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RICARDO SÉRGIO DA SILVA

AVALIAÇÃO DAS ATIVIDADES ANTI-INFLAMATÓRIA, ANTINOCICEPTIVA, ANTIPIRÉTICA E CICATRIZANTE DE ÓLEO FIXO DE *SYAGRUS SCHIZOPHYLLA* EM CAMUDONGOS

Recife
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Tese apresentada ao Programa de Pós-Graduação em Ciências Biológicas da Universidade Federal de Pernambuco, como requisito parcial para obtenção do título de Doutor em Ciências Biológicas.
Área de concentração: Biotecnologia

Orientadora: Profª. Dra. Márcia Vanusa da Silva

Coorientadora: Profª Dra. Kátia Ribeiro Alves

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RESUMO

Syagrus schizophylla (Mart.) Glass. (Arecaceae) é uma palmeira oleaginosa nativa do Nordeste do Brasil, e conhecida popularmente como Aricuriroba. Estudos sobre o seu potencial biotecnológico são escassos, entretanto, há estudos sobre várias espécies desta família que comprovam suas atividades biológicas. Diante do exposto, o objetivo do trabalho foi avaliar as atividades anti-inflamatória, antinociceptiva, antipirética e cicatrizante do óleo de sementes de *S. schizophylla* (OFSs), em camundongos. Para tanto, a toxicidade aguda foi investigada em camundongos em duas fases. Na fase um cada grupo recebeu uma concentração diferente de OFSs (10, 100 e 1000 mg/kg) por gavagem. Na segunda fase, foi administrada altas doses de OFSs (1600 e 2900 mg/kg). Os parâmetros analisados em ambas as fases foram comportamento e mortalidade. Realizou-se ainda o teste de contorção abdominal induzida por ácido acético 0,8%, teste de dor por formalina, edema de pata induzido por carragenina 1%, peritonite aguda (com avaliação da migração leucócitos e neutrófilos e quantificação de citocinas IL1-α e TNF-α) e pirexia induzida pela levedura *Saccharomyces cerevisiae*. A atividade cicatrizante foi investigada em feridas cutâneas induzidas em camundongos tratados durante 15 dias com DMSO 2% (controle negativo), Dersani, Dexpantenol, OFSs (10%, 25% e 100%) ou pomada de OFSs a 5%. A identificação, caracterização e quantificação dos compostos presentes no OFSs por CG-MS e GC-FID revelaram a presença de oito compostos diferentes, sendo o ácido láurico o mais abundante (50,45 ± 2,30%). O óleo não promoveu mortalidade dos animais no teste de toxicidade aguda. O OFSs em concentrações crescentes na segunda fase do teste de toxicidade (10, 100, and 1000 mg/kg) não induziu alterações/modificações persistentes comportamentais durante todo o ensaio, demonstrando possuir um valor de LD50 maior que 5000 mg/kg. As contorções abdominais foram reduzidas utilizando o OFSs, de 16,17, 51,96 e 72,05%, e reduziu-se o tempo de lambedura da pata, de 16,17, 51,96 e 72,05%, respectivamente. A investigação dos mecanismos sugere ação antinociceptiva via sistema opioide. O óleo mostrou-se eficaz na inibição de 100% (400 mg/kg) do edema a partir de 5 horas, com resultado superior a indometacina (20 mg/kg, v.o.). O modelo de peritonite demonstrou migração significativa de leucócitos (37,93, 62,06 e 77,58%, nas concentrações testadas respectivamente) e

neutrófilos (41,02, 66,66 e 87,17%) respectivamente. Além disso as concentrações do óleo de OFSs foram capazes de reduzir os níveis de IL-1β em 59,26, 68,93 e 76,35% e TNF- α em 41,60, 57,52 e 75,44%. A administração do OFSs inibiu a febre nos animais desde a primeira hora de teste, em todas as doses testadas. A morfometria revelou que os animais tratados com Dersani®, dexpantenol, OFSs 10% e 25% apresentaram o menor tempo de reepitelização. O número de fibroblastos foi maior no OFSs 25% (67,04%) e na pomada de OFSs (63%), quando comparado ao grupo controle negativo (45,08%). O estudo mostrou-se promissor para indústria terapêutica, e demonstrou que o OFSs pode ser um contributo para o auxílio de doenças, atuando como agente antinociceptivo, anti-inflamatório, antipirético e cicatrizante. Além da pomada de OFSs estabelecer potencial para se tornar um tratamento tópico alternativo no processo de reparo tecidual.

Palavras-chave: *Syagrus schizophylla*; Inflamação; Nocicepção; Pirexia; Cicatrização de feridas.

ABSTRACT

Syagrus schizophylla (Mart.) Glass. (Arecaceae) is an oleaginous palm tree, native from Brazilian northeast, and is popularly known as “aricuriroba”. There are no scientific reports about its biotechnological potential, however, there is several species from this family proving different biological activities. With that in mind, the aim of the present study was to evaluate the anti-inflammatory, antinociceptive, antipyretic and wound healing potential from the oil from the seeds of *S. schizophylla* (OFSs), as well an ointment formulation containing 5% of OFSs in mice. An acute toxicity effect was investigated, where 3 groups (n=6) in two different phases. In the phase one, each group received different OFSs concentration (10, 100, and 1000 mg/kg orally). At the phase two, the concentration was higher (1600 and 2900 mg/kg). In both phases the behavior and mortality were observed. We also performed abdominal contortion test induced by acetic acid (0.8%), paint test induced by formalin, paw edema induced by carrageenan 1%, acute peritonitis, with leukocytes and neutrophils migration evaluation, IL1-α e TNF-α quantification, and pyrexia induced by *Saccharomyces cerevisiae*. The wound healing activity was investigated in induced cutaneous wounds in mice treated for 15 days, the treatment consisted in DMSO 2% as negative control, two commercial products, Dersani® and dexpanthenol, as positive control, tree different concentrations of OFSs (10%, 25%, and 100%), and our ointment formulation. The chemical characterization was made using GC-MS and GC-FID and revealed the presence of eight different compounds, with lauric acid being the major compound (50.45 ± 2.30%). The OFSs didn’t induce mortality in all tested concentrations in the acute toxic test. As also, didn’t induced any behavior modification during the entire assay, which in turn showed to have a LD50 higher than 5000 mg/kg. The abdominal contortion assay was reduced in 16.17, 51.96 and 72.05% and the paw-licking time in 16.17, 5.96 and 72.05%, respectively. According to our data, there is evidence that the antinociceptive mechanism of action is due the opioid system. The OFSs was able to inhibit in 100% (400 mg/kg) the edema after 5 hours, with the results being superior to indomethacin (20 mg/kg v.o.). The peritonitis model showed significant leukocytes migration (37.93, 62.06, and 77.58%), as well neutrophills (41.02, 66.66, 87.17%) respectively. Besides that, the OFSs were able to reduce the IL-1β in 59.26, 68.93, and 76.35%, and the TNF-α in 41.60, 57.52, and 75.44%, as well, inhibit the fever since the first hour during the assay, in all tested concentration. Histomorphometry revealed that animals treated with Dersani®, dexpanthenol, 10% and 25% OFSs had the shortest re-epithelialization time. The number of fibroblasts was higher in the OFSs 25% (67.04%) and in the OFS ointment (63%), when compared to the negative group (45.08%). Our data shows that *S. schizophylla* is a promising candidate to the therapeutic industry since the OFSs can

contribute to treat several diseases, acting as antinociceptive, anti-inflammatory, anti-pyretic and wound healing agent. Besides that, the ointment may be a potential product that can be applied in the tissue restoration process.

Keywords: *Syagrus schizophylla*; Inflammation; Nociception; Pyrexia; Wound healing.

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LISTA DE ABREVIATURAS E SIGLAS

ANOVA	Análise de variância
BHT	Butilhidroxitolueno
ºC	Celsius
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico
DMSO	Sulfóxido de dimetilo
EDTA	Ácido etilenodiamina tetraacético
FACEPE	Fundação de Amparo à Ciência e Tecnologia de Pernambuco
FID	Detector de ionização de chamas
GC/MS	Cromatografia gasosa acoplada à espectrometria de massas
GC	Cromatografia gasosa
i.p	Via intraperitonial
Il-1β	Interleucina 1 beta
ISO	Organização Internacional de Padronização
K_{ATP}	Canais de potássio sensíveis ao ATP
Kg	Quilo
LA	Ácido láurico
LD50	Dose letal média
LIKA	Laboratório de Imunopatologia Keizo Asami
LPS	Lipopolissacarídeos
M	Molar
MCTI	Ministério da Tecnologia e Inovação
Mg	Miligramas
MM	Massa molar
mm	Milímetros
mm^2	MilÍmetros quadrados
OECD	Organização para Cooperação e Desenvolvimento econômico
OFSs	Óleo fixo de sementes de *Syagrus schizophylla*

S.	Syagrus
SD	Desvio Padrão
UFPE	Universidade Federal de Pernambuco
p-valor	Probabilidade de significância
v.o	Via oral

SUMÁRIO

1 INTRODUÇÃO

O uso de plantas com fins medicinais é realizado de forma empírica, pelo conhecimento tradicional, através de preparações que busquem extrair seus princípios ativos (FIRMO *et al*., 2011; ASADI-SAMANI; RAFIEIAN-KOPAEI; AZIMl, 2013; PADILHA *et al*., 2017). *Syagrus schizophylla* (Mart.) Glass. (Arecaceae) é uma espécie oleaginosa de palmeira que possui potencial ornamental e paisagístico (TEIXEIRA *et al*., 2019; PADILHA *et al.*, 2017; BELTRAME *et al.*, 2019). É conhecida popularmente como aricuriroba, é uma espécie endêmica do Brasil e difundida no Nordeste, sendo encontrada nos estados de Alagoas, Bahia, Pernambuco e Sergipe, principalmente nas áreas costeiras (restinga) e de Mata Atlântica (LEITMAN *et al*., 2015; BELTRAME, JASMIM, VIEIRA, 2019). Os relatos acerca de seu potencial biotecnológico ainda são escassos na literatura. As investigações científicas realizadas até o momento exploram seu potencial nutricional, relatando o alto valor calórico de suas amêndoas, e demonstrando seu uso culinário (PADILHA *et al*., 2017).

A família Arecaceae destaca-se por suas plantas apresentarem enorme potencial terapêutico. Há estudos sobre várias espécies desta família que comprovam diversas atividades biológicas, dentre elas, propriedades antioxidante, antimicrobiana (NONATO *et al.*, 2018), analgésica, antipirética, anti-inflamatória (ELHAKIM; ABDEL-BAKY; BISHAY, 2017), antimalárica (TAYLER *et al*., 2019) e antibacteriana (JOY *et al.*, 2019). A variedade de atividades biológicas supracitadas pode ser proveniente dos inúmeros compostos descritos nesta família. Isso porque as espécies dessa família são ricas em muitos compostos, dentre eles, taninos (JOY *et al.*, 2019), rutinósido de caempferol de vanílico, ácido g-linolênico, ácido linoleico, ácido oleico, ácido cinâmico, ácido cafeico, protocatecuico, ácido ferúlico, ácido sérico, quercetina, entre outros (MARQUES *et al.*, 2016; NONATO *et al.*, 2018).

A presença de ácidos graxos nas espécies da família Arecaceae vem sendo bastante reportada, como ácido oleico, ácido láurico, ácido láurico, ácido cáprico, ácido mirístico e ácido caprílico (LOPES *et al.*, 2018; MARINS *et al.*, 2018; LIMA *et al.*, 2018). Estudos rotineiramente relatam o ácido láurico como composto majoritário de óleos vegetais nas plantas dessa família. Sales *et al.* (2020) destacam o ácido láurico como ácido graxo predominante em plantas da família Arecaceae, e que a presença desse composto permite alta estabilidade oxidativa com alegações funcionais. É importante destacar ainda que os ácidos graxos são utilizados no tratamento de feridas (FERREIRA *et al.*, 2012) e possuem propriedade antineoplásica (FAUSER *et al.*, 2013), além de não serem tóxicose serem compostos com longa vida útil (PARK JUN-HYUN *et al.*, 2019).

O Brasil é o país que possui a maior biodiversidade do planeta, possuindo cerca de 45.000 espécies vegetais catalogadas (FLORA DO BRASIL, 2017). A formulação e efetivação de políticas públicas que valorizem o conhecimento tradicional e científico de plantas medicinais, assim como a sua inserção na saúde pública, simbolizam um marco regulatório e um incentivo à pesquisa de plantas fitoterápicas e medicinais, o que prioriza a biodiversidade do país, o desenvolvimento de tecnologias e inovações das mais diversas fases da cadeia produtiva (SALES *et al.*, 2015). Nesse contexto, é importante e necessário que *S. schizophylla* seja explorada para fins terapêuticos, uma vez que as plantas são utilizadas como terapia alternativa para o tratamento de diversas doenças (BEVILACQUA, 2010; DUTRA *et al*., 2016).

De acordo com a Associação Internacional para o Estudo da Dor (IASP, 2020), a dor trata-se de uma experiência sensorial e emocional desagradável, usualmente causada por lesão tecidual atual ou potencial. A capacidade de sentir dor e assim perceber estímulos nocivos estabelece uma função fisiológica essencial ao organismo, o que representa um sinal de alerta contra ameaças à sua integridade (MARTINI *et al.*, 2018). Persistindo o agente lesivo, ocorre a evolução da inflamação, passando de aguda para ser considerada crônica, podendo durar meses ou anos, causando destruição do tecido e a proliferação do tecido conjuntivo (RANG *et al.*, 2011; NWAEHUJOR *et al.*, 2014). Desse modo, enquanto for transitória, a dor pode ser considerada um sintoma clínico interessante para prevenção e limitação de danos. Entretanto, quando essa condição se torna persistente ela deixa de desempenhar sua função primária, passando a ser considerada debilitante (MARTINI *et al.*, 2018).

Apesar do processo inflamatório ser satisfatório para o corpo humano ele pode desencadear alguns sinais clássicos que podem levar ao desconforto e acabam por interferir na qualidade de vida (AGHASAFARI *et al.*, 2019), bem como pode passar de um impulso de preservação da integridade do corpo para uma inflamação descontrolada (RONCHETTI *et al.*, 2017).

Nesse sentido, é necessário que se faça uma intervenção farmacológica para o tratamento da dor e demais sinais de inflamação (DHINGRA *et al.*, 2015). No entanto, as atuais classes de medicamentos que viabilizam o tratamento dessas condições possuem efeitos colaterais significativos, o que se justifica a busca por novas moléculas que possuam efeitos farmacológicos (YAXLEY; LITFIN, 2016). Desse modo o tratamento da dor e da inflamação tem causado a preocupação da comunidade científica e da indústria farmacêutica, pois há a necessidade urgente de analgésicos e anti-inflamatórios mais eficazes e com menos efeitos adversos (BENEDITO, 2013).

Por se tratar de uma espécie que dispõe de poucos relatos na literatura com relação à

constituição química e propriedades descritas, investigar o potencial biotecnológico de *S. schizophylla* pode direcionar a formação de novos fármacos, sejam estes compostos obtidos por síntese a partir de moléculas protótipos ou por isolamento nas fontes de origem. Diante do exposto, o objetivo do trabalho foi investigar as atividades anti-inflamatória, antinociceptiva, antipirético e cicatrizante do óleo fixo de sementes de *S. Schizophylla* (OFSs), bem como determinar o mecanismo de ação da atividade antinociceptiva em modelos experimentais *in vivo.*

2 OBJETIVOS

2.1 OBJETIVO GERAL

Investigar as atividades anti-inflamatória, antinociceptiva, antipirética e cicatrizante do óleo fixo de *S. Schizophylla* (OFSs) o óleo em camundongos *Swiss*.

2.2 OBJETIVOS ESPECÍFICOS

a) Caracterizar a composição química do OFSs por Cromatografia Gasosa GC-FID e Cromatografia gasosa acoplada à espectrometria de massas GC-MS;
b) Avaliar a toxicidade aguda do OFSs em camundongos;
c) Investigar o potencial antinociceptivo do OFSs mediante o teste de dor por ácido acético e formalina*;*
d) Analisar o potencial anti-inflamatório do OFSs no teste de edema de pata e peritonite por carragenina*;*
e) Investigar o potencial antipirético do OFSs por meio do método de pirexia induzida por leveduras*;*
f) Avaliar a atividade cicatrizante do OFSs e de uma formulação em pomada a base de OFSs a 5% em camundongos;

3 REFERENCIAL TEÓRICO

3.1 PLANTAS MEDICINAIS

O Brasil é o País que dispõe da maior biodiversidade do planeta, possuindo mais de 45.000 espécies vegetais catalogadas (FLORA, 2019). Em diferentes partes do mundo as plantas são consideradas como fundamentais à saúde humana e são utilizadas como terapia alternativa para tratar diversas doenças, desde milhares de anos antes de Cristo (BEVILACQUA, 2010; DUTRA *et al*., 2016; MATTOS *et al*., 2018; PADILHA *et al*., 2017; OLIVEIRA *et al*., 2021).

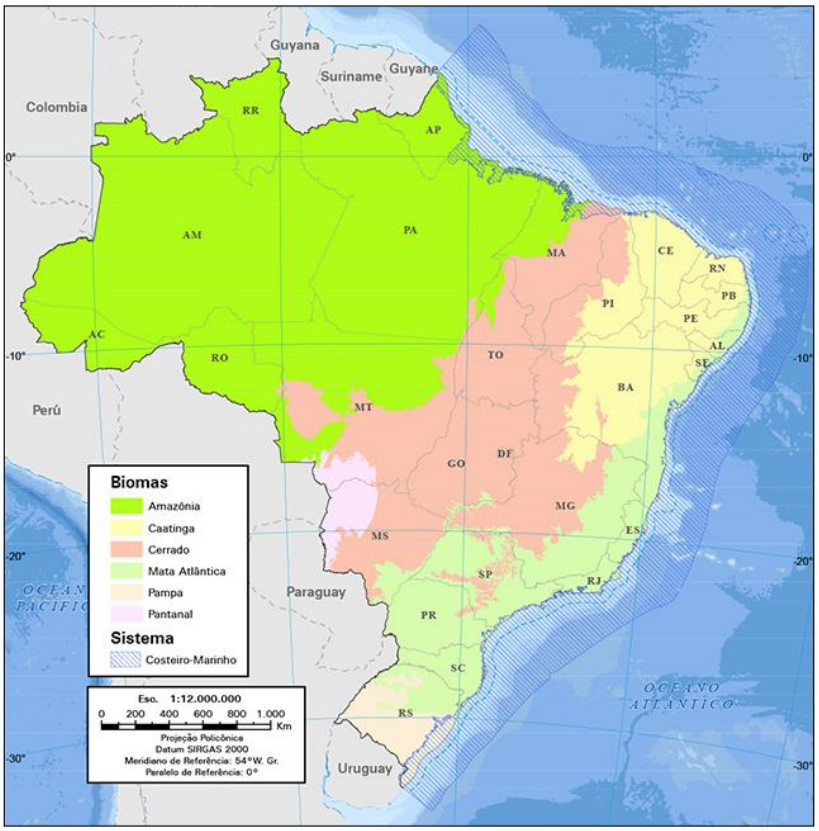
A difusão do conhecimento popular permitiu que as plantas fossem positivamente selecionadas para atuar nas necessidades de cura de diversas enfermidades (SILVA; OLIVEIRA, 2018). O conjunto de saberes que é internalizado nos diversos usuários das comunidades se estabelece como uma prática comum e bem conservada (SILVA; OLIVEIRA, 2018; PANYADEE *et al*., 2019), principalmente em áreas rurais, de todo o mundo (WHO, 2002), onde representa de forma muito frequente o único recurso possível para o tratamento de doenças na comunidade local (ROQUE, 2010).

Além de apresentar uma excelente fonte para a busca de novos compostos farmacologicamente ativos (DUTRA *et al*., 2016; MARTINS; ALVES; MAMPRIM, 2016) algumas plantas medicinais podem estabelecer melhores resultados terapêuticos quando comparado com substâncias sintéticas (JOY *et al*., 2019). Essas plantas representam uma fonte de riqueza da flora de cada país, e a nível mundial, independentemente dos continentes onde estão inseridas, a sua utilização só tem crescido nas últimas décadas, se tornando assim um grande desafio a investigação de suas propriedades biotecnológicas (MOREIRA *et al*., 2015).

3.2 CAATINGA

A Caatinga corresponde a uma das maiores savanas sazonais do mundo, abrangendo grande parte do Nordeste do Brasil e uma pequena parte do Sudeste (Figura 1), sendo constituída por um mosaico de diferentes tipos de floresta, caracterizada por árvores e arbustos com espinhos e adaptações para combater o déficit hídrico. Trata-se de uma área severamente modificada pela agricultura de corte e queima de madeira, caça e ação contínua de rebanhos bovinos e caprinos, sendo que apenas uma porcentagem reduzida encontra-se bem preservada e protegida (ARAÚJO; FERREIRA; ARANTES, 2012; LUCAS DA SILVA *et al*.,2015).

Figura 1 – Distribuição dos biomas da caatinga



Fonte: IBGE

Fonte: IBGE
https://educa.ibge.gov.br/jovens/conheca-o-brasil/territorio/18307-biomas-brasileiros.html

A Caatinga comporta uma variedade de cobertura vegetal, determinada em grande parte pelo clima, topografia e geologia. Sua decídua vegetação ampara a formação de uma camada de matéria orgânica natural que protege o solo em estação seca (LUCAS DA SILVA *et al*., 2015). Diversas comunidades rurais presentes no Nordeste fazem parte de áreas de vegetação da Caatinga, local em que retiram seu sustento, proveniente da agricultura, assim como de produtos não madeireiros, como plantas medicinais, óleos, sementes e frutos. As ervas medicinais se tornam a única alternativa dos moradores dessas comunidades para combater enfermidades, uma vez que é o único recurso disponível (SILVA, 2015).

A conveniência pela exploração racional da biodiversidade vegetal como fonte natural de produtos alimentares sustentáveis e compostos bioativos que promovem saúde vem aumentando devido a sua abundância, segurança e impactos na economia local (MACIEL; YOSHIDA; GOYCOOLEA, 2019). Isto porque a Caatinga dispõe de uma composição vegetal do tipo xerófita, adaptada ao clima seco e árido e cujo metabolismo secundário pode originar moléculas diferenciadas e únicas (MORAIS *et al*., 2005; SILVA ELOI, 2016).

3.3 FAMÍLIA ARECACEAE

3.3.1 Distribuição e características botânicas

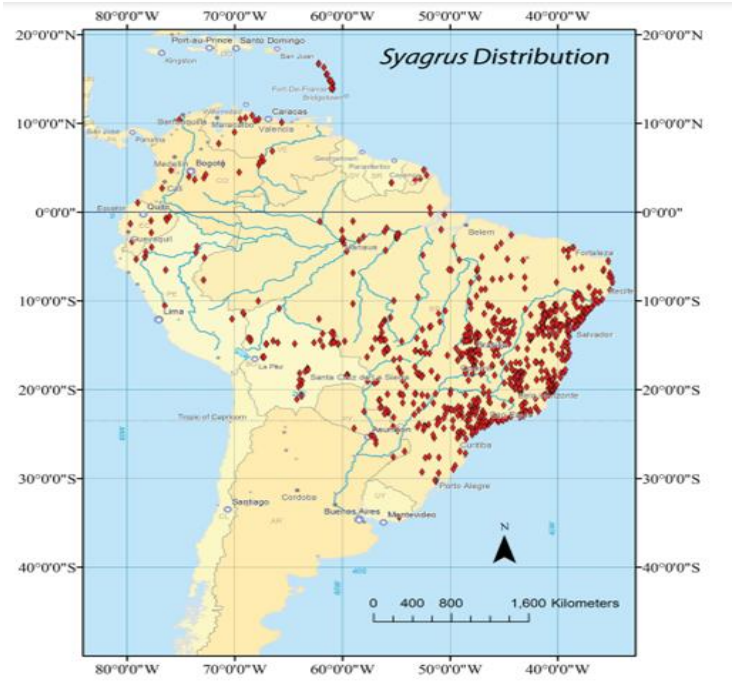
A família das palmeiras (Arecaceae) compreende cerca de 2600 espécies em 181 gêneros que são distribuídos principalmente em regiões tropicais e subtropicais em todo o mundo, embora palmeiras arborescentes também possam ocorrer em regiões áridas de climas desérticos (BAKER; DRANSFIELD, 2016; EMILIO *et al*., 2019).

A riqueza de espécies da família Arecaceae apresenta uma perceptível variação geográfica, porém os processos que impulsionam essa variação ainda não estão esclarecidos na literatura (SVENING *et al*.,2008; EISERHARDT *et al*., 2011). Gama de Souza e colaboradores (2020) destacam que, das espécies presentes nessa família, 48 são nativas do Brasil e ocorrem em regiões de transição entre a Amazônia, Cerrado e Caatinga. Além disso, as plantas dessa família são corriqueiramente utilizadas como fonte de alimento e subsistência, apresentando riqueza de compostos bioativos lipofílicos, principalmente carotenoides, poliácidos graxos insaturados, tocoferóis e vitamina A (GAMA DE SOUZA *et al*., 2020).

3.3.2 Gênero *Syagrus*

O gênero *Syagrus* é pertencente à família Arecaceae e é inserido na subtribo Attaleinae da tribo Cocoseae (subfamília Arecoideae). O epicarpo de seus frutos (Figura 2) é do tipo membranáceo, uma característica peculiar, que diferencia as plantas desse gênero (NOBLICK *et al*., 2017; ELIAS *et al*., 2018). Atualmente existem 65 espécies, 2 subespécies e 67 táxons, em que 57 ocorrem no Brasil. O gênero é distribuído pela região Neotropical (Figura 2), com maior concentração no leste e centro do Brasil.

Figura 2 – Mapa de distribuição do gênero Syagrus



Fonte: Noblick *et al.* (2017, p. 7)

As espécies do gênero *Syagrus* são encontradas em diversos lugares. Algumas habitam florestas tropicais úmidas, como a Amazônia (*S. inajai*) ou a Mata Atlântica (*S. botryophora*). Algumas (*S. coronata, S. vagans*) podem sobreviver a condições extremamente áridas, como a Caatinga. Entretanto, em zonas de transição, em savanas (cerrados) e campos rupestres encontram-se a maior parte deste gênero. As plantas desse gênero podem ser muito altas, com caules variando de colunares a caules subterrâneos curtos (NOBLICK *et al*., 2017). O gênero *Syagrus* possui muitas palmeiras que são ricas em compostos ativos, apresentando muitas propriedades que podem ser utilizadas no auxílio a tratamentos e/ou prevenção de doenças crônicas, como diabetes e Alzheimer. Além disso, o gênero demonstra potencial para a produção de biodiesel, demonstrando assim a sua versatilidade (CORIOLANO *et al*., 2021).

As plantas do gênero *Syagrus* são corriqueiramente relatadas por estabelecer diversas propriedades, sejam mencionadas no uso popular ou testadas cientificamente. São relatadas por conferir várias propriedades biológicas (FARIAS *et al*., 2021), das quais podemos citar, atividade anti-inflamatória de *Syagrus cearensis* citada no uso popular (JUNIOR; LADIO; ALBUQUERQUE, 2011), além das folhas de *Syagrus romanzoffiana* que auxiliam no emagrecimento (DIAS-OLIVEIRA *et al*., 2012) e atividade antichagásica de amêndoas de *Syagrus coronata,* assim como o uso tradicional na para cicatrização de feridas (SOUZA *et al*., 2017). Além disso, estudos sobre algumas plantas do gênero *Syagrus* ainda são pouco relatados, como a espécie *Syagrus schizophylla*, que seu uso etnofarmacológico é mencionado na preparação de um suco medicinal, entretanto, as atividades farmacológicas ainda não foram

investigadas cientificamente (OLIVEIRA *et al*., 2012).

3.4 ÓLEOS FIXOS

A aplicação tópica de óleos fixos vegetais para fins cosméticos e medicinais já é utilizada há muito tempo, uma vez que os produtos tópicos apresentam benefícios de possuir maior biodisponibilidade na pele e terem um efeito localizado, ao invés de efeitos sistêmicos (PATZELT *et al*., 2012).

Muitas espécies vegetais possuem tecidos especializados no armazenamento de gorduras, tais como polpas de frutos e sementes (RAMALHO; SUAREZ, 2013). Óleos fixos de espécie de plantas têm-se tornado populares em virtude da sua grande concentração de ácidos graxos saturados e insaturados (TIMILSENA *et al*., 2017).

Ácidos graxos são ácidos carboxílicos, com cadeia carbônica longa que diferem entre si pelo número de carbonos da sua cadeia principal, quantidade e posição de suas insaturações (RAMALHO; SUAREZ, 2013). Dada a diversidade dos tecidos que armazenam ácidos graxos, existem vários processos de extração e purificação de óleos, uma vez que isso depende das características da oleaginosa. Dentre os processos de extração, podemos identificar algumas operações unitárias básicas envolvidas na extração, dentre elas, a prensagem mecânica, extração à solvente ou autoclavagem (RAMALHO; SUAREZ, 2013).

Mesmo com os avanços tecnológicos, ainda é possível observar processos rudimentares de extração. Há milhares de anos a extração por prensagem mecânica é utilizada pela população para produção de óleos e gorduras. Um exemplo disso é a utilização de prensagem que era utilizada em moinhos de pedra movidos por tração animal, ambos utilizados na antiguidade em diversas cidades do norte da África (RAMALHO; SUAREZ, 2013).

Atualmente o processo de extração de óleos fixos se fundamenta principalmente em duas técnicas: a extração por pressão, com o uso de prensas hidráulicas em que o óleo é removido parcialmente, e a extração por solventes orgânicos (esgotamento por solventes voláteis), em que o solvente mais comumente utilizado é o hexano (CRUZ, 2012).

É sabido que as propriedades de muitos ácidos graxos e outros componentes de óleos vegetais aportam benefícios para a saúde (FOOD, 2014). Isso porque os óleos fixos de origem vegetal possuem uma composição rica em ácidos graxos, que podem variar de acordo com a espécie, mas frequentemente são compostas por: ácido caprílico (8:0), ácido cáprico (10:0), láurico (12:0), mirístico (14:0), ácido palmítico (16:0), palmitoleico (16:1), ácido esteárico (18:0), ácido oleico (18:1), ácido vacênico (18:1 cis 11), ácido linoleico (18:2), ácido linolênico (18:3) e ácido araquídico (20:0) (MEYER, 2013).

Nessa perspectiva, o interesse da indústria farmacêutica no potencial biotecnológico de óleos fixos se dá devido à presença de componentes majoritários com propriedades bioativas (HIDALGO; ZAMORA, 2006; YARA-VARÓN *et al*., 2017). Além de que, a identificação e caracterização de óleos extraídos da flora cultivada pela população local tem potencial para contribuir para o uso sustentável de recursos vegetais locais (ABREU, 2019).

3.4.1 *Syagrus schizophylla*

Syagrus schizophylla (Mart.) Glass. (Tabela 1) é uma espécie oleaginosa de palmeira, com potencial ornamental, conhecida popularmente como "aricuriroba", "coco-babão" ou "coco-caboclo", sendo uma espécie endêmica do Brasil e difundida no Nordeste, por ser encontrada nos estados de Alagoas, Bahia, Pernambuco e Sergipe, principalmente nas áreas costeiras (restinga) e de Mata Atlântica(BELTRAME *et al*., 2018; PADILHA *et al*., 2017; LEITMAN *et al*., 2015; BELTRAME *et al*., 2018; SILVA *et al*., 2016; NOBLICK *et al*., 2017; NOBLICK, 2019).

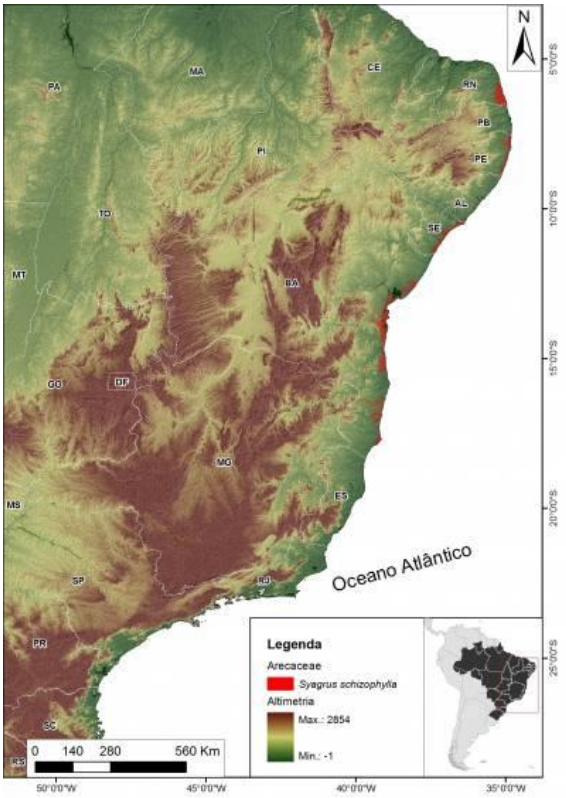
Tabela 1 – Classificação taxonômica da *Syagrus schizophylla* (Mart.) Glassman

Reino	Plantae
Filo	Trachophyta
Classe	Liliopsida
Ordem	Arecales
Família	Arecaceae

Fonte: O Autor (2022).

Syagrus schizophylla é uma espécie amplamente distribuída (Figura 3) e localmente abundante, entretanto, as restingas que a espécie habita enfrentam uma intensa pressão da expansão urbana e turística da especulação imobiliária, de modo que a espécie possa ser ameaçada de extinção em um futuro próximo (CNC FLORA, 2012; NOBLICK, 2019).

Figura 3 – Mapa de distribuição de *Syagrus schizophylla*



Fonte: Centro Nacional de Conservação da Flora (2012).

É uma espécie de palmeira baixa. Com m uma coroa (capitel) densa, um pouco achatada, e um caule com 1–4 m × 10–15 cm, com entrenós muito curtos. Os pecíolos ou margens da bainha apresentam-se armados com dentes ou espinhos, e a base das folhas é muito firme no caule. Seus frutos quando maduros variam da cor amarelo avermelhado a alaranjado e crescem até 3.5 cm (Figura 4). Seu nome indígena tupi “arikuryroba” significa infrutescência longa (arib) com amêndoas (kury) que são amargas (rob) (NOBLICK, 2019).

Figura 4 – Frutos da espécie *Syagrus schozphylla*

Fonte: Noblick (2017, p. 199).

Os relatos sobre o potencial biotecnológico de *Syagrus schizophylla* ainda são escassos na literatura, todavia, investigações científicas realizadas até o momento exploram acerca de seu valor nutricional (PADILHA *et al*., 2017), e relatam sobre a utilização do seu fruto para preparação de suco medicinal em que não se é mencionada a sua aplicabilidade (OLIVEIRA *et al*., 2012).

3.4.2 Dor

Uma das funções importantes para a manutenção da vida é o fornecimento de informações sobre a ocorrência ou ameaça de uma lesão. Para nosso organismo, uma das maneiras de emitir essa resposta é na forma de dor. Entretanto, por diversas vezes a dor pode ir além da sua função protetora, desencadeando assim uma doença (VERMA *et al*., 2015). A dor é definida pela Associação Internacional para o Estudo da Dor (IASP) como "uma experiência sensorial e emocional desagradável que está associada a um dano tecidual potencial (TREEDE *et al*., 2018; RAJA *et al*., 2020; IASP *et al*., 2020; WILLIAMS; CRAIG, 2016; THOMPSON; NEUGEBAUERA, 2018), o que torna uma sensação protetora importante que influencia no comportamento com o intuito de evitar mais lesões e promover a cura (LIGON *et al*., 2016).

A dor é classificada como o 5º sinal vital, e se estabelece como a principal causa da procura por assistência à saúde e de consumo de medicamentos, além de impactar de forma direta a qualidade de vida das pessoas. A investigação de moléculas eficientes no controle de

condições álgicas e com baixos efeitos colaterais têm aumentado ao longo dos anos. Deste modo, as plantas e seus compostos são opções para o controle da dor e para o desenvolvimento de novos fármacos analgésicos (ALMEIDA-OLIVEIRA *et al*., 2014)

O entendimento a respeito da dor avançou bastante nas últimas décadas, uma vez que técnicas moleculares e de imagens funcionais ajudaram na compreensão de mecanismos nociceptivos a nível celular, assim como sobre a função do córtex cerebral na percepção da dor. Isso permitiu uma reavaliação sobre qual o melhor caminho para reduzir principalmente as dores crônicas, graças ao desenvolvimento da pesquisa translacional (COLVIN; OWBOTHAM 2013; JOHNSON, 2016; VARDEH *et al*., 2016).

As plantas medicinais destacam-se pelas contribuições constantes para se ter conhecimento dos mecanismos relacionados à geração, transmissão, manutenção e controle da dor. Consideravelmente, as principais drogas atualmente utilizadas como analgésicos são derivadas de espécies de plantas ou são sintetizadas com base em produtos de origem natural. Entretanto, os analgésicos disponíveis não são ideais para todos os pacientes, nem mesmo para diferentes tipos de dor existentes. Deste modo, a descoberta de novos analgésicos seguros com efeitos colaterais reduzidos é urgentemente imprescindível (DUTRA *et al*., 2016). Nessa perspectiva, o uso dos produtos naturais e seus metabólitos no controle da dor e de doenças tem sido reconhecido pela ciência contemporânea, de maneira que uma gama de medicamentos são provenientes destes (PETROVSKA, 2012).

Apesar de significativos avanços na compreensão da neurofisiologia da dor, o aumento na disponibilidade de procedimentos diagnósticos avançados e a aplicação de modalidades e abordagens terapêuticas, no presente momento, tratamentos disponíveis para dor crônica raramente resultam em resolução completa dos sintomas. Assim, pessoas com dor crônica convivem com algum nível de dor independentemente do tratamento atual ou tratamentos que venham a receber em um futuro próximo (TURK; WILSON; CAHANA, 2011).

A dor sendo caracterizada como uma condição multifacetada e multifatorial, exerce um desafio em seu tratamento e gerenciamento. Terapias convencionais, como analgésicos, anti-inflamatórios não esteroidais (AINEs) e corticosteroides, entre outros, têm sido bem-sucedidos em certa medida em seu manejo e tratamento. No entanto, tais terapias tendem a ser acompanhadas de efeitos indesejáveis e têm um alcance terapêutico limitado (SREEKEESOON; MAHOMOODALLY, 2014). Desta forma, quando a dor torna-se persistente, as terapias tradicionais incluindo analgésicos opioides e não opioides, anti-inflamatórios não esteroidais (AINEs) e corticosteroides, são pouco eficazes (TURK *et al*., 2011; BASHIR; COLVIN, 2013).

De acordo com o Controle Internacional de Narcóticos, 5,5 milhões de pessoas possuem acesso reduzido ou nenhum acesso a analgésicos, incluindo opiáceos, codeína e morfina. (BOURZAC *et al*., 2017). Os anti-inflamatórios não esteroides (AINEs) representam um dos pilares do tratamento da dor associada a uma variedade de condições médicas, e foram desvendados em 1987 (BARKIN; PHARM, 2015; LOPES, DORADO; NARDINO, 2016). Desde então os AINEs tornaram-se uma das classes de medicamentos mais utilizadas no mundo (WALTERS; WOESSNER, 2016).

Essa classe de medicamentos é amplamente utilizada no tratamento da dor associada a diversas indicações, como por exemplo, condições artríticas, mas sua serventia é muitas vezes limitada pela dose, devido aos efeitos adversos, como distúrbios gastrointestinais, eventos cardiovasculares e toxicidade (BARKIN; PHARM, 2015).

3.5 NOCICEPÇÃO

A nocicepção é denominada como um mecanismo sensorial e fisiológico em que os nociceptores, que são receptores sensoriais especializados, detectam os estímulos nocivos, que podem deflagrar em dano tecidual (TRACEY JR, 2017; VARDEH; WOLLER *et al*., 2017). É corriqueiramente caracterizada também como um fenômeno pelo qual ocorre a codificação e o processamento dos estímulos ambientais físicos, químicos ou patológicos que resultam na dor, por meio de uma cascata complexa de eventos, que vai da periferia até as estruturas superiores do sistema nervoso central. O reconhecimento e a avaliação da dor são etapas fundamentais para o sucesso em seu tratamento e devem ser baseados em indicadores fisiológicos, biomarcadores específicos e parâmetros comportamentais (OLIVEIRA ALVES *et al*., 2017).

A relação entre a percepção da dor e a função cognitiva é fundamental, uma vez que esse conceito é central para compreender esse tipo de informação que pode ser estabelecida a partir da mensuração da dor e da nocicepção. De maneira abrangente diferentes medidas de nocicepção/dor refletirão em conhecimentos sobre a função de todo o percurso da dor ou será limitado a uma parte específica dele (JOHSON, 2016).

O sistema imunológico desempenha um papel fundamental na via da dor, por meio da liberação de mediadores moleculares que sensibilizam os nociceptores, que por sua vez têm receptores para detectar as citocinas, os lipídios, as proteases e os fatores de crescimento que são liberados durante a inflamação. A informação é transmitida como potencial de ação, através da medula espinhal até o cérebro, onde é processada como dor (CABRAL SILVA, 2013).

De modo que as diferentes medidas refletem e verificam a atividade em diferentes partes do sistema é estabelecida uma consideração muito importante na escolha de uma técnica para

mensurar a dor para uma determinada aplicação de pesquisa (JOHSON, 2016). Diferentemente de nocicepção, a dor é mais que uma sensação, é uma experiência, podendo englobar componentes sensoriais com influências pessoais e ambientais importantes. Enquanto isso, a palavra nocicepção refere-se ao estímulo doloroso propriamente dito, sem levar em consideração o componente emocional, ou seja, abrange as vias neuroanatômicas, assim como os mecanismos neurológicos e os receptores específicos que identificam o estímulo lesivo (IASP, 2020)

A dor pode ser classificada de acordo com o tipo de lesão e com os mediadores relacionados, recebendo as seguintes denominações: neurogênica, quando ocorre lesão do tecido neuronal; neuropática, quando ocorre a disfunção de um nervo; psicogênica, que ocorre por fatores psicológicos; ou nociceptiva, quando ocorre por estimulação em excesso dos nociceptores. Desse modo, o potencial antinociceptivo de um produto natural, por exemplo, pode ser mensurado por sua capacidade de maximizar o limiar de excitação das terminações nervosas ao estímulo doloroso, ou então, fazer com que os nociceptores não percebam ou não respondam ao estímulo doloroso promovido (CABRAL SILVA, 2013).

Com base no que foi anteriormente supracitado, tem-se a necessidade de descobrir medidas alternativas para o desenvolvimento de medicamentos que atuem no tratamento da dor. Tendo assim, os produtos naturais com uma perspectiva para elucidar essa questão, uma vez que caracteriza uma fonte promissora na pesquisa de moléculas com potencial atividade analgésica (CABRAL SILVA, 2013).

3.6 INFLAMAÇÃO

A inflamação faz parte da resposta biológica natural do corpo a danos nos tecidos e estímulos nocivos, como invasão de patógenos e danos celulares e teciduais, bem como uma resposta protetora envolvendo células imunes, vasos sanguíneos e mediadores moleculares. Trata-se de um processo antigo e evoluído, que envolve o recrutamento e ação de células de imunidade inata e adaptativa (GRETEN *et al*., 2019). Nesse sentido, a inflamação caracteriza um conjunto amplo de resposta fisiológica a um organismo estranho ou lesão (ARULSELVAN *et al*., 2016), cujo objetivo principal é limitar e eliminar as causas do dano celular, assim como, eliminar células atrofiadas e tecido necrosado, promovendo o reparo tecidual (SINGH *et al*., 2016).

A resposta inflamatória, pode ser deflagrada por estímulos de origens diversas (agentes físicos, químicos e biológicos) (CHEN *et al*., 2018) e caracteriza-se pela produção de fluidos, substâncias químicas e células danificadas com alterações nos vasos sanguíneos, recrutamento

e ativação de leucócitos para induzir o reparo celular, resultando em alterações teciduais e funcionais que constituem as cinco principais marcas do processo inflamatório, calor, vermelhidão, inchaço (edema), dor e perda de função (BARNES, 2016).

Atualmente existem algumas terapias anti-inflamatórias desenvolvidas que são baseadas nas propriedades de inibir ou antagonizar a produção ou ação de mediadores pró-inflamatórios. Essa capacidade de regular mediadores inflamatórios é, sem dúvida, um pré-requisito importante para um agente anti-inflamatório, essencialmente quando se trata da modulação do recrutamento de leucócitos (SERHAN; CHIANG; DALLI, 2015; AZIZ *et al*., 2018).

Diversas classes de fármacos já são relatadas para tratamento de doenças inflamatórias, entre elas, os anti-inflamatórios não esteroidais (AINEs) e corticosteroides. Esses fármacos possuem ações antipiréticas, analgésicas e anti-inflamatórias, agindo na inibição da via das ciclooxigenases (COX) no mecanismo da dor, febre e inflamação. No entanto, o uso deles de forma prolongada pode causar graves efeitos colaterais, tais como diarreia, somado a isso são de custo elevado.

Nesse contexto, justifica-se a procura por novas substâncias, com capacidade de auxiliar no tratamento de doenças no qual o processo inflamatório está envolvido, com o objetivo de limitar os efeitos nocivos desse processo, assim como os compostos derivados de origem vegetais são extremamente importantes por serem precursores na descoberta de novas alternativas de tratamento (GUO, 2017).

3.6.1 Pele e cicatrização de feridas

A pele é o maior órgão do corpo humano, e compõe 16% do peso corporal, desempenhando múltiplas funções, dentre elas a de revestimento da superfície do corpo. Este órgão é composto por um tecido epitelial de origem ectodérmica, a epiderme, e um tecido conjuntivo de origem mesodérmica, a derme. Graças à estrutura da epiderme, com suas múltiplas camadas celulares, ela protege o organismo contra desidratação, atrito, agentes químicos e patógenos. Por meio das terminações nervosas sensoriais que possui, a pele recebe constantemente informações sobre o ambiente e as direciona para o sistema nervoso central. Abaixo e em continuidade com a derme, encontra-se a hipoderme ou tecido celular subcutâneo, que não faz parte da pele, mas lhe serve de união com os órgãos subjacentes (JUNQUEIRA; CARNEIRO, 2018).

As feridas são eventos que resultam na abertura ou ruptura da pele e acontecem rigorosamente devido as lesões (LORDANI *et al*., 2018). Os cortes que são formados na

epiderme da pele resultam em infecções deflagradas por microorganismos como bactérias e fungo (SUGUMAR *et al*., 2013; LORDANI *et al*., 2015).

A cicatrização de feridas cutâneas é um mecanismo que caracteriza uma vantagem evolutiva não só para os mamíferos. Em decorrência das funções da pele como barreira química e bacteriana, a cicatrização de feridas cutâneas é um passo crucial para a sobrevivência. Apesar do grande número de trabalhos dispostos na literatura sobre os mecanismos de cicatrização de feridas, otimizatr o processo de reparação tecidual continua sendo o objetivo, uma vez que o processo de regulação fisiológica da cicatrização é um processo complexo, e que depende de muitos tipos de células e mediadores, em uma sequência temporal imensamente sofisticada (SORG *et al*., 2017; COSTA *et al*., 2018).

As feridas podem ser classificadas como abertas ou fechadas e, dependendo da causa subjacente, como agudas ou crônicas com base na fisiologia da cicatrização de feridas. O processo de cicatrização pode ser largamente categorizado em quatro fases: fase de hemostasia (coagulação), fase inflamatória, fase proliferativa (formação de tecido de granulação e síntese de colágeno) e a fase de remodelação, que define a força e a aparência do tecido cicatrizado (AGYARE *et al*., 2015; PEREIRA; BÁRTOLO, 2013). Esse processo pode ser afetado por fatores locais ou fatores sistêmicos como é o caso de infecções (LORETI *et al*., 2015).

A regeneração de uma pele saudável e funcional prossegue estabelecendo um desafio devido à sua estrutura multicamada e à presença de diferentes tipos de células dentro da matriz extracelular de forma ordenada (PEREIRA; BÁRTOLO, 2013). Os agentes curativos convencionais exercem uma atividade central no tratamento de feridas devido à sua eficácia clínica, simplicidade e acessibilidade.

As terapias supracitadas representam uma alternativa econômica para o tratamento de diversas feridas de difícil cicatrização (por exemplo, úlceras, queimaduras e feridas infectadas), possibilitando efeitos terapêuticos que estimulam a processo de cicatrização e melhoram a qualidade do novo tegumento. Essas terapias convencionais também podem ser aplicadas em combinação com práticas clínicas modernas, proporcionando o desenvolvimento de tratamentos terapêuticos, como a redução da resistência bacteriana e redução do tempo de cicatrização (PEREIRA; BÁRTOLO, 2013).

O crescente interesse pela utilização de produtos convencionais para cicatrização de feridas direcionou a um aumento do número de investigações científicas que buscam a eficácia clínica, segurança e efeitos colaterais de terapias. Assim sendo, esses trabalhos tem permitido a execução de novos produtos e práticas clínicas que atualmente são utilizadas por clínicos e cirurgiões no tratamento de lesões. Mesmo com os avanços, esforços adicionais fazem-se

indispensáveis para aprovação de terapias tradicionais e compostos curativos naturais que viabilizem a utilização de curativos naturais no mercado nacional dos sistemas de saúde (PEREIRA; BÁRTOLO, 2013).

3.6.2 Desenvolvimento de formulações com ação cicatrizante

As formulações em pomadas são preparações semissólidas atribuídas ao uso externo e que devem ser facilmente espalháveis (MINISTÉRIO DA SAÚDE, 2012). Uma pomada ideal deve possuir um aspecto homogêneo, não induzir produzir irritação ou sensibilização na pele, e nem retardar cicatrização. As pomadas são habitualmente usadas como emolientes que tornam a pele mais hidratada e flexível, e agem como barreira protetora, que previne a absorção de substâncias perigosas por meio da pele e veículo em que são incorporadas (MIRANDA DE MORAIS, *et al*., 2017).

As pomadas caracterizam-se por formulações para uso tópico, quase sempre constituídas por um ou mais corpos gordurosos de consistência mole, gordura semi-sólida ou gordura plástica, como por exemplo a vaselina (FERREIRA, 2010). As bases para estas podem ser do tipo oleaginosa e de absorção. As oleaginosas são anidras e insolúveis em água. Já as bases de absorção são anidras, insolúveis e não laváveis com água, todavia, podem absorver água. Sendo assim permitem a inclusão de medicamentos solúveis em água diretamente na base ou posteriormente a sua dissolução em quantidade mínima de água. É válido destacar ainda as bases de natureza hidrofílica, como aquelas preparadas pela associação de polietilenoglicóis de pesos moleculares diferentes, instituindo que sejam obtidas preparações de diferentes viscosidades (MINISTÉRIO DA SAÚDE, 2012).

No Brasil temos várias apresentações comerciais disponíveis para utilização no reparo tecidual, dentre outras, temos as seguintes, Dersani ® (Saniplan), Curatec® AGE (LM Farma), Repitelin® (Biolab), Dermosan® (Sunny Day), AGE Cremer óleo® (Cremer), AGEDerm® (Helianto Farmaucêutica Ltda), Lin'Óleo® (V Declair), Primoderm® (LC produtos Naturais com Calêndula) Supriderm® (LC produtos Naturais com calêndula), genericamente denominadas como AGE (Ácidos graxos essenciais) (FERREIRA *et al*., 2012).

Mesmo com os grandes avanços em produtos para o tratamento de feridas por meio de terapias tradicionais, investigar compostos de origem natural, são alternativas plausíveis. Uma vez que essas terapias podem oferecer novas perspectivas para auxiliar no tratamento de doenças na pele, ampliando o acesso aos cuidados de saúde, e possibilitando ultrapassar algumas limitações relacionadas à produtos e terapias, como por exemplo, altos custos, longos

tempos de fabricação e acréscimo da resistência bacteriana (PEREIRA; BÁRTOLO, 2013).

4 RESULTADOS E DISCUSSÃO

4.1 ARTIGO 1 - EMERGING SOURCE OF BIOACTIVE COMPOUNDS FROM ARECACEAE FAMILY: A SYSTEMATIC REVIEW

O artigo "*Emerging source of bioactive compounds from Arecaceae family: a systematic review*" foi publicado no periódico *Research, Society and Development*, volume 10, artigo 10, 2021, link para acesso: https://doi.org/10.33448/rsd-v10i10.18994

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Emerging source of bioactive compounds from Arecaceae family: a systematic review

Fonte emergente de compostos bioativos da família Arecaceae: uma revisão sistemática

Fuente emergente de compuestos bioactivos de la familia Arecaceae: una revisión sistemática

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Abstract

The use of plants for medicinal purposes is performed empirically by traditional knowledge with the use of preparations that seek to extract their active principles, and are considered to be fundamental to human health. In this context, the aim of the present study was to of this study was to carry out a systematic review of the biological activities of the Arecaceae family distributed throughout Brazil. This research was carried out through a comprehensive search using the following databases, Scopus, Portal Periódicos Capes, PubMed, Google Scholar and Science Direct, using the following descriptors: "Arecaceae" and "Biological properties of the family Arecaeae", checked at <www.theplantlist.org/> to check synonyms. It was possible to identify numerous biological activities in the arecaceae family, among the most recurring ones, the antioxidant, antimicrobial and anti-inflammatory activity. These activities are justified by the presence of fatty acids, phenolic compounds, alkaloids and terpenes. Studies routinely report lauric acid as a major in the plants of this family, which makes it a potential compound to cure or assist in the treatment of various diseases.

Keywords: Medicinal plants; Brazilian biodiversity; Biological activities; Arecaceae.

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Resumo

A utilização de plantas com fins medicinais é realizada empiricamente pelos conhecimentos tradicionais com a utilização de preparações que buscam extrair seus princípios ativos, e são consideradas fundamentais para a saúde humana. Nesse contexto, o objetivo deste estudo foi realizar uma revisão sistemática das atividades biológicas da família Arecaceae distribuída por todo o Brasil. Esta pesquisa foi realizada por meio de uma busca abrangente nas bases de dados Scopus, Portal Periódicos Capes, PubMed, Google Scholar e Science Direct, utilizando os seguintes descritores: "Arecaceae" e "Propriedades biológicas da família Arecaeae", verificados em <www .theplantlist.org /> para verificar sinônimos. Foi possível identificar inúmeras atividades biológicas na família das Arecaceae, entre as mais recorrentes, a atividade antioxidante, antimicrobiana e antiinflamatória. Essas atividades são justificadas pela presença de ácidos graxos, compostos fenólicos, alcalóides e terpenos. Os estudos rotineiramente relatam o ácido láurico como um dos principais nas plantas desta família, o que o torna um composto potencial para curar ou auxiliar no tratamento de várias doenças.

Palavras-chave: Plantas medicinais; Biodiversidade brasileira; Atividades biológicas; Arecaceae.

Resumen

La utilización de plantas para fines medicinales es realizada empíricamente por los conocimientos tradicionales con la utilización de preparos que buscan extraer sus principios activos y son considerados fundamentales para la salud humana. En este contexto, el objetivo del estudio fue realizar una revisión sistemática de las actividades bilógicas de la familia Arecaceae repartida por todo el Brasil. Esta investigación fue realizada a través de una búsqueda integral en las bases de datos Scopus, Portal Periódicos Capes, PubMed, Google Scholar y Science Direct, utilizando los siguientes descriptores "Areacaceae" y "Propriedades biológicas da familia Arecaceae", verificados en <www .theplantlist.org/> para la verificación de sinónimos. Fue posible identificar muchas actividades biológicas en la familia de las Arecaceae, entre las más recurrentes, la actividad antioxidante, antimicrobiana y antiinflamatoria. Esas actividades son justificadas por la presencia de ácidos grasos, compuestos fenólicos, alcaloides y terpénicos. Los estudios rutinariamente reportar el ácido láurico como un de los principales en las plantas de esta familia, lo que torna un compuesto potencial para curar o auxiliar en el tratamiento de variadas enfermedades.

Palabras clave: Plantas medicinales; Biodiversidad brasileira; Actividades biológicas; Areacaceae.

1. Introduction

The use of medicinal plants as an alternative to treat several diseases is an old habit in different cultures, which remains until nowadays, especially in developing countries (Mattos, Camargo, Sousa, & Zeni, 2018; Padilha et al., 2017). Some reasons for the use of medicinal plants are due to its low cost, easy access and the belief that natural products are safer when compared to synthetic drugs (Silva & Santana, 2018; Filho, 2010). Thus, several research on medicinal plants are focused on discovering bioactive molecules with benefits to human health and low toxicity (Al-Okbi, 2014; Lee, Lee, Tsai, & Su, 2012), demanding studies to identify plant compounds and related biological activities (Lana, Martins Necchi, Casoti, & Manfron, 2012). For this reason, the phytochemistry study of plants with medicinal properties represents an essential step to define their composition and provides evidence of potential biological activities and mechanism of action (León-mejía et al., 2011; Vinod, Tiwari, & Meshram, 2011).

Natural chemical compounds have been used to treat health problems and historically their derivates are extremely important as nutraceuticals, supplements and therapeutic agents (Lescano & Kassuya, 2014). However, besides the therapeutic purpose, in some cases, the plant chemical compounds may present toxic effects, such as the terpenoids, alkaloids, tannins and glycosides (Pereira & Cardoso, 2012).

Additionally, the use of medicinal plants may present better therapeutic results when compared to synthetic substances. Thus, the preliminary phytochemical analysis is a very important step for the for the beginning of the phytochemical study of the plant to be studied, and may show several classes of bioactive compounds, among them: flavonoids, reducing sugars, alkaloids, tannins, lignins, saponins, steroids (Joy et al., 2019). Therefore, plants present bioactive compounds that can be toxic, mutagenic, carcinogenic and teratogenic, especially when they are consumed without restriction, so, it is important to evaluate the toxicity with biological activities (López-Romero et al., 2018).

Brazil has the greatest biodiversity worldwide, being a source of natural molecules with high biological potential (Khan et al., 2018). Thus, studies that demonstrate the potential of medicinal plants found in Brazilian biomes are essential for

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maintaining the conservation of species, as well as providing scientific evidence regarding the invaluable source of new bioactive molecules for diverse purposes, including for the treatment of several diseases, many of them still without effective treatment (Brasil, 2011).

The Arecaceae family is one the biggest family worldwide and it is strongly distributed in tropical zones, with 181 genus and 2600 species (Emilio et al., 2019; Henrique, Koolen, & Soares, 2019). This family is extremely valuable due to its diversity of species, in Brazil it comprises 37 genera and 293 species, occurring in all Brazilian biomes (Leitman, Soares, Henderson, Noblick & Martins, 2015). The species from this family present morphological and functional differences, like bush species, woody trees, or even grasses (Balslev, Laumark, Pedersen, & Grández, 2016; Santos, Aguiar-Dias, Amarante, & Coelho-Ferreira, 2013). Additionally, there is a big variety of edible fruits, like nuts, berries, or drupes, with different textures, forms, colors, and chemical compositions (Blok, Katan, Jos, & Meer, 1996; James, Gibson, & Cleland, 2000).

Figure 1. *Acrocomia aculeata* (Jacq.) Lodd. ex Martius. A: specimen in natural habitat. B: infructescence.

Source: Rodrigues et al. (2011).

Figure 2. *Cocos nucifera* (Arecaceae). A: specimen in natural habitat. B: fruit.

Source: Adapted from (Belviso et al., 2013) and (Bessa et al., 2016)

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Most species from this family are reported in the literature due to their biological potential, an example is *Syagrus coronata*, which is used for fruit production. This species also has emerged as to its medicinal potential, due to its leishmanicidal activity (Rodrigues et al., 2011), antioxidant (Belviso et al., 2013) and antimicrobial (Bessa et al., 2016). Another species is *Butia odorata*, which is known due to its antioxidant and antitumor potential (Boeing et al., 2019), hypolipidemic and anti-inflammatory (Ramos, Silva, Oliveira, Bona, Hofmann, & Chaves, 2020), antihyperglycemic (Vinholes, Lemos, Lia, Franzon, & Vizzotto, 2017), and antibacterial activity (Maia, 2019). The species *Syagrus schizophylla* also has a range of biological activities, such as antioxidant, antimicrobial (Nonato et al., 2018) analgesic, antipyretic and anti-inflammatory (Elhakim, Abdel-Baky, & Bishay, 2017), antimalarial (Tayler et al., 2019), and antibacterial (Joy et al., 2019). Most of those pharmacological properties are reported in ethnobotanical studies and have been proved in scientific research.

In this context, the present study aimed to carry out a systematic review of the biological activities from the Arecaceae family with occurrence in Brazilian territory.

2. Methodology

The search for articles was performed between the months of September and December of 2020, using the species names, verified in <www.theplantlist.org/> in case of synonyms. The searched databases were Scopus, Portal Periódicos CAPES, PubMed, Google Scholar and Science Direct, using the descriptors: "Arecaceae" and "Biological properties of the family Arecaceae".

This research was carried out through a search between the months of September to December 2020, with the names of the species verified on the site <www.theplantlist.org/> to check synonyms. A comprehensive search for articles was carried out using Scopus, Portal Periódicos Capes, PubMed, Google Scholar and Science Direct, using the following descriptors: "Arecaceae" e "biological properties of the family Arecaceae". Studies published between 2010 and 2020 were included. Complete articles containing the descriptors included in the abstract or keywords were selected. Duplicate articles in the search platforms, review articles, articles of genetic and taxonomic scope and studies on plant metabolism were excluded. The other articles were then selected based on the title, abstract and keywords. Finally, the complete articles were analyzed according to the following criteria (1): phytochemistry; 2): ethnobotanical uses; (3): bioactivities; (4): bioactivities of compounds isolated in the Arecaceae family; (5): types of products used.

3. Results and Discussion

Extracts

Among the articles, 30 of them investigated extracts from 19 different genus and their biological activities, as shown in Table 1. The most used vegetal parts were the fruits (72%). As for essential oil, the leaves were the most used part (66%), followed by the fruits (33%) and fixed oil; the fruits were used in all research.

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Table 1. Biological activities from Arecaceae species.

Specie	Biological activity	Type of product	References
Hyphaene thebaica	Antioxidant and Antimicrobial	Methanolic and Ethanolic extract	(Aboshora et al., 2014)
Phoenix dactylifera	Determination of the nutritional class of compounds present and antioxidante	Ethanol extract	(Abdul-hamid et al., 2020)
Oenacapus bataua	Antimicrobial	Ethanol extract	(Aranaga et al., 2020)
Euterpe precatoria	Antimicrobial	Ethanol extract	(Aranaga et al., 2020)
Cocus nucifera	Antitoxic	Ethanol extract	(Adaramoye & Ola-davies, 2015)
Attalea speciosa	Antimicrobial and immunomodulatory	Ethanol extract	(Barroqueiro et al., 2016)
Orbignya phalerata	Th1 immunomodulatory activity	Aqueous extract	(Guerra, Silva, Aragão-França, Oliveira, & Feitosa, 2011a)
Hyophorbe indica	Antioxidant activity, α-glucosidase inhibition and hypoglycemic activity.	Ethanol extract	(William et al., 2018)
Cocos nucifera	Antimicrobial	Aqueous, ethanol, chloroform and diethyl extracts	(Joy et al., 2019)
Cuminum cyminum	Antimicrobial	Aqueous extract	(Karamian & Kamalnejad, 2019)
Melia azedarach	Larvicide	Methanolic extract	(Koc, Evren, & Cetin, 2016)
Phoenix theophrasti	Larvicide	Methanolic extract	(Koc et al., 2016)
Styphnolobim aponicum	Larvicide	Methanolic extract	(Koc et al., 2016)
Pyracantha coccinea	Larvicide	Methanolic extract	(Koc et al., 2016)
Cocos nucifera	Antimicrobial	Aqueous extract	(Kadja, Atsain-allangba, Kouamé, & Janat, 2020)
Phoenix dactylifera	Hepatoprotetor	Methanolic extract	(Okwuosa, Udeani, Umeifekwem, & Augustine, 2014)
Attalea speciosa,	Antimicrobial	Ethanol extract	(Oliveira et al., 2016)
Mauritia flexuosa	Antimicrobial	Ethanol extract	(Oliveira et al., 2016)
Acrocomia aculeata	Antimicrobial	Ethanol extract	(Oliveira et al., 2016)
Phoenix dactylifera	Protective effect against oxidative testicular damage	Aqueous extract	(Jahromi, Rasooli, Kamali, Ahmadi, & Sattari, 2017)
Bactris setosa	Antioxidant	Aqueous extract	(Rosa, Arruda, Egle, & Arruda, 2016)
Phoenix loureiroi	Intestinal anti-inflammatory activity	Methanolic, ethyl, chloroform extract, ethyl acetate	(Murugan, Saravanan, & Parimelazhagan, 2018)
Cocos nucifera	Antiparasitic and anticâncer	Dichloromethane and methanol extracts	(Tayler et al., 2019)
Cocos nucifera	Synthesis of silver nanoparticles	Methanol extract	(Mariselvam et al., 2014)
Raphia vinifera	Cytotoxicity	Chloroform and methanolic extracts	(Chi, Sop, Mbaveng, & Ombito, 2020)

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Ravenea rivularis	Antioxidant, anti-inflammatory and cytotoxicity against Hep-G2	Metanolic, hexanic, ethyl acetate and butanolic extracts	(Elgindi, Singab, Mahmoud, & Abdullah, 2015)
Orbignya phalerata,	Immune responses	Aqueous extract	(Guerra et al., 2011a)
Raphia hookeri	Antimicrobial and modulation	Methanol extract	(Nguenang et al., 2018).
Caryota mitis lour	Analgesia, antipyretic and anti-inflammatory.	Aqueous and ethanolic extract	(Elhakim et al., 2017)
Cocos nucifera	Antifungal and antioxidante	Methanolic extract	(Thebo et al., 2016)
Hyophorbe indica	Antioxidant, anti-hypoglycemic and metabolite profile.	Ethanol extract	(William et al., 2018)
Ráfia gentiliana	Anti-hyperglycemic and hyperglycemic	Aqueous and ethanolic extract	(Mpiana, Masunda, Longoma, Tshibangu, & Ngbolua, 2013)
Mauritia flexuosa	Antioxidant and antimicrobial	Chloroform extract, ethyl acetate and ethanolic	(Nonato et al., 2018)
Phoenix dactylifera	Hepatoprotection	Methanolic extract	(Okwuosa et al., 2014)
Euterpe oleracea	Antioxidant	Aqueous extract	(Minighin et al., 2019)
Mauritia flexuosa	Antimicrobial and antioxidante	Fraction	(Nonato et al., 2018)
Orbignya speciosa	Antinociceptive	Fraction	(Pinheiro, Boylan, & Fernandes, 2012)
Raphia farinifera	Cytotoxicity	Fraction	(Tapondjou, Siems, Bottger, & Melzing, 2015)
Euterpe oleracea	Anti-inflammatory and antinociceptive	Fixed oil	(Favacho et al., 2011)
Livistona australis	Antioxidant and anti-hyperlipidemic	Fixed oil	(Kassem & Afifi, 2014)
Acrocomia aculeata	Diuretic and anti-inflammatory	Fixed oil	(Lescano & Kassuya, 2014)
Attalea phalerata	Cytotoxicity, Genotoxicity and Clastogenicity	Fixed oil	(Lima et al., 2016)
Attalea phalerata	Cytotoxicity, Genotoxicity and Clastogenicity	Fixed oil	(Lima et al., 2016)
Chamaerops humilis	Antimicrobial	Essential oil	(Inouye, Yamaguchi, & Takizawa, 2001)
Euterpe oleracea	Genotoxicity and clastogenics / anagenic potential	Essential oil	(Marques et al., 2016)

Source: Authors.

Antioxidant activity

The endogenous antioxidant system is essential to maintain integrity and body homeostasis, since several reactive oxygen species (ROS) are constantly generated in cells as products of cellular metabolism. Although these ROS have benefic functions on the organism, at high concentrations they induce toxic effects and are associated with several diseases (Alves et al., 2010; Santos et al., 2014).

Arecaceae species have demonstrated antioxidant potential. The extract obtained from *Hyphaene thebaica* fruits present antioxidant activity in DPPH reduction assay (Aboshora et al., 2014). As for *Hyophorbe indica* leaf extract, which presents compounds known as antioxidants, like gallic acid, catechin and citric acid, also present an antioxidant effect, being able to reduce the DPPH radical, and achieving the IC50 of 35.35 ±0,18 µg/mL (Aboshora et al., 2014). The extract

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from *Bactris setosa*, with a higher content of flavonoids, presents antioxidant activity, in FRAP and β-carotene oxidation assays (Rosa et al., 2016). *Mauritia flexuosa* showed antioxidant activity being able to reduce the ABTS radical and chelate 80.9% of Fe+2 *in vitro*, available at 700 µg/mL (Nonato et al., 2018). Other Arecaceae species that also showed antioxidant activity *in vitro* models are *Euterpe Oleracia* (Minighin et al., 2019), *Hyophorbe indica* (William et al., 2018), *Cocos nucifera* (Kadja et al., 2020; Thebo et al., 2016), and *Ravena rivularis* (Elgindi et al., 2015)

Kassem (Kassem & Afifi, 2014) studied the lipophilic fraction obtained from *Livistona australis* fruit (LALF), which presented oleic acid as major content (59.05%), palmitic acid (20.59%), phytol-diterpene (7.98%) and linoleic acid (0.79%).

Oleic acid (OA) is the main component among the fatty acid contents of LALF. Oleic acid, linoleic acid and phytol inhibited hyperlipidemia probably through the oxidation reaction. The LALF content can play a role with strong antioxidant activity in inhibiting lipid peroxidation and protecting against oxidative degradation of biologically active substances. *In silico* studies, with oleic acid, indicates that it acts as a competitive inhibitor with nitric oxide on the active site of nitric oxide synthase (Kassem & Afifi, 2014). The unsaturated fatty acids play important roles in the immunological system and inflammatory process (Menéndez et al., 2006; Weatherill et al., 2005).

According to the literature, even if some of the studies do not bring exactly the compounds present in the extracts, they still have at least the metabolite class present in these extracts, as disposed of in Table 2. It was possible to observe that the aforementioned studies have in common the occurrence of phenolic and flavonoid compounds, which are known antioxidant molecules (Balasudram, Sundram, & Samman, 2006), being used in several industries, such as food, aesthetics, pharmaceuticals, and textile.

Table 2. Phytochemical compounds present in Arecaceae family.

Species	Vegetal part	Chemical compounds	References
Hyphaene thebaica	Fruit	Unidentified	(Aboshora et al., 2014)
Phoenix dactylifera	Fruit	Unidentified	(Abdul-hamid et al., 2020)
Oenacapus bataua	Root	Unidentified	(Aranaga et al., 2020)
Euterpe precatória	Root	Unidentified	(Aranaga et al., 2020)
Cocus nucifera	Fruit	Unidentified	(Adaramoye & Ola-davies, 2015)
Attalea speciosa	Fruit	Unidentified	(Barroqueiro et al., 2016)
Orbignya phalerata	Fruit	Unidentified	(Guerra et al., 2011a)
Hyophorbe indica	Leaves	Citric acid, procyanidin B3, epicatechin, procyanidin B2, catechin, catechin derivative, procyanidin B1, apigenin-c-hexocide-c-hexocide, Kaempferol, Kaempferol derivative, quinic acid derivative, gallic acid	(William et al., 2018)
Cocos nucifera	Leaves	Tannin, lignins, flavonoids.	(Joy et al., 2019)
Cuminum cyminum	Leaves	Total phenol, flavonoid, ascorbic acid, starch, reducing sugars.	(Karamian & Kamalnejad, 2019)
Melia azedarach	Fruit	Unidentified	(Koc et al., 2016)
Phoenix theophrasti	Fruit	Unidentified	(Koc et al., 2016)
Styphnolobim aponicum	Fruit	Unidentified	(Koc et al., 2016)

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Pyracantha coccínea	Fruit	Unidentified	(Koc et al., 2016)
Cocos nucifera	Fruit peel	Coumarins, flavonoids, steroids, tannins and triterpenes	(Kadja et al., 2020)
Phoenix dactylifera	Leaves	Unidentified	(Okwuosa et al., 2014)
Attalea speciosa,	Leaves	Unidentified	(Oliveira et al., 2016)
Mauritia flexuosa,	Leaves	Unidentified	(Oliveira et al., 2016)
Acrocomia aculeata	Leaves	Unidentified	(Oliveira et al., 2016)
Phoenix dactylifera	Leaves	Unidentified	(Jahromi et al., 2017)
Bactris setosa	Leaves	Unidentified	(Rosa et al., 2016)
Phoenix loureiroi	Leaves	Unidentified	(Murugan et al., 2018)
Cocos nucifera	Peel, Leaf and Fruits	Unidentified	(Tayler et al., 2019)
Cocos nucifera	Inflorescence	Unidentified	(Mariselvam et al., 2014)
Raphia vinífera	Fruit	Saponins (1-4)	(Chi et al., 2020)
Ravenea rivularis	Leaves	Lupeol acetate, betulinic acid, apigenin, luteolin, luteolin-7-O-β-D-glucopyranoside, ferulic acid, caffeic acid and chlorogenic acid	(Elgindi et al., 2015)
Orbignya phalerata,	Fruit	Unidentified	(Guerra et al., 2011a)
Raphia hookeri	Fruit	Alkaloids, triterpenes, steroids and polyphenols, including flavonoids.	(Nguenang et al., 2018)
Caryota mitis lour	Leaves	Unidentified	(Elhakim et al., 2017)
Cocos nucifera	Fruit	Unidentified	(Thebo et al., 2016)
Hyophorbe indica	Leaves	Unidentified	(William et al., 2018)
Ráfia gentiliana	Fruit	Unidentified	(Mpiana et al., 2013)
Mauritia flexuosa	Fruit	Unidentified	(Nonato et al., 2018)
Phoenix dactylifera	Fruit	Unidentified	(Okwuosa et al., 2014)
Euterpe oleracea	Fruit	Unidentified	(Minighin et al., 2019)
Mauritia flexuosa	Fruit	Flavonoids	(Nonato et al., 2018)
Orbignya speciosa	Leaves	Unidentified	(Pinheiro et al., 2012)
Raphia farinifera	Fruit	Unidentified	(Tapondjou et al., 2015)
Euterpe oleracea	Fruit	Palmitic acid, palmitoleic acid and oleic acid	(Favacho et al., 2011)
Livistona australis	Fruit	Oleic acid, linoleic and palmitic acids, diterpene-phytol	(Kassem & Afifi, 2014)
Acrocomia aculeata	Fruit	Oleic acid, palmitic acid and linoleic acid.	(Lescano & Kassuya, 2014)
Attalea phalerata	Fruit	β-carotene and α-carotene	(Lima et al., 2016)
Attalea phalerata	Fruit	β-carotene	(Lima et al., 2016)
Chamaerops humilis	Leaves and fruit	Unidentified	(Inouye et al., 2001)
Euterpe oleracea	Fruit	Oleic, palmitic and palmitoleic fatty acids	(Marques et al., 2016)

Source: Authors.

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Anti-inflammatory and protective activities

Inflammation can be defined as an organism natural response to several types of stimuli, which in turn culminates into tissue damage. During this process, many molecular mechanisms are activated which induces histologic and vascular alterations in the affected area (Ashley, Weil, & Nelson, 2012). Despite that, the inflammation may induce deleterious effects when it persists on the organism and the inflammatory response is too strong. Several Arecaceae species demonstrate anti-inflammatory effect.

Phoenix loureiroi extract was able to reduce intestinal inflammation, in mice, due to oral administration at a concentration of 5 mg/kg, corroborating with the popular use of the fruit to treat intestinal pain (Murugan et al., 2018). Elhakim et al. (2017) verified the anti-inflammatory potential of *Caryota mitis*, its extract was able to attenuate the inflammatory response in mice paw edema induced by carrageenan at a concentration of 400 mg/kg. Besides that, the research also highlighted the absence of toxicity, presenting an average lethal dose (LD_{50}) higher than 5000 mg/kg. *As for Ravenea rivularis*, which extract, presented antioxidant activity, also present anti-inflammatory activity. Is worth to noting that the inflammation process is related to oxidative stress, therefore, it may be possible that the molecules found in the extract present both effects, antioxidant and anti-inflammatory, promoting an efficient attenuation on inflammation process and the diseased related to it (Elgindi et al., 2015).

As for the oils and fatty acids, some authors state that it can reduce the levels of cytokines, like the IL-1 α, TNF- α, IL-6 e IL-1 β, which will result in an anti-inflammatory response (Blok et al., 1996; W. James et al., 2018). Oleic acid, palmitic acid and palmitoleic acid are identified as the main components that play important physiological roles in the human body, due to their chemical structure, these compounds have become the focus of interest for pharmaceutical and food companies (Blok et al., 1996; James et al., 2018) and as seen in the table 2, the oils obtained from Areceae species are usually rich in those compounds.

According to Favacho et al. (2011), the oil obtained from *Euterpe oleracea* fruits showed anti-inflammatory activity *in vivo* in paw edema and ear erythema induced by croton oil. The average effective dose was 1226.8 mg/kg, and the results showed that *E. oleracea* oil presents an anti-inflammatory effect by inhibiting prostaglandins biosynthesis. The microencapsulated oil from *Acrocomia aculeata* fruits also presented anti-inflammatory in paw edema, and pleural edema models, both induced by carrageenan (Lescano & Kassuya, 2014), both species have oleic acid as major compound.

The relation between oleic acid and the therapeutic potential for the treatment of inflammatory diseases is that it can induce tissue repair, as discussed by Grimm et al. (2002), its occurs due to changes in metalloproteinases balance, which are key molecules for the process of tissue healing. As for Calder (2002), the omega-3 unsaturated fatty acid can affect the expression of pro-inflammatory cytokine genes, altering cell membrane's characteristics, cell signaling, cell mobility, the interaction of receptors, membrane and the formation of secondary signs (Grimm et al., 2002).

The balance of the dietary lipids is intended to control the inflammatory response when exacerbated by the intake of unsaturated fatty acids. Studies express those fatty acids participate in the modulation of calcium signaling (Soldati et al., 2002), protein kinase C (May & Calder, 1993), activation of phospholipase C , production of inositol-1,4,5-triphosphate (IP3) and diacylglycerol (DAG). In addition, they are the primary precursors of lipid mediators during the inflammatory process, such as arachidonic acid and prostaglandins (Soldati et al., 2002). With that in mind, there is several pathways that fatty acids can act to attenuate the inflammatory process.

As for the protective effect, it is related with the capacity of a molecule or product prevent damages into a certain cells or tissue before it starts an inflammation process. Some Arecaceae species showerd protective effect in different system, like the hepatoprotective effect described for *Phoenix dactylifera* (Okwuosa et al., 2014), which in turn presented an LD_{50} higher than 6000 mg/kg. The same species also presented a protective effect in bovine testicles (Jahromi et al., 2017). Investigating *Cocos*

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nucifera extract, intending to revert toxic effects induced by cisplatin in mice, Adaramoye and Ola-davies (2015) obtained positive results by administrating 200 mg/kg daily on mice diet, they also noticed a decrease in lipid peroxidation and intensification of antioxidant enzymes activity. And finally, the extract obtained from *Orbignya phalerata* presented a protective effect by modulating the inflammatory response, and the fruit extract from this species associated or not with aluminum particles increased interferons and interleukins concentration (Guerra, Silva, Aragão-França, Oliveira, & Feitosa, 2011b).

Antimicrobial activity

In the last 10 years, at least 10 Arecaceae species were studied as potential antimicrobial activity. The ethanolic extract from *H. thebaica* fruits showed strong antibacterial activity against *Staphylococcus aureus* and *Salmonella typhi*, in the disk diffusion method, it is worth noting that the extract showed positive results against two types of bacteria cells, a Gram-positive and Gram-negative respectively, still, the control drugs, gentamicin, and ampicillin, showed higher zone of inhibition when compared to the extract (Aboshora et al., 2014).

A similar methodology was employed to test the extract from *C. nucifera* leaves, rich in tannin, lignin, and flavonoids, it was able to inhibit *Escherichia coli* growth, with an inhibition halo of 5 mm, 50% less compared to the drug control, ciprofloxacin (a 1 µg) (Joy et al., 2019). Tayler et al. (2019) evaluated the antiparasitic effect from *C. nucifera* Against several parasites, like *Leishmania donovani*, *Trypanosoma cruzi*, and *Plasmodium falciparum*, which showed positive results.

Aranaga et al. (2020), evaluated the antimicrobial potential from several plant extracts, between then: *Onecapaus bataua* and *Euterpe precatoria*, which were able to inhibit the PKnB kinase enzyme, essential to *Mycobacterium tuberculosis*. The IC_{50} from the first species was of 60.9 µg/mL, while the second one showed 77.4 µg/mL, both being able to inhibit the enzymatic activity, however, it was not able to inhibit bacteria growth. The extract capacity of inhibiting the enzymatic activity brings new perspectives to the search of bacteria metabolism modulation mediated by plant extracts, turning them more susceptible, or not, to antibiotics drugs.

An example of modulatory effect was observed in *Raphia hookeri* extract, which was able to decrease the antibiotic concentration until 50% when combined with chloramphenicol, kanamycin, streptomycin, erythromycin, and tetracycline. Also, according to the author, this effect was due to the metabolites present in *R. hookeri*, which could inhibit the efflux bomb present in bacteria, which is a factor that grants bacteria the resistance effect (Nguenang et al., 2018). *M. flexuosa* showed a similar effect, inducing susceptibility to conventional antibiotics in Gram-positive, Gram-negative and Candida species (Nonato et al., 2018).

Another species, rich in phenolic compounds and flavonoids, is *Attalea speciosa*, which was able to inhibit the growth of *S. aureus* resistant to methicillin strains, *Enterococcus faecalis* and *Pseudomonas aerugionosa in vitro*, as also an excellent antiseptic *in vivo* model, being able to modulate the immunologic system, into a less intensive response (Barroqueiro et al., 2016).

An alterntive approach approach is the use of natural products to decrease the virulence for bacteria strains, like inhibiting the biofilm expression. The oil from *Syagrus coronata*, rich in octanoic, dodecanoic, decanoic and γ-eudesmol was able, not only to inhibit and kill bacteria strains resistant to antibiotics, as act over bacterias strains capable of forming a biofilm, with MIC between 156 and 625 µg/mL, and MBC of 312 to 1250 µg/mL (B. S. Santos et al., 2019). The oil from *Chamaerops humilis* leaves, whose authors emphasized that the fact of the leaves present more oil than the fruits, due to the anatomic structures have several storage glands, present antibacterial action against *S. aureus*, *E. coli*, and *P. aeruginosa* (Okkacha, Edine, & Raja, 2013).

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The bioproducts development has also been applied to the Arecaceae family, and it has proved to be efficient, as related by Karamian and Kamalnejad (Karamian & Kamalnejad, 2019). The authors synthesized nanoparticles of silver with the extract from *Cuminum cyminum*, with strong antibacterial activity. Although other studies with bioproducts made from *M. flexuosa* and *A. aculeata* didn't show any promising effect against *S. aureus*, *E. faecalis*, *E. coli* and *P. aeruginosa*, *C. albicans* and *C. parapsiolis*.

Cytotoxicity and anticancer

The use of medicinal plants has been growing progressively, mainly since they have biological activity and are used as a source of new molecules and effects obtained by the synthetic drugs currently commercialized, and may even confer a more potent effect, with a potential for less physiological damage. In addition, the cost of herbal medicines is generally reduced, increasing access to this resource, ensuring quality treatment, with chances of cure and better quality of life (Kharchoufa, Merrouni, Yamani, & Elachouri, 2018; Prasansuklab, Brimson and Tencomnao, 2020).

Even with a lower potential for intoxication, some plant species may present a risk of toxicity, mainly because they produce neurotoxins, cytotoxins and metabolic poisons that will disturb the structural and functional integrity of internal organs, such as the liver, heart, kidneys, gastrointestinal system and lungs. In addition, the dose is also important, as some substances can show positive activity for some illnesses in minimal concentrations, but if there is an increase in the dose, that previously therapeutic compound becomes toxic to the organism and can cause tissue or cellular injuries, especially whether carcinogenesis, hormonal dysregulation and the interruption of reproductive and developmental processes (Kristanc & Kreft, 2016; Nembo, Hescheler, & Nguemo, 2020; Shabbir, Shahzad, & Gobe, 2014).

Euterpe oleraceae, the Brazilian açai, is rich in fatty acids, like vanillic acid, palmitic acid, linolenic acid, linoleic acid and oleic acid. This species well-known for its popular fruit, which is famous in the whole country, but specially the North region.

The chromatographic analysis identified a range of fatty acids in the fruit, such as vanillic acid, palmitic acid, γ-linolenic acid, linoleic acid and oleic acid. Toxicity was assessed in rats at doses of 30 mg/Kg, 100 mg/Kg or 300 mg/Kg. Only at a concentration of 300 mg/Kg the animals showed signs of intoxication, such as diarrhea and hair bristles. In addition to acute toxicity, genotoxicity was performed by comet and micronucleus assays from leukocyte samples from peripheral blood, liver, bone marrow and testicular cells taken from animals that were subjected to the acute test (Marques et al., 2016).

In the comet assay, genetic material was used to measure DNA damage, such as single and double-strand breaks, alkaline sites, DNA-DNA and DNA-protein cross-links. Thus, it was verified that there was no damage, indicating that the oil did not present genotoxicity. According to the micronucleus assay, clastogenicity (chromosome breakdown) and aneugenicity (chromosomal delay due to dysfunction of the mitotic apparatus) were measured, as well as it was possible to estimate the proportion of polychromatic erythrocytes concerning normochromatic erythrocytes, suggesting any disturbances in hematopoiesis. Thus, the study reported a non-genotoxic effect on bone marrow cells, with an average micronucleus of 2.16 to 2.5 at concentrations of 30 mg/kg and 100 mg/kg, while the control reported a presence of an average of 8.5 micronucleated cells. With that, it is possible to affirm that *E. oleracea* oil does not present genotoxicity, however, from the concentration of 300 mg/kg, it is possible to observe an imbalance in homeostasis (Marques et al., 2016).

Studies with *Attalea phalerata* Mart. ex Spreng., well known as "bacuri" *in vivo* and *in vitro* models, were carried out to evaluate toxicity using the *Artemia salina* and MTT assay models, in addition to the comet and micronucleus assays. The results showed that bacuri oil did not induce cell death in the *Artemia salina* and MTT experiments and did not present cytotoxicity. The oil also did not cause significant damage to the DNA of the rats in the four doses used when compared to

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the negative control group, in addition to not showing a significant increase in micronucleated polychromatic erythrocytes (MNPCEs) for the four doses tested. Thus, the study suggested that this species widely used by popular medicine does not cause cytotoxicity, genotoxicity and clastogenicity, and its main component was β-carotene (Lima et al., 2016).

Chi (Chi et al., 2020) isolated 4 saponins from *Raphia vinifera*, being toxic in average concentrations of 3.55 to 7.14 μM in cell lines sensitive to drugs CCRF-CEM, whereas in cell lines resistant to drugs, CEM/ADR5000 concentration mean ranged from 9.19 to 12.29 μM, showing an anticancer potential, since the cell lines tested are leukemic cells. The saponins present in this species induced a cytotoxic effect in a drug-resistant phenotype, showing a potential alternative in the treatment of cancer unresponsive to conventional drugs. Tayler (Tayler et al., 2019), when evaluating the action of *Cocos nucifera*, verified the potential for anticancer activity in MCF-7 breast cancer cell line, all *in vivo* tests, obtaining promising results.

Arboviruses comprise a group of viral diseases transmitted by arthropods (mosquitoes) and have been plaguing the world, causing epidemic crises mainly in developing countries (Mayer, Tesh, & Vasilakis, 2016). Recently, the most prominent outbreaks are dengue (DENV), Zika virus (ZIKV) and chikungunya (CHIKV), which are associated with symptoms of hemorrhagic fever, microcephaly and arthritic disease, respectively (Palmer, Dittmar, Gordesky-gold, Hofmann, & Cherry, 2020). The *Aedes aegypti* mosquito is an important vector for the transmission of arboviral pathogens of dengue, chikungunya, Zika virus and yellow fever. Its life cycle (stage of eggs, larvae and pupae) occurs in an aquatic way until reaching its full development, becoming adult and aerial life. Due to the need for aquatic development, in regions where standing water facilitates its dissemination, therefore, poor regions with few resources for sanitation and water treatment are the places with the highest incidence of the mosquito and consequently the diseases associated with it (Luz, Mesquita, Amaral, & Coutinho, 2020; Omondi et al., 2019). *Phoenix dactylifera* L. is a species widely cultivated in the Arabian Peninsula and especially in Saudi Arabia. The extraction of the essential oil from the spathe (a region that protects the flowers) by hydrodistillation obtained the majority of 3,4-dimethoxytoluene (73.47%), 2,4-dimethoxytoluene (9.47%) and β-karyophylene (5, 47%). In the repellency test, both essential oil and the two major oils (3,4-dimethoxytoluene and 2,4-dimethoxytoluene) were used. According to the results, the essential oil, 3,4-dimethoxytoluene and 2,4-dimethoxytoluene presented a minimum effective dose of 0.051, 0.063 and 0.063 mg / cm2, respectively. These results can illustrate a repellent effect, because when we compare these data with that obtained by the standard DEET repellent (N, N -diethyl-3-methylbenzamide) with a minimum effective dose of 0.018 mg/cm^2, a statistically relevant result. With this, it is possible to verify that the mixture between the oil components is more potent than isolated products, this is due to the synergy between oil compounds, the same does not occur when using the isolated molecule (Demirci, Tsikolia, Barbier, Agramonte, & AlqasoumiL, 2013).

According to Santos (L. M. M. Santos et al., 2017), a study was carried out using oil of *Syagrus coronata*, for larvicidal and ovicidal activity. *S. coronata* is a typical Caatinga species, popularly known as “ouricuri” or “licuri”. According to gas chromatography (GC) analysis, the oil showed prominence for octanoic acid (40.55%) and dodecanoic acid (40.48%). In the larvicidal test, the larvae were reduced by half after 48 hours in the concentrations of 21.07, 19.72 and 51.78 ppm for the samples of oil, dodecanoic acid and octanoic acid, respectively. According to the oviposition, the oil affected the oviposition of the females more intensely, reducing the number of eggs by 35% compared to the control, while the octanoic acid reduced by 31%. The results indicated that the larvicidal activity is due to the action of dodecanoic acid, while the effect of oviposition is probably related to the presence of octanoic acid. Finally, the *Phoenix theophrasti* extract has larvicidal activity, at a concentration of 1000 ppm against larvae of the *Culex pipiens* insect (Tayler et al., 2019).

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Hypoglycemic activity

William (William et al., 2018) demonstrated the hypoglycemic potential of the *Hyophorbe indica* extract, through the in vivo assay of α-glucosidase inhibition with IC50 36.52 ± 0.08 μg / mL. *Raphia gentiliana*, on the other hand, was able to decrease the concentration of glucose in the blood by 27 and 56% after one and two hours, respectively, after ingesting the fruit extract at a concentration of 0.2 g/Kg. In this same study, it was reported that the extract changed the glycemic index by -3.1% and the glycemic load by -1.36% in humans (Mpiana et al., 2013).

4. Final Considerations

The development of the present study showed that the Arecaceae family has a composition rich in fatty acids, phenolic compounds, alkaloids and terpenes, with the main compound of the family lauric acid, a compound already used as a therapeutic alternative to help various diseases. Among the most recurrent biological activities, we can report the antioxidant, antimicrobial and anti-inflammatory activity.

Thus, it is possible to consider that the abundance and the processing capacity of the plants of the Arecaceae family in Brazil bring us the need for more in-depth studies, which allows us to investigate other important activities for future therapeutic innovations. In addition, by adding in-depth scientific research, it will bring the possibility of developing a local production chain, valuing and generating income in the traditional communities that popularize its use. It is also important to note that the development of research on bioactive molecules of Brazilian biodiversity not only brings therapeutic innovations, but also promotes the emergence and development of traditional communities, valuing customs, culture and the history of sub-existence.

The relevance and importance of this work lies in the review of the medicinal potential of the Arecaceae family, and this data collection could serve as a basis for collaboration in future studies and projects for the development of new therapeutic applications for phytotherapics, cosmetics and food.

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References

Abdul-hamid, N. A., Hafizah, N., Maulidiani, M., Mediani, A., Safinar, I., Ling, C., & Abas, F. (2020). Journal of the Saudi Society of Agricultural Sciences Quality evaluation of the physical properties, phytochemicals, biological activities and proximate analysis of nine Saudi date palm fruit varieties. *Journal of the Saudi Society of Agricultural Sciences*, *19*(2), 151–160. https://doi.org/10.1016/j.jssas.2018.08.004

Aboshora, W., Lianfu, Z., Dahir, M., Qingran, M., Qingrui, S., Jing, L., … Ammar, A. (2014). Effect of Extraction Method and Solvent Power on Polyphenol and Flavonoid Levels in Hyphaene Thebaica L Mart (Arecaceae) (Doum) Fruit, and its Antioxidant and Antibacterial Activities. *Tropical Journal of Pharmaceutical Research*, *13*(12), 2057–2063.

Adaramoye, O., & Ola-davies, O. E. (2015). Ameliorative Effects of Chloroform Fraction of Cocos nucifera L. Husk Fiber Against Cisplatin-induced Toxicity in Rats April - June 2016 | Volume 8 | Issue 2. *Phamacognosy Research*, *8*(2), 89–95. https://doi.org/10.4103/0974-8490.172658

Al-Okbi, S. Y. (2014). Nutraceuticals of anti-inflammatory activity as complementary therapy for rheumatoid arthritis. *Toxicology and Industrial Health*, *30*(8), 738–74. https://doi.org/10.1177/0748233712462468

Aranaga, C. A., Fraile, S., Torres, A., Falco, A., Michelangeli, F., & Takiff, H. (2020). Antimycobacterial and PknB Inhibitory Activities of Venezuelan Medicinal Plants. *International Journal of Microbiology*, *2020*.

Ashley, N. T., Weil, Z. M., & Nelson, R. J. (2012). Inflammation: Mechanisms, Costs, and Natural Variation. *Reviews in Advance*, *43*(August), 385–406. https://doi.org/10.1146/annurev-ecolsys-040212-092530

Balslev, H., Laumark, P., Pedersen, D., & Grández, C. (2016). Tropical rainforest palm communities in Madre de Dios in Amazonian Peru. *Revista Peruana de Biologia*, *23*(1), 1–12.

Research, Society and Development, v. 10, n. 10, e426101018994, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i10.18994

Barroqueiro, E. S. B., Prado, D. S., Barcellos, P. S., Silva, T. A., Pereira, W. S., Silva, L. A., & Guerra, R. N. M. (2016). Immunomodulatory and Antimicrobial Activity of Babassu Mesocarp Improves the Survival in Lethal Sepsis Immunomodulatory and Antimicrobial Activity of Babassu Mesocarp Improves the Survival in Lethal Sepsis, (August). https://doi.org/10.1155/2016/2859652

Belviso, S., Ghirardello, D., Giordano, M., Sousa, G., Souza, J. De, Parodi, S., … Zeppa, G. (2013). Phenolic composition, antioxidant capacity and volatile compounds of licuri (Syagrus coronata (Martius) Beccari) fruits as affected by the traditional roasting process. *Food Research International Journal*, *51*(1), 39–45. https://doi.org/10.1016/j.foodres.2012.11.012

Bessa, C. M. A. S., Nascimento, R. S., Alves, R. C. C., Anselmo, J. M., Silva, A. P. S., Silva, A. G., … Correia, M. T. S. (2016). Syagrus coronata seed oils have antimicrobial action against multidrug-resistant Staphylococcus aureus. *Journal of Medicinal Plants Research*, *10*(23), 310–317. https://doi.org/10.5897/JMPR2016.6098

Blok, W. L., Katan, M. B., Jos, W. M., & Meer, V. D. (1996). Critical Review Modulation of Inflammation and Cytokine Production by Dietary (n-3) Fatty Acids. *American Institute of Nutrition*, (January), 1515–15333.

Boeing, J. S., Barizão, É. O., Rotta, E. M., Volpato, H., Nakamura, C. V., Maldaner, L., & Visentainer, J. V. (2019). Phenolic Compounds from Butia odorata (Barb. Rodr) Noblick Fruit and Its Antioxidant and Antitumor Activities. *Food Analytical Methods*.

BRASIL. (2011). *Espécies Nativas da Flora Brasileira de Valor Econômico Atual ou Potencial Plantas para o Futuro - Região Sul*.

Calder, P. C. (2002). Dietary modification of inflammation with lipids. *Proceedings of the Nutrition Society*, *1*(61), 345–358. https://doi.org/10.1079/PNS2002166

Chi, G. F., Sop, R. V. T., Mbaveng, A. T., & Ombito, J. O. (2020). Steroidal saponins from Raphia vinifera and their cytotoxic activity. *Steroids*, *163*(July), 108724. https://doi.org/10.1016/j.steroids.2020.108724

Demirci, B., Tsikolia, M., Barbier, U., Agramonte, N. M., & AlqasoumiL, S. I. (2013). Phoenix dactylifera L. spathe essential oil: Chemical composition and repellent activity against the yellow fever mosquito. *Acta Tropica*, 8–11. https://doi.org/10.1016/j.actatropica.2013.08.003

Elgindi, M. R., Singab, A. N., Mahmoud, I. M., & Abdullah, S. H. (2015). Phytochemical and biological investigation of the leaves of Ravenea rivularis (Arecaceae), *4*(1), 72–78.

Elhakim, I. A. A., Abdel-Baky, A. M., & Bishay, W. (2017). Botanical and biological study of the leaves of caryota mitis lour. family arecaceae cultivated in egypt. *Bulletin of Pharmaceutical Sciences Assiut*, *40*, 71–95.

Emilio, T., Lamarque, L. J., Torres-ruiz, J. M., King, A., Charrier, G., Burlett, R., & Delzon, S. (2019). Embolism resistance in petioles and leaflets of palms. *Embolism Resistance in Palms*, *124*, 1173–1183. https://doi.org/10.1093/aob/mcz104

Favacho, H. A. S., Oliveira, B. R., Santos, K. C., Medeiros, B. J. L., Sousa, P. J. C., Fabio, F., & Carvalho, J. C. T. (2011). Anti-infl ammatory and antinociceptive activities of Euterpe oleracea oil. *Revista Brasileira de Farmacognosia*, *21*(1), 105–114. https://doi.org/10.1590/S0102-695X2011005000007

Filho, A. M. (2010). Desenvolvimento, validação e aplicação de metodologias para determinação de resíduos de agrotóxicos em manga por SPME-GC-MS e SPME-HPLC-UV-Vis, 150.

Grimm, C., Wenzel, A., Groszer, M., Mayser, H., & Seeliger, M. (2002). HIF-1-induced erythropoietin in the hypoxic retina protects against light-induced retinal degeneration. *Nature*, *8*(7), 2–8. https://doi.org/10.1038/nm723

Guerra, R. N. M., Silva, V. M. G., Aragão-França, L. S., Oliveira, P. R., & Feitosa, R. (2011a). Babassu aqueous extract (BAE) as an adjuvant for T helper (Th) 1-dependent immune responses in mice of a Th2 immune response-prone strain. *BMC Immunology*, *12*(1), 13. https://doi.org/10.1186/1471-2172-12-13

Guerra, R. N. M., Silva, V. M. G., Aragão-França, L. S., Oliveira, P. R., & Feitosa, R. (2011b). Babassu aqueous extract (BAE) as an adjuvant for T helper (Th) 1-dependent immune responses in mice of a Th2 immune response-prone strain.

Henrique, H., Koolen, F., & Soares, E. R. (2019). An antimicrobial diketopiperazine alkaloid and co-metabolites from an endophytic strain of Gliocladium isolated from Strychnos cf toxifera. *Natural Product Research*, *26*(21), 2013–2019.

Inouye, S., Yamaguchi, H., & Takizawa, T. (2001). Screening of the antibacterial effects of a variety of essential oils on respiratory tract pathogens, using a modified dilution assay method. *JOURNAL Infect Chemother*, *7*, 251–254.

Jahromi, A. R., Rasooli, R., Kamali, Y., Ahmadi, N., & Sattari, E. (2017). Short-term Effects of Date Palm Extract (Phoenix dactylifera) on Ischemia / Reperfusion Injury Induced by Testicular Torsion / Detorsion in Rats. *Pharmacognosy Research*, (January). https://doi.org/10.4103/0974-8490.199769

James, M. J., Gibson, R. A., & Cleland, L. G. (2000). Dietary polyunsaturated fatty acids and inflammatory mediator production 1,2. *American Society for Clinical Nutrition*, *71*, 1–6.

James, W., John, P., Mumtaz, M. W., Ch, A. R., Adnan, A., Mukhtar, H., & Raza, S. A. (2018). Antioxidant activity, Hypoglycemic potential and metabolite profiling of Hyophorbe indica leaf extract, *31*(6), 2737–2742.

Joy, A., Vinson, B., Anto, L., Dinilkumar, M., Wilson, S., Simon, S., & Jose, J. (2019). Antibacterial screening and phytochemical powder isolated from dorsal side of leaves of Cocos nucifera (Arecacaae). *Journal of Pharmaceutical Sciences and Research*, *11*(7), 2557.

Kadja, B. A., Atsain-allangba, R. M., Kouamé, B. K., & Janat, A. (2020). GSC Biological and Pharmaceutical Sciences Influence of temperature on the phytochemical composition and the antioxidant and anticariogenic activities of extracts from the husk of the fruit of Cocos nucifera L. (Arecaceae), *12*(2), 179–187.

Karamian, R., & Kamalnejad, J. (2019). Green Synthesis of Silver Nanoparticles Using Cuminum cyminum Leaf Extract and Evaluation of Their Biological Activities, *9*(1), 74–85. https://doi.org/10.22052/JNS.2019.01.008

Research, Society and Development, v. 10, n. 10, e426101018994, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i10.18994

Kassem, M., & Afifi, M. S. (2014). Chemical Composition of the Lipophilic Fraction of Livistona australis R. Br. Journal of Natural Products Research Paper Chemical Composition of the Lipophilic Fraction of Livistona australis R. Br. Mart, (Arecaceae) Fruit Pulp and Evaluation of its Antioxidant and Antihyperlipidemic Activities, (January).

Khan, F., Dastagir, N., Lateef, M., Yousuf, M., Mirani, A., Mesaik, A., … Kazmi, S. U. (2018). Immunomodulatory activities of extracts of Caesalpinia pulcherrima Immunomodulatory activities of extracts of Caesalpinia pulcherrima. *Journal of Herbs, Spices & Medicinal Plants*, *0*(0), 1–12. https://doi.org/10.1080/10496475.2018.1463931

Koc, S., Evren, O. H., & Cetin, H. (2016). Short Communication Evaluation of Some Plant Fruit Extracts for the Control of West Nile Virus Vector Culex pipiens Diptera: Culicidae), *10*(December), 595–601.

Kristanc, L., & Kreft, S. (2016). European Medicinal and Edible Plants Associated with Subacute and Chronic Toxicity Part. *Food and Chemical Toxicology*, *131*, 1–51. https://doi.org/10.1016/j.fct.2016.04.007

Lana, D. F. D., Martins Necchi, R. M., Casoti, R., & Manfron, M. P. (2012). Uma Revisão Sobre As Propriedades Farmacológicas, Morfoanatomia E Toxicicidade De Xanthium Cavanillesii Schouw (Asteraceae). *Saúde (Santa Maria)*, *38*(2), 57–70. https://doi.org/10.5902/223658344917

Lee, I., Lee, W., Tsai, C., & Su, I. (2012). Combined extractives of red yeast rice, bitter gourd, chlorella, soy protein, and licorice improve total cholesterol, low-density lipoprotein cholesterol, and triglyceride in subjects with metabolic syndrome. *Nutrition Research*, *32*(2), 85–92. https://doi.org/10.1016/j.nutres.2011.12.011

Leitman, P., Soares, K., Henderson, A., Noblick, L., & Martins, R. C. (2015). Arecaceae in Lista de Espécies da Flora do Brasil. Jardim Botânico do Rio de Janeiro.

León-mejía, G., Espitia-pérez, L., Hoyos-giraldo, L. S., Da, J., Hartmann, A., Antônio, J., & Quintana, M. (2011). Science of the Total Environment Assessment of DNA damage in coal open-cast mining workers using the cytokinesis-blocked micronucleus test and the comet assay. *Science of the Total Environment, The*, *409*(4), 686–691. https://doi.org/10.1016/j.scitotenv.2010.10.049

Lescano, C. H., & Kassuya, C. (2014). Diuretic and anti-Inflammatory activities of the microencapsulated Acrocomia aculeata (Arecaceae) oil on wistar rats. *Journal of Medicinal Food*. https://doi.org/10.1089/jmf.2014.0077

Lima, F. F. De, Emilia, S., Tolouei, L., Karenina, G., Arau, S. De, Lescano, C. H., & Oesterreich, S. A. (2016). Study on the Cytotoxic, Genotoxic and Clastogenic Potential of Attalea phalerata Mart. ex Spreng. Oil Pulp In Vitro and In Vivo Experimental Models, 1–12. https://doi.org/10.1371/journal.pone.0165258

López-Romero, D., Izquierdo-Vega, J. A., Morales-Gonçález, J. A., Madrigal-Bujaidar, E., Chamorro-Cevallos, G., Sánchez-Gutiérrez, M., & Madrigal-Santillián, E. (2018). Evidence of Some Natural Products with Antigenotoxic Effects. Part 2: Plants, Vegetables, and Natural Resin. *Nutrients*, *10*(1954), 1–46. https://doi.org/10.3390/nu10121954

Luz, T. R. S. A., Mesquita, L. S. S., Amaral, F. M. M. A., & Coutinho, D. F. (2020). Acta Tropica Essential oils and their chemical constituents against Aedes aegypti L. (Diptera: Culicidae) larvae. *Acta Tropica*, *212*(May), 105705. https://doi.org/10.1016/j.actatropica.2020.105705

Maia, D. S. V. (2019). *Atividade antibacteriana de extrato de butiá (Butia odorata Barb. Rodr.): mecanismo de ação, aplicação em sistema alimentar e em biofilme bacteriano*.

Mariselvam, R., Ranjitsingh, A. J. A., Raja, A. U., Kalirajan, K., Padmalatha, C., & Selvakumar, P. M. (2014). Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy Green synthesis of silver nanoparticles from the extract of the inflorescence of Cocos nucifera (Family: Arecaceae) for enhanced antibacterial activity. *Spectrochimica Acta Part A: Molecular And Biomolecular Spectroscopy*, *129*, 537–541. https://doi.org/10.1016/j.saa.2014.03.066

Marques, E. S., Froder, J. G., Carvalho, J. C. T., Rosa, P. C. P., Perazzo, F. F., & Maistro, E. L. (2016). Evaluation of the genotoxicity of Euterpe oleraceae Mart. (Arecaceae) fruit oil (açaí), in mammalian cells in vivo. *Food and Chemical Toxicology*, *93*, 13–19. https://doi.org/10.1016/j.fct.2016.04.018

Matos, T. M., Muller, N. T. G., Machado, D., Vettorato, J. G., & Amaral, G. N. (2020). Characterization of Foliar Secondary Metabolites in Butia Yatay (Mart.) Becc. *Revista Tecnológica - Universidade Estadual de Maringá*, 31–38. https://doi.org/10.4025/revtecnol.v28i1.50962

May, C. L., & Calder, P. C. (1993). Unsaturated fatty acids inhibit lymphocyte protein kinase C activity. *Biochemical SocietyTransactions*, (1987), 5153.

Mayer, S. V, Tesh, R. B., & Vasilakis, N. (2016). The Emergence Of Arthropod-Borne Viral Diseases: A Global Prospective On Dengue, Chikungunya And Zika Fevers. *Acta Tropica*, (16), 1–34. https://doi.org/10.1016/j.actatropica.2016.11.020

Minighin, E. C., Souza, K. F., Valenzuela, V. D. C. T., Silva, N. O. C., Anastácio, L. R., & Labanca, R. A. (2019). Effect of in vitro gastrointestinal digestion on the mineral conten, phenolic compounds, and antioxidant capacity of commercial ´ (Euterpe oleracea Mart.) pulps of purple and white ac ¸ aı. *J Food Sci Technol*, 1–13. https://doi.org/10.1007/s13197-019-04207-5

Mpiana, P. T., Masunda, T. A., Longoma, B. F., Tshibangu, D. S. T., & Ngbolua, K. N. (2013). Anti-Hyperglycemic Activity of Raphia gentiliana De Wild. (Arecaceae), *3*(2), 233–240.

Murugan, R., Saravanan, S., & Parimelazhagan, T. (2018). Study of intestinal anti-inflammatory activity of Phoenix loureiroi Kunth (Arecaceae) fruit ScienceDirect Study of intestinal anti-in fl ammatory activity of Phoenix loureiroi Kunth (Arecaceae) fruit. *Biomedicine et Pharmacotherapy*, *93*(September 2017), 156–164. https://doi.org/10.1016/j.biopha.2017.06.028

Nembo, E. N., Hescheler, J., & Nguemo, F. (2020). Biomedicine & Pharmacotherapy Stem cells in natural product and medicinal plant drug discovery — An overview of new screening approaches. *Biomedicine & Pharmacotherapy*, *131*, 110730.

Research, Society and Development, v. 10, n. 10, e426101018994, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i10.18994

Nguenang, G. S., Mbaveng, A. T., Fankam, A. G., Manekeng, H. T., Nayim, P., Wamba, B. E. N., & Kuete, V. (2018). Tristemma hirtum and Five Other Cameroonian Edible Plants with Weak or No Antibacterial Effects Modulate the Activities of Antibiotics against Gram-Negative Multidrug-Resistant Phenotypes, *2018*.

Nonato, C. F. A., Leite, D. O. D., Pereira, R. C., Boligon, A. A., Ribeiro-Filho, J., Rodrigues, F. F. G., & Costa, J. G. M. (2018). Chemical analysis and evaluation of antioxidant and antimicrobial activities of fruit fractions of Mauritia flexuosa L. f. (Arecaceae). *Peerj*, *6*, 1–21. https://doi.org/10.7717/peerj.5991

Okkacha, H., Edine, A. D., & Raja, S. (2013). Research Journal of Pharmaceutical, Biological and Chemical Sciences Antibacterial Activity of Essential Oils of Chamaerops humilis Arecaceae) on Some Pathogenic Bacteria. *Research Journal of Pharmaceutical, Biological and Chemical Sciences Antibacterial*, *4*(4), 626–633.

Okwuosa, C. N., Udeani, T. K., Umeifekwem, J. E., & Augustine, C. (2014). Hepatoprotective Effect of Methanolic Fruit Extracts of Phoenix dactylifera (Arecaceae) on Thioacetamide Induced Liver Damage in Rats. *American Journal of Phytomedicine and Clinical Therapeutics*, *2*(3), 1–11.

Oliveira, A. I. T., Mahmoud, T. S., Nascimento, G. N. L., Silva, J. F., Pimenta, R. S., & Morais, P. B. (2016). Chemical Composition and Antimicrobial Potential of Palm Leaf Extracts from Babaçu (Attalea speciosa), Buriti (Mauritia flexuosa), and Macaúba (Acrocomia aculeata)*? e Scientific World Journa*, 1–6.

Omondi, P., Owino, E. A., Odongo, D., Mwangangi, J. M., Torto, B., & Tchouassi, D. P. (2019). Acta Tropica Di ff erential response to plant- and human-derived odorants in fi eld surveillance of the dengue vector, Aedes aegypti. *Acta Tropica*, *200*, 1–7. https://doi.org/10.1016/j.actatropica.2019.105163

Padilha, M. R. F., Shinohara, N. K. S., Macêdo, I. M. E., Bernardino, A. S. B., Rocha, N. S., & Machado, J. (2017). Syagrus schizophylla: Unconventional Food Plant of the Caatinga Biome with a high caloric value. *Geama*, *3*(2), 53–57.

Palmer, W. H., Dittmar, M., Gordesky-gold, B., Hofmann, J., & Cherry, S. (2020). Drosophila melanogaster as a model for arbovirus infection of adult salivary glands. *Virology*, *543*(September 2019), 1–6. https://doi.org/10.1016/j.virol.2020.01.010

PEREIRA, R. J., & CARDOSO, M. G. (2012). Metabólitos secundários vegetais e benefícios antioxidantes Vegetable secondary metabolites and antioxidants benefits. *Journal of Biotechnology and Biodiversity*, *3*(November), 146–152.

Pinheiro, M. M. G., Boylan, F., & Fernandes, P. D. (2012). Antinociceptive effect of the Orbignya speciosa Mart. (Babassu) leaves: Evidence for the involvement of apigenin. *Life Sciences*, *91*(9–10), 293–300. https://doi.org/10.1016/j.lfs.2012.06.013

Ramos, V. P., Silva, P G, Oliveira, P. S., Bona, N. P., Hofmann, J. F., & Chaves, F. C. (2020). Hypolipidemic and anti-inflammatory properties of phenolic rich Butia odorata fruit extract: potential involvement of paraoxonase activity. *Biomarkers*, *0*(0), 1–26. https://doi.org/10.1080/1354750X.2020.1781261

Rodrigues, I. A., Alviano, D. S., Gomes, M. T., Silva, D. O., Antoniassi, R., Silva, A. J. R., & Rosa, S. S. (2011). In vitro anti- Leishmania amazonensis activity of the polymeric procyanidin-rich aqueous extract from Syagrus coronata. *Journal of Medicinal Plants Research*, *5*(16), 3781–3790.

Rosa, F. R., Arruda, A. F., Egle, M. A., & Arruda, S. F. (2016). Phytochemical Compounds and Antioxidant Capacity of Tucum-Do-Cerrado (Bactris Setosa Mart). *Nutrients*, *8*, 1–17.

Santos, A. C. F., Aguiar-Dias, A. C. A., Amarante, C. B., & Coelho-Ferreira, M. (2013). Estruturas secretoras da lâmina foliar de amapá amargo (Parahancornia fasciculata, Apocynaceae): histoquímica e doseamento de flavonoides. *Acta Amazonica*, *43*(4), 407–413. https://doi.org/10.1590/S0044-59672013000400002

Santos, B. S., Bezerra-Filho, C. M., Nascimento Junior, J. A. A., Brust, F. R., Bezerra-Silva, P. C., Rocha, S. K. L., & Paiva, P. M. G. (2019). Microbial Pathogenesis Anti-staphylococcal activity of Syagrus coronata essential oil: Biofilm eradication and in vivo action on Galleria mellonela infection model. *Microbial Pthogenesis*, *131*(August 2018), 150–157. https://doi.org/10.1016/j.micpath.2019.04.009

Santos, L. M. M., Nascimento, J. S., Santos, M. A. G., Marriel, N. B., Bezerra Silva, P. C., Rocha, S. K. L., & Napoleão, T. H. (2017). Fatty acid-rich volatile oil from Syagrus coronata seeds has larvicidal and oviposition-deterrent activities against Aedes aegypti. *Physiological and Molecular Plant Pathology*, *17*, 1–31. https://doi.org/10.1016/j.pmpp.2017.05.008

Shabbir, A., Shahzad, M., & Gobe, G. C. (2014). Protective activity of medicinal plants and their isolated compounds against the toxic effects from the venom of of Naja (Cobra) species. *Journal of Ethnopharmacology*, *222–227*, 222–227. https://doi.org/10.1016/j.jep.2014.09.039

Silva, A. C., & Santana, L. L. (2018). The risks of the use of medicinal plants during the gestational period: A bibliographic review Abreu. *Acta Toxicologica*, *26*, 118–125.

Soldati, L., Lombardi, C., Adamo, D., Terranegra, A., Bianchin, C., Bianchi, G., & Vezzoli, G. (2002). O ácido araquidônico aumenta o cálcio intracelular nos eritrócitos. Biochem Biophys Res Commun 293: 974-978, 2002. *Biochem Biophys Res Commun*, *293*, 974–978.

Tapondjou, L. A., Siems, K. J., Bottger, S., & Melzing, M. (2015). Steroidal Saponins from the Mesocarp of the Fruits of Raphia farinifera (Arecaceae) and their Cytotoxic Activity Léon. *Natural Product Communications*, *10*(11), 8–11. https://doi.org/10.1177/1934578X1501001134

Tayler, N. M., Boya, C. A., Herrera, L., Moy, J., Ng, M., Pineda, L., & Id, C. S. (2019). Analysis of the antiparasitic and anticancer activity of the coconut palm (Cocos nucifera L. ARECACEAE) from the natural reserve of ´ n Punta Pati ñ o, Darie. *Plos One*, *14*(4), 1–18.

Thebo, N. K., Simair, A. A., Mangrio, G. S., Ansari, K. A., Bhutto, A. A., Lu, C., & Sample, S. (2016). Antifungal Potential and Antioxidant Efficacy in the Shell Extract of Cocos nucifera (L.) Arecaceae) against. *Medicines*, *3*(12), 1–12. https://doi.org/10.3390/medicines3020012

Vinholes, J., Lemos, G., Lia, R., Franzon, R. C., & Vizzotto, M. (2017). Assessment of the antihyperglycemic and antioxidant properties of araçá, butiá and pitanga and changes along the. *Food Bioscience*, 1–39. https://doi.org/10.1016/j.fbio.2017.06.005

Research, Society and Development, v. 10, n. 10, e426101018994, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i10.18994

Vinod, V., Tiwari, P. K., & Meshram, G. P. (2011). Evaluation of mutagenic and antimutagenic activities of neem (Azadirachta indica) seed oil in the in vitro Ames Salmonella / microsome assay and in vivo mouse bone marrow micronucleus test. *Journal of Ethnopharmacology*, *134*(3), 931–937. https://doi.org/10.1016/j.jep.2011.02.003

William, J., John, P., Mumtaz, M. W., Ch, A. R., Adnan, A., Mukhtar, H., & Raza, S. A. (2018). Antioxidant activity, Hypoglycemic potential and metabolite profiling of Hyophorbe indica leaf extract Antioxidant activity, Hypoglycemic potential and metabolite profiling of Hyophorbe indica leaf extract, (November).

Anti-inflammatory, antinociceptive, and antipyretic activities from the fixed oil of the Brazilian specie *Syagrus schizophylla* (Mart.)

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Abstract

Aim: The present study evaluated the phytochemical composition of the fixed oil obtained from *S. schizophylla* almond (OFSs), as well as its anti-inflammatory, antinociceptive, and antipyretic activities *in vivo*, and its antinociceptive mechanism of action.

Materials and methods: The phytochemical evaluation was determined using the Gas Chromatography attached to a Flame Ionization Detector (GC-FID). As for the pre-clinical pharmacological activities, all assays were carried out in swiss mice. The acute toxicity assay was performed by administrating doses of the OFSs, orally, in different concentrations (1.75, 5.5, 17.5, 55, 175, 550 and 2.000 mg/kg). To determinate the antinociceptive activity, the abdominal contraction test was performed using acetic acid and formalin as inducing agents. For the anti-inflammatory activities, the paw edema induced by carrageenan test, and acute peritonitis protocols were applied. And finally, the pyrexia induced by yeast assay was performed to evaluate the antipyretic activity.

Results: The GC-FID analysis revealed the presence of eight compounds, with lauric acid being the major compound. As for the pre-clinical pharmacological results, the acute toxicity test did not present mortality or animal behavior alteration in any of the tested concentrations. The antinociceptive assay pointed a decrease in the abdominal contortion frequency (in 16.17, 51.96

and 72.05%, according to the tested concentrations), with our data suggesting that the OFSs acts in the opioid system. As for the anti-inflammatory activities, both protocols showed that OFSs was able to attenuate the inflammation, being able to inhibit the paw edema formation at 400 mg/kg concentration, 5 hours after carrageenan injection, as well a decreased in the leukocytes and neutrophils migration in the peritonitis test, a decrease was also registered in the IL-1β and TNF-α concentrations. And finally, the OFSs inhibit the fever induced by yeast during the entire experiment in all tested concentrations (100, 200 and 400 mg/kg).

Conclusion: Our data shows that OFSs is a promising natural product that could be explored in the phytotherapeutic industry, being a good candidate for clinical studies, due to their anti-inflammatory, antinociceptive, and anti-pyretic.

Keyword: Biological activities; inflammation; pain; fever; vegetable oil.

Introduction

The Arecaceae is an important family with several therapeutic potentials. There is much research proving its biological activity, highlighting the antioxidant, antimicrobial [1,2] analgesic, antipyretic, anti-inflammatory [3], and antimalarial [4] activities. Those biological activities are due to a range of chemical compounds that occur in this family species, such as tannins [2], vanillic kaempferol, cinnamic acid, caffeic acid, protocatechuic acid, ferulic acid, serum, quercetin, kaempferol, and the fatty acids γ-linolenic, linoleic, and oleic acid [1,5].

The presence of fatty acids in Arecaceae species is also widely reported in the literature, besides the fatty acids mentioned above, some species also present lauric acid, methyl, and ethyl esters, capric acid, myristic acid, and caprylic acid [6,7,8], with lauric acid being the major compound observed in the most phytochemical profiles in this family species. According to Sales et al. [9], the fact that lauric acid is the major fatty acid present in fruits may explain the reason why Arecaceae species have oils with high oxidative stability and stay functional for long periods of time.

In this context, the development of products using species with biotechnological potential, and species that are native to Brazilian biodiversity, such as S. schizophylla, can contribute to establishing new hytotherapeutics for treatment, prevention, and support of the management of several diseases, while it contribute to the local economy [9,11].

Since there are not many reports about *S. schizophylla*, especially in the light of its pharmacological activities, besides its chemical composition, the investigation of *S. schizophylla* potential can guide the characterization of new potential drugs. With that in mind, the present research aimed to evaluate *S. schizophylla* fixed oil phytochemical profile, and evaluate its anti-inflammatory, antipyretic, antinociceptive activities *in vivo*, using swiss mice

as models.

Materials & Methods

Plant Material and oil extraction

Syagrus schizophylla seeds were collected at Coruripe Power Plant located at Coruripe – Alagoas/Brazil (-10.0933332 S, -36.1877785 W). The oil was obtained by hydraulic press (model Tecnal® – TE-098) and stored in amber recipients under 4 °C. A sample of the specimen was deposited in the Herbarium of the Biology Departament at Universidade Federal Rural de Pernambuco (UFRPE), under the voucher Nº 55.148 BR-AL-CORURIPE, B.O. VERAS.

Phytochemical profile

The phytochemical profile was determined by Gas chromatography attached to a Flame Ionization Detector (GC-FID) (Thermo Scientific®, Milan, Italy) and a capillary column VB-5 of silica (ValcoBond® 30 m × 0.25 mm id.; film thickness: 0.25 mm) (Valco® Instruments Company Inc., Houston, TX, USA). Nitrogen was adopted as a carrier gas at a flow rate of 1 L/min and an inlet pressure of 30 psi. As for the oven temperature program, it was initially set at 40 °C, and held for 2 min, later it was increased to 230 °C at 4° C/min and was then held for 5 min. Injector and detector temperatures were set to 250 °C and 280 °C mutually. The sample (1 μL; 2 mg/mL in n-hexane) was injected without splitting. The relative amount of each component was estimated from the corresponding peak area and expressed as a percentage of the total area of the chromatogram. The analyses were carried out in triplicate and the identification of the present compounds was carried out by GC coupled to mass spectrometry (GC-MS).

These analyses were performed using an Agilent® 5975C series GC/MSD (Agilent Technologies®, Palo Alto, CA, USA) quadrupole instrument equipped with an Agilent J&W DB-5 non-polar fused silica capillary column (30 m × 0.25 mm id.; film thickness: 0.25 μm) (Agilent Technologies®, Palo Alto, CA, USA). For each sample, 1 μL was injected in split mode (50:1) with the inlet temperature set at 250 °C. The GC oven temperature was set at 40 °C, and was held for 2 min, was maximized to 230 °C at 4 °C/min and was then set for 5 min. Helium (He) gas was used as carrier gas at a flow of 1 mL/min, established at a constant pressure of 7.0 psi.

The source and quadrupole temperatures were determined for 230 °C and 150 °C, respectively. Mass spectra were acquired at 70 eV (in EI mode) with a sweep speed of 1.0 sweeps of m/z 35–350. The recognition of the individual components was determined against

previously reported values of retention indices, obtained by co-injecting oil samples and a set of linear hydrocarbons C9-C30, and calculated according to the Van den Dool and Kratz equation (1963). Then, the acquired MS data for each component were combined with the data available in the mass spectral library of the GC-MS system (MassFinder® 4, scientific consultancy of Dr. Hochmuth, Hamburg, Germany); NIST08 Mass Spectral Library (ChemSW® Inc. Fairfield, CA, USA); Wiley Registry ™ by Mass Spectral Date 9th Edition (Wiley®, Ho boken, NJ, USA) and with other mass spectral data published [12].

Pre-clinical assays

Males and females swiss mice, with 10 to 12 weeks and body weight between 30 and 35 g, were obtained from the bioterium of the Imunopathology Keizo Asami Laboratory from the Universidade de Pernambuco (UFPE) and kept at Animal Experimentation Laboratory from Biochemistry Department from the UFPE, under temperature of 23 ± 2 °C, and controlled luminosity (12 h of light and 12 h of darkness), with water and food *ad libitum*. After the adaptation period, the animals were divided in different groups to perform the assays. All the experiments were made according to the current guidelines for the care of laboratory animals, with the approval of Committee on Animal Research and Ethics under the protocol 0039/2021.

Acute toxicity

For this assay, female *swiss* mice were used and were divided in seven groups, each group containing 4 animals (n=4). The animals received doses of OFSs daily, orally. After the dosage administration, the animals were kept under continuous observation during the first 4 hours. During 14 days, animal body weight, feed consumption, as well as adverse events, such as convulsions, salivation, pyloreation, bleeding, diarrhea, lethargy, coma, and other toxicity indicator were registered. The median lethal dose (DL_{50}) was calculated according to the Organization for Economic Cooperation and Development protocols, guideline 425 (OECD, 2008), defined according to number of deaths and calculated with the software LC_{50} Modem System.

Antinociceptive activity

The antinociceptive potential was evaluated using two methods, the abdominal contortion induced by acetic acid and the pain induced by formalin, with the last one providing data about the possible antinociceptive mechanism.

Abdominal contortion induced by acetic acid

The abdominal contortion assay was carried out in accordance with the recommended standards described by Radulovic et al. [2015] with adaptations. The nociception was induced by acetic acid at 0.8% (10 mL/Kg) (i.p.). The animals were divided in five experimental groups, each group with five animals (n = 5): control group (NaCl solution at 0.9%); indomethacin (20 mg/kg), morphine (10 mg/kg) and OFSs (100, 200 and 400 mg/kg). All treatments were administrated orally, 1 hour before the nociceptive agent, and the number of contortions were registered between 5 and 15 minutes after the acetic acid administration [16].

Pain induced by formalin and antinociceptive mechanism of action

This assay was performed following the protocol of Vaz et al. [17]. The animals were divided in five experimental groups, each group containing five animals (n = 5): control group (NaCl solution at 0.9%); indomethacin (20 mg/kg), morphine (10 mg/kg) and OFSs (100, 200, and 400 mg/kg), administrated orally 30 minutes before the nociceptive agent.

The nociception was induced with a formalin injection (2.5%) in the paw of the animals. The animals were observed to register the total time of paw licking. The number of paw licking was registered with a stopwatch considering two phases as described by Shibata et al. [18]: the first phase occurred right after the formalin administration and it was due to the direct stimulation on the nociceptors, it lasted for 5 min, while the second phase, occurred due to an inflammatory process and started around 15 to 30 minutes after the injection.

To verify the mechanism of action possibly involved on the antinociceptive effect, the animals were treated 30 minutes before the nociceptive agent, with the following antagonists: naloxone (opioid antagonist 1 mg/kg i.p.), glibenclamide (K_{ATP} channels antagonist at 1 mg/kg i.p.), atropine (competitive antagonist of acetylcholine receptors 1 mg/kg i.p.) and caffeine (adenosine receptor antagonist at 1 mg/kg i.p.).

Anti-inflammatory activity

Paw edema induced by carragenin

The paw edema was induced by 1% carrageenan, injected in the right paw while a Saline solution (0.9%) was injected in the left paw. The animals were divided in five experimental

groups, each group containing five animals (n = 5): control group (NaCl solution at 0.9%); indomethacin (20 mg/kg) and OFSs (100, 200, and 400 mg/kg), orally. The animals were treated 1 hour before the carrageenan injection, and the edema was measured with a pachymeter at different times: 1, 2, 3, 4, and 5 hours after the carrageenan administration. The edema inhibition was calculated following the equation proposed by Winter: Right paw edema – Left paw edema [19].

Peritonitis induced by carrageenan

The assay was performed according to Souza and Ferreira [20] protocol. The experimental groups consisted in five groups, each group containing five animals (n=5), the treatments consisted of different concentrations of OFSs (100, 200, and 400 mg/kg), saline solution (NaCl 0.9%), administered orally, and dexamethasone (10 mg/kg i.p.). The treatments were administrated 1 hour before 1% carrageenan injection (500 µg) on the peritoneal cavity. The animals were euthanized 3 hours after the carrageenan injection. 3 mL of saline solution buffered with PBS and EDTA (1 mM) was injected in the peritoneal cavity to collect leukocytes and neutrophil cells. The peritoneal fluid (20 µL) was diluted in Turk solution (0.4 mL), the cells were stained in hematoxylin-eosin and counted in microscope and the number of the differentiated cells were calculated due to the percentage of total cell number.

An aliquot of the peritoneal fluid was centrifuged at 12,000 g for 15 min at 4ºC, the supernatant was stored in ultra-freezer for future analysis. 100 µL from the peritoneal fluid was used to determinate the TNF-α and IL-1β concentrations, using ELISA kit from Thermo Fisher (Waltham, USA), following the manufacturer instruction.

Antipyretic activity

Finally, the antipyretic activity was performed according to Sobeh et al. [21] protocol. The animals were divided into five groups, each group containing 5 animals, and each group received doses of different treatments: a negative control group (NaCl solution at 0.9%), dypirone (100 mg/kg) and OFSs (100, 200, and 400 mg/kg). In this methodology, the fever is induced by yeast inoculation. The rectal temperature was registered before the yeast inoculation, the inoculum consisted in a suspension of *Saccharomyces cerevisiae* (15% w/v in saline solution) inoculated in a subcutaneous route. After 18 hours, the animals that presented an average increase in the body temperature of 37.5 and 39 ºC received a treatment dose, and

were kept under observation for 6 hours, with temperatures measured in intervals of 1, 2, 3, 4 and 5 hours.

Statistical analysis

Data were analyzed for normality using the Shapiro-Wilk test. In case of normal distribution, the data were submitted to analysis of variance test (ANOVA) followed by Tukey test, for multiple comparison. If the distribution is not normal, the data were submitted to the Kruskal-Wallis's test, followed by Dunn's method. All statistical analyzes were performed using performed and considered significant when $p < 0.05$and were

Results and Discussion

Phytochemical profile

The GC analysis revealed the presence of eight different compound in OFSs, as described in Table 1. Lauric acid was the major compound (50.45 ± 2.30%), followed by caprylic acid (16.46 ± 0.43%), and myristic acid (10.94 ± 0.38%).

Table 1. *Syagrus schizophylla* (OFSs) fixed oil chemical constituents

Compounds	Usual nomenclature	Total area (%) ± SD
Octanoic acid (C8:0)	Caprylic acid	16.46 ± 0.43
Decanoic acid (C10:0)	Capric acid	10.33 ± 0.53
Dodecanoic acid (C12:0)	Lauric acid	50.45 ± 2.30
Tetradecanoate (C14:0)	Myristic acid	10.94 ± 0.38
Hexadecanoic acid (C16:0)	Palmitic acid	3.50 ± 0.72
9,12- Octadecadienoic acid (C18:2)	Linoleic acid	0.52 ± 0.31
9- Octadecenoic acid (Z)- (C18:1)	Elaidic acid	2.65 ± 0.90
Octadecanoic acid (C18:0)	Stearic acid	0.58 ± 0.16

Results expressed as mean and standard deviation (n=3). Fatty acids were identified according to an external standard (FAME Supelco™ mix C4 – C24, Bellefonte, PA, USA) and their percentage (%) calculated according to normalization peak areas.

Research focusing on *S. schizophylla* chemical profile are scarce, however, species from the same genus or family have been studied in the last decades and, not only its chemical composition are characterized, but also its biotechnological potential. Recently, Souza et al. [22] evaluated the phytochemical characterization in fixed oil from *S. coronata* and found the presence of lauric acid as major compound (43.64%), followed by myristic acid (14.32%), both

present in OFSs. Our data is also aligned with Bauer (2013) research, which reported that lauric acid is the major compound present in *S. coronata* (44.2%), as well myristic acid (14.45%), and oleic acid (12.08%).

Another Arecaceae species which is widely studied is *Attalea speciosa*, known as "babaçu", whose oil also presented lauric acid as major compound (46.05%) [23]. Chandrashekar et al. [24], evaluated the hypoglycemic effect of *Cocus nucifera* oil, and found a similar pattern of chemical compounds: lauric acid as major compound (48.5%), followed by myristic acid (21.2%), and oleic acid (5.2%), which suggest that the lauric acid is a signature compound present in Arecaceae species.

According to Lescano et al. [25], the fatty acids have a relevant biotechnology potential, once they can promote an improvement in life quality through the development of new drugs, or even nutraceuticals. As stated by Lappano et al. [26], the medium chain saturated fatty acids are related with certain health benefits, like patients with breast cancer that ingested the coconut oil during the chemotherapy and improved their quality of life. With that in mind, the use of fixed oil from Arecaceae species have been increasingly and recommended, mainly because the benefits of lauric acid, that may provoke inhibitory effects on cancer cells, preventing tumor growth [26].

Acute toxicity

Furthermore, it is very important to evaluate the toxicity of new drugs in potential [27]. OFSs acute toxicity was tested in different concentrations: 1.75, 5.5, 17.5, 55, 175, 550 e 2,000 mg/kg (table 2). The results have shown that OFSs have not induced any type of toxicity, except for the animals that were treated with doses of 2,000 mg/kg, that presented diarrhea symptoms. Besides that, none of the tested concentration was lethal to the animals, with the LD_{50} being higher than 2,000 mg/kg, together, this data suggests that OFSs has a good safety range and can be applied for therapeutic purpose.

Table 2. Effect of *Syagrus schizophylla* fixed oil (OFSs) in the acute toxicity test

Sample	Dose (mg/kg; p.o.)	Behavior effects	Number of dead animals	Mortality (%)
	1.75	N.D.	0/3	0.00
	5.5	N.D.	0/3	0.00

OFSs	17.5	N.D.	0/3	0.00
	55	N.D.	0/3	0.00
	175	N.D.	0/3	0.00
	550	N.D.	0/3	0.00
	2.000	Diarrhea	0/3	0.00

N.D.= No modifications detected.

According to the Globally Harmonized Classification System, *S. schizophylla* fixed oil fits in class 5, which represents the compounds with low, or even absence of toxicity [27,28]. Therefore, the low toxicity may be associated with the presence of fatty acids, mainly because lauric acid, since according to Fauster et al. [29] and Park et al. [30], the lauric acid is a compound with low toxicity, being considered safe and easy to handle. Therefore, natural products usually have more probability to show low toxicity, which make them a promising source for drug development [31,32]. In a study guided by Santos et al. [23] with *S. coronata* fixed oil, the results have not shown any level of toxicity or mortality as well, these results corroborated with our findings.

Antinociceptive activity

Abdominal contortion tests

The OFSs was able to significantly reduce the number of abdominal contortions in the tested concentrations (100, 200, and 400 mg/kg), being able to reduce in 16.17%, 51.96 and 72.05%, respectively, while the animals treated with indomethacin reduced the number of abdominal contortions in 39.7%. These data are disposed in the Figure 1, as well the efficacy of OFSs in attenuating pain and inflammation.

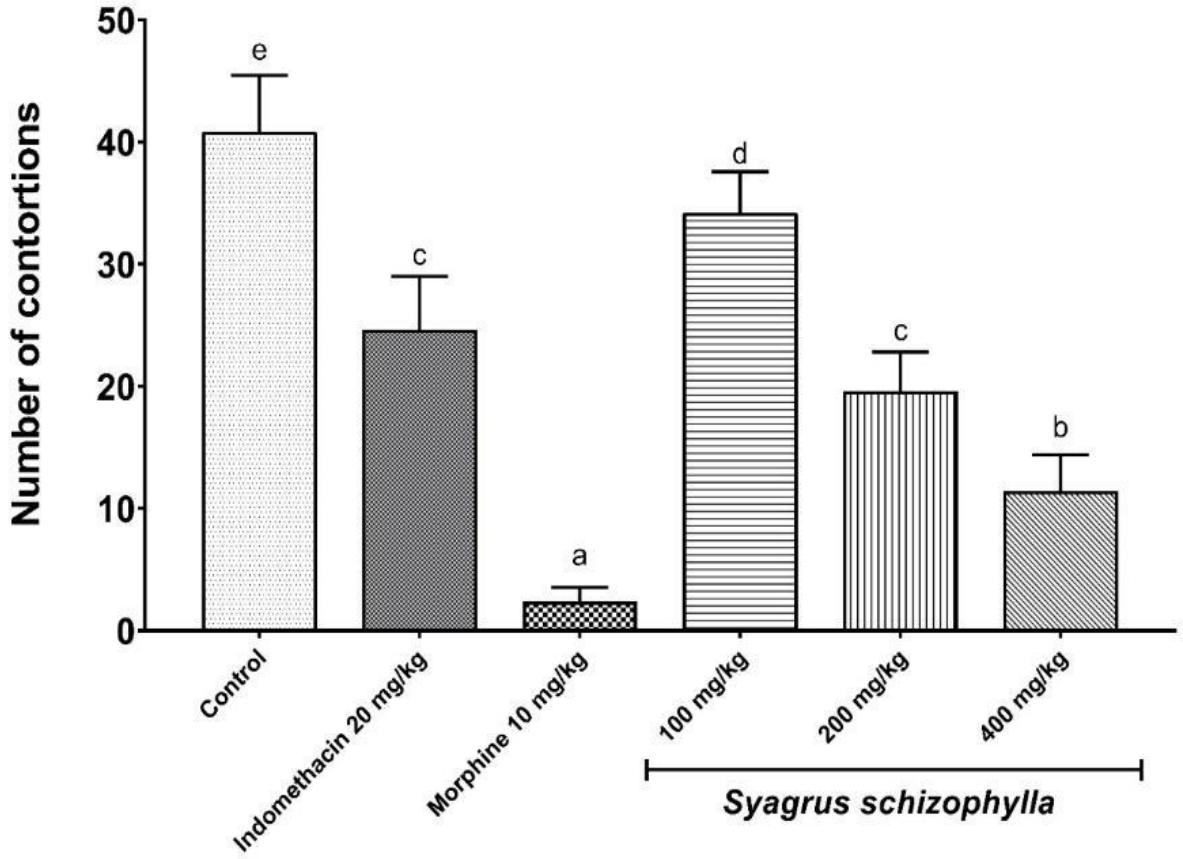


Fig. 1. Effect of OFSs in the abdominal contortion induced by acetic acid. Effect of *S. schizophylla* fixed oil (OFSs) on acetic acid-induced abdominal writhing. Control Group (0.9% saline solution); Indomethacin (20 mg/kg,.), morphine (10 mg/kg) and OFSs (100, 200, and 400 mg/kg, v.o.).* $p < 0.001$ compared to control, one-way ANOVA followed by Tuckey's test.

Similar results are reported in the literature for another Arecaceae species. An example is the report made by Naskar et al. [33], which investigated *C. nucifera* fruits, at concentration of 250, 400, and 500 mg/kg, and they noticed a decrease in contortion number in 21, 24, and 28% respectively.

Formalin test

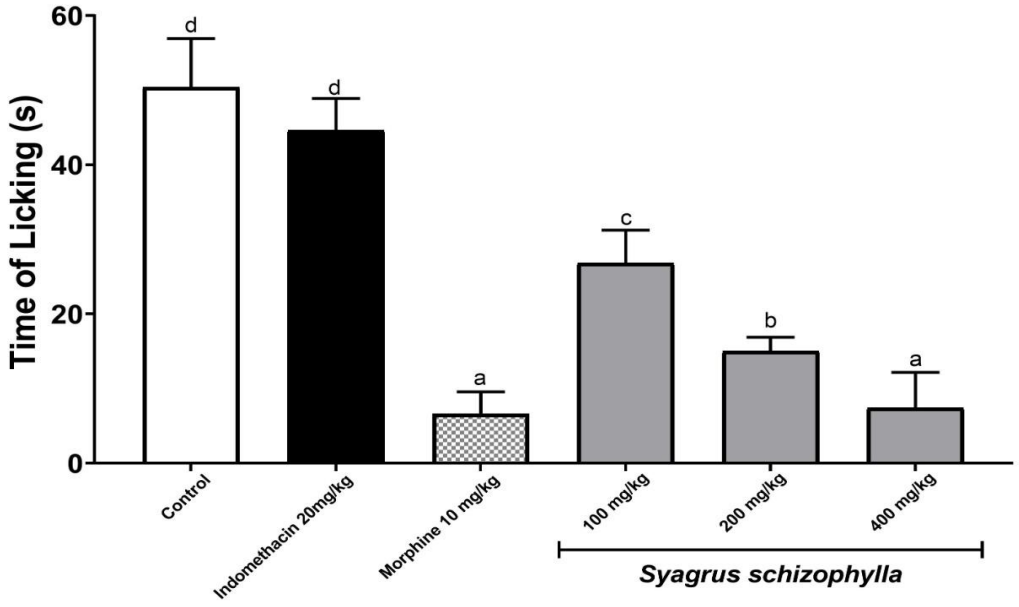
The formalin test was carried out in two phases. The first one is characterized due to the neurogenic pain in the nociceptors between 0 to 5 minutes right after the formalin injection, as for the second phase, which occurs between 15 and 30 minutes after the injection, the pain is due to the inflammation process [36]. General drugs with central action can inhibit the phase 1 and 2 evenly, as for drugs with peripheric action inhibit the phase 2 [37].

The formalin test results showed that the OFSs at concentration of 100, 200, and 400 mg/kg was able to reduce the paw licking time, already in the first phase, in 84.47%, 64.89%,

and 38.77% respectively, when compared to control group. The morphine, at concentration of 10 mg/kg, reduced the paw licking time in 86.51%, while indomethacin has not differentiated from the control group.

The inhibition of paw licking time on the phase 1 (known as neurogenic) corroborate with our results from the abdominal contortion test induced by acetic acid [38]. It is plausible that the oil acts on the chemical inhibition of nociceptive afferent fibers, which are suspended by opioids analgesics, like morphine [39].

For the second phase, the OFSs at 100, 200, and 400 mg/kg also reduced the paw licking time by 57.95, 67.99 and 84.94% respectively. The positive controls, indomethacin (20 mg/kg) and morphine (10 mg/kg) reduced the paw licking time at 87.21 and 96.02% (figure 2).


Time of Licking (s)
60
40
20
0
d
d
a
c
b
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Control
Indomethacin 20mg/kg
Morphine 10 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg
Syagrus schizophylla

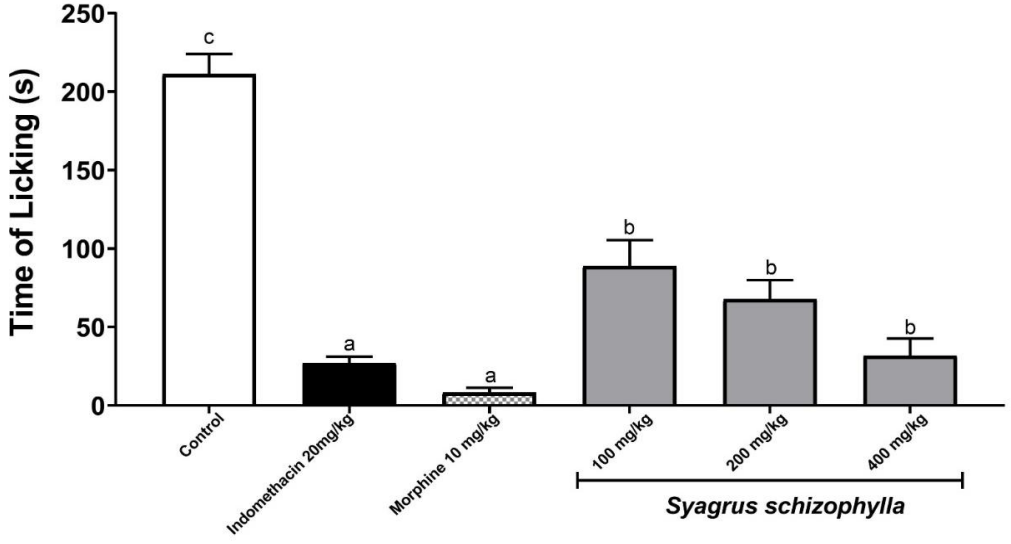
Time of Licking (s)
250
200
150
100
50
0
c
a
a
b
b
b
Control
Indomethacin 20mg/kg
Morphine 10 mg/kg
100 mg/kg
200 mg/kg
400 mg/kg
Syagrus schizophylla

Fig. 2. Fixed oil of *Syagrus schizophylla* (OFSs) on the treatment in the formalin assay. Effect of OFSs and morphine on the formalin test (1st and 2nd phases). Negative control (0.9% saline), morphine (10 mg/kg) and OFSs (100, 200 and 400 mg/kg). Values in each column represent the mean ± s.d. The ANOVA test was performed, followed by the Kruskall-Wallis's test.

The reduction in the paw licking time, in both phases, corroborate with the results obtained from abdominal contortion assay, evidencing the OFSs efficiency on the pain treatment. Zhao et al. [40], investigated the antinocipcetive effect of *Areca catechu*, an Arecaceae species, and verified a reduction in the paw licking time in mice.

No reports were found in the literature in the light of antinociceptive effect of fixed oils from Arecaceae family, using the formaline model. However, Shajib et al. [35] verified that the methanolic extract obtained from *Phoenix sylvestris* at concentrations of 50, 150, 300, and 450 mg/kg was able to reduce the paw licking time in the neurogenic phase, in 16.18%, 42.49%, 55.21%, and 68.21%, as for the inflammatory phase, the paw-licking time was reduced in 28.79%, 54.30%, 64.64%, and 75.68%, respectively. It is important to mention that the extract composition is rich in lauric acid, as well in linoleic acid, both present in OFSs. Besides that, the authors report that the anti-inflammatory activity from the fatty acids cited above may be responsible for the antinociceptive effect observed.

Antinociceptive mechanism

To verify this mechanism, the animals were pre-treated with naloxone (opioid antagonist) and it was verified a partial inhibition of the antinociceptive effect induced by OFSs, reducing the first phase activity by 50.79%, as for the second phase, the inhibition was of

28.59%. Taken together, those results suggest that the antinociceptive action from OFSs involves the opioid system. The same effect was observed when the animals were pre-treated with caffeine (adenosine receptor blocker), which in turn, induced a partial inhibition of the antinociceptive activity on the first phase to 42.06%, as for the second phase, it was reduced to 57.57%, suggesting that the oil also acts as adenosine receptor blocker (Figure 3).

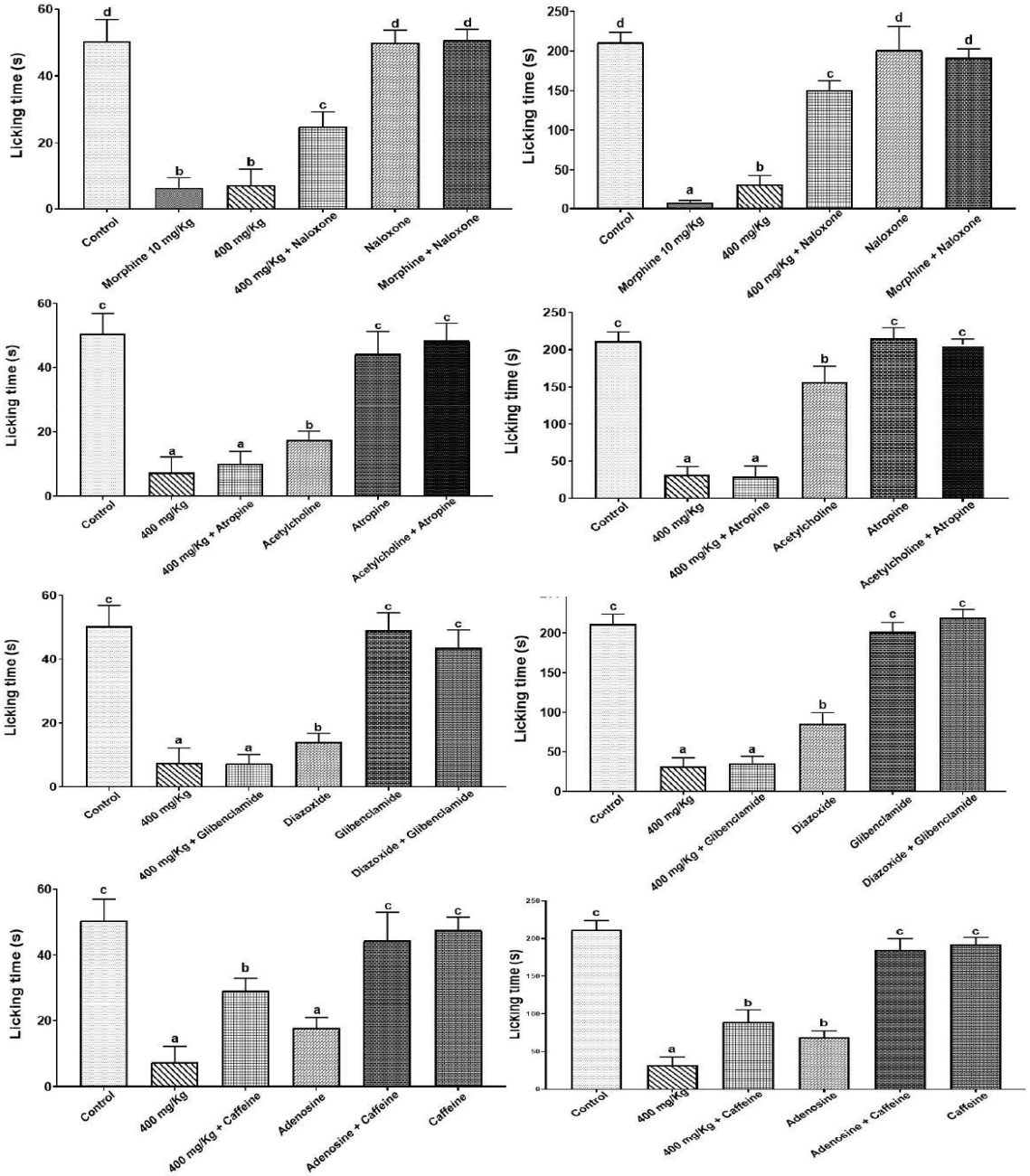

Fig. 3. Antinocipcetive activity of the fixed oil of *S. schizophylla* (OFSs) induced by formalin intraplantar injection. Effect of *S. schizophylla* fixed oil (OFSs) and morphine on the formalin test (1st and 2nd phases). Negative control (vehicle), morphine (10 mg/kg i.p) and OFSs (100, 200 and 400 mg/kg v.o.).

The opioid system comprises an important target for evaluate the action mechanism of new drugs with antinociceptive properties [41]. Opioids drugs are known as the main drug class for pain treatment, thus, search for new drugs to treat inflammation are necessary [42,43]. Naloxone is a non-selective opioid receptor antagonist [37,42].

Anti-inflammatory activity

Paw edema induced by Carrageenan

The results showed that, when compared to the control group, the OFSs at concentrations of 100, 200, and 400 mg/kg inhibited the paw edema volume, reducing the edema formation in 76.96, 82.23, and 93.19% respectively, 5 hours after the experiment (Table 3). Those results are higher than the animals treated with indomethacin, pointing out that OFSs is a strong anti-inflammatory product.

Table 3.
OFSs effect in the paw edema induced by carrageenan

Pre-treatment	**Dose (mg/kg)**	**Edema formation (mm) at hours (h)**					**Average edema formation (mm)**	**Average inhibition (%)**
		1h	**2h**	**3h**	**4h**	**5h**		
Control	-	0.855±0.145^{c}	1.155±0.292^{c}	0.995±0.219^{e}	0.877±0.271^{d}	0.892±0.191^{c}	0.955	-
Indomethacin	20	0.553±0.105^{b}	0.362±0.148^{b}	0.197±0.009^{d}	0.097±0.006^{b}	0.020±0.003^{b}	0.242	74.65
	100	0.522±0.061^{b}	0.295±0.057^{b}	0.152±0.094^{c}	0.102±0.063^{c}	0.043±0.007^{c}	0.220	76.96
OFSs	200	0.370±0.027^{b}	0.232±0.013^{b}	0.108±0.069^{b}	0.073±0.037^{b}	0.022±0.003^{b}	0.163	82.23
	400	0.203±0.016^{a}	0.090±0.06^{a}	0.030±0.005^{a}	0.005±0.008^{a}	0.000±0001^{a}	0.065	93.19

All results were expressed as standard deviation ± mean (S.D.) (n = 5). Different letters mean statistical difference, one-way ANOVA followed by Bonferroni Test.

Our results corroborate with Lima et al. [8], that investigated the fruit pulp oil from *Attalea phalerata* and verified the anti-inflammatory effect. Their results had shown that the paw edema reduced due the oil application, and also induced a decrease in the leukocytes migration by the peritonitis model induced by carrageenan. The author results corroborate with the popular use of *A. phalerata* as anti-inflammatory, and with the aggregate importance to

Arecaceae family.

Peritonitis induced by carrageenan

In the peritonitis assay, the animal treated with OFSs at 100, 200, and 400 mg/kg concentration showed a decrease in leukocytes migration in 37.93, 62.06, and 77.58% respectively, as well in the neutrophil levels in 41.02, 66.66, and 87.17%. For the animals treated with indomethacin, the leukocyte migration decreased in 55.17%, and the neutrophils in 69.23%. The dosages of 200 and 400 mg/kg of OFSs showed better results than the animals treated with indomethacin, additionally a decrease in the pro-inflammatory cytokines IL-1β and TNF-α levels in peritoneal fluid. The OFSs tested concentrations were able to reduce the IL-1β in 59.26, 68.93, and 76.35%, respectively, as for TNF-α were reduced in 41.60, 57.52, and 75.44% (Figure 4).

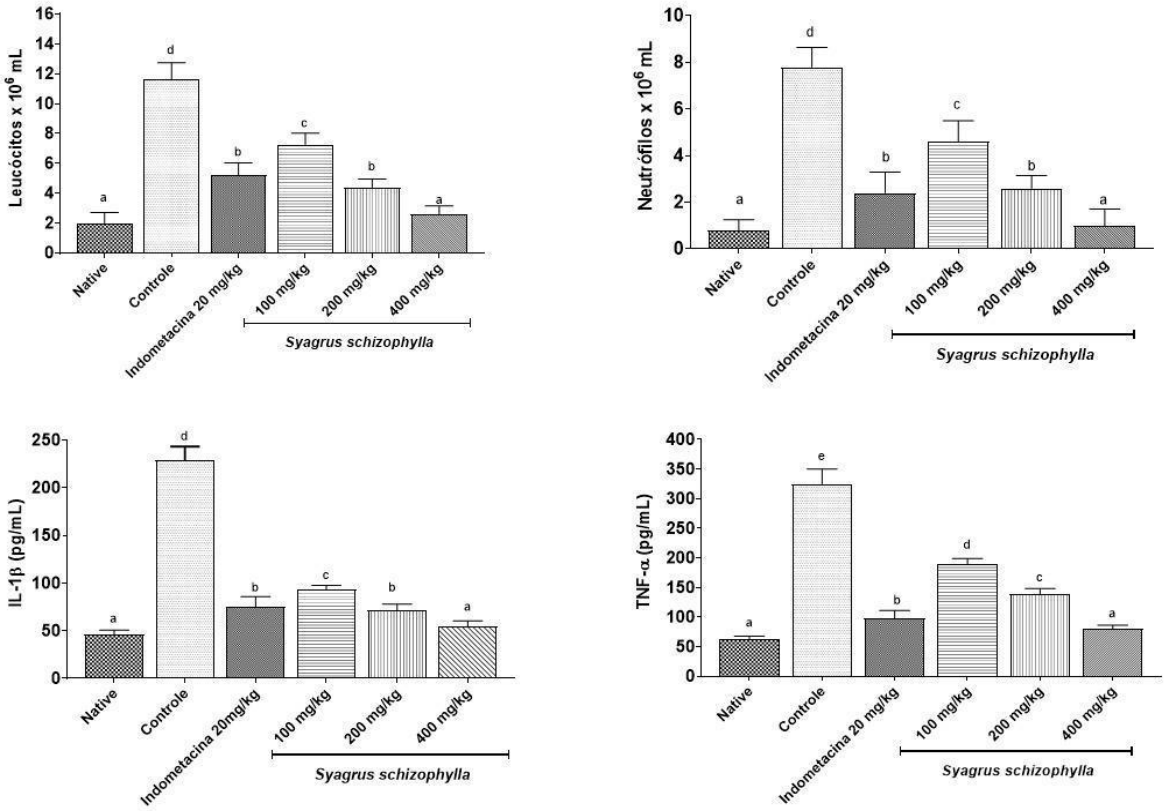

Fig. 4. Effect of treatment of *S. schizophylla* fixed oil (OFSs) on leukocyte and neutrophil migration. Administration (v.o.) of OFSs (100, 200 and 400 mg/kg) and Indomethacin (20 mg/kg, v.o.) in the migration of neutrophils to the peritoneal cavity in mice, induced by 3 mL of carrageenan (100 μg/mL).

The decrease in leukocytes and neutrophils migration suggests that the OFSs

compounds act as an inflammatory mediator, since the leukocytes usually stimulate the pro-inflammatory production. If the leukocytes migration is decreased, it will affect the pro-inflammatory synthesis which in turn will also decrease. Furthermore, even though the oil has the characteristic of an inflammatory mediator, it acts in a controlled manner, not establishing an exacerbated response.

An important clinical sign involves the leukocytes recruitment on the inflammatory areas [44]. Favacho et al. [45] showed that the oil from *Euterpe oleraceae* inhibited the leukocyte migration by 80.14%, as for the animals treated with dexamethasone showed an inhibition of 93.17%, while the animals that did not receive any treatment presented an acute inflammatory response in the peritoneal cavity, with a neutrophil concentration of $3886.58x10^6$ cells/mL after 4 h, corroborating with our findings. Additionally, Arecaceae species have been investigated as anti-inflammatory product, and even if the studies do not elucidate the mechanism of action, those data are still relevant for popular uses and future research.

According to Borges et al. [46], the peritoneal fluid from animals treated with *C. nucifera* presented a similar anti-inflammatory effect, according to our findings, against abdominal sepsis. The same effect was observed in species from another families, like the fixed oil obtained from *Cannabis sativa* which showed a decrease in the migration of inflammatory cells (leukocytes flux) [47]. It is important to highlight that the chemical analysis from fixed oil of *C. sativa* revealed oleic acid as major compound (12.50%). Amorim et al. [48] report similar results with pre-treatment of *Mauritia flexuosa* mesocarp oil, being able to reduce the inflammatory parameters, as well the leukocytes migration and TNF-α levels. Aquino et al. [49] investigated the phytochemical composition of *M. flexuosa* fruits and found that 72.7% of the oil is constituted by oleic acid, followed by palmitoleic acid (19.6%), with lower concentrations of linoleic acid and steraic acid. All the compounds reported by the author are present on OFSs, which suggests that the chemical composition, as well as its proportion, may be a signature of Arecaceae species.

Antipyretic activity

The result from the antipyretic assay shows that a decrease in the temperature after 1 hour of OFSs administration was observed, with the animals presenting lower temperatures and not entering a feverish state.

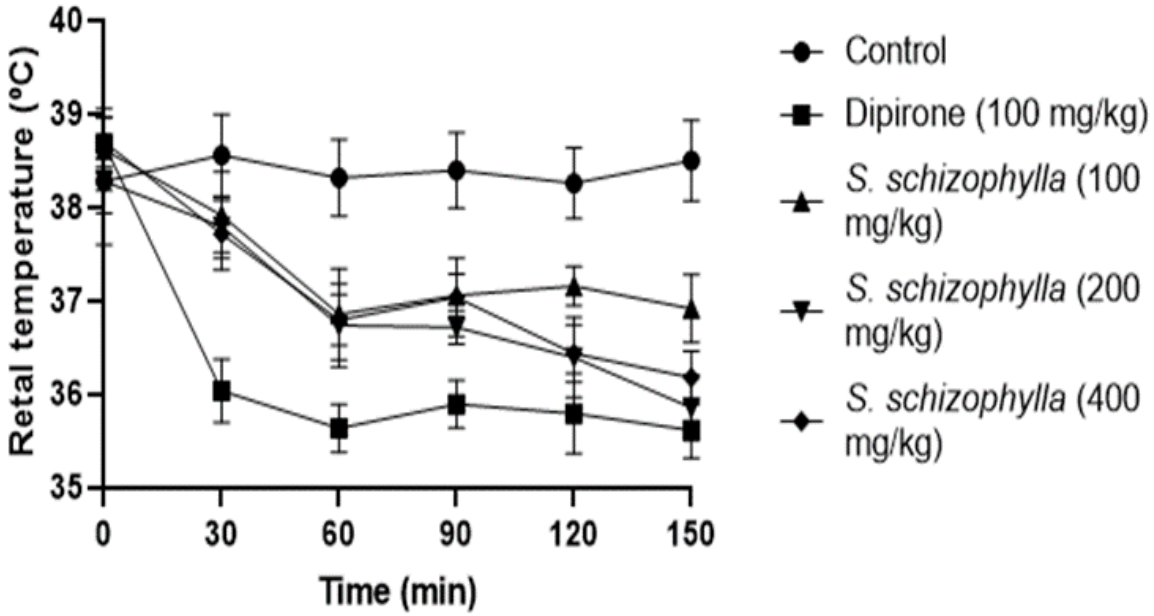

Fig. 5. Antipyretic potential of *S. schizophylla* fixed oil (OFSs) in mice with fever induced by *Saccharomyces cerevisae* infection. * $p < 0.001$ compared to control, one-way ANOVA followed by Tuckey's test.

Researches focusing the fixed oil from Arecaceae species and their relationship with antipyretic effect are scarce in the literature. However, there are few reports evaluating the fixed oil from another plant families, one example is the oil from *Linum usitatissimum* rich in fatty acids, the oil present antipyretic activity similar to aspirin [50], which showed 57.73% of α-linolenic acid. As the OFSs in rich in fatty acids, the observed activities are probably due to those compounds.

Conclusion

Together, those findings stand the first evidence of S. schizophylla fixed oil as a source of potential new drugs, once its composition presents different fatty acids that together promote several pre-clinical benefits. Furthermore, we have reported for the first time the antinociceptive and a potential mechanism of action, anti-inflammatory effect, antipyretic activity, as well absence of acute toxicity in the ingestion of OFSs not yet described for this species. Despite we need further studies in clinical models, the results described in the present work contribute to the strengthening of folk medicine, and to the therapeutic potential of the Aceraceae family.

Acknowledgment

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References

[1] Nonato CFA, Leite DOD, Pereira RC, Boligon AA, Ribeiro-Filho J, Rodrigues FFG, Costa JGM. Chemical analysis and evaluation of antioxidant and antimicrobial activities of fruit fractions of Mauritia flexuosa L. f. (Arecaceae). Peerj 2018;6:1-21. https://doi.org/10.7717/peerj.5991

[2] Joy A, Vinson B, Anto L, Dinilkumar M, Wilson S, Simon S, Jose J. Antibacterial screening and phytochemical powder isolated from dorsal side of leaves of *Cocos nucifera* (Arecacaae). Journal of Pharmaceutical Sciences and Research 2019;11:2557.

[3] Elhakim IAA, Abdel-Baky A M, Bishay W. Botanical and biological study of the leaves of caryota mitis lour. family arecaceae cultivated in egypt. Bulletin of Pharmaceutical Sciences Assiut 2017;40:71–95. https://dx.doi.org/10.21608/bfsa.2017.63167

[4] Tayler NM, Boya CA, Herrera L, Moy J, Ng M, Pineda L, Almanza A, Rosero S, Coronado LM, Correa R, Santamaría R, Caballero Z, Durant-Archibold AA, Tidgewell KJ, Balunas MJ, Gerwick WH, Spadafora A, Gutiérrez M, Spadafora C. Analysis of the antiparasitic and anticancer activity of the coconut palm (*Cocos nucifera* L. ARECACEAE) from the natural reserve of Punta Patiño, Darién. Plos one 2019;14:1–18. https://doi.org/10.1371/journal.pone.0214193

[5] Marques ES, Froder JG, Carvalho JCT, Rosa PCP, Perazzo FF, Maistro EL. Evaluation of the genotoxicity of *Euterpe oleraceae* Mart. (Arecaceae) fruit oil (açaí), in mammalian cells in vivo. Food and Chemical Toxicology 2016;93:13–19. https://doi.org/10.1016/j.fct.2016.04.018

[6] Lopes AS, Pacheco TG, Nimz T, Vieira LN, Guerra MP, Nodari RO, Souza EM, Pedrosa FO, Rogaslski M. The complete plastome of macaw palm Acrocomia aculeata (Jacq.) Lodd. ex mart. and extensive molecular analyses of the evolution of plastid genes in arecaceae. Planta 2018;247:1–20. https://doi.org/10.1007/s00425-018-2841-x

[7] Dario MF, Oliveira FF, Marins DSS, Baby AR, Velasco MVR, Lobenberg R, Bou-Chacra NA. Synergistic photoprotective activity of nanocarrier containing oil of Acrocomia aculeata (Jacq.) Lodd. Ex. Martius-Arecaceae Article. Industrial Crops & Products 2018;112:305–312. https://doi.org/10.1016/j.indcrop.2017.12.021

[8] Lima FF, Emilia S, Tolouei L., Karenina G, Arau S, Lescano CH, Oesterreich SA. Study on the Cytotoxic, Genotoxic and Clastogenic Potential of *Attalea phalerata* Mart. ex Spreng. Oil Pulp In Vitro and In Vivo Experimental Models. PLos One 2016;11:1–

12. https://doi.org/10.1371/journal.pone.0165258

[9] Sales ARR, Albuquerque TN, Xavier LE, Santana AG, Silva OS, Santos SS, Fonseca SB, Meireles BRLA. Caracterização físico-química do oléo de coco babaçu industrial e artesanal e suas aplicações tecnológicas Physical. Brazilian Journal of Development 2020;6:25734–25748. https://doi.org/10.34117/bjdv6n5-140

[10] Oliveira VB, Yamada LT, Fagg CW, Brandão MGL. Native foods from Brazilian biodiversity as a source of bioactive compounds. Food Research International 2012;48:170–179. http://dx.doi.org/10.1016%2Fj.foodres.2012.03.011

[11] Flora do Brasil. Jardim Botânico do Rio de Janeiro 2017. Disponível em: http://floradobrasil.jbrj.gov.br/&gt . Acesso em: 25 jul. 2021.

[12] Snodgrass WT, Elmore J, Adams R. Bladder neck sling and appendicovesicostomy without augmentation for neurogenic incontinence in children. The Journal of urology: 2007:4:1510-1514. https://doi.org/10.1016/j.juro.2006.11.080.

[13] Chinedu E, Arome D, Ameh FS. A new method for determining acute toxicity in animal models. Toxicology International 2013;20:224-226. https://doi.org/10.4103/0971-6580.121674

[14] Organization for Economic Cooperation and development [OECD]. Guideline for testing of chemicals. Guideline: acute oral toxicity-acute toxic class method. Organization for Economic Cooperation and Development, Paris 2001. Disponível em: https://www.oecd-ilibrary.org/docserver/9789264071001en.pdf?expires=1642436206&id=id&accname=guest&checksum=9274FDE504FBDDD15F11330B0512839A. Acesso em: 17/01/2022.

[15] Radulovic NS, Randjelović PJ, Stojanović NK, Cakić ND, Bogdanović GA, Živanović AV. Aboriginal bush foods: A major phloroglucinol from Crimson Bottlebrush, flowers (Callistemon citrinus, Myrtaceae) displays strong antinociceptive and anti-inflammatory activity. Food Research International 2015;77:280-289. http://dx.doi.org/10.1016/j.foodres.2015.02.023

[16] Queiroz AC, Lira DP, Dias TL, Souza ET, Matta CB, Aquino AB, Silva LH, Silva DJ, Mella EA, Agra MF, Filho, JM, Araújo-Júnior JX, Santos BV, Alexandre-Moreira MS. The antinociceptive and anti-inflammatory activities of Piptadenia *stipulacea Benth*. (Fabaceae). Journal of Ethnopharmacology 2010;128:377-383. https://doi.org/10.1016/j.jep.2010.01.041

[17] Vaz ZR, Ccchinel-Filho V, Yunes RA, Calixto JB. Antinociceptive action of 2-(4-bromobenzoyl)-3-methyl-4,6-dimethoxy bonzofuran, a novel xanthoxyline derivative on chemical and thermal models of nociceptive in mice. Journal of Pharmacology and Experimental Therapeutics 1996;278:304-312.

[18] Shibata M, Ohkubo T, Takahashi H, Inoki R. Modified formalin test: Characteristic biphasic pain response. Pain 1989;38:.347-352. https://doi.org/10.1016/0304-3959(89)90222-4

[19] Winter CA, Risley EA, Nuss GW. Antinociceptive action of 2-(4-bromobenzoyl)-3-methyl-4,6-dimethoxy benzofuran, a novel xanthoxyline derivative on chemical and thermal

models of nociception in mice. Proceedings of the Society for Experimental Biology and Medicine 1962;111:544-547.

[20] Souza GEP, Ferreira SH. Blockade by antimacrophage serum of the migration of PMN neutrophils into the inflamed peritoneal cavity. Agents actions 1985;17:1-5. https://doi.org/10.1007/bf01966691

[21] Sobeh M, Mahmoud MF, Abdelfattah MAO, El-Beshbishy HA,El-Shazly AM, Wink M. Hepatoprotective and hypoglycemic effects of a tannin rich extract from Ximenia americana var. caffra root.Phytomedicine 2017:33:36-42. https://doi.org/10.1016/j.phymed.2017.07.003.

[22] Souza TGSS, Silva MM, Feitoza GS, Alcântara, LFM, Silva MA, Oliveira, AM, Aguiar JCROF, Navarro DMAF, Aguiar-Júnior FCAA, Silva MV. Biological safety of *Syagrus coronata* (Mart.) becc. fixed oil: cytotoxicity, acute oral toxicity, and genotoxicity studies. Journal of Ethnopharmacology Biological 2021;272:1–8. https://doi.org/10.1016/j.jep.2021.113941

[23] Santos AA, Silva JW, Santos SM, Rodrigues MF, Silva CJ, Silva MV, Correia MTS, Albuquerque JFC, Melo CML, Silva TG, Martins RD, Aguiar-Junior FCA, Ximenes RM. In vitro and in vivo wound healing and anti-inflammatory activities of babassu Oil (*Attalea speciosa* mart. ex spreng. Arecaceae). Evidence-based complementary and alternative medicine 2020;2020:1–10. https://doi.org/10.1155/2020/8858291

[24] Chandrashekar P, Lokeshr BR, Kishna, AGG. Hypolipidemic effect of blends of Coconut oil with soybean oil or sunflower oil in experimental rats. Food Chemistry 2010;123:728–733. https://doi.org/10.1016/j.foodchem.2010.05.042

[25] Lescano CH, KassuyaC. Diuretic and anti-Inflammatory activities of the microencapsulated Acrocomia aculeata (Arecaceae) oil on wistar rats. Journal of Medicinal Food 2014;18:656-62. https://doi.org/10.1089/jmf.2014.0077

[26] Lappano R, Sebastiani A, Cirillo F, Rigiracciolo, DC, Galli GR, Curcio R, Malaguarnera, Belfiore A, Cappello AR, Maggiolini M. The lauric acid-activated signaling prompts apoptosis in cancer cells. Journal of the cell death differentiation association 2017;18:1–9. https://doi.org/10.1038/cddiscovery.2017.63

[27] Organization for Economic Cooperation and Development [OECD]. Guideline for the testing of chemicals. Guideline: acute oral toxicity –Up-and-down-Procedure (UDP). Organization for Economic Cooperation and Development, Paris 2008. Disponível em: https://www.oecd.org/env/test-no-425-acute-oral-toxicity-up-and-down-procedure-9789264071049-en.htm. Acessado em: 17/01/2022.

[28] Strickland J, Clippinger AJ, Brown J, Allen D, Jacobs A, Matheson J, Lowit A, Reinke EN, Johnson MS, Quinr-Junior MJ, Mattie D, Fitzpatrick SC, Ahir S, Kleinstreuer N, Casey W. Status of acute systemic toxicity testing requirements and data uses by U. S. regulatory agencies. Regulatory Toxicology and Pharmacology 2018;94:183–196. https://doi.org/10.1016/j.yrtph.2018.01.022

[29] Fauser JK, Matthews GM, Cummins AG, Howarth GS. Induction of apoptosis by the Medium-chain length fatty acid Lauric acid in colon cancer cells due to induction of oxidative

stress. Chemotherapy 2013;59:214–224. https://doi.org/10.1159/000356067

[30] Park EJ, Oh JH. Antimicrobial activities of Korean mugwort (*Artemisia iwayomogi* and *Artemisia princeps*) extracts against *Staphylococcus aureus* and Cutibacterium acnes. The Korean Society of Food Preservation 2019;26:381–390. https://doi.org/10.11002/kjfp.2019.26.4.381

[31] Guimarães DO, Momesso LS, Pupo MT. Antibióticos: importância terapêutica e perspectivas para a descoberta e desenvolvimento de novos agentes. Química Nova 2010;33:667-679. http://dx.doi.org/10.1590/S0100-40422010000300035

[32] Ribeiro DA, Macêdo DG, Oliveira LGS, Saraiva ME, Oliveira SF, Souza LRA, Menezes MMA. Potencial terapêutico e uso de plantas medicinais em uma área de Caatinga no estado do Ceará, nordeste do Brasil. Revista Brasileira de Plantas Medicinais 2014;16:912–930. https://doi.org/10.1590/1983-084X/13_059

[33] Naskar S, Mazumder UK, Pramanik G, Saha P, Haldar PK, Gupta M. Evaluation of antinociceptive and anti-inflammatory activity of hydromethanol extract of *Cocos nucifera* L. Inflammopharmacolog 2012;21:7–11. https://doi.org/10.1007/s10787-012-0135-7

[34] Manivannan A, Bhardwaj R, Padmanabhan S, Suneja P, Hebbar KB, Kanade SR. Biochemical and nutritional characterization of coconut (Cocos nucifera L.) haustorium. Food Chem 2018;238:153-159. https://doi:10.1016/j.foodchem.2016.10.127.

[35] Shajib MS, Akter S, Ahmed T, Imam MZ. Antinociceptive and neuropharmacological activities of methanol extract of Phoenix sylvestris fruit pulp. Front Pharmacol 2015;2:1-12. https://doi.org/10.3389/fphar.2015.00212.

[36] Huskaar S, Hole KN. The formalin test in mice: dissociation between inflammatory and non-inlammatory pain. Pain 1987;30:103-114. HTTPS://DOI.ORG/10.1016/0304-3959(87)90088-1

[37] Campos DCO, Costa AS, Lima ADR, Silva FDA, Lobo MDP, Monteiro-Moreira ACO, Moreira RA, Leal LKAML, Miron D, Vasconcelos IM, Oliveira, HD. First isolation and antinociceptive activity of a lipid transfer protein from noni (*Morinda citrifolia*) seeds. International Journal of Biological Macromolecules 2016:86:71–79. https://doi.org/10.1016/j.ijbiomac.2016.01.029

[38] Silva AN, Bonfim HF, Magalhães AO, Rocha ML, Lucchese AM. Composição química e atividade antinociceptiva em modelo animal de óleo essencial de *Myrcia rostrata* D.C. (Myrtaceae). Química Nova 2018;41:982–988. http://dx.doi.org/10.21577/0100-4042.20170274

[39] Amaral JF, Silva MI, Neto MR, Neto PF, Moura BA, Melo CT, Araújo FL, Sousa DP, Vasconcelos PF, de Vasconcelos SM, de Sousa FC. Antinociceptive effect of the monoterpene R-(+)-limonene in mice. Biological and Pharmaceutical Bulletin 2007;30:7:1217-1220. http://doi:10.1248/bpb.30.1217.

[40] Zhao L, Li Y, Yang S, Zhang P, Wang J. Anti-nociceptive effect of total alkaloids isolated from the seeds of *Areca catechu* L (Arecaceae) in mice. Tropical Journal of Pharmaceutical

Research 2017;16:363–369. https://doi.org/10.4314/tjpr.v16i2.15.

[41] Benedito RB. Estudo do mecanismo de ação antinociceptivo e avaliação histopatológica cerebral do (S)-(-)-álcool perílico em camundongos. Tese de doutorado 2013. Available in: https://repositorio.ufpb.br/jspui/bitstream/tede/6802/1/arquivototal.pdf. Acesso em: 16/01/2022.

[42] Eidi A, Oryan, AS, Zringhalam J, RAD M. Antinociceptive and anti-inflammatory effects of the aerial parts of *Artemisia dracunculus* in mice. Pharm Biol 2016;54:549-554. https://doi.org/10.3109/13880209.2015.1056312.

[43] Lavor EM, Fernandes AWC. Andrade TRB, Leal AEBP, Oliveira Júnior RG, Gama SM, Oliveira AP, Silva JC, Moura FAMT, Coutinho HDM, Menezes IRA, Picot L, Silva-Almeida JRG. Essential oils and their major compounds in the treatment of chronic inflammation: A review of antioxidant potential in preclinical studies and molecular mechanisms. Oxidative Medicine and Cellular Longevity 2018;23:01–24. https://doi.org/10.1155/2018/6468593.

[44] Brocco MC, Paulo DNS, Almeida ED, Carraretto AR, Silveira ACO, Gomez RS, Baptista JFA. A study of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) serum levels in rats subjected to fecal peritonitis and treated with intraperitoneal ropivacaine. Peritoneum 2012;27:494–498. https://doi.org/10.1590/s0102-86502012000700011.

[45] Favacho HAS, Oliveira BR, Santos KC, Medeiros BJL, Sousa PJC, Perazzo FF, Carvalho JCT. Anti-infl ammatory and antinociceptive activities of Euterpe oleracea oil. Revista Brasileira de Farmacognosia 2011;21:105–114. https://doi.org/10.1590/S0102-695X2011005000007.

[46] Borges KMB, Azevedo IM, Celani LMS, Medeiros AC. Peritoneal lavage with Coconut water in rats with abdominal peritoneal lavage with coconut water in rats with abdominal sepsis and its effects in peritoneum. Journal of surgical and clinical research 2017;8:42–55. https://doi.org/10.20398/jscr.v8i1.13035.

[47] Carvalho HDO, Gonçalves DES, Picanço KRT, Santos AVTLT, Lucia M, Hu Z, Fernandes CP, Ferreira IM, Carvalho JC. Actions of Cannabis sativa L. fixed oil and nano - emulsion on venom - induced inflammation of Bothrops moojeni snake in rats. Inflammopharmacology 2020;29:1–13. https://doi.org/10.1007/s10787-020-00754-.

[48] Amorim VR, Rodrigues DCN, Silva JN, Ramos CLS, Almeida LMN, Almeida ARC, Rizzo MS, Pereira-Freire JA, Ferreira PM. Anti-inflammatory mechanisms of fruits and by-products from *Mauritia flexuosa*, an exotic plant with functional benefits. Journal of Toxicology and Environmental Health 2021;84:441–457. https://doi.org/10.1080/15287394.2021.1881672.

[49] Aquino JDS, Pessoa DC, Araújo KDLG, Epaminondas PS, Schuler ARP, Souza AGD, Stamford TLM. Refining of buriti oil (Mauritia flexuosa) originated from the Brazilian Cerrado: physicochemical, thermal-oxidative and nutritional implications. Journal of the Brazilian Chemical Society, 2012;23:212-219. https://doi.org/10.1590/S0103-50532012000200004.

[50] Kaithwas G, Murkherjee A, Chaurasia AK, Majumdar DK. Anti-inflamatory, analgesic and antipyretic activities of *Linum usitatissimum* L. (flaxseed/linseed) fixed oil. Indian Journal of Experimental Biology 2011;49:932-9

EVALUATION OF THE HEALING PROPERTIES OF Syagrus schizophylla (Mart.) FIXED OIL AND PLANT-BASED OINTMENT FORMULATION IN CUTANEOUS WOUNDS

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Abstract

Syagrus schizophylla is a palm tree species, popularly known as aricuriroba. Its oleaginous fruits are used in folk medicine in several preparations; however, no scientific reports are proving its therapeutic efficacy in the laboratory. Our research aimed to evaluate the wound healing activity of the fixed oil obtained from *S. schizophylla* seeds (OFSs), and an ointment formulation containing 5% of OFSs in mice. The phytochemical composition was determined by GC-FID. The ointment formulation was evaluated according to its physical-chemical properties. As for the wound healing potential, Swiss mices were submitted to aseptic cutaneous wounds and doses of different treatments were applied daily, for 15 days, the treatments

consisted in two positive controls (Dersani® and dexpanthenol), three different concentrations of OFSs (10%, 25%, and 100%) and a DMSO 2% solution as negative control, in the end of the experiment, the tissue was collected for histomorphometry analysis, as well fibroblast count. The GC-FID revealed the presence of eight compounds, with lauric acid as major compound (50.45 ± 2.30%). At the 10 thrd day after the beginning of the experiment, the animals treated with OFSs 25%,100%, and dexpanthenol, presented full re-epithelization. The histomorphometry revealed that the animals treated with Dersani®, dexpanthenol, OFSs 10% and 25% enhanced the tissue remodeling. The fibroblasts number were higher in OFSs 25% (67.04%) and OFSs ointment (63%), when compared to the negative control group (45.08%). In conclusion, the OFSs was able to induce a faster wound healing process. Together, our results shoows that *S. schizophylla* is a promising candidate to develop products for wound healing purpose.

Keywords: Arecaceae family; *S. schizophylla;* tissue restoration; fixed oil; topical formulation.

Introduction

The skin is the largest organ in the human body, and has an important role in the immunological system, acting as a protective barrier against infections, and minimizing water loss. In contrast, the skin is also one of the most fragile organs in the human body (*7, 20*).

Wound healing is an active, dynamic, and complex process that starts the moment the skin suffers a lesion, that in turn will activate several biological mechanisms to regenerate the damaged tissue (*6, 56*). However, this process is influenced by several factors, which in turn will lead to a faster or slower wound healing activity (*10*). It occurs because wound healing has several stages: hemostasis, inflammation, migration, proliferation, and cell maturation *(63).* And this process is regulated by multiple growth facts and cytokines released in the wound area, external factors can stimulate or inhibit the levels of those cytokines (*12*).

In Brazil, the number of reports of medicinal plants used in folk medicine has increased in the last decades, and it's important to investigate the plant's chemical profile, biological activity, and mechanism of action (17). Especially because these investigations may open paths for the development of new phytotherapy drugs, using chemical compounds from natural sources (11, 64, 24). That research may also help to produce a variety of plant-based products, such as ointment, lotion, sticking plaster, hydrogel, among others, each one of then presents certain limitations, but also, may help to provide a improvement in the healing process, due to the combinations between the plant molecules and appropriate technologies (66).

The search for alternative and integrative therapy for cutaneous wound treatment has increased, especially because access to commercial products is not always easy. With that in mind, medicinal plants are a valuable source of natural products (*25, 1*), an example is an oil obtained from plants, which has been used as anti-inflammatory agents, both by ingestion and topical application in wound treatments (*26, 51*). Thus, the pharmaceutical industry established several advances to provide efficient products that stimulate the wound healing process. However, only 1 to 3% of all cataloged medicines in pharmacopoeias are intended to be used in topical application for cutaneous wounds treatment. Despite

many research investigating wound healing mechanisms, still, there are many questions to be elucidated (*20*). Besides that, the cost of the medicines is also a problem that highlights the need of alternative drugs that are efficient, at a low cost, for most of the population.

Syagrus schizophylla (Mart.) Glass. (Arecaceae) is palm tree species, native to Brazil's northeast region, it possesses fruits with oleaginous seeds and is popularly known as “aricuriroba” and “aricuri” (27), as well “catolé coconut” (29). The literature about S. schizophylla biotechnological potential is scarce, however, many literature reports highlight Arecaceae species with a range of biological activities, such as antioxidant, antimicrobial activity (28), analgesic, antipyretic, and anti-inflammatory (30), antimalaria (65) and antibacterial activities (31).

In addition, the Arecaceae species present fruits and seeds rich in fatty acids, like oleic acid, lauric acid, myristic acid, and caprylic acid, which are known due to their relevant pharmacological potential (35, 71, 37). Studies show that lauric acid (Figure 1) is the predominant fatty acid in plants from this family and point out that the presence of this compound grants high oxidative stability (39), being used in the treatment of wounds (45).

With that in mind, the present work aimed to evaluate the wound healing potential of *S. schizophylla* fixed oil (OFSs) and a plant-based product, that consists of an ointment containing 5% of OFSs, to the determine its therapeutic effect in aseptic cutaneous wounds.

Materials And Methods

Botanical material and oil extraction

Syagrus schizophylla seeds were collected at Coruripe Power Plant located at Coruripe, Alagoas, Brazil (-10.0933332 S, -36.1877785 W). The oil was extracted using a hydraulic press (Tecnal® TE-098) and stored in amber recipients in a refrigerator at 4 °C. An aliquot of the fixed oil was sent to the Chromatography Laboratory of the Department of Fundamental Chemistry (DQF) at UFPE for analysis in GC-FID.

Chemical characterization

Sample preparation for chromatographic analysis: esterification using the boron trifluoride method for oils

Considering the international standardization organization (ISO) orientations, the fatty acids were converted into methyl esters using boron trifluoride (BF3) in methanol (Sigma-Aldrich, code 15716) as a catalyst. 150 mg from the OFSs was resuspended in 2 mL of chloroform, then 0.5 mol/L of sodium hydroxide (NaOH) was added. The mixture was heated up in a water bath at 100 ºC for 5 minutes. For the methanol solution (1.3 M), 2 mL of BF3 were inert to the atmosphere, which in turn was left under reflux for 30 min. The mix was cooled and transferred to a separation funnel with 20 mL of heptane. This mixture was agitated for 1 minute and separated into phases. The organic phase (superior), composed of heptane, was collected and the aqueous phase (inferior) was rejected. The

organic phase was fractionated using column chromatography with gradient elution (pure heptane, heptane: dichlorine [1:1], and pure dichloride). The solvent volume from each fraction was reduced under nitrogen flux at a temperature between 22 and 28 ºC before the CG analysis.

Gas chromatography attached with mass spectrometry

After the esterification process, 1 μL of the sample was inserted in gas chromatography attached with mass spectrometry (GC/MS) in a quadruple system model Agilent 5975C series GC-EM (Agilent Technologies), equipped with an nonpolar column DB-5 (Agilent J&W; 60 m x 0.25 mm di, film thickness of 0.25 μm).

The analysis was carried out in the chromatography laboratory from the fundamental chemistry department (DQF) at UFPE. The GC was initially adjusted for 150 ºC for 2 min and the temperature was maximized at a rate of 5 ºC/min to 230 ºC and maintained for 7.5 min. The sample injection was made at 230 ºC and the interface temperature was 260 ºC. The helium gas was used as the mobile phase at a flow rate of 1.0 mL/min. The mass detector was conducted in scan mode with acquisition de 36.75 min, and solvent cut in 3.25 min, The adopted parameters were: mass range (35-550 amu); filament potential difference (70 Ev); detection potential difference (1.3 sV) using a quadrupole. To identify the methyl esters from the fatty acids, the samples were co-injected with fatty acid standard (FAME-MIX C4-C24, Sigma-Aldrich), and the mass spectra were compared with the ones available in the mass spectrometry library (NIST, Wiley). The fatty esters were quantified by chromatography gas with flame ionization detector (GC-FID) using the Thermo Trace GC Ultra system (Thermo Scientific) equipped with FID and a column of VB-5 (30 m length, 0.25 mm internal diameter and 0.25 μm thickness), at same conditions from the GC-MS investigation.

Plant-based product, ointment with OFSs at 5% formulation

To obtain the ointment formulation, we applied a methodology that consisted of two phases, in the first phase, the OFSs and BHT were added to a recipient, then mixed until complete solubilization (Phase A). Later, phase A was mixed with solid vaseline and homogenized until its complete solubilization (phase B). The pH was measured and maintained at 5.5 and 6.5. After the homogenization process, the ointment was transferred to plastic recipients, for further characterization (Table 1).

Table 1– Plant-based ointment formulation for topic application

Phase	Compound	Function	Concentration (%)
A	BHT	Antioxidant	0,2
	S. schyzophilla oil	Active ingredient	5
B	Solid vaseline	Vehicle	q.s.p.

Stability and characterization of the ointment containing OFSs at 5%

The formulation was submitted to the preliminary stability study, according to the Brazilian guide of cosmetic products stability (46). The stability test was carried out for 12 days, with frosting and defrosting cycles, each one lasting for 24 hours, temperature -5 °C ± 2 °C. At the end of the frosting/defrosting cycles, all the analyses were compared with day 0.

The organoleptic properties were analyzed macroscopically. The color was compared between other tested products with the standard color (base formulation and ingredients). As for the odor, it was also compared with the base formulation or the ingredients. And finally, for the organoleptic properties, after the frosting/defrosting cycle, it was classified as normal, with no alteration; slightly changed; changed, and strongly changed.

All other physical-chemical properties were evaluated according to the Brazilian Pharmacopoeia 6th edition (*48*) and Brazilian guide of cosmetic products stability (*46*).

Animals

Swiss mice (n=35), at 10 weeks old, weight between 30-35 g, obtained from the bioterium of Keizo Asami immunopathology laboratory (LIKA) at UFPE. The animals were maintained in the bioterium for animal experimentation from the Biochemistry Department (UFPE) in environment-controlled rooms, a temperature of 23 ± 2 °C, 12 hours of light/dark cycle, water, and food ad libitum. The assays were performed following the approved protocol from Committee on Animal Use (CEUA/UFPE) under the protocol number 0063/2020.

Wound healing activity Animals

To evaluate the wound healing activity, the mice were divided in seven random groups, each group with five animals. The negative control group received a saline solution at 0.9%, the positive control group received the commercial lotion Dersani®, and another positive control group received dexpanthenol at 5% in an ointment. The experimental groups received the OFSs at 10%, 25%, and 100% concentration, as well a group containing our ointment formulation.

Cutaneous wound and topical treatment

To start the surgical experiment, the mice were previously anesthetized with xylazine hydrochloride 1 mg/kg and ketamine chloride 50 mg/kg, administered by intramuscular injection. After the anesthesia, a trichotomy and antisepsis were made in the dorsal thoracic region, using ethyl alcohol (70%) and sterile saline solution (NaCl 150 mM). The mice skin was demarcated using an adhesive paper mold (0.64 cm^2), and the wound was made with skin excision using surgical material.

The wound treatment consisted of daily topical application of the treatment's solutions/products and an application of post-collection curative every 24 h. The OFSs concentration of 10, 25, and 100%

diluted in DMSO 2%. For the negative control (absence of therapeutic compound) the animals received DMSO 2%, and the positive controls received Dersani® or dexpanthenol. Each treatment consisted of a n of 5 animals.

Wound clinical evaluation

The wounds were evaluated daily for 15 days, in intervals of 24 hours. The following parameters were evaluated: edema, hyperemia, bleeding, secretions, odor, itching, crust presence, and characteristics, necrosis, color, granulation, and scar tissue aspect. All the wounds were photographed, and the diameter was measured with the software ImageJ, for the measurement of the percentage of wound contraction area the following equation was used:

Wound contraction (%): 100X (Wo – Wi) /Wo = % of contraction.
Where, Wo = wound initial area and Wi = wound area day (i).

Histomorphometric analysis of skin wounds

At the end of the 15th day, the animals were sacrificed using lethal doses of xylazine hydrochloride and ketamine chloride, and the skin fragments in the wound area were removed and stored in buffered formalin (10%). Then, samples were fixed and later processed using the conventional histological techniques at the Department of Pathology (UFPE). The sections embedded in paraffin were 5 µm in size and the preparations were stained with hematoxylin-eosin and Masson's trichrome. The histological slides were scanned in the Oral Pathology Laboratory of the Dentistry Department (UFPE). To obtain the microphotographs of the wound site, the Pannoramic Midi (3DHISTECH) blade scanner was used. Then, microphotographs were used to measure the distance between the edges of the scar, as well as the fibroblasts count. This process was done using the Pannoramic Viewer software version 1.15.4 year 2014.

Results and discussion

OFSs Chemical characterization

The phytochemical characterization revealed the presence of eight different compounds, with lauric acid (50.45 ± 2.30%), caprylic acid (16.46 ± 0.43%), and myristic acid (10.94 ± 0.38%) comprising the highest concentrations. Other compounds are also present in concentrations lower than 10% (Table 2).

Table 2. *S. schizophylla* (OFSs) fixed oil constituents

Compounds	Usual nomenclature	Total area (%) ± SD
Octanoic acid, methyl ester	Caprylic acid	16.46 ±0.43
Decanoic acid, methyl ester	Capric acid	10.33 ±0.53
Dodecanoic acid, methyl ester	Lauric acid	50.45 ±2.30
Methyl tetradecanoate	Myristic acid	10.94 ± 0.38
Hexadecanoic acid, methyl ester	Palmitic acid	3.50 ± 0.72
9,12- Octadecadienoic acid, methyl ester	Linoleic acid	0.52 ± 0.31
9- Octadecenoic acid (Z)-, methyl ester	Elaidic acid	2.65± 0.90
Octadecanoic acid, methyl ester	Stearic acid	0.58 ±0.16
Total		95,44

The OFSs composition is similar to another Arecaceae species reported in the literature, especially from the Syagrus genus. Comparing to (*13*) data, *Attalea speciosa* fruits, known as "babaçu", also present lauric acid as major compound (46.05%), followed by myristic acid (15.04%), palmitic acid (8.26%), capric acid (5.33%), caprylic acid (4.59%), stearic acid (2.80%), and linoleic acid (2.71%), all present in OFSs. Similar data were found by (*15*), also studying *A. speciosa*, the lauric acid was present at 54.15%, myristic acid at 10.62%, and caprylic acid at 9.13%. The composition cited above are like our studies. The literature highlights the fatty acid biotechnological potential since they can improve the life quality once they are applied in the development of medicines and nutraceuticals (*11, 22*). From this perspective, (19) reports that the saturated medium-chain fatty acids are related to several health benefits. An example cited by the author is the improvement of life quality by patients that ingest coconut oil during chemotherapy to treat breast cancer.

The chemical profile from Arecacae family oil will be enlightened, once more species from this family are investigated, specifically plants that didn't have its pharmacological potential registered in the literature yet, like *S. schizopjylla*, once the search for medicinal plants usage has increased, about a third from all conventional medicines applied on the wound's treatment are plant-based (*12, 3*). Since immemorial times plants are known to promote wound healing, as well prevent infections (*2, 3*), it is highly important to carry out research focusing on those species.

OFSs ointment

The plant-based ointment formulation was evaluated according to their physical-chemical characteristic, with the technical specifications in Table 3. The analysis was performed according to the Brazilian guide to cosmetic quality control (*47*). According to our data, the OFSs ointment presented visual aspects and homogeneity, appropriate for topical application. The formulation presents transparent color, homogenous aspect, firm consistency, and characteristic scent, and didn't show any alteration, or phase separation, after the centrifugation process. (47) highlights that those characteristics are aligned with formulations usually applied in skin lesion treatment, since the tegument pH is slightly acid, varying between 4 and 6, our formulation attends to the requirements for topical application.

Table 3. Ointment formulation technical specification

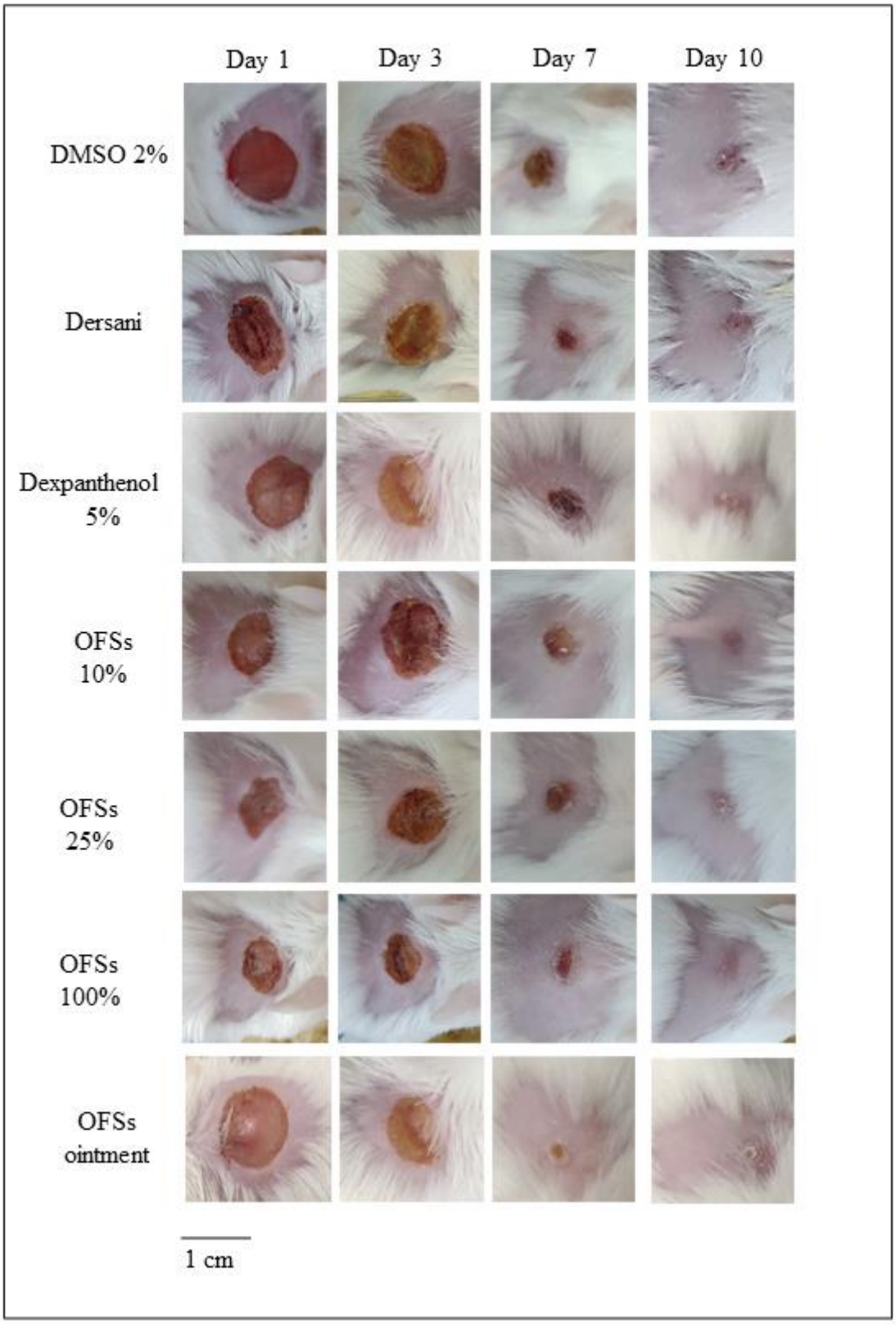
Parameter	Specification
Aspect	Homogenous ointment
Color	White
Scent	Characteristic
pH	5.5 – 6.5
Centrifugation test	Homogenous after 30 minutes at 3.000 rpm

There are no reports in the literature of plant-based formulations using *S. schizophylla.* However, a plant-based ointment, containing the oil from *Mauritia flexuosa* fruits, in two concentrations, 1 and 15%, tested in Wistar mice (51), also presented a homogenous aspect, absence of phase separation, pH varying between 6.23 and 6.45. Besides that, the stability test demonstrates that the samples were stable for 12 days. These results are in line with our results and reinforce the importance of physical-chemical tests for plant-based products.

Macroscopy description of wounds

In the present study, we evaluated the cutaneous wounds for 15 days, evaluating the following aspects: edema, exudate, necrosis, odor, granulation tissue formation, crust, and scar. Figure 3 shows the wound healing process during 10 days of observation, from the incision to the total closure.

Fig. 1 Wound healing process on different treatment days.



The wounds were kept clean and free of infections during the entire experiment. On the first day, the negative control group, and the animals treated with OFSs ointment didn't present crust, while it was present in all other groups. We also observed the edema formation in all animals, however, the

edema was attenuated in the animals treated with Dersani®, dexpanthenol, and OFSs at 25 and 100%, and moderate edema in the animals treated with OFSs at 10% and OFSs ointment when compared to the negative control group, that in turn presented intense edema.Another remarkable difference was the absence of exudate in the animals treated with dexpanthenol, Dersani®, and OFSs at 25% and 100%, while the other groups presented a serous exudate.

On the third day, all animals presented crust, and the negative control group, OF 10% and OFSs formulation, presented mild edema. It worth mentioning that, only the negative control group presented serous exudate, besides that, was possible to note granulation tissue in the wound bothers in the other groups (Dersani®, dexpanthenol, OFSs 25%, and 100%), this granulation tissue was noticeable due to its appearance. On the seventh day, all animals presented an expressive granulation tissue, and the wound area was significantly smaller, indicating the re-epithelialization process. Finally, on the tenth day, only the negative control group presented a wound with crust and not fully closed, as for the other groups, the wound was fully closed, and a scar was present.

Many types of research have been conducted with the aim of optimizing the tissue repair process, providing a better life quality. (70; *9; 13; 33; 52*). Our study is the first one to investigate the *Syagrus schizophylla* wound healing potential, which occurs due to the fatty acid composition present in the *Syagrus* genus, as well as the range of biological activities presented by palm tree species (34).

Our results may be justified due to the different mechanism of action of each compound present in *S. schizophylla* oil, like the fatty acids, (*40*) highlights the anti-inflammatory and antimicrobial activities from lauric acid, which may be evolved with the observed effects, since the wounds were kept clean and aseptic during the entire assay. Those properties improve the tissue repair process, promoting a faster re-epithelialization, as mentioned above, the lauric acid is present in more than 50% of OFSs. Besides that, recently, (41), observed that myristic acid also induces an anti-inflammatory activity, causing an increase in IL-10 concentration in LPS, the IL-10 is associated with anti-inflammatory activity in the tissues (42). Another compound related to several biological activities is palmitic acid, which is widely studied by the pharmaceutical industry (61). With that in mind, the observed wound healing activity is due to its chemical composition, which may act in different ways, and together they exert a positive influence on the wound healing process.

Morphometric analysis

Table 4 shows the wound area, and the wound area contraction during the assay. On the seventh day, the group treated with Dersani® presented the lowest wound area (9.34 ± 8.97 mm), and closure of 88.48%, when compared to the beginning of the experiment. On the tenth day, the re-epithelialization was completed, with total closure of the wound area and a scar, along with the OFSs at 25% and 100%, as well as the dexpanthenol group. As for the OFSs ointment, it presented a small wound area left to achieve total closure, this area corresponds to 0.37 ± 0.69 mm, around 0.25% of the remaining area to

be closed. In this perspective, it is important to highlight that the group treated with OFSs 25% and 100% presented a wound healing performance equivalent to commercial products, like Dersani® and dexpanthenol. On the tenth day, all the OFSs treatments differed from the negative control ($p < 0.005$), except for the animals treated with our formulation.

Table 4. Wound area (mm^2) and percentage of wound contraction. Means represented by different letters, on the same line, differ significantly, Two-way ANOVA test and Tukey test (95% confidence interval, with $p < 0.05$ – $p = 0.0001$)

Assessment time after wound induction	**DMSO 2%**	**Dersani®**	**Bepantol**	**OFSs 10%**	**OFSs 25%**	**OFSs 100%**	**Ointment (OFSs)**
Initial	276.86 ± 31.70	197.38 ± 35.62	214.91 ± 36.16	250.97 ± 28.98	172.72 ± 23.75	195.48 ± 23.52	280.36 ± 33.55
3	233.27 ± 29.68 (b)	144.74 ± 24.83 (a)	169.28 ± 24.45 (a)	163.43 ± 36.42 (b)	141.61 ± 16.11 (a)	150.28 ± 17.83 (a)	248.38 ± 26.98 (b)
7	62.41 ± 16.65 (b)	9.34 ± 8.97 (a)	19.13 ± 6.24 (a)	34.50 ± 12.64 (b)	30.33 ± 6.33 (a)	16.92 ± 2.36 (a)	40.77 ± 23.18 (b)
10	9.18 ± 5.43 (b)	0.32 ± 0.72 (a)	0.12 ± 0.20 (a)	0.86 ± 1.93 (a)	0.00 (a)	0.00 (a)	0.37 ± 0.69 (a)
15	0	0.00	0.00	0.00	0.00	0.00	0.00
% Contraction on 3rd day	13.96 ± 1.44 (b)	26.45 ± 2.79 (a)	23.16 ± 3.50 (a)	16.06 ± 2.33 (a)	23.71 ± 2.72 (a)	26.88 ± 2.12 (a)	11.41 ± 2.51 (b)
% Contraction on 7th day	69.25 ± 3.67 (b)	92.68 ± 4.48 (a)	89.29 ± 3.46 (a)	70.96 ± 4.32 (a)	78.58 ± 6.59 (a)	88.48 ± 2.03 (a)	76.95 ± 9.10 (b)
% Contraction on 10th day	87.78 ± 7.17 (b)	100.00 (a)	100.00 (a)	95.60 ± 11.73 (a)	100.00 (a)	100.00 (a)	99.75 ± 0.93 (b)

(13) showed that the fixed oil obtained from *Attalea speciosa* fruits improves the tissue

restoration process in Swiss mice. It is important to highlight that the author attributes those results to the major compounds, that are also present in our oil, such as lauric acid, and myristic acid. Another investigation showed the wound healing potential from an ointment made with *Mauritia flexuosa*, at 1% and 15%, the authors noticed an improvement in the wound healing process after the third day of application in Wistar mouses, again, the major compounds present in *M. flexuosa* were lauric acid (40%) and myristic acid (29.3%) (*51*). The wound healing potential of Arecaceae species is notorious, and it's due to the chemical composition shared by those species.

Those results may be attached with the difference in mechanism of action between the fixed oil and the OFSs ointment, once the viscosity, as well its saturation from the vegetable oil exerts an important role on its skin penetration ability (*68*). The vegetable oil owns fatty acids that promote permeability due to the lipidic fluidization between the stratum corneum, increasing the transdermal drug delivery (62), and this viscosity is lost when the oil is placed in an ointment formulation, which may explain the OFSs ointment delay to achieve full wound closure.

Histological analysis and fibroblasts

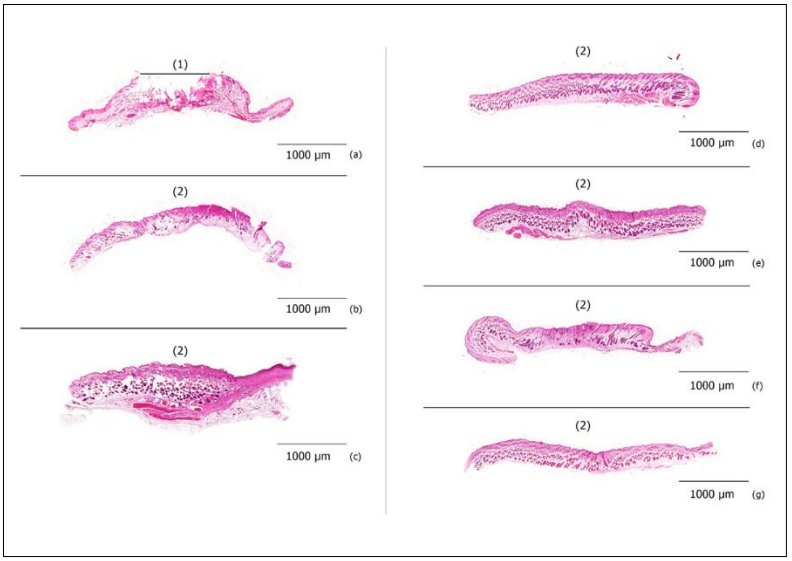
The table 5 shows the histological results from the 15thr day of the assay, the negative control group didn't present a full wound closure, with a distance between the epithelium of 3,451 µm, while the other groups presented a full wound closure, with $p < 0.0001$. We noticed that the animals treated with Dersani®, dexpanthenol 5%, OFSs 10, 25, and 100%, as well the OFSs ointment, presented a full re-epithelialization (Figure 4).

Table 5. Distance between the wound epithelium

Assessment time after wound induction	DMSO 2%	Dersani®	dexpanthenol	OFSs 10%	OFSs 25%	OFSs 100%	Ointment (OFSs)	Valor p
15	3,451 ± 518 µm [(a)]	0,00[(b)]	0,00[(b)]	0,00[(b)]	0,00[(b)]	0,00[(b)]	0,00[(b)]	$p <$ 0,0001

Means represented by different letters, on the same line, differ significantly, Two-way ANOVA test and Tukey test (95% confidence interval, $p < 0.05$ – $p = 0.0001$)

Fig. 2 Histological sections of mice's dorsal skin demonstrating the Control group (a), Dersani® group (b), dexpanthenol group 5% (c), OFSs 10% (d), OFSs 25% (e), OFSs 100% (f) e OFS ointment 5% (g).



The images show the extent of re-epithelialization after 15 days of treatment: (1) distance between epithelium and (2) total re-epithelialization. Staining: Hematoxylin-eosin. 20x magnification.

(43) states that those results are due to the presence of lauric acid which presents antibacterial properties and contribute to the tissue restoration process once the wound infection is avoided. Also, linoleic acid is a fatty acid strongly present in epidermic layers, being an important agent in the fat transport, favoring the integrity and maintenance of the epidermic barrier, and due to that, it enhances the wound healing process. The literature also reports that the linoleic acid acts as an immunogen (*60; 45*). The presence of oleic acid in the OFSs reinforces the synergetic effect between the fatty acids, potentiating the wound healing properties and contributing to the tissue restoration process.

Even though there are no literature reports of *S. schizophylla* biological potential, similar results have been published for another Arecaceae species. (44) studied the coconut oil and found out that it improved the wound healing process in mice, inducing an enhancement in the collagen deposition, and reducing the oxidative stress in the damaged tissue. The authors also attribute the observed activities with medium-chain fatty acids, which are present in the OFSs.

The fibroblast count is shown in Table 6. On the 15thrd day, the animals treated with OFSs 25% presented the highest number of fibroblasts cells (67,04%), followed by OFSs ointment (63%), and dexpanthenol (55,32%), when compared to the negative control group (45,08%) ($p < 0.05$). The lowest number of cells were registered in the animals treated with OFSs 100% (35,76%), OFSs 10% (32,76%), and Dersani® (47,56%). It is important to notice that the highest mean was found in our ointment, being able to induce the highest collagen deposition, as well fibroblast proliferation.

Table 6. Fibroblast count after the surgical procedure on the 15thr day

Treatment	Negative control	Dersani®	Dexpanthenol	Ointment OFSs 5%	OFSs 10%	OFSs 25%	OFSs 100%
Number of fibroblasts	45.08 ± 16.00 (a)	47.56 ± 19.69 (a)	55.32 ± 23.98 (a)	63.00 ± 16.78 (a)	32.76 ± 15.39 (b)	67.04 ± 27.23 (a)	3 5.76 ± 18.29 (b)

* p = 0.2289

(50) highlights that, the improvement in the tissue restoration, and its faster re-epithelialization, is due to the fibroblast proliferation. Our results are aligned with another Arecaceae species research. (13) found similar results studying the oil obtained from A. speciosa, as well as the *M. flexuosa* ointment (51). Both authors report the fibroblasts to increase in the histomorphometry analysis in mice. Besides that, several other research reports the fibroblast importance in the wound healing process (53, 69; 9). With that in mind, it is important to highlight the histomorphometry importance in those studies once the macroscopic analysis can't provide the full wound closure at a microscopic level (9).

Conclusion

The present study proved that the OFSs own a significant wound healing potential, crude, diluted, or in the plant-based formulation. The observed effects are due to the chemical composition of S. schizophylla seeds that present themselves with high antioxidative properties, which in turn may have contributed to the ointment stability, and fatty acids innate properties, which modulated the inflammatory signaling pathway and fibroblasts proliferation on the derma layer. Moreover, it is notorious for the wound healing potential attached to our ointment, and since this is the first reports of S. schyzophylla or any formulation made with it, we strongly recommend further investigation to a better understanding of the S. schizophylla biological activities. And finally, our results show that the OFSs application is as effective as products already marketed, like Dersani® and Dexpanthenol, which makes S. schizophylla a competitive alternative for wound treatment.

References

SOUZA, Zion Nascimento de et al. Utilização de plantas medicinais do gênero Caesalpinia (Fabaceae) na cicatrização de feridas: uma revisão de literatura. Revista Principia - Divulgação Científica e Tecnológica do IFPB, [S.l.], ago. 2021.

Mantle D, Gok MA, Lennard TW. Adverse and beneficialeffects of plant extracts on skin and skin disorders. AdverseDrug React Toxicol Rev2001; 20 (Suppl.): 89–103.

Lania BG, Morari J, Almeida AR, Silva MND, Vieira-Damiani G, Lins KA, César CL, Velloso LA, Maia NB, Cintra ML, Velho PENF. Topical essential fatty acid oil on wounds: Local and systemic effects. PLoS One. 2019 Jan 4;14(1):e0210059.

GHOSH, S. et al. In vitro and in vivo anti-arthritic and anti-inflammatory activity of Bungarus fasciatus venom. J. Toxins, v. 2, p. 1-5, 2015.

OLIVEIRA, A.S.; ZOCOLER, M.A. Desenvolvimento e avaliação da eficácia de cosmeticos sensoriais com ação antiestresse. Colloquium Vitae, vol. 10, n. Especial 5, p.29-34, 2018.

Gurel MS, Naycı S, Turgut AV, Bozkurt ER. Comparison of the effects of topical fusidic acid and rifamycin on wound healing in rats. Int Wound J. 2015 Feb;12(1):106-10.

Mahdavian Delavary B, van der Veer WM, van Egmond M, Niessen FB, Beelen RH. Macrophages in skin injury and repair. Immunobiology. 2011 Jul;216(7):753-62.

OLIVEIRA, F.G.S.; FERNANDES, Y.C. BÜTTNER-PIRES, J.; CARGNIN, S.T.; SINHORIN, A.P.; ALMEIDA, J.R.G.S.; FERRARINI, S.R. Microencapsulated Myrciaria cauliflora Berg. fruit peel extract as a natural pigment for neutralizing shampoo preparation. Scientific Electronic Archives, v. 14, n. 1, p. 50-58, 2021.

Lopes CMI, Baratella-Evêncio L, Souza IA, Oliveira EB, Sá JGA, Santana MAN, Marcelino Neto PP, Santana ES, Silva LAD, Vieira JRC. Evaluation of cytotoxicity and wound healing activity of Avicennia schaueriana in cream. An Acad Bras Cienc. 2019;91(1).

Wild T, Rahbarnia A, Kellner M, Sobotka L, Eberlein T. Basics in nutrition and wound healing. Nutrition. 2010 Sep;26(9):862-6.

Lescano, C. H., & Kassuya, C. (2014). Diuretic and anti-Inflammatory activities of the microencapsulated Acrocomia aculeata (Arecaceae) oil on wistar rats. Journal of Medicinal Food. https://doi.org/10.1089/jmf.2014.0077

Ibrahim N', Wong SK, Mohamed IN, Mohamed N, Chin KY, Ima-Nirwana S, Shuid AN. Wound Healing Properties of Selected Natural Products. Int J Environ Res Public Health. 2018 Oct 25;15(11):2360.

Santos JAA, da Silva JW, Dos Santos SM, Rodrigues MF, Silva CJA, da Silva MV, Correia MTS, Albuquerque JFC, Melo CML, Silva TG, Martins RD, Aguiar Júnior FCA, Ximenes RM. In Vitro and In Vivo Wound Healing and Anti-Inflammatory Activities of Babassu Oil (Attalea speciosa Mart. Ex Spreng., Arecaceae). Evid Based Complement Alternat Med. 2020 Sep 24;2020.

OLIVEIRA, Y. L. C. et al. Antimicrobial activity and phytochemical screening of Buchenavia tetraphylla (Aubl.) RA Howard (Combretaceae: Combretoideae). The Scientific World Journal, v. 2012, 2012.

Nobre CB, Sousa EO, Camilo CJ, Machado JF, Silva JMFL, Filho JR, Coutinho HDM, Costa JGM. Antioxidative effect and phytochemical profile of natural products from the fruits of "babaçu" (Orbignia speciose) and "buriti" (Mauritia flexuosa). Food Chem Toxicol. 2018 Nov;121:423-429.

Mantle D, Gok MA, Lennard TW. Adverse and beneficialeffects of plant extracts on skin and skin disorders. AdverseDrug React Toxicol Rev2001; 20 (Suppl.): 89–103

Lana, D. F. D., Martins Necchi, R. M., Casoti, R., & Manfron, M. P. (2012). Uma Revisão Sobre As Propriedades Farmacológicas, Morfoanatomia E Toxicicidade De Xanthium Cavanillesii Schouw (Asteraceae). Saúde (Santa Maria), 38(2), 57–70. https://doi.org/10.5902/223658344917

Nobre CB, Sousa EO, Camilo CJ, Machado JF, Silva JMFL, Filho JR, Coutinho HDM, Costa JGM. Antioxidative effect and phytochemical profile of natural products from the fruits of "babaçu" (Orbignia speciose) and "buriti" (Mauritia flexuosa). Food Chem Toxicol. 2018 Nov;121:423-429.

Lappano R, Sebastiani A, Cirillo F, Rigiracciolo DC, Galli GR, Curcio R, Malaguarnera R, Belfiore A, Cappello AR, Maggiolini M. The lauric acid-activated signaling prompts apoptosis in cancer cells. Cell Death Discov. 2017 Sep 18;3:17063.

Sorg H, Tilkorn DJ, Hager S, Hauser J, Mirastschijski U. Skin Wound Healing: An Update on the Current Knowledge and Concepts. Eur Surg Res. 2017;58(1-2):81-94. doi: 10.1159/000454919. Epub 2016 Dec 15. PMID: 27974711.

Wild T, Rahbarnia A, Kellner M, Sobotka L, Eberlein T. Basics in nutrition and wound healing. Nutrition. 2010 Sep;26(9):862-6. doi: 10.1016/j.nut.2010.05.008. PMID: 20692599.

Lescano CH, Iwamoto RD, Sanjinez-Argandoña EJ, Kassuya CA. Diuretic and Anti-Inflammatory Activities of the Microencapsulated Acrocomia aculeata (Arecaceae) Oil on Wistar Rats. J Med Food. 2015 Jun;18(6):656-62. doi: 10.1089/jmf.2014.0077. Epub 2014 Nov 4. PMID: 25369069; PMCID: PMC4458740.

Silva, C.S.M., de Araújo, J.A., Silveira, T.S. et al. Wound Healing Activity of Topical Formulations Containing Mauritia flexuosa Oil. Rev. Bras. Farmacogn. 31, 225–231 (2021). https://doi.org/10.1007/s43450-021-00149-2.

LUCIANO, Leonardo Luca et al. Utilização de óleo de moringa na cicatrização de feridas cutâneas em ratos. Research, Society and Development, v. 10, n. 1, p. e23710110981-e23710110981, 2021.

RIBEIRO, Daiany Alves et al. Potencial terapêutico e uso de plantas medicinais em uma área de Caatinga no estado do Ceará, nordeste do Brasil. Revista Brasileira de Plantas Medicinais, v. 16, p. 912-930, 2014.

DE MORAIS, Selene Maia et al. Fatty acid profile and anti-inflammatory activity of fixed plant oils. Acta Scientiae Veterinariae, v. 45, p. 1-8, 2017.

CANCELA, Francisco. A flora da antiga capitania de Porto Seguro na viagem de Wied-

Neuwied, 1815-1817: prática científica, inventário naturalista e colaboração indígena. História, Ciências, Saúde-Manguinhos, v. 28, p. 811-837, 2021.

Nonato CFA, Leite DOD, Pereira RC, Boligon AA, Ribeiro-Filho J, Rodrigues FFG, da Costa JGM. Chemical analysis and evaluation of antioxidant and antimicrobial activities of fruit fractions of Mauritia flexuosa L. f. (Arecaceae). Peer J. 2018 Nov 28;6:e5991. doi: 10.7717/peerj.5991. PMID: 30519510; PMCID: PMC6272029.

PADILHA, Maria do Rosário Fátima et al. Syagrus schizophylla: Unconventional Food Plant of the Caatinga Biome with a high caloric value| Syagrus schizophylla: Planta alimentícia não convencional do bioma de caatinga com alto valor calórico. Revista Geama, p. 53-57, 2017.

ABD ELHAKIM, Islam Abd Elhakim A.; ABDEL-BAKY, Afaf M.; BISHAY, D. W. BOTANICAL AND BIOLOGICAL STUDY OF THE LEAVES OF CARYOTA MITIS LOUR. FAMILY ARECACEAE CULTIVATED IN EGYPT. Bulletin of Pharmaceutical Sciences. Assiut, v. 40, n. 1, p. 71-95, 2017.

JOY, Anumol et al. Antibacterial screening and phytochemical powder isolated from dorsal side of leaves of Cocos nucifera (Arecaceae). Journal of Pharmaceutical Sciences and Research, v. 11, n. 7, p. 2555-2557, 2019.
DARIO, Michelli F. et al. Synergistic photoprotective activity of nanocarrier containing oil of Acrocomia aculeata (Jacq.) Lodd. Ex. Martius—Arecaceae. Industrial Crops and Products, v. 112, p. 305-312, 2018.

Sofrona E, Tziveleka LA, Harizani M, Koroli P, Sfiniadakis I, Roussis V, Rallis M, Ioannou E. In Vivo Evaluation of the Wound Healing Activity of Extracts and Bioactive Constituents of the Marine Isopod Ceratothoa oestroides. Mar Drugs. 2020 Apr 18;18(4):219. doi: 10.3390/md18040219. PMID: 32325719; PMCID: PMC7230750.

Lacerda Coriolano D, Menezes Estevam Alves MH, Macário Ferro Cavalcanti I. Biological Potential of Products Obtained from Palm Trees of the Genus Syagrus. Evid Based Complement Alternat Med. 2021 Aug 19;2021:5580126. doi: 10.1155/2021/5580126. PMID: 34457025; PMCID: PMC8397564.

Santana Lopes A, Gomes Pacheco T, Nimz T, do Nascimento Vieira L, Guerra MP, Nodari RO, de Souza EM, de Oliveira Pedrosa F, Rogalski M. The complete plastome of macaw palm [Acrocomia aculeata (Jacq.) Lodd. ex Mart.] and extensive molecular analyses of the evolution of plastid genes in Arecaceae. Planta. 2018 Apr;247(4):1011-1030. doi: 10.1007/s00425-018-2841-x. Epub 2018 Jan 16. PMID: 29340796.

Ferreira LC, Grabe-Guimarães A, de Paula CA, Michel MC, Guimarães RG, Rezende SA, de Souza Filho JD, Saúde-Guimarães DA. Anti-inflammatory and antinociceptive activities of Campomanesia adamantium. J Ethnopharmacol. 2013 Jan 9;145(1):100-8. doi: 10.1016/j.jep.2012.10.037. Epub 2012 Oct 31. PMID: 23123269.

DE LIMA, João Alberto Lins et al. Attalea speciosa Mart. ex Spreng (Arecaceae): Uma revisão integrativa quanto às principais características biotecnológicas. Brazilian Journal of Development, v. 6, n. 7, p. 45844-45861, 2020.

LAPPANO, Rosamaria et al. The lauric acid-activated signaling prompts apoptosis in cancer

cells. Cell death discovery, v. 3, n. 1, p. 1-9, 2017.

DE SALES, Airton Ricart Rodrigues et al. Caracterização físico-química do oléo de coco babaçu industrial e artesanal e suas aplicações tecnológicas. Brazilian Journal of Development, v. 6, n. 5, p. 25734-25748, 2020.

KANED, Tejas D. et al. Cocos nucifera pharmacological activities–An overview. International Journal, v. 1, n. 01, p. 01-18, 2021.

Alonso-Castro AJ, Serrano-Vega R, Pérez Gutiérrez S, Isiordia-Espinoza MA, Solorio-Alvarado CR. Myristic acid reduces skin inflammation and nociception. J Food Biochem. 2022 Jan;46(1):e14013. doi: 10.1111/jfbc.14013. Epub 2021 Nov 22. PMID: 34811755.

Jiang Y, Zhao W, Xu S, Wei J, Lasaosa FL, He Y, Mao H, Bolea Bailo RM, Kong D, Gu Z. Bioinspired design of mannose-decorated globular lysine dendrimers promotes diabetic wound healing by orchestrating appropriate macrophage polarization. Biomaterials. 2022 Jan;280:121323. doi: 10.1016/j.biomaterials.2021.121323. Epub 2021 Dec 15. PMID: 34942563.

LIEBERMAN, Shari; ENIG, Mary G.; PREUSS, Harry G. A review of monolaurin and lauric acid: natural virucidal and bactericidal agents. Alternative & Complementary Therapies, v. 12, n. 6, p. 310-314, 2006.

Nevin KG, Rajamohan T. Effect of topical application of virgin coconut oil on skin components and antioxidant status during dermal wound healing in young rats. Skin Pharmacol Physiol. 2010;23(6):290-7. doi: 10.1159/000313516. Epub 2010 Jun 3. PMID: 20523108.

FERREIRA, Adriano Menis et al. Utilização dos ácidos graxos no tratamento de feridas: uma revisão integrativa da literatura nacional. Revista da Escola de Enfermagem da USP, v. 46, n. 3, p. 752-760, 2012.

BRASIL. Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Guia de Estabilidade de Produtos Cosméticos. 1ª Edição. Brasília: ANVISA, 2004. 52 p.

BRASIL. Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Guia de Controle de Qualidade de Produtos Cosméticos. 1ª Edição. Brasília: ANVISA, 2007. 26 p.

BRASIL. Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Farmacopeia Brasileira. 6ª Edição, ANVISA. Brasília, 2010.

Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. Acta Derm Venereol. 2013 May;93(3):261-7. doi: 10.2340/00015555-1531.

Ulger BV, Kapan M, Uslukaya O, Bozdag Z, Turkoglu A, Alabalık U, Onder A. Comparing the effects of nebivolol and dexpanthenol on wound healing: an experimental study. Int Wound J. 2016 Jun;13(3):367-71. doi: 10.1111/iwj.12314. Epub 2014 Jul 15. PMID: 25040679; PMCID: PMC7949647.

DA SILVA, Carlena SM et al. Wound Healing Activity of Topical Formulations Containing Mauritia flexuosa Oil. Revista Brasileira de Farmacognosia, v. 31, n. 2, p. 225-231, 2021.

HARTATI, Hartati et al. Evaluation Of Antioxidant, Antimicrobial And Wound Healing Activity Of Poikilospermum Suaveolen. Jurnal Teknologi (Sciences and Engineering), v. 84, n. 1, p. 41-48, 2022.

Khoshneviszadeh, M., Ashkani-Esfahani, S., Namazi, M. R., Noorafshan, A., Geramizadeh, B., & Miri, R. (2014). Topical simvastatin enhances tissue regeneration in full-thickness skin wounds in rat models. Iranian journal of pharmaceutical research : IJPR, 13(1), 263–269.

KAUSHIK, Atul et al. Effect of statin on perioperative myocardial injury in isolated valve surgery. Asian Cardiovascular and Thoracic Annals, v. 29, n. 5, p. 369-375, 2021.

AROLLADO, Erna C. et al. Cocos nucifera L. endosperm promotes healing of excised wound in BALB/c mice. Marmara Pharmaceutical Journal, v. 22, n. 1, 2018.

Weimann E, Silva MBB, Murata GM, Bortolon JR, Dermargos A, Curi R, Hatanaka E. Topical anti-inflammatory activity of palmitoleic acid improves wound healing. PLoS One. 2018 Oct 11;13(10):e0205338. doi: 10.1371/journal.pone.0205338. PMID: 30307983; PMCID: PMC6181353.

Rajoo A, Ramanathan S, Mansor SM, Sasidharan S. Formulation and evaluation of wound healing activity of Elaeis guineensis Jacq leaves in a Staphylococcus aureus infected Sprague Dawley rat model. J Ethnopharmacol. 2021 Feb 10;266:113414. doi: 10.1016/j.jep.2020.113414. Epub 2020 Sep 24. PMID: 32980488.

Budovsky A, Yarmolinsky L, Ben-Shabat S. Effect of medicinal plants on wound healing. Wound Repair Regen. 2015 Mar-Apr;23(2):171-83. doi: 10.1111/wrr.12274. PMID: 25703533.

Datta HS, Mitra SK, Patwardhan B. Wound healing activity of topical application forms based on ayurveda. Evid Based Complement Alternat Med. 2011;2011:134378. doi: 10.1093/ecam/nep015. Epub 2011 May 26. PMID: 19252191; PMCID: PMC3136177.

Bajay, H. M., S. A. Jorge, and S. R. P. E. Dantas. "Curativos e coberturas para o tratamento de feridas." Jorge AS, Dantas SRPE. Abordagem Multiprofissional do tratamento de Feridas. São Paulo: Atheneu (2003): 247-59.

James MJ, Gibson RA, Cleland LG. Dietary polyunsaturated fatty acids and inflammatory mediator production. Am J Clin Nutr. 2000 Jan;71(1 Suppl):343S-8S. doi: 10.1093/ajcn/71.1.343s. PMID: 10617994.

Viljoen JM, Cowley A, du Preez J, Gerber M, du Plessis J. Penetration enhancing effects of selected natural oils utilized in topical dosage forms. Drug Dev Ind Pharm. 2015;41(12):2045-54. doi: 10.3109/03639045.2015.1047847. Epub 2015 Jul 10. PMID: 26161938.

Gonzalez ACO, Costa TF, Andrade ZA, Medrado ARAP (2016) Wound healing - a literature review. An Bras Dermatol 91:614–620. https:// doi.org/10.1590/abd1806-4841.20164741

SHEDOEVA, Aleksandra et al. Wound healing and the use of medicinal plants. Evidence-Based Complementary and Alternative Medicine, v. 2019, 2019.

Tayler, N. M., Boya, C. A., Herrera, L., Moy, J., Ng, M., Pineda, L., … Id, C. S. (2019). Analysis of the antiparasitic and anticancer activity of the coconut palm (Cocos nucifera L . ARECACEAE) from the natural reserve of Punta Patio , Darie. Plos One, 14(4), 1–18.

EL-KASED, Reham F. et al. Honey-based hydrogel: In vitro and comparative In vivo evaluation for burn wound healing. Scientific reports, v. 7, n. 1, p. 1-11, 2017.

MOORE, Z. et al. Tratamento de Feridas em Equipa. Journal of Wound Care, v. 23, n. 5, 2014. Moo.

CERQUEIRA, A. D. MÓSCA, M.; ANA, D.; MÓSCA, M. Investigação in vivo da penetração de óleos e sua influência na barreira cutânea 1. 2012.

SONMEZ, Ertan et al. The efficacy of absorbable polysaccharide haemostats in wound healing. Blood Coagulation & Fibrinolysis, v. 26, n. 1, p. 50-53, 2015.

GÁL, Peter et al. Effect of Atropa belladonna L. on skin wound healing: biomechanical and histological study in rats and in vitro study in keratinocytes, 3T3 fibroblasts, and human umbilical vein endothelial cells. Wound Repair and Regeneration, v. 17, n. 3, p. 378-386, 2009.
DARIO, M. F. et al. Synergistic photoprotective activity of nanocarrier containing oil of Acrocomia aculeata (Jacq.) Lodd. Ex. Martius—Arecaceae. Industrial Crops and Products, v. 112, n. March, p. 305–312, 2018.

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Author Contributions
All authors have contributed to this study. Ricardo Sérgio da Silva: designed the study, performed the assays, analyzed the data, wrote the article; Paulo Henrique Oliveira de Miranda: Study design, performed the assay, manuscript review and translation; Luzia Abilio da Silva: Performed the study and revised the manuscript; Paulo Henrique Eloi Fernandes: Performed the assays, revised the manuscript, graphics and manuscript formatting; Kátia Alves Ribeiro: Revised the manuscript and performed the assays; Silvânia Tavares Paz: Performed the histological process of the biological material; Fernanda Granja da Silva Oliveira: Study design, final review of the manuscript.; Bruno de Oliveira de Veras: reviewed the methodologies; Augusto César Leal da Silva Leonel: Slides scanning; Maria Tereza dos Santos Correia: Manuscript review; Daniela Maria do Amaral Ferraz Navarro: GC/FID analysis; Júlio César Ribeiro de Oliveira Farias de Aguiar: Manuscript review, assisted the GC/MS; Jeymesson Raphael Cardoso Vieira: Review of the work and assisted in the histological analyses; Márcia Vanusa da Silva: Orientation and manuscript review.
Ethics approval

This study was performed in line with the principles of the animal ethic. Approval was granted by the Ethics Committee on Animal Use of the Federal University of Pernambuco (CEUA/UFPE) under the protocol number 0063/2020.

5 CONCLUSÃO

Os resultados obtidos demonstram que a utilização do OFSs é segura, por não apresentar toxicidade nas doses testadas. A composição química do OFSs apresenta importantes ácidos graxos, que podem estar relacionados fortemente com a redução da dor, inflamação e febre. O OFSs (25% e 100%) acelera o processo de cicatrização em camundongos, sugerindo a maior porcentagem de reepitelização em 15 dias, e apresentando resultados semelhantes a grupos de formulações comerciais testadas, como o dersani e dexpantenol.

Os resultados obtidos demonstram ainda que a aplicação de OFSs, em óleo ou pomada, induz a uma cicatrização e reepitelização mais rápida,. Tanto o óleo quanto a pomada representam excelentes candidatos à terapia alternativa de regeneração tecidual. o que reforça a premissa de que os ácidos graxos contribuem para as propriedades medicinais demonstradas. Ainda assim, ensaios clínicos e outros modelos experimentais são indispensáveis

Deste modo, pode-se dizer que o OFSs é um produto promissor para a indústria terapêutica e pode ser um forte aliado para tratamento de diversas doenças, atuando como agente antinociceptivo, anti-inflamatório, antipirético e cicatrizante.

REFERÊNCIAS

AGHASAFARI, P.; GEORGE, U.; PIDAPARTI, R. A review of inflammatory mechanism in airway diseases. **Inflammation Research**, v. 68, n. 1, p. 59–74, 2019.

ARULSELVAN, Palanisamy et al. Role of antioxidants and natural products in inflammation. **Oxidative medicine and cellular longevity**, v. 2016, 2016.

ASADI-SAMANI, MAJID; RAFIEIAN-KOPAEI, MAHMOUD; AZIMI, NAFISEH. Gundelia: a systematic review of medicinal and molecular perspective. **Pakistan Journal of Biological Sciences**, v. 16, n. 21, p. 1238-1247, 2013.

AZHAR, N. et al. A putative "chemokine switch" that regulates systemic acute inflammation in humans. **Scientific reports**, v. 11, n. 1, p. 1-14, 2021.

AZIZ, N.; KIM, M. Y.; CHO, J. Y. Anti-inflammatory effects of luteolin: A review of in vitro, in vivo, and in silico studies. **Journal of ethnopharmacology**, v. 225, p. 342-358, 2018.

BAKER, W. J.; DRANSFIELD, J. Beyond Genera Palmarum: progress and prospects in palm systematics. **Botanical Journal of the Linnean Society**, v. 182, n. 2, p. 207-233, 2016.

BARKIN, R. L. Topical nonsteroidal anti-inflammatory drugs: the importance of drug, delivery, and therapeutic outcome. **American journal of therapeutics**, v. 22, n. 5, p. 388-407, 2015.

BELTRAME, R. A.; JASMIM, J. M.; VIEIRA, H. D. Morphological characterization and germination of Syagrus schizophylla (Mart.) Glass. (ARECACEAE). **Comunicata Scientiae**, v. 10, n. 1, p. 54-64, 2019.

BENEDITO, R. B. **Estudo do mecanismo de ação antinociceptivo e avaliação histopatológica cerebral do (S)-(-)-álcool perílico em camundongos**, 2013. Disponível em: https://repositorio.ufpb.br/jspui/handle/tede/6802. Acesso em: 04/01/2022.

BEVILACQUA, H. G. C. R. **Planejamento de horta medicinal e comunitária.** Divisão Tec. Esc. Municipal de Jardinagem / Curso de Plantas medicinais – São Paulo, 2010.

CHEN, J. et al. Combination of Span 20 and pH-assisted walnut oil extraction during aqueous extraction process. **LWT**, v. 91, p. 477-483, 2018.

CNC, Flora. ***Syagrus schizophylla*** **in Lista Vermelha da flora brasileira versão 2012.2** Centro Nacional de Conservação da Flora. Disponível em <http://cncflora.jbrj.gov.br/portal/pt-br/profile/Syagrus schizophylla>. Acesso em: 27 jan. 2022.

COLVIN, L. A.; ROWBOTHAM, D. J. I. Managing pain: recent advances and new challenges. **British journal of anaesthesia**, v. 111, n. 1, p. 1-3, 2013.
CORIOLANO, L. D.; MENEZES, E. A. M. H.; MACÁRIO, F. C. I. Biological Potential of Products Obtained from Palm Trees of the Genus Syagrus. **Evid Based Complement**

Alternat Med, v. 19, 2021. doi: 10.1155/2021/5580126.

CRUZ, M. R. **Extração de óleo da torta de pinhão manso (Jatropha curcas L.) com etanol para a remoção de éster de forbol**. 2012. 57 f. Dissertação (Mestrado) - Curso de Ciências e Tecnologia de Alimentos, Universidade Federal de Viçosa, Viçosa - Minas Gerais, 2012.

COSTA, A. G. et al. Development of Software for Obtaining Image Attributes for Evaluation of the Wound Healing Process. In: **2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)**. IEEE, 2018. p. 1-4.

DATOVO, L. R. C. B. et al. DESENVOLVIMENTO DE FORMA FARMACEUTICA SEMI-SÓLIDA PARA VEICULAR TINTURA de Arnica Montana1. **Revista Pesquisa e Ação**, v. 3, n. 1, 2017.

DGAC LOPES; DORADO, S.; NARDINO, R. B. **Anti-inflamatórios não esteroidais (AINES): Mecanismos farmacológicos, emprego terapêutico e os seus riscos à saúde**, 2016.

DHINGRA, L. et al. Longitudinal analysis of pain and illicit drug use behaviors in outpatients on methadone maintenance. **Drug and Alcohol Dependence**, v. 149, p. 285–289, 2015.

DUTRA, R. C. et al. Medicinal plants in Brazil: Pharmacological studies, drug discovery, challenges and perspectives. **Pharmacological Research**, [s.l.], v. 112, p.4-29, out. 2016. Elsevier BV. http://dx.doi.org/10.1016/j.phrs.2016.01.021.

EISERHARDT, W. L.; SVENNING, J-C; KISSLING, W. D.; BALSLEV, H. Geographical ecology of the palms (Arecaceae): determinants of diversity and distribution across spatial scales. **Annals of Botany**, v.108, p. 1391–1416, 2011.

ELHAKIM, I. A. A.; ABDEL-BAKY, A. M.; BISHAY, W. Botanical and biological study of the leaves of caryota mitis lour. family arecaceae cultivated in egypt. **Bulletin of Pharmaceutical Sciences Assiut**, v. 40, p. 71–95, 2017.

ELIAS, G. A. et al. Palmeiras (arecaceae) em santa catarina, sul do brasil. **Revista Brasileira de Agroecologia**, v. 13, n. 5, p. 262-263, 2018.

EMILIO, T.; LAMARQUE, L. J.; TORRES-RUIZ, J. M.; KING, A.; CHARRIER, G.; BURLETT, R.; DELZON, S. Embolism resistance in petioles and leaflets of palms. **Embolism Resistance in Palms**, p.1173–1183, 2019. doi.org/10.1093/aob/mcz104

ETIENNE, R.; VIEGAS, F. P. D.; VIEGAS JR, C. Aspectos fisiopatológicos da inflamação e o planejamento de fármacos: uma visão geral atualizada. **Revista Virtual de Química**, v. 13, n. 1, 2021.

FARIAS, P. A. M. et al. Propriedades terapêuticas de plantas do gênero Syagrus: uma revisão integrativa Therapeutic properties of plants of the genus Syagrus: an integrative. **Brazilian Journal of Development**, v. 7, n. 8, p. 76999-77010, 2021.

FAUSER, J. K. et al. Induction of apoptosis by the Medium-chain length fatty acid Lauric

acid in colon cancer cells due to induction of oxidative stress. **Chemotherapy**, v. 59, p. 214–224, 2013.

FERREIRA, A. M. et al. Utilização dos ácidos graxos no tratamento de feridas: uma revisão integrativa da literatura nacional. **Revista da Escola de Enfermagem da USP**, v. 46, p. 752-760, 2012.

FERREIRA, G. **Pomada base tipo Lanovaselina**. In: Relatório de Conclusão de Aula Prática. Universidade Presidente Antônio Carlos – UNIPAC, Ipatinga, 2010.

FIRMO, W. D. C. A. et al. Contexto histórico, uso popular e concepção científica sobre plantas medicinais. **Cad. Pesq.**, v. 18, n. n. especial, p. 90–95, 2011.

FLORA, do Brasil. 2017. Jardim Botânico do Rio de Janeiro. Disponível em: <http://floradobrasil.jbrj.gov.br/ >. Acesso em: 25 out. 2021.

FOOD. Dossiê Óleos In: **Food Ingredients Brasil**, n. 31, 2014.

FORNI, J. E. et al. Perfil sócio-demográfico e clínico de uma coorte de pacientes encaminhados a uma Clínica de Dor. **Revista Dor**, v. 13, n. 2, p. 147-151, 2012.

GAMA, S. F. G, ARAÚJO, F.F.; PAULO, F. D.; ZANOTTO, A. W.; NERI-NUMA, I.A.; PASTORE, G. M. Brazilian fruits of Arecaceae family: An overview of some representatives with promising food, therapeutic and industrial applications. **Food Res Int**., 2020. doi: 10.1016/j.foodres.2020.109690.

GRETEN, F. R.; GRIVENNIKOV, S. I. Inflammation and cancer: triggers, mechanisms, and consequences. **Immunity**, v. 51, n. 1, p. 27-41, 2019.

GUO, X.; CHITALE, P.; SANJANA, N. E. Target discovery for precision medicine using high-throughput genome engineering. **Precision Medicine, CRISPR, and Genome Engineering**, p. 123-145, 2017.

HARIRFOROOSH, S.; ASGHAR, W.; JAMALI, F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. **Journal of Pharmacy & Pharmaceutical Sciences**, v. 16, n. 5, p. 821-847, 2013.

HIDALGO, F. J.; ZAMORA, R. Peptides and proteins in edible oils: Stability, allergenicity, and new processing trends. **Trends in Food Science & Technology**, v. 17, n. 2, p. 56-63, 2006.

IASP. **Pain Terminology**. (2020). Disponível em: <Available online: http://www.iasp-pain.org/AM/Template.cfm?Section=Pain _Definitions&Template=/CM/HTML Display.cfm&ContentID=1728#Pain>. Acesso em: 8 dez. 2021.

JOHNSON, C. Research tools for the measurement of pain and nociception. **Animals**, v. 6, n. 11, p. 71, 2016.

JOY, A. et al. Antibacterial screening and phytochemical powder isolated from dorsal side of leaves of Cocos nucifera (Arecaceae). **Journal of Pharmaceutical Sciences and Research**, v. 11, n. 7, p. 2555-2557, 2019.

JÚNIOR, W. S. F.; LADIO, A. H.; ALBUQUERQUE, U. P. Resilience and adaptation in the use of medicinal plants with suspected anti-inflammatory activity in the Brazilian Northeast. **Journal of ethnopharmacology**, v. 138, n. 1, p. 238-252, 2011.

JUNQUEIRA, L. C.; CARNEIRO, J**. Histologia Básica: texto e Atlas**. Editora Guanabara Koogan.13 ed., 2018.

LEITMAN, P., SOARES, K., HENDERSON, A., NOBLICK, L., MARTINS, R.C. Syagrus in Flora do Brasil. **Jardim Botânico do Rio de Janeiro**. (2015). Disponível em: http://www.floradobrasil.jbrj.gov. br/reflora/ floradobrasil/FB15746. Acessado em: 3 fev. 2022.

LIGON, C. O.; MOLONEY, R. D.; GREENWOOD-VAN MEERVELD, Beverley. Targeting epigenetic mechanisms for chronic pain: a valid approach for the development of novel therapeutics. **Journal of Pharmacology and Experimental Therapeutics**, v. 357, n. 1, p. 84-93, 2016.

LIMA, F. F. et al. Anti-inflammatory, antiproliferative and cytoprotective potential of the Attalea phalerata Mart. ex spreng. pulp oil. **Plos one**, v. 13, n. 4, p. 1–16, 2018.

LIN, T. K.; ZHONG, L.; SANTIAGO, J. L. Anti-Inflammatory and Skin Barrier Repair Effects of Topical Application of Some Plant Oils. **Int J Mol Sci**, v. 19, n. 1, 2017. doi: 10.3390/ijms19010070.

LOPES, A. S. et al. The complete plastome of macaw palm Acrocomia aculeata (Jacq.) Lodd. ex mart.] and extensive molecular analyses of the evolution of plastid genes in arecaceae. **Planta**, v. 247, n. 4, p. 1–20, 2018.

LORENZI, H.; NOBLICK, L.; KAHN, F.; et. al. Flora Brasileira - Arecaceae (Palmeiras). Nova Odessa, SP: Instituto Plantarum, 2010. 384 p.

LORETI, Eduardo Henrique et al. Use of laser therapy in the healing process: a literature review. **Photomedicine and laser surgery**, v. 33, n. 2, p. 104-116, 2015.

LUCAS DA SILVA, I. L.; COELHO, L. C. B. B.; SILVA, L. A. O. Biotechnological potential of the Brazilian Caatinga biome. **Advances in Research**, v. 5, n. 1, p. 1-17, 2015.

MACIEL, V. B. V., YOSHIDA, C. M. P., GOYCOOLEA, F. M. Agronomic Cultivation, Chemical Composition, Functional Activities and Applications of Pereskia Species. **A Mini Review. Curr Med Chem**, v. 26, n. 24, p. 4573-4584, 2019.

MACIEL, V. B. V.; YOSHIDA, C. M. P.; GOYCOOLEA, F. M. Agronomic cultivation, chemical composition, functional activities and applications of Pereskia species–a mini review. **Current Medicinal Chemistry**, v. 26, n. 24, p. 4573-4584, 2019.

MAGALHÃES, P. K. A.; ARAUJO, E. N.; SANTOS, A. M.; VANDERLEI, M. B.; SOUZA, C. C. L.; CORREIA, M.S., FONSECA, S.A.; PAVÃO, J. M. J. S.; SOUZA, M. A.; COSTA, J. G.; SANTOS, A. F.; MATOS-ROCHA, T. J. Ethnobotanical and ethnopharmacological study of medicinal plants used by a traditional community in Brazil's northeastern. **Braz J**

Biol, 2021. doi: 10.1590/1519-6984.237642.

MARINS, D. et al. Synergistic photoprotective activity of nanocarrier containing oil of Acrocomia aculeata (Jacq.) Lodd. Ex. Martius-Arecaceae Article. **Industrial Crops & Products**, v. 112, n., p. 305–312, 2018.

MARQUES, E. S. et al. Evaluation of the genotoxicity of Euterpe oleraceae Mart. (Arecaceae) fruit oil (açaí), in mammalian cells in vivo. **Food and Chemical Toxicology**, v. 93, p. 13–19, 2016.

MARTINI, Alessandra C. et al. Past to future: what animal models have taught us about Alzheimer's disease. **Journal of Alzheimer's Disease**, v. 64, n. s1, p. S365-S378, 2018.

MARTINS, C. C.; ALVES, L. F. A.; MAMPRIM, A. P. Effect of plant extracts and a disinfectant on biological parameters and pathogenicity of the fungus Beauveria bassiana (Bals.) Vuill. (Ascomycota: Cordycipitaceae). **Brazilian Journal Of Biology**, [s.l.], v. 76, n. 2, p. 420-427, 2016. doi.org/10.1590/1519-6984.17914.

MATHEWS, K.; KRONEN, P. W.; LASCELLES, D.; NOLAN, A.; ROBERTSON, S.; STEAGALL, P. V.; WRIGHT, B.; YAMASHITA, K**. Guidelines for recognition, assessment and treatment of pain:** WSAVA Global Pain Council members and co-authors of this document: J Small Anim Pract, v. 55, n. 6, p. 10-68, 2014.

MEYER, B. Re: **Food-frequency questionnaire for assessing long-chain ω-3 fatty-acid intake**. 2013.

MINISTÉRIO DA SAÚDE. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. **Práticas integrativas e complementares:** plantas medicinais e fitoterapia na Atenção Básica/Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. – Brasília: Ministério da Saúde, 2012

MORAIS, S. M.; CATUNDA, F. E. A.; DA SILVA, A. R. A.; NETO, J. S. M.; RONDINA, D.; LEAL CARDOSO, J. H. Atividade antioxidante de óleos essenciais de espécie dee Croton do nordeste do Brasil. **Química Nova**, v. 29, n. 5, p. 907–910, 2006. https://doi.org/10.1590/S0100-40422006000500004

MOREIRA, S. C. F. C. **Estudo da aplicabilidade de pétalas de Calendula officinalis L. em produtos alimentares enriquecidos**. 2015. Tese de Doutorado. Disponível em: http://hdl.handle.net/10284/5394. Acesso em : 10/01/2022.

NOBLICK, L. R. A revision of the genus Syagrus (Arecaceae). **Phytotaxa**, v. 294, n. 1, p. 1-262, 2017.

NOBLICK, L. R. **Guia para as palmeiras do Nordeste do Brasil.** UEFS Editora, Feira de Santana, 2019.

NONATO, C. F. A. et al. Chemical analysis and evaluation of antioxidant and antimicrobial activities of fruit fractions of Mauritia flexuosa L. f. (Arecaceae). **Peerj**, v. 6, p. 1–21, 2018.

NWAEHUJOR, C. O. et al. Anti-inflammatory and anti-oxidant activities of Mallotus

oppositifolius (Geisel) methanol leaf extracts. **Arabian Journal of Chemistry**, v. 7, n. 5, p. 805–810, 2014.

OLIVEIRA, M. et al. Aplicação de terpenos como agentes analgésicos: uma prospecção tecnológica. **Revista geintec-gestao inovacao e tecnologias**, v. 4, n. 4, p. 1292-1298, 2014.

OLIVEIRA, S. G.; DE MOURA, F. R.; DEMARCO, F. F.; NASCENTE, P. D. A. S.; PINO, F. A.; LUND, R. G. An ethnomedicinal survey on phytotherapy with professionals and patients from Basic Care Units in the Brazilian Unified Health System. **J Ethnopharmacol**, v. 140, n. 2, p. 428-37, 2012. doi:10.1016/j.jep.2012.01.054.

OLIVEIRA, V. B. et al. Native foods from Brazilian biodiversity as a source of bioactive compounds. **Food Research International**, v. 48, n. 1, p. 170-179, 2012.

PADILHA, M. R. F.; SHINOHARA, N. K. S.; MACÊDO, I. M. E.; BERNARDINO, A. S. B., ROCHA, N. S.; MACHADO, J. Syagrus schizophylla: Unconventional Food Plant of the Caatinga Biome with a high caloric value. **Geama**, v. 3, n. 2, p. 53–57, 2017.

PANYADEE, P. et al. Plantas medicinais em quintais de quatro grupos étnicos na Tailândia. **Journal of ethnopharmacology**, v. 239, p. 111927, 2019.

PARK, E. J.; OH, J. Antimicrobial activities of Korean mugwort (Artemisia iwayomogi and Artemisia princeps) extracts against Staphylococcus aureus and Cutibacterium acnes. **The Korean Society of Food Preservation**, v. 26, n. 4, p. 381–390, 2019.

PATZELT, A. et al. In vivo investigations on the penetration of various oils and their influence on the skin barrier. **Skin Research and Technology**, v. 18, n. 3, p. 364-369, 2012.

PEREIRA, R. F.; BARTOLO, P. J. Traditional therapies for skin wound healing. **Advances in wound care**, v. 5, n. 5, p. 208-229, 2016.

PETROVSKA, B. B. Historical review of medicinal plants' usage. **Pharmacognosy reviews**, v. 6, n. 11, p. 1, 2012.

RAJA, S. N.; CARR, D. B.; COHEN, M.; FINNERUP, N. B.; FLOR, H.; GIBSON, S. et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. **Pain**, v. 23, 2020.

RAMALHO, H. F.; SUAREZ, P. A. Z. A química dos óleos e gorduras e seus processos de extração e refino. **Revista Virtual de Química**, v. 5, n. 1, p. 2-15, 2013.

RANG, H. P. et al. **Rang & Dale's pharmacology**. Elsevier: Health Sciences, 2011.

RONCHETTI, S.; MIGLIORATI, G.; DEL, D. V. Association of inflammatory mediators with pain perception. **Biomedicine & Pharmacotherapy**, v. 96, n. 2017, p. 1445–1452, 2017.

ROQUE, A. Uso e diversidade de plantas medicinais da Caatinga na comunidade rural de Laginhas, município de Caicó, Rio Grande do Norte (nordeste do Brasil). **Revista brasileira de plantas medicinais**, v. 12, p. 31–42, 2010.

SALES, A. R. R. et al. Caracterização físico-química do oléo de coco babaçu industrial e artesanal e suas aplicações tecnológicas Physical. **Brazilian Journal of Development**, v. 6, n. 5, p. 25734–25748, 2020.

SANTOS SOUZA, T. G. et al. Biological safety of Syagrus coronata (Mart.) Becc. Fixed oil: Cytotoxicity, acute oral toxicity, and genotoxicity studies. **Journal of Ethnopharmacology**, v. 272, p. 113941, 2021.

SERHAN, C. N. et al. Lipid mediators in the resolution of inflammation. **Cold Spring Harbor perspectives in biology**, v. 7, n. 2, p. a016311, 2015.

SILVA, C. G. et al. Levantamento etnobotânico de plantas medicinais em área de Caatinga na comunidade do Sítio Nazaré, município de Milagres, Ceará, Brasil. **Revista Brasileira de Plantas Medicinais**, v. 17, p. 133-142, 2015.

SILVA, J. C. et al. Modelos experimentais para avaliação da atividade antinociceptiva de produtos naturais: uma revisão. **Brazilian Journal of Pharmacy**, v. 94, p. 18-23, 2013

SILVA, M. F. et al. **Uma análise do bioma caatinga no município de Gado Bravo-PB através do Índice Vegetação por Diferença Normalizada**. 2016. Disponível em: <http://tede.bc.uepb.edu.br/jspui/handle/tede/2293>. Acesso em: 9 maio 2019.

SILVA, M. I.; OLIVEIRA, H. B. Desenvolvimento de software com orientações sobre o uso de plantas medicinais mais utilizadas do sul de Minas Gerais. **Brazilian Applied Science Review**, v. 2, n. 3, p. 1104-1110, 2018.

SORG, H. et al. Skin wound healing: an update on the current knowledge and concepts. **European Surgical Research**, v. 58, n. 1-2, p. 81-94, 2017.

SREEKEESOON, D. PRIYAMKA; MAHOMOODALLY, M. FAWZI. Ethnopharmacological analysis of medicinal plants and animals used in the treatment and management of pain in Mauritius. **Journal of ethnopharmacology**, v. 157, p. 181-200, 2014.

SVENNING, J. et al. High tropical net diversification drives the New World latitudinal gradient in palm (Arecaceae) species richness. **Journal of Biogeography**, v. 35, n. 3, p. 394-406, 2008.

TAYLER, N. M. et al. Analysis of the antiparasitic and anticancer activity of the coconut palm (Cocos nucifera L. ARECACEAE) from the natural reserve of´n Punta Patiño, Darie. **Plos one**, v. 14, n. 4, p. 1–18, 2019.

TEIXEIRA, N. et al. Edible fruits from Brazilian biodiversity: A review on their sensorial characteristics versus bioactivity as tool to select research. **Food Research International**, v. 119, p. 325–348, 2019.

THOMPSON, J. M.; NEUGEBAUER, V. Cortico-limbic pain mechanisms. **Neuroscience letters**, v. 702, p. 15-23, 2019.

TIMILSENA, Y. P., VONGSVIVUT, J.; ADHIKARI, R., ADHIKARI, B. Physicochemical and thermal characteristics of Australian chia seed oil. **Food Chem**, 2017. doi:

10.1016/j.foodchem.2017.02.021.

TRACEY, J. R.; DANIEL, W. Nociception. **Current Biology**, v. 27, n. 4, p. R129-R133, 2017.

TREEDE, R. The International Association for the Study of Pain definition of pain: as valid in 2018 as in 1979, but in need of regularly updated footnotes. **Pain reports**, v. 3, n. 2, 2018.

TURK, D. C.; WILSON, H. D.; CAHANA, A. Treatment of chronic non-cancer pain. **The Lancet**, v. 377, n. 9784, p. 2226-2235, 2011.

VARDEH, D.; NARANJO, J. F. Anatomy and physiology: mechanisms of nociceptive transmission. In: **Pain Medicine**. Springer, Cham, p. 3-5, 2017.

VERMA, V.; SHEIKH, Z.; AHMED, A. S. Nociception and role of immune system in pain. **Acta Neurologica Belgica**, v. 115, n. 3, p. 213-220, 2015.

WALTERS, K. M.; WOESSNER, K. M. An overview of nonsteroidal antiinflammatory drug reactions. **Immunology and Allergy Clinics**, v. 36, n. 4, p. 625-641, 2016.

WILLIAM, J.; JOHN, P.; MUMTAZ, M. W.; CH AR, ADNAN A, MUKHTAR, H.; SHARIF S, RAZA, S. A. Antioxidant activity, Hypoglycemic potential and metabolite profiling of Hyophorbe indica leaf extract. **Pak J Pharm Sci**. 2018, v. 31, n. 6, p. 2737-2742.

YARA-VARÓN, E. et al. Vegetable oils as alternative solvents for green oleo-extraction, purification and formulation of food and natural products. **Molecules**, v. 22, n. 9, p. 1474, 2017.

YAXLEY, J.; LITFIN, T. Non-steroidal anti-inflammatories and the development of analgesic nephropathy: a systematic review. **Renal Failure**, v. 6049, p. 0–7, 2016.

APÊNDICE A - SÚMULA CURRICULAR

1) Formação

Ano	Título ou atividade	Instituição
2016	Graduação	Licenciatura em Ciências Biológicas
2018	Mestrado	Morfotecnologia
2018	Doutorado	Ciências Biológicas
2020-2021 2021-2021 -2018-2018 2020-2021	Outros cursos, treinamentos ou certificações (se for ocaso)	Especialização em Docência e Gestão da Educação à Distância Capacitação em Meio ambiente – 20h (Secretaria do Meio Ambiente e Sustentabilidade de Pernambuco, SEMAS/PE, Brasil); Avaliação da Experiência: Princípios de uma nova Perspectiva de avaliação. (Carga horária: 40h). Instituto Federal de Pernambuco, IFPE, Brasil; Docência do Ensino Superior – 240 h.

2) Histórico profissional

- Professor de Ciências – Escola Municipal Maurina Rodrigues dos Santos (2017-2018)
- Coordenador Pedagógico – Escola Municipal Maurina Rodrigues dos Santos (2018-2018);
- Professor Colaborador (Acompanhamento e gerenciamento de Atividades de Ensino, Pesquisa e Extensão) – Programa Internacional Despertando Vocações para Licenciatura
- (2016-2018);
- Professor dos Cursos de Farmácia, Fisioterapia e Pedagogia (Disciplinas Ministradas; Introdução à Profissão Farmácia, Citologia e Embriologia, Histologia dos sistemas Humanos Educação de Jovens e adultos – Uninassau Olinda (2019-2020);
- Professor Colaborador – Realizando o acompanhamento e gerenciamento de Atividades de Ensino, Pesquisa e Extensão) – Programa Internacional Despertando Vocações para Ciências da saúde (2019 – Atual);
- Professor Colaborador – Centro Universitário São Miguel - UNISÃOMIGUEL (2021 – Atual)
- Chefe do departamento de Controle e Preservação ambiental – Prefeitura Municipal de Passira (2021 – Atual).

3) Palestras Ministradas

- SÉRGIO-DA-SILVA, R. Substitutos de pele e Compostos bioativos na Cicatrização de feridas cutâneas (Palestra). 2020.
- SÉRGIO-DA-SILVA, R. Tópicos em desenvolvimento Acadêmico-Científico. 2019.
- SÉRGIO-DA-SILVA, R. PEREIRA, D. R. O Uso crescente de Fitoterápicos na Pesquisa Científica no Brasil. 2019.
- SÉRGIO-DA-SILVA, R. O Networking na área da Saúde: Oportunidade ou oportunismo? 2019.
- SÉRGIO-DA-SILVA, R. A atuação do Biólogo na Área da Biotecnologia (Palestra). 2018.

4) Participação Em Mesa Redonda

- BALBINO, V. Q.; LINS, A. J. C. C.; SÉRGIO-DA-SILVA, R. Atualizações Tecnológicas em Saúde, 2019.

5) Artigos Publicados no Período

- OROZCO, V. R.; GARCIA, N. A. G.; TORRES, S. M. E.; OROZCO, D. L.; TELES, G. H.; AMORIM, L. C.; SÉRGIO-DA-SILVA, R. Isolamento e caracterização morfológica de Acanthamoeba spp em caixas de água de edifícios residenciais. Research, society and development, v. 10, p. file:///C:/User, 2021.
- SILVA, R. S.; SANTANA, E. S.; SILVA, L. A.; SANTANA, E. R. B.; BERENGUER, F. A.; PADILHA, R. J. S. A.; SILVA, M. G. F.; HARAND, W.; LIMA, C. S. A.; YARA, R.; VIEIRA, J. R. C. Phytochemical evaluation of Conocarpus erectus leaves. Rev. Bras. Pl. Med., v. 2019, p. (2019) 21:45-49, 2021.
- SOUZA, G. F.; SANTOS, D. K. D. N.; SÉRGIO-DA-SILVA, R.; BARROS, B. R. S.; CRUZ FILHO, I. J.; RAMOS, B. A.; SILVA, T. D.; SILVA, P. A.; LIMA-NETO, R. G.; GUSMAO, N. B.; NASCIMENTO, M. S.; MELO, C. M. L. to date 0 Altmetric Listen Listen with webReader Focus Short Communication Evaluation of cytotoxic, immunomodulatory effects, antimicrobial activities and phytochemical constituents from various extracts of *Passiflora edulis* F. flavicarpa (Passifloraceae). Natural product research, v. 1, p. https://www.tan, 2020.
- MELO, C. M. L.; DA CRUZ FILHO, I. J.; DE SOUSA, G.F.; DE SOUZA SILVA, G.A.; SÉRGIO-DA-SILVA, R. ; ROCHA, G. J. Lignin isolated from Caesalpinia

pulcherrima leaves has antioxidant, antifungal and immunostimulatory activities. International Journal of biological Mcromolecules, v. 1, p. https://www.sci, 2020.

- SILVA, K. S.; OLIVEIRA, F. G. S.; MIRANDA, P. H. O.; SANTANA, E. S.; SOUZA, Z. N.; AMORIM, L. C.; SILVA, R. S. Phytotherapeutic properties of the Caesalpiniagenus present in the Caatinga biome. Scientific electronic archives, v. 13, 2021.
- SOUZA, Z. N.; SILVA, L. A.; SILVA, K. S.; SANTOS, J. A. A.; SILVA, R. S. Utilização de plantas medicinais do gênero Caesalpinia (Fabaceae) na cicatrização de feridas: uma revisão de literatura'. PRINCIPIA (JOÃO PESSOA). 2021.
- SCOPEL, B. R.; MIRANDA, P. H. O.; SILVA, R. S.; OLIVEIRA, J. V. A.; SILVA, M. V. Biological activities and chemical profile from Batis maritima (Bataceae), a halophyte species with bioprospecting potential. RESEARCH, SOCIETY AND DEVELOPMENT, 2021.

6) Artigos aceitos para publicação

- MELO, C. M. L.; SILVA, R. S. Pectin-Like Polysaccharide Extracted From The Leaves Caesalpinia Pulcherrima Is A Promising Antioxidant And Immunomodulator Agent. Brazilian Archives Of Biology And Technology, 2022.
- SILVA, R. M.; SÉRGIO-DA-SILVA, R. A formação do professor e a utilização de recursos para o ensino. Scientific electronic archives. 2021.

- SÉRGIO-DA-SILVA, R.; SANTOS, D. K. D. N.; SOUZA, G. F.; MELO, C. M. L. Antifungical and immunomodulatory activities from Caesalpinia pulcherrima extracts. Scientific electronic archives. 2021.
- FRANÇA, L. S. S.; SUZANA CINTHIA GOMES DE MEDEIROS, SILVA; SILVA, R. S. Concepções de estudantes sobre o Ensino de Botânica em escolas Estaduais de Vitória de Santo Antão-PE. Revista Ciências em Extensão, 2021.
- SILVA, K. S.; OLIVEIRA, F. G. S.; MIRANDA, P. H. O.; SANTANA, E. S.; SOUZA, Z. N.; AMORIM, L. C.; SÉRGIO-DA-SILVA, R. Phytotherapeutic properties of the Caesalpinia genus present in the Caatinga biome. Scientific Electronic archives, 2021.

7) Organização de Livros

- PEREIRA, D. R. (Org.) ; REGO, M. L. (Org.) ; SÉRGIO-DA-SILVA, R. (Org.) . Ciências da Saúde e suas contribuições sociais. 1. ed. Recife: Editora IIDV, 2020. v. 1. 222p .

8) Capítulos de livros publicados

- SILVA, R. S.; NASCIMENTO, A. R. N.; ASSUNÇÃO, E. R.; SILVA, R. M.; COSTA, D. G.; OROZCO, D. L. R.; FERREIRA, F. R. S.; SILVA, S. M.; SANTANA, S. L.; CORREIA, J. M. A função social da escola e os acaminhos para o desenvolvimento de uma gestão democrática e participativa. In: Discursos, Práticas, Ideias e Subjetividades na Educação. ed.II: Atena Editora, 2021, p. 75-85.
- SILVA, R. S.; CARMO NETO, E. F.; SANTANA, S. L.; SILVA, L. A.; AMORIM, L. C.; MIRANDA, P. H. O.; NASCIMENTO, A. R. N.; OROZCO, D. L. R.; SILVA, R. M. Desafios do Ensino à distância em tempos de pandemia. In: Deflagração de Ações voltadas à Formação Docente 2.1 ed.Ponta Grossa/PR: Atena Editora, 2021, p. 163-172.
- SILVA, R. S.; Santana, S. L.; Carmo Neto, E. F.; Silva, R. M.; Lima, G. H.; Pereira, M. G.; Amorim, L. C.; Miranda, P. H. O.; Silva, L. A.; Santana, E. S. S.; SILVA, S. C. G. M. Desenvolvimento de coletores recicláveis: Trabalhando Educação ambiental em uma escola municipal de Passira/PE. In: Conservação e Meio Ambiente. II ed.: Atena Editora, 2021, p. 291-299.
- MELO, C. M. L.; BARROS, B. R. S.; SANTOS, D. K. D. N.; SÉRGIO-DA-SILVA, R.; AGUIAR, L. M. S.; SOUZA, G. F.; CRUZ FILHO, I. J. O benefício do uso das folhas de *M. emarginata* (aceroleira) para saúde Orgânica. In.1 ed.Belo Horizonte/MG: Atena Editora, 2019, v.1, p. 160.
- VIANA, E.; SÉRGIO-DA-SILVA, R. Os desafios ao longo da Trajetória intelectual: Persistência e Vocação In: Memorial PDV.II ed.Recife: Editora IIDV, 2019, v.1, p. 7.

9) Orientação de trabalhos para submissão em congressos

- NASCIMENTO-DE-SOUZA, Z.; BARROS, B. R. S.; SOARES, K. S.; SÉRGIO DA SILVA, R.; MOUTINHO, C. M. L. Plantas medicinais utilizadas no nordeste do Brasil: uma revisão de literatura. In: I Congresso Internacionalk de Ciências da saúde, 2019, Boa Viagem. Democratização do conhecimento e valorização profissional: caminhos para o desenvolvimento. Recife: Instituto internacional Despertando Vocações, 2019. v. 1.

- SILVA, M. D.; SILVA, A. C.; MELO, J. V.; MOURA, M. K. A.; SÉRGIO-DA-SILVA, R. Alimentação Saudável : a vivência da Pedagogia de Projetos no Contexto da Educação Básica. In: Congresso Nacional de Educação, 2018, Recife. Anais V Conedu. Paraíba-PB: Editora Realize, 2018. v. 1.
- MOURA, E. J.; SILVA, K. S.; SILVA, M. J. C.; SILVA, E. V.; SÉRGIO-DA-SILVA, R. Levantamento de Plantas Medicinais em Áreas Rurais do IFPE Vitória de Santo Antão. In: III Congresso Internacional das Licenciaturas, 2018, João Pessoa. Ciência, tecnologia e desenvolimento rural:compartilhando conhecimentos inovadores e experiências, 2018. v. 1.
- SILVA, K. S.; MOURA, E. J.; BARROS, B. R. S.; SILVA, E. V.; SÉRGIO-DA-SILVA, R. O uso popular de *Lippia alba* (Mill) NE Br. como fitoterápico na Região Nordeste do Brasil. In: III Congresso Internacional das Ciências Agrárias - PDVAGRO, 2018, João Pessoa. Ciência, Tecnologia, desenvolvimento Rural: Compartilhando conhecimentos Inovadores e experiências, 2018. v. 1.
- MOURA; E. J.; SILVA, K. S.; AGUIAR, L. M. S.; SILVA, E. V.; SILVA, R. S. Aplicações biológicas do gênero Caesalpinia L. (Leguminosae Caesalpinoideae). In: III Congresso Internacional das Ciências Agrárias, 2018.Desenvolvimento do campo: a ciência do campo: A ciência e tecnologia a serviço da sustentabilidade. João Pessoa: Instituto Internacional Despertando Vocações.

10) Resumos expandidos publicados em congressos

- SILVA , A. C.; MOURA, M. K. A.; FRANCA, L. S. S.; MELO, J. V.; SÉRGIO-DA-SILVA, R. Bingo dos Elementos Químicos: A importância do Lúdico no Processo de Ensino-Aprendizagem. In: Congresso Nacional de Educação, 2018, Recife. Anais V Conedu. Campina Grande-PB: Portal Realize, 2018. v. 1.
- FRANCA, L. S. S.; MELO, J. V.; SILVA, A. C.; MOURA, M. K. A.; SÉRGIO-DA-SILVA, R. A Percepção de estudantes da licenciatura em Ciências Biológicas sobre o Uso da ludicidade. In: Congresso Nacional de Educação, 2018, Recife. Anais V Conedu. Paraíba-PB: Editora Realize, 2018. v. 1.
- SILVA, R. S.; NASCIMENTO, J. M. S.; SILVA, V. M.; SILVA, S. C. G. M.; SANTANA, S. L. S. A importância da iniciação científica na Educação básica. In: V Congresso Internacional das Licenciaturas, 2018, João Pessoa.Integrar e inovar saberes para a democratização do conhecimento, 2018. v. 1.

- NASCIMENTO, J. M. S.; SILVA, K. A. S.; SOUZA, C. G. A.; SILVA. R. S. O teatro de fantoches como ferramenta ativa para o ensino e aprendizagem de ciências. In: V Congresso Internacional das Licenciaturas, 2018, João Pessoa.Integrar e inovar saberes para a democratização do conhecimento, 2018. v. 1.

11) Lista de Orientações concluídas

- Raquel Patrícia Farias de Barreto Lima. A Tecnologia como Contribuição do Processo de Ensino-aprendizagem. 2019. Trabalho de Conclusão de Curso. (Graduação em Pedagogia) - Centro Universitário Maurício de Nassau - UNINASSAU Olinda. Orientador: Ricardo Sérgio da Silva.
- Letícia Stéfany Santos de França. Concepções de Estudantes do Ensino médio sobre o Ensino de Botânica em Escolas Estaduais de Vitória de Santo Antão/PE. 2019. Trabalho de Conclusão de Curso. (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco. Orientador: Ricardo Sérgio da Silva.
- Fernanda Cibelly de Souza Silva. Sexualidade e vida: análise dos métodos didáticos de Ciências apresentados pelos professores do Município de Passira - PE com foco nas normas da BNCC (Co-orientador). 2020. Trabalho de Conclusão de Curso. (Graduação em Ciências Biológicas) - Centro Universitário da Vitória de Santo Antão. Orientador: Ricardo Sérgio da Silva.
- Henrique José da Costa. Elaboração de um modelo didático na forma de dominó interativo para estudos de doenças relacionadas com Pombos da família Columbridae (Co-orientador: Ricardo Sérgio da Silva).

12) Participação em bancas de TCC

- ALMEIDA, M. B.; SILVA, R. S. Participação em banca de Renato Bagetti Fonseca de Souza.Os Cursos de Bacharelado em Educação Física no Estado de Pernambuco prepara o Profissional de para lidar com lesões. 2021. Trabalho de Conclusão de Curso (Graduação em Educação Física) - Universidade Federal de Pernambuco.
- SÉRGIO-DA-SILVA, R. Participação em banca de Diêgo Delbano Braz de Oliveira. A compreensão a partir dos usuários do SUS do município de Bom Jardim em relação ao descarte adequado de medicamentos vencidos. 2020. Trabalho de Conclusão de Curso (Graduação em Bacharelado em Farmácia) - Centro Universitário da Vitória de Santo Antão.

- SÉRGIO-DA-SILVA, R. Participação em banca de Anderson Alves de Aguiar.Terapia Medicamentosa utilizada em pacientes acometidos por hanseníase. 2020. Trabalho de Conclusão de Curso (Graduação em Bacharelado em Farmácia) - Centro Universitário da Vitória de Santo Antão.
- SÉRGIO-DA-SILVA, R.; SILVA, M. J. Participação em banca de Ailton Clemente da Silva.Inclusão Educacional e Barreiras Atitudinais na Atuação de Professores de Ciências do Ensino Fundamental na Cidade de Passira/PE. 2019. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.
- SÉRGIO-DA-SILVA, R. Participação em banca de Georon Ferreira De Sousa. Investigação Fitoquímica E Potencial Biológicos De Extratos Orgânicos De Passiflora Edulis F. Flavicarpa (Passifloraceae) - Membro Suplente. 2019. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.
- SILVA, R. C.; SILVA, L. R. S.; SÉRGIO-DA-SILVA, R. Participação em banca de Maria Gorete da Silva."Seleção Natural: Uma visão de estudantes do Ensino médio de uma escola da rede estadual de Pernambuco".. 2018. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.
- SILVA, R. S.; CRUZ FILHO, I. J. Participação em banca de Júlio César Ribeiro de Oliveira Farias de Aguiar.Estudo da remoção de uma mistura binária de antibióticos, amoxilina e cefalexina, usando adsorvente vegetal, bagaço de feijão verde. 2018. Trabalho de Conclusão de Curso (Graduação em Química Industrial) - Universidade Federal de Pernambuco.
- SÉRGIO-DA-SILVA, R. Participação em banca de Maria das Dores da Silva.TCC 1: Inserção da história em quadrinhos no Ensino de Evolução: Trabalhando o Conceito de Seleção Natural no Ensino Médio. 2018. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.
- SILVA, R. C.; SILVA, M. G.; OLIVEIRA, R. A.; SÉRGIO-DA-SILVA, R. Participação em banca de Maria Gorete da Silva.TCC 2: Seleção Natural: Uma visão de estudantes do Ensino médio de uma escola da rede estadual de Pernambuco. 2018. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.
- CAVALCANTI, D. R.; SÉRGIO-DA-SILVA, R. Participação em banca de Josefa Ferreira Guimarães.Sífilis gestacional e os desafios no diagnóstico para o controle da transmissão vertical. 2021. Trabalho de Conclusão de Curso (Graduação em

Biomedicina) - Centro Universitário da Vitória de Santo Antão.

- SÉRGIO-DA-SILVA, R. Participação em banca de Anderson Alves de Aguiar.Terapia Medicamentosa utilizada em pacientes acometidos por hanseníase. 2020. Trabalho de Conclusão de Curso (Graduação em Bacharelado em Farmácia) - Centro Universitário da Vitória de Santo Antão.
- SÉRGIO-DA-SILVA, R.; SILVA, M. J.. Participação em banca de Ailton Clemente da Silva.Inclusão Educacional e Barreiras Atitudinais na Atuação de Professores de Ciências do Ensino Fundamental na Cidade de Passira/PE. 2019. Trabalho de Conclusão de Curso (Graduação em Ciências Biológicas) - Universidade Federal de Pernambuco.

13) Trabalhos completos publicados em anais de congressos

- LIMA, G. H.; SILVA, R. S.; LIMA, K. E. C.; CAVALCANTE, P. S. Mobile Learning: a Utilização do Aplicativo Nearpod em uma Disciplina de Zoologia III no Curso se Licenciatura em Ciências Biológicas. In: V Congresso Internacional das Licenciaturas, 2018, João Pessoa. INTEGRAR E INOVAR SABERES PARA A DEMOCRATIZAÇÃO DO CONHECIMENTO, 2018. v. 1.

14) Outras informações biográficas relevantes

- Coordenador do I Congresso Internacional de Ciências da Saúde (COINTER 2018). Possui experiência como Professor do Nível Fundamental, Médio e Superior. Palestrante e Professor Colaborador do Programa Internacional Despertando Vocações /IFPE (Vitória de Santo Antão), realizando o acompanhamento e gerenciamento de ações de Ensino, Pesquisa e Extensão.

15) Links para a página Lattes e ORCID

- Para acesso ao currículo da plataforma Lattes consulte: http://lattes.cnpq.br/8354808367373706
- Para acesso ao Perfil ORCID consulte: https://orcid.org/0000-0002-2900-6807

ANEXO A – PARECER DO COMITÊ DE ÉTICA EM ANIMAIS

Universidade Federal de Pernambuco
Centro de Biociências
Av. Prof. Nelson Chaves, s/n
50670-420 / Recife – PE – Brasil
Fones: 2126 8842
ceua@ufpe.br

Recife, 24 de setembro de 2021

Ofício nº68/21

Da Comissão de Ética no Uso de Animais (CEUA) da UFPE
Prof. Márcia Vanusa da Silva
Departamento de Bioquimica
Centro de Biociencias
processo nº0063/2020

Certificamos que a proposta intitulada "**Investigação do potencial anti-inflamatório, antinociceptivo e antipirético do óleo fixo de sementes de *syagrus schizophylla* (mart.) glassman em modelos experimentais in vivo".** registrado com o **nº0063/2020** sob a responsabilidade da **Prof. Márcia Vanusa da Silva** envolve a produção, manutenção ou utilização de animais pertencentes ao filo Chordata, subfilo Vertebrata (exceto humanos), para fins de pesquisa científica (ou ensino) - encontra-se de acordo com os preceitos da Lei nº 11.794, de 8 de outubro de 2008, do Decreto nº 6.899, de 15 de julho de 2009, e com as normas editadas pelo CONSELHO NACIONAL DE CONTROLE DE EXPERIMENTAÇÃO ANIMAL (CONCEA), e foi aprovada pela COMISSÃO DE ÉTICA NO USO DE ANIMAIS (CEUA) DA UNIVERSIDADE FEDERAL DE PERNAMBUCO (UFPE), em reunião de 31/08/2021

Finalidade	() Ensino (x) Pesquisa Científica
Vigência da autorização	05/09/2021 a 05/03/2022
Espécie/linhagem/raça	Camundongo heterogênico
Nº de animais	161
Peso/Idade	30-35g /10-12
Sexo	Macho (125) e Femea (36)
Origem: Biotério de Criação	Biotério do Laboratório de Imunopatologia Keizo Asami (LIKA)
Destino: Biotério de Experimentação	Biotério experimentação animal do Departamento de Bioquímica da UFPE.

Atenciosamente

Prof. Sebastião R. F. Silva
Presidente CEUA/UFPE
SIAPE 2345691
UFPE