5th BCNP Brazilian Conference on Natural Products
XXXI RESEM
Atibaia – SP – Brazil
ISBN: 978-85-66836-10-3
Oct. 26–29th 2015

Marine Natural Products as Leads to Potential Drugs: Chemogenomics Approaches Applied on a Database of Secondary Metabolites from *Laurencia sp.*

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Abstract: Algae of the genus *Laurencia* are extremely prolific in the production of bioactive metabolites with innovative molecular skeletons. However, there is still very little information about their mechanisms of action (MOAs). In this context, the use of chemogenomics coupled to a Naïve Bayesian algorithm developed by the groups of Bender and Glen at the Centre for Molecular Informatics, Cambridge University, UK, has helped the identification of important molecular biological targets of various molecular classes and may be applied to the study of the MOAs of secondary metabolites of *Laurencia* with therapeutic potential. Thus, in this work, we have used a few computational methods to predict biological targets and rationalize the predicted activities of secondary metabolites from the Seaweed Molecular Database (SWMDB) [1]. Firstly, we used a target prediction tool available in the software BioSar. Next, we selected interesting molecules and targets based on either the real possibility of obtaining the isolated metabolites or gaining access to biological testing. Furthermore, we have used ligand-based methods to identify similar compounds to those in the SWMDB database. In this process, we used the CHEMBL18 database, molecular similarity search with a KNIME workflow using fingerprints and, finally, we performed shape similarity calculations with ROCS [2] using a library of conformers generated with Omega software [3]. Structure-based pharmacophore queries were performed with MOE in order to gain deeper insights into putative interactions of the metabolites and their selected targets based on scores derived from BioSar. In addition, we have also calculated drug-like properties of the compounds according to Lipinski's rule of five (Ro5) [4], aiming at getting insight into early ADMET properties while also performing Multidimensional Scaling (MDS) analysis based on MOLPRINT2D fingerprints [5] of metabolites from the SWMDB database, which were compared to a few databases of approved drugs [6]. These studies provided us with putative acetylcholinesterase inhibitors, *e.g.* Elatol and debromo-elatol from *Laurencia dendroidea*, which are currently under pharmacological investigation in our research group.

References:

[1] Davis, G. D., Vasanthi, A. H. 2011. Seaweed metabolite database (SWMD): A database of natural compounds from marine algae. Bioinformation. 5:361-64.

[2] Grant, J. A., Gallardo, M. A., Pickup, B. J. 1996. A fast method of molecular shape comparison: A simple application of a Gaussian description of molecular shape. J. Comp. Chem. 17:1653-66.

[3] Kirchmair, J., Wolberg, G., Laggner, C., Langer, T. J. 2006. Comparative performance assessment of the conformational model generators omega and catalyst: a large-scale survey on the retrieval of protein-bound ligand conformations. Chem. Inf. Model. 46:1848-61.

[4] Lipinski, C. A., Lombardo, F., Dominy, B. W., Feeney, P. J. 1997. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Delivery Rev. 23:3-25.

[5] Bender, A., Mussa, H. Y., Glen, R. C., Reiling, S. J. 2004. Similarity searching of chemical databases using atom environment descriptors (MOLPRINT 2D): evaluation of performance. Chem. Inf. Comput. Sci. 44:1708-18.

[6] Irwin, J. J., Shoichet, B. K. 2005. ZINC-a free database of commercially available compounds for virtual screening. J. Chem. Inf. Model. 45:177-82.