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Design, synthesis and SAR studies of ٤-allyoxyaniline amides as potent ١٥-lipoxygensae inhibitors

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View references (٣٨)

Abstract

A group of ٤-allyloxyaniline amides ٥a-o were designed, synthesized and evaluated as potential inhibitors of soybean ١٥-lipoxygenase (SLO) on the basis of eugenol and esteragol structures. Compound ٥e showed the best $IC_{٥٠}$ in SLO inhibition ($IC_{٥٠}$ = ٠,٦٧ ± ٠,٠٦ μM). All compounds were docked in SLO active site retrieved from RCSB Protein Data Bank (PDB entry: ١IK٣) and showed that allyloxy group of compounds is oriented towards the $Fe^{٢+}$-OH moiety in the active site of enzyme and fixed by hydrogen bonding with two conserved $His^{٥١٣}$ and $Gln^{٧١٦}$. It is resulted that molecular volume of the amide moiety would be a major factor in inhibitory potency variation of the synthetic amides, where the hydrogen bonding of the amide group could also involve in the activity of the inhibitors.

Reaxys Database Information

View Compounds View Reactions

Author keywords

Docking; Esteragol; Eugenol; Linoleic acid; SLO

Indexed Keywords

EMTREE drug terms: aniline derivative; arachidonate ١٥ lipoxygenase; lipoxygenase inhibitor; n١ [٤ (allyloxy)phenyl] ١ admantancarboxamide; unclassified drug

EMTREE medical terms: article; drug activity; drug binding site; drug design; drug structure; drug synthesis; hydrogen bond; IC ٥٠; structure activity relation

MeSH: Aniline Compounds; Drug Design; Esters; Eugenol; Lipoxygenase Inhibitors; Models, Molecular; Molecular Conformation; Structure-Activity Relationship

Medline is the source for the MeSH terms of this document.

Species Index: Glycine max; Puffinus auricularis

Chemicals and CAS Registry Numbers: arachidonate ١٥ lipoxygenase, ٨٢٢٤٩-٧٧-٢;Aniline Compounds; Esters; Eugenol, ٩٧-٥٣-٠; Lipoxygenase Inhibitors

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