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Research Article

DIABETES MELLITUS AND PPAR-γ

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Abstract

Diabetes is a disorder in which the person exhibits a high blood sugar level. It is mainly because the pancreas does not produce enough insulin or the cell response is low. This metabolic disorder also leads to several associated disorders. The rate of diabetic incidence is more in developing countries. The present paper deals with the docking of naturally available ligands with PPAR- γ. It was reported that the ligand Chrysin showed the highest dock results with 256.523 on C-Docker.

Keywords: C-Docker, PPAR- γ, Diabetes, Natural Drugs.

INTRODUCTION

Diabetes is considered to be the instigator of the retinopathy, cataractgenesis, nephropathy etc[1]. It is noted worldwide that more than 285 million people are "diabetic"[2] more than 18 million people are reported with diabetic cataract[3] and around 20 % of the cataract procedures are done for diabetic patients[4]. When there is a deficiency of insulin hormone, it leads to a metabolic disorder called diabetes which is primly because of type 1 diabetes mellitus and type 2 diabetes mellitus[5,6]. It was reported by WHO that India tops the world with a number of 32 million diabetic patients[7]. In the countries like India and Srilanka alone it was reported that 10-16 % of the urban population diabetic[8-10]. Diabetes is associated with several disorders[11,12]. Hence the need to address diabetes has gained importance. In view of achieving an anti diabetic drug, the present paper deals with peroxisome proliferator activated receptor-gamma (PPAR-γ) a member of the nuclear receptor family. They regulate the gene expression[13] and also have a role in cellular differentiation, development and metabolism and tumorigenesis[14]. The research performed by Issemann and Green[15] through on the biological and physiological functions of (PPAR γ) and hence they are a potential target for obesity and diabetes[16]. The objective of the present paper is to dock the PPAR-gamma with the naturally available ligands.

MATERIALS AND METHODS

Ligand and Protein Preparation

Chemsketch software was used to draw the ligand structures. 10 ligand molecules were drawn and were imported on to the Discovery studio for docking after minimization. The protein for the present study, 2Q6S was selected upon the high resolution of Ramachandhran plot. Minimization of the protein was done after the removal of hetero atoms and the water molecules.

ADMET Studies

The ADMET studies were performed for the ligands. The ADMET studies represent the physiological properties of the ligand.

Docking

The protein-ligand docking was done in the Accelerys Discovery Studio. The c-docker algorithm was used to perform the process.

RESULT

Ligand and Protein

The ligands drawn on chemsketch were subjected to minimization. From the protein 2Q6S, the active site was identified, and a sphere was built around the active site.

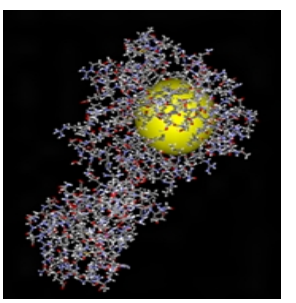


Figure 1: Protein with active site

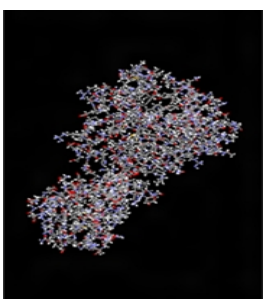


Figure 2: Protein with sphere

ADMET: The ADMET studies revealed the following

	Name	ADMET_BBB	ADMET_Absorpti	ADMET_Solubility	ADMET_Hepatotc	ADMET_CYP2D6	ADMET_PPB_Leve
1	6-dehydroxylongi...	-1.633	0	-2.471	1	0	0
2	ailanquassi A	-1.669	0	-2.717	1	0	0
3	ailanqussian B		0	-1.79	1	0	0
4	ailantinol A		0	-2.286	1	0	0
5	ailantinol B		1	-1.88	1	0	0
6	alfa-hydroxy-13;...	-0.175	0	-4.444	1	0	0
7	alfa-hydroxyeury...	-1.633	0	-2.485	1	0	0
8	bruceanols D		1	-3.323	1	0	0
9	bruceanols E		1	-3.17	1	0	0
10	bruceanols G		1	-2.864	1	0	0
11	bruceanols H		0	-3.983	0	0	0
12	castelatin	-1.629	0	-2.461	1	0	0
13	chaparramarin	-1.459	0	-3.196	1	0	0
14	eurylactone A	0.031	0	-5.294	1	0	0
15	eurylactone B		2	-1.399	1	0	0
16	gutolactone		1	-3.054	1	0	0
17	neoquassin	-0.593	0	-4.113	1	0	0
18	peninsularinone		3	-3.127	1	0	0
19	perforaquqssin B	-0.228	0	-5.074	1	0	0
20	perforaquassin	-0.455	0	-4.503	1	0	0
21	picrasinol D	-1.401	0	-2.693	1	0	0
22	polyandrol	-1.463	0	-3.479	1	0	0

Figure 3: ADMET Results

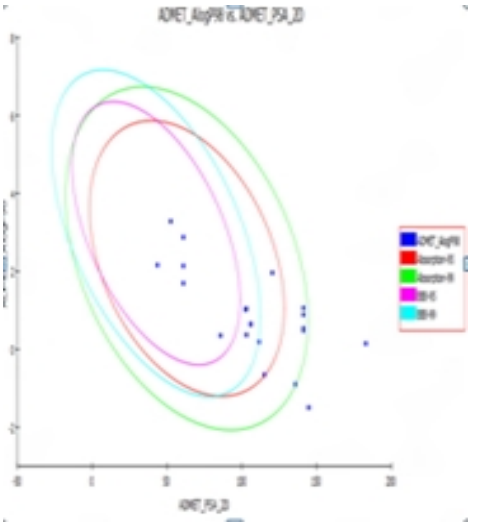
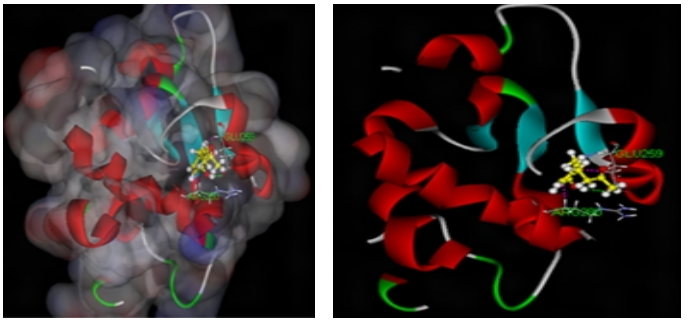


Figure 4: ADMET Results

Name	- CDOCKER_ENERGY	- CDOCKER_INTERACTION_ENERGY	Name	- CDOCKER_ENERGY	- CDOCKER_INTERACTION_ENERGY
acacetin	6.759	13.914	chrysin	-214.876	-70.781
acacetin	6.163	13.445	chrysin	-216.013	-70.483
acacetin	4.092	11.738	chrysin	-219.934	-72.149
acacetin	3.228	13.05	chrysin	-220.363	-70.977
acacetin	2.51	11.221	chrysin	-222.921	-72.136
acacetin	2.492	11.76	chrysin	-223.817	-71.345
acacetin	2.028	12.031	diedzein	7.285	14.88
allicin	-17.008	6.104	diedzein	6.71	14.403
allicin	-17.105	5.609	diedzein	6.595	14.224
allicin	-18.359	7.005	diedzein	5.678	13.17
allicin	-18.361	7.146	diedzein	4.388	12.723
allicin	-18.382	5.375	diedzein	3.616	12.518
allicin	-18.48	7.081	diedzein	3.295	11.617
allicin	-18.815	6.462	dihydroxyquercetin	12.668	18.286
apigenin	10.979	15.516	dihydroxyquercetin	4.609	11.194
apigenin	10.051	14.566	dihydroxyquercetin	4.33	10.729
apigenin	8.91	13.587	dihydroxyquercetin	-0.949	6.581
apigenin	6.327	10.991	dihydroxyquercetin	2.521	11.137
apigenin	2.521	11.137	epicatechin	-154.375	-48.965
apigenin	-195.147	-85.593	epicatechin	-195.419	-62.394
apigenin	-212.614	-71.341	epicatechin	-196.756	-60.956
catechin	-142.541	-40.203	epicatechin	-197.534	-62.154
catechin	-144.83	-39.239	epicatechin	-197.734	-61.615
catechin	-146.309	-39.257	epicatechin	-200.682	-61.728
catechin	-183.358	-47.561	epicatechin	-206.682	-65.751
catechin	-252.558	-90.55	gingiral	-92.459	-29.174
catechin	-252.976	-89.516	gingerone	16.866	19.565
catechin	-256.014	-89.237	gingerone	14.153	15.148
chrysin	-256.523	-91.182	gingerone	12.417	15.795

Table 1: C-Docker Results



Docking: The prepared protein and ligands were docked using the C-docker.

Figure 5: Protein Ligand Docking

Interacting bonds: ARG 280 and GLU 259

The dock result showed Chrysin (-256.523) to be an excellent ligand and represents a good drug for Diabetes. The amino acids which are attached to hydrogen bonds are ARG 280 and GLU 259.

CONCLUSION

Diabetes mellitus is a condition which not only effects the eye but also effects the other organs[17]. Diabetes is associated with several other disorders. It is hence very important to address this problem with priority. In the present experiment we could successfully identify the natural ligands which inhibit the PPAR Gamma, a potential drug target. The results showed Chrysin to be an excellent drug for Diabetes.

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