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Research Article

AN IN SILICO APPROACH TO CURTAIL THE ACTION OF OBESITY PROTEINS WITH PHYTOCONSTITUENTS

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A B S T R A C T

Obesity is recently becoming a global health problem with alarming number of prevalence. The obesity itself is not defined as a disease but rather a disease process which can end up in various health problems. Most of the synthetic drugs used for obesity have side effects and hence, development of alternative agents are required. But its challenging as it act by multiple factors like genetic, hormonal, environmental and dietary. The present study attempts to curtail the action of proteins by docking with phytoconstituents. Three targeted proteins were subjected for the study and the proteins selected were Fat mass and obesity associated protein, Resistin, and Leptin. Ligands were phytoconstituents belonging to different classes seen in fruits, vegetables and were docked using autodock tool. The binding efficiency of the ligands with each receptors were compared with synthetic drug orlistat. Results obtained were comparable with synthetic drug with daidzein being the better among phytoconstituents. Moreover, hydrogen bond interactions made by quercetin, catechin with targeted proteins were more than the synthetic drug. As these constituents are clinically safer, future efforts can be taken to frame a diet choosing food items containing these constituents for obese patients which will help to curtail the proteins using different mechanisms.

INTRODUCTION

Obesity is recently becoming a global health problem with alarming number of prevalence. The obesity itself is not defined as a disease but rather a disease process which can end up in various health problems. Height and weight are the measurements currently used in clinical practice to perform obesity diagnosis. One of the most useful parameter is to correlate height and weight is the body mass index (Bonamichi B *et.al.,* 2018). According to World Health Organization, classification of obesity is tabulated in the table 1.

Table 1 Classification of obesity

BMI(Kg/m2)	Classification	Risk of related diseases
18.5 -24.9	Normal	Normal
25.0 – 29.9	Over weight	High
30.0 – 34.9	Obesity class I	Super high
35.0 – 40.0	Obesity class II	Super super high
>40.0	Obesity class III	Established disease

It is one of the most prevalent disorder which requires proper diagnosis and multidisciplinary long term treatment.

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environment in which patient consumes meal. Also, there are many biochemistry pathways and mechanisms which could lead to the metabolic syndrome. One of them is Fat Mass and Obesity associated protein (FTO) (Kaviya M., 2016). FTO protein plays important role in regulating fat accumulation in the body. Some other proteins associated with obesity are Resistin and Leptin. Resistin which is also known as adipose tissue specific secretory factor increases the production of LDL in human liver cells and degrades the LDL receptors in liver. Leptin is a hormone that regulates the amount of fat stored in the body. It plays an important role in adjusting both the sensation of hunger and adjusting energy expenditure (Sumaryada T*et.al.,* 2018).

Nowadays many synthetic anti-obesity drugs are in the market but its side effects make it not suitable for long term use. Hence, there is a need to identify newer drugs without side effects. As Hippocrates quoted ”Let your food be your medicine”, an effort was taken to screen the action of important phyto constituents seen in fruits, vegetables, seeds which we use in daily life against the targeted proteins; FTO, Resistin and Leptin (Akhila.S *et al*., 2015 & Gandhi S P *et al*., 2019). Molecular docking is the technique employed to identify the binding efficiency of phytoconstituents with targeted proteins and preferred orientation of one molecule to other which bound to each other to form a stable complex. The

preferred orientation will help in the prediction of binding energy and will be helpful in identifying the specific biological response it induces on the body (Chowdary R *et al.,* 2017). In the present study, we aimed to curtail the action of proteins by docking with phytoconstituents.

METHODOLOGY

Protein targets (Sumaryada Tet.al., 2018).

Three targeted proteins were subjected for the study and the proteins selected were Fat mass and obesity associated protein [FTO] (PDB ID: 3LFM), Resistin (PDB ID: 1LV6), and Leptin (PDB ID: 1AX8). All the proteins were downloaded from protein data bank and depicted in the figures 1, 2 and 3.

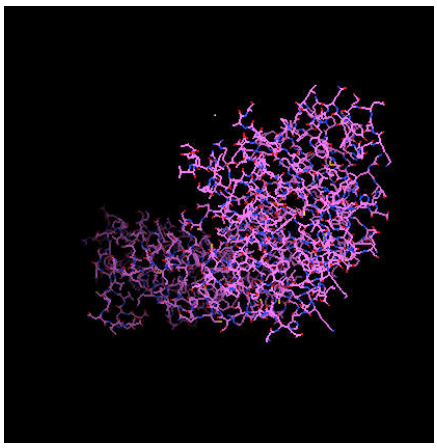

Fig 1 3 LFM (FTO Protein)

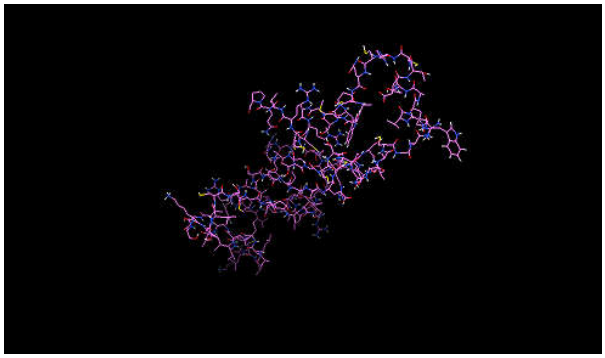

Fig 2 1LV6 (Resistin)

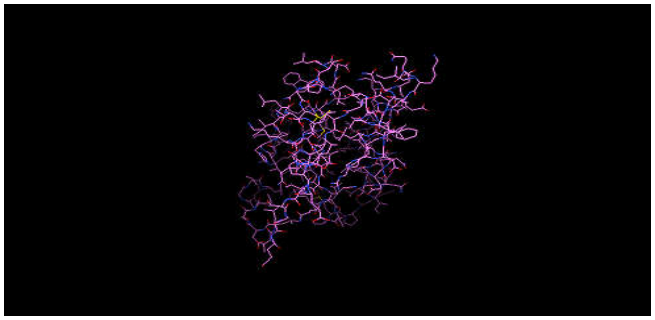

Fig 3 1AX8 (Leptin)

Ligand preparation

Phytoconstituents selected for the study were collected after a thorough review on food ingredients usually fruits, vegetables, seeds used in the daily life and also reported to be preferred in the anti-obese diet. All the ligands used for the study were drawn using chemsketch and converted to pdb files using online tool CORINA. Smiles of the standard drug, orlistat was obtained from Pubmed and converted to PDB file using CORINA.

Docking analysis (Chowdary R *et al.,* 2017 & Veintramuthu S *et al*., 2018)

Molecular docking is the process by which two molecules fit together in 3D space and is a key tool in structural biology and computer aided drug design. Autodock tools 1.5.6 was used to carry out the molecular docking and the ligand binding to three different proteins were calculated. Prepared protein and the prepared ligand PDBQT files were used to prepare the autogrid and the grid points in X, Y and Z axis were set at 60X 60 X 60. Lamarckian Genetic Algorithm was used for dock ng conform 60. Docking was performed based on Lamarckian genetic algorithm.

RESULTS

The phytoconstituents were subjected to docking studies against three obesity associated proteins; FTO, resistin and leptin and the results were compared with orlistat drug. The binding energy obtained for phytoconstituents against each protein FTO, Resistin and Leptin were tabulated in the table 2,3 and 4 respectively. The interaction of constituents with proteins were depicted in the figures 4,5,6,7 and 8 respectively.

Table 2 Interaction of FTO with ligands

Ligands	Binding energy	No: of H bonds formed
Caffeic acid	-5.36	2
Coumaric acid	-4.28	1
Quercetin	-5.13	2
Genistein	-6.18	1
Daidzein	-6.84	1
Apigenin	-5.92	1
Luteolin	-5.47	2
Catechin	-5.45	3
Malvidin	-5.16	2
Capsaicin	-5.02	1
Nicotine	-5.48	2
Resveratrol	-5.1	1
Orlistat (synthetic drug)	-7.15	0

Table 3 Interaction of Resistin with Ligands

Ligands	Binding energy	No: of H bonds formed
Caffeic acid	-3.01	1
Coumaric acid	-3.76	3
Quercetin	-5.19	4
Genistein	-4.43	1
Daidzein	-5.81	2
Apigenin	-5.18	3
Luteolin	-4.9	4
Catechin	-4.23	1
Malvidin	-3.93	1
Capsaicin	-3.36	0
Nicotine	-5.48	1
Resveratrol	-3.49	2
Orlistat (synthetic drug)	-7.16	0

Table 4 Interaction of leptin with ligands

Ligands	Binding energy	No: of H bonds formed
Caffeic acid	-3.20	2
Coumaric acid	-3.61	1
Quercetin	-5.13	3
Genistein	-5.25	1
Daidzein	-5.99	1
Apigenin	-5.93	0
Luteolin	-4.62	1
Catechin	-5.15	5
Malvidin	-4.69	4

Capsaicin	-4.19	1
Nicotine	-5.15	2
Resveratrol	-5.46	1
Orlistat (synthetic drug)	-5.31	1

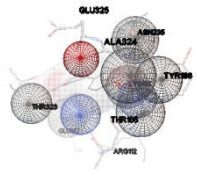

Figure 4 Interaction of FTO protein (wire frames) with daidzein

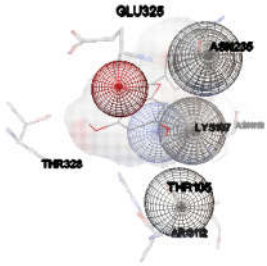

Figure 5 Interaction of FTO protein with catechin

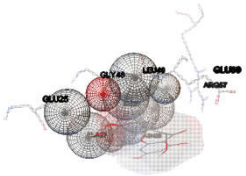

Figure 6 Interaction of Resistin with Quercetin

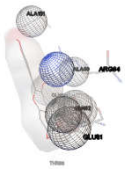

Figure 7 Interaction of leptin with catechin

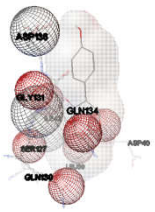

Figure 8 Interaction of Leptin with daidezin

DISCUSSION

Obesity, a metabolic disorder is increasing in alarming rate and is a major threat throughout the world. Some synthetic drugs like orlistat is widely used but the side effects of the same demands better, clinically safe medications as it has to be used for long term periods. Hence, the present study aimed to screen some phytoconstituents belonging to different classes and commonly seen in fruits and vegetables against three different target proteins.

This helped to identify the phytoconstituents which act better against obesity with different mechanisms. The phytoconstituents such as Daidzein which is a isoflavonoid found to be the best phytoconstituent to bind with all the three proteins and prevent obesity. Flavanols like quercetin and flavan 3 ol, catechins also showed good binding efficiency and fairly large number of H bonds and thereby helepful in preventing obesity. The phytoconstituents used in the study states clearly its benefit in fighting obesity and confirms the importance of these molecules. Newer drugs can be designed using these clinically safe constituents which acts by different mechanisms towards the same goal.

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Author Disclosure Statement

"No competing financial interests exist.

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