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In silico Screening of Myristicin, Elemicin, Isoelemicin and Malalabaricone C for their activity towards obesity related enzyme 17β-hydroxysteroid dehydrogenase (1BHS)

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Abstract

Screening of some of the compounds found in nutmeg extract Myristicin, Elemicin, Isoelemicin and Malalabaricone C against a protein target 1BHS associated with type 2 diabetes mellitus have been carried out and discussed in the current study.

The 3D structures of the ligands and the protein were obtained from PubChem database and Protein Data Bank respectively.

Each ligand was prepared and docked against the target protein using AutoDock Vina. Activity of each compounds towards the obesity related protein 1BHS was predicted. Among the four phytochemicals, highest binding affinity and most number of hydrogen bonding were observed for Malalabaricone C.

Key words: Myristicin, Elemicin, Isoelemicin, Malalabaricone C, 1BHS

Introduction

Obesity and type-2 diabetes are metabolic disorders which have affected billions of adults globally. The disease has become an epidemic with rapid rise in the number of overweight and obese population the developed and developing countries. As per WHO estimation, there were more than 1.9 billion overweight adults as of 2016. Out of these over 650 million adults were obese. Traditional medicinal plants contain active phytoconstituents which possess lower side effects.[i] New drug molecules can be discovered using those phytochemicals.

Nutmeg (*Myristica fragrans*) seeds have been used since ancient times, as a spice and flavoring agent in most part of the world. Apart from culinary uses, nutmeg has been also used in traditional medicinal practice to treat stomach ailments, headaches and fever to name a few.[ii] Essential oil extracted from nutmeg known to have antimicrobial, antiseptic, antiparasitic, anti-inflammatory, and antioxidant properties.[iii]

There are a few reports on the anti-obesity properties of nutmeg extracts. Phi *et al.* studied Tetrahydrofuran lignans isolated from nutmeg were studied for their activity as AMPK activator.[iv] In this communication, an *in silico* study was performed to screen Myristicin, Elemicin, Isoelemicin and Malalabaricone C as antidiabetics against known target such as 17β-hydroxysteroid dehydrogenase. Conversion of testosterone to androstenedione and vice versa happens in presence of the enzyme 17β-hydroxysteroid dehydrogenase (17β -HSD).

This enzyme is involved in metabolism of lipids and increase in the level of this enzyme leads to insulin resistant and obesity. It has been found that this enzyme can be linked to obesity and polycystic ovarian syndrome (PCOS) in women. In post-menopausal women the level of 17β -HSD found to be in higher than normal.[v]

3D structures of Myristicin, Elemicin, Isoelemicin and Malalabaricone C were obtained from PubChem database (https://pubchem.ncbi.nlm.nih.gov/). PyMol software was used to convert .sdf format of the structures into .pdb format. Ligand files were then saved in the format of .pdbqt in AutoDock. The compounds chosen for the study are shown in figure 1.

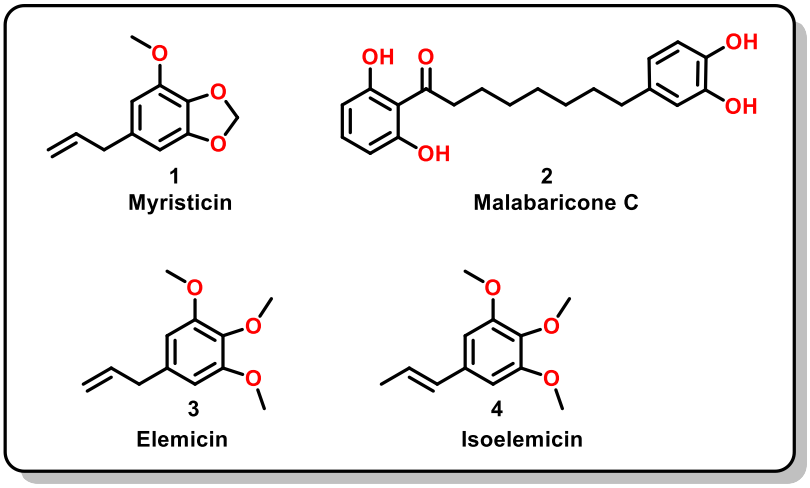

Figure 1: Chemical structures of the selected compounds Myristicin (1), Malabaricone C (2), Elemicin (3) and Isoelemicin (4)

Structure of the target protein was obtained from Protein Data Bank (https://www.rcsb.org). Water molecules were removed and the protein was prepared

Docking was performed using AutoDock Vina.[vi] Nine best docking poses were obtained for a particular ligand after the docking with the protein. To visualize the ligand-protein interaction, pose with minimum binding energy was selected.

Binding energy and number of hydrogen bond interaction of the molecules with each protein are shown in **Table 1**.

	Binding energy and number of hydrogen bond of protein 1BHS with each ligand							
	Myristicin		**Malabaricone C**		**Elemicin**		**Isoelemicin**	
PDB ID	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**
1BHS	-5.7	0	-7.4	2	-5.7	0	-5.8	0

Table 1: Binding energy (BE) and number of hydrogen bonds (NHB) of ligand protein interaction

Among the four phytochemicals those were studied, **Malabaricone C (2)** exhibited had the highest binding affinity with the protein with binding energy of -7.4 kcal/mol. It had also highest number of hydrogen bonds with the protein whereas others did not show any hydrogen bonding. Binding affinity of individual molecules with the protein target and number of hydrogen bond interactions are summarized in **Table 1**.

The best poses of each molecules as visualized in PyMol software are shown in the figures given below.

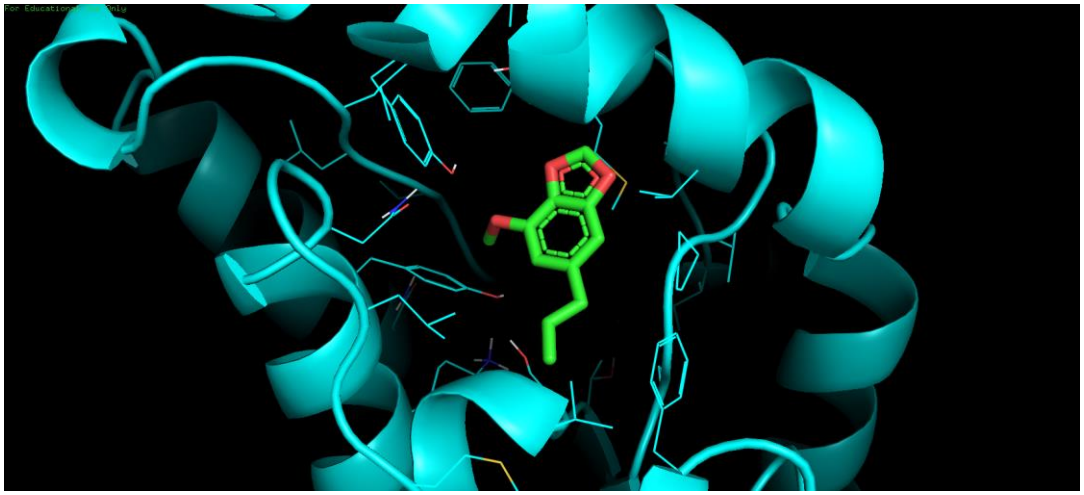

Figure 2: Protein-ligand interaction of 1BHS and Myristicin

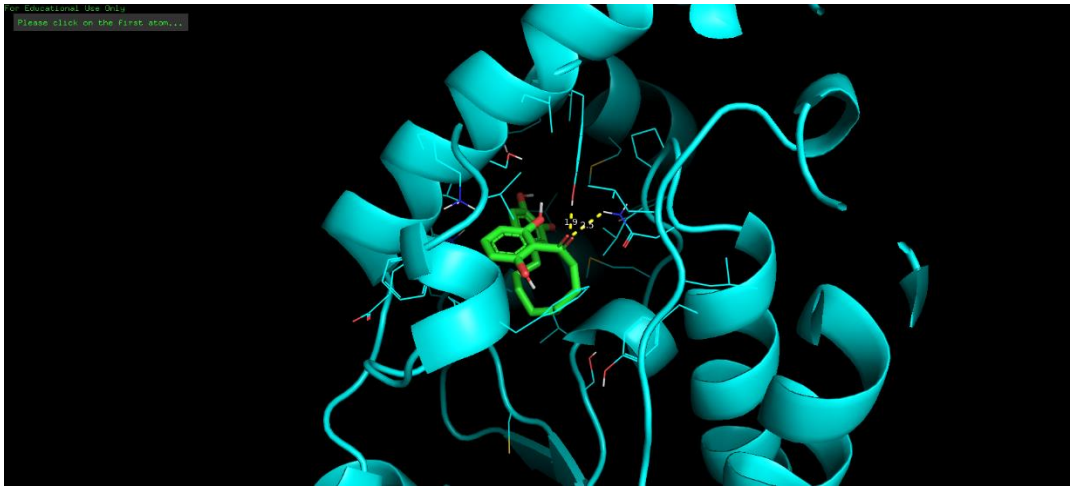

Figure 3: Protein-ligand interaction of 1BHS and Malabaricone C

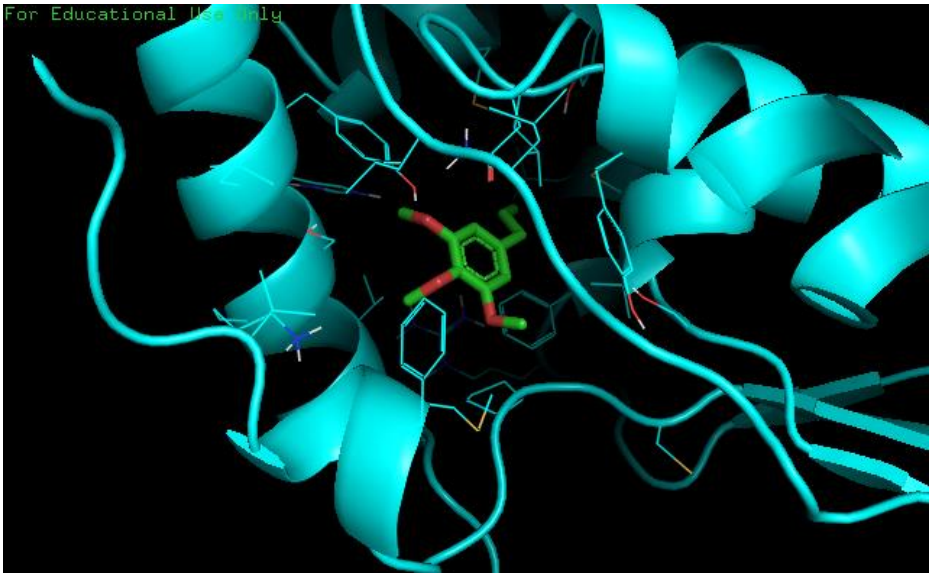

Figure 4: Protein-ligand interaction of 1BHS and Elemicin

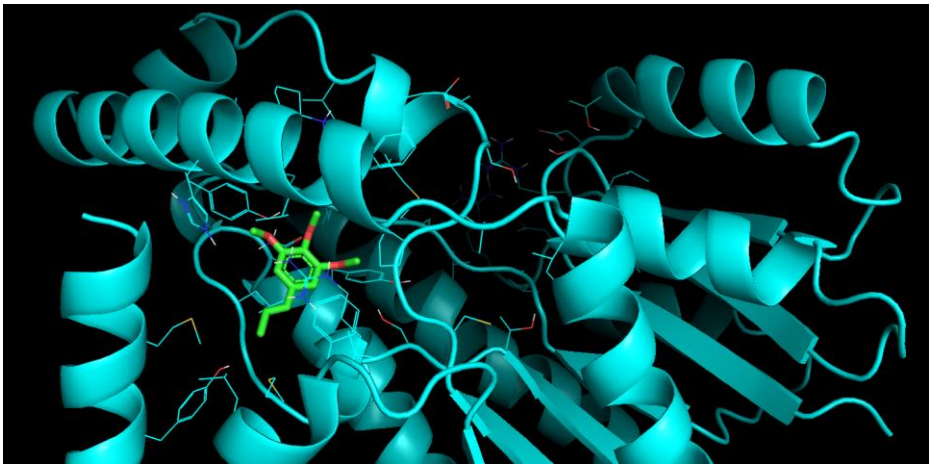

Figure 5: Protein-ligand interaction of 1BHS and Isoelemicin

Conclusion

The current study demonstrates that among the studied phytochemicals malabaricone C has highest binding affinity to the enzyme 17β-hydroxysteroid dehydrogenase. This *in silico* study can be used to further develop lead molecules to treat obesity related diseases.

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