

## Investigating mushroom LMW compounds as potential Bcl-2 inhibitors: docking studies using AutoDock4

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The B cell CLL/lymphoma-2 (Bcl-2) family is functionally classified as either anti-apoptotic or pro-apoptotic, and the regulation of its interactions dictates survival or commitment to apoptosis. Bcl-2 family is also implicated in a wide range of diseases. In some types of cancers, including lymphomas and epithelial cancers, protein overexpression of anti-apoptotic Bcl-2 family, such as the Bcl-2 protein is indicative of cancer in an advanced stage, with a poor prognosis and resistant to chemotherapy [1]. Several reports indicate that mushrooms have the ability to promote apoptosis in tumour cell lines, but the mechanism of action is not fully understood. Inhibition of the interaction between Bcl-2 (anti-apoptotic protein) and pro-apoptotic proteins could be an important step in the mechanism of mushroom induced apoptosis. Therefore, the discovery of compounds with the capacity to inhibit Bcl-2 is an ongoing research topic on cancer therapy.

In this work, docking studies were performed using a dataset of 40 low molecular weight (LMW) compounds present in mushrooms. The docking software AutoDock 4 was used and docking studies were performed using 5 selected Bcl-2 crystal structures as targets. Compounds with the lowest predicted binding energy (pred $\Delta$ G) are expected to be the more potent inhibitors. Among the tested compounds, steroids presented the lowest pred $\Delta$ G with several exhibiting values below -9 kcal/mol. The results are corroborated by several reports that state that steroids induce apoptosis in several tumor cells. It is thus feasible that they might act by preventing Bcl-2 from forming complexes with the respective proapoptotic protein interaction partners, namely Bak, Bax, and Bim. Moreover, previous studies on our research group demonstrated that 48 h treatment of MCF-7 cells (breast carcinoma) with *Suillus collinitus* methanolic extract caused a decrease in Bcl-2, highlighting the antitumor potential of this mushroom species [2].

In conclusion, the process of apoptosis promoted by mushroom extracts may be related to the inhibition of Bcl-2 by the steroid derivatives herein studied. However, further studies are needed to confirm this hypothesis.

[1] MH Kang, CP Reynolds, Clin Cancer Res 2009, 15, 1126-32.

[2] JA Vaz, ICFR Ferreira, C Tavares, G M Almeida, A Martins, MH Vasconcelos, Food Chem, 2012, 135, 596-602.

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Pour le comité d'organisation  
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