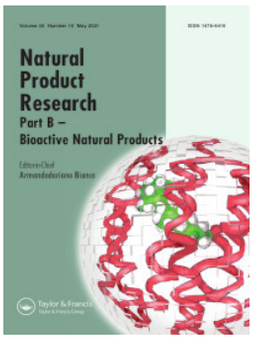

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Natural Product Research

Formerly Natural Product Letters

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/gnpl20

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To cite this article: Pollyana Mendonça de Assis, Rafael Cypriano Dutra, Cristine Bastos do Amarante, Maria das Graças Afonso Miranda Chaves, Carolina Paula de Souza Moreira, Marcos Antônio Fernandes Brandão & Nádia Rezende Barbosa Raposo (2021) *Plinia cauliflora* (Mart.) Kausel: toxicological assays, biological activities, and elemental analysis of organic compounds, Natural Product Research, 35:10, 1727-1731, DOI: 10.1080/14786419.2019.1633642

To link to this article: https://doi.org/10.1080/14786419.2019.1633642

NATURAL PRODUCT RESEARCH
2021, VOL. 35, NO. 10, 1727–1731
https://doi.org/10.1080/14786419.2019.1633642

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SHORT COMMUNICATION

Plinia cauliflora (Mart.) Kausel: toxicological assays, biological activities, and elemental analysis of organic compounds

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ABSTRACT

Jaboticaba, *Plinia cauliflora* (Mart.) Kausel, is a Brazilian berry traditionally used in folk medicine as treatment for some health conditions. Phenolic compounds such as flavonoids and anthocyanins have previously been detected in the fruit. This current study aimed to evaluate the toxicological effects of jaboticaba peel extract (JPE) on *Artemia salina*, L929, and MDA-MB-231 cell lines. Besides, JPE antioxidant, acetylcholinesterase, and antifungal activities, and elemental analysis CHNS were also tested. JPE had moderate toxicity (LD_{50} = 360.92 μg mL^{-1}) on *A. salina*, non-toxic effect on L929 cell line, and decreased the viability of cancer cell line MDA at 1,000 μg mL^{-1} and 500 μg mL^{-1} concentrations. The antioxidant activity toward 2,2-diphenyl-1-picrylhydrazyl (DPPH) performed IC_{50} = 37.45 ± 0.17 μg mL^{-1}, whereas 45.7% of acetylcholinesterase activity was inhibited. By its elemental composition, JPE is an alternative food supplement and dermocosmetic component. Antifungal potential toward Candida strains was not observed.

ARTICLE HISTORY
Received 20 October 2018
Accepted 7 June 2019

KEYWORDS
Jaboticaba; cell viability; antiproliferative; antioxidant capacity; acetylcholinesterase activity; elemental analysis

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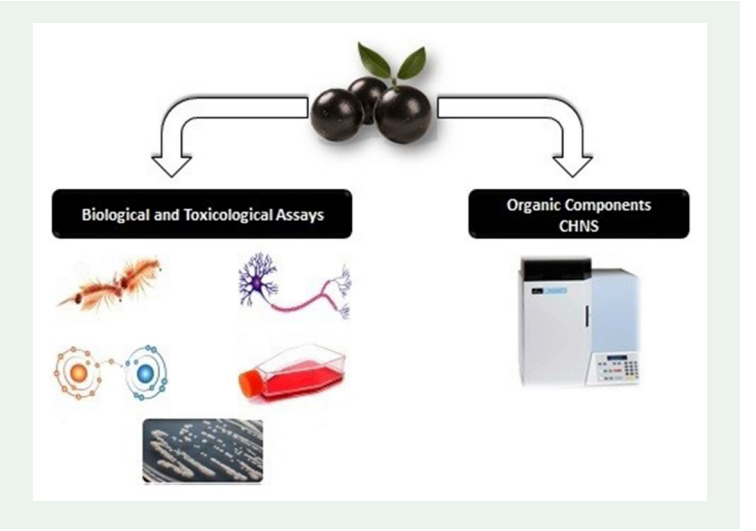
Supplemental data for this article can be accessed at https://doi.org/10.1080/14786419.2019.1633642.



1. Introduction

Jaboticaba, *Plinia cauliflora* (Mart.) Kausel is a Brazilian native berry that belongs to the Myrtaceae family (Bailão et al. 2015). It may also be called *Myrciaria cauliflora* (Mart.) O.Berg., a synonym for the plant species (Sobral et al. 2015). The fruit is consumed *in natura* or in processed forms such as jams, ice creams, and liquors. In folk medicine, parts of the plant are used as a natural treatment for asthma, diarrhea, and inflammation (Donado-Pestana et al. 2018). These effects have been attributed to the secondary metabolites compounds that are found in the fruit. Previously, studies have detected phenolic compounds in jaboticaba peels such as flavonoids, anthocyanins, and ellagitannins, and these groups are well known for their antioxidant, anti-inflammatory, and chemo-preventive activities (Silva et al. 2016; Betta et al. 2018). However, the pharmacological activities of jaboticaba are still not completely elucidated.

Considering jaboticaba as a potential source of compounds, which can be applied in different fields of study including in pharmaceuticals, the activities of the hydroalcoholic extract of the fruit peels were evaluated. In this regard, toxicological assays were performed on *Artemia salina*, murine fibroblasts (L929) and estrogen receptor (ER)-negative breast carcinoma (MDA-MB-231) cells. Moreover, the extract was evaluated for its antioxidant and acetylcholinesterase activities, as well as elemental analysis (carbon, hydrogen, nitrogen, and sulfur content – CHNS) and antifungal activity in four Candida species.

2. Results and discussion

2.1. The toxic potential in artemia salina

Compounds with $LC_{50} < 1000$ μg mL^{-1} are described as having good correlation between toxic effects on brine shrimps and biological properties (Nguta et al. 2011).

They may be associated with antitumor, insecticide, and antimicrobial activities (Rosa et al. 2016). Jaboticaba peel extract (JPE) showed moderate toxicity with an LC_{50} = 360.92 μg mL^{-1}. Interesting, there are no reports available on *P. cauliflora* and its lethality over *A. salina* until the moment. Evaluation of biological activities of substances through *A. salina* assay is a useful tool for detecting preliminary toxicity, although it does not provide sufficient clue about how the mechanism occurs (Khan et al. 2018).

2.2. Cell viability assay

JPE was tested on L929 and MDA-MB-231 cell lines at concentrations ranging from 1,000 μg mL^{-1} to 7.81 μg mL^{-1}. JPE was non-toxic to L929 cells when compared with control groups. Interestingly, JPE was found to be toxic on the MDA-MB-231 cells at concentrations of 1,000 μg mL^{-1} to 500 μg mL^{-1}.

Some secondary metabolites found in jaboticaba are related to antiproliferative effects against cancer cell lines. *M. cauliflora* skin is rich in flavonoids, compounds that have been described as potentially antiproliferative against those cells (Baldin et al. 2016). Moreover, ellagic acid and anthocyanins, also found in *M. cauliflora* peels, are potential suppressors for leukemia and colon cells (Leite-Legatti et al. 2012). Based on the results from *Artemia salina* assay and the antiproliferative effect on MDA-MB-231 cells, JPE may be a good candidate for more investigative studies on its suppressive activity over *in vitro* neoplastic cells.

2.3. Acetylcholinesterase activity

JPE inhibited 45.7% of acetylcholinesterase activity against 99.7% performed by the positive control physostigmine. The IC_{50} values found were 1,867 and 2 μg mL^{-1} for the extract and control, respectively. Alkaloids are known as the main group of compounds with the capacity to inhibit acetylcholinesterase; other classes of phytochemicals such as flavonoids and terpenes have been reported as having the same activity as well (Pinho et al. 2013). Those compounds have been previously identified in members of *Myrciaria* genus.

Oxidative stress is one of the pathways that can lead to neuronal damage, contributing to the inflammation process (Rajmohamed et al. 2017). The loss of cholinergic neurons is related to the clinical symptoms of Alzheimer's disease, which affects over 40 million people worldwide (Bengt et al. 2016). A natural product that performs a good antioxidant activity and is capable of inhibiting acetylcholinesterase is a good candidate for more specific studies.

2.4. Elemental analysis CHNS

Carbon was the most abundant mineral (45.06%) in the jaboticaba peel, followed by hydrogen (6.73%), nitrogen (1.22%) and sulfur (1.04%). From the nitrogen content, we got the value of total protein (7.63%). Mineral elements are fundamental to the regulation of physiological processes. Macronutrients deficiencies are still a concern

especially in developing countries, so supplementing food with jaboticaba peels could be a possible and cheap alternative to overcome this problem. Another alternative use for jaboticaba would be in cosmetic formulations. Sulfur, commonly present in cosmetics and topical formulations (Leslie et al. 2004), was found in the fruit skin. Incorporation of sulfur in dermocosmetics has demonstrated efficacy against facial dermatosis and acne vulgaris (Del Rosso 2009; Draelos 2010).

2.5. Antifungal activity

None of the four *Candida* species tested were affected by JPE. When compared to the reference drug amphotericin B (MIC = 0.0312 to 2 μg mL^{-1}), JPE was ineffective with activity >5,000 μg mL^{-1}.

3. Conclusion

P. cauliflora peels showed moderate toxicity when submitted to *Artemia salina* assay. JPE was non-toxic to murine non-cancer cell lines L929, providing the clue that this extract may be suitable for topical formulations. Interestingly, the viability of human breast cancer cell line MDA-MB-231 decreased when exposed to the extract concentrations of 1,000 μg mL^{-1} and 500 μg mL^{-1}. Our data suggest that jaboticaba skin is a candidate in the study of new potential anticancer drugs. JPE also demonstrated the antioxidant capacity and acetylcholinesterase inhibition activity, and these results open up many possibilities to use jaboticaba skins in the pharmaceutical, cosmetic, and food industries. For the food industry, the mineral composition of the fruit peel suggests new use as a nutritional supplement. Therefore, our results are remarkable as jaboticaba peels have demonstrated significant bioactivities and, yet most are commonly trashed.

4. Experimental

Please refer to the supplementary material online for more on the 'Experimental' section.

Disclosure statement

The authors declare no conflict of interest.

Funding

The authors gratefully acknowledge PROPESQ/UFJF, FAPEMIG, CNPq and CAPES.

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