UNIVERSIDADE FEDERAL DE PERNAMBUCO

CENTRO ACADÊMICO DE VITÓRIA DE SANTO ANTÃO

JOSÉ TELES DE OLIVEIRA NETO

ATIVIDADE ANTI-INFLAMATÓRIA DO EXTRATO DE *Solanum campaniforme* ROEM. & SCHULT (SOLANACEAE) E DE SEUS ALCALOIDES ESTEROIDAIS

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CURSO DE BACHARELADO EM ENFERMAGEM

NÚCLEO DE ENFERMAGEM

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TCC apresentado ao Curso de Bacharelado em Enfermagem da Universidade Federal de Pernambuco, Centro Acadêmico de Vitória, como requisito para a obtenção do título de Bacharel em Enfermagem.

Orientador: Dr.ª Roberta Jeane Bezerra Jorge
Coorientador: Msc. Marcela Albuquerque de Oliveira

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Aprovado em: 29/11/2018.

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RESUMO

Solanum campaniforme (Roem. & Schult.) é um arbusto popularmente conhecido como “jurubeba brava” e pode ser encontrado em todas as regiões brasileiras, sendo no Nordeste, distribuído nos estados do Maranhão, Ceará, Paraíba e Pernambuco. Entre os compostos bioativos extraído das folhas *S. campaniforme*, três novos alcaloides esteroidais (1-3) foram caracterizados e testados em estudos anteriores contra ação do veneno de *Bothrops pauloensis* mostraram inibição relevante das atividades proteolíticas *in vitro*, redução dos efeitos mitóxicos, hemorrágicos e necrosantes e também diminuição da área e intensidade hemorrágica e inibiram a lesão necrótica na pele de camundongos. Diante do exposto, buscando dar seguimento aos estudos do efeitos biológicos da planta e dos seus metabólitos secundários, investigamos o potencial efeito anti-inflamatório do extrato de *Solanum campaniforme* e seus alcaloides isolados. O estudo foi realizado com camundongos Swiss machos, por meio do edema de orelha induzido por óleo de cróton. Os dados foram analisados no software GraphPad Prisma® (5.0) utilizando a ANOVA, seguido por pós-teste de Dunnet e $p < 0,05$ considerado como valores estatisticamente significantes. Concluímos que o extrato metanólico e os alcaloides esteroidais isolados da *Solanum campaniforme* possuem atividade anti-inflamatória.

Palavras-chave: Alcalóides de Solanáceas. Plantas Medicinais. Solanaceae.

ABSTRACT

Solanum campaniforme Roem & Schult. Is a shrub popularly known as "jurubeba brava" and can be found in all Brazilian regions, being in the Northeast, distributed in the states of Maranhão, Ceará, Paraíba and Pernambuco. Among bioactive compounds extracted from *S. campaniform*e leaves, three new steroidal alkaloids (1-3) were characterized and tested in previous studies against the action of Bothrops pauloensis venom showed significant inhibition of proteolytic activities in vitro, reduction of mitoxic, hemorrhagic and necrosis and also decreased area and hemorrhagic intensity and inhibited the necrotic lesion in the skin of mice. In view of the above, seeking to follow the studies of the biological effects of the plant and its secondary metabolites, we investigated the potential anti-inflammatory effect of the extract of *Solanum campaniforme* and its isolated alkaloids. The study was performed with Swiss Swiss mice, using ear edema induced by chroton oil. Data were analyzed using GraphPad Prisma® software (5.0) using ANOVA, followed by Dunnet's post-test and $p < 0.05$ considered as statistically significant values. We conclude that the methanolic extract and steroidal alkaloids isolated from *Solanum campaniforme* have anti-inflammatory activity.

Keywords: Alkaloids of Solanaceae. Medicinal plants. Solanaceae.

SUMÁRIO

ARTIGO

O PRESENTE TRABALHO ESTÁ APRESENTADO NO FORMATO DE ARTIGO REQUERIDO PELA REVISTA **BRAZILIAN JOURNAL OF PHARMACOGNOSY,** CUJAS NORMAS PARA SUBMISSÃO DE ARTIGOS SE ENCONTRAM EM ANEXO.

Atividade anti-inflamatória do extrato de *Solanum campaniforme* Roem. & Schult (Solanaceae) e de seus alcaloides esteroidais

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Resumo: *Solanum campaniforme* (Roem. & Schult.) é um arbusto popularmente conhecido como “jurubeba brava” e pode ser encontrado em todas as regiões brasileiras, sendo no Nordeste,

distribuído nos estados do Maranhão, Ceará, Paraíba e Pernambuco. Entre os compostos bioativos extraído das folhas *S. campaniforme*, três novos alcaloides esteroidais foram caracterizados e testados em estudos anteriores contra ação do veneno de *Bothrops pauloensis* mostraram inibição relevante das atividades proteolíticas *in vitro*, redução dos efeitos mitóxicos, hemorrágicos e necrosantes e também diminuição da área e intensidade hemorrágica e inibiram a lesão necrótica na pele de camundongos. Diante do exposto, buscando dar seguimento aos estudos do efeitos biológicos da planta e dos seus metabólitos secundários, investigamos o potencial efeito anti-inflamatório do extrato de *Solanum campaniforme* e seus alcaloides isolados. O estudo foi realizado com camundongos Swiss machos, por meio do edema de orelha induzido por óleo de cróton. Os dados foram analisados no software GraphPad Prisma® (5.0) utilizando a ANOVA, seguido por pós-teste de Dunnet e $p < 0,05$ considerado como valores estatisticamente significantes. Concluímos que o extrato metanólico e os alcaloides esteroidais isolados da *Solanum campaniforme* possuem atividade anti-inflamatória.

Palavras-chave: Alcalóides de Solanáceas, Plantas Medicinais, Solanaceae.

Conflito de interesse: Todos os autores não têm nada para declarar.

Introdução

A inflamação é uma das principais reações da resposta imune celular aos microrganismos e outras doenças. Essa reação ocorre através do recrutamento de leucócitos (fagócitos, neutrófilos e monócitos, principalmente), macrófagos e proteínas plasmáticas do sangue e, devido ao seu acúmulo e ativação são capazes de combater os microrganismos e atuar nos diversos processos inflamatórios (Abbas; Lichtman; Pillai, 2015).

Entre os fármacos mais comuns utilizados na inflamação estão os glicocorticoides e os Anti-inflamatórios Não Esteroidais (AINEs). Os glicocorticoides atuam na inibição da transcrição dos genes da ciclooxigenase-2, citocinas e interleucinas, entre outros mecanismos. Já os AINEs são inibidores da cicloxigenase e atuam inibindo a biossíntese de prostaglandinas através da ação direta da COX. Ambos são potentes agentes anti-inflamatórios e imunossupressores (Rang et al., 2016).

No entanto, o uso prolongado de grande parte dos fármacos anti-inflamatórios está associado a uma série de efeitos colaterais (hipertensão, insuficiência renal, hiperglicemia etc.) (Katzung; Masters; Trevor, 2014). Diante disso, as plantas medicinais são uma fonte de substâncias bioativas com propriedades terapêuticas, profiláticas ou paliativas, visto que a flora brasileira é considerada uma das mais ricas fontes de material com potencial farmacológico e biotecnológico do mundo devido à diversidade de espécies e aos conhecimentos oriundos da medicina tradicional. É cada vez maior o interesse pelas plantas medicinais nativas do Brasil, especialmente pelas empresas farmacêuticas e de biotecnologia de outros países (Fátima et al., 2008).

A família Solanaceae, possui 96 gêneros, aproximadamente, incluindo o gênero *Solanum,* e 2.500 espécies amplamente distribuída por toda região tropical e de clima temperado no mundo, com centros de diversidade ocorrentes nas Américas Central e do Sul, bem como na Austrália e na África, com menor frequência na Europa e na Ásia (Wink, 2003).

Solanum é reconhecido como o maior e o mais complexo gênero da família Solanaceae, com cerca de 1500 espécies, onde muitas são consideradas de interesse medicinal e econômico. As plantas do gênero *Solanum* produzem uma grande variedade de compostos bioativos, sendo os alcaloides esteroidais e glicoalcaloides os mais característicos (Wink, 2003).

Algumas espécies do gênero *Solanum* apresentam potencial anti-inflamatório como: *Solanum lycopersicum* L. (Navarrete *et al.*, 2015); *Solanum lycocarpum* (Costa *et al.*, 2015); *Solanum Melogena Linn.* (Umamageswari *et al.*, 2015); *Solanum erianthum* (Chen *et al.*, 2013) entre outras.

Entre a diversidade de uso incluindo variadas aplicações terapêuticas, inclusive anti-inflamatória, destaca-se *Solanum campaniforme* (Roem. & Schult.) um arbusto popularmente conhecido como "jurubeba brava", encontrado em todas as regiões brasileiras, sendo no Nordeste, distribuído nos estados do Maranhão, Ceará, Paraíba e Pernambuco (Stehmann et al., 2010).

Estudos realizados por Jorge (2011) e Torres e colaboradores (2013) demonstraram o potencial antiofídico de alcaloides isolados, até antes não estudados, das folhas de *S. campaniforme*, no qual foi possível observar inibição significativa das atividades proteolíticas *in vitro* e redução dos efeitos miotóxicos, hemorrágicos e necrosantes promovidos pelo veneno total de *Bothrops pauloensis* induzidos em camundongos.

Em face do exposto, buscando dar seguimento aos estudos dos efeitos biológicos dos metabólitos secundários, o presente estudo realizou uma investigação preliminar do potencial efeito anti-inflamatório do extrato de *Solanum campaniforme* e seus alcaloides isolados.

Materiais e Métodos

Material vegetal

As folhas de *S. campaniforme* foram coletadas durante o estágio de floração no município de Guaramiranga – CE em outubro de 2007, pelo professor Edilberto Rocha Silveira, do Departamento de Química orgânica e Inorgânica da Universidade Federal do Ceará. A planta foi identificada pelo professor Edson Paula Nunes do Departamento de Biologia da Universidade Federal do Ceará. A exsicata da planta (# 41038) encontra-se depositada no Herbário Prisco Bezerra (EAC) daquele Departamento.

As folhas foram pulverizadas e submetidas à extração com metanol. Processos cromatográficos foram adotados para o isolamentos e purificação das substâncias (Torres, 2011).

Extrato metanólico e alcaloides esteroidais isolados de Solanum campaniforme

Neste estudo utilizamos o extrato metanólico das folhas de *Solanum campaniforme* e três alcaloides esteroidais isolados, de esqueleto solanidano: 1 -22,23-epoxi-solanida-1,4,9-trien-3-ona (1), 2-22,23-epoxi-solanida-1,4-dien-3-ona (2) 3-3,9-dihidroxi-22,23-epoxi-9-10-secosolanida-1,3,5(10)-trieno (3), isolados das folhas, os quais foram cedidos pela Prof.ª Dr.ª Otília Deusdênia Loiola Pessoa - Departamento de Química da Universidade Federal do Ceará (UFC).

Drogas e reagentes

Todos os substratos e reagentes para os ensaios *in vitro* a serem utilizados neste trabalho foram pró-análise e obtidos de fornecedores credenciados (Sigma®, EUA).

Animais e aspectos éticos

Nos testes *in vivo* foram utilizados camundongos Swiss machos, com tempo de vida de aproximadamente 8 e 12 semanas de idade. Os animais foram mantidos no Biotério do Laboratório de Etnofarmacologia Aplicada (LEA), Departamento de Antibióticos – UFPE, com temperatura controlada (22 ± 2 ºC) e ciclo claro/escuro de 12h, com água e ração *Ad libitum*. Todos os procedimentos experimentais realizados estão de acordo com as leis brasileiras para experimentação com animais e foram aprovados pela Comissão de Ética no Uso Animal da Universidade Federal de Pernambuco (Protocolo de aprovação: 23076.017574/2015-23).

Ensaios

Edema de orelha induzido por óleo de cróton

Os animais (n = 6) foram anestesiados com pentobarbital sódico (50 mg/kg, i.p.) e 20 µL do óleo de cróton a 2% diluído em acetona foi aplicado na superfície interna da orelha direita dos animais. A orelha esquerda recebeu por via de administração tópica somente acetona e funcionou como controle negativo. O extrato metanólico (0,1; 0,3 e1 mg/orelha) e o fármaco-padrão (0,1 mg/orelha de dexametasona) foram aplicados em seguida e diluídos no mesmo volume de acetona,

através da via de administração tópica. Após seis horas, os animais foram eutanasiados por overdose de anestésicos (300 mg/kg de Ketamina + 30mg/kg de xilazina intraperitoneal e uma amostra de 6 mm de diâmetro retirada de cada orelha com auxílio de um *punch* de biópsia. As amostras foram pesadas em balança analítica (Shimadzu, Japão) e o edema foi calculado pela diferença do peso das amostras da orelha esquerda (controle negativo) e da orelha direita (grupos testes e controle positivo) do mesmo animal (Tubaro, 1985). A mesma metodologia foi utilizada no ensaio com os alcaloides esteroidais isolados, contudo em concentração única de 2µg/orelha.

Análise estatística

Os dados foram analisados utilizando a ANOVA, seguido por pós-teste de Dunnet. Os valores foram expressos como média ± desvio padrão (d.p,) e o nível de significância mínimo foi de $p < 0,05$ como estatisticamente significante. Todos os resultados foram analisados com software GraphPad Prisma® (5.0).

Resultados

Nos testes *in vivo* com o extrato metanólico da *S. campaniforme* observamos significância estatística nas três concentrações utilizadas, principalmente nas concentrações de 0,1 e 0,3 mg/kg, quando comparadas ao controle negativo (Figura 1). E no ensaio com as substâncias isoladas, os três alcaloides esteroidais (1-3) foram estatisticamente iguais, quando comparados ao controle negativo (Figura 2) e também demonstraram potência semelhante com a dexametasona ao reduzir o edema.

Discussão

Um estudo realizado por Umamageswari & Yasmeen (2015), utilizando camundongos Swiss (toxicidade oral aguda) e ratos Wistar (ensaio anti-inflamatório), revelou que o extrato aquoso das folhas de *Solanum melongena* Linn., apresentou no estudo fitoquímico a presença de flavonoides, alcaloides, taninos e esteróis, principalmente. Concluíram que a *S. melongena* Linn. apresenta atividade anti-inflamatória, visto que não houveram alterações nos ensaios de toxicidade e o extrato aquoso foi capaz de reduzir o edema de pata no estudo anti-inflamatório.

O efeito anti-inflamatório de *Solanum integrifolium* foi comprovado após a análise do mecanismo do extrato de seu fruto verde. Uma parte do metanol (ME) que apresentou um índice fenólico elevado, foi responsável por produzir um efeito inibidor na liberação do óxido nítrico (NO) induzido por LPS e a citotoxicidade em macrófagos RAW 264.7, além disso, demonstra uma baixa expressão de genes pró-inflamatórios (iNOS, inibidores de COX-2, IL-1β, IL-6, CCL2 / MCP-1, e CCL3 / MIP1α) (Wang et al., 2014).

Outro estudo realizado por Navarrete e colaboradores (2015), mostrou que a *Solanum lycopersicum* L. e o ácido ferúlico têm propriedades que podem contribuir para a prevenção de doenças inflamatórias crônicas, através da atividade redutora sobre a expressão do TNF-α e citocinas IL-1β em macrófagos (agentes presentes na inflamação), impedindo a ativação do NF-kB (fator nuclear kappa B), o qual está envolvido na resposta celular a estímulos, como por exemplo: citocinas etc.

Um estudo realizado com frações obtidas das folhas *Solanum lycocarpum* e o extrato etanólico foi realizado a fim de determinar sua composição fenólica, entre outras características, como por exemplo: atividade anti-inflamatória, antioxidante, antibacteriana e o seu potencial citotóxico. Após a análise, constatou-se que o diclorometano, acetato de etilo e frações de

hidroetanólicos são os responsáveis pela atividade antioxidante. Já as outras caraterísticas testadas se deram através dos compostos: frações de hexano e diclorometano (antibacteriana); hidroetanólico (anti-inflamatória); acetato de etilo (efeito citotóxico). Essas atividades estão relacionadas, parcialmente, aos flavanóides (Costa et al., 2014).

Conhecida popularmente com "baga-de-veado", a *Solanum corymbiflorum* é utilizada na medicina popular para o tratamento de inflamações cutâneas e, através de um estudo utilizando o extrato das folhas dessa espécie com modelo de edema induzido por óleo de cróton em camundongos Swiss machos, está comprovado que a *S. corymbiflorum* possui atividade anti-inflamatória em aplicação local nas desordens da pele (Piana et al., 2016).

Além disso, outro estudo mostrou que o extrato bruto das folhas de *Solanum anomalum* possui atividade anti-inflamatória através de diferentes modelos de inflamação (carragenina, albumina de ovo e edema de orelha induzido por xileno) em camundongos, confirmando o seu uso na medicina tradicional para o tratamento de doenças inflamatórias (Okokon et al., 2016).

Esses resultados corroboram com os achados do nosso trabalho, visto que, no extrato metanólico da *S. campaniforme*, apresentou uma redução do edema, principalmente nas concentrações de 0,1 e 0,3 mg/orelha quando comparados ao controle negativo. Também observamos que no ensaio realizado com os alcaloides esteroidais isolados houve a redução do edema nos três alcaloides utilizados, sendo o alcaloide SC-05 o mais significativo estatisticamente, quando comparado ao controle negativo e o positivo, demonstrando também um potencial anti-inflamatório das substâncias isoladas.

Baseados nos resultados, o estudo do extrato metanólico e os alcaloides esteroidais isolados da *Solanum campaniforme* demostraram potencial anti-inflamatório. Contudo, enfatizamos que mais estudos devem ser realizados com a espécie estudada, a fim comprovar a sua capacidade anti-inflamatória em diferentes modelos farmacológicos e as alterações histomorfométricas. Com isso, pretendemos elucidar os possíveis mecanismos de ação envolvidos na atuação do extrato e das

substâncias isoladas de *S. campaniforme* como fonte potencial de compostos anti-inflamatórios para auxiliar em terapias principais ou complementares.

Agradecimentos

Este estudo foi apoiado pelo Conselho Nacional de Desenvolvimento Científico e Tecnológico (Pibic/UFPE/CNPq). Agradeço aos pesquisadores do Laboratório de Etnofarmacologia Aplicada - Departamento de Antibióticos/UFPE, por terem colaborado com a realização desse trabalho.

Contribuições dos autores

O José Teles de Oliveira Neto (aluno de graduação) contribuiu no trabalho de laboratório, análise dos dados e elaboração do trabalho. A Maria da Conceição de Menezes Torres (Doutora) contribuiu na coleta de amostras de plantas, identificação. O Francisco Carlos Amanajás de Aguiar Júnior (Doutor) contribuiu para a leitura crítica do manuscrito. A Marcela Albuquerque de Oliveira (aluna de Doutorado) e a Roberta Jeane Bezerra Jorge (Doutora) elaboraram o estudo, supervisionaram o trabalho de laboratório e contribuíram para a leitura crítica do manuscrito. Todos os autores leram o manuscrito final e aprovaram a submissão.

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Outras informações importantes:

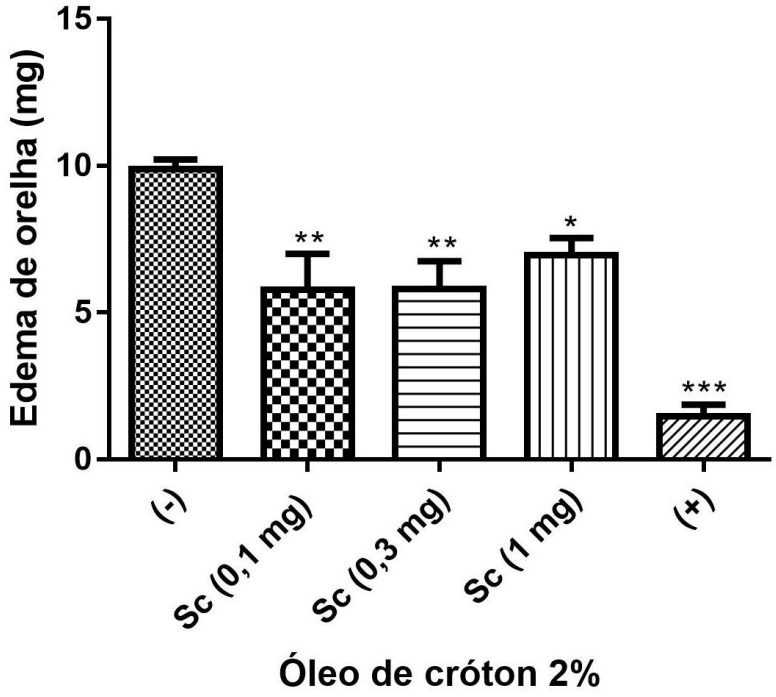


Figura 1 – Edema de orelha induzido por óleo de cróton 2% tratado com o extrato metanólico da *S. campaniforme*. A orelha esquerda recebeu somente acetona e funcionou como controle negativo. O extrato (0,1; 0,3 e1 mg/orelha) e o fármaco-padrão (0,1 mg/orelha de dexametasona) foram diluídos no mesmo volume de acetona e aplicados em seguida na orelha direita do grupo tratado e no controle positivo, respectivamente.

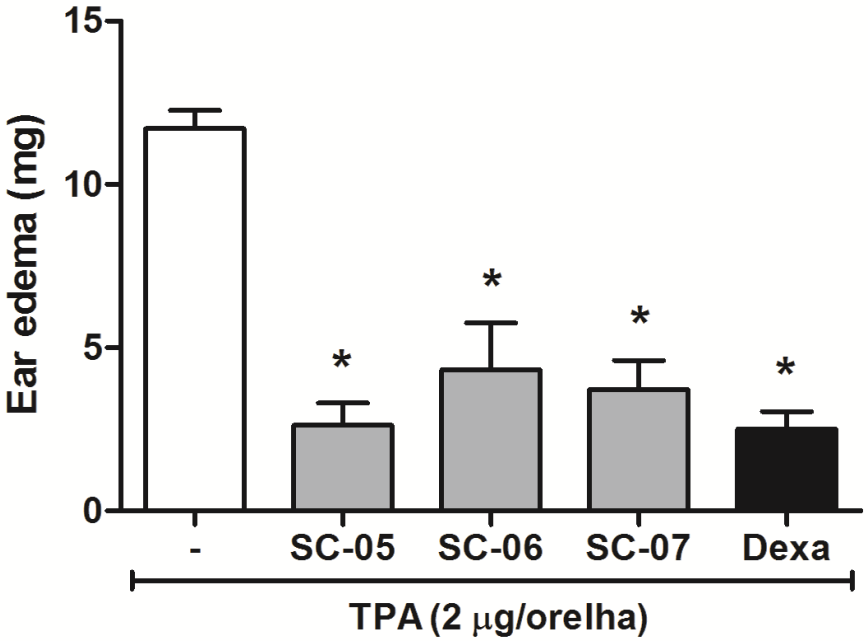
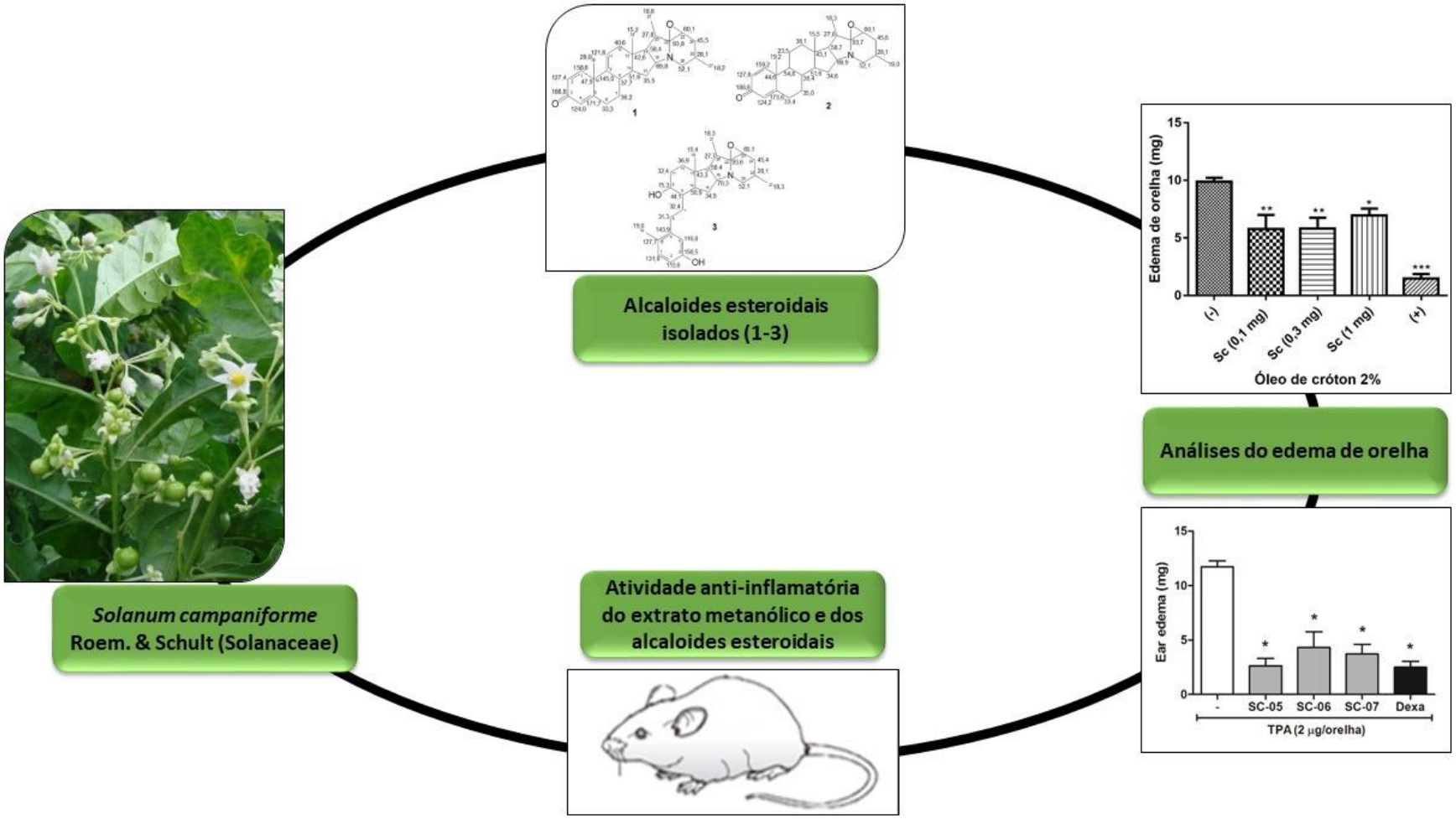


Figura 2 – Edema de orelha induzido por óleo de cróton tratado com os alcaloides esteroidais isolados da *S. campaniforme*. A orelha esquerda recebeu somente acetona e funcionou como controle negativo. Os alcaloides (SC-05, SC-06 e SC-07) (2µg/orelha) e o fármaco-padrão (0,1 mg/orelha de dexametasona) foram diluídos no mesmo volume de acetona e aplicados em seguida na orelha direita do grupo tratado e no controle positivo, respectivamente.


Alcaloides esteroidais isolados (1-3)
Análises do edema de orelha
Edema de orelha (mg)
(-)
Sc (0,1 mg)
Sc (0,3 mg)
Sc (1 mg)
(+)
Óleo de cróton 2%
Ear edema (mg)
SC-05
SC-06
SC-07
Dexa
TPA (2 µg/orelha)
Atividade anti-inflamatória do extrato metanólico e dos alcaloides esteroidais
Solanum campaniforme
Roem. & Schult (Solanaceae)

ANEXO A – NORMAS DE PUBLICAÇÃO DA REVISTA

Revista Brasileira de Farmacognosia

Instructions for Authors

Introduction

The Revista Brasileira de Farmacognosia-Brazilian Journal of Pharmacognosy is a periodical dedicated to the publication of original scientific work, reviews and communications in the field of Pharmacognosy (the study of crude drugs and substances derived from natural sources used as medicines).

Types of articles

The Brazilian Journal of Pharmacognosy accepts for publication original scientific work, reviews and communication articles written **only** in English.

• *Original papers:* Original papers are research articles describing original experimental results. The manuscript should be arranged in the following order: Graphical abstract, Title, Abstract, Keywords, Introduction, Material and Methods, Results, Discussion, Acknowledgements, Authorship, References, Figures with Legends, Tables, Structural Formulae and Supplemental files (if applicable). Results and Discussion sections may appear as a combined 'Results and Discussion' section. The normal length of the main text of an Original Paper (excluding references, tables, figures and figure legends) is approximately 3,000 words. Longer manuscripts may be accepted only in exceptional and well justified cases.

• *Short communications:* This section will cover mainly the isolation of known compounds from new neotropical sources, or complementary results of on-going work. The text should be arranged as follows: Graphical abstract, Title, Abstract of 200 words, Keywords, Introductory Remarks, Material and Methods with brief experimental details without subheadings, Results and Discussion as one body of text without headlines, Acknowledgements, Authorship, References (up to 20 citations) and Figures and/or Tables (up to 3). The text should not exceed 2,000 words.

• *Reviews*: Authors are invited to submit a review article that provides concise and critical updates on a subject, and with around 100 references. The main purpose of reviews is to provide a concise, accurate introduction to the subject matter and inform the reader critically of the latest developments in the field. They should be concise and include details of the search strategy used, such as time frame, search terms, used databases. A review should be an article that produces knowledge and not just a kind of survey of the existing literature. The review must be a response to an initial question. Reviews of a particular herbal drug will be considered if they contain the newest issue and a perspective on future directions.

Authors are strongly recommended to prepare a manuscript using a A4-sized paper, double-spaced, with Times New Roman size-12 font, fully justified, with margins of 2 cm.

Submission checklist

You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details.

Ensure the following:

i. One author has been designated as the corresponding author with contact details: Institutional e-mail address; full postal address.
ii. All authors, with their respective email addresses, should be entered into the system.
iii. All necessary files have been uploaded: Graphical abstract, Manuscript; Include keywords; All figures with Legends; All tables (including titles, description, footnotes); and Supplemental files (if applicable).
iv. All figure and table citations in the text match the files provided;
v. Manuscript has been 'spell checked' and 'grammar checked;
vi. All references mentioned in the Reference List are cited in the text, and vice versa;
vii. Permission has been obtained for use of copyrighted material from other sources (including the Internet);
viii. Relevant declarations of interest have been made;
ix. Journal policies detailed in this guide have been reviewed.

Before you begin

Ethics in publishing

Please see our information page on Ethical guidelines for journal publication.

Human and animal rights

If the work involves the use of human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals. Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

All articles involving studies with humans or animals should have the approval and authorization of the Ethics Committees on Research on Human Beings or on Animals of the institution to which the author(s) belong.

Declaration of interest

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. If there are no conflicts of interest then please state this: 'Conflicts of interest: none'. For more information, please contact the Managin Editor at revista@sbfgnosia.org.br.

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Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. To verify originality, your article may be checked by the originality detection service CrossCheck.

Contributors

Each author is required to declare his or her individual contribution to the article: all authors must have materially participated in the research and/or article preparation, so roles for all authors should be described. The statement that all authors have approved the final article should be true and included in the disclosure.

Authorship

All authors should have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Changes to authorship

Authors are expected to consider carefully the list and order of authors **before** submitting their manuscript and provide the definitive list of authors at the time of the original submission. Any addition, deletion or rearrangement of author names in the authorship list should be made only **before** the manuscript has been accepted and only if approved by the journal Editor. To request such a change, the Editor must receive the following from the **corresponding author**: (a) the reason for the change in author list and (b) written confirmation (e-mail, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of

addition or removal of authors, this includes confirmation from the author being added or removed.
Only in exceptional circumstances will the Editor consider the addition, deletion or rearrangement of authors **after** the manuscript has been accepted. While the Editor considers the request, publication of the manuscript will be suspended. If the manuscript has already been published in an online issue, any requests approved by the Editor will result in a corrigendum.

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You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should be stated.

Open Access

This is an open access journal: all articles will be immediately and permanently free for everyone to read and download.

Article Processing Charges

The Brazilian Society of Pharmacognosy (SBFgnosia) pays for most of the publishing costs incurred by the journal. But, authors are required to pay a small publication fee to the Brazilian Society of Pharmacognosy in order to share in the costs of production:

Payments will be received through the PayPal system for Overseas, which is a safe, flexible and well-established service for on-line payments, or by Bank transfer. Brazilian authors could make a bank deposit/transfer to Banco do Brasil account.

Sociedade Brasileira de Farmacognosia (CNPJ: 76.259.381/0001-90)

Processing fees:

- Corresponding author non-member of the SBFgnosia: US$ 450
- Corresponding author member of SBFgnosia: US$ 350
- Corresponding author member of SBFgnosia for more than two successive years US$ 300
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A limited number of waivers for article processing charges are also available at the editors' discretion, and authors wishing to apply for these waivers should contact the editors prior to submit their manuscripts.

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Language services

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the English Language Editing service available from journal's webpage.

Submission

Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (*e.g.*, Word, LaTeX) are required to typeset your article for

final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail.

Please submit your article via: https://www.evise.com/evise/jrnl/BJP

Additional information

- All plant, microorganism and marine organism materials used in the described research should be supported by an indication of the site (including GPS coordinates, if possible) and country of origin, the name of the person identifying the biological material and the location of the voucher specimen.

- Authors should be prepared to provide documentary evidence that approval for collection was afforded from an appropriate authority in the country of collection and, if applicable, to follow the rules concerning the biodiversity rights.

- The journal will not accept responsibility for research works that do not comply with the legislation of the country of residence of the author.

- We strongly recommend that authors avoid stating that the popular or traditional use of a certain herb was confirmed by pre-clinical, *in-vitro* or *in vivo* tests using animals.

- The Brazilian Journal of Pharmacognosy strongly encourages the submission of original works in which the experimental procedures were conducted taking into consideration green chemistry principles, such as by employing green solvents and environmental resource saving experimental designs in any step of the investigation.

- The following **immediate rejection criteria** apply

i. the manuscript does not fall into the areas of interest of the journal;

ii. manuscripts not formatted in accordance with the standards of the journal;

iii. the manuscript results are preliminary;

iv. manuscripts reporting activity data without comparison with a reference, without a positive control/appropriate control or not based on adequate statistics;

v. the biological source (e.g. plant, microorganism, marine organism etc.) is not clearly identified, authenticated and documented;

vi. experimental work on antioxidant activity of crude extracts without isolation, identification and content estimation of the active compounds; phenolic compounds are widely spread in nature and fully recognized as antioxidants or scavengers.

vii. experimental work on antimicrobial activity with crude extracts without isolation and identification of the active compounds, with large MIC values (µg/ml) for antimicrobial activity (≥250 µg/ml for plant extracts and ≥50 µg/ml for pure compounds) and without appropriate identification of culture collections/strain designation codes;

viii. experimental work on essential oils with only one sample of a single plant specimen with a single chromatographic analysis and without appropriate statistical analyses; without oil yield (%) and characterization and component quantification not undertaken using GC-MS-FID. Analyses of the retention indices of the components not calculated using *n*-alkane homologous series together with analyses of some of the isolated natural components. Biological activity of essential oil without chemical characterization.

ix. too preliminary data using in-vitro assays will not be acceptable if (i) no information on the type of activity is given; (ii) single dose or very high concentrations (must show dose–response studies); (iii) repetition of a simple bioassay (usually one assay with replicates); (iv) lack of appropriate controls (solvents; positive or negative substances according to the study); (v) no IC50 values (if applicable).

x. use of only the brine shrimp assay (*Artemia salina*) to access the toxicity of extracts;

xi. isolation and bioassay of well-known compounds with small or no relationship to the activity, or to the medicinal use of the plant without clear justification;

xiii. manuscripts reporting pharmacological or biological activities of crude extracts without chemical and technical standardization. Standardization of the plant extracts is considered to be the complete description of manufacturing parameters such as granulometry, solvent-plant ratio, time of extraction, solvent composition etc., together with marker quantification and chromatographic fingerprint analyses.

In addition to these Guidelines, a template (for original papers) is available at http://www.sbfgnosia.org.br/revista/templates.html.

Preparation

Peer review

This journal operates a single blind review process. All contributions will be initially assessed by the editor for suitability for the journal. Papers deemed suitable are then typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final.

Use of word processing software

Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

The manuscript should be arranged in the following order: Graphical abstract, Title, Abstract, Keywords, Introduction, Material and Methods, Results, Discussion, Acknowledgements, Authorship, References, Figures with Legends, Tables, Structural Formulae and Supplemental files (if applicable).

Subdivision - unnumbered sections

Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

Essential title page information

Title: Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

Author names and affiliations: Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author. Author affiliations should be presented in decreasing hierarchical order (e.g. Harvard University, Harvard Business School, Boston, USA) and should be written as established in its own language (e.g. Université Paris-Sorbonne; Harvard University, Universidade de São Paulo).

Corresponding author: Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that the institutional e-mail address is given and that contact details are kept up to date by the corresponding author.

Present/permanent address: If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Abstract

A structured abstract of ≤ 300 words, by means of appropriate headings, should provide the context or background for the research and should state its purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving

specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations. The journal does not accept abbreviations in the abstract.

Immediately after the abstract, provide a maximum of six keywords in alphabetical order and separated by commas, to represent the content of the article.

Please avoid using the plant name species in the keywords as it should be already in the title and/or in the abstract. Choose representative words to help indexation and readers to reach your article.

Graphical abstract

A Graphical abstract is mandatory for this journal. It should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership online. Authors must provide images that clearly represent the work described in the article. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: please provide an image with a minimum of 531 x times; 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files.

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Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

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Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.

Plant name species

Plant names should be complete, including author name and family, according to http://www.theplantlist.org/ or http://www.tropicos.org, and http://floradobrasil.jbrj.gov.br/2010/

Structural Formulae

Chemical structures are not considered as figures, should be numbered sequentially in bold letters according to their citations in the manuscript, and placed closed to the desired point in the manuscript body. Structures should be drawn according to the style set by the American Chemical Society.

Chemical structures of well-known compounds will not be published.

Abbreviations

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

Units

Follow internationally accepted rules and conventions: use the International System of Units (SI). If other units are mentioned, please give their equivalent in SI.

Math formulae

Please submit math equations as editable text and not as images. Present simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. In principle, variables are to be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Results

Results should be clear and concise.

Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

Authors contributions

The role of each author involved in the development of the study and/or the elaboration of the manuscript must be clearly described, and he/she should be referred to by his/her initials.

Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements: Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States

Institutes of Peace [grant number aaaa].It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding. If no funding has been provided for the research, please include the following sentence: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Artwork

The journal uses recycled paper, so colour figures are accepted and will abe available only on the online version.

Image manipulation

Whilst it is accepted that authors sometimes need to manipulate images for clarity, manipulation for purposes of deception or fraud will be seen as scientific ethical abuse and will be dealt with accordingly. For graphical images, this journal is applying the following policy: no specific feature within an image may be enhanced, obscured, moved, removed, or introduced. Adjustments of brightness, contrast, or color balance are acceptable if and as long as they do not obscure or eliminate any information present in the original. Nonlinear adjustments (*e.g.* changes to gamma settings) must be disclosed in the figure legend.

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General points

• Make sure you use uniform lettering and sizing of your original artwork.

• Preferred fonts: Arial (or Helvetica), Times New Roman (or Times), Symbol, Courier.

• Number the illustrations according to their sequence in the text.

• Use a logical naming convention for your artwork files.

• Indicate per figure if it is a single, 1.5 or 2-column fitting image.

• For Word submissions only, you may still provide figures and their captions, and tables within a single file at the revision stage.

• Please note that individual figure files larger than 10 MB must be provided in separate source files.

Formats

Regardless of the application used, when your electronic artwork is finalized, please 'save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.

TIFF (or JPG): Color or grayscale photographs (halftones): always use a minimum of 300 dpi.

TIFF (or JPG): Bitmapped line drawings: use a minimum of 1000 dpi.

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Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); the resolution is too low.

• Supply files that are too low in resolution.

• Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then the journal will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version.

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Ensure that each illustration has a caption. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules.

References

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Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal

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This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. This identifier will not appear in your published article.

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Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

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Text: All citations in the text should be chronologically and refer to:

Author in lower case, followed by the publication year between parenthesis, *e.g.* Pereira (1999); at the end of the citation: Author in lower case and year, both between parenthesis. *e.g.* (Silva, 1999) or (Silva and Souza, 1998) or (Silva et al., 1999) or (Silva et al., 1995a,b); textual citation: the page must be provided, *e.g.* (Silva, 1999, p. 24).

List: References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c' etc., placed after the year of publication.

Examples:

Reference to a journal publication: Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2010. The art of writing a scientific article. J. Sci. Commun. 163, 51-59.

Reference to a book: Strunk Jr., W., White, E.B., 2000. The Elements of Style, fourth ed. Longman, New York.

Reference to a chapter in an edited book: Mettam, G.R., Adams, L.B., 2009. How to prepare an electronic version of your article, in: Jones, B.S., Smith , R.Z. (Eds.), Introduction to the Electronic Age. E-Publishing Inc., New York, pp. 281-304.

Reference to a website: Cancer Research UK, 1975. Cancer statistics reports for the UK. http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/ (accessed 13 March 2003).

Reference to a dataset: [dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T., 2015. Mortality data for Japanese oak wilt disease and surrounding forest compositions. Mendeley Data, v1. https://doi.org/10.17632/xwj98nb39r.1.

Scientific meetings: Oliveira, R.M.M.W., Lolli, L.F., Santos, C.A.M., 2006. Possible involvement of GABAAbenzodiazepine receptor in the anxiolytic-like effect induced by *Passiflora actinia* extracts in mice. 19th ECNP Congress. Paris, France.

Patents: whenever possible the Chemical Abstracts Service number should be informed. Ichikawa, M., Ogura, M., Lijima, T., 1986. Antiallergic flavones glycoside from *Kalanchoe pinnatum*. Jpn. Kokai Tokyo Koho JP 61,118,396, apud Chemical Abstracts 105: 178423q.

Journal abbreviations source

Journal names should be abbreviated according to the https://www.library.caltech.edu/journal-title-abbreviations.

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Authors Inquiries

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ANEXO B – PARECER DO COMITÊ DE ÉTICA

Universidade Federal de Pernambuco
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Recife, 15 de dezembro de 2015.

Ofício nº 128/15

Da Comissão de Ética no Uso de Animais (CEUA) da UFPE
Para: **Prof.ª Roberta Jeane Bezerra Jorge**
Núcleo de Ciências da Vida
Centro Acâdemico do Agreste
Universidade Federal de Pernambuco
Processo nº 23076.017574/2015-23

Os membros da Comissão de Ética no Uso de Animais do Centro de Ciências Biológicas da Universidade Federal de Pernambuco (CEUA-UFPE) avaliaram seu projeto de pesquisa intitulado, **"Estudo do potencial anti-inflamatório de alcalóides esteroidais isolados de *Solanum campaniforme* Roem. & Schult. (Solanaceae)."**

Concluímos que os procedimentos descritos para a utilização experimental dos animais encontram-se de acordo com as normas sugeridas pelo Colégio Brasileiro para Experimentação Animal e com as normas internacionais estabelecidas pelo National Institute of Health Guide for Care and Use of Laboratory Animals as quais são adotadas como critérios de avaliação e julgamento pela CEUA-UFPE.

Encontra-se de acordo com as normas vigentes no Brasil, especialmente a Lei 11.794 de 08 de outubro de 2008, que trata da questão do uso de animais para fins cientificos e didáticos.

Diante do exposto, emitimos **parecer favorável** aos protocolos experimentais a serem realizados.

Origem dos animais: Biotério do Departamento de Antibióticos – CCB/UFPE; Animais: camundongos heterogênicos Swiss, 60 dias, 25-35g, 84 machos e 84 fêmeas; camundongos isogênicos BALB/c, 60 dias, 20-25g, 20 machos e 20 fêmeas; Nº total de animais no protocolo: 208.

Atenciosamente,

Prof. Dr. Pedro V. Carelli
Presidente da CEUA / CCB - UFPE
UFPE SIAPE 1801584