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Molecular modeling of potential inhibitors of inflammatory cascade enzymes from bioactive components of *Matricaria suaveolens*

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Introduction. Inflammatory processes underlie the development of a wide range of pathological conditions – from acute pain syndromes to chronic degenerative diseases. Modern non-steroidal anti-inflammatory drugs (NSAIDs) act by inhibiting the enzymes cyclooxygenase (COX-1, COX-2) and lipoxygenase (LOX-5) and are highly effective; however, their use is often accompanied by side effects such as gastrotoxicity, nephrotoxicity, and an increased cardiovascular risk [1].
This highlights the need to search for new, safer anti-inflammatory agents of natural origin. Plants of the genus *Matricaria* are known for their high content of flavonoids, phenolic acids, and other bioactive compounds that can potentially affect the key enzymes of the inflammatory cascade [2]. In particular, sweet chamomile (*Matricaria suaveolens*) represents a promising source of such substances; however, its molecular mechanisms of anti-inflammatory action remain insufficiently studied. The **aim** of this study was to perform *in silico* prediction of the affinity of biologically active compounds identified in *Matricaria suaveolens* toward key enzymes of the inflammatory response – LOX-5, COX-1 and COX-2.
Materials and methods. Molecular docking was performed using AutoDock Vina and AutoDockTools 1.5.6 software. The methodology was verified by re-docking of native ligands, and the mean root mean square deviation did not exceed 2.1 Å, confirming the validity and reliability of the docking protocol.
Results and discussion. Molecular modeling showed that among the bioactive compounds of *Matricaria suaveolens*, the highest affinity toward the LOX-5 enzyme was demonstrated by luteolin and its glycosides (*luteolin-3,7-diglucoside*, *luteolin-7-O-glucoside*), as well as by 3,5-dicaffeoylquinic acid and rutin (binding energy greater than –9 kcal/mol). Their activity is determined by the formation of stable hydrophobic and hydrogen bonds with the amino acid residues His130, Arg101, and Thr137, ensuring strong fixation within the enzyme's active site. For COX-1, the most active compounds were luteolin, isorhamnetin, chlorogenic, and neochlorogenic acids, whose interactions with Ser530, Gly526, and Ala527 were similar to those of diclofenac. In contrast, isorhamnetin-3-glucoside exhibited low affinity due to its limited ability to penetrate the enzyme's hydrophobic pocket. In the case of COX-2, the highest affinity (–9.6 to –9.8 kcal/mol) was observed for luteolin, isorhamnetin, and 4,5-dicaffeoylquinic acid. Their spatial orientation closely replicates that of celecoxib, indicating a high probability of competitive enzyme inhibition.
Thus, the flavonoids and phenolic acids of *Matricaria suaveolens* may serve as natural inhibitors of the key inflammatory cascade enzymes – LOX-5, COX-1, and COX-2, confirming the plant's significant anti-inflammatory potential.
Conclusions. The most promising natural inhibitors of inflammatory enzymes: LOX-5 – luteolin, its glycosides, dicaffeoylquinic acids, hyperoside; COX-1 – luteolin, isorhamnetin, neo- and chlorogenic acids; COX-2 – luteolin, isorhamnetin, 4,5-dicaffeoylquinic acid. The obtained results indicate a high anti-inflammatory potential of flavonoids and phenolic acids from *Matricaria suaveolens*, which justifies their use in the development of plant-based anti-inflammatory preparations.

References

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