

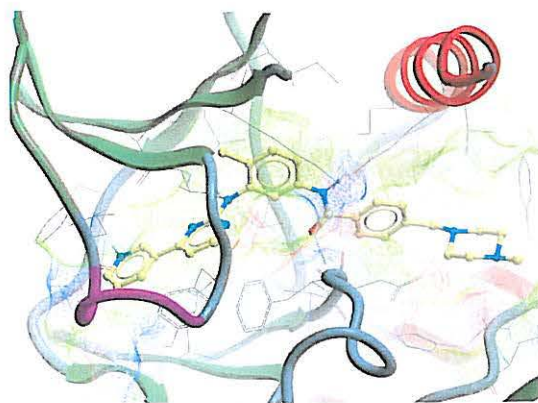
# Revista Portuguesa de Farmácia

Edição da Sociedade Portuguesa de Ciências Farmacêuticas

2.º Encontro Nacional de Química Terapêutica  
2<sup>nd</sup> National Meeting on Medicinal Chemistry

28 a 30 Novembro 2010  
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**LIVRO DE RESUMOS**  
**ABSTRACT BOOK**



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## DOCKING STUDIES USING PROTEINS INVOLVED IN BREAST CANCER AND LOW MOLECULAR WEIGHT COMPOUNDS FOUND IN WILD MUSHROOMS

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Mushrooms are a vast and yet largely untapped source of powerful new pharmaceutical products. In particular, and most importantly for modern medicine, they represent an unlimited source of compounds with antitumor and immunostimulating properties [1]. Particularly, the intake of some wild mushrooms has shown to reduce the risk of breast cancer in Chinese women [2] and inhibited the proliferation of human tumour cell lines [3].

A large number of LMW (low molecular weight) compounds have been identified in wild mushrooms including phenolic acids, flavonoids, tocopherols and carotenoids [4]. In this study we used AutoDock4 to perform molecular docking in order to evaluate which LMW compounds may be involved in the inhibition of the activity of proteins related to human breast cancer. The protein targets selected were aromatase (EC: 1.14.14.1), estrone sulfatase (EC: 3.1.6.2) and 17-hydroxysteroid dehydrogenase type 1 activity (17 $\beta$ -HSD-1; EC: 1.1.1.62). A representative dataset of 43 LMW compounds was selected and molecular docking was performed against the three protein targets. 4-O-caffeoylquinic, naringin and lycopene stand out as the top ranked potential inhibitors for aromatase, estrone sulfatase and 17 $\beta$ -HSD1, respectively. All the compounds with good estimated Ki (inhibition constant) values were manually inspected in order to investigate the binding mode to the catalytic site of each protein target.

This study suggests the LMW compounds to look for in wild mushrooms when searching for species with anti-breast cancer activity. Furthermore, the information provided shows several interesting starting points for further development of Aromatase, Estrone Sulfatase and 17 $\beta$ -HSD1 inhibitors, as also for the development of nutraceuticals or functional foods.

[1] Ferreira ICFR, Vaz JA, Vasconcelos MH, Martins A. Compounds from wild mushrooms with antitumor potential. *Anti-cancer Agents in Medicinal Chemistry*, 2010, 10, 424-436.

[2] Zhang M, Huang J, Xie X, Holman CDJ. Dietary intakes of mushrooms and green tea combine to reduce the risk of breast cancer in Chinese women. *International Journal of Cancer*, 2009, 124, 1404-1408.

[3] Vaz JA, Heleno SA, Martins A, Almeida GM, Vasconcelos MH, Ferreira ICFR. Wild mushrooms *Clitocybe alexandri* and *Lepista inversa*: *In vitro* antioxidant activity and growth inhibition of human tumour cell lines. *Food and Chemical Toxicology*, 2010, 48, 2881-2884.

[4] Ferreira ICFR, Barros L, Abreu RMV. Antioxidants in wild mushrooms. *Current Medicinal Chemistry*, 2009, 16, 1543-1560.

### Acknowledgements

FCT (COMPETE/QREN/UE, PTDC/AGR-ALI/110062/2009 research project) for financial support.