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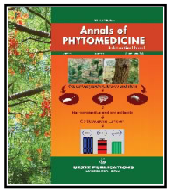

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In silico approach for discovery of drug against the peroxisome proliferator-activated receptor gamma for diabetes treatment

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Abstract

Type 2 diabetes occurs when the body cannot manage glucose efficiently and plasma glucose concentration remains high. This condition generally occurs due to deficiency of insulin or resistant against the insulin hormone. It affects a wide range of people from various socioeconomic sectors and ethnic groups. At least 462 million individuals worldwide have type 2 diabetes; with that number of people suffering from diabetes is expected to reach 693 million by 2045 globally. Due to the availability of a huge number of antidiabetic drugs in the market, still, there is a shortage of the effective and safe drugs in the market. This has raised concerns to find novel drugs. This study focused on finding novel drug a gainst the peroxisome proliferator-activated receptor gamma as a potential target. As it regulates lipid metabolism and glucose homeostasis. Molecular docking was done by AutoDock Vina for the identification of new potential drugs candidate against the peroxisome proliferator-activated receptor gamma. After docking, ligand suitability as a drug candidate also evaluated checking by ADME analysis. Forty docked compounds were evaluated for the pharmacological properties and also compare with standard drug compound. The results were observed that these compounds small litters samin, kobusin, methylpluviatilol, planinin, piperitol, and saltillin could be potential drug candidates for PPARG activation.

1. Introduction

Diabetes is a serious illness that emerges when the body is unable to provide insulin or the pancreas can no longer provide the proper amount of insulin. This condition usually appears when the blood glucose levels are high above its threshold limit 126 mg/dL (7.0 mmol/l) for long time and it is called hyperglycemia (Francois *et al.* 2015). According to the World Health Organization, there are two major forms of diabetes. Type 1 diabetes, T1D is a type of juvenile diabetes that occurs as a result of the body's deterioration of insulin-producing cells. T2D, this condition is referred to as type 2 diabetes. It usually takes place when the cells can no longer use the glucose efficiently (Nolan *et al.*, 2019). High blood pressure and diabetes can also be triggered by other risk factors such as hyperglycemia. The lifestyle changes have also contributed to the rising cases of these conditions. The number of people with diabetes is expected to increase to 693 million by 2045. This condition can cause long-term damage to various organs, such as kidneys, eyes, and blood vessels (Cole *et al.*, 2020).

The peroxisome proliferator activated receptor gamma function is to improve glucose homeostasis by regulating the cell cycle and insulin sensitivity. It is also involved in the development of inflammatory activities. This receptor is a potential therapeutic target for treating diabetes and metabolic syndrome. It increases endothelial cell function by reducing inflammation in diabetes and atherosclerosis. By reducing hepatic glucose synthesis and improving peripheral glucose clearance, PPARG activation increases the action of insulin in insulin-sensitive tissue (Mirza *et al.*, 2019).

However, due to the huge number of drugs available in the market, many countries have been experiencing a shortage of effective and affordable antidiabetic drugs. This has raised the concerns of the public regarding the safety and efficacy of these drugs. Numerous antidiabetic drugs can be found in nature. Using a computer aided drug design technique is one of the most important methodologies in drug discovery and development in recent years (Selvaraj, 2018). Usually, it takes around 10 to 15 years for a new drug to be developed. Through, the use of CAD, pharmaceutical companies were able to speed up the process by identifying the most promising compounds (Selvaraj, 2018). The term "Molecular Docking" refers to a technique that is used to bring molecules together in computer aided drug design Technique to identify which ligands and receptors are the best matches. This procedure involves identifying the conformations of the ligand and the site where it should be placed. In the current study, we tried to identify a new drug candidate that may be utilized to treat diabetes.

2. Materials and Methods

2.1 Retrieval of protein structure

Peroxisome proliferator-activate receptor gamma is a key target for the treatment of type 2 diabetes. It plays a crucial role in the regulation of lipid metabolism and glucose control (Jay *et al.*, 2007). It is also known to improve the function of endothelial cells. PPARG

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is a protein that regulates insulin's action in insulin-sensitive tissue in people who are diabetic (Monsalve *et al*., 2013). The protein data bank (PDBhttp://www.rcsb.org/pdb/) was used to acquire the crystal structure of the target protein peroxisome proliferator-activated receptor gamma. X-beam crystallography was chosen as the test approach for X-beam resolution, with a claim of 2.30 A PPARG ligand-binding domain to SR10171 was found (PDB: 6C5Q) (Frkic *et al*., 2018).

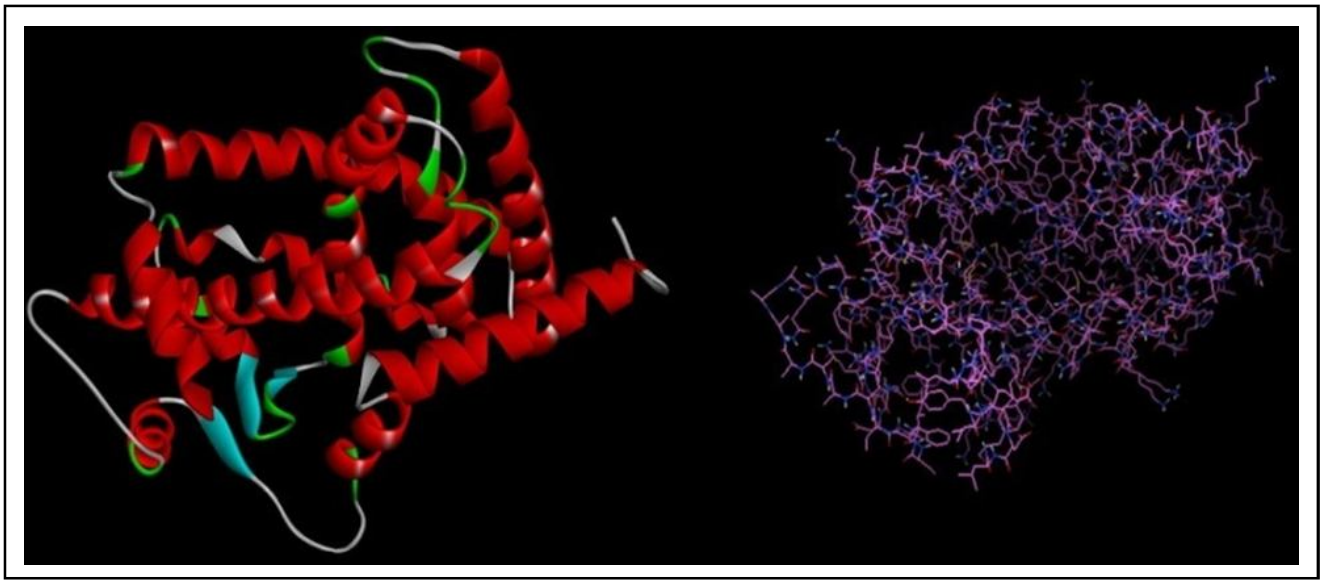

Figure 1: Peroxisome proliferator-activated receptor gamma (PDB: 6C5Q) was obtained through the discovery studio 2021. Helixes are colored red, beta sheets are colored cyan, turns are colored green, and coils are colored white.

2.2 Select and retrieval of ligands

For the present study, we have chosen one common conventional medicines, pioglitazone (Tseng, 2022), as well as forty bioactive compounds shown in Tables 1, 2. The pub chem database (https://pubchem.ncbi.nlm.nih.gov/) was used to retrieve the 3D structures in SDF format, this database comprises a range of chemically validated compounds as well as a wealth of information for depicting substances in pub-chem (Hähnke *et al*., 2018). Later, the structures of those molecules were converted into PDB format using graphic user interface Open Babel Convertor (http://openbabel.org/wiki/Main) (Istyastono, 2012).

Table 1: List of bioactive compounds

Sl.No.	Ligand name	Pub-Chem CID	Sources (plant founds in)
1	Pioglitazone	4829	Thiazolidinedione
2	Asarinin	11869417	*Asarum maculatum*
3	Pluviatilol	70695727	*Piper mullesua*
4	Piperundecalidine	44453654	*Piper longum*
5	EPI-MAGNOLIN A	10454576	*Magnolia biondii*
6	Sylvatesmin	3083590	*Magnolia biondii*
7	Lariciresinol	332427	*Brassica*
8	Diasesartemin	73118	*Hernandi corbigera*
9	Methylpluviatilol	5320622	*Stauranthus*
10	Planinin	129290	*Piper mullesua*
11	Okanin	5281294	*Acacia doratoxylon*
12	Saltillin	5378171	*Camellia sinensis*
13	Myricetin	5281672	*Elegia nuda*
14	Diosmetinidin	14842007	*Galium verum*
15	Aquilarixanthone	51034839	*Aquilaria sinensis*
16	Corallocin B	132524619	*Hericium coralloides*

17	Membrin	10893644	*Annona mucosa*
18	Pinoresinol	73399	*Brassica*
19	Medioresinol B	132492668	*Syzygium cumini*
20	SCHEMBL16917560	476860	*Larrea tridentata*
21	Pinoresinol diacetate	234825	*Araucaria angustifolia*
22	Silibinin	31553	*Asteraceae*
23	Brartemicin	44139747	*Nonomuraea*
24	Mesosyringresinol	101757722	*Hibiscus taiwanensis*
25	Yangambin	443028	*Hernandi corbigera*
26	Syringaresinol	100067	*Ficus septica*
27	Prunetin	5281804	*Iris milesii*
28	Eudesmin	234823	*Machilus kurzii*
29	Sesamin	72307	*Pandanus boninensis*
30	Terameprocol	476861	*Larrea tridentata*
31	Dihydroclusin	3978441	*Piper borbonense*
32	Kobusin	182278	*Pandanus utilis*
33	Piperitol	10247670	*Kala usambarensis*
34	Gallocatechin	65084	*Saxifraga cuneifolia*
35	Abiespiroside A	50925084	*Abies delavayi*
36	Sesartemin	342737	*Ocotea fasciculata*
37	Hedyosumin E	25019245	*Hedyosmum orientale*
38	schisandrin C	119112	*Schisandra bicolor*
39	Corilagin	73568	*Euphorbia fischeriana*
40	Silymarin	5213	*Anastatica hierochuntica*
41	Butein	5281222	*Dahlia pinnata*

2.3 AMDE drug likeness properties

The concept of absorption explains the journey of drugs through the body. When a drug enters the body, it is absorbed by one part of the body and then distributed to another. The process of metabolism involves various chemical reactions that occur after drugs have been metabolized. Then, the body's natural process of removing drugs involves various routes, such as the urine, saliva, milk and stool in a process called excretion (Lakhera *et al*., 2021).

The initial screening of a compound for drug-like properties is usually carried out according to a set of rules and guide lines. Some of these include Veber's rule, the Mueggerule, the Egan rule, Lipinski's rule, and the Lipophilicity rule. The concept of the rule of five Lipinski's rule is based on the idea that if a chemical compound has not violated the other rules, it can be considered an orally active drug. Doing so will allow the compound to reach the markets and become more widely used (Lin *et al*., 2014).

Other basic rules help in determining the structure and function of a drug. These include molecular weight, hydrogen-bond donors, MLOGP, and molar refractivity. The drug screening tests are used to identify drug-like and non-drug-like structures in a drug candidate. They are performed using the "SWISS-ADME" software (http://www.swissadme. Ch). This software allows us to perform various analytical tasks such as druglikeness analysis, pharmacokinetics, lipophilicity analysis, and various other aspects of drug development. In virtual screening, it is often seen that some drugs fail to follow all the screening rules (Yadav *et al*., 2020).

2.4 Molecular docking

In drug design, molecular docking is considered a tool that helps predict the interactions between two molecules when they are bound together (Antony *et al*., 2015). In this work, we have employed the software "AutoDock Vina," a grid-based software that automatically calculates the ideal grid positions for protein and ligand docking. It does so by detecting the best possible grids for protein-ligand docking. It is a suite for determining the binding of a small molecule or drug to a 3D protein structure. At AutoDock Vina, we take into account various parameters such as binding modes and exhaustiveness, which equals 8, energy difference of 4 kcal/mol, a grid box with center coordinates of X=24.118000, Y=-26.150550, and Z=20.413175 of the position of the target protein (Lakhera *et al*., 2021). The goal of the studies is to perform molecular docking on 6C5Q to determine the optimal position of the target protein to study the effects of an activator, (PPARG). A large number of water molecules were found with the protein (PPARG). The structures

were dehydrated, polarhydrogen was added, the Kollman and Gasteiger-type charges were added, and A4D atoms were assigned to the protein 3D structure (Lakhera *et al*., 2021). The ligands are also prepared using AutoDock Vina. Later ligands and the protein are saved in PDQT. Based on the parameters that have been examined, the best protein-ligand complex is chosen rely on its binding energy.

3. Results

3.1 ADME study evaluation

Studies related to the ADME parameters, biocompatibility, and pharmacological proper ties of the molecules must also be supported in the development of new drugs. Many of the failures in the development of new drugs are due to inadequate gastrointestinal and brain access. Due to the increasing number of tools being developed for drug discovery, researchers are continuously striving to improve the efficiency and effectiveness of the process. Swiss ADME is an online server that can predict the various parameters of a drug's absorption, distribution, and metabolism, as well as its medicinal chemistry (Daina *et al*., 2017).

The data is initially described in terms of a two-dimensional chemical structure and canonical SMILES. Those data would be collected by Swiss ADME and then divided into various sections. The 40 (forty) compounds (and pioglitazone) were evaluated for their drug-like properties, following the screening process. Swiss ADME was then used to analyze the various parameters of these compounds. The various parameters of the compounds analyzed by Swiss ADME include AMDE of compounds are measured using the various parameters of the gastrointestinal absorption, blood-brain barrier, and pan-assay interference structure and the area of the polar atoms that are attached to the hydrogena referred to as the TPSA. The presence of high levels of prodrugsatin (PSA) has been known to improve the drug's ability to permeate (Geldenhuys and Allen, 2012). This is because the compounds with high levels of this chemical have poor permeating cell membranes.

The result of this study was represented in a graphical classification model called the BOILED-Egg; it can predict passive diffusion through the interaction between the blood-brain barrier and the gastrointestinal tract. It was also able to take into account the position of the WLOGP-TPSA in certain chemical spaces (Nag *et al*., 2021).

In our study, 21 (twenty-one) phytochemicals were found to have gastrointestinal absorption properties, while 17 (seventeen) compounds exhibited a blood-brain barrier permeation property. 2 (two) compounds were found to be out of range (Figure 2).

The active transport system of P-glycoproteins is responsible for the removal of various drugs and other xenobiotics from the cells. The effects of a concentration gradient are known to affect the oral bioavailability of drugs. When a concentration gradient is applied, the P-glycoproteins act by binding to various substrates and converting them into efflux.

Additionally, All the ligands have been studied *via* bioavailability radar. Bioavailability radar displays the availability of a particular phytochemical for users to visualize its drug-like properties (Daina *et al*., 2017). Figures (3,4,5,6) represent the bioavailability radar for the forty phytochemicals, those has been chosen. The bioavailability radar can visualize a given molecule's various chemical properties. The optimal range for each one is shown in the pink area and includes the size, polarity, amount of lipophilicity, and flexibility. All of these properties must be depicted in a pink area to make it look like a drug-like substance (Figure 3, Figure 4, Figure 5, Figure 6).

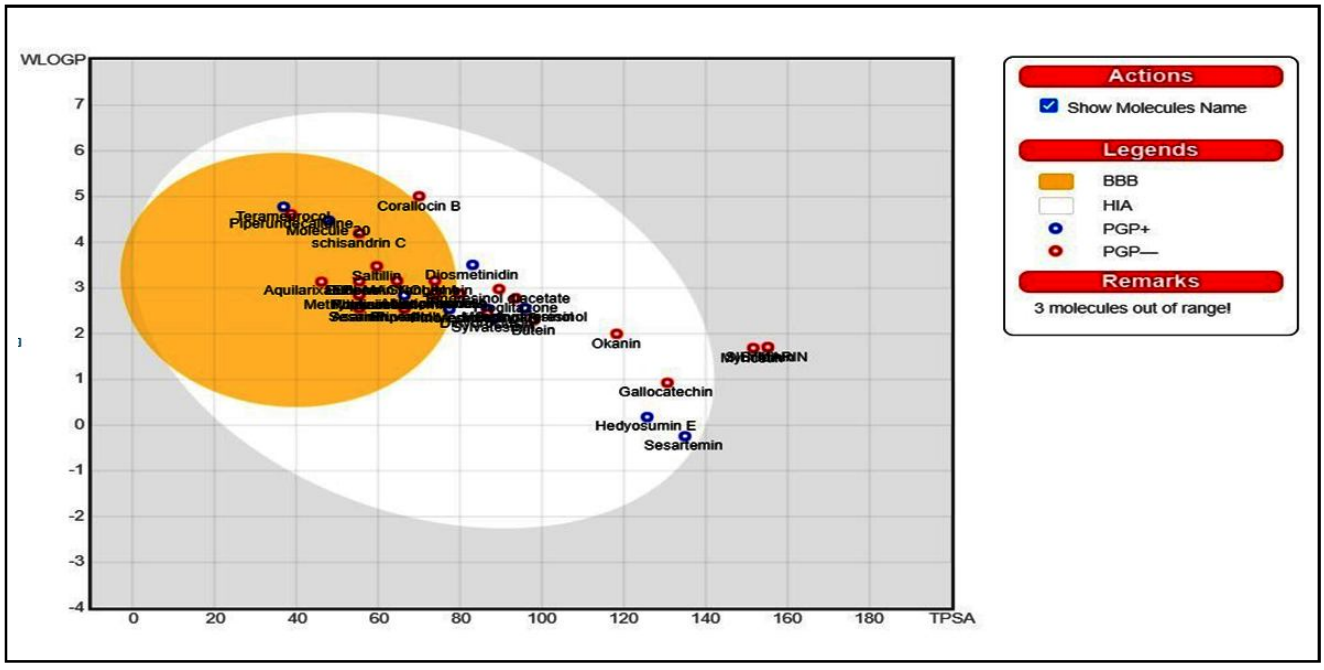

Figure 2: BOILED-Egg: It predicts the passive diffusion through the interaction between the blood-brain barrier and the gastro intestinal tract, the position of the WLOGP-TPSA in a certain chemical space. For 40 (forty) phytochemicals and (pioglitazone).

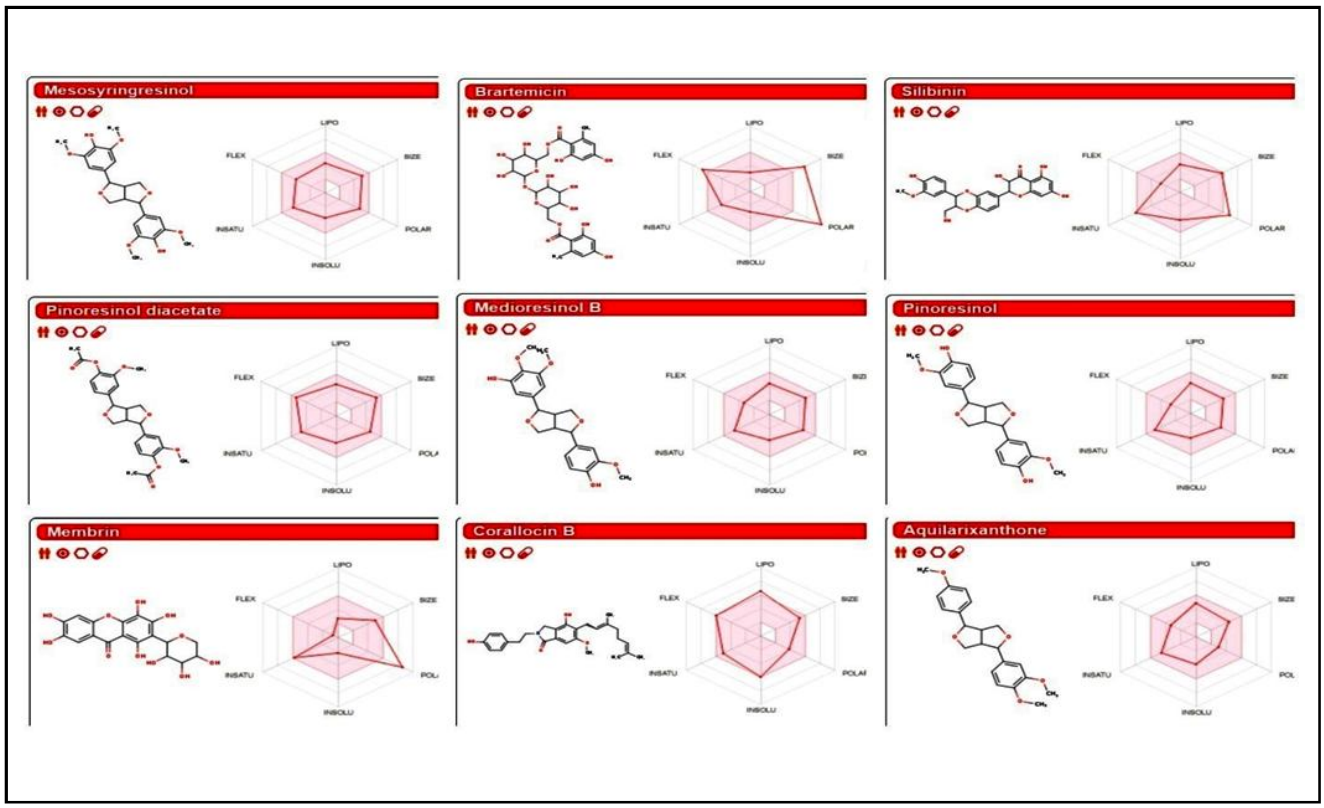

Figure 3: The bioavailability radar for mesosyringresinol, brartemicin, silibinin, pinoresinol diacetate, medioresinol B, pinoresinol, membrin, corallocin B and aquilarixanthone receptively.

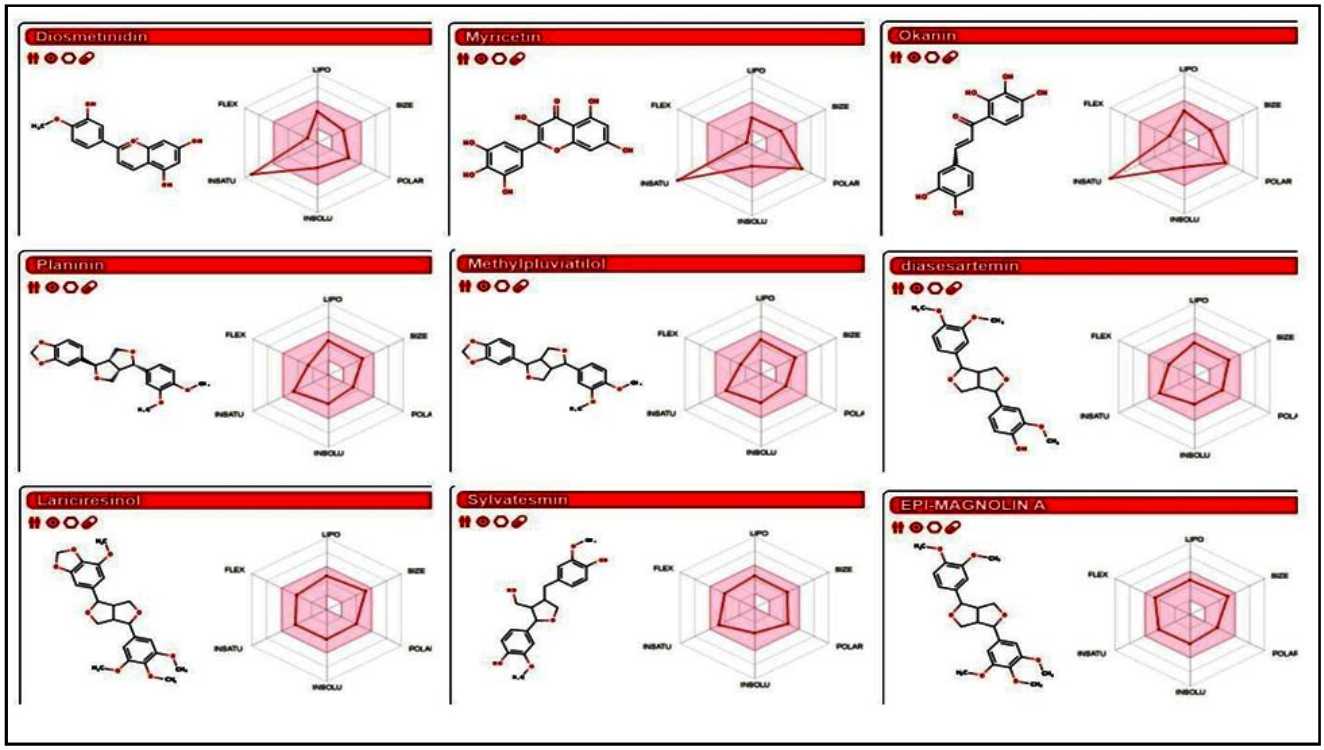

Figure 4: Bioavailability radar for diosmetinidin, myricetin, okanin, planinin, methylpluviatilol, diasesartemin, laricire-sinol, sylvatesmin and EPI-mangolin A receptively.

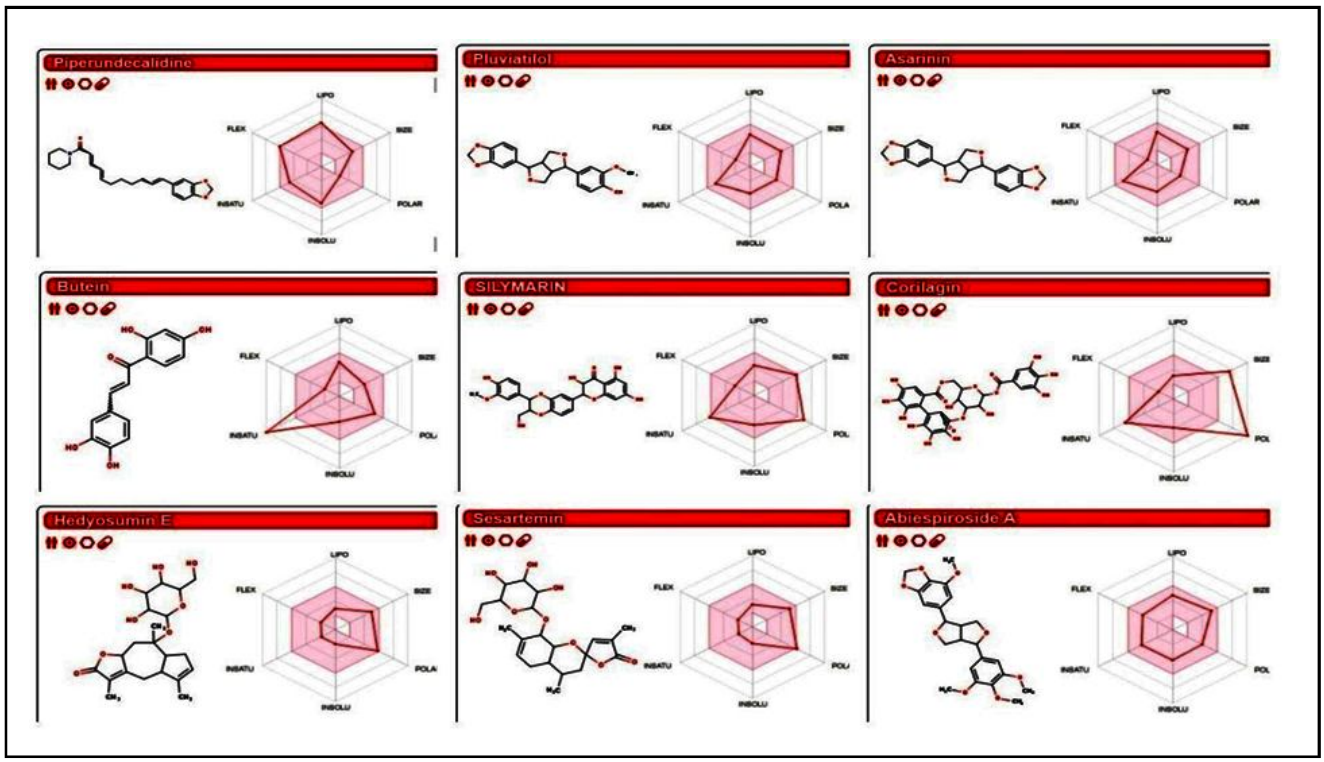

Figure 5: The bioavailability radar for piperundecalidine, pluviatilol, asarinin, butein, silymarin, corilagin, hedyosumin E, sesartemin and abiespiroside A receptively.

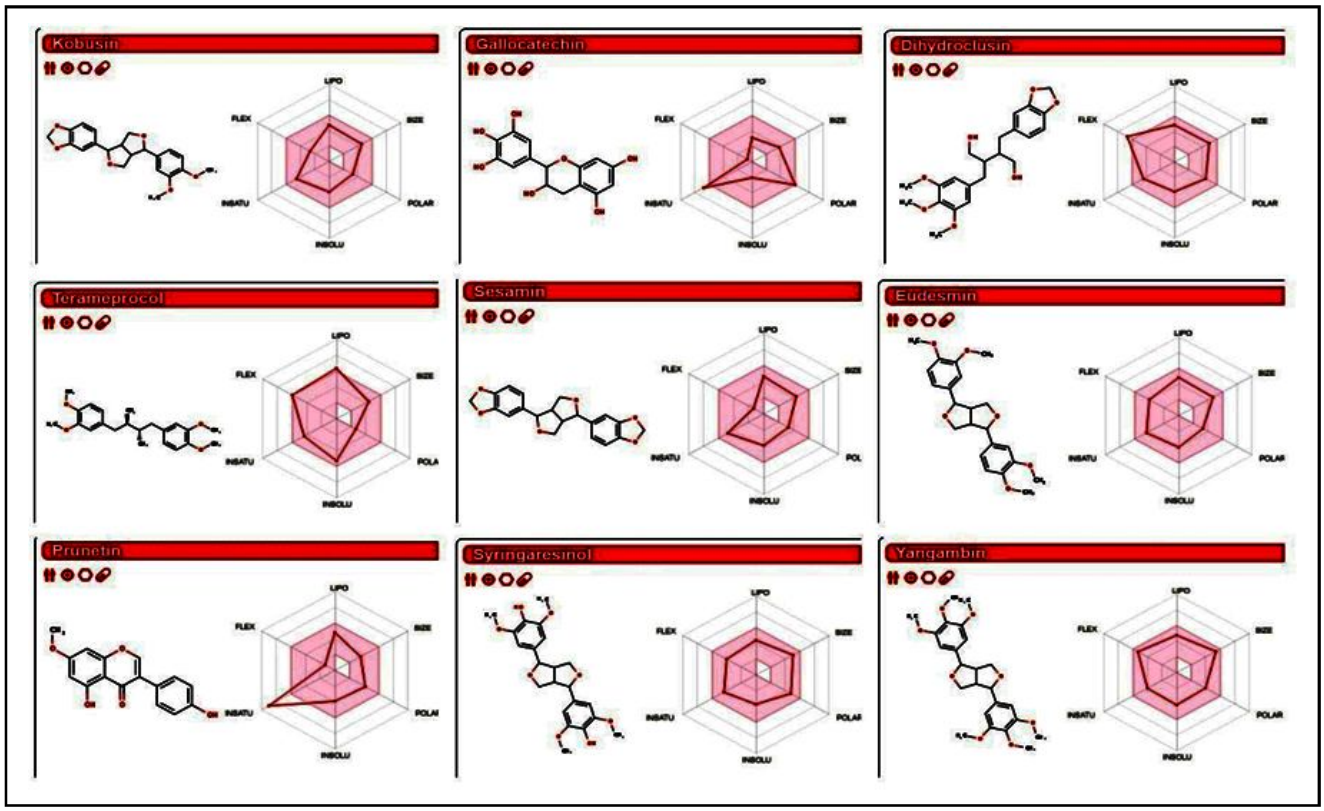

Figure 6: The bioavailability radar for kobusin, gallocatechin, dihydroclusin, terameprocol, sesamin,eudesmin, prunetin, syringaresinol and yangambin receptively.

Only 12 (twelve) out of 40 (forty) phytochemicals are represented in Table 3, Table 4; only those with the best properties to be drug candidates have been included. Those phytochimcals are sesamin, asarinin, kobusin, piperitol, pinoresinol, piperundecalidine, pluviatilol, schisandrin C, planinin, saltillin, membrin and methylpluviatilol.

Table 3: Prediction AMDE result of selected molecules from using SWISS ADME online tool

Compound name	Sesamin	Asarinin	Kobusin	Piperitol	Piperundecalidine	Pinoresinol
Molecular weight	354.5 g/mol	354.35 g/mol	370.40 g/mol	356.37 g/mol	367.48 g/mol	358.39 g/mol
Num. rotatable bonds	2	2	4	3	9	4
Num. H bond acceptors	6	6	6	6	3	6
Num. H-bond donors	0	0	0	1	0	2
Molar refractometry	90.00	90.00	96.92	92.45	113.84	94.90
TPSA	55.38 Å2	55.38 Å2	55.38 Å2	66.38 Å2	38.77 Å2	77.38 Å2
ConsensusLog Po/w	2.79	2.79	2.92	2.56	4.68	2.26
GI absorption	High	High	High	High	High	High
BBB permeant	Yes	Yes	Yes	Yes	Yes	Yes
P-gy substrate	No	No	No	No	No	No
Cytochrome P450	NO	NO	NO	NO	NO	NO
Log Kp (skin permeation)	-6.56 cm/s	-6.56 cm/s	-6.56 cm/s	-6.71 cm/s	-4.44 cm/s	6.87 cm/s
Lipinski	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Bioavailability score	0.55	0.55	0.55	0.55	0.55	0.55
PAINS	0 alert	0 alert	0 alert	0 alert	0 alert	0 alert
Leadlikeness	No	NO	No	No	No	No
Synthetic accessibility	4.12	4.12	4.30	4.19	3.53	3.99

Table 4: prediction AMDE result of selected molecules from using SWISS ADME online tool

Compound name	Pluviatilol	schisandrin C	Planinin	Saltillin	Membrin	Methylpluviatilol
Molecular weight	356.37 g/mol	384.42 g/mol	370.40 g/mol	282.29 g/mol	356.41 g/mol	370.40 g/mol
Num. rotatable bonds	3	2	4	2	5	4
Num. H bond acceptors	6	6	6	4	5	6
Num.H-bond donors	0	0	0	1	0	0
Molar refractometry	92.45	104.03	96.92	81.40	97.35	96.92
TPSA	66.38 Å2	55.38 Å2	55.38 Å2	59.67 Å2	46.15 Å2	55.38 Å2
Consensus Log Po/w	2.56	4.11	2.92	3.25	3.07	2.92
GI absorption	High	High	High	High	High	High
BBB permeant	Yes	Yes	Yes	Yes	Yes	Yes
P-gy Substrate	No	No	No	No	No	No
Cytochrome P450	NO	Yes	NO	NO	NO	NO
LogKp(skin permeation)	-6.71cm/s	-5.09 cm/s	-6.56 cm/s	5.13 cm/s	-6.37cm/s	-6.56 cm/s
Lipinski	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0	Yes; 0
Bioavailability score	0.55	0.55	0.55	0.55	0.55	0.55
PAINS	0 alert	0 alert	0 alert	0 alert	0 alert	1 alert
Leadlikeness	NO	No	No;	No	No	No
Synthetic accessibility	4.19	4.37	4.30	3.08	4.07	4.30

3.2 Molecular docking

The docking of the PPARG protein was performed using AutoDock Vina. 40 (forty) ligand were selected for the study. Alongside, pioglitazone is conventional medicine for diabetes type 2 treatment (Da Silva and De Queiroz, 2019). All compounds were prepared for docking against the PPARG target. Only ligands with the best properties (AMDE) to be drug candidates and high binding affinities with an excellent docking score have been studied further (Singh *et al*., 2017). 27 (twenty-seven) bioactive compounds were discovered to have higher docking scores and binding affinities than commonly used synthetic drugs (pioglitazone). However, out of those 27 (twenty-seven) bioactive compounds, only12 (twelve) ligands follow the ADME and drug-likeness rules. These compounds are very stable and have a high molar refractivity. All of the components have a total number of over 20 atoms and are compliant with the Ghose filtration system. The binding affinity score of each component has been calculated by taking the number of times a given protein has been docked for a given ligand. Based on the lowest binding affinity score, the most stable structure is selected. The docking score results are shown in (Table 6).

Sesamin, kobusin, methylpluviatilol, planinin, piperitol, saltillin, schisandrin C, asarinin, pluviatilol, membrin, piperun, decalidine and pinoresinol which have previously been proven to be promising drug candidate. They showed substantial binding to PPARG with binding energies of (-9.5, -9.0, -9.0, -8.9, -8.8, -8.6, -8.6, -8.5, -8.5,-8.4, -8.3, and 8.2) kcal/mol, respectively, (Tables 3.2.5). On another hand existing medicine for diabetes type 2 pioglitazone was having a binding energy of -8.0 kcal/mol (Table 6). To gain a deeper understanding of the interaction pattern of best ligands with the target protein. The interaction between proteins and ligands was plotted, and the crucial amino acid residues involved in the interaction were identified as shown in Table5.

This study reported that several bioactive compounds possess antidiabetic activityes, pecially sesamin, kobusin, methyl-pluviatilol, planinin, piperitol, and saltillin can activate PPARG for the treatment of diabetes type 2.

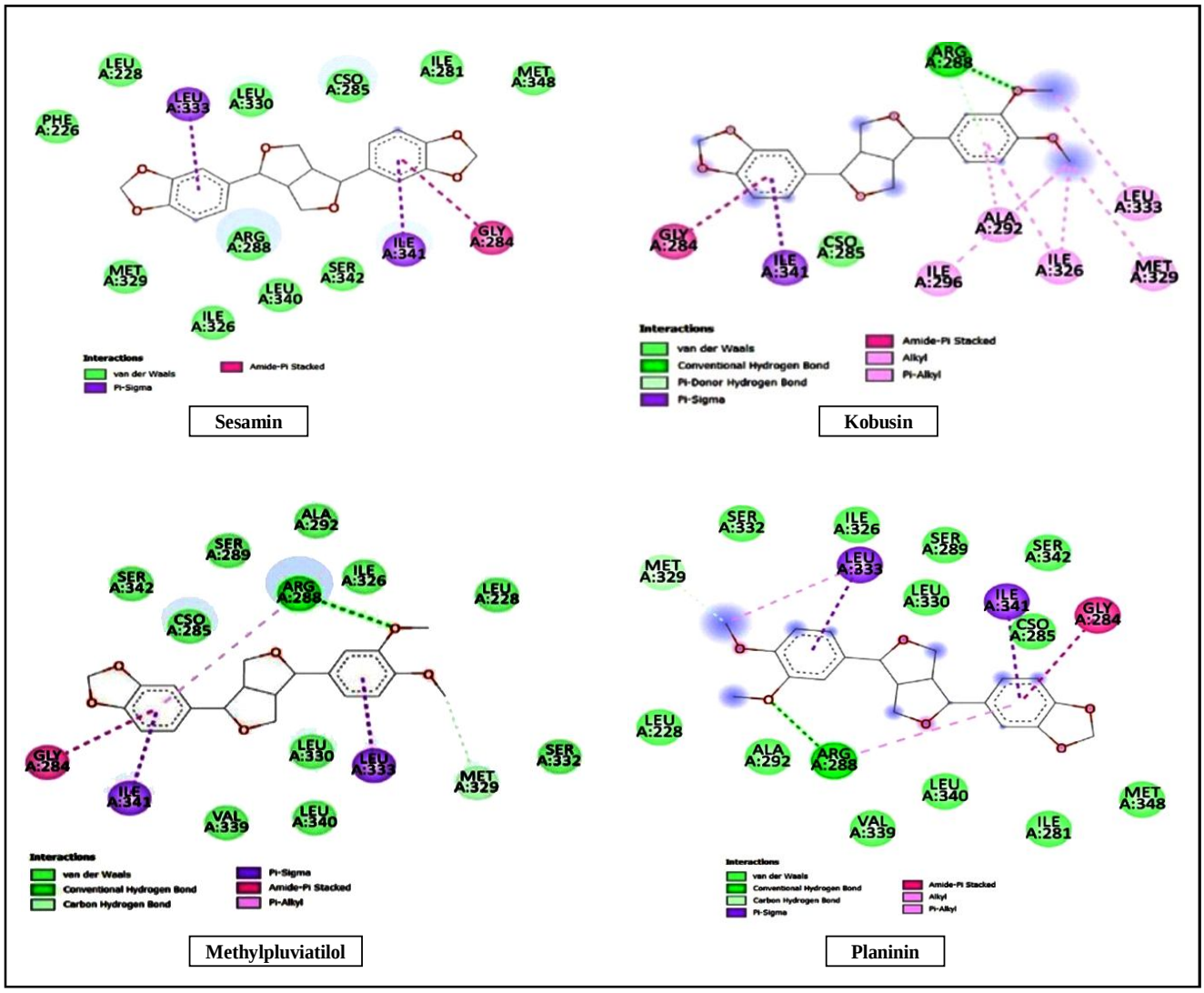

Figure 8: Sesamin, kobusin, methylpuviatilo and planin interaction with PPARG.

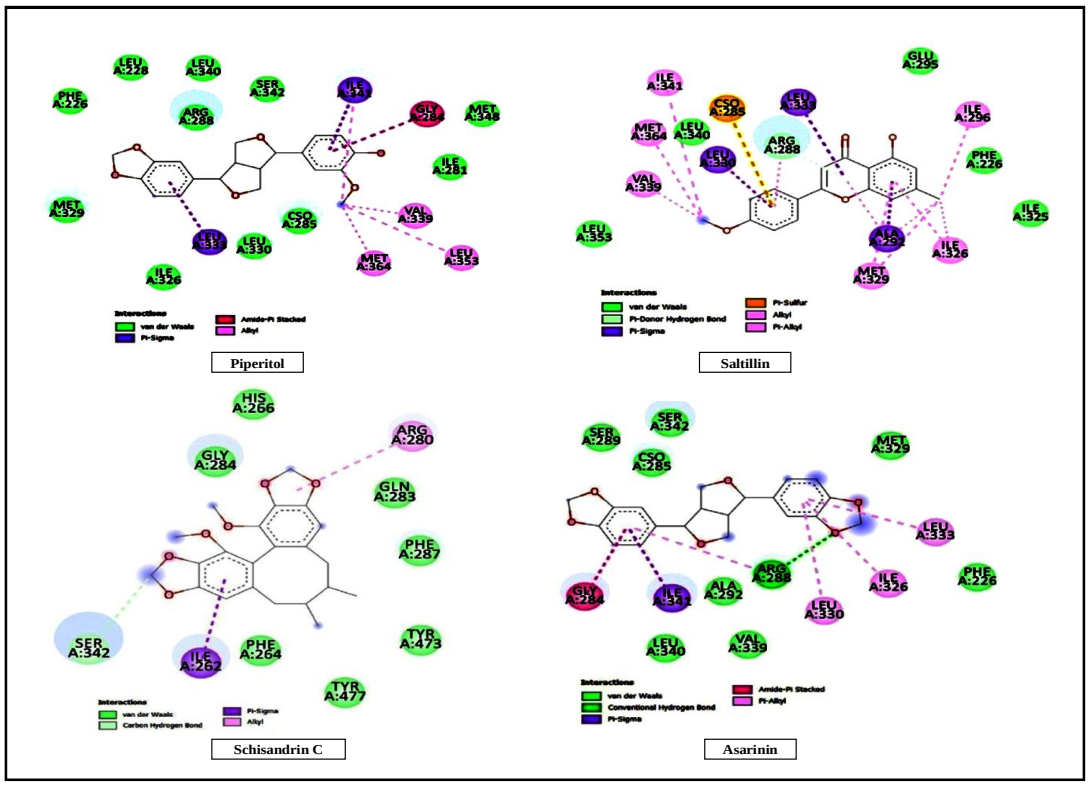

Figure 9: Piperitol, saltillin, schinsandrin C and asarinin with PPARG.

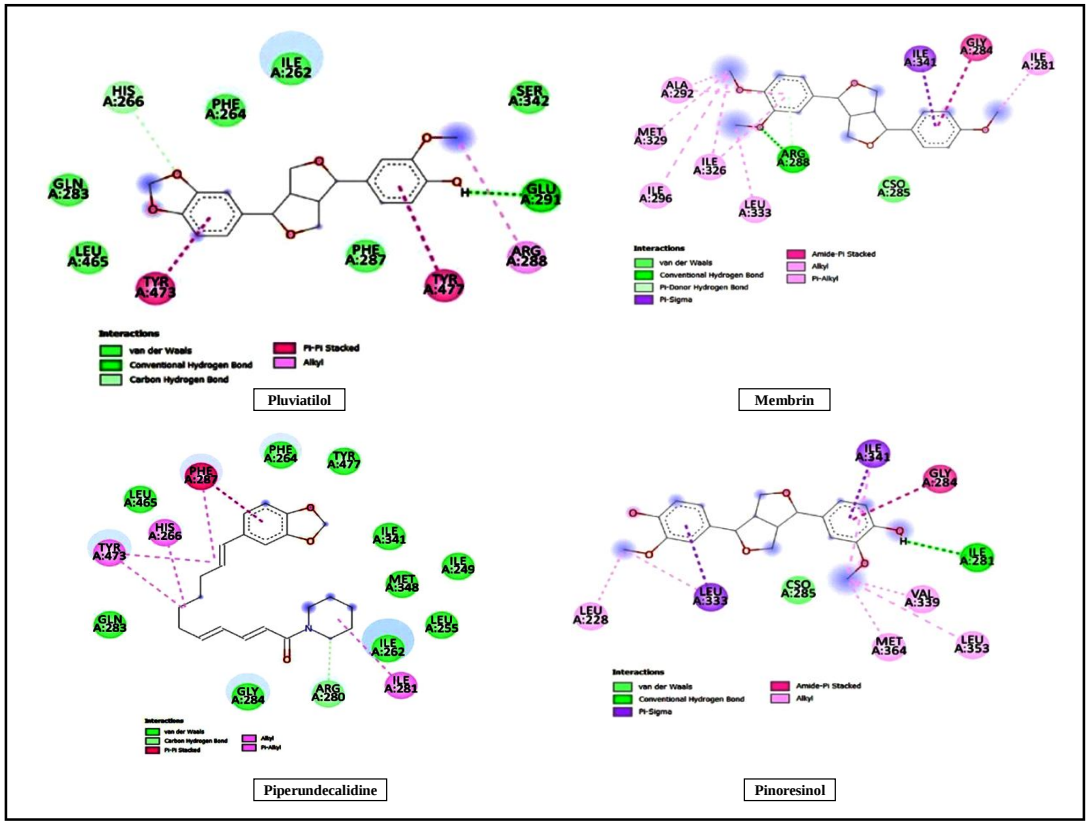

Figure 10: pluviatilol, membrin, piperundecalidine and pinoresinol with PPARG.

Table 5: Amino acid residues involved in the interaction between ligands with PPARG

S.No.	Ligand	Amino acid residue
1.	Sesamin	PHE226, LEU228, LEU330, CSO285, ILE281, MET348, SER342, LEU340, ARG288, ILE326, MET329, PHE226, LEU228
2.	Kobusin	ARG288, LEU33, MET392, ILE326, ALA292, ILE296, COS285, ILE341, GLY284
3.	Methylpluviatilol	SER342, SER289, ALA292, COS285, ARG288, ILE326, LEU228, SER332, MET329, LEU335, LEU330, LEU340, VAL339, ILE341, GLY284
4.	Planinin	MTE329, SER332, ILE326, SER289, ILU330, SER342, CSO285, MET348, ILE281, LEU340, VAL339, ALA292, LEU228, LEU333, LEU330, ILE341, GLY284, ARG228.
5.	piperitol	PHE226, LEU228, LEU340, SER342, ARG288, MET348, ILE281, CSO285, LEU330, ILE326, MET329, ILE341, GLY284, VAL339, LEU353, MET364
6.	Saltillin	PHE226, LEU228, LEU340, SER342, ARG288, MET348, ILE281, CSO285, LEU330, ILE326, MET329, ILE341, GLY284, VAL339, LEU353, MET364.
7.	Schisandrin C	GLY284, HIS226, GLN283, PHE287, TYR, TYR477, PHE264, ARG280, ILE262, SER342
8.	Asarinin	SER289, SER342, CSO285, ME329, PHE226, LEU340, VAL339, LEU33, ILE326, LEU330, ARE228, ALA292, ILE341, GLY284
9.	Pluviatilol	PHE264, ILE262, SER342, PHE287, LEU465, GLN283, HIS226, GLU291, ARG288, TYR477
10.	Membrin	ILE341, GLY284, ILE281, CSO285, ARG288, LEU33, ILE326, ILE296, MET329, ALA292
11.	Piperundecalidine	PHE264, TYR477, ILE341, ILE249, MET348, LEU255, GLY284, GLN283, LEU465, TYR473, HIS226, PHE287, ILE281, ARG280
12.	Pinoresinol	ILE341, GLY284, ILE281, VAL339, LEU353, MET364, CSO285, LEU33, LEU228

Table 6: Docking score for selected ligand alongside pioglitazone against PPARG

S.No.	Ligand	Docking score (kcal/mol)
1	Pioglitazone (conventinal medicine for T2D)	-8.0
2	Silibinin	-10.1
3	Silymarin	-9.7
4	Sesamin	-9.5
5	Kobusin	-9.0
6	Methylpluviatilol	-9.0
7	Corilagin	-9.0
8	Corallocin B	-9.0
9	Planinin	-8.9
10	Piperitol	-8.8
11	Saltillin	-8.6
12	schisandrin C	-8.6
13	Asarinin	-8.5
14	Pluviatilol	-8.5
15	Sesartemin	-8.5
16	Brartemicin	-8.5
17	Membrin	-8.4
18	Okanin	-8.4
19	Piperundecalidine	-8.3
20	Medioresinol B	-8.3
21	Hedyosumin E	-8.3

22	Gallocatechin	-8.3
23	Pinoresinol	-8.2
24	Abiespiroside A	-8.2
25	Pinoresinol diacetate	-8.2
26	Eudesmin	-8.2
27	Butein	-8.1
28	Mesosyringresinol	-8.1
29	Diosmetinidin	-8.1
30	Lariciresinol	-8.0
31	Aquilarixanthone	-8.0
32	Yangambin	-7.9
33	Prunetin	-7.9
34	Myricetin	-7.9
35	Syringaresinol	-7.8
36	Terameprocol	-7.8
37	Sylvatesmin	-7.8
38	Dihydroclusin	-7.7
39	Diasesartemin	-7.7
40	EPI-MAGNOLIN A	-7.3
41	SCHEMBL16917560	-7.3

4. Discussion

When the body is unable to effectively control glucose and the plasma glucose concentration remains high, type 2 diabetes (T2D) develops. Type 2 diabetes can be managed with a range of drugs, including (pioglitazone), which regulates fat and carbohydrate metabolism. When this medicine is administered; however, serious negative effects can develop. This has prompted concerns about the availability of new medications with minimal adverse effects.

As a result, natural compounds have been extensively studied for their agonist action against PPARG.

Using the AutoDock Vina programme, which predicts the interactions between ligands and proteins 40 (forty) bioactive compounds were chosen for the investigation.

All of the compounds interact with the PPARG, according to the docking studies. However, 29 (twenty-nine) of the bioactive compounds had the best docking score.

Furthermore, AMDE research was conducted utilising Swiss ADME, an internet server that predicts drug-like features. Only 12 (twelve) phytochemicals out of 40 (forty) had the best qualities to be medication candidates, according to the findings.

The results show that sesamin, kobusin, methylpluviatilol, planinin, piperitol, saltillin, schisandrin C, asarinin, pluviatilol, membrin, piperundecalidine and pinoresinol are all interesting therapeutic candidates. when compared to docking and AMDE investigations. These compounds exhibit favorable interactions with the target. Natural sources of PPARG upregulation were found to be useful in the treatment of diabetes.

This research contributes to the field of evidence for those bioactive compounds' antidiabetic properties and aids in the development of new diabetes drugs.

5. Conclusion

The study revealed that the compounds sesamin, kobusin, methylpluviatilol, planinin, piperitol, and salt illin exhibited efficient effects when compared to standard drugs. The results also showed that these compounds could be potential drug candidates for peroxisome proliferator-activated receptor gamma activation. The goal of this study was to find a new drug that could activate peroxisome proliferator-activated receptor gamma from natural plants with no side effect.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

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