Rev Rene. 2021;22:e59963.
DOI: 10.15253/2175-6783.20212259963
www.periodicos.ufc.br/rene

Review Article

Pharmacological actions of bacuri butter (Platonia insignis Mart.): an integrative review

Atividades farmacológicas da manteiga de bacuri (Platonia insignis Mart.): revisão integrativa

How to cite this article:
Ribeiro JF, Figueiredo MLF, Carvalho ALM, Sousa Neto BP. Pharmacological actions of bacuri butter (Platonia insignis Mart.): an integrative review. Rev Rene. 2021;22:e59963. DOI: https://doi.org/10.15253/2175-6783.20212259963

José Francisco Ribeiro[1]
Maria do Livramento Fortes Figueiredo[1]
André Luís Menezes Carvalho[1]
Benedito Pereira de Sousa Neto[1]

[1]Universidade Federal do Piauí.
Teresina, PI, Brazil.

Corresponding author:
José Francisco Ribeiro
Qd – 28; Cs-6; St – C; Mocambinho.
CEP: 64010360. Teresina, PI, Brazil.
E-mail: jotafribeiro@yahoo.com.br

ABSTRACT

Objective: to identify the pharmacological activities of *bacuri* butter (*Platonia insignis* Mart.). **Methods:** an integrative review, carried out in the databases of Latin American and Caribbean Literature in Health Sciences, Cumulative Index to Nursing and Allied Health Literature, EMBASE, MEDLINE/PubMed, Web of Science, Cochrane Library and SCOPUS, without the time and language restriction. The selection consisted of 13 pre-clinical trials. The information assessment descriptively took place, comparing with the pertinent findings. **Results:** it was observed that 50.0% of the publications were indexed in MEDLINE/PubMed, most publications were from England (61.5%), followed by Brazil and the United States, both with 13.3%. It is noteworthy that 100.0% of the articles were pre-clinical trials; pharmacological activities for antioxidants (38.4%) and antileishmanicides (30.7%). It was found that 38.4% of the trials presented toxicity tests. **Conclusion:** *bacuri* butter (*Platonia insignis* Mart.) Showed pharmacological activities in pre-clinical trials, such as antioxidants, antileshimaniasis, anticonvulsant and wound healing.

Descriptors: Clusiaceae; Benzophenones; Drug Compounding; Drug Synergism; Drug Therapy.

RESUMO

Objetivo: identificar as atividades farmacológicas da manteiga de bacuri (*Platonia insignis* Mart.). **Métodos:** revisão integrativa, realizada nas bases de dados Literatura Latino-americana e do Caribe em Ciências da Saúde, *Cumulative Index to Nursing and Allied Health Literature*, EMBASE, MEDLINE/PubMed, *Web of Science*, *Cochrane Library* e SCOPUS, sem delimitação temporal e de idioma. A seleção se constituiu de 13 ensaios pré-clínicos. A avaliação das informações ocorreu de forma descritiva, confrontando com os achados pertinentes. **Resultados:** observou-se que 50,0% das publicações foram indexadas na MEDLINE/PubMed, maioria das publicações ocorreram na Inglaterra (61,5%), seguidas do Brasil e dos Estados Unidos, ambos com 13,3%. Destaca-se que 100,0% dos artigos foram ensaios pré-clínicos; atividades farmacológicas para antioxidante (38,4%) e antileishmanicidas (30,7%). Registrou-se que 38,4% dos ensaios apresentaram testes de toxicidade. **Conclusão**: a manteiga de bacuri (*Platonia insignis* Mart.) apresentou atividades farmacológicas em ensaios pré-clínicos, como antioxidantes, antileshimaniose, anticonvulsivante e cicatrização de feridas.

Descritores: Clusiaceae; Benzofenonas; Composição de Medicamentos; Sinergismo Farmacológico; Tratamento Farmacológico.

Received: June 30th 2020; Accepted: Sep. 9th 2020.

Introduction

The use of medicinal herbs is understood as a promising option. Vegetables are capable of biosynthesizing compounds for self-protection in response to environmental damage. The relevance is clarified by the wide diversity of metabolites generated by these species, with different chemical, physical and biological properties, most of which are possibly bioactive against various diseases, considering the empirical use. In this context, compounds synthesized by species native to Brazil that have pharmacological action and with low toxicity may represent alternatives for the treatment of many diseases[1].

Platonia insignis, traditionally called *bacurizeiro*, a fruitful, woody tree, has a dense and diverse population, easily found from the Amazon to Piauí, in Brazil. It belongs to the family *Clusiaceae*, consisting of approximately one thousand species and forty-seven genus, spread in tropical, subtropical, and temperate regions. In Brazil, the use of *Platonia insignis* in medical practices is very common, being indicated as healing, antimicrobial, digestive, diuretic, antitumor, cytotoxic and antioxidant[2].

Bacurizeiro (*Platonia insignis* Mart.) Is characterized by having fleshy fruits with more than one seed, with rounded, oval, or concave configuration and average weight according to the region. There are those who produce bulky fruits, weighing more than 1 kg. The number of seeds varies from one to six[3].

The oil or butter extracted from the seeds of *bacuri* (*Platonia Insignis* Mart.) has been used as a raw material for making soap, as well as treating skin diseases and formulating healing substances for animal wounds[4]. Currently, herbal medicine researchers have shown increasing interest in *Platonia insignis* (mainly seeds), to optimize the biological effects[4].

Bacuri butter has excellent absorption, attributed to the components immersed in it, such as tripalmitin (50 to 55.0%), which guarantees a high permeability action on the skin. The palmitoleic acid (5.0%) has an emollient and humidifying pharmacological activity[3-4].

In the hexane extract of *bacuri* seeds, a chemical compound, polyprenylated polycyclic acylfloroglucinol, was isolated, in tautomeric form, called *garcinielliptone* FC, a little-known compound in the genus Platonia, in which was found the polyprenylated benzophenone with several pharmacological activities[5].

Polyprenylated benzophenones are secondary metabolites of plants causing increasing interest, mainly because of their pharmacological properties. Previous in vitro studies have shown that the compound *garcinielliptone* FC, a substance isolated from *bacuri* seeds, has an antioxidant, blood vessel relaxing and antiparasitic effect[6].

Research related to the genus *Platonia* isolated several biologically active natural substances, xanthones and chloroglucinol derivatives, which constitute the main class of metabolites existing in the *Clusiaceae* family. These derivatives have been extensively investigated for biological activities, including pharmacological activities[7].

Bacuri butter formulations are still at an early stage of discovery to officially work as drugs in the treatment of diseases in humans. However, pre-clinical trials are necessary. Given the context, this study aimed to identify the pharmacological activities of *bacuri* butter (*Platonia insignis* Mart.).

Methods

An integrative review was carried out, established by theoretical framework, following the steps: 1) choice of the guiding question, 2) sample or publication investigation, 3) recruitment of the sample's articles, 4) collecting of information from the included articles, 5) evaluation and meaning of the retrieved data and 6) presentation of the review or evaluation of the collected findings[8].

For the creation of the guiding question, the acronym PICO was adopted, determining: P (population): *Platonia insignis* Mart., I (interest): *Garcinielliptone* FC; *Clusiaceae*, C (it does not have) and O (context): composition of medicines. Thus, the guiding

question was: what are the pharmacological actions of *bacuri* butter (*Platonia insignis*)?

Primary original articles were included, without the time and language restriction, that addressed the pharmacological actions of *bacuri* butter (*Platonia insignis* Mart.). Congress abstracts, theses, dissertations, reviews, and editorials were excluded.

The investigation was carried out in June 2020, through searches carried out in the bases Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE, Cochrane Library, Web of Science, SCOPUS and Latin American and Caribbean Literature in Health Sciences (LILACS). Interval interception was performed with the descriptors and the title words, using the Boolean operator and as a strict combination, applying the strategies: 1) *Platonia insignis* Mart. and *Garcinielliptone FC* and drug compounding; 2) *Garcinielliptone FC* and *Clusiaceae* and drug compounding 3) *Platonia insignis* Mart and *Garcinielliptone FC* and drug compounding. The descriptors were accessed through the presence of the terms of the Medical Subject Headings (MeSH), Descriptors in Health Sciences (DeCS) and List of Headings of the Cumulative Index of Nursing Literature.

The articles were accessed through the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (Coordination for the Improvement of Higher Education Personnel). The selection was developed by two reviewers, independently, in two stages: the first, the title and abstract were read, and in the second, the full text. In cases of disagreement, there was a discussion between the two evaluators to reach a consensus.

The search resulted in 49 publications. In the first stage, according to established standards, 15 productions were selected. In the second, two productions were removed, totaling 13 articles, which comprised the total number of articles for analysis. Figure 1 outlines the selected articles.

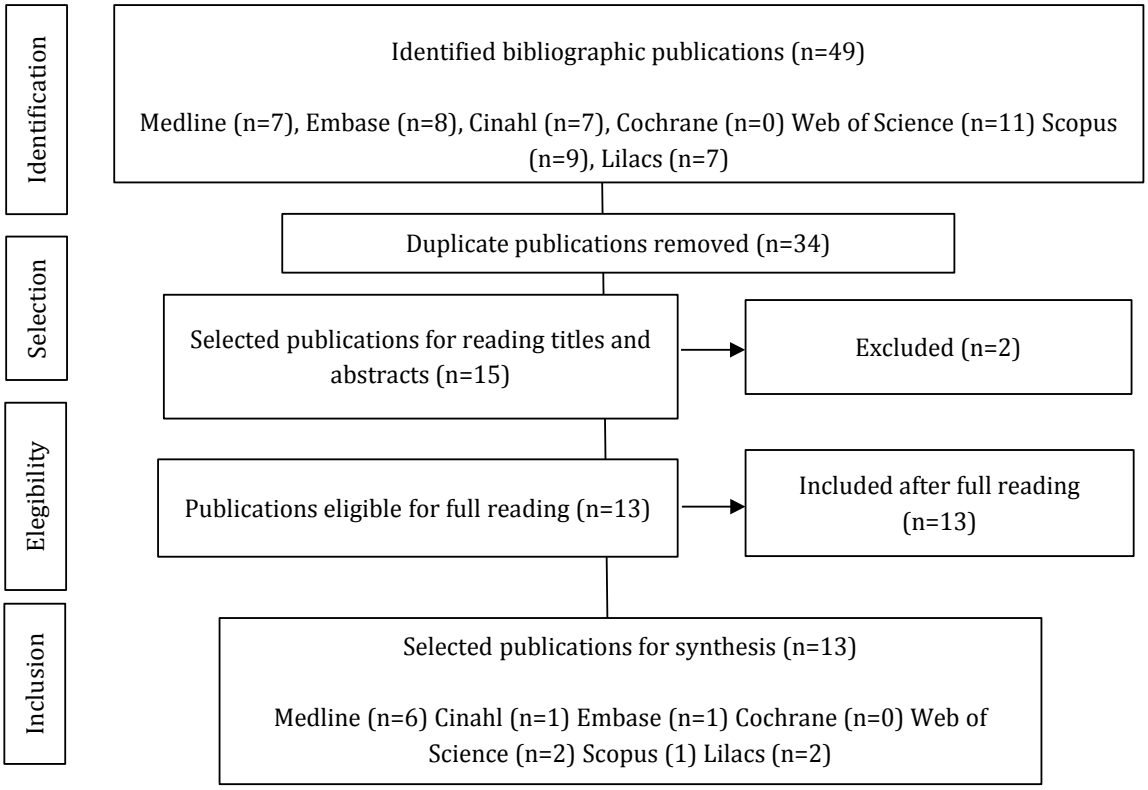

Figure 1 – Flowchart of publications, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes protocol[9]. Teresina, PI, Brazil, 2020

The organization of the information retrieved from the articles was transcribed into a previously prepared document, considering information about the main author, journal and year of publication, design/sample, pharmacological action, and category of evidence.

The category of evidence was classified according to the model proposed by the authors[8], who consider: category I – a systematic review or meta-analysis of valuable clinical trials; category II - very limited controlled randomized controlled trial; category III - clinical trial supported by a non-randomized design; category IV - cohort and case-control study with adequate design; category V – a systematic review of descriptive and qualitative research; category VI - descriptive or qualitative research; category VII - judgment of authorities or narratives of expert committees. The synthesis of the results was carried out quantitatively and descriptively.

Results

The results are shown in Figure 2, in the following order: main author, journal and year; design/sample; and pharmacological action. It was observed that most of the articles came from international journals, published in the English language, only one in Portuguese and indexed in the MEDLINE/PubMed databases. The most evident country was England, with the largest number of publications (61.5%), followed by Brazil and the United States, both with 13.3%. It is noteworthy that 100% of the articles were evidence II pre-clinical trials. It was registered that 38.4% of the information indicated pharmacological actions for antioxidants; cutaneous leishmaniasis (30.7%); epilepsy (15.3%); scarring; schistosomiasis; cancer and immunomodulator were 3.9%, respectively. As for the toxicity represented by cytotoxicity, genotoxicity, and mutagenicity, it was observed that 38.4% had tests for toxicity associated with the pharmacological action (Figure 2).

Authors, Journals Place/year	**Titles**	**Design/sample**	**Pharmacological action**	**Evidence category**
Santos Júnior RQ, et al. Conscientiae Saúde. Brazil/2010[10]	Histologic study of skin of wounds healing using the cream of *bacuri* (Platonia insignis)	Pre-clinical trial/46 male Wistar rats	Wound healing	II
Costa Júnior JS, et al. Epilepsy Behav. United States/2011[11]	Evaluation of possible antioxidant and anticonvulsant effects of the ethyl acetate fraction from Platonia insignis Mart. (*Bacuri*) on epilepsy models	Pre-clinical trial/240 male Wistar rats	Antioxidant	II
Costa Júnior JS, et al. Pharm Biol. England/2012[12]	Superoxide dismutase and catalase actions in rat hippocampus pretreated with garcinielliptone FC from Platonia insignis	Pre-clinical trial/57 male Wistar rats	Antioxidants and anticarcinogenic	II
Costa Júnior JS, et al. Nat Prod Res. England/2013[13]	Cytotoxic and leishmanicidal properties of garcinielliptone FC, a prenylated benzophenone from Platonia insignis	Pre-clinical trial/human cancer cells: colon, lung, and breast) and Leishmania promastigotes, from Amazon	leishmanicides	II
Costa Júnior JS, et al. Basic Clin Pharmacol Toxicol. England/2013[14]	Investigation of biological actions of dichloromethane and ethyl acetate fractions of Platonia insignis Mart. seed	Pre-clinical trial/Artemia salina and *Saccharomyces cerevisiae*	Antioxidants	II

(the Figure 2 continue in the next page...)

Silva AP, et al. Pharmacol Biochem Behav. United States/2014[15]	Behavioral and neurochemical studies in mice pretreated with garcinielliptone FC in pilocarpine-induced seizures	Pre-clinical trial/50 male and female Swiss mice, weighing 25-35g, divided into five groups of 10	Antiepileptic	II
Silva AP, et al. Toxicol In Vitro. England/2015[16]	Garcinielliptone FC: Antiparasitic action without cytotoxicity to mammalian cells	Pre-clinical trial/*Schistosoma mansoni* (BH strain), *Mesocricetus auratus* hamsters, infected by 150 *S. mansoni cercariae*	Anti-schistosomal	II
Silva APSCL, et al. Phytomedicine. Germany/2016[17]	Pre-clinical toxicology of garcinielliptone FC, a tautomeric pair of polyprenylated benzophenone, isolated from Platonia insignis Mart seeds	Pre-clinical trial/Swiss mice of both sexes, weighing 25-30g, divided into three separate groups of five animals matched by weight and size	Antiepileptic and antioxidant	II
Lustosa AKMF, et al. Braz J Pharmacognosy. Brazil/2016[6]	Immunomodulatory and toxicological evaluation of the fruit seeds from Platonia insignis, a native species from Brazilian Amazon Rainforest	Pre-clinical trial/female Wistar rats (200-250g, n=5 per group) and male Balb/males (25-30g)	Antioxidant Immunomodulator	II
Silva PL, et al. Basic Clin Pharmacol Toxicol. England/2017[18]	Evaluation of DNA damage in HepG2 cells and mutagenicity of garcinielliptone FC, A bioactive benzophenone	Pre-clinical trial/*Salmonella Typhimurium* (five strains of 400 cells per concentration)	Immunomodulator	II
Coelho VR, et al. Basic Clin Pharmacol Toxicol. England/2018[19]	A 28-day sub-acute genotoxic and behavioural assessment of garcinielliptone FC	Pre-clinical trial/60 male Swiss mice	Antioxidant	II
Coêlho ES, et al. Drug Dev Ind Pharm. England/2018[20]	Emulgel based on amphotericin B and *bacuri* butter (Platonia insignis Mart.) for the treatment of cutaneous leishmaniasis: characterization and in vitro assays	Pre-clinical trial/*Leishmaniasis promastigotes* in 96-field cell culture plates	Anti-leishmaniasis	II
Bezerra EA, et al. Toxicol In Vitro England/2020[21]	Selective anti-amastigote and immunomodulatory effects on macrophages infected by Leishmania amazonensis	Pre-clinical trial/Mice (25 - 30) and promastigotes of *Leishmania amazonensis*	Anti-leishmaniasis	II

Figure 2 – Distribution of selected studies, according to authors, journals, places, year, titles, types of study, samples, pharmacological actions, and evidence categories. Teresina, PI, Brazil, 2020

Discussion

The insufficient production of scientific papers that addressed *bacuri* butter in clinical trials is considered an important limitation of this study. Thus, this study aims to contribute to research in natural products and the development of formulations containing *bacuri* butter for human treatments, because of the absorption potential and reduced adverse effect of this product.

It is highlighted that the investigation of new drugs from plants has supported the discovery of metabolites with important therapeutic potential for the development of new herbal medicines, through isolation, clarification of the structure, composition and bioactivity analysis[21]. The continuous search for robust pre-clinical trials with medicinal plants is evident, however, there is limited research that addres-

ses the pharmacological actions of *bacuri* butter (*Platonia insignis* Mart.), mainly in clinical trials.

Cutaneous leishmaniasis is a condition with a high incidence and the ability to cause deformities. The first-choice treatment, recommended by the World Health Organization, with pentavalent antimonial, is offensive and very toxic. Therefore, the development of a drug for topical treatments can happen as a positive option and less harmful to the user's health[22]. As for the pharmacological action of *bacuri* butter for cutaneous leishmaniasis, it was observed in a preclinical trial that the authors detected that the compounds developed showed a promising antileishmanial action and a high potential for topical use[19].

Traditionally, the leishmaniasis treatment is carried out with antimonial, drugs settled for use since 1945, marketed as N-methyl glucamine antimoniate (Glucantime), in Latin America and Africa, and the sodium stibogluconate Pentostam, in the United States and Europe. The antimonials marketed in India and China, Pentostam, show similar results for the clinical forms of American cutaneous leishmaniasis. The most common side effects of antimonials are: joint pain, muscle pain, anorexia, nausea, vomiting, epigastric discomfort, heartburn, itching, hyperthermia, migraine, increased liver enzymes and alkaline phosphatase, acute kidney disorder, by modifying the release of vasopressin and renal tubular cytotoxicity, pancreas inflammation[23-24]. It was also evident in research whose purpose was to evaluate the cytotoxic and leishmanicidal effects of *bacuri* butter, using in vitro models, that the experimental findings showed that the benzophenone garcinielliptone poliisoprenilada, compounds of *bacuri* butter, has low toxicity to the host and high leishmanicidal toxicity[25].

As for human schistosomiasis, a neglected tropical disease, originated by worms of the genus Schistosoma, responsible for more than 280,000 deaths per year, the treatment of this disease currently comes from a single drug, praziquantel (PZQ). The care with resistance to PZQ and the insensitivity of juvenile schistosomes has increased the interest in using medicinal plants for alternative drug therapies[26]. As an example, it was found that formulations with *bacuri* butter showed *in vitro* action for *Schistosoma mansoni*, granting toxicity to the cells of this helminth[15,26]. Besides *bacuri* formulations, there are other herbal medicines with pharmacological actions like *bacuri* butter.

Another research aimed at analyzing the effect of the hexane and crude ethanolic extracts obtained from *Phyllanthus amarus* (stone breaker), in mice infected with *Schistosoma mansoni*, the authors detected anti-schistosomiasis actions, however, acting differently, according to the parasite's age[27].

Regarding epilepsy observed by a temporary and reversible change in brain activity, which has not been caused by fever, drugs or metabolic disorders and is expressed by repeated epileptic seizures, drug therapy, in some cases, requires regular adjustments of the drugs valproate, carbamazepine , lamotrigine and other anticonvulsants in addition or exchange to lithium[27]. As a future option for the epilepsy treatment, a behavioral and neurochemical study in mice provided anticonvulsant action[14].

As for antioxidant agents, research on the role of cellular nutrients shows that certain nutritive substances from food have enhanced antioxidant action, showing a propensity to convert and decrease the oxidation action of free radicals, inhibiting the harmful consequences to the body and instability in the production of free radicals and their suppression by antioxidant protection, given that oxidative stress causes damage to cell membranes, as well as nucleic acids, proteins and polysaccharides, leading to initial changes and the spread of different diseases[28]. Pharmacological actions of *bacuri* butter as an antioxidant were also observed[9,16]. *Bacuri* seed and pulp are sources of vitamin C, which guarantees antioxidant action.

As for toxicity, it was found that 64.5% of preclinical trials did not reveal the existence of preclinical toxicity, such as cytotoxic, genotoxic, and mutagenic, it is believed that these experiments followed previous criteria of other research with *bacuri* butter, which

analyzed the toxicity, considering that the test of this element presents itself as the first step in experimental studies.

It was detected in a topical formulation of amphotericin B with *bacuri* butter, to evaluate antileishmanial action, through *in vitro* tests, in which *bacuri* butter and the drug presented low toxicity to host cells. This proposition clarifies the need to perform toxicity tests *in vitro* and *in vivo*, recommended for the use of medicines for humans, issued by international or national regulatory bodies, analyzed, and then adopted to be used in the toxicity assessment. Thus, based on the compilation of these demonstrated regulations, tests are advised to assess toxicity in vitro cytotoxicity, genotoxicity, acute and repeated dose toxicity, carcinogenicity, reproductive and developmental toxicity, evidence of local tolerance, additional toxicokinetic and toxicity studies, including safety pharmacology[19,29].

Herbal medicines, before being used by humans, must be assessed for toxicity, which aims to ensure its safety for the use. *Bacuri* butter showed significant action in terms of potential, low toxicity to cells was observed in preclinical tests and, in some cases, very toxic to the cells of agents harmful to the host organism[11,17,30].

Regarding immunomodulatory action, *bacuri* butter (*Platonia insignis* Mart.) showed an increase in the organic response against certain microorganisms or substances unwanted to the organism, besides a high potential for immunomodulatory action, observed in the wound healing process and reduction of cancer cells[8,16].

Conclusion

Evidence has shown that *bacuri* butter has pharmacological actions, such as antioxidants, antileishmanicides, antischistosomiasis, antiepileptics, anticancer and immunomodulators, according to preclinical tests carried out, findings of great relevance for the execution of robust clinical trials.

Collaborations

Ribeiro JF collaborated with the review's concept, analysis, and data interpretation. Figueiredo MLF and Carvalho ALM contributed to writing the article and relevant critical review of the intellectual content. Sousa Neto BP participated in the final approval of the version to be published.

References

1. Agra MDF, Silva KN, Basílio IJLD, Freitas PF, Barbosa-Filho JM. Survey of medicinal plants used in the region Northeast of Brazil. Rev Bras Farmacogn. 2008; 18(3):472-508. doi: https://doi.org/10.1590/S0102-695X2008000300023

2. Rufino MSM, Alves RE,Brito ES, Pérez JJ, Saura CF, Mancini-Filho J. Bioactive compounds and antioxidant capacities of 18 non-traditional tropical fruits from Brazil. Food Chem. 2010; 121(4):996-1002. doi: https://dx.doi.org/10.1016/j.foodchem.2010.01.037

3. Carvalho JEU, Alves SDM, Nascimento WMO, Müller CH. Características físicas e químicas de um tipo de bacuri (Platonia insignis Mart.) sem sementes. Rev Bras Frutic. 2002; 24(2):573-5. doi: https://doi.org/10.1590/S0100-29452002000200060

4. Silva BMH, Serruya H, Rocha Filho GN, Oliveira GRL, Silva CJA, Soares MJG. Estudo químico das sementes de bacuri. Acta Amaz. 1986; 16:363-8. doi: https://doi.org/10.1590/1809-43921986161368

5. Arcanjo DDR, Costa-Júnior JS, Moura LHP, Ferraz ABF, Rossatto RR, David JM, et al. Garcinielliptone FC, a polyisoprenylated benzophenone from Platonia insignis Mart., promotes vasorelaxant effect on rat mesenteric artery. Nat Prod Res. 2014; 28(12):923-7. doi: https://dx.doi.org/10.1590/1809-43921986161368.

6. Lustosa AKMF, Arcanjo DDR, Ribeiro RG, Rodrigues KAF, Passos FFB, Piauilino CA, et al. Immunomodulatory and toxicological evaluation of the fruit seeds from Platonia insignis, a native species from Brazilian Amazon rainforest. Rev Bras Farmacogn. 2016; 26(1):77-82. doi: https://doi.org/10.1016/j.bjp.2015.05.014

7. Almanza GR, Quispe R, Mollinedo P, Rodrigo G, Fukushima O, Villagomez R, et al. Antioxidant and antimutagenic polyisoprenylated benzophenones and xanthones from Rheedia acuminata. Nat Prod Commun. 2011; 6(9):1269-74 doi: https://doi.org/10.1177/1934578X1100600916

8. Whittemore R, Knafl K. The integrative review: updated methodology. J Adv Nurs. 2005; 52(5):546-53. doi: https://doi.org/10.1111/j.1365-2648.2005.03621.x

9. Mendes KDS, Silveira RCCP, Galvão CM. Revisão integrativa: método de pesquisa para a incorporação de evidências na saúde e na enfermagem. Texto Contexto Enferm. 2008; 17(4):758-64. doi: https://doi.org/10.1590/S0104-07072008000400018

10. Santos Júnior RQ, Soares LC, Maia Filho ALM, Araujo KS, Santos ÍMSP, Costa Júnior JSC, et al. Histologic study of skin of wounds healing using the cream of bacuri (Platonia insignis Mart.). Conscientiae Saúde [Internet]. 2010 [cited Jul 13, 2020]; 9(4):575-81. Availabble from: https://www.redalyc.org/articulo.oa?id=92921672004

11. Costa Júnior JS, Almeida AAC, Tomé AR, Citó AMGP, Saffi J, Freitas RM. Evaluation of possible antioxidant and anticonvulsant effects of the ethyl acetate fraction from Platonia insignis Mart. (Bacuri) on epilepsy models. Epilepsy Behav. 2011; 22(4):678-84. doi: https://doi.org/10.1016/j.yebeh.2011.09.02

12. Costa Júnior JS, Almeida AAC, Costa JP, Citó AMGP, Saffi J, Freitas RM. Superoxide dismutase and catalase activities in rat hippocampus pretreated with garcinielliptone FC from Platonia insignis. Pharm Biol. 2012; 50(4):453-7. doi: https://doi.org/10.3109/13880209.2011.611146

13. Costa Júnior JS, Almeida AMC, Ferraz ABF, Rossatto RR, Silva TG, Silva PBN, et al. Cytotoxic and leishmanicidal properties of garcinielliptone FC, a prenylated benzophenone from Platonia insignis. Nat Prod Res. 2013; 27(4-5):470-4. doi: 10.1080/14786419.2012.695363

14. Costa Júnior JS, Ferraz ABF, Sousa TO, Silva RAC, Lima SG, Feitosa CM, et al. Investigation of biological activities of dichloromethane and ethyl acetate fractions of Platonia insignis Mart. seed. Basic Clin Pharmacol Toxicol. 2013; 112(1):34-41. doi: https://doi.org/10.1111/j.1742-7843.2012.00924.x

15. Silva APSCL, Lopes JSL, Vieira PS, Pinheiro EEA, Silva MLG, Silva FJCCL, et al. Behavioral and neurochemical studies in mice pretreated with garcinielliptone FC in pilocarpine-induced seizures. Pharmacol Biochem Behav. 2014; 124:305-10. doi: https://doi.org/10.1111/j.1742-7843.2012.00924.x

16. Silva AP, Silva MP, Oliveira CG, Monteiro DC, Pinto PL, Mendonça RZ, et al. Garcinielliptone FC: antiparasitic activity without cytotoxicity to mammalian cells. Toxicol In Vitro. 2015; 29(4):681-7. doi: https://doi.org/10.1016/j.tiv.2014.12.014

17. Silva APSCL, Oliveira GLS, Medeiros SC, Sousa AML, Lopes LS, David JM, et al. Pre-clinical toxicology of garcinielliptone FC, a tautomeric pair of polyprenylated benzophenone, isolated from Platonia insignis Mart seeds. Phytomedicine. 2016; 23(5):477-82. doi: https://doi.org/10.1016/j.phymed.2016.02.013

18. Silva PL, Silva J, Garcia ALH, Boaretto FBM, Grivicich I, Conter LU, et al. Evaluation of DNA damage in HepG2 cells and mutagenicity of garcinielliptone FC, A bioactive benzophenone. Basic Clin Pharmacol Toxicol. 2017; 120(6):621-7. doi: https://doi.org/10.1111/bcpt.12753

19. Coelho VR, Prado LS, Rossato RR, Ferraz ABF, Vieira CG, Souza LP, et al. A 28-day sub-acute genotoxic and behavioural assessment of garcinielliptone FC. Basic Clin Pharmacol Toxicol. 2018; 123(2):207-12. doi: https://doi.org/10.1111/bcpt.13010

20. Coêlho ES, Lopes GLN, Pinheiro IM, Holanda JNP, Alves MMM, Carvalho NN, et al. Emulgel based on amphotericin B and bacuri butter (Platonia insignis Mart.) for the treatment of cutaneous leishmaniasis: characterization and in vitro assays. Drug Dev Ind Pharm. 2018; 44(10):1713-23. doi: https://doi.org/10.1080/03639045.2018.1492610

21. Bezerra ÉA, Alves MMM, Amorim LV, Carvalho RCV, Cruz LPL, Costa Júnior JS, et al. Garcinielliptone FC: Selective anti-amastigote and immunomodulatory effects on macrophages infected by Leishmania amazonensis. Toxicol In Vitro. 2020; 63:104750. doi: https://doi.org/10.1016/j.tiv.2019.104750

22. Piccinelli AL, Campone L, Dal Piaz F, Cuesta-Rubio O, Rastrelli L. Fragmentation pathways of polycyclic polyisoprenylated benzophenones and degradation profile of nemorosone by multiple-stage tandem mass spectrometry. J Am Soc Mass Spectrom. 2009; 20(9):1688-98. doi: https://doi.org/10.1016/j.jasms.2009.05.004

23. Chattopadhyay A, Jafurulla M. A novel mechanism for an old drug: amphotericin B in the treatment of visceral leishmaniasis. Biochem Biophys Res Commun. 2011; 416(1-2):7-12. doi: https://doi.org/10.1016/j.bbrc.2011.11.023

24. Reis SR, Gomes LHM, Ferreira NM, Nery LR, Pinheiro FG, Figueira LP, et al. Ocorrência de flebotomíneos (Diptera: Psychodidae: Phlebotominae) no ambiente peridomiciliar em área de foco de transmissão de leishmaniose tegumentar no município de Manaus, Amazonas. Acta Amaz. 2013; 43(1):121-3. doi: https://doi.org/10.1590/S0044-59672013000100016

25. Amato VS, Paula JG, Boulos MIC, Nicodemo EL, Boulos M, Neto VA. Tratamento da leishmaniose tegumentar americana. Rev Bras Med. 1996; 53(4):202-14. doi: https://doi.org/10.1590/S0365-05962007000200002

26. Souza AC, Alves MMM, Brito LM, Oliveira LGC, Sobrinho-júnior CPC, Costa ICG, et al. Platonia insignis Mart., a Brazilian Amazonian Plant: the stem barks extract and its main constituent lupeol exert antileishmanial effects involving macrophages activation. Evid Based Complement Alternat Med. 2017; 2017:3126458. doi: https://doi.org/10.1155/2017/3126458

27. Oliveira CNF, Frezza TF, Garcia VL, Figueira GM, Mendes TMF, Allegretti SM. Schistosoma mansoni: In vivo evaluation of Phyllanthus amarus hexanic and ethanolic extracts. Exp Parasitol. 2017; 183:56-63. doi: https://doi.org/10.1016/j.exppara.2017.10.008

28. Hopker CDC, Berberian AP, Massi G, Willig MH, Tonocchi R. The individual with epilepsy: perceptions about the disease and implications on quality of life. CoDAS. 2017; 29(1):e20150236. doi: https://dx.doi.org/10.1590/2317-1782/20172015236

29. Olela B, Mbaria J, Wachira T, Moriasi G. Acute oral toxicity and anti-inflammatory and analgesic effects of aqueous and methanolic stem bark extracts of piliostigma thonningii (Schumach.). Evid Based Complement Alternat Med. 2020; 2020:5651390. doi: https://doi.org/10.1155/2020/5651390

30. Valente D, Costa-Amaral IC, Carvalho LVB, Santos MVC, Castro VS, Rodrigues DRF, et al. Utilização de biomarcadores de genotoxicidade e expressão gênica na avaliação de trabalhadores de postos de combustíveis expostos a vapores de gasolina. Rev Bras Saúde Ocup. 2017; 42(suppl 1):1-21. doi: https://doi.org/10.1590/2317-6369000124415