

Inhibitors of salicylic acid binding protein 2 (SABP2) study through docking and molecular dynamics approaches

Ricardo Fagundes da Rocha, Vanessa Petry do Canto, Gustavo Pozza Silveira, Paulo Augusto Netz

Instituto de Química, Universidade Federal do Rio Grande do Sul (UFRGS)
Avenida Bento Gonçalves, Número 9500, Bairro Agronomia, Porto Alegre-RS, Brazil
ricardo.fagundes@ufrgs.br

Introduction: Plants can be damaged by several agents, such as temperature variations and microorganisms attack. However, vegetable cells contain protection mechanisms, which act mediated by salicylic acid (SA) production and present acute and chronic responses. Additionally, the signal transmission to distal plant regions is dependent of methyl salicylate (MeSA) that is synthesized from SA. After arriving in distal cells, MeSA needs to be reconverted into SA to trigger the defense signaling. The deesterification reaction is catalyzed by an esterase called salicylic acid binding protein 2 (SABP2), which is inhibited by the product SA. Thereby, the development of SA analogues can be an interesting strategy to optimize SABP2 action. **Aim:** Therefore, the present work aims to describe potential inhibitors (analogues of salicylic acid) for SABP2 through docking and molecular dynamics approaches. **Materials and methods:** Initially, the structures of SA, MeSA and 87 other ligands were drawn, and the protonation degree of each one was calculated with MarvinSketch, generating 101 relevant forms at pH = 7,00 (+/- 1,00). Thereafter, a ligands' optimization step was conducted with Gaussian09 while the SABP2 protein structure was downloaded from Protein Data Bank (PDB), <http://www.rcsb.org/pdb/home/home.do>. Docking analysis was performed with AutoDockingVina and results were checked with AutoDockTools. Molecular dynamics was accomplished with Gromacs and the chosen force field was Amber. **Partial results:** Thirty one structures presented interactions at enzyme active site and energy scores equal or lower than SA. The SA score was $-6.7 \text{ kcal.mol}^{-1}$. Among the 31 structures is the 2-(1H-Tetrazol-5-yl)phenol presenting energy score of $-7.5 \text{ kcal.mol}^{-1}$ for protonated structure and $-7.8 \text{ kcal.mol}^{-1}$ for the unprotonated. Currently, analysis of molecular dynamics results is in processing.

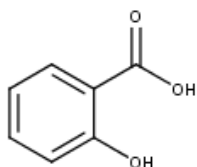


Figure 1: salicylic acid

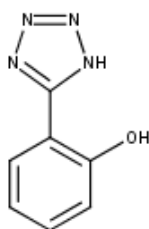


Figure 2: 2-(1H-tetrazol-5-yl)phenol



Figure 3: SABP2 and ligands at active site

Conclusions: The 31 structures with favorable score and positioned at active site, such as 2-(1H-Tetrazol-5-yl)phenol, are promising inhibitors for SABP2 and the ongoing molecular dynamics analysis can infer about the enzyme's conformational changes and the flexibility of residues located at active site. **Keywords:** Docking. Molecular dynamics. SABP2. Salicylic acid. **Supported by:** CAPES, CNPq, FAPERGS and UFRGS.

References

- Chen, Z.; Zheng, Z.; Huang, J.; Lai, Z. e Fan, B. *Plant. Signal. Behav.* **2009**, 4(6), 493-6.
Forouhar, F.; Yang, Y.; Kumar, D.; Chen, Y.; Fridman, E.; Park, S. W.; Chiang, Y.; Acton, T. B.; Montelione, G. T.; Pichersky, E.; Klessing, D. F. e Tong, L. *Proc. Natl. Acad. Sci.* **2005**, 102(5), 1773-8.
Tripathi, D.; Jiang, Y. L. e Kumar, D. *FEBS Lett.* **2010**, 584(15), 3458- 63.