

# A theoretical model to study the interactions of xanthene-1,2,3-triazolyl-*N*-riboside and xanthene-piperidinyl-benzisoxazole based conjugates with the insulin: Design, docking and ADME studies

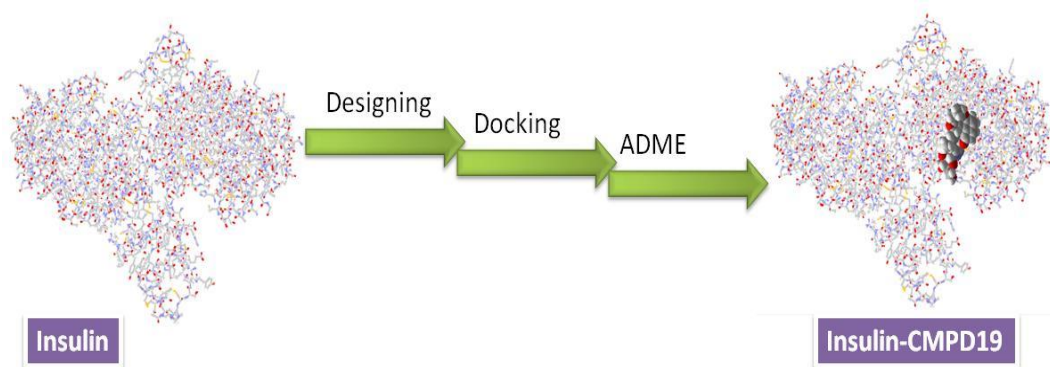
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## Abstract

Literature reported the insulin is an important for the humans and it is secreted in the pancreas and controls, regulates the glucose level. It also controls the mechanism and growth. On decreasing the amount of insulin can caused diabetes, several cancers and other disease. Therefore, there is a need to find promising candidates can binds with insulin and stabilize them. Organic compounds containing hetero atoms have lots of biological potency in different area, therefore, researchers are designing new biological potent compounds. Further, *insilico* studies attracted the researchers in last one decade mainly to get the drug in less time with a clear strategy. In the present work, authors have designed two types of conjugates, xanthenes with trizole as well benzisoxazole and study their interaction with the insulin using computational methods. The library of compounds was screened through molecules docking in terms of binding energy between the designed compound and the active site of the receptor. Further, their ADME properties are investigated. CMPD19 showed best binding affinity with the insulin and may be considered as oral drug based on the bioactive scores.



**Keywords:** Conjugates compounds; insulin; docking; ADME

## Introduction

Insulin hormone which is the major secretion of the  $\beta$ -cells of endocrine gland (pancreas), regulates the extent of glucose in blood by promoting glucose uptake or by quashing glucose production. Diabetes mellitus (DM) is a result of the failure of insulin making or malfunction of tissue sensitivity to insulin [1-9]. Type 1 diabetes mellitus (T1DM) is caused due to the loss of  $\beta$ -cells of pancreas through immune destruction, which leads to inadequate insulin production. Hence, the T1DM patients needed to give insulin from outside for maintaining the required glucose level in the blood [10-13]. The declined tissue sensitivity towards insulin hormone leads to type 2 diabetes mellitus (T2DM). In order to cure T2DM, the hepatic glucose production is reduced and the peripheral glucose utilization is boosted by working on two different approaches, one is to enhance the release of insulin and the other is to improve the action of insulin [14, 15]. Nevertheless, these treatment methods no longer remains very effective when the disease progresses on advance stages and type 2 diabetic patients requires insulin therapy. Therefore, to identify new molecular targets for the development of novel remedial approaches to restore insulin action always be a matter of good research.

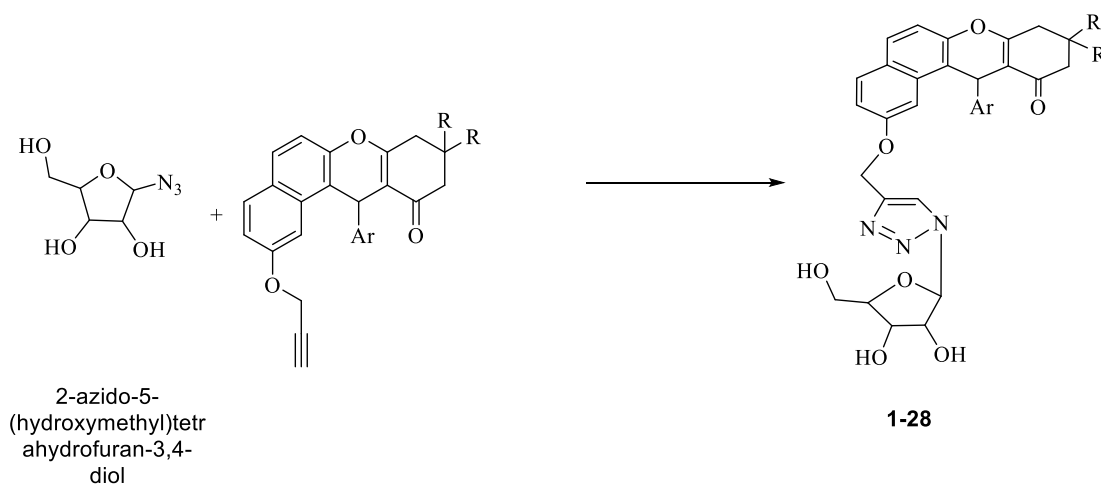
Benzo[*a*]xanthenes play very important role in pharmaceutical chemistry due to their several biological activities [16]. Molecular hybrids holding 1,2,3-triazole own a diversity of medicinal properties including anti-microbial, anti-tumor, anti-alzheimer, anti-diabetic / hypoglycemic activities [17-22]. Further 1,2,3-Triazolyl-*N*-Glycosides/ *N*-glycosides are proven to be very effective anti-diabetic agents [23]. The benzisoxazoles exemplify one of the most privileged structure motifs in medicinal chemistry and different biological studies are increasing day by day on benzisoxazole-containing compounds. The unique benzisoxazole framework shows potent medicinal properties like anti-bacterial, anti-tumor, anti-inflammatory, anti-glycation, anti-psychotic, anti-diabetic etc [24-29].

Keeping in mind the bio-mimicry i.e. bio-motivated design and rational design two or more different biologically active molecules could be joined in a single molecular entity to obtain the hybrid molecules with two distinct pharmacophores and dual mode of action. Hence the technique of molecular hybridization is used in drug design and discovery to get the molecules having improved biological activity with the same or

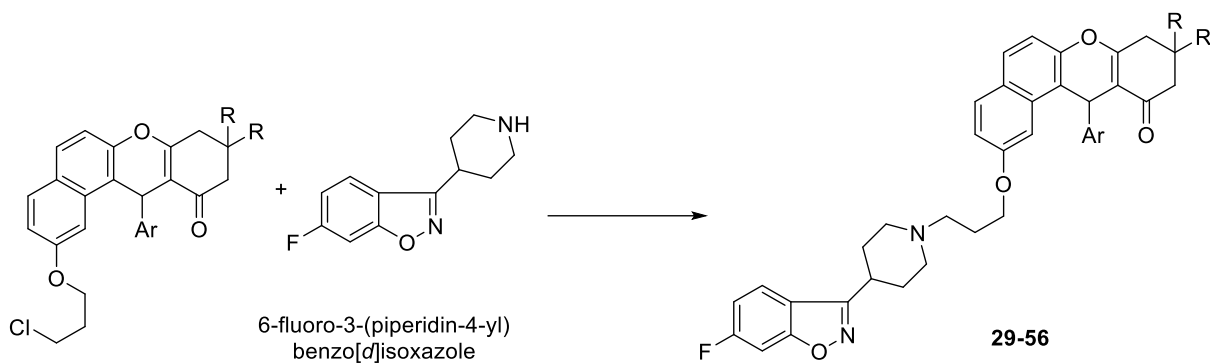
different mode of action compared to the precursors [30, 31]. Computational approaches could also be valuable tool to take decision for the synthesis of molecules to make libraries of desired compounds. Herein, the authors have designed two schemes to get conjugates of xanthenes with the triazole and benzisoxazole. Further, the screening of the compounds was done using the docking and ADME properties to get a promising candidate.

## Experimental

Designing of biological potent xanthenes based conjugates to study the interaction with the insulin as in Scheme 1 and 2. Authors have designed the synthesis of xanthene-1,2,3-Triazolyl-*N*-ribose via the reaction between the sugar or the 2-azido-5-(hydroxymethyl)tetrahydrofuran-3,4-diol with xanthenes as in **Scheme 1** to get compounds **1-28**. Further, synthesis of xanthene-piperidinyl benzisoxazole hybrids is designed via the reaction between 6-fluro-3-(piperidin-4-yl)benzo[d]isoxazole and xanthenes as in **Scheme 2** to get compounds **29-56**. Compounds **1-28** and **29-56** are obtained on changing the substituents (Ar and R) on the cyclic ring of xanthenes as mentioned in **Table 1**.



**Scheme 1** Design the synthesis of xanthene-1,2,3-triazolyl-*N*-ribose via the reaction between the sugar or the 2-azido-5-(hydroxymethyl)tetrahydrofuran-3,4-diol with xanthenes



**Scheme 2** Design the synthesis of xanthene-piperidinyl benzisoxazole hybrids via the reaction between 6-fluoro-3-(piperidin-4-yl)benzo[d]isoxazole and xanthenes

**Table 1** A library of compounds on varying Ar and R in Scheme 1 & 2

For Scheme 1 (1-28)			For Scheme 2 (29-56)		
C. No	Ar	R	C. No	Ar	R
1	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	29	4-FC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
2	4-BrC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	30	4-BrC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
3	4-FC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	31	4-ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
4	4-ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	32	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
5	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	33	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
6	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	34	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
7	3,4-(OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CH <sub>3</sub>	35	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>
8	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	36	3,4-(OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CH <sub>3</sub>
9	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	37	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
10	4-Me <sub>2</sub> CHC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	38	4-Me <sub>2</sub> CHC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
11	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	39	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>
12	2-Naphthyl	CH <sub>3</sub>	40	1-Naphthyl	CH <sub>3</sub>
13	1-Naphthyl	CH <sub>3</sub>	41	2-Naphthyl	CH <sub>3</sub>
14	9-Anthryl	CH <sub>3</sub>	42	9-Anthryl	CH <sub>3</sub>
15	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	43	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H
16	3,4-(OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H	44	4-Me <sub>2</sub> CHC <sub>6</sub> H <sub>4</sub>	H
17	C <sub>6</sub> H <sub>5</sub>	H	45	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H
18	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	46	1-Naphthyl	H
19	4-Me <sub>2</sub> CHC <sub>6</sub> H <sub>4</sub>	H	47	2-Naphthyl	H
20	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	48	9-Anthryl	H
21	2-Naphthyl	H	49	4-FC <sub>6</sub> H <sub>4</sub>	H
22	1-Naphthyl	H	50	4-BrC <sub>6</sub> H <sub>4</sub>	H

23	9-Anthryl	H	51	4-ClC <sub>6</sub> H <sub>4</sub>	H
24	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	52	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H
25	4-ClC <sub>6</sub> H <sub>4</sub>	H	53	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H
26	4-BrC <sub>6</sub> H <sub>4</sub>	H	54	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H
27	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	55	C <sub>6</sub> H <sub>5</sub>	H
28	4-FC <sub>6</sub> H <sub>4</sub>	H	56	3,4-(OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	H

### Molecular docking

All the compounds designed are drawn using Chemdraw and then they were optimized using MM2 for the study. Protein data bank file for the insulin is taken from the RCSB and the ID is 5mam. Then, the pdb is prepared for the docking by the removal of the ligands/ cofactors/ solvents and then addition of atoms, if any. The interactions between the insulin and the designed compounds was performed using molecular docking with the help of a computational tool i.e. iGemdock. The screening is done based on the binding energy for the formation of the complex between the compound and the insulin. This binding is obtained by the electrostatic and van der Waals interaction along with the hydrogen bonding. Further, the molecular interactions of best five compounds with insulin at residues level were studied [32-47].

### Absorption, distribution, metabolism, and excretion (ADME) properties of the designed compounds

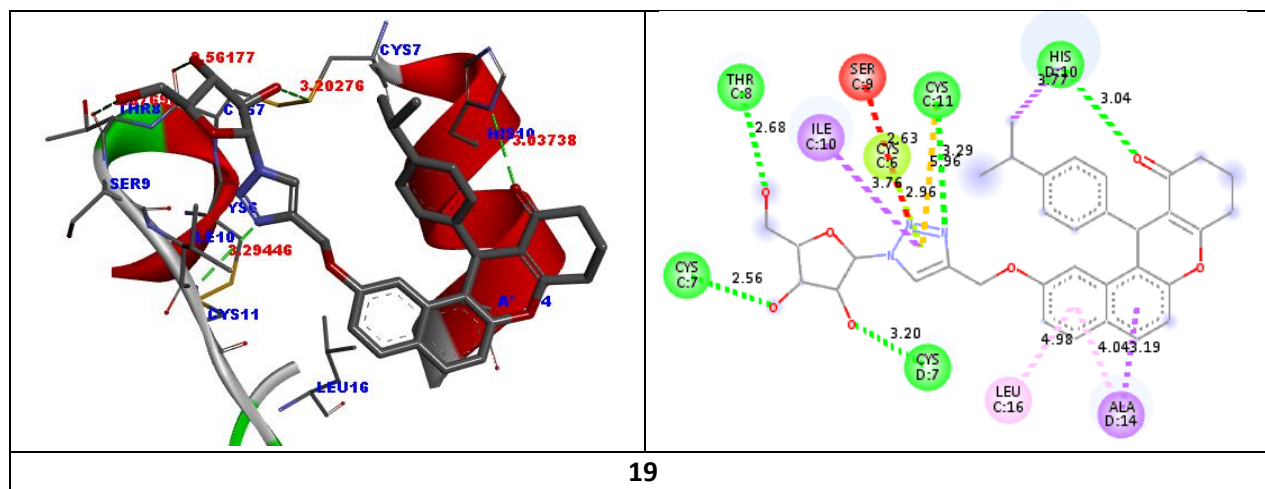
Absorption, distribution, metabolism, and excretion (ADME) properties of the compounds were determined using <http://www.swissadme.ch/>, an online web-server. It is used to explain the disposition of a molecule in the organism. These properties of a molecule affect the tissues in the organisms and explain the pharmacology of the molecule.

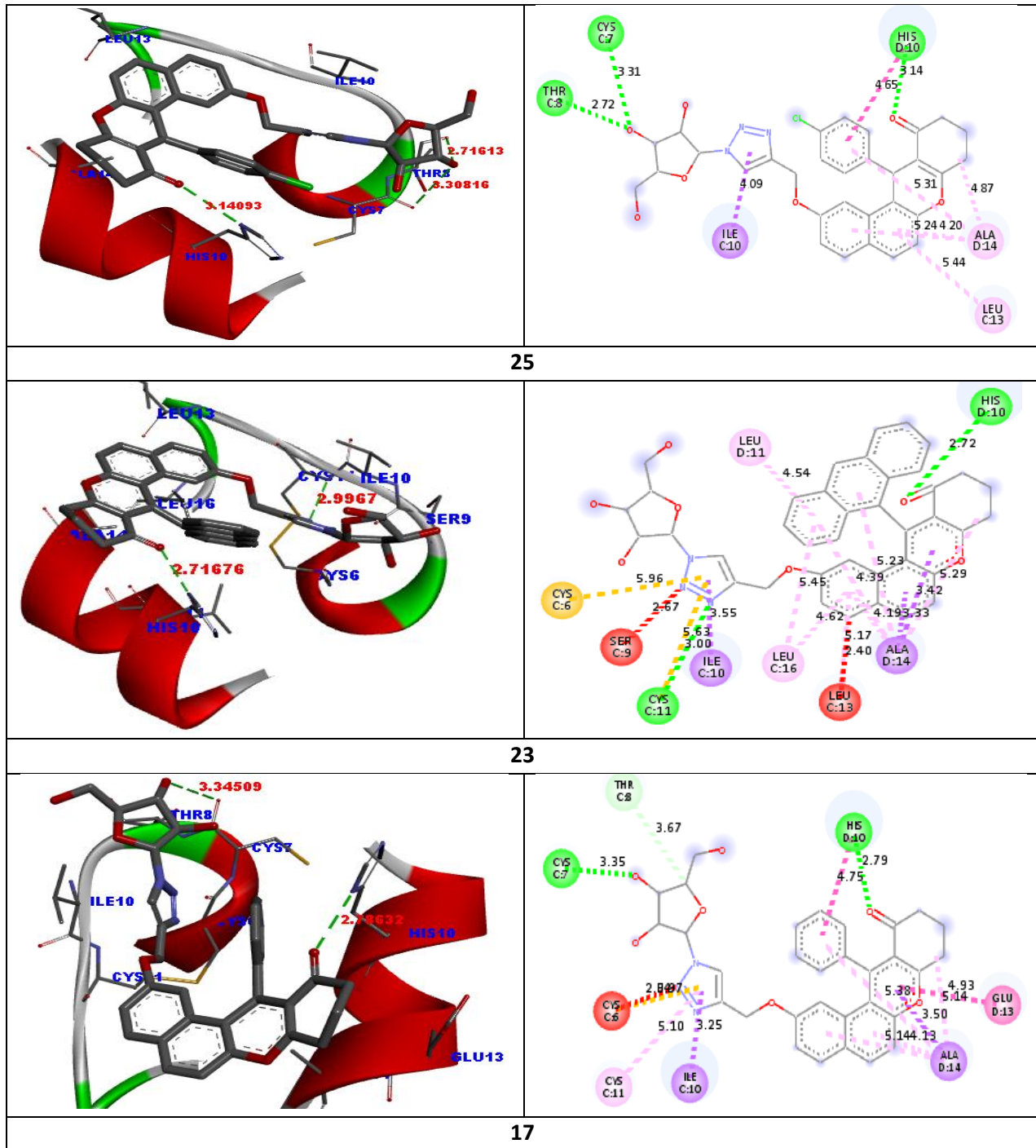
## Result & discussion

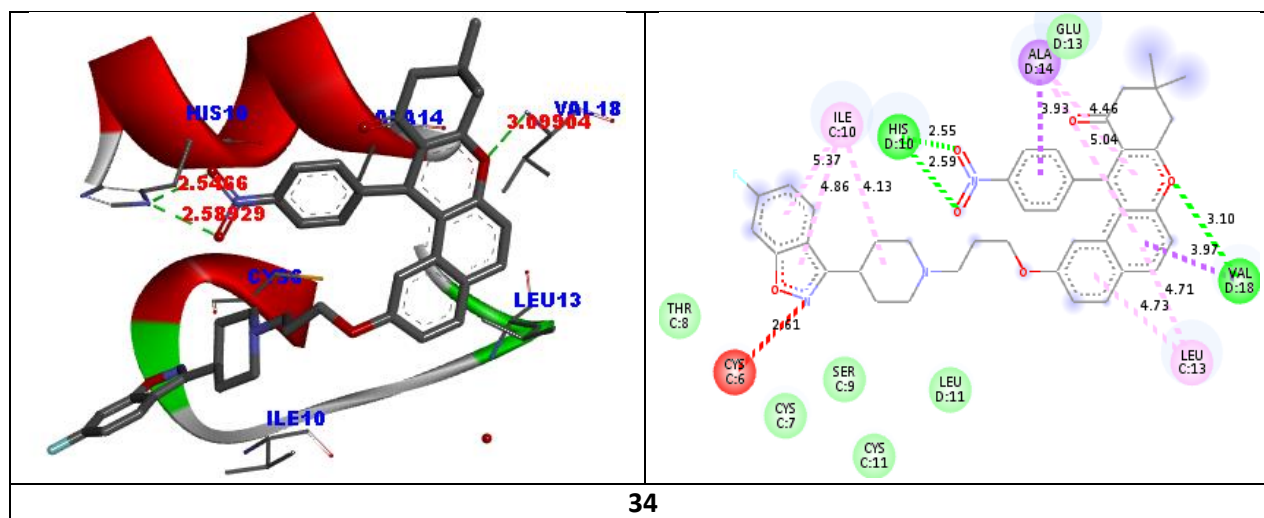
### Molecular docking

Docking of the all the designed 56 compounds were docked with insulin and the binding energy for the formation of the complex is given in **Table 2**. Binding energy for the formation of the complex between the insulin and best five compounds are 19, 25, 23, 17 & 34 with their binding energy are -126.26, -123.617, -119.702, -110.639 and -110.414 kcal/mol. From this, it is understood that the compounds designed from Scheme 1 are more biologically potential. Out of all designed compounds, **CMPD19** showed the best binding affinity with the insulin. Energy contributed from the van der Waals interaction is significant for the formation of complex between the CMPD19 and insulin. Two and three dimensional view for the interaction best five compounds with the amino-acids of the insulin is given in **Figure 1** and the types of interactions is given in **Table 3**.

**CMPD19** showed different types of interactions with the insulin and these are hydrogen bonding (classical and non-classical), hydrophobic and others. CMPD19 forms hydrogen with CYS-C-7; THR-C-8; CYS-D-7; CYS-C-11 and HIS-D-10 of insulin with distance of 2.56; 2.68; 3.20; 3.29 and 3.04 Å. It also forms hydrophobic interactions with LEU-C-16; ALA-D-14; ILE-C-10 and HIS-D-10 of insulin with distance of 4.98; 3.19, 4.04; 3.76 and 3.77 Å. Some other interactions are also observed between the CMPD19 with CYS-C-6 and CYS-C-11 with distance of 2.96 and 5.96 Å.







**Figure 1** Interaction view of the best five compounds (19, 25, 23, 17 & 34) based on the docking with insulin

**Table 2** Total energy obtained on applying docking of the designed compounds with insulin

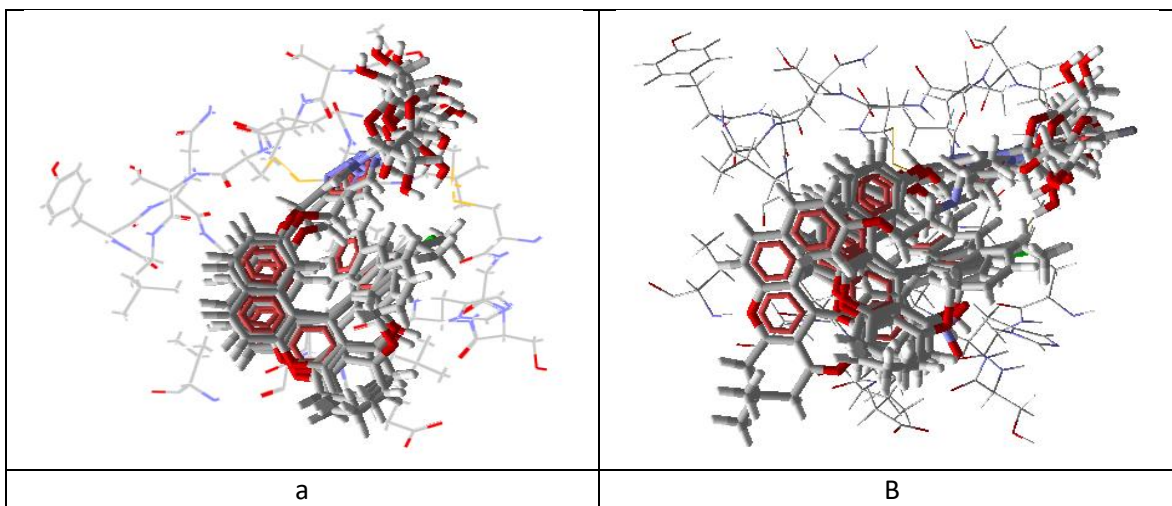
C. No.	Total Energy	EVDW	E <sub>H-Bonding</sub>	E <sub>Elec</sub>	C. No.	Total Energy	EVDW	E <sub>H-Bonding</sub>	E <sub>Elec</sub>
1	-103.475	-90.9092	-13.1713	0.605098	29	-105.663	-91.1232	-14.5398	0
2	-100.223	-90.6664	-9.55675	0	30	-93.7386	-85.6796	-8.05902	0
3	-95.0079	-89.264	-5.7439	0	31	-92.7295	-88.9469	-3.78254	0
4	-97.4916	-87.2296	-10.262	0	32	-85.4703	-79.1663	-6.30399	0
5	-95.6749	-87.009	-8.66584	0	33	-91.0151	-89.2924	-1.72264	0
6	-100.133	-87.9581	-12.1752	0	<b>34</b>	<b>-110.414</b>	<b>-89.1574</b>	<b>-21.8205</b>	<b>0.56412</b>
7	-103.348	-87.1948	-16.1531	0	35	-96.7847	-83.024	-13.7608	0
8	-102.658	-78.129	-24.5294	0	36	-100.94	-85.6775	-15.2626	0
9	-89.5631	-73.8248	-15.7383	0	37	-107.718	-97.6659	-11.0423	0.990078
10	-99.0018	-80.0554	-18.9465	0	38	-84.5454	-80.3046	-4.24082	0
11	-105.862	-89.5569	-16.3048	0	39	-99.4778	-96.7699	-2.70791	0
12	-104.492	-92.6053	-11.887	0	40	-96.5244	-87.0244	-9.5	0
13	-108.332	-93.1772	-15.155	0	41	-88.0899	-85.5899	-2.5	0
14	-109.462	-87.3984	-22.0637	0	42	-92.2911	-89.2969	-2.99414	0
15	-94.9422	-81.1558	-13.7863	0	43	-105.287	-95.1022	-11.3535	1.1691
16	-103.122	-89.0381	-14.0836	0	44	-97.9091	-92.8259	-5.08316	0
<b>17</b>	<b>-110.639</b>	<b>-98.2899</b>	<b>-12.3486</b>	<b>0</b>	45	-101.413	-101.413	0	0
18	-104.74	-86.6321	-18.1079	0	46	-102.368	-97.3683	-5	0
<b>19</b>	<b>-126.26</b>	<b>-104.354</b>	<b>-21.9062</b>	<b>0</b>	47	-93.7946	-92.0404	-1.75423	0
20	-104.294	-93.6311	-10.6631	0	48	-108.539	-102.539	-6	0
21	-96.517	-81.515	-15.002	0	49	-94.2811	-87.3834	-6.89776	0
22	-101.87	-89.5003	-12.3695	0	50	-90.8006	-84.1727	-6.6279	0
<b>23</b>	<b>-119.702</b>	<b>-103.659</b>	<b>-16.0435</b>	<b>0</b>	51	-103.799	-100.608	-3.19042	0
24	-101.262	-90.7072	-10.5546	0	52	-106.444	-93.9568	-12.4869	0
<b>25</b>	<b>-123.617</b>	<b>-102.086</b>	<b>-21.5304</b>	<b>0</b>	53	-91.3455	-89.3	-2.04543	0
26	-97.0398	-84.1852	-12.8547	0	54	-107.579	-100.834	-7	0.255258
27	-109.683	-101.762	-8.51703	0.596614	55	-96.9498	-86.4498	-10.5	0
28	-108.675	-94.2878	-14.3874	0	56	-103.849	-93.4877	-10.3616	0



**Table 3** Different interaction of the best five compounds (19, 25, 23, 17 & 34) with insulin through molecular docking

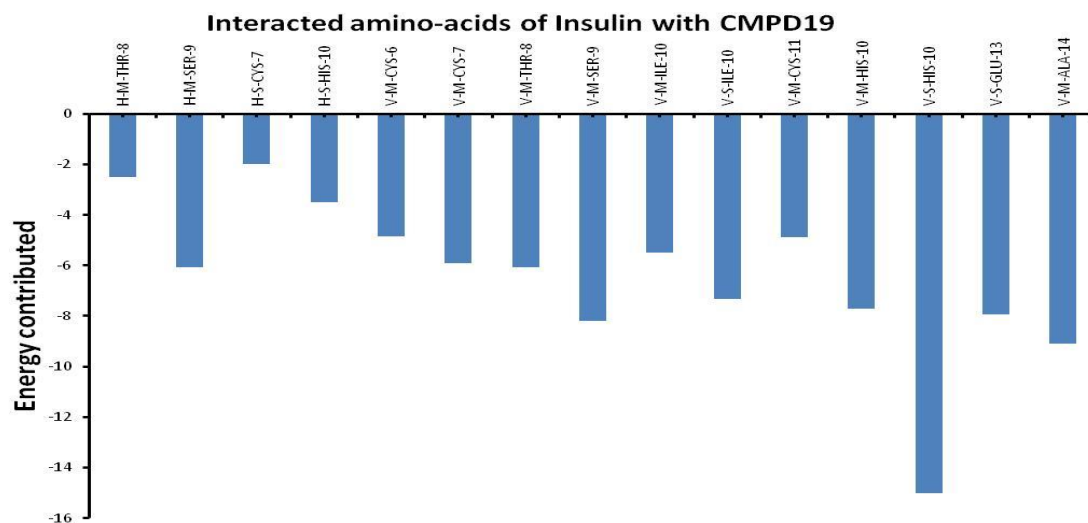
C. No.	H-bonds			Hydrophobic	Miscellaneous			
	Classical	Non-classical						
19	CYS-C-7; THR-C-8; CYS-D-7; CYS-C-11; HIS-D-10;	2.56; 2.68; 3.20; 3.29; 3.04			LEU-C-16; ALA-D-14; ILE-C-10; HIS-D-10	4.98; 3.19, 4.04; 3.76; 3.77	CYS-C-6; CYS-C-11	2.96; 5.96
25	CYS-C-7; THR-C-8; HIS-D-10	3.31; 2.72; 3.14			ILE-C-10; HIS-D-10; ALA-D-14; LEU-C-13	4.09; 4.65; 4.87, 4.20, 5.24; 5.44		
23	CYS-C-11; HIS-D-10	3.00; 2.72			LEU-D-11; LEU-C-16; ALA-D-14; CYS-C-6; CYC-C-11	4.54; 4.62, 5.45; 4.39, 5.23, 3.33, 3.42; 5.96; 5.63	CYS-C-6	5.63, 5.96
17	HIS-D-10; CYC-C-7	2.79; 3.35	THR-C-8	3.67	CYS-C-11; ILE-C-10; HIS-C-10; ALA-D-14; GLU-D-13	5.10; 3.25; 4.75; 5.38, 5.14, 4.13; 4.93	CYS-11	5.97
34	VAL-18; HIS-10	3.10; 2.59, 2.55			ILE-10; LEU-13; VAL-18; ALA-14	5.37, 4.86; 4.73, 4.71; 3.97; 3.93, 5.04, 4.48	CYC-6	2.61

The superimposed views of the best four and five compounds with the insulin are given in the **Figure 2**. From this, it can be clearly understood that these compounds binds to the same active site of the receptor of the insulin.



**Figure 2** Superimposed views of the best (a) four and (b) five compounds with the insulin

It is also important to understand to find the interaction of the promising compound with the amino-acids of the receptor at the active site. Significant energy contributions from the interacted amino-acids of insulin with CMPD19 are V-S-HIS-10, V-M-ALA-14 and V-M-THR-8 as in **Figure 3**.



**Figure 3** Plot for the significant energy contribution of the insulin with **CMPD19****ADME properties of the compounds**

The designed compounds in the Scheme 1 and 2 are studied for the ADME properties. Different physio-chemical properties (molecular weight, number of heavy atoms, number of rotational bonds, number of hydrogen bond donors and number of hydrogen bond acceptors) of the compounds are determined. Further, number of violations for the drug likeness (Lipinski's rule of five, Ghosh, Veber, Egan and Muegge) are determined using the web-server as in **Table 4**. The number of violations for the Lipinski's rule of five, Ghosh, Veber, Egan and Muegge of screened **CMPD19** are 1, 3, 0, 1 and 0. Usually, Lipinski's rule of five is considered by the researchers to understand the behavior of compounds to act as drug. If the number of violation in Lipinski's rule of five is 0 or 1, then the compound is acceptable. For the selection of a compound to be a drug then it is important for the compound to reach the target in enough concentration so the expected biological action can take place. In view of it, **CMPD19** may be considered as a promising drug candidate.

**Table 4** Physio-chemical descriptors of the designed compounds as in **Table 1**

C. No.	Mol. wt. (g/mol)	No. of heavy atoms	No. of rotatable bonds	No. of H-bond donors	No. of H-bond acceptors	Drug likeness (No. of Violations)				
						Lipinski	Ghosh	Vebar	Egan	Muegge
1	628.63	46	7	3	11	2	3	1	1	3
2	662.53	44	6	3	9	1	3	0	1	1
3	601.62	44	6	3	10	1	3	0	1	1
4	618.08	44	6	3	9	1	3	0	1	1
5	597.66	44	6	3	9	1	3	0	1	0
6	613.66	45	7	3	10	2	3	1	1	1
7	643.68	47	8	3	11	2	3	1	1	3
8	583.63	43	6	3	9	1	3	0	1	0
9	628.63	46	7	3	11	2	3	1	1	3
10	625.71	46	7	3	9	1	3	0	1	1
11	651.63	47	7	3	12	1	3	0	1	2
12	633.69	47	6	3	9	1	3	0	1	2
13	633.69	47	6	3	9	1	3	0	1	2
14	683.75	51	6	3	9	1	4	0	1	3
15	585.60	43	7	3	10	2	3	1	1	0
16	615.63	45	8	3	11	2	3	1	1	3
17	555.58	41	6	3	9	1	2	0	1	0

18	600.58	44	7	3	11	2	3	1	1	3
19	597.66	44	7	3	9	1	3	0	1	0
20	623.58	45	7	3	12	1	3	0	1	2
21	605.64	45	6	3	9	1	3	0	1	2
22	605.64	45	6	3	9	1	3	0	1	2
23	655.70	49	6	3	9	1	3	0	1	3
24	569.60	42	6	3	9	1	3	0	1	0
25	590.02	42	6	3	9	1	2	0	1	0
26	634.47	42	6	3	9	1	2	0	1	1
27	600.58	44	7	3	11	2	3	1	1	3
28	573.57	42	6	3	10	1	2	0	1	0
29	648.74	48	7	0	8	2	4	0	1	3
30	709.64	48	7	0	7	2	4	0	1	3
31	665.19	48	7	0	7	2	4	0	1	3
32	644.77	48	7	0	7	2	4	0	1	3
33	660.77	49	8	0	8	2	4	0	1	3
34	675.74	50	8	0	9	2	4	0	1	3
35	630.75	47	7	0	7	2	4	0	1	3
36	690.80	51	9	0	9	2	4	0	1	3
37	675.74	50	8	0	9	2	4	0	1	3
38	672.83	50	7	0	8	2	4	0	1	3
39	698.75	51	8	0	10	2	4	0	1	3
40	680.81	51	7	0	7	2	4	0	1	3
41	680.81	51	7	0	7	2	4	0	1	3
42	730.86	55	7	0	7	2	4	0	1	3
43	647.69	48	8	0	9	1	4	0	1	3
44	644.77	48	8	0	7	2	4	0	1	3
45	670.69	49	8	0	10	2	4	0	1	3
46	652.75	49	7	0	7	2	4	0	1	3
47	652.75	49	7	0	7	2	4	0	1	3
48	702.81	53	7	0	7	2	4	0	1	3
49	620.68	46	7	0	8	2	4	0	1	3
50	681.59	46	7	0	7	2	4	0	1	3
51	637.14	46	7	0	7	2	4	0	1	3
52	616.72	46	7	0	7	2	4	0	1	3
53	632.72	47	8	0	8	2	4	0	1	3
54	647.69	48	8	0	9	1	4	0	1	3
55	602.69	45	7	0	7	2	4	0	1	3
56	662.75	49	9	0	9	2	4	0	1	3

Later, other bioactive scores ( $\text{LogP}_{o/w}$ , GI absorption, BBB permeability, P-gp binder,  $\text{LogK}_p$  and others) of the designed compounds are determined as in **Table 5**.  $\text{LogP}_{o/w}$  is an important parameter in development of drug designing and it is a partition coefficient between the n-octanol and water.  $\text{LogP}_{o/w}$  of CMPD is 3.39 and considered to moderately polar in nature and may be considered for oral drug. Further, it has low GI absorption and

not a good permeable to blood brain barrier. P-gp of CMPD19 has a good ATP-binding cassette transporter for active efflux through biological membranes.

**Table 5** Various bioactive score of the designed compounds as in **Table 1**

C. No.	Log P <sub>o/w</sub>	GI absorption	BBB permeant	P-gp substrate	Log K <sub>p</sub> (cm/s)	Lead-likeness	TPSA (Å <sup>2</sup> )
1	2.40	Low	No	Yes	-7.88	No	181.98
2	3.68	Low	No	Yes	-7.47	No	136.16
3	3.35	Low	No	Yes	-7.53	No	136.16
4	3.58	Low	No	Yes	-7.25	No	136.16
5	3.43	Low	No	Yes	-7.31	No	136.16
6	3.09	Low	No	Yes	-7.69	No	145.39
7	3.04	Low	No	Yes	-7.89	No	154.62
8	3.07	Low	No	Yes	-7.49	No	136.16
9	2.41	Low	No	Yes	-7.88	No	181.98
10	3.88	Low	No	Yes	-6.94	No	136.16
11	4.04	Low	No	Yes	-7.27	No	136.16
12	3.88	Low	No	Yes	-6.91	No	136.16
13	3.95	Low	No	Yes	-6.91	No	136.16
14	4.63	Low	No	Yes	-6.32	No	136.16
15	2.45	Low	No	No	-8.11	No	145.39
16	2.38	Low	No	No	-8.32	No	154.62
17	2.36	High	No	No	-7.91	No	136.16
18	1.82	Low	No	Yes	-8.30	No	181.98
19	3.36	Low	No	Yes	-7.36	No	136.16
20	3.65	Low	No	Yes	-7.69	No	136.16
21	3.39	Low	No	Yes	-7.32	No	136.16
22	3.30	Low	No	Yes	-7.32	No	136.16
23	4.06	Low	No	Yes	-6.74	No	136.16
24	2.78	Low	No	Yes	-7.73	No	136.16
25	3.02	Low	No	Yes	-7.67	No	136.16
26	3.14	Low	No	Yes	-7.90	No	136.16
27	1.74	Low	No	Yes	-8.30	No	181.98
28	2.83	Low	No	Yes	-7.95	No	136.16
29	7.66	Low	No	No	-4.36	No	64.80
30	7.97	Low	No	No	-4.31	No	64.80
31	7.89	Low	No	No	-4.08	No	64.80
32	7.71	Low	No	No	-4.15	No	64.80
33	7.33	Low	No	No	-4.52	No	74.03
34	6.57	Low	No	No	-4.71	No	110.62
35	7.30	Low	No	No	-4.32	No	64.80
36	7.28	Low	No	No	-4.73	No	83.26

37	6.69	Low	No	No	4.71	No	110.62
38	8.29	Low	No	No	-3.77	No	64.80
39	8.38	Low	No	No	-4.11	No	64.80
40	8.21	Low	No	No	-3.74	No	64.80
41	8.21	Low	No	No	-3.74	No	64.80
42	6.44	Low	No	Yes	-3.15	No	64.80
43	6.12	Low	No	No	-5.13	No	110.62
44	7.73	Low	No	No	-4.20	No	64.80
45	6.80	Low	No	No	-4.53	No	64.80
46	7.66	Low	No	No	-4.15	No	64.80
47	7.64	Low	No	No	-4.15	No	64.80
48	8.37	Low	No	Yes	-3.57	No	64.80
49	7.12	Low	No	No	-4.78	No	64.80
50	7.41	Low	No	No	-4.73	No	64.80
51	7.34	Low	No	No	-4.50	No	64.80
52	7.16	Low	No	No	-4.57	No	64.80
53	6.77	Low	No	No	-4.94	No	74.03
54	6.01	Low	No	No	-5.13	No	110.62
55	6.82	Low	No	No	-4.74	No	64.80
56	6.69	Low	No	No	-5.15	No	83.26

## Conclusion

Insulin is used to control the mechanism and growth in humans. With decrease in amount of the insulin may cause diabetes and some other diseases. Therefore, there is a need to explore to find the promising molecules for the binding with insulin. A library of the conjugates based on the xanthenes with ribose and benzisoxazole are designed studied their interaction with insulin using molecular docking and ADME properties. Based on the molecular docking, it showed the best binding affinity with insulin. Further, based on the ADME scores, CMPD19 may be a promising candidate.

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