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Swiss ADME Evaluations of the Drug-Likeness Aspects and Pharmacokinetics of Secondary Metabolites Identified in *Rehmannia glutinosa*

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ABSTRACT

Modern pharmaceutical techniques may be used for examined for traditional medicinal plants. In the modern of computer science Insilco techniques like screening and network analysis are now frequently used to shed light on the pharmacological mechanisms of action of these plants. The uses of Insilco screening, pharmacokinetic screening, and network pharmacology, can assist in identifying the mode of action of potential therapeutic agents from the plants. The current study was developed to predict the pharmacokinetic and drug-likeness properties of 19 bioactive compounds from *Rehmannia glutinosa* using Swiss ADME modelling. The current study observed on utilizing the Swiss ADME Insilco ADME tool for the physicochemical and pharmacological description of the secondary metabolites that *Rehmannia glutinosa* contains.

KEYWORDS: *Rehmannia glutinosa*, pharmacological properties, secondary metabolites, Swiss ADME, drug-likeness.

1 INTRODUCTION

Rehmannia glutinosa Libosch is a traditional Chinese medicinal herb and is in the family of Scrophulariaceae. In China, *Rehmannia glutinosa* is considered as a "top grade" herb. It has various pharmacological actions on multiple body systems. [1] *The* paper studies *Rehmannia glutinosa* root processing effects. Processing involves 9 cycles of rice wine, drying and steaming. Chemical changes during processing are analyzed using NMR and FT-MS. Hydrolysis is identified as the major chemical process.[2] Metabolite composition changes significantly through processing cycles *Rehmannia glutinosa* contains diverse bioactive compounds including Iridoid glycoside, flavonoids, phenolic acids, and polysaccharides. It is also used for stress relief, cancer prevention, liver and kidney protection, and immune system support. *Rehmannia glutinosa* plant has a wide range of health benefits, cultural significance, and practical application. The Swiss ADME website, that makes it easier to calculate physicochemical descriptors and predicted ADME parameters, pharmacokinetic characteristics, drug-like nature, and medicinal chemistry friendliness of small molecules, is a helpful resource for this purpose. The aim in the present investigation was to examine individual ADME behavior and interpret outcomes with the Swiss ADME (http://www.swissadme.ch/index.php). Swiss ADME is a web-based tool that provides users with access to various computational model. [3] predict the absorption, distribution, metabolism, and excretion (ADME) properties of small molecules.[1] The use of SwissADME extends beyond mere predictions; it plays a pivotal role in the early stages of drug discovery by facilitating the identification of promising candidates with optimal pharmacokinetic profiles. By integrating various computational methodologies, such as those from pkCSM, researchers can enhance their understanding of how structural modifications affect ADME properties, ultimately guiding the design of more effective therapeutic agents.[4]

Furthermore, the accessibility of these tools allows for rapid iterations in lead optimization, significantly reducing both time and cost compared to traditional experimental approaches. As the field evolves, the synergy between in silico modelling and experimental validation is expected to yield even more sophisticated insights into molecular behavior, paving the way for innovative drug development strategies that are informed by robust predictive analytics.

2 MATERIALS AND METHODS

2.1 Swiss ADME:

Swiss Institute of Bioinformatics developed by Swiss ADME software, through the website of www.swissadme.ch. To be able to estimate the individual ADME activities of the compounds produced by Rehmannia glutinosa, the web server offered the Swiss ADME Submission page on Google. The simplified molecular input line entry system (SMILES) defined each molecule in the input list, and provided one molecule per line.[5]

2.2 Structure and bioavailability radar:

Canonical SMILES is a two-dimensional chemical structure. To determine a substance of interest's drug-likeness. lipophilicity (LIPO), size (SIZE), polarity (POLAR), insolubility (INSOLU), unsaturation (INSATU), and flexibility (FLEX) is six physiochemical properties using bioavailability radar. The following are specific demands for each property: Size should have a molecular weight (MW) of 150–500 g/mol, lipophilicity should have an XLOGP3 score between -0.7 and +5.0, Topological polar surface area (TPSA) should be between 20 and 130 0A2 to polarity, logarithm of solubility (log S) should not be higher than 6, the fraction of carbons in sp3 hybridization should not be less than 0.25 for saturation, and flexibility should have no more than nine rotatable bonds.[6]

2.3 Physicochemical properties:

In physiochemical features such as molar refractivity, TPSA, proportion csp3, number of rotatable bonds, number of H-bond acceptors, number of H-bond donors, number of heavy atoms, number of aromatic heavy atoms, and molecular weight. open Babel version 2.3.0. is used for calculate the value. [7,6]

2.4 Lipophilicity:

Lipophilicity is used for drug discovery and design.in medicinal chemistry most informative and successful physicochemical property. It can be shown empirically as distribution coefficients (log D) or partition coefficients (log P). The partition equilibrium of a unionized solute between water and an immiscible organic solvent is represented by log P. Greater lipophilicity [8]is correlated with greater log P values.[9] Swiss ADME is five freely accessible models: XLOGP3, WLOGP, MLOGP, SILICOS-IT, and iLOGP. XLOGP3 is an atomistic method that incorporates a knowledge-based library and [10] corrective elements [11]. The foundation of WLOGP is a fragmental system and an atomistic approach. [12] MLOGP is a topological technique based on a linear connection used for 13 implemented molecular descriptors [1]. [13,12] SILICOS-IT is 7 topological descriptors and 27 pieces based on the hybrid approach. The generalized-born and solvent-accessible surface area (GB/SA) model is used in the physics-based LOGP method to calculate the free energies of solvation in water and octanol. The consensus log P o/w is the values determined by the arithmetic mean of the five proposed techniques.[6]

2.5 Solubility:

The point at which increased the solute's concentration in the solution cannot result in greater amounts is termed as the saturation concentration, is used to measure solubility.[14] When a drug's maximum dosage strength disintegrates in 250 millilitres or less water-soluble media with a pH of between 1 and 7.5, it is said to be highly soluble. Two topological methods to predict water solubility in Swiss ADME are employed. The first approach uses the ESOL model, which separates solubility into classes based on the logarithmic scale (Insoluble<-10, Poorly soluble<-6, Moderately soluble<-4, Soluble<-2, Very soluble<0), as opposed to the fundamental general solubility equation.[15] Molecular weight can be utilized to change the linear coefficient (R2=0.75). Every projected value is shown as the molar solubility in water (log S) expressed as a decimal logarithm. Swiss ADME additionally offers qualitative solubility classes and values pertaining to solubility articulated in terms of molarity (mol/L) and mass concentration (mg/mL).

2.6 Pharmacokinetics:

A graphical representation illustrating two derived descriptors, ALOGP and PSA, respectively, delineates the distinctions within a region characterized by advantageous properties for gastrointestinal (GI) absorption. The Egan egg is the name given to the circular area that is most densely packed with well-absorbed molecules. In order to establish the BOILED-Egg (Brain or Intestine

L Estimate D permeation predictive model), this egg is utilized to evaluate the model's predictive capabilities regarding passive gastrointestinal absorption and its forecasting of cerebral accessibility via passive diffusion. For drug discovery and development, the BOILED-Egg model provides a quick, spontaneous, effective, and reliable way to predict passive GI absorption.[16] The area occupied by molecules exhibiting a greater extent of absorption by the gastrointestinal tract is denoted by the white region, whereas the yellow region, referred to as the yolk, represents the area with the greatest probability of permeating the brain[17,6]More than 50–90% of medicinal compounds are bio-transformed by cytochrome p450 (CYP) the isoenzymes are represented by their five principal isoforms, namely CYP1A2, CYP3A4, CYP2C9, CYP2C19, and CYP2D6.The intestinal epithelium has a large amount of P-gp, which is responsible for pumping xenobiotics back into the intestinal lumen and from the brain's capillary endothelial cells back into the capillaries.[19,18] Five key isoforms of cytochrome p450 (CYP) enzymes—CYP1A2, CYP3A4, CYP2C9, CYP2C19, and CYP2D6—bio transform between 50 and 90 percent of medicinal compounds. Xenobiotic substances are transported back into the intestinal lumen. and from the brain's capillary endothelial cells back into the capillaries. [19,18] P-glycoprotein is extensively disseminated throughout the intestinal epithelial tissue.. Swiss ADME utilizes the support vector machine (SVM) methodology for the binary classification of datasets that contain established substrates/non-substrates or inhibitors/non-inhibitors. The label "Yes" or "No" will be applied to the resultant molecule based on whether it is anticipated to be a substrate for both CYP and P-gp, respectively. 1033 molecules from the training set were used to build the SVM model for the P-gp substrate, while 415 molecules from the test set were used for testing. The ten-fold cross-validation demonstrated an accuracy of 0.80 and an area under the curve of 0.86. The external validation revealed an accuracy of 0.80 and an area under the curve of 0.87. For the Cytochrome P-450 2C9 inhibitor molecule, the support vector machine model was developed utilizing a training set comprising 5940 molecules and subsequently tested on 2075 molecules. The ten-fold cross-validation produced an accuracy of 0.78 and an area under the curve of 0.85. The external validation yielded an accuracy of 0.71 and an area under the curve of 0.81. The support vector machine model for the Cytochrome P-450 2D6 inhibitor molecule was formulated utilizing a training set of 3664 molecules and tested on 1068 molecules. The ten-fold cross-validation indicated an accuracy of 0.79 and an area under the curve of 0.85. Ultimately, the SVM model was developed utilizing a training set comprising 7518 compounds and subsequently assessed on 2579 molecules pertaining to the Cytochrome P-450 3A4 inhibitor molecule; the implementation of 10-fold cross-validation resulted in an accuracy (ACC) of 0.77 and an area under the curve (AUC) of 0.85, whereas the external validation produced an ACC of 0.78 and an AUC of 0.86.

2.7 Medicinal chemistry:

The objective of this segment is to assist medicinal chemists in their ongoing endeavors to formulate novel pharmaceuticals. Regardless of the protein targets, chemicals known as PAINS (Pan Assay Interference Compounds, frequent hits, or promiscuous compounds) show robust assay results. These compounds have been substantiated to exhibit activity in numerous assays, thereby rendering them promising candidates for subsequent investigation. SwissADME advises prudence should such moieties be identified in the molecule under evaluation.[20] In a different strategy, Brenk expands lead optimization options by concentrating on smaller and less hydrophobic molecules instead of those that fall under "Lipinski's rule of 5." Nitro groups, sulfates, phosphates, 2-halopyridines, and thiols are examples of chemicals that should be avoided because they include potentially mutagenic, reactive, and unfavourable groups. The ClogP/ClogD values must be between 0 and 4, the number of hydrogen-bond donors must be less than 4, the number of hydrogen-bond acceptors must be fewer than 7, and the number of heavy atoms must be between 10 and 27 according to the Brenk model. Furthermore, only restricted complexity compounds— They are considered medicinal if they have fewer than five ring systems, fewer than eight rotatable links, and no ring systems with more than two fused rings. Lead likeness aims to provide high affinity leads for high throughput screening (HTS), allowing for more interaction exploration during the lead optimization phase. Leads are expected to undergo chemical modifications that reduce their size and improve their lipophilicity, making them less hydrophobic than drug-like molecules. Lead optimization is typically carried out using a rule-based methodology, where molecules with a ClogP between 1 and 3.0 and a molecular weight between 100 and 350 Da are considered superior than compounds that resemble medicines and, consequently, lead.

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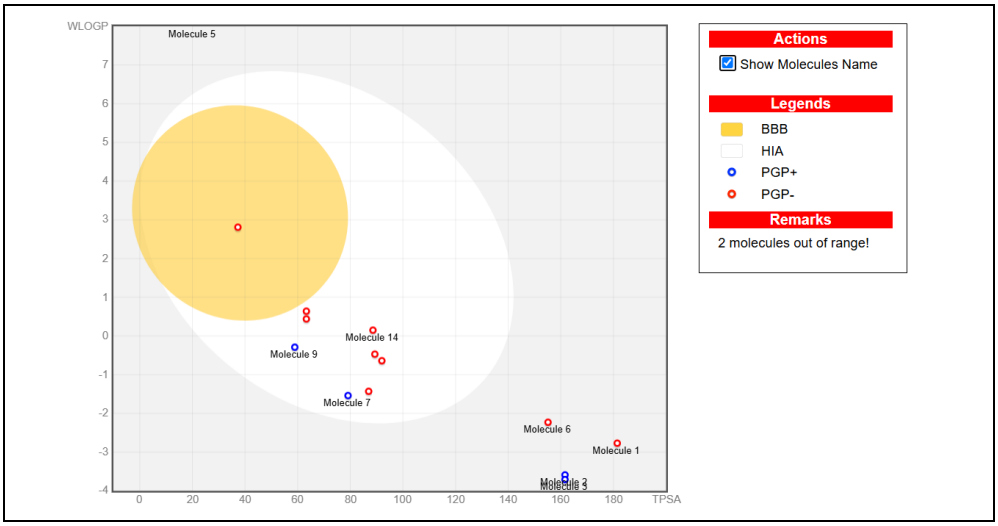

Figure 1: Model of the Phytoconstituents in Boiled Eggs of *Rehmannia glutinosa*

3 RESULTS

Table 1: General phytoconstituents of *Rehmannia glutinosa*

Sr. No	Small molecule	Pub chem ID	Molecular formula	Canonical SMILES	Molecular weight (in g/mol)
1	Iridoid	453214	C20H24O12	COC(=O)C1=CO[C@H]([C@H]2[C@@H]1C=C[C@@]23C=C(C(=O)O3)CO)O[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O	456.4
2	Catalpol	91520	C15H22O10	C1=CO[C@H]([C@H]2[C@@H]1[C@@H]([C@H]3[C@@]2(O3)CO)O)O[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O	362.33
3	Dihydrocatalpol	575531	C15H24O10	C1CO[C@H]([C@H]2[C@@H]1[C@@H]([C@H]3[C@@]2(O3)CO)O)O[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O	364.34
4	Sesquiterpenes	139087999	C15H24O2	CC(C)[C@H]1[C@@H](CC(=C)[C@@H]2[C@@H]1[C@@H](CC2)C(=O)C)O	236.35
5	Aucubin	91458	C15H22O9	C1=CO[C@H]([C@H]2[C@@H]1[C@@H](C=C2CO)O)O[C@H]3[C@@H]([C@H]([C@@H]([C@H](O3)CO)O)O)O	346.33
6	Triterpene	259846	C30H50O	CC(=C)[C@@H]1CC[C@]2([C@H]1[C@H]3CC[C@@H]4[C@]5(CC[C@@H](C([C@@H]5CC[C@]4([C@@]3(CC2)C)C)(C)C)O)C)C	426.7
7	Geniposide	107848	C17H24O10	COC(=O)C1=CO[C@H]([C@H]2[C@@H]1CC=C2CO)O[C@H]3[C@@H]([C@H]([C@@H]([C@H](O3)CO)O)O)O	388.4
8	Rehmaglutin A	5320903	C9H14O5	C1CO[C@H]2[C@H]3[C@@H]1[C@@H]([C@H]([C@]3(CO2)O)O)O	202.2
9	Rehmaglutin C	21637649	C9H12O5	C1[C@H]2[C@@H](C=C([C@]2(OC1=O)CO)CO)O	200.19
10	Rehmaglutin D	5320906	C9H13ClO4	C1CO[C@H]2[C@H]3[C@@H]1[C@@H]([C@H]([C@]3(CO2)O)Cl)O	220.65
11	Stachyose	439531	C24H42O21	C([C@@H]1[C@@H]([C@@H]([C@H]([C@H](O1)OC[C@@H]2[C@@H]([C@@H]([C@H](	666.6

				[C@H](O2)OC[C@@H]3[C@H]([C@@H]([C@H]([C@H](O3)O[C@]4([C@H]([C@@H]([C@H](O4)CO)O)O)CO)O)O)O)O)O)O)O)O	
12	Terpenoids	22311	C10H16	CC1=CCC(CC1)C(=C)C	136.23
13	Monosaccharide	9578507	C43H63NO11	C[C@H]1CC[C@]2(C[C@@H]3C[C@H](O2)C/C=C(/[C@H]([C@H](/C=C/C=C/4\CO[C@H]\5[C@@]4([C@@H](C=C(/C5=N/O)C)C(=O)O3)O)C)O[C@H]6C[C@@H]([C@H]([C@@H](O6)C)O)OC)\C)O[C@@H]1C7CCCCC7	770
14	histidine	6274	C6H9N3O2	C1=C(NC=N1)C[C@@H](C(=O)O)N	155.15
15	Isoleucine	6306	C6H13NO2	CC[C@H](C)[C@@H](C(=O)O)N	131.17
16	Leucine	6106	C6H13NO2	CC(C)C[C@@H](C(=O)O)N	131.17
17	Lysine	5962	C6H14N2O2	C(CCN)C[C@@H](C(=O)O)N	146.19
18	Methionine	6137	C5H11NO2S	CSCC[C@@H](C(=O)O)N	149.21
19	L-Phenylalanine	6140	C9H11NO2	C1=CC=C(C=C1)C[C@@H](C(=O)O)N	165.19

Table 2: Lipophilicity of the Phytoconstituents of *Rehmannia glutinosa*

Sr. No.	Small molecule	Ilogp	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log $P_{o/w}$
1	Iridoid	2.14	-1.61	2.77	-2.04	-2.31	-1.32
2	Catalpol	1.45	-3.22	-3.59	-2.96	-2.91	-2.25
3	Dihydrocatalpol	1.17	-3.34	-3.71	-2.81	-2.50	-2.24
4	Sesquiterpenes	2.82	2.37	2.81	2.63	2.76	2.68
5	Aucubin	0.56	-3.02	-2.80	-2.29	-2.78	-2.07
6	Triterpene	4.72	9.87	8.02	6.92	6.82	7.27
7	Geniposide	2.48	-2.34	-2.23	-1.86	-1.91	-1.17
8	Rehmaglutin A	1.05	-1.75	-1.54	-0.94	-0.69	-0.77
9	Rehmaglutin C	0.98	-2.50	-1.43	-0.78	-0.08	-0.76
10	Rehmaglutin D	1.42	-0.47	-0.29	0.20	0.43	0.26
11	Stachyose	0.77	-7.99	-9.75	-8.02	-8.01	-6.60
12	Terpenoids	2.72	4.57	3.31	3.27	2.97	3.37
13	Monosaccharide			6.07			
14	histidine	-0.03	-3.23	-0.64	-3.74	-0.06	-1.54
15	Isoleucine	1.29	-1.72	0.44	-1.82	-0.15	-0.39
16	Leucine	1.15	-1.52	0.44	-1.82	-0.15	-0.38
17	Lysine	0.97	-3.05	-0.47	-2.67	-0.72	-1.19
18	Methionine	1.12	-1.87	0.15	-2.20	-0.15	-0.59
19	L-Phenylalanine	1.08	-1.52	0.64	-1.11	0.86	-0.01

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Table 3: Water solubility of the phytoconstituents of *Rehmannia glutinosa*.

Small molecule	ESOL				Ali				SILICOS-IT			
	LogS (ESOL)	Solubility		Class	Log S (ESOL)	Solubility		Class	Log S (ESO)	Solubility		Class
		mg/mL	mol/L			mg/mL	mol/L			mg/mL	mol/L	
Iridoid	-1.26	2.51e+01	5.50e-02	Very soluble	-1.69	9.30e+00	2.04e-02	Very soluble	1.77	2.71e+04	5.94+01	Soluble
Catalpol	0.21	5.82e+02	1.61e+00	Highly soluble	0.40	9.03e+02	2.49e+00	Highly soluble	3.03	3.89e+05	1.07e+03	Soluble
Dihydrocatalpol	0.27	6.77e+02	1.86e+00	Highly soluble	0.52	1.21e+03	3.32e+00	Highly soluble	2.56	1.34e+05	3.67e+02	Soluble
Sesquiterpenes	-2.67	5.09e-01	2.16e-03	Soluble	-2.79	3.80e-01	1.61e-03	Soluble	-2.20	1.48e+00	6.28e-03	Soluble
Aucubin	0.18	5.23e+02	1.51e+00	Highly soluble	0.45	9.81e+02	2.83e+00	Highly soluble	2.76	2.00e+05	5.77e+02	Soluble
Triterpene	-8.64	9.83e-07	2.30e-09	Poorly soluble	-10.22	2.58e-08	6.05e-11	Insoluble	-6.74	7.69e-05	1.80e-07	Poorly soluble
Geniposide	-0.38	1.63e+02	4.19e-01	Very soluble	-0.38	1.62e+02	4.16e-01	Very soluble	1.69	1.91e+04	4.91e+01	Soluble
Rehmaglutin A	0.01	2.06e+02	1.02e+00	Highly soluble	0.60	8.10e+02	4.01e+00	Highly soluble	1.03	2.18e+03	1.08e+01	Soluble
Rehmaglutin C	0.63	8.46e+02	4.23e+00	Highly soluble	1.22	3.29e+03	1.65e+01	Highly soluble	0.18	3.05e+02	1.52e+00	Soluble
Rehmaglutin D	-0.91	2.70e+01	1.22e-01	Very soluble	-0.30	1.10e+02	5.00e-01	Very soluble	-0.16	1.52e+02	6.90e-01	Soluble
Stachyose	1.79	4.08e+04	6.12e+01	Highly soluble	1.44	1.82e+04	2.73e+01	Highly soluble	7.24	1.17e+10	1.75e+07	Soluble
Terpenoids	-3.50	4.33e-02	3.18e-04	Soluble	-4.29	6.93e-03	5.09e-05	Moderately soluble	-2.26	7.54e-01	5.53e-03	Soluble
Monosaccharide												
histidine	1.09	1.93e+03	1.24e+01	Highly soluble	1.87	1.15e+04	7.39e+01	Highly soluble	-0.69	3.18e+01	2.05e-01	Soluble
Isoleucine	0.63	5.57e+02	4.25e+00	Highly soluble	0.90	1.05e+03	8.02e+00	Highly soluble	-0.14	9.61e+01	7.33e-01	Soluble
Leucine	0.50	4.17e+02	3.18e+00	Highly soluble	0.70	6.52e+02	4.97e+00	Highly soluble	-0.14	9.61e+01	7.33e-01	Soluble
Lysine	1.51	4.68e+03	3.20e+01	Highly soluble	1.74	7.99e+03	5.47e+01	Highly soluble	-0.18	9.61e+01	6.58e-01	Soluble
Methionine	0.68	7.09e+02	4.75e+00	Highly soluble	0.53	5.04e+02	3.38e+00	Highly soluble	-0.23	8.75e+01	5.86e-01	Soluble
L-Phenylalanine	-0.08	1.38e+02	8.35e-01	Very soluble	0.70	8.21e+02	4.97e+00	Highly soluble	-1.86	2.30e+00	1.39e-02	Soluble

Table 4: Pharmacokinetic Parameters of the Phytoconstituents of *Rehmannia glutinosa*

Molecules	GI absorption	BBB permeant	P-Gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp (cm/s)
Iridoid	Low	No	No	No	No	No	No	No	-10.23 cm/s
Catalpol	low	No	Yes	No	No	No	No	No	-10.80 cm/s
Dihydrocatalpol	Low	No	Yes	No	No	No	No	No	-10.89 cm/s
Sesquiterpenes	High	Yes	No	No	No	No	No	No	-6.06 cm/s
Aucubin	Low	No	Yes	No	No	No	No	No	-10.56 cm/s
Triterpene	Low	No	No	No	No	No	No	No	-1.90 cm/s
Geniposide	Low	No	No	No	No	No	No	No	-10.33 cm/s
Rehmaglutin A	High	No	Yes	No	No	No	No	No	-8.78 cm/s
Rehmaglutin C	High	No	Yes	No	No	No	No	No	-9.30cm/s
Rehmaglutin D	High	No	Yes	No	No	No	No	No	-7.98 cm/s
Stachyose	low	No	Yes	No	No	No	No	No	-16.04 cm/s
Terpenoids	low	Yes	No	No	No	Yes	No	No	-3.89 cm/s
Monosaccharide									
histidine	High	No	No	No	No	No	No	No	-9.54 cm/s
Isoleucine	High	No	No	No	No	No	No	No	-8.32 cm/s
Leucine	High	No	No	No	No	No	No	No	=8.18 cm/s
Lysine	High	No	No	No	No	No	No	No	-9.36 cm/s
Methionine	High	No	No	No	No	No	No	No	-8.54 cm/s
L-Phenylalanine	High	No	No	No	No	No	No	No	-8.39 cm/s

Table 5: Drug likeness of the Phytoconstituents of *Rehmannia glutinosa*

Molecules	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability score
Iridoid	Yes,1 violation:Nor>10	No; 1 violation: WLOGP<-0.4	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, H-acc>10	0.11
Catalpol	Yes; 1 violation: NHorOH>5	No; 1 violation: WLOGP<-0.4	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: XLOGP3<-2, TPSA>150, H-don>5	0.55
Dihydrocatalpol	Yes; 1 violation: NHorOH>5	No; 1 violation: WLOGP<-0.4	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: XLOGP3<-2, TPSA>150, H-don>5	0.55
Sesquiterpenes	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Aucubin	Yes; 1 violation: NHorOH>5	No; 1 violation: WLOGP<-0.4	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: XLOGP3<-2, H-don>5	0.55
Triterpene	Yes; 1 violation: MLOGP>4.15	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Geniposide	Yes; 0 violation	No; 1 violation: WLOGP<-0.4	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: XLOGP3<-2, TPSA>150	0.11
Rehmaglutin A	Yes; 0 violation	No; 1 violation: WLOGP<-0.4	yes	Yes	Yes	0.55
Rehmaglutin C	Yes; 0 violation	No; 1 violation: WLOGP<-0.4	Yes	Yes	No; 1 violation: XLOGP3<-2	0.55
Rehmaglutin D	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Stachyose	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 4 violations: MW>480, WLOGP<-0.4, MR>130, #atoms>70	No; 2 violations: Rotors>10, TPSA>140	No; 1 violation: TPSA>131.6	No; 5 violations: MW>600, XLOGP3<-2, TPSA>150	0.17

					, H-acc>10, H-don>5	
Terpenoids	Yes; 0 violation	No; 1 violation: MW<160	Yes	Yes	No; 2 violations: MW<200, Heteroatoms<2	0.55
Monosaccharide	Violation					
histidine	Yes; 0 violation	No; 3 violations: MW<160, WLOGP<-0.4, MR<40	Yes	Yes	No; 2 violations: MW<200, XLOGP3<-2	0.55
Isoleucine	Yes; 0 violation	No; 2 violations: MW<160, MR<40	Yes	Yes	No; 1 violation: MW<200	0.55
Leucine	Yes; 0 violation	No; 2 violations: MW<160, MR<40	Yes	Yes	No; 1 violation: MW<200	0.55
Lysine	Yes; 0 violation	No; 3 violations: MW<160, WLOGP<-0.4, MR<40	Yes	Yes	No; 2 violations: MW<200, XLOGP3<-2	0.55
Methionine	Yes; 0 violation	No; 2 violations: MW<160, MR<40	Yes	Yes	No; 1 violation: MW<200	0.55
L-Phenylalanine	Yes; 0 violation	Yes	Yes	Yes	No; 1 violation: MW<200	0.55

Table 6: Medicinal Chemistry Properties of Phytoconstituents of *Rehmannia glutinosa.*

Molecules	Pains	Brenk	Leadlikeness	Synthetic accessibility
Iridoid	0 alert	2 alerts: isolated_alkene, more_than_2_esters	No; 1 violation: MW>350	6.45
Catalpol	0 alert	1 alert: Three-membered_heterocycle	No; 1 violation: MW>350	5.72
Dihydrocatalpol	0 alert	1 alert: Three-membered_heterocycle	No; 1 violation: MW>350	5.39
Sesquiterpenes	0 alert	1 alert: isolated_alkene	No; 1 violation: MW<250	3.86
Aucubin	0 alert	1 alert: isolated_alkene	Yes	5.79
Triterpene	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	5.49
Geniposide	O alert	1 alert: isolated_alkene	No; 1 violation: MW>350	5.80
Rehmaglutin A	0 alert	0 alert	No; 1 violation: MW<250	4.47
Rehmaglutin C	0 alert	1 alert: isolated_alkene	No; 1 violation: MW<250	3.99
Rehmaglutin D	0 alert	1 alert: alkyl_halide	No; 1 violation: MW<250	4.52
Stachyose	0 alert	0 alert	No; 2 violations: MW>350, Rotors>7	7.32
Terpenoids	0 alert	1 alert: isolated_alkene	No; 2 violations: MW<250, XLOGP3>3.5	3.46
Monosaccharide	0 alert	0 alert		
histidine	0 alert	0 alert	No; 1 violation: MW<250	2.29
Isoleucine	0 alert	0 alert	No; 1 violation: MW<250	1.65
Leucine	0 alert	0 alert	No; 1 violation: MW<250	1.39
Lysine	0 alert	0 alert	No; 1 violation: MW<250	1.75
Methionine	0 alert	0 alert	No; 1 violation: MW<250	2.43
L-Phenylalanine	0 alert	0 alert	No; 1 violation: MW<250	1.46

Among the 19 molecules of tested lipophilicity of monosaccharaide molecule does not show as compare to others molecule. importance of lipophilicity plays a crucial role in drug design and pharmacokinetics, influencing how compounds are absorbed, distributed, metabolized, and excreted within the body.

Water solubility is crucial in various fields, including chemistry, biology, and environmental science, as it affects the behavior of substances in solutions, influencing reactions, transport, and bioavailability. Most of the molecule are high solubility.

Pharmacokinetic importance lies in understanding how drugs are absorbed, distributed, metabolized, and excreted by the body, which is crucial for optimizing therapeutic efficacy and minimizing adverse effects. The majority molecule shows the low absorption and metabolite the CYP1A2 CYP2C19 CYP2D6, CYP3A4 inhibitors.

medicinal chemistry is crucial in the development of new drugs and therapies, as it combines principles from chemistry, biology, and pharmacology to design and optimize compounds that can effectively treat diseases. The majority molecule shows the 0 alert pains.

Drug likeness is crucial in pharmaceutical development as it helps predict the bioavailability and therapeutic potential of a compound, guiding researchers in selecting suitable candidates for further testing. The majority molecule shows the Lipinski's rules, verbs is yes and bioavailability score is 0.55.

4 DISCUSSIONS

Ayurveda is the oldest and earliest system used to observe the effectiveness and it is used for the drug development in herbs. To World Health Organization (WHO) reports that 30% at one time or another all-plant species are used for medicinal purposes.[21] In computer-based drug designing employ the advancement of ADME characteristics of the drug which results in drug discovery in its early stages.[22][23][24] Pharmacokinetics, or the fate of a medicinal substance in the body, is traditionally thought of by dissecting the several actions that affect the target's access into discrete factors. Pharmacokinetics, or the fate of a medicinal substance in the body, is traditionally thought of by dissecting the several actions that affect the target's access into discrete factors. Then, using SWISSADME techniques, these ADME characteristics (for Absorption, Distribution, Metabolism, and Excretion) can be [25] identified and separated independently. Early ADME estimation during the discovery phase has been shown to significantly lower the percentage of pharmacokinetics-related failure during the clinical phases.[26] For the prediction of ADME, computer models have been promoted as a viable substitute for experimental methods, particularly in the early stages when there are many chemical structures under investigation but few molecules available.[27] is regarded as one of the most significant herbs in traditional Chinese medicine because of its many health advantages, which include anti-inflammatory and immune-boosting effects. The phytochemical phytoconstituents of the plant were enlisted for their potential therapeutic effects, which include compounds such as iridoids, flavonoids, and polysaccharides that contribute to its efficacy in promoting overall health and wellness. The role of significance in *Rehmannia glutinosa* extends beyond its components, as the synergistic effects of these phytochemicals may enhance their therapeutic potential, making it a vital ingredient in various herbal formulations aimed at treating chronic conditions and enhancing vitality. The main component of the Re*hmannia glutinosa* plant is the presence of iridoids, which are known for their ability to modulate immune responses and reduce inflammation, alongside flavonoids that provide antioxidant benefits and promote cardiovascular health. The presence of iridoids, which are known for their ability to modulate immune responses and reduce inflammation, alongside flavonoids that provide antioxidant benefits and promote cardiovascular health. The significant role of phytochemicals in *Rehmannia glutinosa* extends to their ability to support overall wellness, as these compounds work in harmony to improve metabolic functions and bolster the body's natural defences against various diseases.

5 Conclusion

In conclusion, while *Rehmannia glutinosa* shows promise as a therapeutic agent, further clinical studies are necessary to fully understand its efficacy, optimal dosages, and safety profile. As with any herbal remedy, individuals need to consult healthcare professionals before incorporating it into their health regimen. The growing interest in herbal medicine has led to an increased focus on the potential of *Rehmannia glutinosa*, prompting researchers to explore its active compounds and their mechanisms of action within the body. Understanding these mechanisms will not only enhance our knowledge of this herb but also pave the way for developing targeted therapies that harness its benefits while minimizing risks associated with herbal treatment. For future studies, researchers aim to investigate the long-term effects of *Rehmannia glutinosa* on various health conditions, including its role in managing chronic diseases and improving overall wellness.

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