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Case study: Nutraceutical

Target identification for existing nutraceutical molecule

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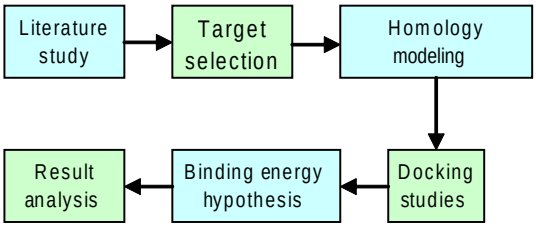
Customer type

Nutraceutical Company

Software modules

BioPredicta

VLife Engine



Application

Inverse docking

Techniques

Homology modeling

Protein - ligand docking

Binding energy analysis

Background:

Migraine is a neurological disorder characterized by severe and disabling head ache, disordered vision and gastrointestinal disturbances. The etiology of the disease is still not known clearly though there is strong evidence suggesting the role of serotonergic control system. Several nutraceuticals have demonstrated beneficial effects in complex diseases like migraine.

Design challenge:

The customer compound was reported to have its beneficial effect in the condition of migraine. The mechanism through which it exerts its anti – migraine property was not known. This study was aimed at finding out the most probable targets on which the compound acts by using computational methods.

Project work:

Most of the proteins involved in the pathophysiology of migraine are GPCR's (G-protein coupled receptors) whose crystal structures is not known. The structures of these receptors were modeled using BioPredicta module of VLifeMDS. The targets for which crystal structures were available were taken from Protein Data Bank. They were cleaned with respect to their bond orders, missing atoms and residues.

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VLifeMDS

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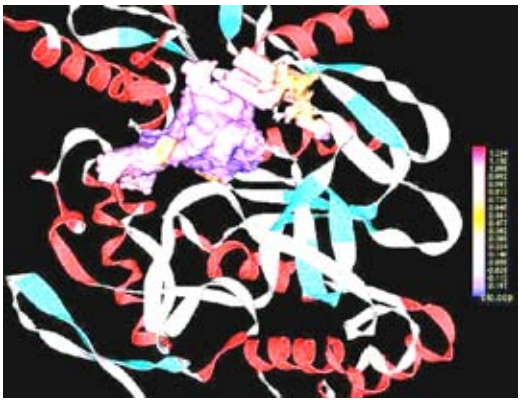
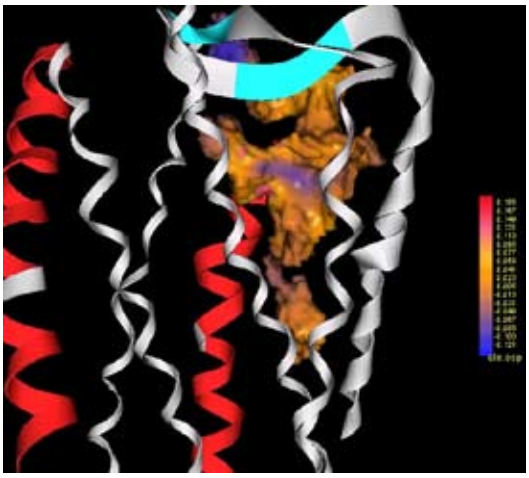


Active Site of eNOS into which customer ligand is docked



Active site cavity of 5HT1B receptor into which customer ligand is docked

Then the customer ligand was docked into these structures/ models and their interaction energies were determined. While docking both the ligand and the receptor were kept flexible. From ability of binding of this compound to various protein targets involved in migraine, we have provided to the customer a list of probable targets through which the compound acts to relieve the disease condition.

Result analysis:

The binding affinity of the customer compound into various targets was determined using the formula:

E bind = E complex – (E protein + E ligand),

Where,

E bind = binding energy,

E complex = energy of complex

E protein = energy of protein

E ligand = energy of ligand

Based on these binding energies the targets to which the compound will bind were prioritized. The possible mechanism for the action of the compound was reported to the customer. The suggested target binding was subsequently verified by *in vitro* assays.

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