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***Ganoderma lucidum* Methanolic Extract: Chemical Characterization in Phenolic Compounds and Study of Growth Inhibitory Activity in Human Tumour Cell Lines**

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Ganoderma lucidum is one of the most extensively studied mushroom species due to its medicinal properties. It has been used as functional food and as chemopreventer in some countries for thousands of years, and became a popular dietary supplement ingredient in Western countries.^[1] Some of its pharmacological properties have been related to antitumour properties, attributed to a wide variety of bioactive components such as polysaccharides, triterpenes, sterols, lectins and some proteins.^[2,3] Nevertheless, the bioactive properties of its phenolic compounds have not been studied. The aim of this work was to study the potential antitumor activity of the methanolic extract of this mushroom. This extract of *Ganoderma lucidum*, collected in Northeast Portugal, was characterized in phenolic compounds by high performance liquid chromatography coupled to photodiode array detection and mass spectrometry (HPLC-DAD-MS). The extract was further submitted to evaluation of growth inhibitory activity in four human tumour cell lines (MCF-7, NCI-H460, HCT15 and AGS), by the sulforhodamine B assay.

The extract presented a moderate growth inhibitory activity in all the cell lines tested ($GI_{50}=93.3 \pm 18.1$ – 112.6 ± 11.7 $\mu\text{g/mL}$). The following compounds were identified in the extract: *p*-hydroxybenzoic acid (0.58 ± 0.04 mg/100 g dw), *p*-coumaric acid (0.38 ± 0.03 mg/100 g dw) and cinnamic acid (0.28 ± 0.03 mg/100 g dw). Future work will elucidate the mechanism of action of the studied extract leading to the observed cell growth inhibition.

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References

- [1] R. Sullivan, J. E. Smith, N. J. Rowan, *Perspect. Biol. Med.* **2006**, *49*, 159–170.
[2] R. R. M. Paterson, *Phytochemistry* **2006**, *67*, 1985–2001.

- [3] I. C. F. R. Ferreira, J. A. Vaz, M. H. Vasconcelos, A. Martins, *Anti-Cancer Agents Med. Chem.* **2010**, *10*, 424–436.

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Indication of Brain Penetrable Compounds in Plant Extracts by PAMPA-BBB–LC-MS Assay

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Plant extracts with proven neurological bioactivity are attractive and potential targets for central nervous system (CNS) drug discovery. In the vast majority of cases, however, the molecular mechanism of action and the constituents responsible for activity remain unclear or uncertain due to the complexity of natural products. To overcome this issue, predicting and evaluating the blood–brain barrier (BBB) permeability of natural products is of key importance. Parallel artificial membrane permeability assay (PAMPA) is a robust, 96-well plate assay-based in vitro method for assessing the rate of transcellular passive permeability of drug candidates through the BBB. The goal of our study was to validate the applicability of the PAMPA-BBB assay coupled with LC-MS for identifying brain penetrable compounds in really complex mixtures. Our validation set contained 43 natural product drugs and natural product-like drugs with experimental blood–brain partition coefficients ($\log BB = \log(C_{\text{brain}}/C_{\text{blood}})$) ranging evenly from -2.0 to 1.0 in value. In order to measure the effective permeability (P_e) and membrane retention (MR%) of each test compound, rapid LC-MS methods were developed. Finally, we demonstrate the applicability and advantages of PAMPA-BBB assay with the extract of *Corydalis cava* and *Tanacetum parthenium*, containing several CNS active benzyloquinoline alkaloids and sesquiterpene lactones, respectively.