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ISOLATION, STRUCTURAL ELUCIDATION, AND POTENTIAL ANTIDIABETIC ACTIVITY OF α-GALLOYLPUNICALAGIN FROM THE LEAVES OF Terminalia phaecoarpa

José Hugo de S. Gomes[1*], Rodrigo M. de Pádua[1], Steyner de F. Cortês[2], Fernão C. Braga[1]

josehugoufmg@gmail.com

1-Faculdade de Farmácia, UFMG, Av. Antônio Carlos, 6627, Belo Horizonte, MG, Brazil. 2-Instituto de Ciências Biológicas, UFMG, Av. Antônio Carlos, 6627, Belo Horizonte, MG, Brazil.

Diabetes is a highly prevalent chronic disease, affecting approximately 830 million people worldwide[1]. Despite therapeutic advances, current treatments remain of limited effectiveness, and bioactive natural products have emerged as an important source of therapeutic innovation. Species of *Terminalia* have different ethnomedicinal uses, and the potential antidiabetic activity of some species has been demonstrated in various experimental models. *T. phaeocarpa* is an endemic tree distributed across the Brazilian Cerrado and Atlantic Forest biomes, whose chemical composition and biological activities have never been investigated. The present study aimed to perform a phytochemical investigation of *T. phaeocarpa* leaves and to assess their potential antidiabetic activity through *in vitro* inhibition of the α-glucosidase enzyme[2]. An ethanolic extract was prepared by percolation with 96 °GL EtOH, followed by fractionation between immiscible solvents. The extract induced significant α-glucosidase inhibition (pIC_{50} = 5.46 ± 0.05), as did the derived ethyl acetate (FrEtOAc; pIC_{50} = 5.79 ± 0.11) and methanol/water (7:3) (FrMeOH:H_2O; pIC_{50} = 5.74 ± 0.05) fractions. UHPLC-ESI-MS/MS analysis of the extract, FrEtOAc, and FrMeOH:H_2O led to the identification of 38 phenolic compounds, including tannins, flavonoids, and organic acids. The obtained chromatograms revealed a major peak in FrEtOAc. To isolate this constituent, FrEtOAc was fractionated over a Sephadex LH-20 column, yielding a tannin-enriched fraction in MeOH/acetone (1:1). Subsequent preparative RP-HPLC purification afforded a single ellagitannin. Both the tannin-enriched fraction (pIC_{50} = 1.61 ± 0.04) and the isolated ellagitannin (IC_{50} = 1.56 ± 0.93 µM; pIC_{50} = 5.95 ± 0.27) were evaluated for *in vitro* α-glucosidase inhibition, confirming that the biological activity was concentrated in these samples. The chemical structure of the ellagitannin was elucidated by UHPLC-MS together with extensive ^1H and ^{13}C NMR analyses, including one- and two-dimensional experiments (HSQC, HMBC, and NOESY). The spectroscopic data allowed its unequivocal identification as 1-α-*O*-galloylpunicalagin, a compound not previously reported in *T. phaeocarpa*. This is the first report on the biological activity and chemical composition of *T. phaeocarpa*. Based on previous evidence of polyphenol activity in diabetes, it is feasible to supposed that other polyphenols identified in the species may also contribute to the observed biological effects.

Keywords: *Terminalia phaeocarpa, ^1H NMR, α-galloylpunicalagin, in vitro, α-glucosidase, IC50*

[1] WHO - World Health Organization. Diagnosis and management of type 2 diabetes (HeartsD). Geneva, Switzerland: 2025. Disponível em <https://apps.who.int/iris/handle/10665/331710>.>
[2] Gomes JHS et al., 2021. Hypoglycemic and enzyme inhibitory effects of *Terminalia phaeocarpa*. J. Ethnopharmacol.