Original Article

Comparative In-Silico Screening Of Potent Peptides Lead Using Docking Strategy And AI Approaches For The Treatment Of Diabetes

Himanshi Sengar[1], Chalsi[1], Anjali Saini[1], Kandasamy Nagarajan[1*], Pankaj Bhatt, Garima Kapoor[1], Sheena Mehta[1], Siddheshwari Mishra[2], Anil Ahlawat[2], Ajay Shrivastava[2], Surbhi Kamboj[1]

[1]KIET School of Pharmacy, KIET Group of Institutions, 13 km milestone, Ghaziabad, Delhi-NCR, 201206, India
[2]KIET Group of Institutions, 13 km milestone, Ghaziabad, Delhi-NCR, 201206, India
Correspondence author email id: rknagaraaja@gmail.com
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Abstract

Diabetes mellitus is a disease of inadequate control of blood levels of glucose. Insulin resistance in impaired cell function is a major hallmark of type 2 diabetes, the currently standard medicine available for the treatment is Glimepiride or Metformin which generally causes VitaminB12 deficiency so prevent these types of things and make them more bio-friendly peptide-based drugs with help of AI (Machine Learning). Swiss ADME tool is used to predict physicochemical parameter evaluation and then evaluate toxicity by pro-tox II software and select those classes that lie between 5-6 and then checks receptor-ligand interaction by Swiss dock against SGLT-2 receptor (PDB code -7VSI). By docking result the most promising peptide is Cysteine-Tryptophan and Glycine-Leucine with ΔG value of -9.46 & -8.56 respectively followed by Cysteine-Threonine, Valine-Threonine in comparison to standard drug Glimepiride of ΔG value of -10.75 and according to SVM results Glycine class combination seems to be most promising. So, comparative study shows that there is some similarity to the man- made technique and Machine learning results.

Keywords: Diabetes mellitus, Docking, Peptides and Machine learning.

Introduction

Diabetes mellitus is one of the most prevalent types of disease that is impacting almost every age group. The hallmark of this disease is the body's failure in the management of glucose leading to various interlinked diseases like renal failure, cardiovascular diseases, and neurological disorders. Diabetes is categorized into two types i.e., type 1 and type 2. Type 1 diabetes is insulin-dependent diabetes mellitus. Being an autoimmune disorder, type 1 is featured by the elimination of the beta–cells of the pancreas and inadequate secretion of insulin, also characterized by type 4 hypersensitivity. Insulin resistance in impaired cell function is a major hallmark of type 2 diabetes. Diabetes can be the result of various factors from certain changes like environmental and epigenetic factors. Autoantibodies, genetic, and environmental factors are the etiology factors for autoimmunity targeted against islet cells. Auto-antibodies target insulin and GAD-65. Patients with the HLA-DR-4-DQ8 haplotype and HLA-DR-3-DQ2 for GAD65 are more likely to be susceptible to the incidence of insulin antibodies. IA-2, IA-2beta, and ZNT8 are tyrosine phosphate molecules attacking antibodies. Genes responsible for the growth and progression of autoantibodies include INS, IL2RA, IFIH1, and CTSH. Environmental factors encompass infection with the retrovirus, environmental pollutants, etc. [1]. T1 diabetes-causing chemical toxins are nitrates, nitrites, N - nitro so compounds, and polychlorinated biphenyls. Epigenetic factors are the mediators for the environmental risk factors, encompassing facts beyond genetics. Epigenetic changes are characterized by DNA methylation, miRNA dysregulation, and histone modifications. The

methylation of DNA can be seen at CpG- 34, CpG- 135, CpG- 19, and CpG- 180. Lys 9 of the H3 histone protein shows an increase in acetylation. miRNA modifications cause alterations in the immune response, cell cycle, and apoptosis. Diabetes therapeutic target includes HDACs, DNA methyltransferase, Sirtuin 1, protein tyrosine phosphate 1B, dipeptidyl peptidase 4 inhibitors, peroxisome proliferator-activated receptor – y and sodium-glucose linked transporter i.e, SGLT1 and SGLT 2[2]. Glucagon-like peptide (GLP -1) receptor is one of the new emerging approaches in the treatment of diabetes that works by inducing insulin from the pancreatic beta cells and restricts the release of glucagon. Serum diagnostic markers are the commonly used biomarkers for the detection of hallmarks of T1 diabetes-like hyperglycemia, C- peptide, and autoantibodies. Autoantibodies are utilized as primary biomarkers for the diagnosis and prediction of T1 diabetes. Under nucleic acid, DNA methylation is also used as a biomarker. The presence of amylin DNA and not methylated insulin signifies the destruction of beta-cells. miRNA are also potent biomarkers for T1 diabetes prediction [3]. There are limited diabetes therapies available, which is causing a rapid rise in the number of diabetes patients. Inadequate therapies force us to move towards a safer, more efficient, easy-to-administer, and budget-friendly approach in the treatment of diabetes. A compound found in natural products like plants can be a coaxing alternative in the treatment of diabetes as it has fewer side effects than the present therapies. Momordica Charantia, commonly known as the bitter gourd is an emerging natural plant product. Its extract has blood glucose regulating activity that makes it an important subject for further advanced research. It has various anti–diabetic properties possessing compounds like peptides, vicine, and polypeptide – P, alkaloids, charantin, sterol, glycosides, mcIRBP, triterpenoids, cucurbatanoid compound, flavonoids, and phenols. Biological polymers and peptides are also an emerging interest of advanced research in the treatment of diabetes ex- GLP 1, an anti-diabetic hormone, together with GIP, an anti-diabetic polypeptide that has an incretion effect that results in insulin release. The peptide approach has demonstrated a huge therapeutic efficacy in animal models as well as human clinical studies due to its proper tolerance. Appropriate peptides need to be investigated for enhancing the quality of diabetes treatment.

Chronic kidney disease (CKD) is one of the severe side effects of type 1 diabetes mellitus (T1DM). Various machine learning (ML) algorithms can be put into use to develop models to quickly diagnose (CKD) in patients with T1DM using routine checkup data. RFF, KNN and MICE data imputation techniques and SMOTE Tomek resampling techniques are used for this research's purpose to preprocess the primary data set. Developed prediction models are again evaluated using ten ML algorithms including logistic regression (LR), K- nearest neighbor (KNN), Gaussian naïve bayers (GNB), random forest (RF), extreme gradient boosting (XGB) and light gradient – boosted machine (light GMB). Various parameters of models including sensitivity, specificity, accuracy and precision are ranked using three feature ranking techniques (XGB, RF and extra tree). The RF classifier was found best. Although end stage kidney disease has declined in type 1 diabetes patients over the past decades, probably due to increased use of renin angiotensin systems (RAS) blockers, it still remains a life-threatening complication. Chronic kidney disease is a significant factor in determining mortality rate in type 1 diabetes mellitus T1DM is born from an autoimmune attack against pancreatic beta – cells. Potential drugs and targets are prioritized in this study. Some potential drugs for the use of investigational purposes for the treatment of type 1diabetes are melatonin, resveratrol, lapatinib, geldanamycin, eugenol and fostaminib. After inspecting based on molecular docking analysis, lapatinib – ERBB2 and eugenol – ESR1 resulted in having highest and lowest binding energy. The traditional treatment for type 1 diabetes is continuous subcutaneous infusion or daily injections of insulin for blood sugar control. Another fact about T1D management is preservation of pancreatic beta cells[4]. Transcriptone analysis of pancreatic beta cells and peripheral blood mononuclear cells (PBMCs) are significant terms for investigation in the area of gene expression profiles in T1D. Recently, the support vector machine (SVM) was suggested to carry out the genome – wide disease risk predictions based on GWAS (genome wide association studies) data. It outperformed logistic regression on type 1 diabetes datasets. Cardiac arrhythmia relating to hypoglycemia is also another significant cause of death in diabetic patients. SVM can also be presented for hypoglycemic detection using the ECG parameters as inputs. Hypoglycemia detection is a crucial factor for type 1 diabetes treatment[5]. It is the acute and common factor of type 1 diabetes. It is the factor which significantly needs to be limited. Hypoglycemia could also result in ECG alterations.

The first step towards moving into the project was to obtain deep knowledge about the disease taken into consideration i.e., diabetes. Type 1 diabetes is the focus of this project. Every aspect of the disease is touched including the target, standard drug, and molecular targets [6]. I have gone through major sites and portals like google scholar, PubMed,

kip-is, encyclopedia, etc. Some interesting facts are found about type 1 diabetes. Diabetes is a combination of interlinked diseases like cardiac diseases, renal failure, and neurological disorders. Type 1 diabetes is insulin-dependent diabetes mellitus. Some major molecular targets of type 1 diabetes are DNA methyl-transferases, sirtuin 1, etc. Major causes of diabetes are genetic factors, autoantibodies, and epigenetic factors. Bio screening is done by using SWISS DOCK and SWISS ADME. Appropriate peptides are taken into consideration based on various major factors like ADME properties, toxicity, etc. Through the pro-tox tool peptides interactions which are having high ADR and bad ADME properties are filtered off. The best docking interaction is chosen. The outcome of this project is investigational research on peptides in the treatment of type 1 diabetes.

Experimental material and Methodology

Materials

The Configuration of the system in which the docking study was performed along with other online tools of drug design was running on Intel® Core™ i7-1255U processor Deca-core 1.70 GHz , system type 64-bit operating system, x64-based processor, Installed RAM: 16 GB.

Methodology

Based on literature studies one hundred forty (140) small-chain dipeptide molecules were taken for the study and subjected to SWISSADME, out of them ten molecules were selected for further study. The toxicity of all the compounds was tested with the help of the PROTOX online tool. SWISS ADME online tool was selected for checking the pharmacokinetic properties including GI absorption.

SWISSADME:

A free online tool to assess small molecules' pharmacokinetics, druglikeness, and medicinal chemistry.The permeability glycoprotein (PGP) substrate was used to examine the bioavailability of each molecule, as well as the drug's metabolic profile against different types of cytochrome P450 inhibition (CYP1A2, CYP2C1, CYP2C9, CYP2D6, CYP3A4). To check the drug-likeliness property of the Lipinski rule of five, molecules were collected for the study and submitted to SWISS ADME online TOOL.

PROTOX-II: A Virtual Laboratory for Predicting Small Molecule Toxicity. His LD50 values for toxic doses are often expressed in mg/kg body weight[7]. The median lethal dose, or LD50, is the dose at which 50% of subjects die after exposure to a substance.

SVM: It is a supervised machine learning type classifier, using labeled data for classification. In this study, an SVM-based classification model has been created. Here, two common anti-diabetic medications and a total of 22 shorter-chain dipeptides were taken into account. The smaller chain dipeptides were transformed into a form that the SVM algorithm could understand. Preprocessing the data set is necessary for better classification, so in this case, we simply change 0 for low value and 1 for high value. In this work, we used a Support Vector Machine (SVM) and Gaussian classifier to classify the drug data set based on their gradient. For better classification we need to do the preprocessing of a dataset, so to carry out the preprocess we need to make them as a numeric value. We assign 0 as the lowest value and 1 as the highest value.

We classify the drugs into four categories drug 1, drug 2, drug 3, and drug 4. In Google scholar, Kipris,etc[8]. The Molinspiration-cheminformatics online tool was used for all the smaller chain dipeptides to predict the various physicochemical parameters along with the bioactivity score on enzyme inhibition as a general way of identifying the best suitable potent molecule. Open Babel tool is used to convert file format and do edits to the structure.

GAUSSIEN CLASSIFIER: This classifier is similar to SVM in that is used for predictive modelling. A Gaussian classifier is an algorithm that predicts the data result based on possibilities However, SVM is frequently susceptible to unbiased classification datasets when there are more positive examples than negative examples.

As a general method of selecting the most effective potent molecule, the online Molinspiration Chemo- informatics tool was used to forecast the different physicochemical properties as well as the bioactivity score on enzyme inhibition for each of the smaller chain dipeptides. Online PASS tools are used for locating behavior directed at a specific target that may have harmful and toxic effects. Based on early findings using a target protein the selective dipeptides were

docked using the free Swiss Dock programmer available online. Metformin is the reference medication used to compare docking with the tested dipeptides. Envisioning and Comprehensive 3D analysis of bonding interaction and 2D work was completed using the UCSF Chimera visualization tool and Bio via Discovery studio.

Results and Discussion

Identification of potent peptide lead and comparative bio-screening is done using a docking strategy for finding a suitable peptide lead for the treatment of diabetes.

Detailed docking investigation by utilizing the tool SWISS DOCK is done for finding the most promising docking interaction. Leu-Glu, Arg-Phe, Val-Gly, Val-met, Cal-Thr, Cys-Gly, Cys-Thr, and Cys-Trp are selected for docking. Advanced docking also helps us to find the binding mode of the ligand with the molecule.

The data was prepared and after finding properties from ADME and other software of particular compounds, they have been compared with the standard drug Metformin and Glimpiride.

By comparing the Molinspirations data and PASS data, only GLYCINE and ARGININE peptides were selected for comparison with the standard drug glimpiride. It has the best therapeutic potency against T1 diabetes. It is the most stable interaction of all other dipeptide combinations.

As a result of our data set classification, our accuracy was found. When we validate our drug data set to an unknown drug sample, we found that glycine and arginine interactions are very close to our given drug sample.

SVM classification drug 1 came as the final result which is GLYCINE and peptides and the Gaussian classifier of drug 4 came as the final result which is ARGININE and peptides.

Supervised machine learning models (SVM classifier and Gaussian classifier) are used in the process of this project. This study is a major example that highlights that A. I can also be used as the new therapeutic medical investigational approach for advanced research in the medical field. “Artificial intelligence is the simulation of human intelligence processes by machines, especially computer systems. Specific applications in Artificial intelligence include expert systems, natural language processing, speech recognition, and machine vision. A day-to-day example of Artificial intelligence is Google search engine. When we type something in the goggle, it automatically recommends us many related searches. It also automatically detects our voice through the voice detection feature and we can also chat with its Google assistance feature. It saves our time and money on animal testing.

Table 1a represents results of Swiss ADME Physicochemical characteristic features of smaller chain dipeptides

S.No.	Molecule	MW	Heavy atoms	Aromatic heavy atoms	Rotatable bonds	H-bond acceptors	MR	TPSA
1	Glycine alanine	146.14	10	0	4	4	0.3363	0.9242
2	Glycine-Arginine	231.25	16	0	8	5	0.5715	1.5682
3	Glycyine-aspartic acid	190.15	13	0	6	6	0.4021	1.2972
4	Glycine-asparagine	189.17	13	0	6	5	0.4134	1.3551
5	Glycine-cysteine	178.21	11	0	5	4	0.4156	1.3122
6	Glycine-glutamine	203.2	14	0	7	5	0.4615	1.3551

7	Glycine-glutamic acid	204.18	14	0	7	6	0.4502	1.2972
8	Glycine-glycine	132.12	9	0	4	4	0.2882	0.9242
9	Glycine-histidine	212.21	15	5	6	5	0.5026	1.211
10	Glycine-isoleucine	188.22	13	0	6	4	0.4805	0.9242
11	Glycyl-leucine	188.22	13	0	6	4	0.4805	0.9242
12	Glycine-lysine	203.24	14	0	8	5	0.5076	1.1844
13	Glycine-methionine	206.26	13	0	7	4	0.5083	1.1772
14	Glycine-phenylalanine	222.24	16	6	6	4	0.5812	0.9242
15	Glycine-proline	172.18	12	0	3	4	0.4514	0.8363
16	Glycine-serine	162.14	11	0	5	5	0.3479	1.1265
17	Glycine-threonine	176.17	12	0	5	5	0.396	1.1265
18	Glycine-tryptophan	261.28	19	9	6	4	0.6997	1.0821
19	Glycine-tyrosine	238.24	17	6	6	5	0.6014	1.1265
20	Glycine-valine	174.2	12	0	5	4	0.4324	0.9242

Table 1b represents results of Swiss ADME Pharmacokinetics and Drug likeness characteristic features of smaller chain dipeptides

S.No.	Molecule	GI absorption	BBB permeate	Pgp substrate	CYPYESA2 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	log Kp (cm/s)	Lipinski	Bioavailability Score
1	Glycine alanine	High	NO	NO	NO	N0	N0	-9.78	YES	0.55
2	Glycine-Arginine	Low	N0	NO	NO	N0	N0	-11.15	YES	0.55
3	Glycyine-aspartic acid	Low	N0	NO	NO	N0	N0	-11.11	YES	0.56
4	Glycine-asparagine	Low	N0	NO	NO	N0	N0	-10.97	YES	0.55
5	Glycine-cysteine	Low	N0	NO	NO	N0	N0	-10.04	YES	0.55
6	Glycine-glutamine	Low	N0	NO	NO	N0	N0	-10.8	YES	0.55
7	Glycine-glutamic acid	Low	N0	NO	NO	N0	N0	-11.1	YES	0.56
8	Glycine-glycine	High	N0	NO	NO	N0	N0	-9.18	YES	0.55
9	Glycine-histidine	High	N0	NO	NO	N0	N0	-10.36	YES	0.55
10	Glycine-isoleucine	High	N0	NO	NO	N0	N0	-9.58	YES	0.55
11	Glycyl-leucine	High	N0	NO	NO	N0	N0	-9.1	YES	0.55
12	Glycine-lysine	High	N0	NO	NO	N0	N0	-11.35	YES	0.55
13	Glycine-methionine	High	N0	NO	NO	N0	N0	-9.79	YES	0.55
14	Glycine-phenylalanine	High	N0	NO	NO	N0	N0	-9.26	YES	0.55
15	Glycine-proline	High	N0	NO	NO	N0	N0	-9.56	YES	0.55

16	Glycine-serine	Low	N0	NO	NO	N0	N0	-10.63	YES	0.55
17	Glycine-threonine	Low	N0	NO	NO	N0	N0	-10.29	YES	0.55
18	Glycine-tryptophan	High	N0	NO	NO	N0	N0	-9.75	YES	0.55
19	Glycine-tyrosine	High	N0	NO	NO	N0	N0	-9.08	YES	0.55
20	Glycine-valine	High	N0	NO	NO	N0	N0	-9.27	YES	0.55

Table 2A represents the results of Swiss ADME Physicochemical characteristic features of smaller chain dipeptides

S.No.	Molecule	MW	Heavy atoms	Aromatic heavy atoms	Rotatable bonds	H-bond acceptors	MR	TPSA
1	Arg-ala	245.28	17	0	8	5	0.6196	1.5682
2	Arg-arg	330.39	23	0	12	6	0.8548	2.2122
3	Arg-Asn	288.3	20	0	10	6	0.6967	1.9991
4	Arg-Asp	289.29	20	0	10	7	0.6854	1.9412
5	Arg-cys	277.34	18	0	9	5	0.6989	1.9562
6	Arg-glu	303.31	21	0	11	7	0.7334	1.9412
7	Arg-gln	302.33	21	0	11	6	0.7448	1.9991
8	Arg-gly	231.25	16	0	8	5	0.5715	1.5682
9	Arg-his	311.34	22	5	10	6	0.7859	1.855
10	Arg-Ile	287.36	20	0	10	5	0.7638	1.5682
11	Arg-leu	287.36	20	0	10	5	0.7638	1.5682
12	Arg-lys	302.37	21	0	12	6	0.7909	1.8284
13	Arg-met	305.4	20	0	11	5	0.7916	1.8212
14	Arg-phe	321.37	23	6	10	5	0.8644	1.5682
15	Arg-pro	271.32	19	0	7	5	0.7347	1.4803
16	Arg-ser	261.28	18	0	9	6	0.6312	1.7705
17	Arg-thr	275.3	19	0	9	6	0.6793	1.7705
18	Arg-val	273.33	19	0	9	5	0.7157	1.5682

To check the drug-likeliness property of the Lipinski rule of five and GIT absorption, molecules were collected for the study and submitted to SWISS ADME online TOOL. Among glycine and arginine combinations, Gly–Trp , Gly-Leu, Gly-Val,Gly-Cys,Arg-Phe were considered to be the best dipeptides ,which further incorporated to docking and toxicity.

Table 2b represents results of Swiss ADME Pharmacokinetics and Drug likeness characteristic features of smaller chain dipeptides

S.No.	Molecule	GI absorption	BBB permeate	Pgp substrate	CYPYESA2 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	log Kp (cm/s)	Lipinski	Bioavailability Score
1	Arg-ala	Low	N0	NO	NO	N0	N0	-10.96	YES	0.55
2	Arg-arg	Low	N0	YES	NO	N0	N0	-12.93	NO	0.17
3	Arg-Asn	Low	N0	YES	NO	N0	N0	-12.3	NO	0.55
4	Arg-Asp	Low	N0	YES	NO	N0	N0	-11.84	NO	0.55
5	Arg-cys	Low	N0	NO	NO	N0	N0	-11.21	YES	0.55
6	Arg-glu	Low	N0	NO	NO	N0	N0	-11.67	NO	0.55
7	Arg-gln	Low	N0	YES	NO	N0	N0	-12.13	NO	0.55
8	Arg-gly	Low	N0	NO	NO	N0	N0	-11.15	YES	0.55
9	Arg-his	Low	N0	NO	NO	N0	N0	-11.53	NO	0.55
10	Arg-Ile	Low	N0	NO	NO	N0	N0	-11.01	YES	0.55
11	Arg-leu	Low	N0	NO	NO	N0	N0	-10.88	YES	0.55
12	Arg-lys	Low	N0	NO	NO	N0	N0	-11.47	NO	0.55
13	Arg-met	Low	N0	NO	NO	N0	N0	-11.28	YES	0.55
14	Arg-phe	Low	N0	NO	NO	N0	N0	-10.87	YES	0.55
15	Arg-pro	Low	N0	NO	NO	N0	N0	-10.99	YES	0.55

16	Arg-ser	Low	N0	NO	NO	N0	N0	-11.8	NO	0.55
17	Arg-thr	Low	N0	NO	NO	N0	N0	-11.58	NO	0.55
18	Arg-val	Low	N0	NO	NO	N0	N0	-10.96	YES	0.55

Table 3a represents docking and toxicity

COMPOUNDS	TOXICITY CLASS	SGLT2	DPP4
GLYCINE-TRYPTOPHAN	3	-6.9	9.24
LEUCINE-GLYCINE	5	-8.56	-7.97
ARG-PHE	4	-7.25	-8.61
VAL-GLY	5	-7.39	-7.2
VAL-MET	5	-7.13	-7.79
VAL-THR	5	-7.74	-7.22
VAL-TRP	3	-6.86	-8.09
CYS-GLY	5	-7.49	-7.72
CYS-THR	5	-8.26	-7.73
CYS-TRP	5	-9.46	-8.59
GLIMPIRIDE	5	-10.75	-9.84
METFORMIN	4	-6.98	-6.48

A detailed docking investigation by utilizing the tool SWISS DOCK is done for finding the most promising docking interaction. Identification of potent peptide lead and comparative bio-screening is done using a docking strategy for finding a suitable peptide lead for the treatment of diabetes. The docking result concluded that glycine combinations (gly-trp,gly-leu,gly-cys) and among cysteine combinations (cys-gly, cys-thr, cys-trp) were chosen best among all.

SVM RESULTS

Figure 1: Drug1 contains 95% above score belonging to the test sample anti-diabetic (Glimepiride) drug shown in graph

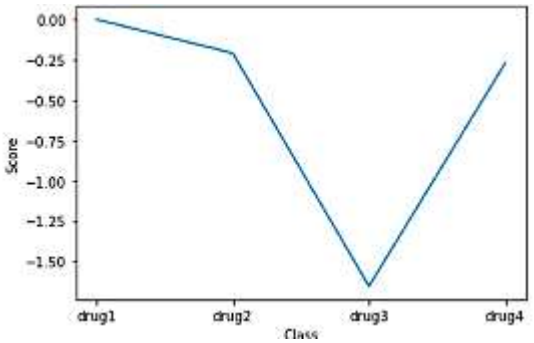
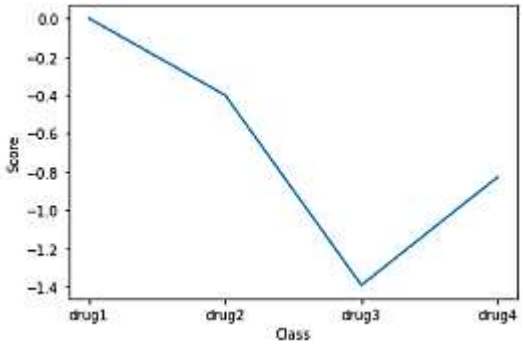
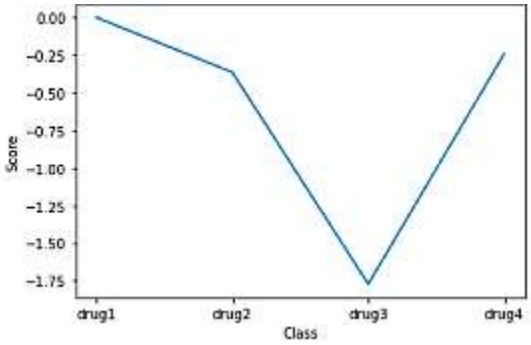


Figure 2: Drug1 contains 95% above score belonging to the test sample anti-diabetic (Glimepiride) drug shown in graph



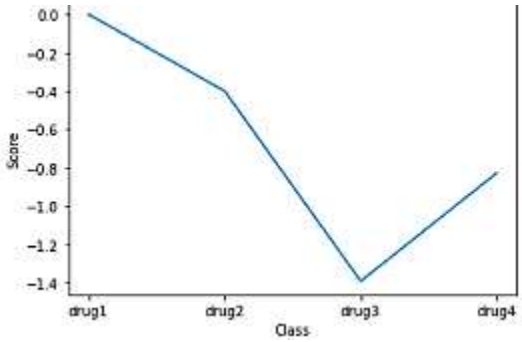
In the above graph we assume that drug 1 shows above 95% score as compared to others drugs 2,3, and 4 which was justify that the smaller chain dipeptides shown similar action as the drug 1 (Glimepiride).

Figure 3: Drug1 contains 95% above score belonging to the test sample anti-diabetic (Glimepiride) drug shown in graph



In the above graph we assume that drug 1 shows above 95% score as compared to others drugs 2,3, and 4 which was justify that the smaller chain dipeptides shown similar action as the drug 1 (Glimepiride).

Figure 4: Drug1 contains 95% above score belonging to the test sample anti-diabetic (Glimepiride) drug shown in graph



In the above graph we assume that drug 1 shows above 95% score as compared to others drugs 2,3, and 4 which was justify that the smaller chain dipeptides shown similar action as the drug 1 (Glimepiride).

Conclusion

Based on literature studies one hundred forty [140] small-chain dipeptide molecules were taken for the study and subjected to SWISSADME, out of them ten molecules (Leu-Glu, Arg-Phe, Val-Gly, Val-met, Cal-Thr, Cys-Gly, Cys-

Thr, and Cys-Trp) were selected for further study. Then the selected dipeptides were further filtered off based on toxicity and efficacy by using the tool Pro Tox-II, through this the dipeptides with considerable ADRs are cut out from the list. A detailed docking investigation by utilizing the tool SWISS DOCK is done for finding the most promising docking interaction. The data was prepared and after finding properties from ADME and other software of particular compounds. After analyzing all result from docking, SVM, Gaussian classifier.

ORDER	SWISS ADME RESULT	DOCKING RESULT	SVM RESULT	GAUSSIAN RESULT
1	Glycine -tryptophan	Cysteine-tryptophan (-9.46)	Glycine-Leucine	Arginine class
2	Leucine-glycine	Cysteine-threonine (-8.26)	Glycine-Tryptophan	
3	Arginine-phenylalanine	Glycine-leucine (-8.56)	Glycine-valine	
4	Glycine-valine	Glycine-tryptophan (-9.24)	Glycine-cysteine	
5	Valine-threonine	Arginine-phenylalanine (-8.69)	Glycine-phenylalanine	
6	Valine-tryptophan	Valine-tryptophan (-8.03)	Glycine-arginine	
7	Cysteine-glycine			
8	Cysteine-threonine			
9	Cysteine-tryptophan			

After SWISSADME, Among glycine and arginine combinations, Gly–Trp , Gly-Leu, Gly-Val,Gly-Cys,Arg-Phe were considered to be the best dipeptides On docking (cysteine-tryptophan) was seen most promising lead dipeptide, and on the other hand, Artificial intelligence approaches. By comparing Molinspiration and PASS data, only the GLYCINE and ARGININE peptides were selected for comparison with the standard drug, Glimpiride. It has the highest therapeutic effect on T1 diabetes. This is the most stable interaction among all other dipeptide combinations.

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Conflict of Interest

All authors declare that there is no competing interest.

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