Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
Impact Factor (RJIF): 6.35
www.phytojournal.com
JPP 2025; 14(4): 655-664
Received: 08-05-2025
Accepted: 12-06-2025

Anusha Vanjarapu,
Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Affiliated to Osmania University, Tarnaka, Hyderabad, Telangana, India

Dr. Neelima Kudumula
Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Affiliated to Osmania University, Tarnaka, Hyderabad, Telangana, India

Corresponding Author:
Dr. Neelima Kudumula
Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Affiliated to Osmania University, Tarnaka, Hyderabad, Telangana, India

Pharmacokinetic screening of the phytochemicals present in *Vitex negundo* using Swiss ADME

Anusha Vanjarapu and Neelima Kudumula

DOI: https://www.doi.org/10.22271/phyto.2025.v14.i4i.15525

Abstract
Background: It is a significant medical plant, of the Indian subcontinent and belongs to the family Lamiaceae which still requires exploring its physicochemical and, pharmacokinetic screening. Widely used in traditional medicine, Jaundice, wounds, body aches, toothaches, asthma, eye discomfort, and headaches are the main conditions that *Vitex negundo* is used to report. After numerous studies and researches conceal that it poses high pharmacological activities and as computational mechanics, i.e., in-silico and pharmacokinetic screening of phytoconstituents can increase among the possibilities, active compounds that show how medicinal plants work. Its common name is "Sarvaroganivarini". It has been recognized to feature some pharmacological actions such as Analgesic, Anti-inflammatory, Anti-Pyretic, Nephroprotective, Anti-Venom snake, and anti-HIV activities.
Methods: The free-to-use software tool Swiss ADME, was used in the current research to evaluate the ADME properties for pharmacological and Pharmacognostic profiling of *Vitex negundo*.
Results: Though the plant contains around 120 phytoconstituents, through the use of the software, phytoconstituents only from the root part of the plant were evaluated for their physicochemical and pharmacokinetic features. Negundin B, one of the examined constituents, exhibits favorable qualities and may be exploited in future research. The values can also be used as monographs by scientists and researchers to create potential semi- and synthetic medications for a variety of uses.
Conclusion: Researchers can further investigate *in vitro* and *in vivo* studies using the findings from these investigations which reveal the pharmaceutical benefits of the traditional medicinal plant.

Keywords: Swiss ADME, *Vitex negundo*, phytoconstituents, Insilco, Sarvaroganivarini.

1. Introduction
The use of herbal remedies derived from medicinal plants was well understood by prehistoric people. Uniyal *et al.* states a famous quote of the Bengalis which is "A man cannot die of disease in an area where *Vitex negundo* is found" [1]. *Vitex negundo* in Indian traditional systems is referred to as "Sarvaroganivarini"[2] which translates as a cure for all diseases [3].
Vitex negundo commonly called Nergundi, belongs to family Lamiaceae and was originally called as 'chaste tree' and is a large aromatic shrub woody in texture thrives mainly in the Indian sub-constituent. It is an herbal medicine that does not merely cure a specific disease but aims to return the body to its original state of health [4].
Based on phylogenetic studies of DNA sequences, Vitex and other genera were moved from the Verbenaceae to the Lamiaceae family in the 1990s. Linnaeus created the genus in 1753 and the family Verbenaceae with four varieties [5].
A common plant used in folk medicine is *Vitex negundo*, which is used to treat jaundice, wounds, body aches, toothaches, asthma, migraines, eye pain, fever, colds, malaria, and as an antidote for snake bites. Its chemical makeup is being increasingly ascribed to these effects.
More than 80% of people around the world who live in less developed nations rely on traditional medicine and people depend on herbs for basic needs including food, housing, clothing, flavor, and medicine. *Vitex negundo* [6] is one of the medicinal plants recommended by Ayurveda and conventional medicine for the treatment of many illnesses.
Traditional herbal medicines and Ayurveda acceptance have increased over a period of time as they have minimal side effects and safe therapeutic effects, so people these days are more relieved on drug resources of plant origin [7]. *Vitex negundo* globally is domesticated in America, Europe, Indo-Malaysia, and West- Indies, and most importantly in Asia. India is spread throughout the outer Himalayas and ascends to an altitude of nearly 1500 meters.
All parts of the plant *Vitex negundo* including roots and fruits, consists of plenty of secondary metabolites that bestow the plant with a profusion of medicinal advantages.

If an efficient method for predicting a large number of chemical constituents has been developed, we can then base our evaluation of the chemical properties of medicinal plants on this method.

The study of how herbal medicines are Absorbed, Distributed, Metabolized, and Excreted (ADME) has recently attracted more attention. The ADMET properties of compounds are important at every stage of the drug research and development process. Modern drug development incorporates pharmacokinetic research. Several pieces of literature show that there are few studies on the ADME effects of herbal remedies in people.

A medicine must have enough concentrated molecules at the target site in the body for it to be effective. One of the primary justifications for stopping drug development is the neglect of pharmacokinetics aspects.

So, utilizing Swiss ADME, a free piece of online software, our primary task is to concentrate on assessing the physicochemical and pharmacokinetic factors of the phytochemical elements of *Vitex negundo*.

2. Materials and Methods

Swiss ADME (www.swissadme.ch)

The Swiss Institute of Bioinformatics' Swiss ADME program had been accessed using a server of web to view the Swiss ADME submission page on Google. The purpose was to determine the ADME behavior of phytoconstituents found *in Vitex* negundo on an individual basis. Results for each molecule were present in both a graphical and an Excel spreadsheet. The list was created to include one input per molecule, based on calculations made using Windows 10Pro and 20H2, as specified by (Egan *et al*., 200) using the SMILES notation [8].

Bioavailability Radar

The first section displayed the conventional SMILES-equipped two-dimensional (2D) chemical structures. It enables an initial look at how drug-like the compounds are by taking into account six physicochemical properties SIZE, Lipophilicity, Polarity, Insolubility, Instauration, and Flexibility.

Size: MW ranging from 150 to 500 g/mol, XLOGP3 between -0.7 and +0.5 for lipophilicity Polarity: TPSA between the 20 & 1300, with maximum logS of 6. No more than 9 flexible bonds and a fraction of at least 0.25 carbons in the sp3 hybridization are required for saturation [9, 10].

Lipophilicity

Lipophilicity is a crucial factor in the development of new drugs (Leeson and Springthorpe, 2007) [11], as it completes the physicochemical property in medicinal chemistry that is the most successful and informative (Testa *et al*., 2000) [12]. It is empirically proved as a distribution coefficient or as a partition feature (Log P) (Log D). The curve P illustrates the unionized solute partition equilibrium between the water & an organic solvent which is immiscible. The higher the values of LogP, the more lipophilicity (Planey & Arnott, 2012) [13].

Swiss ADME offers 5 publicly accessible models, namely SILICOS-IT, XLOGP3, MLOGP, iLOGP, and WLOGP to analyze the lipophilicity character in molecules. XLOGP3, an atomistical method with knowledge-based library and correction variables (Cheng, 2007) [14], MLOGP, a topological approach archetype proposed on a linear relationship having 13 molecular descriptors applied [15]; WLOGP, a completely atomistic application of method based on a fragmentary system (Moriguchi *et al*., 1992 & Moriguchi *et al*., 1994) [16, 17]. The generalized-born along with the solvent accessible surface area (GB/SB) model's computation of the solvation-free energies in n-octanol& water serves as the foundation for the physics-based technique known as iLOGP; An arithmetic average of the values predicted through 5 suggested techniques is called consensus logP o/w.

Water Solubility

Fundamentally, the substance solubility relied on various factors such as the solvent used, pressure &temperature. The saturation point, where the solute concentration in the solution does not rise with the addition of more solute, is used to gauge the range of solubility. (Lachman *et al*., 1986) [18]. It is considered to be very soluble while a medication's greatest dosage strength dissolves in 250 ml of aqueous medium having a pH scale of 1-7.5 or lower. Swiss ADME employs 2 topological approaches to calculate the solubility of water; the 1st is utilizes the model of ESOL (Solubility class: Insoluble-10 badly-6, moderately-4 soluble-2 exceedingly 0 highly soluble; Log S Scale.

From the basic universal solubility equation, both are different (Yalkowsky and Valvani, 1980) [19]. Despite avoiding the melting point parameter, SILICOS-IT developed the 3rd predictor of Swiss ADME, where the linear coefficient is connected by molecular weight (R_2=0.75). The linear relationship between the predicted and experimental values is strong and reliable, with a linear correlation coefficient of 0.69 and 0.81, respectively. (Solubility class: Log S Scale: Insoluble-10 badly-6, Moderately-4, Soluble-2very 0 strongly). All projected numbers are represented by the solubility in water's decimal logarithm. (Log S).

The Swiss ADME provides additional information on solubility including qualitative solubility classes, as well as solubility in mol/l and mg/ml.

Pharmacokinetics

The distinction can be seen on a map of the 2 computed descriptors, ALOGP against PSA, in an area that has favorable gastrointestinal (GI) absorption characteristics. The Egan Egg model generates an approach to forecast the GI absorption passively that is useful for drug development &discovery. This method is quick, spontaneous, and effective in its imitation, but it is also raucous. It is used to evaluate the power of the model's ability to forecast brain access by passive diffusion as well as passive absorption by the gastrointestinal tract. (Brito-Sanchez *et al*., 2015 and Di and *et al*. 2012) [21, 20]. The white region of molecules is the space that allows for the largest amount of absorption in the tract of GI, whereas the molecules (the yolk) yellow region is the space that allows for the greatest possibility of chemicals entering the brain. (Montannari and Ecker, 2015) [22]. Isoenzymes of Cytochrome p450 (CYP), which is one of the enzyme's five primary isoforms, are responsible for the biotransformation of more than 50-90% of medicinal substances. (CYP3A4, CYP2C9, CYP1A2, and, CYP2D6as well as CYP2C19) [21, 22, 23]. P-gp, which is broadly dispersed throughout the intestinal epithelium, is the protein that is responsible for pumping xenobiotics from the capillary endothelial cells in that region back in to the intestinal lumen and into the brain capillaries. (Ndombera *et al*., 2019 and Ogu and Maxa, 2000) [24, 25].

Swiss ADME uses SVM techniques for binary categorization of datasets comprising known inhibitors, non-inhibitors, and substrates. The outcome molecules will either yield "Yes" or

"No", depending on whether the investigated molecule "is "expected to function as a substrate for both P-gp and CYP. Using 1033 molecules as the training set and 415 molecules as the test set, the 10-fold CV: ACC=0.72/AUC=0.77, External: ACC=0.88/AUC=0.94 and SVM model for P-gp substrate were created and evaluated, respectively. The SVM model for Cytochrome P-450 1A2 inhibitor compounds was created on 1945 molecules (training set) and tested on 3000 molecules (test set). The test set size was 3000 molecules, and the 10-fold CV was ACC=0.83/AUC=0.90, External: ACC=0.84/AUC=0.91. In order to build the SVM model for the Cytochrome P-450 2C19 inhibitor molecule, 9272 molecules were used as the training set, and 3000 molecules were used as the test set. The external model's ACC and AUC values for the 10-fold CV were 0.80 and 0.86, respectively. The 10-fold CV: ACC=0.78/AUC=0.85, External: ACC=0.71/AUC=0.81 was used to develop the SVM model for the Cytochrome P-450 2C9 inhibitor compound. The training set for the SVM model for the Cytochrome P-450 2D6 inhibitor" compound consisted of 3664 molecules, and the test set consisted of 1068 molecules. External: ACC=0.81 and AUC=0.87; CV=0.79 and AUC=0.85. The Cytochrome P-450 3A4 inhibitor chemical's model of SVM has been built on 7518 molecules (the training set) and evaluated on 2579 molecules (the test set, 10-fold).

Drug likeness

Swiss ADME examines chemical libraries and removes molecules from the collection that have characteristics that are incompatible with a desirable pharmacokinetic profile. This is done with the goal of enhancing the condition of Swiss ADME's exclusive chemical collections. It does this by using five different rule-based filters from major Pharma companies. The primary pioneer rule of 5 for categorizing small molecules on the basis of their physiochemical property characteristics is the Lipinski filter (Pfizer). Molecular Weight (MW) less than 500, N or O 10, MLOGP greater than 4015, and NH or OH five are a few of them.

Lipinski considers all nitrogen and oxygen to be H-Bond acceptors, while he considers all nitrogen and oxygen that contain at least one hydrogen to be H-Bond donors. This interpretation is based on his definition of the term. On the basis of the physicochemical features, the existence of functional groups, and their substructures, aliphatic fluorines are described as tiny molecules by the Ghose filter (Amgen), however, alanine nitrogen is neither a donor nor an acceptor. Small molecules must contain between 20 and 70 atoms to qualify, whereas big molecules must contain between 160 and 480 Da, WlogP must be between -0.4 and 5.66, and MR must be between 40 and 130. (Ghose *et al*., 1999 and Ghose *et al*., 1998) [26, 27]. If a molecule has 12 or fewer H-bond acceptors &donors, at least 10 rotatable bonds, and a TPSA of 140 or less, the Veber filter (GSK filter) model classifies it as drug-like. Improved rotatable counts of bonds which associated with lower permeation rates, while decreased TPSA corresponds with higher penetration rates. Compounds with these characteristics would have high oral bioavailability. (Veber *et al*., 2002) [28]. The mechanisms involve in the membrane permeability of small molecules, according to Egan filter (Pharmacia filter), will have an impact on how well a medication is absorbed. If molecules possess WLOGP 5088 or TPSA 131.6, respectively, these models depict them as drugs. Because the active transport and efflux routes were accounted for in the Egan computational model for Human Passive Intestinal intake (HIA) of the Small Compounds (HIA), the model was able to accurately estimate drug intake. (Egan and colleagues, 2000). The Muegge filter is an autonomous pharmacophore pint filter that differentiates between drug-like chemicals and other compounds (also known as the Bayer filter).

These models classify molecules as drugs, for instance, if they have a molecular weight between the 200 & 600 Da, a TPSA of 150, a certain rings number, an XLOGP among -2 & 5, a certain carbon atoms number, a certain hetero atoms number, a certain rotatable bonds number, a certain number of H-bond acceptors and donors, and a certain number of rings. The Abbott bioavailability score attempts to predict whether a substance will have at least 10% oral bio-availability in rodents or measurably high permeability of Caco-2, that determines whether a substance will have F>10 and on the basis of predominate charge at the biological pH in model of rat. It aims on rapid chemical library scanning to find the best [29].

Medicinal Chemistry

This section's primary objective is to provide assistance to medicinal chemists in their continued efforts to deliver medical treatments and medications. The molecules that are referred to as PAINS, which are also known as frequent hits or promiscuous chemicals, display a strong response in assays independent of the protein targets that have been tested. It has been demonstrated that these compounds, in particular, are active in a number of different tests; hence, they are viable starting points for further exploration. In the event that such moieties are discovered in the substances that are being evaluated, the Swiss ADME will issue warnings. (2010) according to Baell and Holloway [30]. On the way to increase the potential for lead optimization, Brenk takes into account compounds that are smaller and less hydrophobic in order models rather than those that fall under "Lipinski's rule of 5". After substances with possibly mutagenic, responsive, and opposed groups, including thiol groups, sulphates, nitro, phosphates, and 2-halopyridineswere excluded, this occurred. Brenk models limit the C log P/ClogD to values between 0 and 4, as well as the number of heavy atoms among 10 & 27.

Furthermore, only moderately complex compounds, those with no more than five ring systems, no more than two fused rings, and no more than eight rotatable bonds are believed to have therapeutic effects. (2008) (Brenk *et al*). Lead likeness is created to give lead an extremely high affinity with the help of HTS (High Throughput Screening), which enables the new interactions exploitation that will most likely be molecules. Molecules having molecular weights among 100 & 350 Da as well as Clog P values among 1 & 3.0 have been subjected to lead optimization with the help of a rule-based technique. These molecules are often considered to be superior to drug-like compounds and, as a result, lead-like. (Teague *et al*., 1999; Hann and Keseru, 2012) [31, 32].

Nowadays, a great deal of computer-based drug designing is used to anticipate the ADMET properties of the medications, which results in early-stage drug development. The reasoning for these *in silico* methods is based on the substantially lower time and cost requirements compared to conventional ADMET profiling. For instance, screening 20,000 or more molecules in an *in silico* model just takes a minute, whereas performing the same task in a "wet" laboratory might take 20 weeks. As a result, of the accumulated ADME data that was made accessible with software in the year 1990, several pharmaceutical companies have been now implementing computational models, in several instances, are replacing the

"wet" screens. This is happening because the data was made available in the late 1990s. Because of this shift in conceptualization, a number of theoretical methodologies for the prediction of ADMET values have been developed.

3. Results

In (Table 2) The bioavailability radar results show that Negundin B, (+)-Lyoniresinol, (+)-Diasyringareinol, 6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde shows Orally bioavailable, Whereas (+)-Lyoniresinol-3α-O-β-D-glucoside is showing Too polar and flexibility nature thus it's not orally bioavailable, Vitrofolal F, Vitrofolal E, and Negundin A are unsaturation are orally not bioavailable.

In **(**Figure 1), According to the study, phytochemicals have low gastrointestinal absorption, with almost 80% of the molecules passing through the blood-brain barrier (BBB), and they are all non-P-pg substrates. Vitrofolal E can pass through the BBB and is removed from the brain by the P-glycoprotein. Neither is (+)-Lyoniresinol-3-O-D-glucoside absorbed or entered.

Negundin A, Negundin B, 6-hydroxy-4[4-hydroxy-3-methoxy-phenyl], (+)-Diasyringareinol, (+)-Lyoniresinol, (+)-Lyoniresinol-3-O-D-glucoside, and Vitrofolal FGI or digestive absorption of -3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde.

In (Table 5) (+)-Lyoniresinol-3α-O-β-D-glucoside is having low GI absorption which is not a suitable compound.

Vitrofolal E is having BBB penetration which shows it acts as good blood-brain barrier.

In (Table 6) (+)-Lyoniresinol-3α-O-β-D-glucoside has 3 violations which does not obey Ghose filter, Lipinski rule of 5, Egan rule, Veber rule, Muegge rule, bioavailability score also low with 0.9917 score.

In **(**Table 7) All the phytoconstituents show 0 alerts in PAINS alerts.

Except for Negundin B, (+)-Lyoniresinol, (+)-Lyoniresinol-3α-O-β-D-glucoside shows 0 alerts in Break alerts.

Vitrofolal E shows Lead likeness.

4. Discussion

CADD has significantly changed the development and research paths in medication candidate discovery as a result of the quick expansion in chemical and biological knowledge. The computational tools utilization in the discovery of a drug procedure is frequently praised in terms of execution, financing, and timing. The software was used to collect phytoconstituents from plants, analyse them for their physicochemical and pharmacokinetic characteristics, and show the results in reliable tables and figures. One of the components under investigation, Negundin B, demonstrates positive traits that could be used in future studies. The values could be utilized by scientists and researchers as monographs to develop potential semi- and synthetic drugs for a range of uses. To assess the ADME properties of *Vitex negundo i*n the current research, we utilized the Swiss ADME online software tool, which users can use freely.

5. Conclusion

One of the components under investigation, Negundin B, demonstrates positive traits that could be used in future studies. The values could be utilized by scientists and researchers as monographs to develop potential semi- and synthetic drugs for a range of uses.

6. Acknowledgment

The officials at Sarojini Naidu Vanita Pharmacy Mahavidyalaya in Hyderabad are very much appreciated by the authors of this study for providing the essential facilities so that this research project could be carried out.

7. Conflict of Interest

The authors state that there has been no conflict of interest.

Abbreviations

ADMET: Absorption, Distribution, Metabolism, Excretion; ADMET: Absorption, Distribution, Metabolism, Excretion, toxicity; Pains: Pan Assay Interference Compounds; SMILES: Simplified molecular-input line-entry system; CNS: Central nervous system; WlogP: Water Partition Coefficient; P-gp: P-glycoprotein; TPSA: Topological Polar Surface; BBB: Blood Brain Barrier; GI: Gastrointestinal.

Ethics approval and consent to participate

Not Applicable.

Patient consent

Not Applicable

Summary

Traditional Indian medicines play an important role in several ailments. Vitex negundo is a medicinal plant utilized for the treatment of jaundice, wounds, body aches, toothaches, asthma, eye discomfort, and migraines. etc. *In silico* screening along with a pharmacokinetic screening of phytoconstituents could increase among the possibilities, of active compounds that show how medicinal plants work. In the current investigation, we evaluated the ADME properties of Vitex negundo using the Swiss ADME online software program, that is open-source and free for anybody to access. This allowed us to perform both pharmacological and Pharmacognostic profiling. Researchers and scientists can also utilize the values as monographs to generate prospective semi and synthetic drugs for application ranges.

Funding

There was no funding for this manuscript.

Tables and Figures

Table 1: General characteristics of Phyto-constituents of *Vitex negundo*.

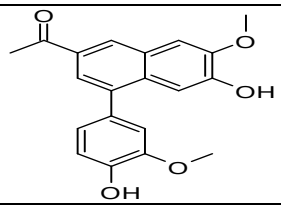
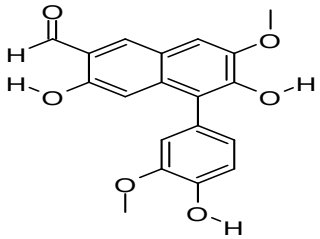
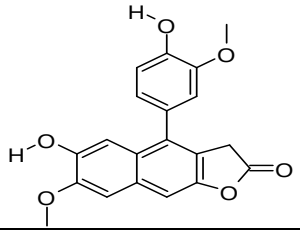
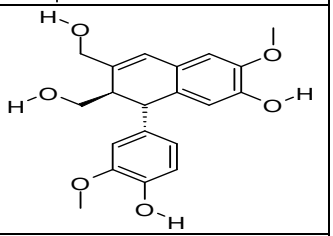
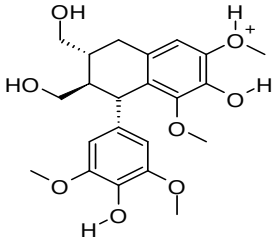
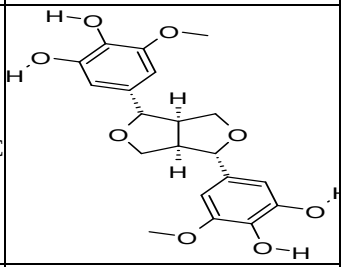
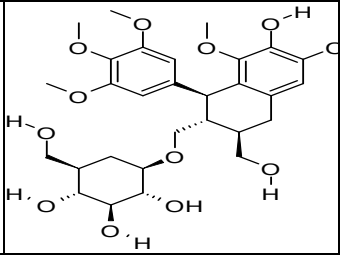
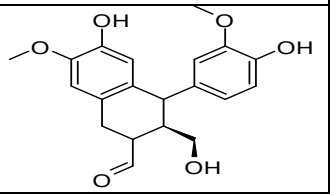
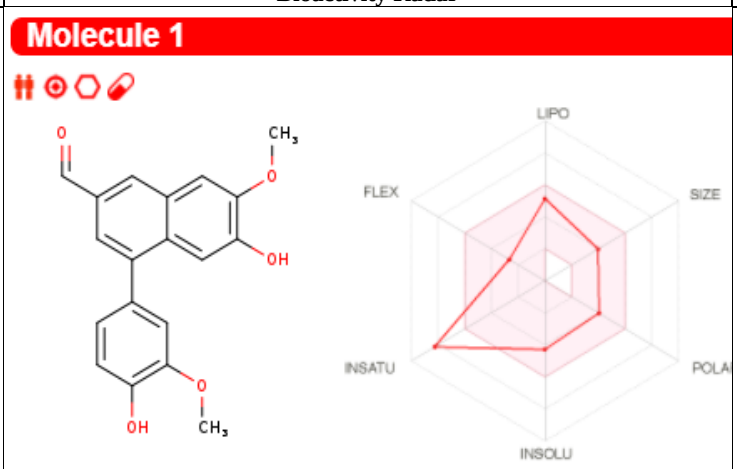
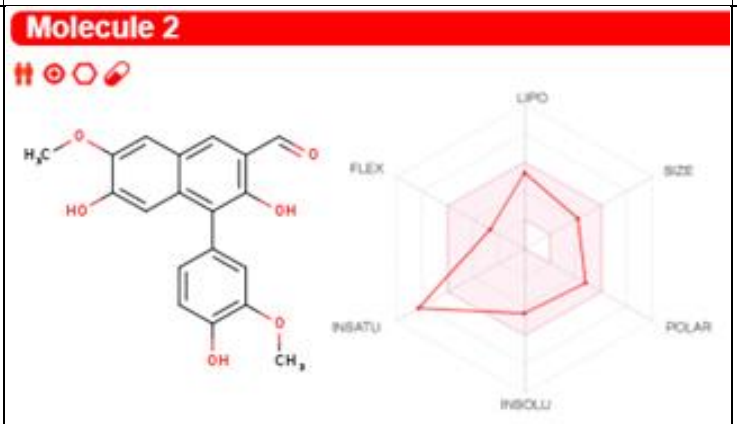
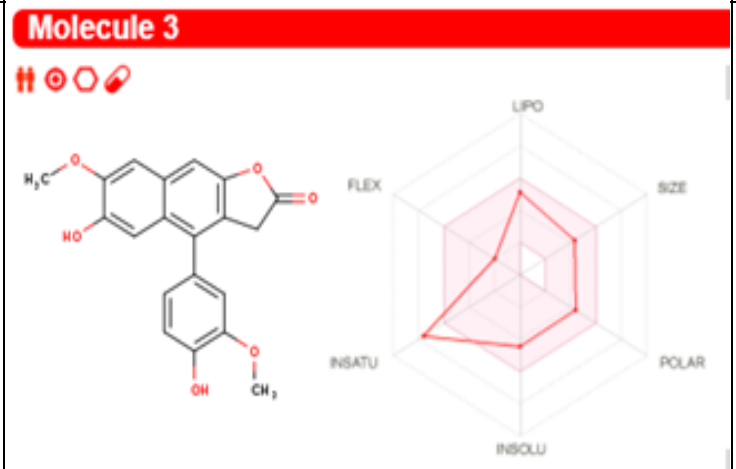
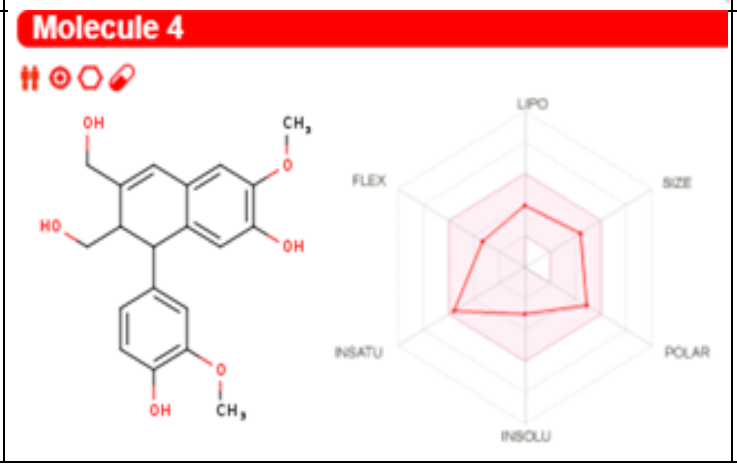
Phyto-Constituent	Molecular weight	Molecular formula	Smile Notation	Structures
Vitrofolal E	324.1	$C_{19}H_{16}O_5$	COC1=C(C=CC(=C1)C2=CC(=CC3=CC(=C(C=C32)O)OC)C=O)O	
Vitrofolal F	340.09	$C_{19}H_{16}O_6$	COC1=CC2=CC(=C(C(=C2C=C1O)C3=CC(=C(C=C3)O)OC)O)C=O	
Negundin A	352.09	$C_{20}H_{16}O_6$	COC1=CC2=CC3=C(CC(=O)O3)C(=C2C=C1O)C4=CC(=C(C=C4)O)OC	
Negundin B	358.14	$C_{20}H_{22}O_6$	COC1=C(C=CC(=C1)C2C(C(=CC3=CC(=C(C=C23)O)OC)CO)CO)O	
(+)-Lyoniresinol	420.18	$C_{22}H_{28}O_8$	COC1=CC(=CC(=C1O)OC)C2C(C(CC3=CC(=C(C(=C23)OC)O)OC)CO)CO	
(+)-Lyoniresinol-3α-O-β-D-glucoside	582.23	$C_{28}H_{38}O_{13}$	COC1=CC(=CC(=C1O)OC)C2C(C(CC3=CC(=C(C(=C23)OC)O)OC)CO)COC4C(C(C(C(O4)CO)O)O)O	
(+)-Diasyringareinol	418.16	$C_{22}H_{26}O_8$	COC1=CC(=CC(=C1O)OC)C2C3COC(C3CO2)C4=CC(=C(C(=C4)OC)O)OC	
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde	358.14	$C_{20}H_{22}O_6$	COc3cc2CC(C=O)[C@H](CO)C(c1ccc(O)c(OC)c1)c2cc3O	

Table 2: Bioavailability radar of Phyto-constituents.

Phyto-Constituents	Bioactivity Radar	Results
Vitrofolal E		In this example, the compound is predicted to be unsaturated compound, so it is Orally not bioavailable.
Vitrofolal F		In this example, the compound is predicted to be unsaturated compound, so it is Orally not bioavailable
Negundin A		In this example, the compound is predicted to be unsaturated compound, so it is Orally not bioavailable
Negundin B		In this example, the compound is predicted to be Orally bioavailable

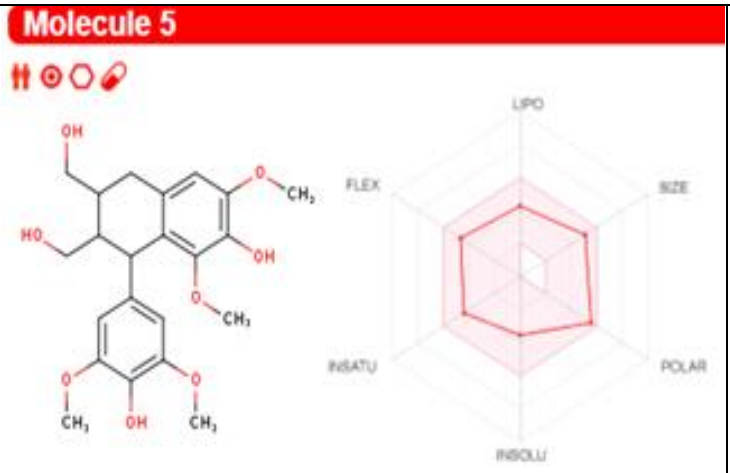
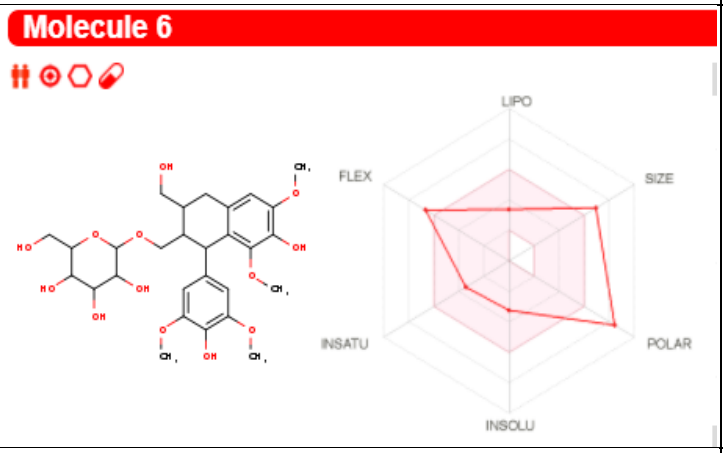
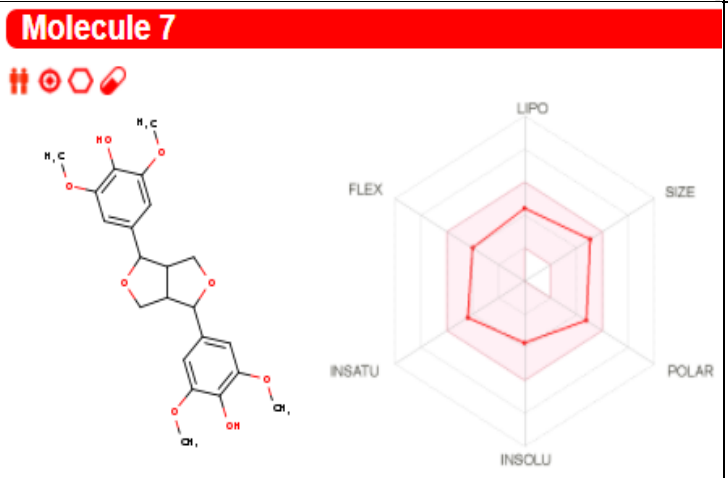
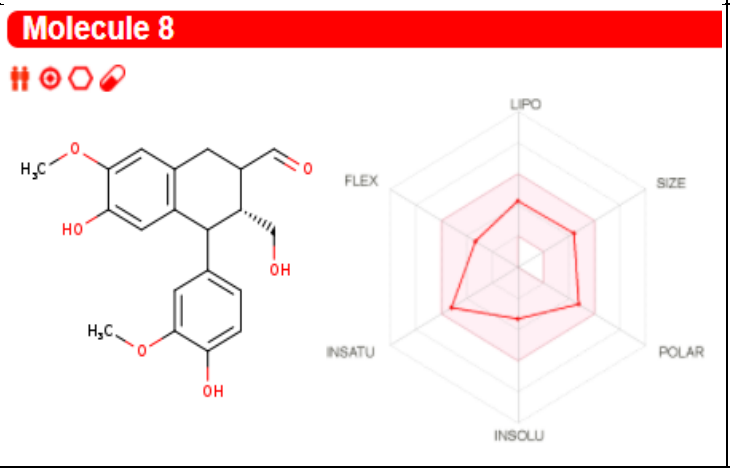
(+)-Lyoniresinol		In this example, the compound is predicted to be Orally bioavailable
(+)-Lyoniresinol-3α-O-β-D-glucoside		In this example, the compound is predicted to be flexible and too polar so it is Orally not bioavailable
(+)-Diasyringareinol		In this example, the compound is predicted to be Orally bioavailable
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde		In this example, the compound is predicted to be Orally bioavailable

Table 3: Computed Lipophilicity of phytoconstituents of *Vitex negundo*.

Phyto-constituent	ILOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log Po/w
Vitrofolal E	2.72	3.49	3.75	1.87	3.83	3.13
Vitrofolal F	2.73	3.69	3.45	1.33	3.35	2.91
Negundin A	2.9	3.46	3.4	1.98	3.82	3.11
Negundin B	2.72	1.46	2.14	1.09	2.52	1.98
(+)-Lyoniresinol	2.92	1.99	2.04	0.56	2.69	2.04
(+)-Lyoniresinol-3α-O-β-D-glucoside	4.71	0.4	-0.14	-1.61	0.66	0.8
(+)-Diasyringareinol	3.52	2.23	2.56	0.56	2.78	2.33
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldeyde	2.76	-0.14	-2.51	-3.77	-2.43	-1.22

Table 4: Computed water solubility of phytoconstituents of *Vitex negundo*.

Phytoconstituents	ESOL				ALI				SILICOS-IT			
	Log S (ESOL)	Solubility		Class	Log S (ESOL)	Solubility		Class	Log S (ESOL)	Solubility		Class
		Mg/mL	Mol/L			Mg/ml	Mol/L			Mg/ml	Mol/L	
Vitrofolal E	-4.28	1.71E-02	5.26E-05	Moderately soluble	-4.77	5.53E-03	1.70E-05	Moderately soluble	-5.62	7.76E-04	2.39E-06	Moderately soluble
Vitrofolal F	-4.48	1.12E-02	3.28E-05	Moderately soluble	-5.4	1.35E-03	3.97E-06	Moderately soluble	-5.04	3.13E-03	9.18E-06	Moderately soluble
Negundin A	-4.46	1.22E-02	3.45E-05	Moderately soluble	-4.93	4.13E-03	1.17E-05	Moderately soluble	-5.83	5.15E-04	1.46E-06	Moderately soluble
Negundin B	-2.99	3.64E-01	1.02E-03	Soluble	-3.15	2.52E-01	7.03E-04	Soluble	-4.03	3.32E-02	9.27E-05	Moderately soluble
(+)-Lyoniresinol	-3.53	1.23E-01	2.92E-04	Soluble	-4.09	3.41E-02	8.11E-05	Moderately soluble	-4.26	2.23E-02	5.53E-05	Moderately soluble
(+)-Lyoniresinol-3a-O-b-D-glucoside	-3.26	3.20E-01	5.49E-04	Soluble	-4.1	4.60E-02	7.89E-05	Moderately soluble	-2.47	1.97E+00	3.39E-03	Soluble
(+)-Diasyringareinol	-3.74	7.63E-02	1.82E-04	Soluble	-3.88	5.54E-02	1.32E-04	Soluble	-4.4	1.67E-02	3.98E-05	Moderately soluble
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde	-3.38	2.63E-01	4.20E-04	Soluble	-4.75	1.11E-02	1.77E-05	Moderately soluble	0.25	1.11E+03	1.77E+00	Soluble

Table 5: Computed pharmacokinetic parameters of phytoconstituents of *Vitex negundo*.

Phyto-Constituents	GI Absorption	BBB Permeation	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	P-gp substrate	Log Kp(cm/s)
Vitrofolal E	High	Yes	yes	yes	yes	yes	yes	no	-5.80cm/s
Vitrofolal F	High	No	Yes	No	Yes	Yes	Yes	No	-5.76cm/s
Negundin B	High	No	No	No	No	Yes	No	Yes	-7.45cm/s
Negundin A	High	No	Yes	No	Yes	Yes	Yes	No	-5.99cm/s
(+)-Lyoniresinol	High	no	No	No	No	Yes	No	Yes	-7.45cm/s
(+)-Lyoniresinol 3a-O-b-D-glucoside	Low	No	No	No	No	No	No	Yes	-9.57cm/s
(+)-Diasyringareinol	High	no	No	No	No	Yes	No	Yes	-7.27cm/s
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde	High	No	No	No	No	Yes	No	Yes	-7.07cm/s

Table 6: Computed drug likeness of phytoconstituents of *Vitex negundo*.

Phytoconstituents	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability Score
Vitrofolal E	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Vitrofolal F	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Negundin A	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Negundin B	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
(+)-Lyoniresinol	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
(+)-Lyoniresinol-3α-O-β-D-glucoside	No; 3 violations: MW>500, N or O>10, NH or OH>5	No; 3 violations: MW>480, MR>130, #atoms>70	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: TPSA>150, H-acc>10, H-don>5	0.17
(+)-Diasyringareinol	Yes;0 violation	Yes	Yes	Yes	Yes	0.55
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde	Yes;0 violation	Yes	Yes	Yes	Yes	0.55

Table 7: Computed medicinal chemistry properties of phytoconstituents of *Vitex negundo*.

Phyto-constituents	Pains	Brenk	Lead likeness	Synthetic accessibility
Vitrofolal E	0 alert	1 alert: aldehyde	Yes	2.29
Vitrofolal F	0 alert	1 alert: aldehyde	No; 1 violation; XLOGP3>3.5	2.59
Negundin A	0 alert	1 alert: Phenol ester	No; 1 violation: MW>350	2.92
Negundin B	0 alert	0 alert	No; 1 violation: MW>350	4.13
(+)-Lyoniresinol	0 alert	0 alert	No; 1 violation: MW>350	4.4
(+)-Lyoniresinol-3α-O-β-D-glucoside	0 alert	0 alert	No;2 violations: MW>350, Rotors>7	6.19
(+)-Diasyringareinol	0 alert	2 alerts	No; 1 violation: MW>350	-
6-Hydroxy-4[4-hydroxy-3-methoxy-phenyl]-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-napthaldehyde	0 alert	1 alert: aldehyde	No;1 violation; MW>350	3.81

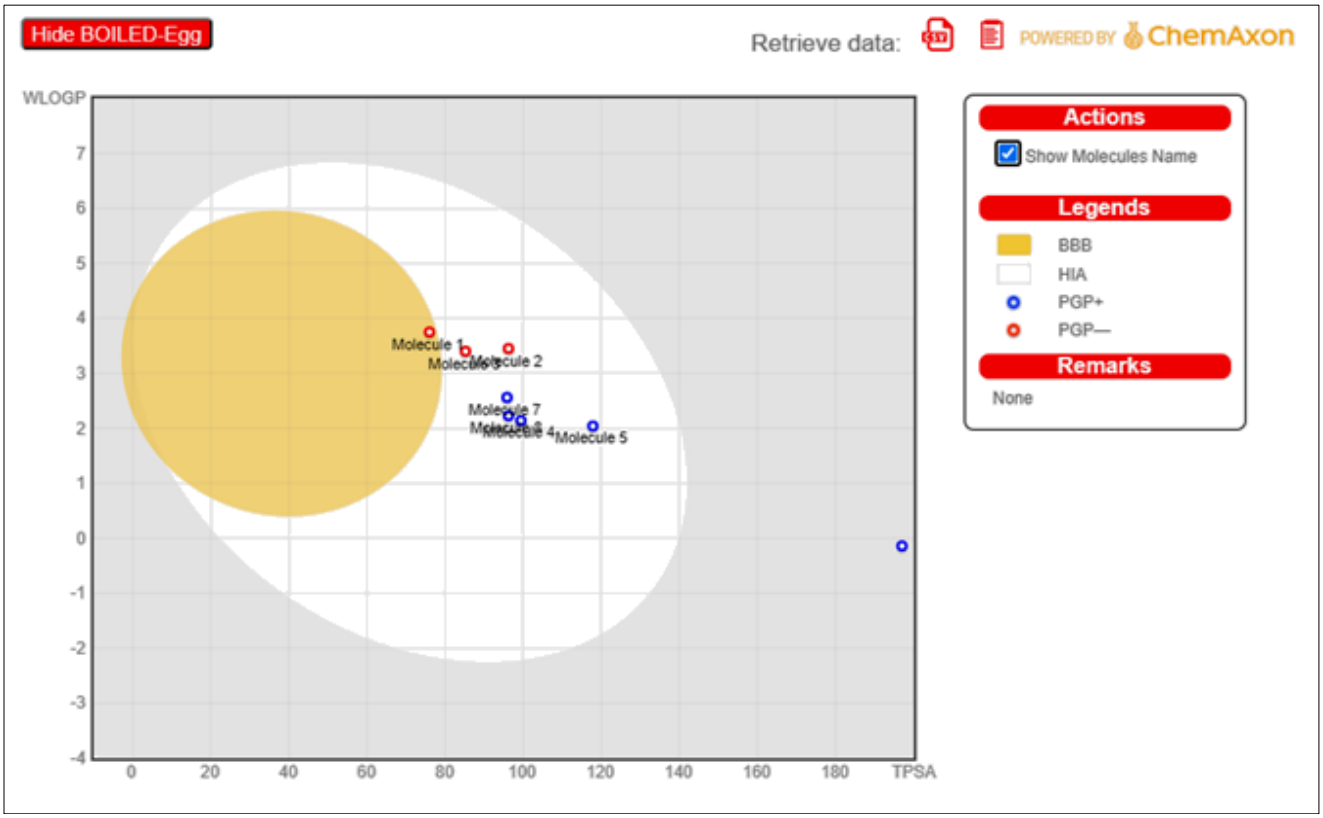


Fig 1: The boiled egg model prediction of GI absorption and BBB penetration of the Phytoconstituents of *Vitex negundo* by using Swiss ADME.

References

1. Ladda PL, Magdum CS. *Vitex negundo* Linn: ethnobotany, phytochemistry and pharmacology. Int J Adv Pharm Biol Chem. 2012;1(1):111-120.
2. Suganthi N, Dubey S. Phytochemical constituents and pharmacological activities of *Vitex negundo* Linn. J Chem Pharm Res. 2016;8(2):802-807.
3. Vishwanathan B. A review on *Vitex negundo* L. Eur J Behav Sci. 2010;3(1):30-42.
4. Vimal A, Vikram L, Singhal S, Anil B. *Vitex negundo* - a Chinese chaste tree. Int J Pharm Innov. 2011;1(5):9-20.
5. Koiral N, Dhakal C, Munankarmi NN, Ali SW, Hameed A, Martins N, *et al*. *Vitex negundo* Linn: phytochemical composition, nutritional analysis, and antioxidant and antimicrobial activity. Cell Mol Biol. 2020;66(4):1-7. DOI: 10.14715/cmb/2020.66.4.1. PMID: 32583767.
6. Basri F, Sharma HP, Firdaus S, Jain P, Ranjan A. A review of ethnomedical plant - *Vitex negundo* Linn. Int J Adv Res. 2014;2(3):882-894.
7. Zheng CJ, Li HQ, Ren SC, Xu CL, Rahman K, Qin LP, *et al*. Phytochemical and pharmacological profile of *Vitex negundo*. Phytother Res. 2015;29(5):633-647. DOI: 10.1002/ptr.5303. PMID: 25641408.
8. Egan WJ, Merz KM, Baldwin JJ. Prediction of drug absorption using multivariate statistics. J Med Chem. 2000;43(21):3867-3877. DOI: 10.1021/jm000292e. PMID: 11052792.
9. Daina A, Michielin O, Zoete V. Swiss ADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017;7:42717. DOI: 10.1038/srep42717.
10. O'Boyle NM, Banck M, James CA, Morley C. Open Babel: An open chemical toolbox. J Cheminform. 2011;3:33. DOI: 10.1186/1758-2946-3-33.
11. Leeson PD, Springthorpe B. The influence of drug-like concepts on decision-making in medicinal chemistry. Nat Rev Drug Discov. 2007;6(11):881-890. DOI: 10.1038/nrd2445. PMID: 17971784.
12. Testa B, Crivori P, Reist M. The influence of lipophilicity on the pharmacokinetic behaviour of drugs: concepts and examples. Perspect Drug Discov Des. 2000;19(1):179-211. DOI: 10.1023/A:1008741731244.
13. Arnott JA, Planey SL. The influence of lipophilicity in drug discovery and design. Expert Opin Drug Discov. 2012;7(10):863-875. DOI: 10.1517/17460441.2012.714363. PMID: 22992175.

14. Cheng T, Zhao Y, Li X, Lin F, Xu Y, Zhang X, *et al*. Computation of octanol-water partition coefficients by guiding an additive model with knowledge. J Chem Inf Model. 2007;47(6):2140-2148. DOI: 10.1021/ci700257y. PMID: 17985865.
15. Wildman SA, Crippen GM. Prediction of physicochemical parameters by atomic contributions. J Chem Inf Comput Sci. 1999;39(5):868-873. DOI: 10.1021/ci990307l.
16. Moriguchi I, Hirono S, Liu Q, Nakagome I, Matsushita Y. Simple method of calculating octanol/water partition coefficient. Chem Pharm Bull. 1992;40(1):127-130. DOI: 10.1248/cpb.40.127.
17. Moriguchi I, Hirono H, Nakagome I. Comparison of reliability of log P values for drugs calculated by several methods. Chem Pharm Bull. 1994;42(4):976-978. DOI: 10.1248/cpb.42.976.
18. Lachman LH, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. Philadelphia: Lea & Febiger; 1986.
19. Yalkowsky SH, Valvani SC. Solubility and partitioning I: solubility of nonelectrolytes in water. J Pharm Sci. 1980;69(8):912-922. DOI: 10.1002/jps.2600690814. PMID: 7400936.
20. Di L, Artursson P, Avdeef A, Ecker GF, Faller B, Fischer H, *et al*. Evidence-based approach to assess passive diffusion and carrier-mediated drug transport. Drug Discov Today. 2012;17(15-16):905-912. DOI: 10.1016/j.drudis.2012.03.015. PMID: 22507594.
21. Sánchez BY, Ponce MY, Barigye SJ, Goenaga YI, Pérez MC, Thu LTH, *et al*. Towards better BBB passage prediction using an extensive and curated data set. Mol Inform. 2015;34(5):308-330. DOI: 10.1002/minf.201400118. PMID: 27490276.
22. Montanari F, Ecker GF. Prediction of drug-ABC transporter interaction-recent advances and future challenges. Adv Drug Deliv Rev. 2015;86:17-26. DOI: 10.1016/j.addr.2015.03.001. PMID: 25769815.
23. Ogu CC, Maxa JL. Drug interactions due to cytochrome P450. Proc (Bayl Univ Med Cent). 2000;13(4):421-423. DOI: 10.1080/08998280.2000.11927719. PMID: 16389357.
24. Ndombera FT, Maiyoh GK, Vivian CT. Pharmacokinetic, physicochemical and medicinal properties of N-glycoside anticancer agent more potent than 2-deoxy-D-glucoside in lung cancer cells. J Pharm Pharmacol. 2019;7(4):165-176. DOI: 10.17265/2328-2150/2019.04.003.
25. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001;46(1-3):3-26. DOI: 10.1016/s0169-409x(00)00129-0. PMID: 11259830.
26. Ghose AK, Viswanadhan VN, Wendoloski JJ. Prediction of hydrophobic (lipophilic) properties of small organic molecules using fragmental methods: An analysis of ALOGP and CLOGP methods. J Phys Chem A. 1998;102(21):3762-3772. DOI: 10.1021/jp980230o.
27. Ghose AK, Viswanadhan VN, Wendoloski JJ. A knowledge-based approach in designing combinatorial or medicinal chemistry libraries for drug discovery: A qualitative and quantitative characterization of known drug databases. J Comb Chem. 1999;1(1):55-68. DOI: 10.1021/cc9800071. PMID: 10746014.
28. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. J Med Chem. 2002;45(12):2615-2623. DOI: 10.1021/jm020017n. PMID: 12036371.
29. Martin YC. A bioavailability score. J Med Chem. 2005;48(9):3164-3170. DOI: 10.1021/jm0492002. PMID: 15857122.
30. Baell JB, Holloway GA. New substructure filters for removal of Pan assay interference compounds (PAINS) from screening libraries and for their exclusion in bioassays. J Med Chem. 2010;53(7):2719-2740. DOI: 10.1021/jm901137j. PMID: 20131845.
31. Hann MM, Keserü GM. Finding the sweet spot: The role of nature and nurture in medicinal chemistry. Nat Rev Drug Discov. 2012;11(5):355-365. DOI: 10.1038/nrd3701. PMID: 22543468.
32. Teague SJ, Davis AM, Leeson PD, Oprea T. The design of lead-like combinatorial libraries. Angew Chem Int Ed Engl. 1999;38(24):3743-3748.