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Protein-ligand docking study: diterpenes from *Juniperus brevifolia* as anticancer and antimicrobial agents

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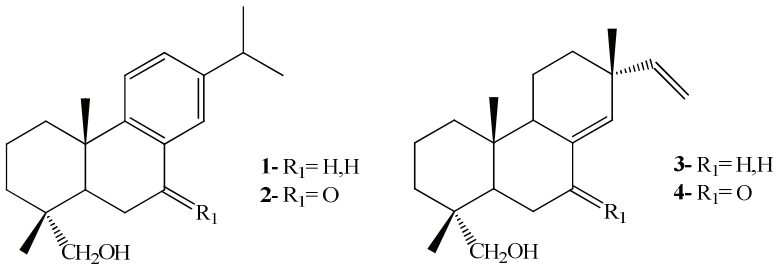
From leaves of *Juniperus brevifolia*, an endemic conifer from Azores, were isolated and structurally characterized, several dehydroabietane and sandaracopimarane derivatives.[1] Some of them (**1**-**4**), displayed antiproliferative activity against cancer cell lines (HeLa, A-549 and MCF-7) and bactericidal effect against *Bacillus cereus* at different concentrations tested.[2] However, it is not known how these compounds interact with most often proteins involved in the antimicrobial and cytotoxic mechanisms. Protein-ligand docking is mainly used to predict (energy and conformation wise) how small molecules bind to a protein of known 3D structure and to predict possible molecular targets for a set of compounds. In this work, the docking studies were performed, using the FlexScreen program, in order to pick molecular targets from a large set of common anticancer (63) and antimicrobial (39) targets to the selected compounds **1**-**4**. The predicted interactions established between the compounds under study and the anticancer targets revealed that the compounds **1** and **3** interact preferentially with phosphatidylinositol-3,4,5-trisphosphate 5-phosphatase 2, whereas compounds **2** and **4** interact preferentially with human mitochondrial peptide deformylase and α-tubulin, respectively. Studying the interactions between the compounds **1** and **3** and the antimicrobial targets we predict that these compounds interact preferentially with RNA polymerase and peptide deformylase. These results provide additional understanding of the cytotoxic and antimicrobial effects of diterpenes studied. These preliminary computational docking predictions of therapeutic targets were established working with just 4 compounds, and to obtain more reliable predictions the number of compounds needs to be increased.



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References

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[2] Moujir, L. M.; Seca, A. M.L.; Araújo, L.; Silva, A. M.S.; Barreto, M. C. *Fitoterapia* **2011**, *82*, 225.