RESEARCH ARTICLE

In-Silico Evaluation, and Qsar Analysis of Para-Coumaric Acid Derivatives as Potential Antidiabetic Agents

Aarti Yadav[1], Rosaline Mishra[1*], Radha Goel[2], Praveen Kumar Gaur[1], Rahul Kaushik[1], Swati Biswas[1], Govind Gupta[1]

[1]Metro College of Health Sciences and Research, Greater Noida, Uttar Pradesh, India

[2]Lloyd Institute of Management and Technology, Greater Noida, Uttar Pradesh, India

Corresponding Author Email ID: rosalinemishra3@gmail.com

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Abstract

Introduction: Diabetes Mellitus, an international health crisis with Increased death and disability, demands ongoing efforts to discover new, effective, and safe antidiabetic drugs. Para-coumaric acid, a naturally occurring phenolic compound, shows promising antidiabetic potential. This study focused on designed and evaluating five novel para-coumaric acid derivatives (Cn1-Cn5) as potential antidiabetic agents.

Material and Methods: In silico evaluations, including QSAR, ADMET and Molecular docking. QSAR analysis identified crucial chemical descriptors related to antidiabetic activity, achieving a high correlation coefficient ($R^2 = 0.9995$).

Results and Discussion: These findings suggest that para-coumaric acid derivatives could serve as promising candidates for antidiabetic drug development. ADMET properties assessed through pkCSM software confirmed favourable pharmacokinetics and toxicity profiles for all derivatives, which also complied with The Five Rules of Lipinski, indicating drug-like properties. Molecular docking (using PyRx), revealed strong binding affinities of the derivatives with alpha-amylase, a key antidiabetic target.

Conclusion: These studies highlighted para-coumaric acid's binding affinity to alpha-amylase (-8.7 kcal/mol), suggesting dual-target antidiabetic potential.

Keywords: Para-coumaric acid, Diabetes Mellitus, *In-Silico* studies, Anti-diabetic agents, Molecular Docking.

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Introduction

Diabetes is a multifaceted syndrome defined by persistent hyperglycemia and is categorized into type 1 diabetes (T1D), type 2 diabetes (T2D), other specific types, and gestational diabetes mellitus. T2D, which accounts for approximately 96% of all diabetes cases, is characterized by a non-autoimmune, progressive decline in functional insulin secretion by pancreatic β-cells, often occurring alongside insulin resistance (IR) and what has traditionally been termed metabolic syndrome (MS).[1] However, given that the term "metabolic" does not inherently distinguish between physiological and pathological states, the more precise terminology "metabolic dysfunction syndrome" (MDS) is proposed as a replacement for MS. T2D is recognized as a major noncommunicable chronic disease with significant public health implications, although its pathogenesis is not yet fully elucidated.

Persistent hyperglycemia in T2D contributes to target organ damage (TOD) through an elevated risk of panvascular complications, encompassing both microvascular disorders—such as diabetic retinopathy, nephropathy, and neuropathy—and macrovascular diseases, including cardiovascular, cerebrovascular, and peripheral vascular conditions. Unlike T1D, which primarily manifests as hyperglycemia, T2D is increasingly viewed as a downstream manifestation of MDS. It frequently coexists with other metabolic abnormalities such as preobesity/obesity (where "preobesity" is considered a more accurate term than "overweight"), metabolic dysfunction-associated steatotic liver disease (MASLD), dyslipidemia, and in some cases, hypertension. These upstream conditions are largely linked to modifiable lifestyle factors and act as independent risk factors for the development of cardiovascular-kidney-metabolic syndrome and T2D, underscoring their preventable nature.[1]

Understanding T2D as a consequence of broader metabolic dysfunction necessitates a paradigm shift in clinical management. The term "chronic diabetic complications" is considered misleading, as it places undue emphasis on hyperglycemia while neglecting the broader metabolic contributors to TOD. Instead, the term "MDS-related TOD" is proposed to more accurately reflect the underlying pathophysiology. This reconceptualization supports a more integrated and holistic therapeutic approach that prioritizes comprehensive metabolic control and organ protection, rather than a narrow focus on glycemic management alone.

The IDF Diabetes Atlas serves as a comprehensive and authoritative resource on the global, regional, and national prevalence of diabetes, along with associated morbidity, mortality, and healthcare expenditures. It also provides an overview of the pathophysiology, classification, and diagnostic criteria of diabetes. The Atlas outlines the global burden across various diabetes types and populations, while emphasizing evidence-based interventions for the prevention of type 2 diabetes and optimal management strategies for all forms of diabetes to mitigate complications. The credibility of the Atlas' estimates is grounded in a robust methodology involving the selection and analysis of high-quality data sources. Each edition undergoes a thorough review by the IDF Diabetes Atlas Committee, which comprises experts from all seven IDF regions. These estimates are primarily derived from population-based studies published in peer-reviewed journals. The 10th edition has also incorporated data from national diabetes registries, reflecting the growing availability of electronic medical records and national surveillance systems. Additionally, eligible data from national health surveys, such as the World Health Organization's STEPS program, are utilized. Findings from the 10th edition reinforce that diabetes remains one of the most rapidly escalating global health crises of the 21st century. As of 2021, an estimated 537 million individuals are living with diabetes, a figure projected to rise to 643 million by 2030 and to 783 million by 2045. Furthermore, approximately 541 million people were estimated to have impaired glucose tolerance in 2021. The same year, over 6.7 million deaths among adults aged 20–79 was attributed to diabetes-related causes. The prevalence of type 1 diabetes among children and adolescents continues to rise, with over 1.2 million affected in 2021. Annual healthcare costs related to diabetes are nearing one trillion USD and are expected to surpass this amount by 2030. The Atlas also highlights that hyperglycaemia in pregnancy affects roughly one in six pregnancies. Alarmingly, nearly 45% of individuals with diabetes remain undiagnosed, the majority of whom have type 2 diabetes. This underlines the critical need for enhanced early detection strategies and the provision of timely, adequate care to reduce the burden of undiagnosed and poorly managed diabetes.[2]

Overview of P-Coumaric Acid

Secondary metabolites in plants are chemical substances produced via different pathways. They have biological functions and constitute components of diets for humans and animals. They are mainly located inberry, crop, grains, avarious other naturalnourishmentitem. phytochemicals recreate a significant role in the treatment or control of the diseases and are used in traditional medicine. It's a polyphenol they are naturally occurring in various plants, vegetables, & fruits.Para-coumaric acid (p-CA), molecular weight of 164.16 g/mol, is a phenolic compound classified within the 3-hydroxycinnamic acid (HCA) group. It represents a category of 2 metabolites in plants, and they are botanically produced via thechorismate biosynthesis pathway, utilizing 2-amino-3-phenyl-propanoic acid and 4-hydroxy-L-phenylalanine is a starting material. It can change into phenolic acids (such as3,4-dihydroxycinnamic acid., trans-ferulic acid, 3-O-Caffeoylquinic acid, and4-hydroxy-3,5-dimethoxy-cinnamic acid), phytochemicals., monolignols annatural productvarious other secondary metabolite. p-coumaric acid is the predominant found in nature and exists in two variations: cis p-Coumaric acid and trans p-Coumaric Acid[3]. Compounds from the HCA family, including p-CA, are also present in the green bark of woody vascular plants. The free or bound form of p-CA is commonly found in fruits (such as apple, pear, grape, orange, tomato, and berries), vegetables (like beans, potato, and onion), and cereals (including maize, oat, and wheat). In these plants, p-CA serves as a part of lignins and tannins, being the most common phenolic acids in cereals. p-CA creates conjugates with various substances such as alcohols, amines, sugar moiety, lignins, tannins, sterols, hydroxyl acids, and more. The conjugates of p-coumaric acid can be Both soluble and insoluble in water based on the compounds they are associated with. Analogues of p-CA may exhibit even greater bioactivity than free p-CA; however, this analogue stands shorter prone to absorption inupper alimentary canal.[4]

Because of its many medicinal uses, such as as ant inflammatory, antioxidant,[5] and anti-melanogenic, anti-ulcer, anti-microbial, anti-hypertensive and anticancer properties.[6,7] These properties have led to significant interest in developing p-coumaric acid derivatives with enhanced potency and selectivity for specific biological targets. In this research paper, we performed silico studies of Fivep-coumaric acid derivatives (CN1-CN5) i.e QSAR, ADMET, Molecular Docking. These In silico studies demonstrated the potent antidiabetic activity of design p-coumaric acid derivatives.

Results And Discussion

Key chemical descriptors linked to antidiabetic activity were identified using statistical research in orderto build a link between quantitative structure and activity (QSAR). With a strong correlation coefficient (R2) of 0.9995, the QSAR analysis revealed important chemical descriptors associated with antidiabetic action.

QSAR Predicted IC_{50} Value

R^2 value is found to be: 0.9995 & Q^2 value is found to be: 0.9992
Generated QSAR equation:

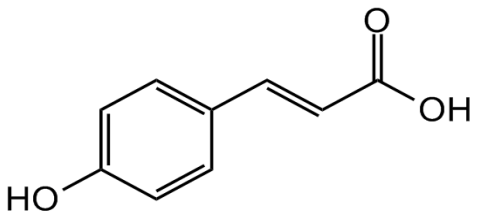


Figure 1: Structure of .p-coumaric acid

PIC 50 value
= 2.792194797231E+000 + -4.445280495587E-001*(SP-4) + -4.515030130010E-001*(SP-2) + 1.917935923251E-001*(ATSC0p) + 5.570458666921E-002*(Zagreb)

QSAR Graph

Drug Likeliness study (As per Lipinski rule)

All designedanalogues were adhered to Lipinski's concept, indicating that they might be medicines. All designed derivatives passLipinski's concept for drug test compatibility's. All five designed derivatives results summarized in Table 1.

In-silico Pharmacokinetic studies

The pkCSM analysis suggested beneficial ADMET profiles among the drugs. The main objective of this study to acquiring knowledge about how medications are metabolized within a biological system. As a result, one of the most important aspects of computational drug design is the ADMET research.

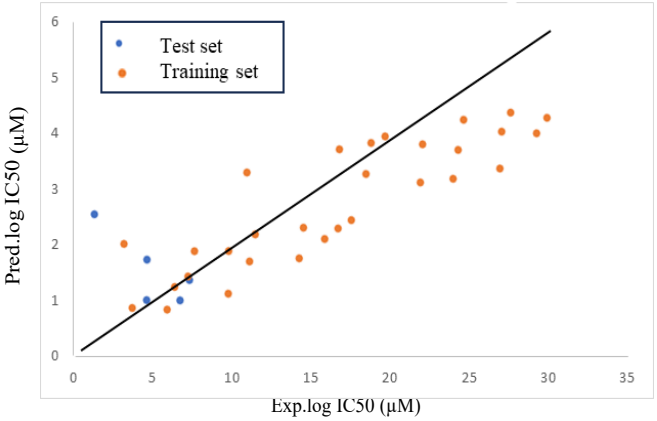


Figure 2: QSAR Graph

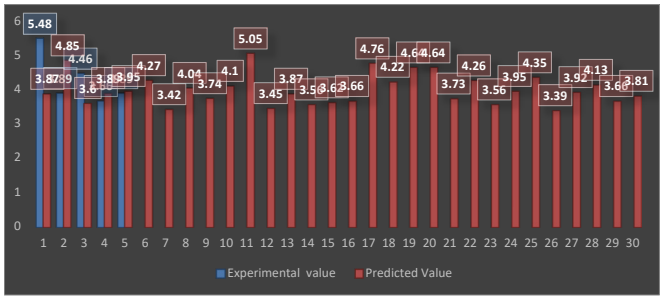


Figure 2 (b): Graph of Experimental and Predicted Value

Absorption

Absorption parameters are extremely important in pharmacokinetics. Because they affect a compound's potency and bioavailability. The critical absorption properties for five compounds (Cn1 to Cn5) are listed in table 2 below. It focused on its water solubility, reaction with P-glycoprotein, gastrointestinal absorption in people, the skin permeability, and the Coca2 permeable.

The two main variables that influence a substance's absorption and bioavailability are permeability and solubility (logS). While Cn1 and Cn5 have lower solubility, Cn2 has the highest solubility and prefers gastric absorption. The high permeability of Cn3, Cn4, and Cn5 enhances intestine absorption, whereas Cn1 and Cn2 have lower permeability. Cn3 has the highest absorption rate (92.211%), indicating exceptional bioavailability, while all of the substances exhibit excellent intestinal absorption (>88%). Because of their low skin permeability, none of the five derivatives can be delivered trans dermally.

Distribution

Human VDss (Volume of Distribution at Steady State) measures how widely a substance is dispersed throughout the body. The compounds Cn2 and Cn5 exhibit superior dispersion inside the body, as indicated by their greatest VDss values of 0.856 and 0.292, respectively. VDss values for Cn3, Cn4, and Cn1 are comparatively lower (0.229, 0.184, and 0.008, respectively), suggesting that their distribution may be more constrained. The proportion of a drug that is free (unbound) and available for pharmacological activity in circulation is known as proportion Unbound (FU) (Human). The largest fraction unbound (0.374) is seen in Cn2, suggesting that there is more medication available in the circulation.

Similar to BBB permeability, Cn1 has the best CNS permeability (-2.002), indicating a higher likelihood of reaching the CNS. The other compounds (Cn2, Cn3, Cn4, and Cn5) show low CNS permeability with values ranging from -2.395 to -1.977, indicating limited ability to penetrate the CNS.Cn1 has the best CNS permeability (-2.002), which is comparable to the BBB permeability and suggests a higher chance of accessing the CNS. With values ranging from -2.395 to -1.977

Metabolism

CYP2D6 Substrate is a crucial enzyme in drug metabolism that can impact how effectively medications are removed

Table 1: Drug Likeliness properties of p-coumaric acid (As per Lipinski Rule)

Compd.	*Mol. Wt.*	*HBA*	*HBD*	*Log P*
CN1	318.376	2	3	3.7169
CN2	282.343	3	3	2.1805
CN3	296.37	3	2	2.7878
CN4	267.328	2	2	3.2828
CN5	301.773	2	2	3.4606

Table 2: Absorption parameters of p-coumaric acid

Compounds	*Water solubility*	*Coca2 Permeability*	*Intestinal absorption (Human)*	*Skin permeability*	*P-glycoprotein substrate*	*P-glycoprotein I inhibitor*	*p-glycoprotein II inhibitor*
Cn1	-4.133	0.943	89.284	-2.914	Yes	Yes	Yes
Cn2	-2.722	0.979	88.825	-3.017	Yes	No	No
Cn3	-3.727	1.3	92.211	-2.871	No	No	No
Cn4	-3.593	1.33	89.964	-2.764	No	No	No
Cn5	-4.1	1.332	89.767	-2.761	Yes	No	No

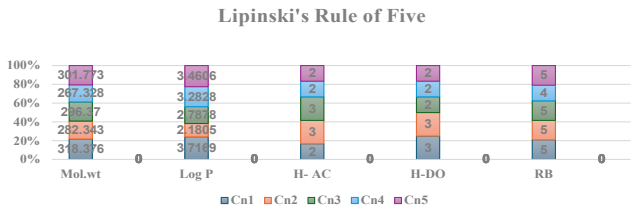


Figure 3: Lipinski's Rule of Five

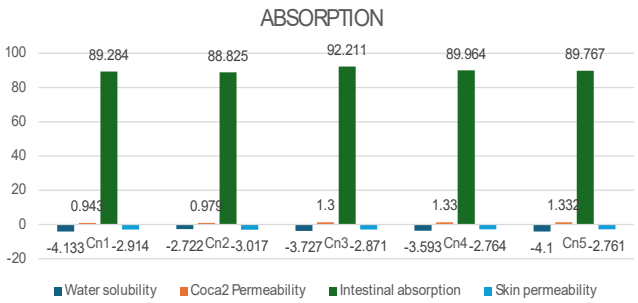


Figure 4: Absorption

Table 3: Distribution properties of p-coumaric acid

Compound number	*VDss (hum) Nume CNS (Log L/Kg*	*Fraction unbounded*	*BBB Permeability Num (log BB)*	*CNS Permeability (log PS)*
Cn1	0.008	0.132	0.091	-2.002
Cn2	0.856	0.374	-0.392	-2.395
Cn3	0.229	0.104	0.01	-2.209
Cn4	0.184	0.09	0.062	-1.977
Cn5	0.292	0.066	0.02	-2.07

Table 4: Metabolism parameters of p-coumaric acid

Comp	*CYP2D6 substrate*	*CYP3A4 substrate*	*CYP1A2 inhibitor*	*CYP2C19 inhibitor*	*CYP2C9 inhibitor*	*CYP2D6 inhibitor*	*CYP3A4substrate*
Cn1	No	Yes	Yes	Yes	Yes	No	Yes
Cn2	No	Yes	Yes	No	No	Yes	No
Cn3	No	Yes	Yes	Yes	Yes	No	Yes
Cn4	No	Yes	Yes	Yes	Yes	No	Yes
Cn5	No	Yes	Yes	Yes	Yes	No	No

Table 5: Computed excretion parameters of p-coumaric acid

Compounds	Total clearance (log ml/min/Kg)	Renal OCT2 Substrate (Y/N)
Cn1	0.462	No
Cn2	1.028	Yes
Cn3	0.501	Yes
Cn4	0.226	Yes
Cn5	-0.172	Yes

Table 6: Computed Toxicity parameters of p-coumaric acid

Compound	*AMES toxicity (Y/N)*	*Max tolrtated dose (hum)*	*hERG I inhibitor (Y/N)*	*hERG II inhibitor (Y/N)*	*Oral rat acute tox (LD50)*	*Oral rat chr. Tox (LOAEL)*	*Hepatotoxicity (Y/N)*	*Skin sensitization (Y/N)*	*T. Pyriformis toxicity*	*Minnor toxicity (log mM)*
Cn1	No	0.548	No	No	2.267	1.043	No	No	0.95	0.385
Cn2	Yes	0.277	No	No	2.519	1.507	No	No	0.878	1.23
Cn3	Yes	0.305	No	No	2.369	1.795	No	No	2.114	0.461
Cn4	Yes	0.375	No	No	2.348	2.178	No	No	1.934	0.003
Cn5	Yes	0.335	No	No	2.435	1.96	No	No	1.03	0.066

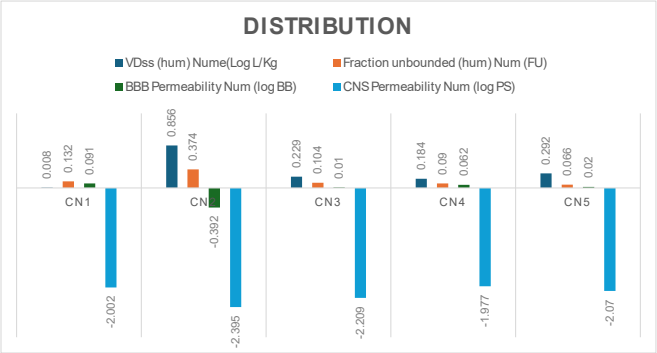


Figure 5: Distribution

Table 7: Compounds binding affinity

Compound no.	*Binding Affinity (kcal/mol)*
CN1	-8.1
CN2	-7.8
CN3	-7.4
CN4	-7.7
CN5	-8.0

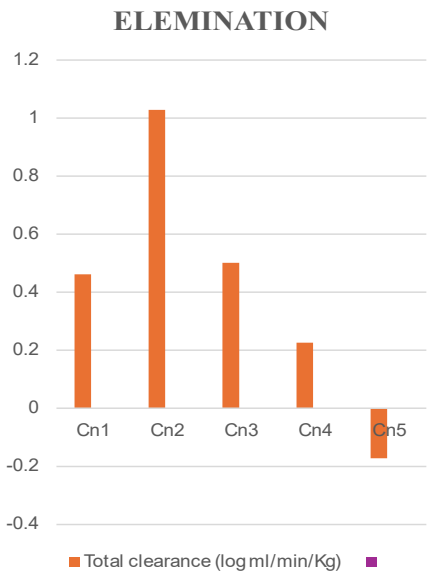


Figure 6: Elemination

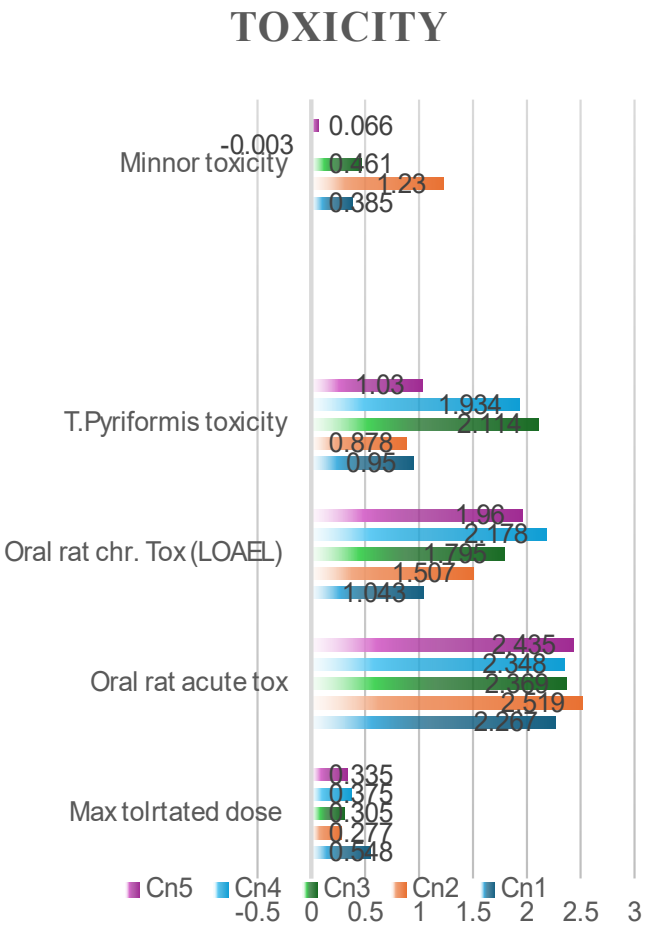


Figure 7: Toxicity

from the body. Despite being CYP2D6 substrates, none of the five substances (Cn1, Cn2, Cn3, Cn4, and Cn5) are substantially metabolized by this enzyme. CYP3A4 substrate is a significant liver protease responsible for contributing to the way certain medications are metabolized. As CYP3A4 substrates, these compounds (Cn1, Cn2, Cn3, Cn4, and Cn5) are all metabolized by this enzyme.

Excretion

Total clearance, which includes metabolic and excretory processes, shows how well a substance is eliminated from the body. The highest total clearance (1.028) for Cn2 indicates that it is removed from the body rather quickly. With a moderate overall clearance of 0.462, Cn1 exhibits an average level of elimination efficiency. Cn3 exhibits a marginally lower clearance (0.501), suggesting that it is eliminated more slowly than Cn1.The lowest clearance (0.226) for Cn4 indicates a slower rate of removal. The negative clearance score (-0.172) for Cn5 may suggest inadequate clearance leading to buildup in the body or poor removal. The renal excretion of several medications is mediated bySLC22A2. Kidney tissue cell receive substrate of SLC22A2 for excretion.

Toxicity

Cn1 is the least toxic overall, with no AMES toxicity, no hERG II inhibition, and the lowest chronic LOAEL.Cn4 has no hERG II inhibition and no significant minnow toxicity, making it a potentially safer candidate for specific uses. Cn4 Unique in not inhibiting hERG II and showing minimal aquatic toxicity. Cn2 to Cn5: Exhibit higher mutagenicity and varying degrees of other toxicological parameters.

ADMET Study: -To estimate a compound's toxic effects, delivery, metabolic processes, elimination, and absorbed (Cn1, Cn2, Cn3, Cn4, Cn5) are indicated in below graphical representation.

Computational Docking studies

The docking analyses were conducted on each and every designed compound to investigate their ability to occupy and interact with the active site of Alpha amylase inhibitor (PDB ID: 4W93). CN5 have shown high binding affinity (-8.7kcal/mol) compare than CN1, CN2, CN3, CN4. Below Table 7 have shown all compounds binding affinity (Figure 8).

Materials And Methods

A research study was conducted in order to find studies on para coumaric acid acts as antidiabetic agent. The PubMed database, ScienceDirect, Scopus, and Google Scholar are 4 scientific databases that were explored using these keywords: "Synthesis of para coumaric acid", "Antidiabetic activity", "Para Coumaric acid", "Alpha Amylase", "β- Glucosidase".The search was focused only on publications in English and studies involving on animals.

QSAR Study

QSAR techniques modeling, that statistically combines the structural components of a chemical structure elements, is one of the best techniques for forecasting a compound's biological activity or function. QSAR models are frequently employed for ecological reasons toxicity or drug development and are increasingly crucial for scientific assessment at the levels of molecule aspects. Quantum chemistry may be stored in a collection of descriptions that characterize a biological activity of the chemical, together with spatial, hydrophobic, electronic, and steric variables. QSAR necessitates certain chemical descriptors, which can becalculated using the Molecular Operating Environment, Swiss ADME web tool, PaDEL-descriptor, E-, and other pertinent software programs and platforms, or they can be acquired empirically through experiments.[8]

2D QSAR Model Development

We compiled thirty (30) p-coumaric acid analogues from reliable journals and analyzed their experimental effects on diabetes medications. The 35 compounds were randomly assigned toa test set 5 compound and the training set of thirty compounds during the QSAR model building process to evaluate the reliability of the created models.[9]

Biological activities

Equation 1. below was used to convert the biological activities of p-coumaric acid derivatives, which are effective medicines, from percent (%) to logarithmic scales. This enhanced predictability thereby bringing the biological activity rates within an average distribution.[10]

$$pBA=\log\left[\left(\frac{\text{Molecular weight(g/o/mol)}}{\text{Dose (g/mol)}}\right)\left(\frac{\text{percentage (\%)}}{\text{100 - percentage (\%)}}\right)\right]$$

Equation. 1

Signifier computation

After gathering thirty compounds from the past research for the training set and five newly designed compounds for the test set, the optimized structures were saved in Structure Data File and exported to the Public Domain Chemical Descriptor LibraryPaDEL signifiersoftware, which was created by Yap Chun Wai of the Pharmaceutical Data Exploration Laboratory.[11] The QSAR programmers can estimate multiple types chemical propertiesfingerprints and descriptors using this program, such asStatic Electricity, algorithmic,serial correlation ,quantitative and thermodynamic properties.[12]

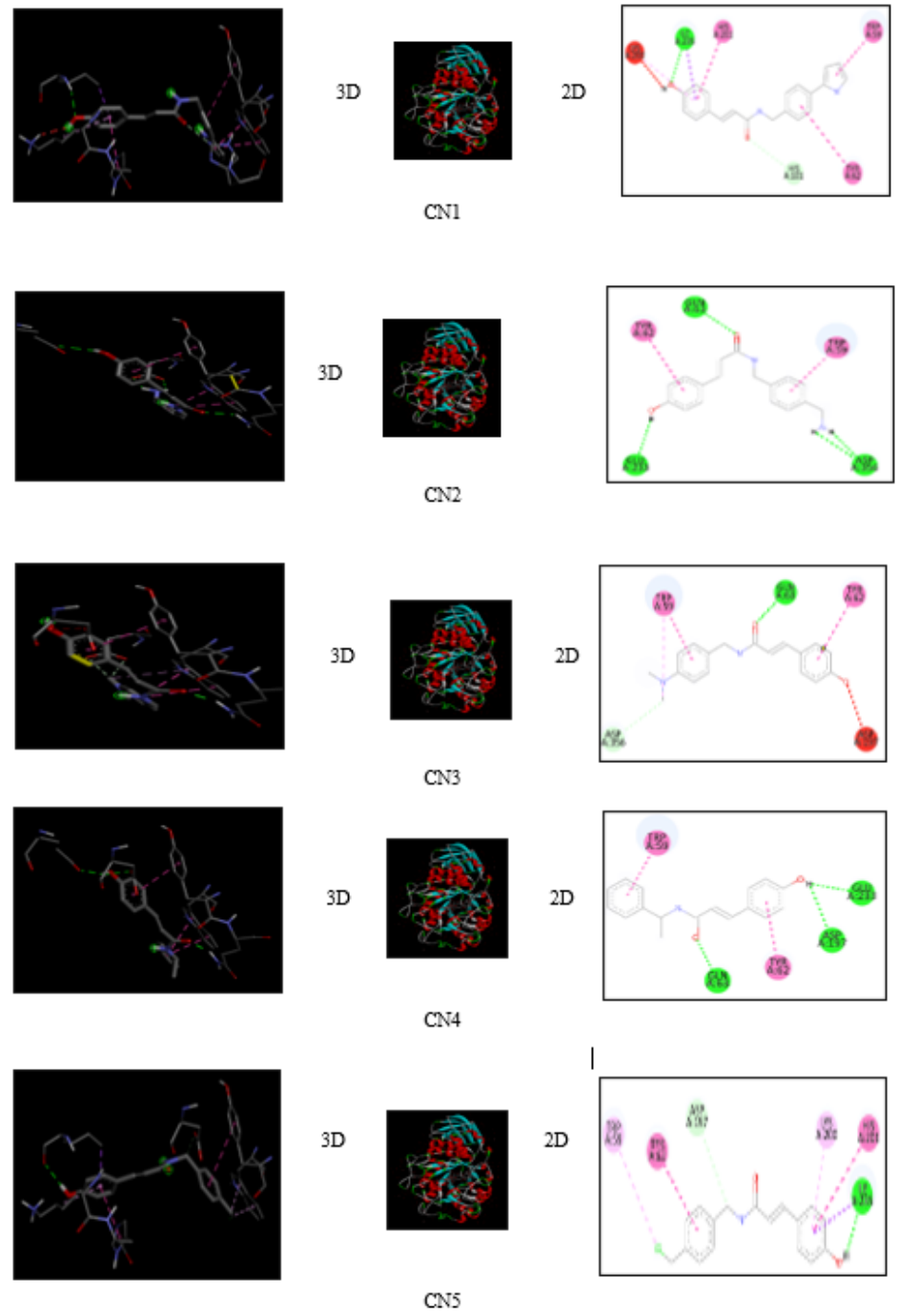
Data pretreatment and division

Data Pre-treatment GUI 1.2, which was downloaded from Drug Theoretics and Cheminformatics (DTC) Laboratory, was used to apply a variable reduction method to the PaDEL descriptors output in an MS Excel sheet. This was done in order to eliminate constant and highly inter-correlated descriptors based on user-specified variance and correlation coefficient cut-off value. Using Kennard-Stone's algorithm division approach, the Dataset Division GUI 1.0 program was utilized to ensure a logical selection of training and test sets (Figure 9).[13]

QSAR Model generation and Validation

Internal validation

The Leave-One-Person-Out cross-validation (LOOCV) approach was used for cross-validation. Every molecular



➢ Docking Interaction of Acarbose (Standard drug) with 4W93 protein binding affinity **-6.1(kcal/mol)**

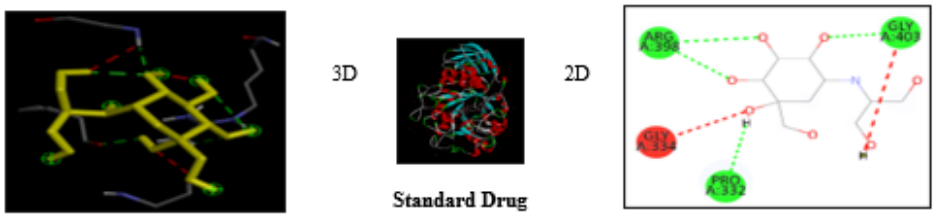
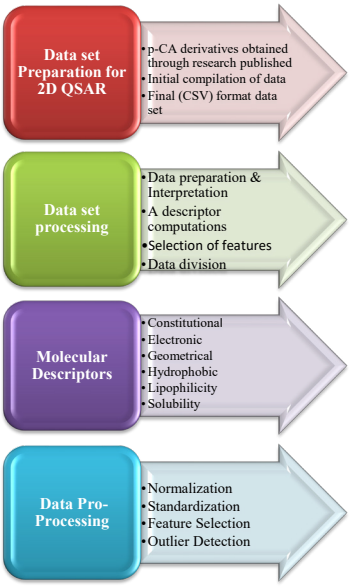


Figure 8: Docking Interaction 2D and 3 D images visualization via Discovery Studio

Table 8: Smiles notations of designed p-coumaric acid derivatives

Compd.	Smiles
CN1	OC1=CC=C(/C=C/C(NCC2=CC=C(C3=CC=CN3)C=C2)=O)C=C1
CN2	OC1=CC=C(/C=C/C(NCC2=CC=C(CN)C=C2)=O)C=C1
CN3	OC1=CC=C(/C=C/C(NCC2=CC=C(N(C)C)C=C2)=O)C=C1
CN4	OC1=CC=C(/C=C/C(NC(C)C2=CC=CC=C2)=O)C=C1



QSAR Model generation and Validation

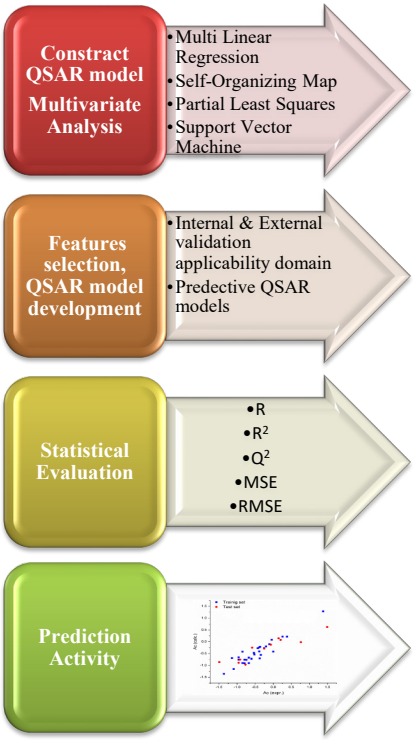


Figure 9: QSAR model workflow

entity to the initial data set was removed a single time, then the actions of the deleted component was forecast by employing the statistical model created by the molecule that was left in order to calculate the rotation estimation, slope coefficients (rCV2). The formula that characterizes a model's inner constancy was used to compute the cross validated regression value (rCV2). The MLR-plus validation program was also used to generate a number of internal validation measures for the models. Create molecular descriptors for the derivatives using programs such as ChemDes. To guarantee predictive dependability, validate the model using statistical techniques (cross-validation, R2, and Q2). Create a 2D QSAR model by applying regression analysis to correlate molecular descriptors with biological activity.[14,15]

$$r2 = \frac{1-\Sigma(Ypred-Y)2}{\Sigma(Y-\bar{Y})2r}$$

The average activity of all molecules in the training set is denoted by $\bar{Y}$, while rCV2 stands for cross validation regression coefficient, Y exploratory and Y pred activity of the molecules in the training set, respectively.

External validation

The model created by the training set was used to predict individual molecule's activity within the test set for independent verification. The equation that follows is used to determine the correlation coefficient (r2) number.where γ training represents the median activity among all the compounds within the training set, the correlation coefficient is the regression coefficient, and Experimental and Ypred are the activity of the molecules in the training set, respectively. Every molecule to the test set is covered by both summaries. The prediction ability of this current system for an outside data set can be determined by the coefficient of regression (r2) number.

$$r^2_{cv}=1-\frac{\Sigma(Y_{pred(test)}-Y_{(test)})^2}{\Sigma(Y(test)-\bar{Y}(training))^2}$$

In-silico Studies

- *Drug Likeness Study (As per Lipinski rule)*

Drug likeness refers to the molecular properties that indicate whether a compound is suitable for development as a drug. This encompasses factors that influence absorption, distribution, Drug likeliness study mainly involves comparison

of molecular properties of the test compounds with structural features of known drugs. The classical method to determine the drug likeliness is to check compliance of Lipinski rule of five. In general, as per the rule, any orally active drug should have not more than one violation of the following criteria: not more than 5 hydrogen bond donors; not more than 10 hydrogen bond acceptors; molecular mass should be less than 500 D and logP should be less than 5.[16]

In-silico Pharmacokinetic studies

All the structure were constructed on ChemBioDraw program and stored as a mol document. the data structures were changed into SMILES form to perform several in-silico studies on different web server tools. The pharmacokinetic studies involved the determination of individual parameters known as. The pkCSM software were examined as well used to assess pharmacokinetic characteristics, such toxic effects, delivery, metabolic processes, elimination, and absorption.[17]

Molecular Docking studies

All the Designed analogues were investigated for binding properties with anti-diabetic target protein. In this study, we designed p-coumaric acid derivatives targeting antidiabetic and performed molecular docking on alpha amylase inhibitor (PDB ID:4W93). The docking study was performed by pyrx. The RCSB Protein Data Bank was used to obtain the structures of alpha amylase inhibitor, which were thenremove water molecules, extra chain, ligands, and unnecessary components. Hydrogen atoms were added after the water molecules were removed, and perform energy minimization. The docking investigations were carried out using pyrxand the docking data were examined, and hydrogen bond interactions, docking score.[18]

Conclusion

A strong prediction model for the antidiabetic action of para-coumaric acid analogues was suggested by the synergistic results of the QSAR, ADMET, and molecular docking studies. Additionally, the QSAR analysis produced an excellent correlation coefficient (R2 = 0.9995). All designed analogues followed to Lipinski's rule of five, showing that they could be potential medicines. The pkCSM analysis revealed the compounds' strong ADMET profiles. In the end, molecular docking was used to investigate the proposed compounds' capacity for inhibiting alpha amylase after QSAR and ADMET parameter analysis.Based on binding energy data, it was determined that all five compounds had a higher affinity for the active site and could form stable complexes. Para-coumaric acid design derivatives exhibit good pharmacokinetic properties and strong binding interactions with significant diabetes targets.In comparison to the standard drug acarbose with 4W93 protein interaction shows -6.1 binding score, and our designed of five compounds were shown to have a higher affinity for the therapeutic region and be able to form robust complexes through binding energy evidence. According to molecular docking assessments, the compound CN5 reveals the most effective relationship with its targeted protein (alpha amylase inhibitor), as demonstrated by its best binding energy of -8.7 kcal/mol among the five analogues. The compounds' promise as novel antidiabetic medications is demonstrated by these results, which also highlight the need for more pharmacological investigations to validate their safety and effectiveness.

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Conflict of Interests

There is no Conflict of Interest involved

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