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EVALUATION OF NATURAL OCCURRING ALKALOIDS AS ANTI-OBESITY AGENTS: AN *IN SILICO* APPROACH

Ashwin T, Radhakrishnan N
MBBS Student, Saveetha Medical College and Hospital, SIMATS, Chennai, India
Department of Biochemistry, Saveetha Medical College and Hospital, SIMATS, Chennai, India

INTRODUCTION

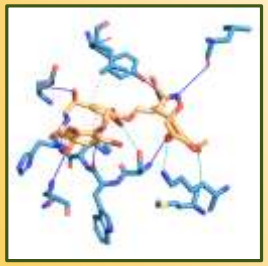
- Alkaloids are class of naturally occurring organic compounds having diverse and important physiological roles on humans and other animals. For instance morphine, quinine, ephedrine, nicotine are few well known alkaloids.
- Alkaloids have been used to treat various disorder, including inflammation, allergies, cancer, diabetes, and many others.
- Alkaloids have been reported to possess various biological activities such as antiviral, anticancer, analgesic, antitubercular, antiproliferative, antibacterial, antioxidant activities.

AIM AND OBJECTIVE

- Based on the above background, the objective of the present study was to assess the anti-obesity activity of selected alkaloids using molecular docking approach.

MATERIALS AND METHODS

1. Ligands were chosen based on literature research
2. Ligands were prepared using Chem Draw 2D, 3D software
3. Target enzymes were identified and downloaded from Protein Data Bank (PDB ID: 3LFM)
4. Target enzymes were prepared using Chimera Software
5. Docking was carried out using SwissDock free web server
6. Best docked pose swiss binding energy value was noted for each ligand and expressed as (-ve) kcal/mol
7. Best docked pose binding site was analyzed for each ligand using protein ligand interaction profiler (PLIP)



It is an docked image of asperversiamides and the fat mass associated protein

RESULT

The *in silico* absorption and distribution (AD) analysis showed that all the selected ligands (except barettin) have exhibited plasma glycoprotein interaction, as shown in the table 1.

Docking analysis showed that Crambescidine has exhibited the highest Swissdock binding energy (-9.84 kcal/mol), whereas Chaetoglobosin has exhibited the lowest Swissdock binding energy (-6.96 kcal/mol) with the target protein (FTO), as shown in the table 2.

Table 1 represents the Absorption and Distribution (AD) properties of selected alkaloids using pkCSM online server

ligands	WS[1]	IA[2]	SP[3]	P-gp*	P-gpI♦	P-gpII■	VDss°	FU**	BBB***
asperversiamides	-3.375	78.067	-2.771	Yes	Yes	No	0.428	0.296	-0.625
chaetoglobosin	-4.559	88.135	-2.856	Yes	Yes	Yes	0.543	0.049	-0.441
barettin	-2.892	93.028	-2.735	No	No	No	0.011	0.389	0.052
lamellarin 14	-3.464	100	-2.735	Yes	Yes	Yes	-1.024	0.272	-1.651
isofistularin 3	-4.036	52.507	-2.736	Yes	Yes	Yes	-1.234	0.247	-2.932
neoamphimedine	-3.9	100	-3.137	Yes	No	No	-0.84	0.147	0.046

Table 2 represents the Swissdock binding energy of selected alkaloids using Swissdock online server

Ligand name	Swissdock binding energy (kcal/mol)	Interactions of amino acids residues	Bond distance (A°) HA	Bond distance (A°) DA
chaetoglobosin	-6.96	Lys211	3.06	3.81
		Lys211	3.26	3.81
		Gln468	2.23	3.01
		Gln468	2.88	3.79
neoamphimedine	-8.11	Arg96	2.69	3.66
		Arg96	3.22	4.07
		Arg322	2.82	3.44
crambescidine	-9.84	Lys216	2.35	3.29
protuboxepin E	-6.54	Gln402	2.77	3.44
		Gln402	3.69	4.09
cycolpenol	-7.17	Asn235	2.20	3.04
		Leu236	3.01	3.92
		Arg239	2.46	3.29

DISCUSSION AND CONCLUSION

- Ser229, Phe317, Leu91, Trp230, His232, His321 amino residues showed interaction with Fat mass and Obesity associated (FTO) protein. The present finding was in par with previous report (Mohammad *et al.*, 2015).
- Sumaryada and colleagues (2018) have reported the catechin and its derivatives as anti-obesity agent using molecular docking method.
- Prabhakar and co-workers (2022) have reported three seaweed compounds namely (BT012, RL074 and RL442) as exhibited anti-obesity agent using *in silico* method.
- In the present study, 27 ligands have been showed to dock with protein. The present findings provide new insight in understanding the 27 selected alkaloids as anti-obesity agents via by modulating the fat mass and obesity associated protein (FTO), which might be useful as anti-sliming agents.

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