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# In Silico Identification of Protein Targets Associated to the Insecticide Activity of Eugenol Derivatives

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# Introduction

- The search for environmental-friendly approaches in insect pest control has attracted many researchers hoping to find more specific and less toxic alternatives.
- Eugenol is a natural compound that is the major component of clove oil and has demonstrated antimicrobial and antioxidant activity.
- The search for new eugenol derivatives with higher efficiency was boosted to find additional alternatives to known insecticides.
- Limitation: lack of knowledge of the specific protein target and the binding conformation of these molecules.
- In this study, we report the application of an integrated molecular modelling - inverted virtual screening protocol for the identification of potential protein targets for a series of eugenol derivatives

# Methods

Literature search

- Other VS studies
- Targets of known pesticides

Re-Docking

- Protocol Optimization for each target
- Comparison with crystallographic ligand

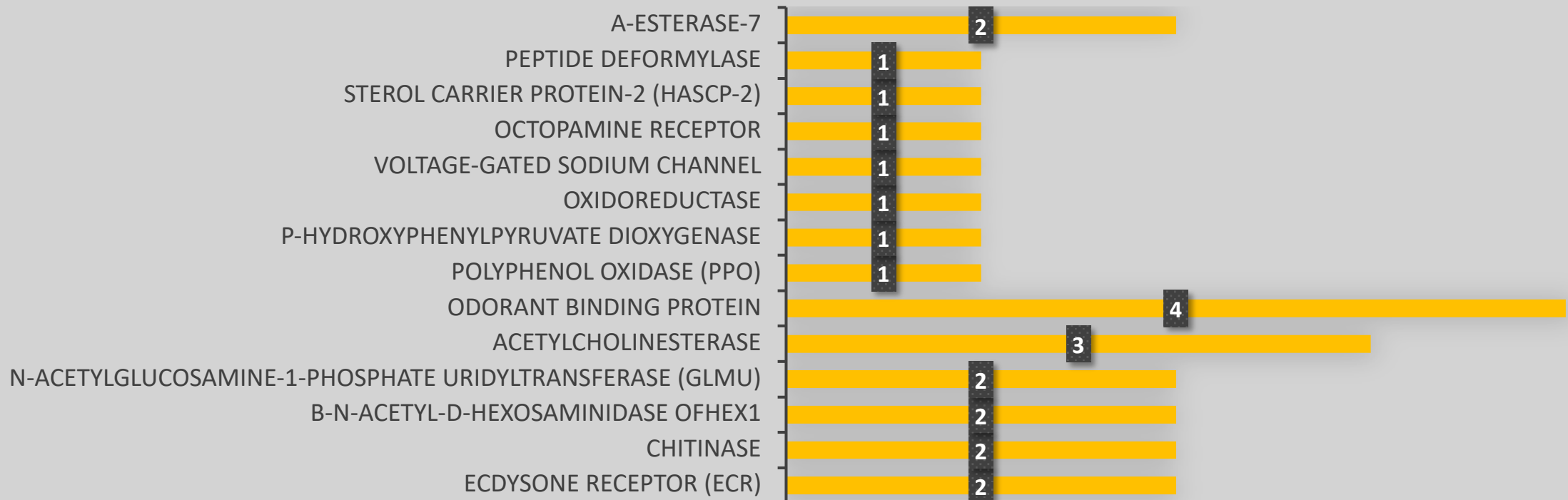
Inverted Virtual Screening

Docking all the eugenol derivatives into each structure

Six different scoring functions: PLP, ASP, ChemScore, GoldScore, Vina and LeDock  
Optimization of: docking box and dimensions, search efficiency and number of runs

# Selected Targets

The literature was explored for other virtual screening studies performed on known targets to minimize the candidate pool. Of 18 studies found, 14 targets were selected to continue the study.





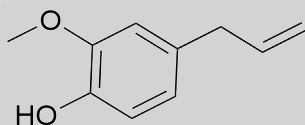
# Eugenol derivatives

Eugenol and eleven derivatives (EU1-EU3e) were selected as new potential insecticides. These molecules have been previously synthesized and validated experimentally with good insecticidal activity

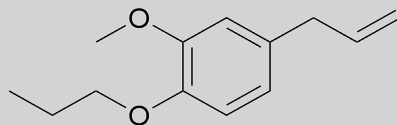


Docking in all the targets with all SF: PLP, ASP, ChemScore, GoldScore, Vina and LeDock.

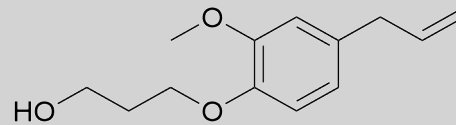
A ranked list was prepared based on the average scores of each target.



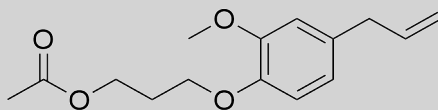
EU1



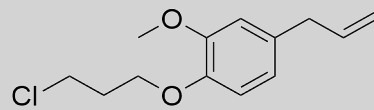
EU2a



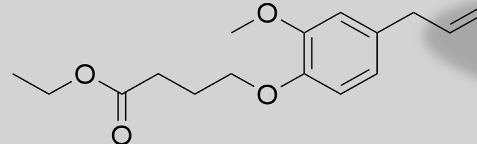
EU2b



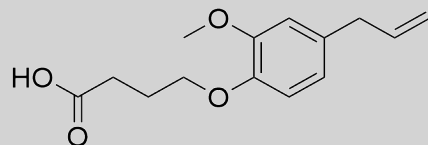
EU2c



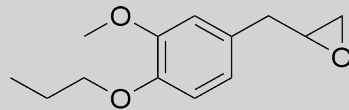
EU2d



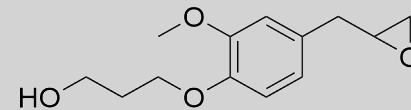
EU2e



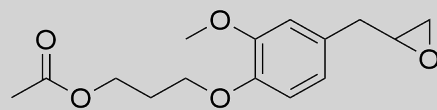
EU2f



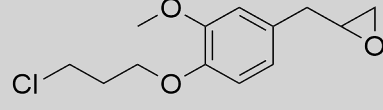
EU3a



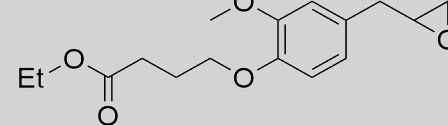
EU3b



EU3c



EU3d



EU3e

# Results & Discussion

Ranking	PLP	ASP	ChemScore	GoldScore	Vina	LeDock	Overall Ranking
Odorant Binding Protein	1	4	1	3	2	2	1
Acetylcholinesterase	2	1	2	5	1	5	2
Chitinase	4	2	5	2	6	7	3
Octopamine receptor	3	5	3	1	5	10	4
Peptide deformylase	6	11	12	4	7	1	5
Oxidoreductase	5	12	4	6	11	4	6
beta-N-acetyl-D-hexosaminidase OfHex1	7	3	9	7	3	13	7
ecdysone receptor (EcR)	9	9	8	10	4	3	8
Alpha-esterase-7	8	6	7	12	9	8	9
Sterol carrier protein-2 (HaSCP-2)	13	8	6	14	8	6	10
p-hydroxyphenylpyruvate dioxygenase	10	7	11	13	10	12	11
Polyphenol oxidase (PPO)	11	10	10	9	14	14	12
N-Acetylglucosamine-1-phosphate uridylyltransferase (GlmU)	12	13	13	11	12	9	13
Voltage-gated sodium channel	14	14	14	8	13	11	14

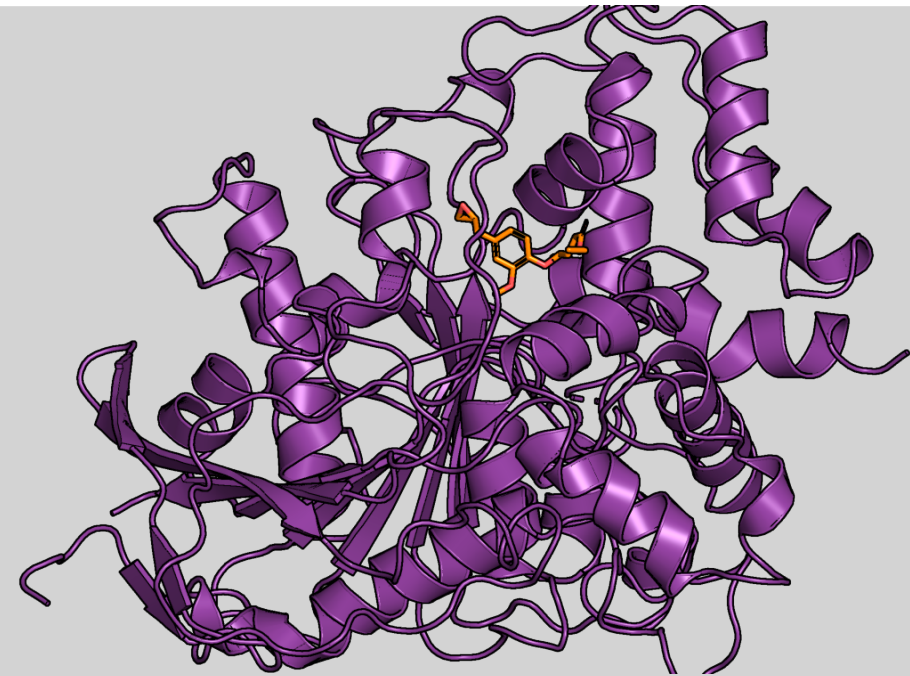
Targets that presented highest binding affinity for eugenol derivatives

Targets that presented lowest binding affinity for eugenol derivatives

# Results & Discussion



Odorant Binding Proteins (OBPs) are a large family of proteins crucial for insect survival and reproduction. Very small targets and are ideal to perform rapid screenings. Are a emergent target for new repellents.

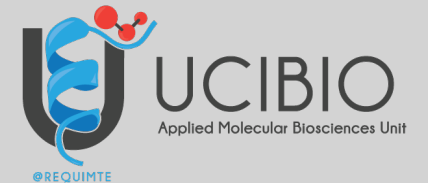


Acetylcholinesterase (AChE) is a serine hydrolase responsible for regulating the levels of acetylcholine. One of the most common targets of synthetic pesticides with some pests already showing resistance. Finding new pesticide alternatives is crucial.

# Conclusion

- This work presents a simple approach for the application of inverted virtual screening in identification of possible targets for new insecticides.
- Eugenol derivatives were docked into each target with six different scoring functions (PLP, ASP, ChemScore, GoldScore, Vina and LeDock). The consistency of the scores was evaluated and a ranked list was created.
- Eugenol derivatives showed an increased binding affinity for odorant binding proteins and acetylcholinesterase.
- Since there is, already, in the PDB database a structure of an OBP bound to eugenol, we can confirm our theory and can say that eugenol derivatives, could be used as repellents.
- Additional computational and experimental studies need to be performed to further optimize and develop this hypothesis.

# Aknowlegments



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