International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

In-Silico Pharmacological Assessment of Pueraria tuberosa DC

Aarcha Jayakishore[1], Atul Thorat[2]

[1]UG Cancer Biology Student, School of Allied Healthcare and Sciences, JAIN (Deemed-to-be University), Bangalore.
[2]Assistant Professor, School of Allied Healthcare and Sciences, JAIN (Deemed-to-be University), Bangalore.

ABSTRACT:
Pueraria tuberosa DC, a traditional medicinal herb, is widely recognised for its therapeutic benefits. The study aims to estimate the pharmacological probability of its phytocompounds through an extensive ADME (Absorption-Distribution-Metabolism-Excretion) investigation. We discovered substantial bioactive compounds in *Pueraria tuberosa* using the online database IMPPAT (Indian Medicinal Plants, Phytochemistry, and Therapeutics). Our analysis revealed a miscellaneous range of chemical constituents with excellent pharmacological profiles, indicating favourable absorption and distribution properties. The findings accentuate the therapeutic value of *Pueraria tuberosa*, validating its historic use in the management of various diseases. This study corroborates the foundation for further research and drug development efforts by emphasizing the pharmacological properties of its phytochemicals. We conducted a detailed examination of the phytocompounds discovered in *Pueraria tuberosa*, comparing fourteen compounds based on ADME features such as lipophilicity, water solubility, medicinal chemistry, pharmacokinetics, and drug-likeness. Overall, this study advocates for further exploration into *Pueraria tuberosa* as a potential candidate for the development of herbal-based medicines, thereby contributing to the emergent interest in phytomedicine and the quest for novel therapeutic agents.

Keywords: ADME, IMPPAT, Pharmacological, Phytomedicine, Phytocompounds, *Pueraria tuberosa*, Therapeutic agents.

INTRODUCTION

India possesses a rich intellectual and textual inheritance that dates back several centuries. Ayurveda, the Indian aboriginal system of medicine, emanating from the Vedic period (circa 4500-1600 BC), has been an integral part of Indian culture. Plants have long been utilized as a rich source of effective and safe medicines due to their natural healing potential (Thorat and Mishra, 2016). Natural source of chemicals has continuously garnered substantial interest from scientists exploring disease treatments, as these compounds are accountable for the therapeutic properties of plants. Biochemical compounds synthesized by plants exhibit pharmacological activities (Mishra and Thorat, 2017; Bultum et al., 2022). Phytochemicals, exclusively, have been recognized for their multifaceted biological activities, including antioxidant, antimicrobial, anticancer, and anti-inflammatory properties (Sharma et al., 2018; Kowalska). These phytochemicals, along with other natural products, represent a biologically relevant chemical space produced by numerous organisms that have evolved to accomplish high levels of fitness under assorted

selective pressures. This characteristic of phytocompounds has intrigued scientists, inspiring them to identify and develop pharmacological agents for various health conditions (Varma et al., 2023).

Pueraria tuberosa DC, a perennial plant of the family Fabaceae, is scattered throughout Southeast Asia (Maji et al., 2014). It is known by numerous vernacular names, including Bhuikuṁbhada, Bīlaikaṅda, Surāl, Vidāri, Vidārīkand and Pātāl kohada. In ancient Ayurvedic texts, it is mentioned by different Sanskrit names such as Kṣhirvallī, Sīta, Swādukaṅda, Ikṣugandhā, Gajavājipriyā, Kroṡtri, Kaṅdapalāśa, Kṣhirśukla, Payśvini, Swādukaṅda, and Vidārī (Thorat and Mishra, 2016). The plant's rhizome/tuber is extensively used in ethno-medicine as well as in traditional systems of medicine, principally in Ayurveda (Maji et al., 2014). Pueraria species are highly esteemed for their health and cosmetic benefits and are additionally utilized in agriculture to reduce soil erosion. They are used across numerous conventional practices to treat menopausal syndrome-related infirmities, with the tuber constituting the most often employed part of the plant in indigenous medicine (Wang et al., 2020). In Ayurveda, *P. tuberosa* is described as a plant with significant nutritional value and is also known for its diuretic, aphrodisiac, energizing and galactagogue properties (Kirtikar and Basu, 1935 and Maji et al., 2014). Extracts and purified compounds of *P. tuberosa* showed a range of pharmacological activities, including anti-stress, anti-inflammatory, antidiabetic, anticonvulsant, hepatoprotective, anticancer, antifertility, europrotective, hypolipidemic, antioxidant, nootropic, cardioprotective, antiulcerogenic, immunomodulatory, wound healing and nephroprotective properties. The plant is particularly used as a tonic, antitumor, antirheumatic, antiallergic, and for the treatment of malaria, typhoid fever, and cough (Anonym, 1978; Jeon et al., 2005; Sadguna et al., 2015; Bharti et al., 2021).

IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics) is a methodically curated database that encompasses the directory of naturally occurring medicinal plants, their phytochemicals and therapeutical potential. (Mohanraj et al., 2018). *In-silico* development of therapeutic preparations can be aided by the availability of a carefully maintained database including data on plants, their associated natural compounds, and a repository for their chemical structures (Jensen et al., 2014). ADME (Absorption - Distribution - Metabolism - Excretion) is an expeditious and convenient method used for predicting the pharmacological properties of innumerable chemical constituents, holding significant importance in the drug development process (Hou and Wang, 2008). The term ADME designates the pharmacokinetics of a drug, defining how the drug behaves in the human body after administration, including its transit across the membrane and body, metabolic processes, and routes of excretion or elimination (Doogue and Polasek, 2013). The properties such as P-glycoprotein substrate, Blood Brain Barrier influence the properties of absorption. The following phytochemical chemical metabolism have the ability to inhibit CYP450 enzymes, and several other properties helps in the designing of drugs (Shen et al., 2010, Cheng et al., 2011 and Wang et al., 2011) .

Analyzing and anticipating the pharmacological basis of the therapeutic activity of *Pueraria tuberosa* using Swiss ADME analysis, considering the physiochemical properties of the phytoconstituents of the medicinal plant, which predict the pharmacokinetic properties, drug-like nature, solubility, lipophilicity, medicinal chemistry. The present study was designed in *Pueraria tuberosa* for *in-silico* ADMET screening

METHODOLOGY

In-silico Collection of Phytocompounds of *Pueraria tuberosa* DC

Indian Medicinal Plants-Phytochemicals-Therapeutics or IMPPAT is the most comprehensive database on phytochemicals of Indian medicinal plants. IMPPAT provides an integrative platform for using

cheminformatic30 methods to accelerate natural product-based drug development. IMPPAT (Indian Medicinal Plants-Phytochemicals-Therapeutics) which helps in the curation of Indian Medicinal Plants their Phytochemicals and Therapeutic uses. With the help of IMPPAT we have curated the phytochemicals and computed physiochemical properties and predicted Absorption, Distribution, Metabolism, Excretion (ADME) properties using cheminformatic tools. At present, IMPPAT has about 9500 phytocompounds with their physiologically relevant data (Mohanraj et al., 2018 and Roshni et al., 2022).

Swiss ADME- an online resource

Swiss ADME, produced by the Swiss Institute of Bioinformatics, is an online resource that offers free access to a variety of parameters and predictive models. This online tool estimates the pharmacokinetics property, lipophilicity, physicochemical properties, drug-likeness, and medicinal chemistry of one or more compounds. Users can acquire findings in the form of tables or Excel sheets by submitting the compounds into the Simplified Molecular Input Line Entry System (SMILES). This aids in simplifying the analysis and comprehend critical pharmacokinetic data, facilitates medication development. (Daina et al., 2017, Fan and De Lannoy, 2014, Lipinski, 2000 and Tsopelas et al., 2017).

Structure and bioavailability radar

The graphical representation of drug-likeness requirements is crucial when assessing the oral bioavailability of substances. A drug's biological activities is determined by 6 crucial physicochemical variables: lipophilicity, size, polarity, solubility, saturation, and flexibility. Specific thresholds are specified for all parameters in order to precisely assess drug-likeness. Molecular weight, a measurement of size, should range around 150 and 500 g/mol. Lipophilicity, estimated by XLOGP3, ought to lie within -0.7 and +6.0. For solubility, the logarithmic value for solubility (log S) ought to stay below an established limit. Saturation is determined by the percentage of sp^3 hybridised carbon to the overall carbon count of the molecule, which should be a minimum of 0.25. The topological polar surface area (TPSA) ranges from 20 to 130 Å and is utilised for evaluating polarity. The flexibility is determined by the number of rotatable bonds, which should not exceed nine (Delaney, 2004, Tian et al., 2015, Cheng et al., 2007 and Daina et al., 2017).

Physiochemical property

Physicochemical characteristics furnish comprehensive explanations of molecules structures and behaviours. Relevant parameters include molecular weight, molecular refractivity, polar surface area (PSA), and the number of specific atom types such heavy atoms, aromatic heavy atoms, rotatable bonds, hydrogen bond acceptors, and hydrogen bond donors. These values have been obtained with Open Babel version 2.3.0 (Daina et al., 2017 and Boyle et al., 2011). Topological polar surface area (TPSA) is a fragmental methodology to estimate the polar surface area. This technique considers sulphur and phosphorus as polar atoms, which contributed to the overall calculations of PSA (Ertl et al., 2000).

Lipophilicity

Lipophilicity is a significant consideration in drug discovery and design, influencing solubility, cell membrane penetration, transport to molecular targets, receptor binding, potency, selectivity, and overall impact on metabolism and pharmacokinetics. It is essential in defining the ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) qualities of a drug (Arnott and Planey, 2012). Lipophilicity is often determined using log P and log D. Log P, additionally referred to as the logarithmic n-octanol-water partition coefficient, quantifies the partition equilibrium of a unionised solute between water and an immiscible organic solvent. The distribution coefficient, log D, indicates the ratio of the compound's complete forms in each phase. A higher log P value demonstrates additional lipophilicity,

which typically correlates with improved ability to cross cell membranes and interact with target receptors (Testa et al., 2000). Swiss ADME has five openly accessible models to determine the lipophilicity of compounds: XLOGP3, WLOGP, MLOGP, SILICOS-IT, and iLOGP. Among these, the logarithmic partition coefficient between n-octanol and water (log P_o/w) is regarded as an essential indicator of lipophilicity (Cheng et al., 2007 and Mannhold et al., 2009).

XLOGP3 is an atomistic, knowledge-based approach calculated using the XLOGP program, incorporating correction aspects (Cheng et al., 2007). WLOGP remains entirely reliant on an atomic approach that employs the fragmentation mechanism established by Wildman and Crippen (Wildman and Crippen, 1999). MLOGP employs a topological technique, as implemented by Moriguchi et al. (Moriguchi et al., 1992). SILICOS-IT offers a hybrid approach that combines fragmental and topological methodologies, as predicted according to the FILTER-IT program, and comprises 27 fragments and 7 topological descriptors. iLOGP is an in-house, physics-based approach for assessing lipophilicity based on free energies of solvation in water and n-octanol using the Generalized-Born and Solvent Accessible Surface Area (GB/SA) model (Daina et al., 2017).

Solubility

Solubility is a significant factor in drugs development, because it significantly impacts drug bioavailability following oral delivery. It is essential to drugs absorption. A compound's water solubility and lipophilicity are highly linked (Ottaviani et al., 2010). Factors like temperature, pressure, and the type of solvent used can impact solubility. The saturation concentration measures the extent of solubility by identifying the point at which the concentration of the solute in the solution reaches equilibrium and no longer increases with more solute (Lachman et al., 1986). Water solubility is determined using the following approaches: Log S (ESOL), Log S (Ali), and Log S (SILICOS-IT). The ESOL and Ali models, both topological methods readily available in Swiss ADME, are frequently utilised to predict water solubility. The ESOL model characterises solubility as follows: Insoluble (< -10), Poorly soluble (< -6), Moderately soluble (< -4), Soluble (< 2), and Highly soluble (< 0) (Yalkowsky and Valvani, 1980). The Ali model, inspired by the ESOL model, applies a similar scale with slightly distinct thresholds: insoluble (< -10), poorly soluble (< -6), moderately soluble (< -4), soluble (< -2), and highly soluble (< 0). Both models diverge from the fundamental universal solubility equation by exhibiting variable linear relationships with experimental results. The ESOL and Ali models display substantial linear correlations, with R^2 values of 0.69 and 0.81, respectively. The SILICOS-IT model's fragmental approach provides a linear correlation coefficient of $R^2 = 0.75$. (Ali et al., 2012, Delaney, 2004 and Mahanthesh et al., 2020)

Pharmacokinetics

The pharmacokinetics section compiles all predictions regarding a molecule's ADME characteristics, aiding with estimating its absorption, distribution, metabolism, and excretion characteristics. The second section captures data on all absorbed molecules to assist in an evaluation of their ADME properties. The BOILED Egg model, an elliptical visualisation tool, has been utilised to explain the absorption properties of these compounds. This model presents a quick and effective prediction of passive human gastrointestinal absorption and the ability to cross the blood-brain barrier (Daina and Zoete, 2016 and Di et al., 2011). Understanding the functioning of P-glycoprotein (P-gp) becomes essential given that it safeguards the central nervous system (CNS) by aggressively pumping foreign chemicals back into the intestinal lumen and capillaries from the brain's capillary endothelial cells (Szaka et al., 2008). Knowing whether a chemical is a substrate or non-substrate of P-gp is crucial for assessing its ability to penetrate

biological barriers, such as the blood-brain barrier or the gastrointestinal wall (Montanari and Ecker, 2015).

Understanding drug metabolism requires an analysis of how chemicals interact with cytochrome P450 enzymes. Among these enzymes, CYP3A4 and CYP2D6 play significant functions in drug biotransformation, regulating metabolic pathways and excretion (Testa et al. 2009). Inhibition of these isoenzymes is the primary cause of drug-drug interactions, which can lead to undesirable side effects, suboptimal drug clearance, and excessive drug accumulation (Kirchmair et al., 2015). Swiss ADME employs a binary classification technique and applies the support vector machine (SVM) algorithm to datasets comprising known substrates, non-substrates, inhibitors, and non-inhibitors. The model anticipates whether the substance under research is a substrate for P-gp and cytochrome P450 enzymes, giving insights into possible relationships and metabolic behaviour (Mitchell, 2014).

Drug likeness

The qualitative characterisation of a molecule's bioavailability is essential to its development as an oral medicine. In order to simplify the chemical libraries and eliminate substances that fail to meet the acceptable pharmacokinetic profiles, five rule-based filters were used (Daina et al., 2017). Swiss ADME offers five different rule-based filters: Lipinski, Veber (GSK), Egan (Pharmacia), Muegge (Bayer), and Ghose (Amgen). Each set of filters evaluated various factors to determine a molecule's suitability as a drug. The Lipinski filter, also referred to as the Rule of Five, divides smaller molecules based around their physicochemical attributes, such as molecular weight (MW) less than 500, MLOGP less than 4.14, and nitrogen or oxygen atom count < 5 (Lipinski et al., 2001). The Veber filter classifies drug-like molecules as those that possess a topological polar surface area (TPSA) of 140 $Å^2$ or less and 10 or fewer rotatable bonds (Veber et al., 2002). The Egan filter necessitates WLOGP of 5.88 or less and TPSA of 13.6 $Å^2$ or less. This filter evaluates chemicals based on the physicochemical processes and permeability of the membrane (Egan et al., 2000). The Muegge and Ghose filters consider additional variables such as the bioavailability score, which is determined by total charge, TPSA, and compliance with the Lipinski filter. These filters classify compounds based on their bioavailability, assigning probabilities of 11%, 17%, 56%, or 85% (Martin and Park, 2005).

Medicinal Chemistry

Medicinal chemists play a substantial part in leading the pursuit for novel medications, and countless essential features impact the drug development process. One of these characteristics is PAINS (Pan Assay Interference Compounds), a group of compounds which demonstrate robust assay reactions but have no relationship with protein targets. If PAINS has been identified during the examination, SWISS ADME gives a warning (Baell and Holloway, 2010). Another significant attribute is Brenk, which recognises chemicals that are chemically reactive, metabolically unstable, or have poor pharmacokinetic characteristics, causing structural alerts. Brenk's molecules tend to be smaller and less hydrophobic, rendering Lipinski's rule of five less applicable. In addition, lead-likeness describes molecules having 10 to 27 heavy atoms, a maximum of four hydrogen bond donors, and less than seven hydrogen bond acceptors. These variables contribute in the assessment of molecules as lead candidates in drug development (Brenk et al., 2008).

RESULTS

IMPPAT data base

Table 1: Phytochemical data of *Pueraria tuberosa* DC from IMPPAT database.

Sr. No.	Plant part	IMPPAT Phytochemical identifier	Phytochemical name	SMILE
1	Tuber	IMPHY014037	1,14-Dihydroxy-7,7-Dimethyl-8,12,20-Trioxapentacyclo[11.8.0.02,11.04,9.014,19]Henicosa-2(11),3,5,9,15,18-Hexaen-17-One	O=C1C=CC2(C(=C1)OCC1(C2Oc2c1cc1c(c2)OC(C=C1)(C)C)O)O
2	Tuber	IMPHY005114	Anhydrotuberosin	Oc1ccc2c(c1)OCc1c2oc2c1cc1c(c2)OC(C=C1)(C)C
3	Tuber	IMPHY014836	Beta-Sitosterol	CC[C@@H](C(C)C)CC[C@H]([C@H]1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O)C
4	Root	IMPHY014836	Beta-Sitosterol	CC[C@@H](C(C)C)CC[C@H]([C@H]1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O)C
5	Whole plant	IMPHY004566	Daidzein	Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O
6	Root	IMPHY004566	Daidzein	Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O
7	Tuber	IMPHY004566	Daidzein	Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O
8	Tuber	IMPHY004643	Genistein	Oc1ccc(cc1)c1coc2c(c1=O)c(O)cc(c2)O
9	Tuber	IMPHY004138	Genistin	OC[C@H]1O[C@@H](Oc2cc(O)c3c(c2)occ(c3=O)c2ccc(cc2)O)[C@@H]([C@H]([C@@H]1O)O)O
10	Whole plant	IMPHY010265	Gluconic Acid	OC[C@H]([C@H]([C@@H]([C@H](C(=O)O)O)O)O)O
11	Not men	IMPHY007169	Pterocarpan	c1ccc2c(c1)C1Oc3c(C1CO2)cccc3

	tioned			
12	Not mentioned	IMPHY004578	Puerarin	OC[C@H]1O[C@H]([C@@H]([C@H]([C@@H]1O)O)O)c1c(O)ccc2c1occ(c2=O)c1ccc(cc1)O
13	Whole plant	IMPHY004578	Puerarin	OC[C@H]1O[C@H]([C@@H]([C@H]([C@@H]1O)O)O)c1c(O)ccc2c1occ(c2=O)c1ccc(cc1)O
14	Root	IMPHY004578	Puerarin	OC[C@H]1O[C@H]([C@@H]([C@H]([C@@H]1O)O)O)c1c(O)ccc2c1occ(c2=O)c1ccc(cc1)O
15	Tuber	IMPHY004578	Puerarin	OC[C@H]1O[C@H]([C@@H]([C@H]([C@@H]1O)O)O)c1c(O)ccc2c1occ(c2=O)c1ccc(cc1)O
16	Tuber	IMPHY013046	Puerarone	Oc1ccc2c(c1)occ(c2=O)c1cc2C=CC(Oc2cc1O)(C)C
17	Tuber	IMPHY013182	Puerarostan	COc1c(O)ccc2c1oc(=O)c1c2oc2c1cc(c(c2)O)CC=C(C)C
18	Tuber	IMPHY014842	Stigmasterol	CC[C@@H](C(C)C)/C=C/[C@H]([C@H]1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O)C
19	Root	IMPHY014842	Stigmasterol	CC[C@@H](C(C)C)/C=C/[C@H]([C@H]1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O)C
20	Not mentioned	IMPHY002579	Tuberosin	Oc1ccc2c(c1)OC[C@]1([C@@H]2Oc2c1cc1c(c2)OC(C=C1)(C)C)O
21	Whole plant	IMPHY002579	Tuberosin	Oc1ccc2c(c1)OC[C@]1([C@@H]2Oc2c1cc1c(c2)OC(C=C1)(C)C)O
22	Root	IMPHY002579	Tuberosin	Oc1ccc2c(c1)OC[C@]1([C@@H]2Oc2c1cc1c(c2)OC(C=C1)(C)C)O
23	Tuber	IMPHY002579	Tuberosin	Oc1ccc2c(c1)OC[C@]1([C@@H]2Oc2c1cc1c(c2)OC(C=C1)(C)C)O
24	Tuber	IMPHY010858	Tuberostan	COc1ccc2c(c1)oc(=O)c1c2oc2c1cc1c(c2)OC(C=C1)(C)C

IMPPAT was used to identify all 24 phytoconstituents from plant components, including the roots, tubers, and whole plant, as shown in the above table. Nevertheless, certain phytoconstituents were discovered to be common, For example, it has been found that Daidzein, Tuberosin, and Puerarin were shared by all three sections. 14 compounds were chosen for Swiss ADME investigation out of the twenty-four compounds.

Table 2: Physicochemical Properties of select phytochemicals of *P. tuberosa*

Molecule	**Name of the Phytochemical**	**Formula**	**Molecular weight**	**No. heavy atoms**	**No. arom. heavy atoms**	**Fraction Csp3**	**Num. rotatable bonds**	**Num. H-bond acceptors**	**Num. H-bond donors**	**Molar Refractivity**	**TPSA**
Molecule 1	1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one	C20H18O6	354.35	26	6	0.35	0	6	2	91.91	85.22
Molecule 2	Anhydrotuberosin	C20H16O4	320.34	24	15	0.2	0	4	1	92.33	51.83

Molecule 3	Beta-sitosterol	C29H50O	414.71	30	0	0.93	6	1	1	133.23	20.23
Molecule 4	Daidzein	C15H10O4	254.24	19	16	0	1	4	2	71.97	70.67
Molecule 5	Genistein	C15H10O5	270.24	20	16	0	1	5	3	73.99	90.9
Molecule 6	Genistin	C21H20O10	432.38	31	16	0.29	4	10	6	106.11	170.05

Molecule 7	Gluconic acid	C6H12O7	196.16	13	0	0.83	5	7	6	38.54	138.45
Molecule 8	Pterocarpan	C15H12O2	224.25	17	12	0.2	0	2	0	64.65	18.46
Molecule 9	Puerarin	C21H20O9	416.38	30	16	0.29	3	9	6	104.59	160.82
Molecule 10	Puerarone	C20H16O5	336.34	25	16	0.15	1	5	2	96.09	79.9

Molecule 11	Puerarostan	C21H18O6	366.36	27	17	0.19	3	6	2	104.02	93.04
Molecule 12	Stigmasterol	C29H48O	412.69	30	0	0.86	5	1	1	132.75	20.23
Molecule 13	Tuberosin	C20H18O5	338.35	25	12	0.3	0	5	2	91.84	68.15
Molecule 14	Tuberostan	C21H16O5	348.35	26	17	0.19	1	5	0	100.38	61.81

Table 3: Lipophilicity of the select phytocompounds of *P. tuberosa*

Name of the phytocompounds	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one	2.49	0.68	1.39	0.55	2.02	1.43
Anhydrotuberosin	3.26	4.1	4.62	2.58	4.35	3.78
Beta-sitosterol	5.05	9.34	8.02	6.73	7.04	7.24
Daidzein	1.77	2.47	2.87	1.08	3.02	2.24
Genistein	1.91	2.67	2.58	0.52	2.52	2.04
Genistin	2.44	0.86	0.05	-1.61	0.35	0.42
Gluconic acid	-0.06	-3.37	-3.49	-2.9	-2.26	-2.42
Pterocarpan	2.51	3.15	2.97	2.81	3.28	2.95
Puerarin	1.77	0.01	0.06	-1.52	0.81	0.23
Puerarone	2.62	3.39	3.95	1.64	3.9	3.1
Puerarostan	3.51	4.66	4.62	2.55	4.62	3.99
Stigmasterol	5.08	8.56	7.8	6.62	6.86	6.98
Tuberosin	3.09	3.36	2.75	1.9	3.1	2.84
Tuberostan	3.74	4.37	4.78	3.1	4.78	4.15

The table above displays high values for iLOGP, XLOGP3, WLOGP, MLOGP, and Silicos-IT Log P. Beta-sitosterol represents the Consensus Log P value, while glutamic acid represents the low value.

Table 4: Solubility of the phytochemicals of *P. tuberosa*

Name of the phytocompound	ESOL				Ali				SILICOS-IT			
	ESOL LogS	ESOL Solubility (mg/ml)	ESOL Solubility (mol/l)	ESOL Class	Ali LogS	Ali Solubility (mg/ml)	Ali Solubility (mol/l)	Ali Class	Silicos-IT LogSw	Silicos-IT Solubility (mg/ml)	Silicos-IT Solubility (mol/l)	Silicos-IT class
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0	-2.64	8.19E-01	2.31E-03	Soluble	-2.	3.18E+00	8.99E-03	Soluble	-2.96	3.89E-01	1.10E-03	Soluble

.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one					05							
Anhydrotuberosin	-4.87	4.31E-03	1.34E-05	Moderately soluble	-4.89	4.09E-03	1.28E-05	Moderately soluble	-6.09	2.63E-04	8.20E-07	Poorly soluble
Beta-sitosterol	-7.9	5.23E-06	1.26E-08	Poorly soluble	-9.67	8.90E-08	2.15E-10	Poorly soluble	-6.19	2.69E-04	6.49E-07	Poorly soluble
Daidzein	-3.53	7.51E-02	2.95E-04	Soluble	-3.6	6.41E-02	2.52E-04	Soluble	-4.98	2.64E-03	1.04E-05	Moderately soluble
Genistein	-3.72	5.11E-02	1.89E-04	Soluble	-4.23	1.59E-02	5.88E-05	Moderately soluble	-4.4	1.07E-02	3.94E-05	Moderately soluble
Genistin	-3.18	2.85E-01	6.60E-04	Soluble	-4.01	4.18E-02	9.67E-05	Moderately soluble	-2.69	8.77E-01	2.03E-03	Soluble
Gluconic acid	1.4	4.89E+03	2.49E+01	Highly soluble	1.04	2.14E+03	1.09E+01	Highly soluble	3.02	2.04E+05	1.04E+03	Soluble
Pterocarpan	-3.74	4.11E-02	1.83E-04	Soluble	-3.21	1.39E-01	6.20E-04	Soluble	-4.76	3.86E-03	1.72E-05	Moderately soluble
Puerarin	-2.62	9.89E-01	2.37E-03	Soluble	-2.94	4.79E-01	1.15E-03	Soluble	-2.97	4.49E-01	1.08E-03	Soluble

Puerarone	-4.47	1.14E-02	3.40E-05	Moderately soluble	-4.75	6.02E-03	1.79E-05	Moderately soluble	-5.81	5.17E-04	1.54E-06	Moderately soluble
Puerarostan	-5.32	1.77E-03	4.84E-06	Moderately soluble	-6.34	1.67E-04	4.56E-07	Poorly soluble	-6.37	1.56E-04	4.25E-07	Poorly soluble
Stigmasterol	-7.46	1.43E-05	3.46E-08	Poorly soluble	-8.86	5.71E-07	1.38E-09	Poorly soluble	-5.47	1.40E-03	3.39E-06	Moderately soluble
Tuberosin	-4.41	1.32E-02	3.89E-l5	Moderately soluble	-4.47	1.15E-02	3.40E-05	Moderately soluble	-4.66	7.40E-03	2.19E-05	Moderately soluble
Tuberostan	-5.17	2.35E-03	6.75E-06	Moderately soluble	-5.38	1.44E-03	4.13E-06	Moderately soluble	-7.13	2.58E-05	7.40E-08	Poorly soluble

In the table given above high solubility was shown by Gluconic acid for ESOL and Ali, while in SILIOCS-IT none of the compound showed high solubility. 1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo [11.8.0.02,11.04,9.014,19] henicosa-2(11),3,5,9,15,18-hexaen-17-one, Daidzein, Pterocarpan, Puerarin these compounds are the common molecules that are soluble according to ESOL and Ali characteristics, other compounds that showed solubility in ESOL are Genistein and Genistin. According to SILICOS-IT, 1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one, Genistin and Gluconic acid showed solubility. Anhydrotuberosin, Puerarone, Tuberosin and Tuberostan are the common compounds that are moderately soluble according to ESOL and Ali. Other compounds that showed moderate solubility according to Ali are Genistein, Genistin. According to SILICOS-IT the compounds that showed moderate solubility are Daidzein, Genistein, Pterocarpan, Puerarone, Stigmasterol, Tuberosin. The common compounds that showed poor solubility according to ESOL and Ali characteristics is Stigmasterol, Beta-sitosterol. Compounds that showed poor solubility according to SILICOS-IT are Tuberostan, Puerarostan, Beta-sitosterol, Anhydrotuberosin.

Table 5: Pharmacokinetic properties of the phytochemicals of *P. tuberosa*

Name of the phytocompounds	GI absorption	BBB permeant	Pgp substrate	CYP 1A2 inhibitor	CYP 2C19 inhibitor	CYP 2C9 inhibitor	CYP 2D6 inhibitor	CYP 3A4 inhibitor	log Kp (cm/s)
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one	High	No	Yes	No	No	No	No	No	-7.98
Anhydrotuberosin	High	Yes	Yes	Yes	Yes	No	No	Yes	-5.34
Beta-sitosterol	Low	No	No	No	No	No	No	No	-2.2
Daidzein	High	Yes	No	Yes	No	No	Yes	Yes	-6.1
Genistein	High	No	No	Yes	No	No	Yes	Yes	-6.05
Genistin	Low	No	Yes	No	No	No	No	No	-8.33
Gluconic acid	Low	No	No	No	No	No	No	No	-9.89
Pterocarpan	High	Yes	Yes	Yes	No	No	Yes	No	-5.43
Puerarin	Low	No	No	No	No	No	No	No	-8.83
Puerarone	High	No	No	Yes	No	Yes	No	Yes	-5.94
Puerarostan	High	No	No	No	Yes	Yes	No	No	-5.23
Stigmasterol	Low	No	No	No	No	Yes	No	No	-2.74

Tuberosin	High	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-5.98
Tuberostan	High	Yes	No	Yes	Yes	Yes	No	No	-5.32

Compounds that showed GI absorption are 1,14-Dihydroxy-7,7-dimethyl-8,12,20 trioxa pentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one, Anhydrotuberosin, Daidzein, Genistein, Pterocarpan, Puerarone, Puerarostan, Tuberosin, Tuberostan and the compounds that does not depict GI absorption are Stigmasterol, Puerarin, Gluconic acid, Genistin, Beta-sitosterol. Compounds that exhibit BBB permeant Anhydrotuberosin, Daidzein, Pterocarpan, Tuberosin, Tuberostan and compounds that does not display BBB permeant are 1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one, Beta-sitosterol, Genistein, Genistin, Gluconic acid, Puerarin, Puerarone, Puerarostan, Stigmasterol.

Table 6: Drug likeness properties of the phytochemicals of *P. tuberosa*

Name of the phytocompounds	**Lipinski #violations**	**Ghose #violations**	**Veber #violations**	**Egan #violations**	**Muegge #violations**	**Bioavailability Score**
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one	0	0	0	0	0	0.56
Anhydrotuberosin	0	0	0	0	0	0.55
Beta-sitosterol	1	3	0	1	2	0.55
Daidzein	0	0	0	0	0	0.55
Genistein	0	0	0	0	0	0.55
Genistin	1	0	1	1	2	0.55
Gluconic acid	1	2	0	1	3	0.56
Pterocarpan	0	0	0	0	0	0.55
Puerarin	1	0	1	1	2	0.55
Puerarone	0	0	0	0	0	0.55
Puerarostan	0	0	0	0	0	0.55
Stigmasterol	1	3	0	1	2	0.55
Tuberosin	0	0	0	0	0	0.55
Tuberostan	0	0	0	0	0	0.55

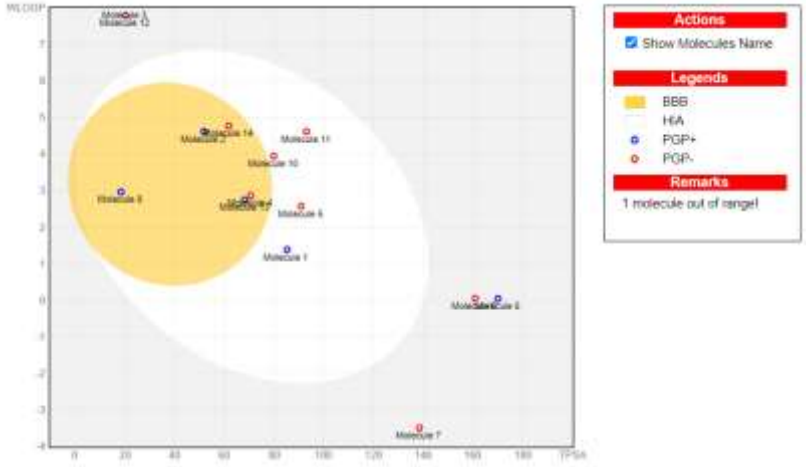
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa 2(11),3,5,9,15,18 hexaen-17-one, Daidzein, Genistein, Pterocarpan, Puerarone, Puerarostan, Tuberosin and Tuberostan these nine compounds are follow the Lipinski rule of 5, which is essential for the compound to be druggable.

Table 7: Medicinal chemistry properties of the phytochemicals of *P. tuberosa*

Name of the phytocompounds	PAINS #alerts	Brenk #alerts	Leadlikeness #violations	Synthetic Accessibility
1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19]henicosa-2(11),3,5,9,15,18-hexaen-17-one	0	0	1	4.82
Anhydrotuberosin	0	0	1	3.83
Beta-sitosterol	0	1	2	6.3
Daidzein	0	0	0	2.79
Genistein	0	0	0	2.87
Genistin	0	0	1	5.12
Gluconic acid	0	0	1	3.33
Pterocarpan	0	0	1	3.29
Puerarin	0	0	1	4.98
Puerarone	0	0	0	3.71
Puerarostan	0	2	2	3.66
Stigmasterol	0	1	2	6.21
Tuberosin	0	0	0	4.31
Tuberostan	0	1	1	3.77

All of these compounds don't show any PAINS alerts.

Figure 1: BOILED-Egg representation of the phytochemicals found in *P. tuberosa*



DISCUSSION

Ayurveda, one of the world's oldest medical systems, utilized natural sources with no known adverse effects for discovering medicinally useful and efficient chemicals obtained from botanicals for drug development. Today, treatment with herbs is used extensively in developed as well as developing nations (Ekor, 2014, Thorat and Mishra, 2016). The characteristics of these chemicals can be easily obtained using numerous resources and websites, such as Swiss ADME (Daina et al., 2017). Reports from the World Health Organization (WHO) indicate that more than 30% of all plant species have been utilized for medicinal purposes at some point (Uniyal et al., 2006). The first phase of drug discovery is the prediction of ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) characteristics, which can be performed easily using computer-based drug design (Lombardo et al., 2003). In silico compound profiling delivers significant advantages over traditional approaches in terms of time and expense. While wet screen examination of chemical characteristics is tedious and costly, ADMET screening may evaluate over 20,000 compounds in one minute (Hodgson, 2001). This fast screening capability helps to speed the drug discovery process and identify feasible medication candidates.

In this study, we used the free online Swiss ADME software application for evaluating the ADME features of *Pueraria tuberosa* DC. Tuberosin, Daidzein, Puerarin, beta-Sitosterol, Stigmasterol, Genistin, Anhydrotuberosin, Tuberostan, Puerarone, Puerarostan, 1,14-Dihydroxy-7,7-dimethyl-8,12,20-trioxapentacyclo[11.8.0.02,11.04,9.014,19] henicosa-2(11),3,5,9,15,18-hexaen-17-one, Gluconic acid, and Pterocarpan were identified by the software. Those phytochemicals are obtained from various parts of plants, including the root, tuber, and whole plant. Certain phytochemicals, such Tuberosin, Daidzein, and Puerarin, are found in all three plant parts. The ADME features of these phytoconstituents were thoroughly studied and summarised in relevant tables. This information is crucial to researchers and scientists, since it provides a foundation for the discovery of possible synthetic and semisynthetic drugs with a wide range of applications. The use of computational silico techniques into the drug development pipeline improves the efficiency of identifying new therapeutic compounds from sources that are natural. Researchers can accelerate the development of novel, safe, and effective herbal-based drugs by combining the best features of traditional wisdom and modern technology. This integrative strategy has significant possibilities for treating contemporary health issues and enhancing the medicinal potential of naturally occurring substances.

CONCLUSION

Computational techniques significantly accelerate the drug discovery process. By simulating and analysing millions of compounds, researchers can identify potential drug candidates more quickly and efficiently, thereby reducing the cost and resources required for experimental testing. These techniques allow scientists to explore a vast and multifaceted range of chemical space, facilitating the identification of compounds with desirable properties. Additionally, computational methods help in predicting the possible side effects and toxicity of candidate compounds. By analysing molecular structures and properties, researchers can assess the safety profile of drugs before they proceed to clinical trials. This approach enhances the efficiency of the drug development pipeline and ensures that only the most promising candidates advance to further stages, ultimately leading to the discovery of safe and effective new medications.

REFERENCES

1. AK Thorat and DN Mishra (2016). Medicinal plants for the treatment of *Mūtrakṛcchra* in the *Bṛhattrayī* and *Mādhava Cikitsā* treatises of *Āyurveda*. International Journal of Herbal Medicine. 4(4): 01-08.
2. Mishra D.N. and Thorat A.K. (2017). Antimicrobial, Phytochemical and GC-MS Analysis of *Abutilon indicum* (Linn.) Sweet Parts used as Ayurvedic Drug for Painful Urination as Per *Mādhav Cikitsā*. 10(7): 723-734.
3. R.P. Vivek-Ananth, Karthikeyan Mohanraj, Ajaya Kumar Sahoo, and Areejit Samal (2023), IMPPAT 2.0: An Enhanced and Expanded Phytochemical Atlas of Indian Medicinal Plants. American Chemical Society. 8: 8827 – 8845. https://doi.org/10.1021/acsomega.3c00156
4. Lemessa Etana Bultum, Gemechu Bekele Tolossa, Gwangmin Kim, Ohhyeon Kwon & Doheon Lee, (2022). In silico activity and ADMET profiling of phytochemicals from Ethiopian indigenous aloes using pharmacophore models. Sci Rep. 12: 22221. DOI-https://doi.org/10.1038/s41598-022-26446-x
5. Amal K Maji 1, Subrata Pandit, Pratim Banerji, Debdulal Banerjee, (2014). Pueraria tuberosa: a review on its phytochemical and therapeutic potential. Natural Product Research, 28(23):2111-27. doi: 10.1080/14786419.2014.928291.
6. Shengguang Wang, Shiming Zhang, Shaoping Wang, Peng Gao, Long Dai, (2020). A comprehensive review on Pueraria: Insights on its chemistry and medicinal value. Biomedicine & Pharmacotherapy, 131: 110734. DOI- https://doi.org/10.1016/j.biopha.2020.110734
7. Bharti R, Chopra BS, Raut S and Khatri N (2021) Pueraria tuberosa: A Review on Traditional Uses, Pharmacology, and Phytochemistry. Front. Pharmacol. 11:582506. doi: 10.3389/fphar.2020.582506
8. Kirtikar, K.R. and Basu, B.D. (1935) Indian Medicinal Plants, Vol. II. Lalit Mohan Publication, Allahabad, 1347-1348.
9. V. Sadguna, K. Sarikha, T. Raj Komuraiah and Md. Mustafa, (2015). Anti-microbial Activity of Pueraria tuberosa DC, an Economically and Medicinally Important Plant. Int.J.Curr.Microbiol.App.Sci 4(5):152-159.
10. Anonym, (1978). Ayurvedic FormularyofIndia. Government of India, Ministry of Healthand Family Planning, Department of Health, New Delhi.
11. Jeon G.C., Park M.S.,Yoon D.Y., Shin C.H., Sin H.S., Um S.J. 2005. Antitumoractivity of spinasterol isolated from Puerariaroots. Exp. Mol. Med., 37: 111120.
12. A. Daina, O. Michielin, V. Zoete. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci. Rep.; 7:42717. doi: 10.1038/srep42717.
13. Fan, J., & De Lannoy, I. A. M. (2014). Pharmacokinetics. Biochemical Pharmacology, 87(1), 93–120. https://doi.org/10.1016/j.bcp.2013.09.007
14. Lipinski, C. A. (2000). Drug-like properties and the causes of poor solubility and poor permeability. Journal of Pharmacological and Toxicological Methods, 44(1): 235–249. https://doi.org/10.1016/S1056-8719(00)00107-6
15. Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. 46: 3–26.
16. Tsopelas, F., Giaginis, C., & Tsantili-kakoulidou, A. (2017). drug discovery Ac ce pt t. Expert Opinion on Drug Discovery, 0(0). https://doi.org/10.1080/17460441.2017.1344210

17. Delaney, J. S. (2004). ESOL : Estimating Aqueous Solubility Directly from Molecular Structure. 1000–1005.
18. Cheng, T., Zhao, Y., Li, X., Lin, F., Xu, Y., Zhang, X., Li, Y., & Wang, R. (2007). Computation of Octanol - Water Partition Coefficients by Guiding an Additive Model with Knowledge. 2140–2148.
19. Boyle, N. M. O., Banck, M., James, C. A., Morley, C., Vandermeersch, T., & Hutchison, G. R. (2011). Open Babel : An open chemical toolbox. 1–14.
20. Ertl, P., Rohde, B., & Selzer, P. (2000). Fast Calculation of Molecular Polar Surface Area as a Sum of Fragment-Based Contributions and Its Application to the Prediction of Drug Transport Properties. 3714–3717.
21. Arnott, J. A., & Planey, S. L. (2012). The influence of lipophilicity in drug discovery and design. 909–921.
22. Testa, B., Crivori, P., Reist, M., & Carrupt, P. (2000). The influence of lipophilicity on the pharmacokinetic behavior of drugs : Concepts and examples. 179–211.
23. Mannhold, R., Poda, G. I., Ostermann, C., & Tetko, I. V. (2009). Calculation of Molecular Lipophilicity : State-of-the-Art and Comparison of Log P Methods on More Than 96 , 000 Compounds. Journal of Pharmaceutical Sciences, 98(3), 861–893. https://doi.org/10.1002/jps.21494
24. Wildman, S. A., & Crippen, G. M. (1999). Prediction of Physicochemical Parameters by Atomic Contributions. 868–873.
25. Moriguchi I, Shuichi H, Liu Q, Nakagome I, Matsushita Y. (1992). Simple Method of Calculating Octanol/Water Partition Coefficient. Chem. Pharm. Bull. 40:127-130.
26. Ottaviani, G., Gosling, D. J., Patissier, C., Rodde, S., Zhou, L., & Faller, B. (2010). European Journal of Pharmaceutical Sciences What is modulating solubility in simulated intestinal fluids? European Journal of Pharmaceutical Sciences, 41(3–4): 452–457. https://doi.org/10.1016/j.ejps.2010.07.012
27. Lachman LH, Lieberman, Kanig JL. (1986). The Theory and Practice of Industrial Pharmacy, Lea & Febiger, 3rd edition.
28. Yalkowsky, S. H., & Valvani, S. C. (1980). Solubility and Partitioning I : Solubility of Nonelectrolytes in Water. 69(8).
29. Daina, A., & Zoete, V. (2016). A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. 1117–1121. https://doi.org/10.1002/cmdc.201600182
30. Di, L., Fish, P. V, & Mano, T. (2011). Bridging solubility between drug discovery and development. 00(00), 1–10. https://doi.org/10.1016/j.drudis.2011.11.007
31. Montanari, F., & Ecker, G. F. (2015). Prediction of drug–ABC-transporter interaction — recent advances and future challenges. Advanced Drug Delivery Reviews https://doi.org/10.1016/j.addr.2015.03.001
32. Kirchmair, J., Göller, A. H., Lang, D., Kunze, J., Testa, B., Wilson, I. D., Glen, R. C., & Schneider, G. (2015). Predicting drug metabolism: experiment and/or computation? Nature Publishing Group, 14(6): 387–404. https://doi.org/10.1038/nrd4581
33. Mitchell, J. B. O. (2014). Machine learning methods in chemoinformatics. https://doi.org/10.1002/wcms.1183
34. Lipinski, C. A. (2000). Drug-like properties and the causes of poor solubility and poor permeability. Journal of Pharmacological and Toxicological Methods, 44(1): 235–249. https://doi.org/10.1016/S1056-8719(00)00107-6

35. Veber, D. F., Johnson, S. R., Cheng, H., Smith, B. R., Ward, K. W., & Kopple, K. D. (2002). Molecular Properties That Influence the Oral Bioavailability of Drug Candidates. 2615–2623. https://doi.org/10.1021/jm020017n
36. Martin, Y. C., & Park, A. (2005). A Bioavailability Score. 3164–3170. https://doi.org/10.1021/jm0492002
37. Baell, J. B., & Holloway, G. A. (2010). New Substructure Filters for Removal of Pan Assay Interference Compounds (PAINS) from Screening Libraries and for Their Exclusion in Bioassays. 2719–2740. https://doi.org/10.1021/jm901137j
38. Brenk, R., Schipani, A., James, D., Krasowski, A., Gilbert, I. H., Frearson, J., & Graham, P. (2008). Lessons Learnt from Assembling Screening Libraries for Drug Discovery for Neglected Diseases. 435–444. https://doi.org/10.1002/cmdc.200700139
39. Cheng, F., Yu, Y., Zhou, Y., Shen, Z., Xiao, W., Liu, G., Li, W., Lee, P. W., & Tang, Y. (2011). Insights into molecular basis of cytochrome P450 inhibitory promiscuity of compounds. *Journal of Chemical Information and Modeling*, 51(10): 2482–2495. https://doi.org/10.1021/ci200317s
40. Doogue, M. P., & Polasek, T. M. (2013). The ABCD of clinical pharmacokinetics. *Therapeutic Advances in Drug Safety*, *4*(1), 5–7. https://doi.org/10.1177/2042098612469335
41. Hou, T., & Wang, J. (2008). *Structure – ADME relationship : still a long way to go ?* 759–770.
42. Jensen, K., Panagiotou, G., & Kouskoumvekaki, I. (2014). Integrated Text Mining and Chemoinformatics Analysis Associates Diet to Health Benefit at Molecular Level. *PLoS Computational Biology*, 10(1). https://doi.org/10.1371/journal.pcbi.1003432
43. Mohanraj, K., Karthikeyan, B. S., Vivek-Ananth, R. P., Chand, R. P. B., Aparna, S. R., Mangalapandi, P., & Samal, A. (2018). IMPPAT: A curated database of Indian Medicinal Plants, Phytochemistry and Therapeutics. *Scientific Reports*, 8(1): 1–17. https://doi.org/10.1038/s41598-018-22631-z
44. Shen, J., Cheng, F., Xu, Y., Li, W., & Tang, Y. (2010). Estimation of ADME properties with substructure pattern recognition. *Journal of Chemical Information and Modeling*, *50*(6): 1034–1041. https://doi.org/10.1021/ci100104j
45. Wang, Z., Chen, Y., Liang, H., Bender, A., Glen, R. C., & Yan, A. (2011). P-glycoprotein substrate models using support vector machines based on a comprehensive data set. *Journal of Chemical Information and Modeling*, 51(6): 1447–1456. https://doi.org/10.1021/ci2001583
46. Roshnia, J., Vaishali, R., Ganesha, K. S., Dharani, N., Alzahrani, K. J., Banjer, H. J., Alghamdi, A. H., Theyab, A., Ahmed, S. S. J., & Patil, S. (2022). Multi-target potential of Indian phytochemicals against SARS-CoV-2: A docking, molecular dynamics and MM-GBSA approach extended to Omicron B.1.1.529. Journal of Infection and Public Health, 15(6): 662–669.
47. Moriguchi I, Shuichi H, Liu Q, Nakagome I, Matsushita Y. (1992). Simple Method of Calculating Octanol/Water Partition Coefficient. Chem. Pharm. Bull. 40:127-130.
48. Mahanthesh, M. T., Ranjith, D., Yaligar, R., Jyothi, R., Narappa, G., & Ravi, M. V. (2020). Swiss ADME prediction of phytochemicals present in Butea monosperma (Lam.) Taub. Journal of Pharmacognosy and Phytochemistry, 9(3): 1799-1809.
49. Cheng, F., Yu, Y., Zhou, Y., Shen, Z., Xiao, W., Liu, G., Li, W., Lee, P. W., & Tang, Y. (2011). Insights into molecular basis of cytochrome P450 inhibitory promiscuity of compounds. *Journal of Chemical Information and Modeling*, *51*(10), 2482–2495. https://doi.org/10.1021/ci200317s

50. Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, *7*(January), 1–13. https://doi.org/10.1038/srep42717
51. Dimasi, J. A., Hansen, R. W., & Grabowski, H. G. (2003). *The price of innovation : new estimates of drug development costs*. *22*, 151–185. https://doi.org/10.1016/S0167-6296(02)00126-1
52. Doogue, M. P., & Polasek, T. M. (2013). The ABCD of clinical pharmacokinetics. *Therapeutic Advances in Drug Safety*, *4*(1), 5–7. https://doi.org/10.1177/2042098612469335
53. Ekor, M. (2014). *The growing use of herbal medicines : issues relating to adverse reactions and challenges in monitoring safety*. *4*(January), 1–10. https://doi.org/10.3389/fphar.2013.00177
54. Hodgson, J. (2001). *F EATURE ADMET — turning chemicals into drugs Rapidly resolving the pharmacokinetic and toxicological properties of drug candidates remains a key challenge for drug developers* .
55. Hou, T., & Wang, J. (2008). *Structure – ADME relationship : still a long way to go ?* 759–770.
56. Jensen, K., Panagiotou, G., & Kouskoumvekaki, I. (2014). Integrated Text Mining and Chemoinformatics Analysis Associates Diet to Health Benefit at Molecular Level. *PLoS Computational Biology*, *10*(1). https://doi.org/10.1371/journal.pcbi.1003432
57. Lombardo, F., Gifford, E., & Shalaeva, M. Y. (2003). *In Silico ADME Prediction : Data , Models , Facts and Myths*. 861–875.
58. Mohanraj, K., Karthikeyan, B. S., Vivek-Ananth, R. P., Chand, R. P. B., Aparna, S. R., Mangalapandi, P., & Samal, A. (2018). IMPPAT: A curated database of Indian Medicinal Plants, Phytochemistry and Therapeutics. *Scientific Reports*, *8*(1), 1–17. https://doi.org/10.1038/s41598-018-22631-z
59. Shen, J., Cheng, F., Xu, Y., Li, W., & Tang, Y. (2010). Estimation of ADME properties with substructure pattern recognition. *Journal of Chemical Information and Modeling*, *50*(6), 1034–1041. https://doi.org/10.1021/ci100104j
60. Uniyal, S. K., Singh, K. N., Jamwal, P., & Lal, B. (2006). Traditional use of medicinal plants among the tribal communities of Chhota Bhangal, Western Himalaya. *Journal of Ethnobiology and Ethnomedicine*, *2*, 1–8. https://doi.org/10.1186/1746-4269-2-14
61. Wang, Z., Chen, Y., Liang, H., Bender, A., Glen, R. C., & Yan, A. (2011). P-glycoprotein substrate models using support vector machines based on a comprehensive data set. *Journal of Chemical Information and Modeling*, *51*(6), 1447–1456. https://doi.org/10.1021/ci2001583