International Journal of Modern Agriculture, Volume 9, No.4, 2020
ISSN: 2305 - 7246

Computational Study of Selected Phytochemicals from Nutmeg Extracts for Their Binding Affinity with Obesity Related Enzyme Retinol Binding Protein (1GGL)

Rosy Mallik [1]

[1] Centurion University of Technology and Management, Odisha, India

Corresponding author*:*

Rosy Mallik
Centurion University of Technology and Management, Odisha, India

Abstract

In silico screening of some phytochemical compounds of nutmeg (myristica fragrans) were performed against Retinol binding protein III (1GGL). This protein is associated with obesity. A computational study has been carried out and the results are discussed here.

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

Free molecular docking software AutoDock Vina was used to prepare the ligands and dock against the target protein. The affinity of each compound for Retinol binding protein could be predicted from the binding energy. Among the chosen phytochemicals, Malalabaricone C exhibited highest binding affinity and most number of hydrogen bonding towards 1GGL.

Key words: Phytochemicals, nutmeg extracts, antiobesity, Malalabaricone C, retinol binding protein III

Introduction

Increase in overweight, more seriously obese population remains a concern to the economically advanced world seeking for remedy/cure. More than 4 million people die every year due to obesity and obesity related health problems. The percentage of adults as well as adolescents being affected by this disease has increased alarmingly in last 4 decades. Being a metabolic disorder, the link between obesity and dietary factors are apparent. Certain phytochemicals have been proved to target different stages of fat metabolism by interacting with related proteins.[i] Phytoconstituents present in traditional medicinal plants possess lower side effects.[ii] These phytochemicals can be used to discover new anti-obesity drugs.

Apart from being a culinary must have in the kitchens around the world, Nutmeg (*Myristica fragrans*) seeds and its mace have been also used in therapeutic applications since ancient times. Traditionally, it has been used to alleviate stomach related ailments such as indigestion, vomiting and nausea.[iii] Essential oil of nutmeg also possess antimicrobial, antiseptic, antiparasitic, anti-inflammatory, and antioxidant properties.[iv]

Potential of nutmeg extracts as prospective anti-obesity agents have been the subject of a few research as well. Tetrahydrofuran lignans isolated from nutmeg were studied for their activity as AMPK activator by Phi *et al.*[v] Mutcharidi *et al. reported the antidiabetic effect of nutmace lignans by actvating PPARγ receptor.*[vi]

Diet induced obesity can be linked to lipid homeostasis involving Retinol binding protein III. In insulin resistant state, level of this protein is increased in adipose tissue.[vii]

Result and Discussion

In this communication, an *in silico* study was conducted to find out inhibition potential of nutmeg phytochemicals such as Myristicin, Elemicin, Isoelemicin and Malalabaricone C against the target Retinol binding protein III.

Retrieving the 3D structures of the molecules (i.e, Myristicin, Elemicin, Isoelemicin and Malalabaricone C) from PubChem database[viii]. .sdf format of the structures were converted into .pdb format using PyMol software. Ligand files were then saved in the format of .pdbqt in AutoDock.

Structure of the target protein was obtained from Protein Data Bank (https://www.rcsb.org). The protein was prepared by removing water molecules and saved as .pdbqt file.

Docking was performed using AutoDock Vina.[ix] For each phytochemical compound, nine best docking poses were obtained after the docking with the protein. Pose with minimum binding energy was selected as the best pose and considered for visualization of ligand-protein interaction.

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

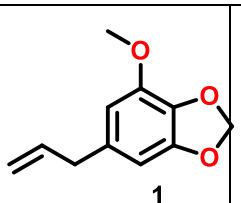
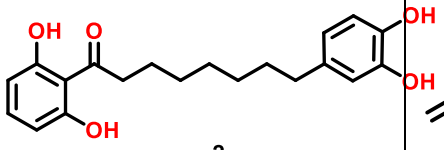
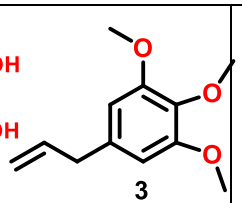
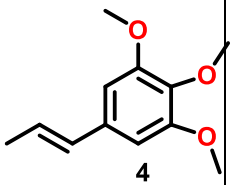
	Binding energy and number of hydrogen bond of protein 1GGL with each ligand							
	 **1 Myristicin**		 **2 Malabaricone C**		 **3 Elemicin**		 **4 Isoelemicin**	
PDB ID	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**	**BE (kcal/mol)**	**NHB**
1GGL	-6.1	2	-7.9	3	-5.7	3	-5.9	3

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

Malabaricone C (2) exhibited the highest binding affinity with the protein among all the phytochemicals those were studied. The best pose had binding energy of -7.9 kcal/mol. Best pose of Myristicin had 2 H-bonds, whereas Malabaricone C, Elemicin and Isoelemicin had 3 H-bonds each with the binding site amino acid residues of the protein.

Table 1 summarizes the binding affinity of individual molecules with the protein target and number of hydrogen bond interactions.

The images of the best pose of each molecule as visualized in PyMol software and the bond length are shown in the figures 1 to 4 given below.

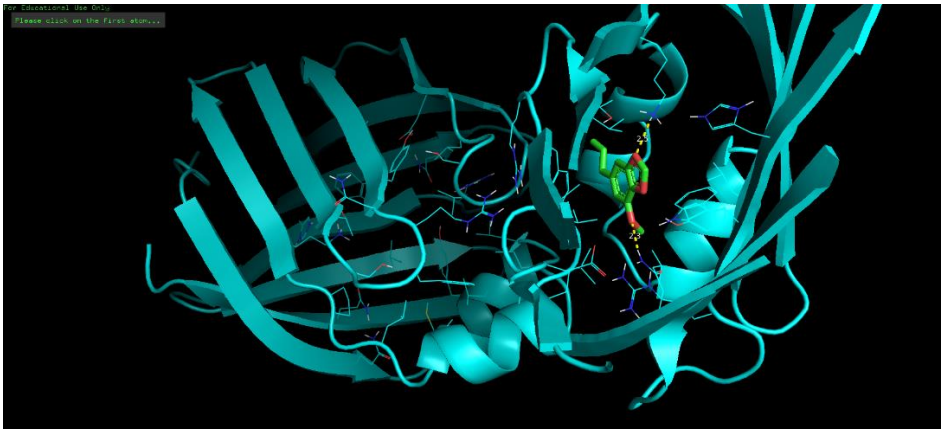


Figure 1: Protein-ligand interaction of 1GGL and Myristicin

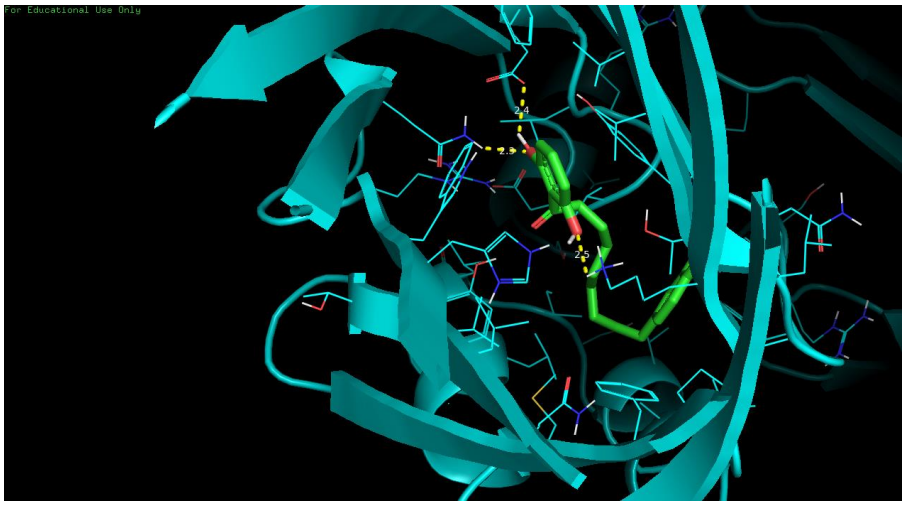


Figure 2: Protein-ligand interaction of 1GGL and Malabaricone C

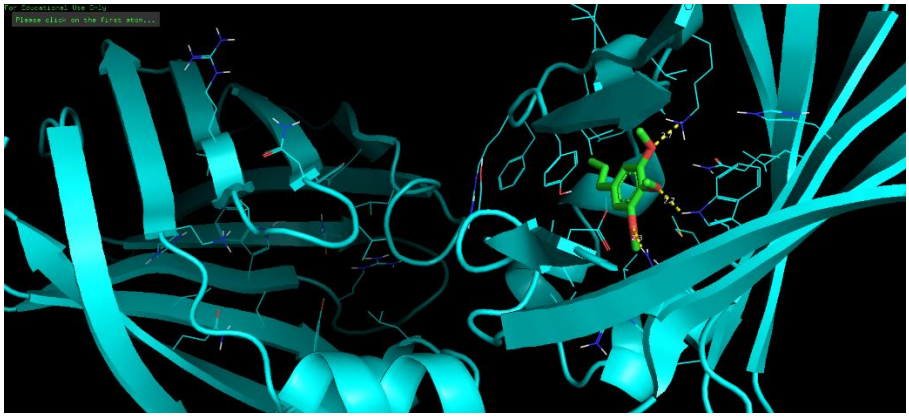


Figure 3: Protein-ligand interaction of 1GGL and Elemicin

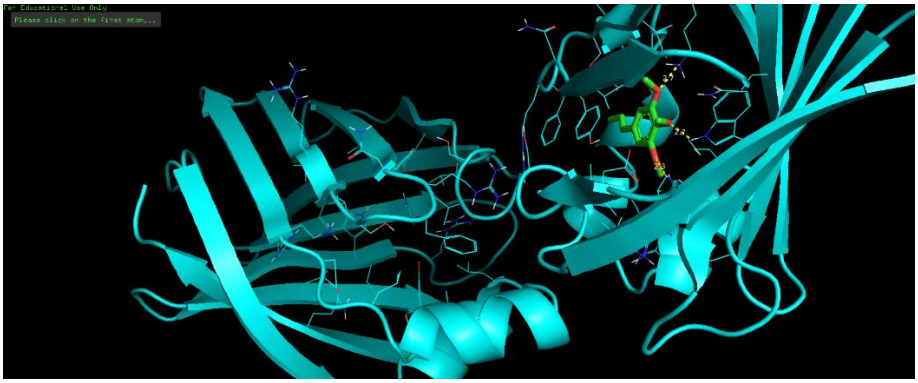


Figure 4: Protein-ligand interaction of 1GGL and Isoelemicin

Conclusion

It can be established from the presented computational study that some phytochemicals present in nutmeg seeds exhibit binding affinity towards obesity related protein and can be studied further and modified to be potential therapeutic agents to treat obesity. Among all the molecules, Malabaricone C showed highest binding affinity to the retinol binding protein III. This *in silico* study can be used to further develop lead molecules to address obesity related diseases.

References

1. a) Williams D. J.; Edwards D.; Hamernig I.; Jian L.; James A. P.; Johnson S.K.; Tapsell L. C. Vegetables containing phytochemicals with potential anti-obesity properties: A review Food Research International, 2013, 52, 323-333: b) Rahman H. A.; Saari N.; Abas F.; Ismail A.; Mumtaz M. W.; Hamid A. A. Anti-obesity and antioxidant activities of selected medicinal plants and phytochemical profiling of bioactive compounds, International Journal of Food Properties, 2017, 20, 2616-2629.

2. Moreira DDL, Teixeira SS, Monteiro MHD, De-oliveira ACAX, Paumgartten FJR. Traditional use and safety of herbal medicines. Rev Bras Farmacogn 2014, 2, 248-57.

3. a) DeMilto L., Frey R.J., In: J. L. Longe (ed.), the Gale Encyclopedia of Alternative Medicine. Farmington Hills, Mich: Thomson/Gale. 2005. b) Muchtaridi; Subarnas, A.; Apriyantono, A.; Mustarichie, R. Identification of Compounds in the Essential Oil of Nutmeg Seeds (Myristica Fragrans Houtt.) That Inhibit Locomotor Activity in Mice. Int. J. Mol. Sci. 2010, 11, 4771–4781.

4. a) Baser, K.H.; Bunchbauer, G. Handbook of Essential Oils: Science, Technology, and Applications; CRC Press NW: Boca Raton, FL, USA, 2010. b) Y. Ozaki, S. Soedigdo, Y.R. Wattimena and A.G.Suganda, Antiinflammatory effect of mace, aril of Myristica fragrans Houtt. and its active principles. Japan J. Pharmacol., 1989.49, 1989. 155-163.

5. Phi Hung Nguyen, Thi Van Thu Le, Hu Won Kang, Jooyoung Chae, Sang Kyum Kim, Kwang-iI Kwon, Dae Bang Seo, Sang Jun Lee, Won Keun Oh; AMP-activated protein kinase (AMPK) activators from Myristica fragrans (nutmeg) and their anti-obesity effect; Bioorganic & Medicinal Chemistry Letters, 2010, 20, 4128–4131.

6. Muchtaridi et al. Journal of Applied Pharmaceutical Science 2016, 6, 048-053.

7. Zizola CF, Schwartz GJ,Vogel S. Cellular retinol-binding protein type III is a PPAR gamma target gene and plays a role in lipid metabolism. Am J Physiol Endocrinol Metab 2008;295:E 1358-68.

8. Kim, S.; Chen, J.; Cheng, T.; Gindulyte, A.; He, J.; He, S.; Li, Q.; Shoemaker, B.A.; Thiessen, P.A.; Yu, B.; et al. PubChem 2019 update: Improved access to chemical data. Nucleic Acids Res. 2018, 47, D1102–D1109.

9. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading. J Comput Chem 2010, 31, 455-61