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SHORT COMMUNICATION

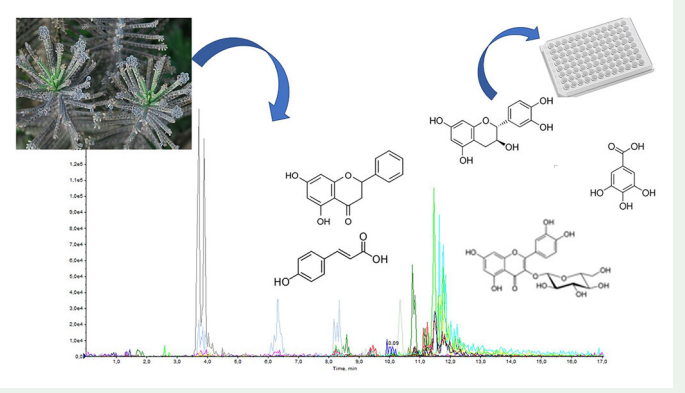
Phenolic profile by HPLC-ESI-MS/MS and enzymatic inhibitory effect of *Bryophyllum delagoense*

Edenize Maria Katrucha[a], Jéssica Lopes[a], Milena Paim[b], Júlia Candiani dos Santos[a], Diogo Alexandre Siebert[c], Gustavo Amadeu Micke[c], Luciano Vitali[c], Michele Debiasi Alberton[b] and Adrielli Tenfen[a]

[a]Curso de Graduação em Farmácia, Sociedade de Educacional Santa Catariana, UniSociesc, Jaraguá do Sul, SC, Brazil; [b]Curso de Graduação em Farmácia, Fundação Universidade Regional de Blumenau, FURB, Blumenau, SC, Brazil; [c]Curso de Pós-Graduação em Química, Universidade Federal de Santa Catarina – UFSC, Florianópolis, SC, Brazil

ABSTRACT

Bryophyllum delagoense (Eckl. & Zeyh.) Druce, native to Madagascar, is popularly known as "abyssian cactus" and popularly used in folk medicine as an analgesic and healing agent. The study methodology was divided into the phytochemical study: fractionation and identification of phenolic compounds by HLPC-ESI-MS/MS from the methanolic extract (ME), and fractions (DCMF and EAF) of leaves of *B. delagoense*, and biological activity with acetylcholinesterase and α-glucosidase inhibition of extracts and fractions by in vitro enzymatic techniques. Twenty-seven phenolic compounds were identified, being the highest concentration of syringic acid (87.848 mg g^{-1}). The DCMF fraction showed the best biological activity for inhibition of α-glucosidase enzyme (0.125 mg mL^{-1}).



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1. Introduction

Oxidative stress is associated with the development of Alzheimer's disease (AD) and Diabetes mellitus (DM) (Prati et al. 2014). Although there are classical pharmacological

CONTACT Adrielli Tenfen adrielli.tenfen@gmail.com

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treatments for AD [cholinesterase (ChEs) inhibitors] and DM (competitive α-glucosidase inhibitors) (Sun et al. 2017), these drugs cause several side effects when administered alone in high doses. For this reason, the use of lower doses of drugs in combination with natural products (with antioxidant properties) that exhibit synergistic therapeutic effects can enhance the drug activity and decrease its toxicity (Sun et al. 2017). In this context, natural compounds have been investigated regarding their relationship (structure-function) of specific components such as phenolic compounds with these disorders. In addition, AD and DM are a multifactorial disease, where a set of biochemical events and protein target are involved. Considering that, more than one molecular target is involved and the discovery of chemical entities capable to act simultaneously on multiple molecular targets are needed (Dias et al. 2015).

In this context, *Bryophyllum* (with several species as the synonym *Kalanchoe*) genus (Crassulaceae) comprises a group of plants with therapeutic applications in traditional medicine, which are used in the treatment of infections, rheumatism, inflammation and oxidative stress (Nayak et al. 2010). Considering the chemotaxonomy and the important activities already described for the *Bryophyllum* and *Kalanchoe* genus, as well as the necessity of new bioactive compounds for the treatment of AD and DM and the few studies involve *Bryophyllum delagoense* [synonym *Kalanchoe delagoensis* Eckl. & Zeyh.], the purpose of this study is to assess the phenolic profile of this plant and to evaluate the potential of anticholinesterase and α-glucosidase inhibitory activities from the leaves of this species.

2. Results and discussion

In the leaves of *B. delagoense*, 27 phenolic compounds were identified (Table S1). Among these phenolic compounds, 12 (4-aminobenzoic acid, *p*-anisic acid, 4-hydroxymethylbenzoic acid, syringaldehyde, aromadendrin, epicatechin, hispidulin, ellagic acid, chlorogenic acid, salicylic acid, galangin, naringenin) were first described in the *Bryophyllum* genus.

In ME, 20 phenolic compounds were described, among them naringenin (30.016 mg g^{-1}) and syringic acid (19.733 mg g^{-1}) were in major concentration. The same was found in EAF, being 54.660 and 87.848 mg g^{-1}, respectively. In this fraction, 22 phenolic compounds were identified. It is important to emphasise that naringenin is a polyhydroxylated flavonoid that demonstrated several health benefits, such as an antioxidant and neuroprotective effects (Md et al. 2018).

The most interesting result for the biological activity was observed for the DCMF fraction, which showed IC_{50} of 0.125 mg mL^{-1} for α-glucosidase inhibition and 0.50 mg mL^{-1} for acetylcholinesterase inhibition. In this fraction, the compounds which presented the highest concentration were gallic acid with (2.639 mg g^{-1}), syringic acid (2.807 mg g^{-1}) and isoquercetin (2.199 mg g^{-1}). According to literature, phenolic compounds, such as gallic acid and quercetin-type flavonoids inhibits the enzyme α-glucosidase (Yin et al. 2014). The α-glucosidase activity of phenolic compounds exists because of the high number of OH groups attached to the enzyme B-ring, they have a large C-ring size and a high degree of polymerisation. The inhibition mode of polyhydroxylated phenolic compounds to α-glucosidase suggests that the compounds

bind at both the active site and other regions of the enzyme, resulting in structural changes and activity inhibition (Stefano et al. 2018).

Regarding the ability of the samples to inhibit the acetylcholinesterase enzyme, the most prominent result was also observed for the DCMF fraction. In this sample, there are some compounds, such as gallic acid, presented inhibitory activity (Morais et al. 2013). It is important to highlight that, despite being in a lower concentration, *p*-coumaric acid is present in the ME (1.07 mg g^{-1}) and DCMF (3.869 mg g^{-1}) also has reported activity against acetylcholinesterase (Trevisan et al., 2003), such as catechins derived compounds (epicatechin), that were found in the EAF fraction (0.063 mg g^{-1}) (Salustiano 2014).

Studies regarding the structural–activity relationship (SAR) correlating flavonoids and the of inhibition of anticholinesterase (AChEI), concluded that the maximum AChEI activity of most of flavonoids is due to the presence and position of hydroxyl (OH) groups at rings A and ring B, and due to the unsaturation of ring C (Khan et al. 2018). This pattern of hydroxylation is present in some phenolic compounds identified in *B. delagoense* by the present work.

Regarding the *Bryophyllum* and *Kalanchoe* genus, some biological activities were described, especially anti-inflammatory (Araújo et al. 2019) and cytotoxic activities. A review of some *Kalanchoe* species report few cytotoxic effects in human cells and in mice studies, especially from non-polar fractions and extracts (Fernandes et al. 2019). In addition, the ethyl acetate fraction from leaves extract of *B. pinnatum*, lowered blood glucose of alloxan-induced diabetic rats and inhibited α-amylase and α-glucosidase, with IC_{50} 137.89 and 110.15 μg mL^{-1}, respectively. The authors attributed the observed activity to quercetin and kaempferol (Ibitoye et al. 2018), and therefore are in good agreement with this work. Finally, there are no studies reporting cytotoxic activity for *B. delagoense*.

These findings suggest that several compounds from the *Bryophyllum* genus show potential antidiabetic and anti-AD properties, and they should be better investigated in further studies to confirm these activities.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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ORCID

Diogo Alexandre Siebert http://orcid.org/0000-0002-9741-4597
Michele Debiasi Alberton http://orcid.org/0000-0003-3490-9936

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