**Exploring Potential Antimicrobial Agent Targeting *Helicobacter* *Pylori* MTAN**

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**Background and aims.** *Helicobacter pylori* *(H. pylori)* is a gram-negative microaerophilic bacterium that colonizes the human stomach and contributes to gastrointestinal diseases. Targeting its essential enzyme, 5′-Methylthioadenosine nucleosidase (MTAN), involved in menaquinone biosynthesis via the futalosine pathway, represents a promising approach as this pathway is absent in the beneficial human microbiome. This study aims to explore phytochemicals from *Foeniculum vulgare* Mill., *Centella asiatica* L., and *Anethum graveolens* L. of the Apiaceae family, which are well-known for their antibacterial and gastroprotective properties, as potential MTAN inhibitors using *in silico* methods.

**Methods.** The 3D pharmacophore model based on the MTAN structure (PDB ID: 6DYV) was constructed using MOE 2022.02, comprising five key features: one hydrogen bond acceptor, one hydrogen bond donor on the receptor, one π–π or hydrophobic interaction, one hydrophobic interaction, and one exclusion volume. Molecular docking was performed and evaluated based on three criteria: (i) the ligand’s ability to interact with the MTAN binding site of *H. pylori*, (ii) binding affinity (kcal/mol), and (iii) specific interactions between the ligand and MTAN residues. Compounds with good binding affinities were selected for molecular dynamics simulations using GROMACS 2023.

**Results.** Of 404 screened phytochemicals, 43 matched all pharmacophore criteria. Among them, compound N222 (p-menthane-2,8,9-triol 2-O-β-D-glucopyranoside) from *Anethum graveolens* L. demonstrated favorable MTAN interactions and structural stability, maintaining high-frequency binding to active site residues during 100 ns MD. Although N217 (Centellasaponin B) form *Centella asiatica* L. showed better binding affinity (–8.08 kcal/mol), N222 exhibited more stable and specific binding patterns (–7.08 kcal/mol), along with good drug-likeness properties.

**Conclusion/Discussion.** N222, a phytochemical derived from *Anethum graveolens* L., demonstrates potential as a novel MTAN inhibitor against *H. pylori*. This study highlights the value of in silico screening and structural analysis in early antimicrobial discovery from natural sources

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