EBTM
Encontro de
Biotecnologia Medicinal

ICMB
Iberian Congress on
Medicinal Biotechnology

BOOK OF ABSTRACTS

P.PORTO ESCOLA SUPERIOR DE SAÚDE

2 ICMB
Iberian Congress on
Medicinal Biotechnology

5 EBTM
Encontro de
Biotecnologia Medicinal

21 OCT 2022

P.PORTO ESCOLA SUPERIOR DE SAÚDE

Wild mushrooms for Alzheimer's disease

Margarida Lobo-Silva[1], Filipa S. Reis[2,3], Clara Grosso[4], Diana Valverde Pérez[5], Lillian Barros[2,3], & Rosário Martins [1,4]

1. ESS|P.PORTO, School of Health, Polytechnic Institute of Porto, Porto, Portugal; **2.** CIMO|Centro de Investigação de Montanha, Instituto Politécnico de Bragança, Bragança, Portugal; **3.** Laboratório Associado para a Sustentabilidade e Tecnologia em Regiões de Montanha (SusTEC), Instituto Politécnico de Bragança, Bragança, Portugal; **4.** REQUIMTE/LAQV|Instituto Superior de Engenharia do Instituto Politécnico do Porto, Porto, Portugal; **5.** CINBIO|Universidad de Vigo, Vigo, Spain; **6.** CIIMAR|Interdisciplinary Centre of Marine and Environmental Research, Porto, Portugal.

Alzheimer's disease (AD) is among the most incident, debilitating, and widespread forms of dementia [1]. AD causes the decline of cognitive function, making overall day-to-day tasks difficult and even impossible [2]. Despite extensive research, its origin and progression are still unclear, and no efficient treatment is available to prevent disease progression or mitigate symptoms [3]. Due to the low efficiency in the available treatments, natural compounds have arisen as an alternative. These are gaining crescent relevance and have been explored, given their promising results as immunomodulatory, anti-inflammatory, or neuroprotective factors [4]–[7]. Mountain natural resources, specifically mushrooms, are among the most studied sources of bioactive molecules. The Montesinho Natural Park, located in northeast Portugal, has incredible mushroom biodiversity, which has been exploited to obtain health-beneficial compounds, namely with anti-inflammatory potential [8]–[11]. This work aimed to study different mushroom extracts and isolated compounds for the prevention and progression of AD. So far, our work aimed at bringing insight into the effect of extract administration in neuroblastoma and endothelial cell lines through the MTT viability assay, as well as studying their effects on acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), enzymes known to be involved in AD pathogenesis through a modified Ellman's method: dry extracts were resuspended in tris-HCl 50mM + 10% DMSO to concentrations between 2 and 0.03125 mg/mL for enzymatic inhibition assays. To be considered promising, extracts must not cause cellular death of over 15-20% and cause enzymatic inhibition. So far, our results using nine mushroom extracts show low-to-no cytotoxicity in concentrations between 100 and 6.25 µg/mL in endothelial and neuroblastoma cell lines. High concentrations of *Lycoperdon umbrinum* extract caused cytotoxicity levels of approximately 35% in endothelial cells after 24h treatment; different extracts caused cell proliferation in both cell lines, the most evident being 128% in the lowest concentrations of *Russula delica* and *Boletus fragrans*. The most promising results were obtained for *Boletus aereus*, which, while not cytotoxic, inhibited both enzymes by 60%. Around 30% AChE inhibition was achieved for the two highest concentrations of *Agaricus silvicola* and *Boletus fragrans* making both extracts good candidates for further studies.

Keywords: Alzheimer's disease, Neurodegenerative disease, Natural products, Bioactive compounds

References:

1. H. Niu, I. Álvarez-Álvarez, F. Guillén-Grima, and I. Aguinaga-Ontoso, "Prevalence and incidence of Alzheimer's disease in Europe: A meta-analysis," 2017. [Online]. Available: www.elsevier.es/neurologia

2. M. Prince et al., "World Alzheimer Report 2014 Dementia and Risk Reduction AN ANALYSIS OF PROTECTIVE AND MODIFIABLE FACTORS SUPPORTED BY Dr Maëlenn Guerchet Dr Matthew Prina," 2014. [Online]. Available: www.daviddesigns.co.uk

3. J. M. Long and D. M. Holtzman, "Alzheimer Disease: An Update on Pathobiology and Treatment Strategies," Cell, vol. 179, no. 2. Cell Press, pp. 312–339, Oct. 03, 2019. doi: 10.1016/j.cell.2019.09.001.

4. W. Lee et al., "Role of Mushrooms in Neurodegenerative Diseases," in Medicinal Mushrooms, Springer Singapore, 2019, pp. 223–249. doi: 10.1007/978-981-13-6382-5_8.

5. G. Venturella, V. Ferraro, F. Cirlincione, and M. L. Gargano, "Medicinal mushrooms: Bioactive compounds, use, and clinical trials," Int J Mol Sci, vol. 22, no. 2, pp. 1–31, Jan. 2021, doi: 10.3390/ijms22020634.

6. N. Kushairi et al., "Modulation of neuroinflammatory pathways by medicinal mushrooms, with particular relevance to Alzheimer's disease," Trends in Food Science and Technology, vol. 104. Elsevier Ltd, pp. 153–162, Oct. 01, 2020. doi: 10.1016/j.tifs.2020.07.029.

7. S. K. Yadav et al., "A Mechanistic Review on Medicinal Mushrooms-Derived Bioactive Compounds: Potential Mycotherapy Candidates for Alleviating Neurological Disorders," Planta Med, vol. 86, no. 16, pp. 1161–1175, 2020, doi: 10.1055/a-1177-4834.

8. E. Pereira, L. Barros, A. Martins, and I. C. F. R. Ferreira, "Towards chemical and nutritional inventory of Portuguese wild edible mushrooms in different habitats," Food Chem, vol. 130, no. 2, pp. 394–403, 2012.

9. I. C. F. R. Ferreira, L. Barros, and R. M. v Abreu, "Antioxidants in Wild Mushrooms," Current Medicinal Chemistry , vol. 16, pp. 1543–1560, 2009.

10. S. A. Heleno, L. Barros, M. J. Sousa, A. Martins, and I. C. F. R. Ferreira, "Tocopherols Composition of Portuguese Wild Mushrooms with Antioxidant Capacity," Food Chem, vol. 119, pp. 1443–1450, 2010.

11. O. Taofiq et al., "The contribution of phenolic acids to the anti-inflammatory activity of mushrooms: Screening in phenolic extracts, individual parent molecules and synthesized glucuronated and methylated derivatives," Food Res Int, vol. 76, no. Pt 3, pp. 821–827, 2015, doi: 10.1016/j.foodres.2015.07.044.

Acknowledgements: The authors are grateful to the Foundation for Science and Technology (FCT, Portugal) for financial support through national funds FCT/MCTES (PIDDAC) to CIMO (UIDB/00690/2020 and UIDP/00690/2020) and SusTEC (LA/P/0007/2021); and to the national funding by FCT, P.I., through the institutional scientific employment program-contract for L. Barros' contract. F.S. Reis thanks FCT for her employment program–contract (2021.03728.CEECIND). Further acknowledgments are due to the European Regional Development Fund (ERDF) through the Regional Operational Program North 2020, within the scope of Project GreenHealth (Norte-01-0145-FEDER-000042).