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Rosemary (*Rosmarinus officinalis*) against *Streptococcus mutans* adhesins

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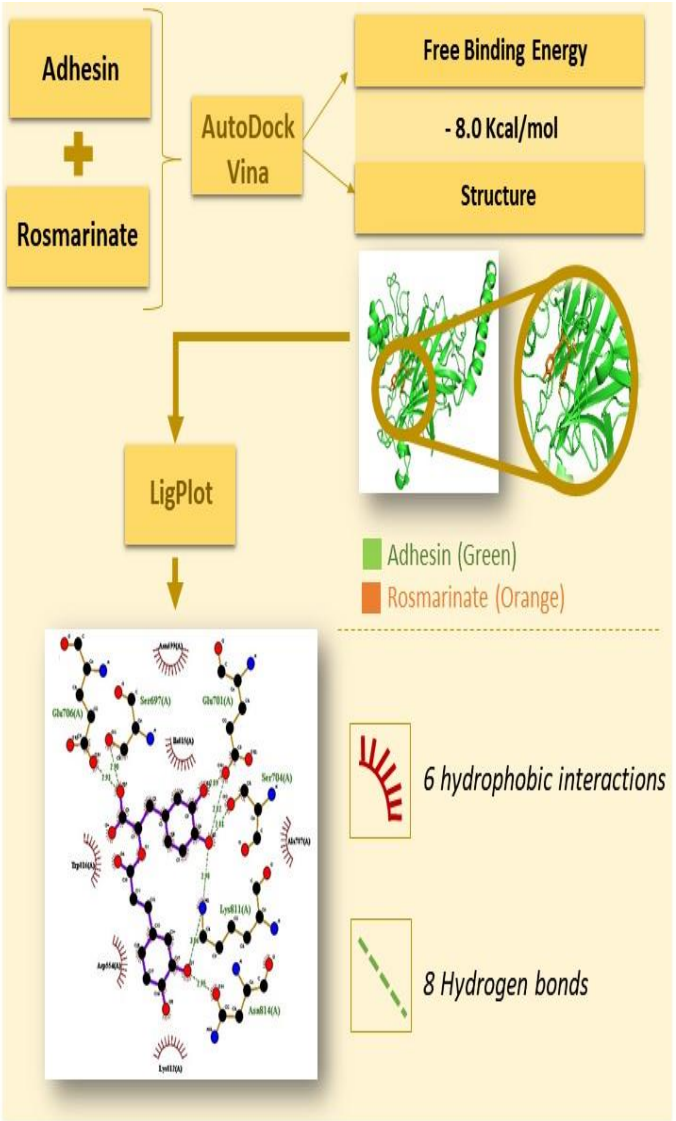
Graphical Abstract



Abstract. *The Streptococcus mutans is one of the main causes of pathologies such as caries. To generate its effects, S.mutans has several mechanisms, including adhesion between microorganisms and microorganisms in tooth enamel. Adhesins are surface or cell wall proteins of S. mutans fundamental to the adhesion process. Thus, blocking this type of protein could represent an inhibition or deceleration of the caries process. The Rosemary (R. officinalis L.) can promote several pharmacological effects due to the interaction between the molecules of the plant and the organic systems. The objective of this study was to verify the possible interaction between Rosemary and adhesion protein (antigen I / II) of S. mutans through molecular docking. First, we prepare the receptor (adhesin) by removing the heteroatoms using the UCSF Chimera. Then, we made several preparations in the receptor and in the ligand (Rosemary) using AutoDock Tools. Finally, the docking simulation took place in AutoDock Vina. The V-region of S. mutans antigen I/II (adhesin) and Alecrim connected with a free binding energy of -8.0 Kcal/mol. The molecules established 08 hydrogen bonds and 06 hydrophobic interactions. Considering the anti-microbial action of rosemary associated with its binding potential in adhesins demonstrated in the docking, Rosemary can be a potent aid in combating caries in dental products.*

Introduction

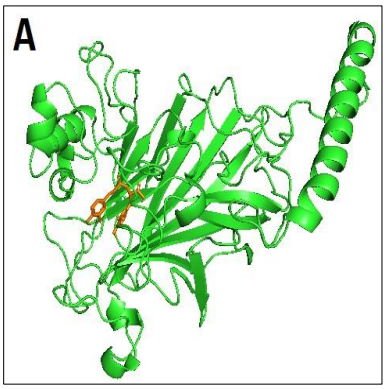
O Streptococcus mutans is a type of gram-positive and anaerobic cocccus present in smooth surface caries lesions (1). Although caries is multifactorial (2), the S. mutans may be the primary etiologic agent in some types of caries (3). The adhesins of S. mutans are surface proteins fundamental in the plate-biofilm interaction (4,5), being this interaction necessary for the formation of caries. In this context, strategies to inhibit the function of adhesins can be decisive for the prevention of caries. The Rosmarinus officinalis L. (rosemary) is a medicinal plant native to the Mediterranean region (6), which demonstrated antibacterial action (7) and could act on adhesins to prevent cavities. Therefore, the objective of this study was to verify the potential for binding between Rosemary and a S. mutans adhesin.

Materials and Methods

The adhesion structure (receptor) was obtained from Protein Data Bank PDB (PDB ID: 1JMM; name Crystal structure of the V-region of Streptococcus mutans antigen I/II) (8) and Rosemary (ligand) was obtained from Pubchem (PubChem ID: 5099; name Rosmarinate/Labiatenic acid) (9). We used the UCSF chimera (available to download at http://www.cgl.ucsf.edu/chimera/download.html) for remove heteroatoms from the adhesin. Then, we prepare receptor and ligand input files using AutoDockTools software for AutoDockVina (10). To perform a blind (coverage of all protein and high number for exhaustiveness) docking simulations, we configure grid box as: size x = 56 Å; size y = 66 Å; and size z = 68 Å; and center box coordinates are x = 43.104 Å center; y = 20.547 Å center; z = -5.781 Å; considering exhaustiveness as 500. Molecular docking simulations were performed with AutoDock Vina (10). The Free Energy of Binding (FEB) of docked ligand-receptor was estimated in Kcal/mol. Visual analysis of docking results was performed with PyMol (available for download https://pymol.org/2/) and for check the types of connections between molecules we used the LigPlot (11).

Results and Discussion

The V-region of S. mutans antigen I/II (adhesin) and Alecrim connected with a free binding energy of -8.0 Kcal/mol. The molecules established 08 hydrogen bonds through the following adhesin amino acids: Glutamine (three bonds); Serine (two bonds); Lysine (two bonds) and Asparagine (one bond). Besides that,occurred 06 hydrophobic interactions between molecules, involving Asparagine; Interleucine; Alanine; Lysine; Aspartate and Tryptophan (adhesin amino acids). Considering the anti-microbial action of rosemary (7) *associated with its binding potential in adhesins demonstrated in the docking, Rosemary can be a potent aid in combating caries in dental products.*



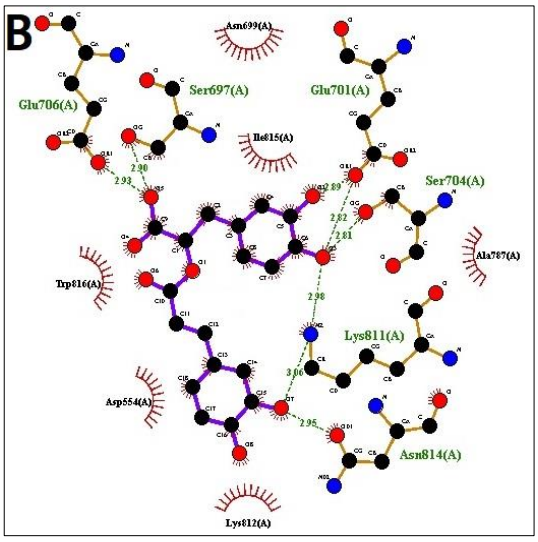


Figure 1: V-region of S. mutans antigen I/II (adhesin) (green) connected to Rosmarinate (orange) (A). Adhesin and Rosmarinate interaction detailed (B): Black or red circles – Adhesin or Rosmarinate atoms; Purple strokes – bonds between the atoms of Rosmarinate; Orange strokes – bonds between the atoms of Adhesin; Dotted green lines – Hydrogen bonds with distances (numbers) between Adhesin's amino acids and Rosmarinate and red semi-circles with lines - hydrophobic interactions.

Conclusions

Molecular docking demonstrated the potential of Rosemary as an aid in the fight against caries, being able to compose dental products.

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