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Swiss ADME properties screening of the phytochemical compounds present in *Bauhinia acuminata*

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Abstract
In modern years, conventional medicinal plants analysis have constantly increased multinationally because plants allow them to complement modern pharmacological approaches. As computer mechanics approach, i.e *in silico* screening and pharmacokinetic screening can augment active compounds among the candidates and indicate mechanism of action of medicinal plants. The plant is well known for its precautionary action in tuberculosis. It has been established to possess some pharmacological activities such as Cytotoxic [1], antibacterial [2, 3], anti-nociceptive [4], thrombolytic activity [5], antioxidant [6], anthelmintic [7], anti-diarrheal [8], Hepatoprotective [9]. The present focus on the use of *in silico* ADME tool called Swiss ADME for pharmacological and pharmacognostic profiling of *Bauhinia acuminata*. The results of these studies can be further carried forward by researcher to investigate the *in vitro* and *in vivo* studies to reveal the pharmacological basis of traditional medicinal plants.

Keywords: Swiss ADME, *Bauhinia acuminata*, phytoconstituents

Introduction
The prehistoric people have great consciousness of the tradition of medicinal plants as herbal medicines. In the world, more than 80% of the living in minor developed countries reveal on customary medicine and humans are dependent on herbs for their basic requirements such as food stuffs, clothing, flavor, shelter, fragrance, and medicines (Divya and Mini, 2011 & Manoj Kumar Mishra, 2016, Gurib-Fakim, 2006 and Brijesh & Madhusudan, 2015) [10, 11, 12, 13]. The Discovery of drugs in medicinal plants affords better and vital leads, besides diverse pharmacological activities such as cytotoxic, anti-diarrheal, antimicrobial, anti-inflammatory, antioxidant, anthelmintic, anti-nociceptive, hemolytic activity. The plant is well known for its precautionary action in tuberculosis. As per the recommendations of Ayurveda *Bauhinia acuminata* is the one of important medicinal plants for the treatment of disorders. (Yi F *et al.*, 2016) [14].

Bauhinia acuminata is a plant belonging to the family of Fabaceae; it is an evergreen large shrub that grows in the areas of Southeast Asia such as Indonesia, Philippines, and the Malaysia. For conventional drugs, bark, leaves, stem, blooms, and Roots have been utilized.

Chemical constituents present in *Bauhinia acuminata* leaves are palmitic acid, three phallic acid esters, gallic acid, and ursolic acid. The leaves and stems of B. acuminata showed the presence of carbohydrate, saponins, phenolic compounds, flavonoids, oils, and fats, alkaloids, steroids, anthocyanoside, anthraquinone, terpenoids, amino acid, resins, sugars and cardiac glycosides. In phytochemical screening, leaf oil identified 13 compounds in B. acuminata through GC-MS analysis are Quercetin, Neophytadiene, Rhoeagenine, Alpha humulene, Isoaromadendrene epoxide (Vasudevan *et al.*, 2013), Butanedioic acid diethyl ester, 9,12,15-octadecatrienoic acid, Beta-ionone, 9,12-octadecadienoic acid, Alpha muurolol, Bauhinione, Beta-sitosterol,Kaempferol-3-glucoside**.** Phytochemical screening of plant extracts showed the occurrence of cardiac glycosides, saponins, alkaloids, flavonoids, tannins and steroid compounds (Dongray *et al.*, 2016) [15].

Recently interest in the absorption, distribution, metabolism and excretion (ADME) studies of herbal remedies are rising. ADMET properties of chemicals play vital roles in every stage of drug discovery and development. Pharmacokinetic studies have been integrated into modern drug development. A wide range of literature hunt indicates that there are limited data on ADME properties of herbal medicines in humans.

For a drug to be active, the molecule should reach to its target in the body in ample concentration. Neglected pharmacokinetic properties are one of the major reasons for terminating drug development.

Hence our main job is to focus on the evaluation of physicochemical and pharmacokinetic parameters of the phytochemical constituents of Bauhinia *acuminate*, using Swiss ADME which is freely accessible online software.

Materials and Methods

Swiss ADME (www.swissadme.ch)

Swiss ADME software of Swiss institute of bioinformatics (http://www.sib.swiss) was accessed in a web server that displays the Submission page of Swiss ADME in Google was used to estimate individual ADME behaviors of the phytoconstituents from *Bauhinia acuminata*. The list is made to contain one input per molecule, defined by a simplified molecular-input line-entry system (SMILES) and the results are presented for each molecule in tables and excel spreadsheet (Egan *et al.*, 2000) [16]. Calculated on Window 10 Pro, Version 20H2.

Bioavailability radar

The two-dimensional chemical structures with canonical SMILES were shown in the first section. The bioavailability radar empowers a preliminary glimpse at the drug-likeness of the molecules of interest which considers six physicochemical properties are taken into account: LIPO (Lipophilicity), SIZE, POLAR (Polarity), INSOLU (Insolubility), INSATU (Insaturation) and FLEX (Flexibility) respectively. Lipophilicity: XLOGP3 between-0.7 and + 5.0, size: MW between 150 and 500 g/mol, polarity: TPSA between 20 and 130 0A2, solubility: log *S* not higher than 6, saturation: fraction of carbons in the sp3 hybridization not less than 0.25 and flexibility: no more than 9 rotatable bonds (Daina *et al.*, 2017) [17].

Lipophilicity

Lipophilicity is a paramount parameter in drug discovery and design (Leeson & Springthorpe, 2007) [19] because it complements the single most informational and successful physicochemical property in medicinal chemistry (Testa *et al.*, 2000) [20]. It is experimentally demonstrated as partition coefficients (log P) or as distribution coefficients (log D). Log P portrays the partition equilibrium of an un-ionized solute amidst water and an immiscible organic solvent. Larger the log P values corresponds greater Lipophilicity (Arnott & Planey, 2012) [21]. To evaluate the Lipophilicity character in a compound, Swiss ADME provides five freely available models i.e. XLOGP3, WLOGP, MLOGP, SILICOS-IT and iLOGP respectively. XLOGP3, an atomistic accost including corrective factors and knowledge-based library (Cheng, 2007) [22]; WLOGP, application of purely atomistic method stationed on the fragmental system (Wildman and Crippen, 1999) [23]; MLOGP, an archetype of the topological method suggested on a linear relationship with implemented 13 molecular descriptors (Moriguchi *et al.*, 1992 & Moriguchi *et al.*, 1994) [24, 25]; SILICOS-IT, a mongrel method entrust on 27 fragments and 7 topological descriptors; iLOGP, a physics-based method lean on free energies of solvation in n-octanol and water calculated by the generalized-born and solvent accessible surface area (GB/SA) model; Consensus log P o/w is an arithmetic mean of the values predicted by the five proposed methods (Daina *et al.*, 2017) [18].

Water Solubility

The solubility of a compound radically confides on the solvent used, ambient temperature and pressure. The breadth of solubility is measured as the saturation concentration whereupon adding more solute does not increase its concentration in the solution (Lachman *et al.*, 1986 & Savjani *et al.*, 2012) [26]. A drug is considered highly soluble when the highest dose strength will be soluble in 250 mL over the pH range of 1 to 7.5 less of aqueous media. Two topological approaches included in Swiss ADME to predict water solubility, the first one is the application of ESOL model (Solubility class: Log S Scale: Insoluble<-10 poorly<-6, moderately<-4 soluble<-2 very<0<highly) and the second one is adapted from Ali *et al.*, 2012 [27] (Solubility class: Log S Scale: Insoluble<-10 poorly<-6, moderately<-4 soluble<-2very<0<highly). Both differ from the fundamental general solubility equation (Yalkowsky & Valvani, 1980) [27] since they avoid the melting point parameter but the linear correlation between predicted and experimental values were strong (R2=0.69 and 0.81 respectively). The third predictor of Swiss ADME was developed by SILICOS-IT (Solubility class: Log S Scale: Insoluble<-10 poorly<-6, moderately<-4 soluble<-2 very<0<highly) where the linear coefficient is corrected by molecular weight (R2=0.75). All predicted values are the decimal logarithm of the molar solubility in water (log S). Swiss ADME also provides solubility in mol/l and mg/ml along with qualitative solubility classes.

Pharmacokinetics

The delineation exists in a region of agreeable properties for GI absorption on a plot of two computed descriptors; ALOGP versus PSA respectively. The region most populated by well-absorbed molecules is elliptical; it was called Egan egg, which is used to assess the predictive power of the model for GI passive absorption and prediction for brain access by passive diffusion to finally lay the BOILED-Egg (Brain or Intestinal Estimate D permeation predictive model). The BOILED-Egg model produces a rapid, spontaneous, efficient imitate yet boisterous method to forecast the passive GI absorption helpful for drug discovery and development (Di *et al.*, 2012 & Brito-Sanchez *et al.*, 2015) [28]. The white region is the space of the molecules with a greater extent of absorption by GI tract, the yellow region (yolk) is the space with the highest probability to permeate to the brain (Daina *et al.*, 2017, Daina *et al.*, 2016 & Montanari and Ecker, 2015) [18]. Cytochrome p450 (CYP) isoenzymes biotransforms more than 50-90% of therapeutic molecules from its five major isoforms (CYP1A2, CYP3A4, CYP2C9, CYP2C19, CYP2D6) [29, 30, 31]. P-gp is broadly dispersed in intestinal epithelium which pumps xenobiotic back into the intestinal lumen and from the capillary endothelial cells of the brain back into the capillaries (Ogu & Maxa, 2000 and Ndombera *et al.*, 2019) [32, 33]. Swiss ADME adopts support vector machine algorithm (SVM) for the datasets of known substrates/non- substrates or inhibitors/non-inhibitors for binary classification. The resultant molecule will return "Yes "or "No" if the molecule under investigation is expected to be a substrate for both P-gp and CYP respectively. The SVM model for P-gp substrate was built on 1033 molecules (training set) and tested on 415 molecules (test set), 10 fold CV: ACC=0.72/AUC=0.77, External: ACC=0.88/AUC=0.94 respectively. The SVM model for Cytochrome P-450 1A2 inhibitor molecule was built on 9145 molecule (training set) and tested on 3000 molecules (test set), 10 fold CV:

ACC=0.83/AUC=0.90, External: ACC=0.84/AUC=0.91. The SVM model for Cytochrome P-450 2C19 inhibitor molecule was built on 9272 molecule (training set) and tested on 3000 molecules (test set), 10 fold CV: ACC=0.80/AUC=0.86, External: ACC=0.80/AUC=0.87. The SVM model for Cytochrome P-450 2C9 inhibitor molecule was built on 5940 molecule (training set) and tested on 2075 molecules (test set), 10 fold CV: ACC=0.78/AUC=0.85, External: ACC= 0.71/AUC=0.81. The SVM model for Cytochrome P-450 2D6 inhibitor molecule was built on 3664 molecule (training set) and tested on 1068 molecules (test set), 10 fold CV: ACC=0.79/AUC=0.85, External: ACC=0.81/AUC=0.87. The SVM model for Cytochrome P-450 3A4 inhibitor molecule was built on 7518 molecule (training set) and tested on 2579 molecules (test set), 10 fold CV: ACC=0.77/ AUC=0.85, External: ACC=0.78/AUC=0.86.

Drug likeness

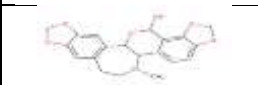
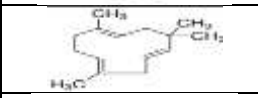
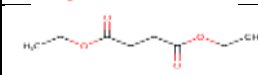
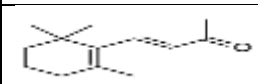
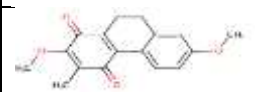
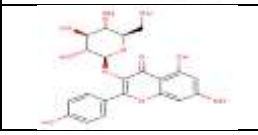
Swiss ADME performs filtering of chemical libraries to exclude molecules with peculiarities incompatible with an acceptable pharmacokinetic profile with five disparate ruled based filters elemental from considerable Pharma companies intended to improve the condition of proprietary chemical collections (Daina *et al.*, 2017) [18]. The Lipinski filter (Pfizer) is the prime pioneer rule of five that characterize small molecules based on their physicochemical property profiles which include Molecular Weight (MW) less than 500, N or O ≤ 10, MLOGP ≤ 4.15, NH or OH ≤ 5. Lipinski considers stringently that all nitrogens and oxygen as H-bond acceptors and all nitrogens and oxygens with at least one hydrogen as H-bond donors. Besides, aliphatic fluorines are acceptors and alinine nitrogen is neither donor nor acceptor. The Ghose filter (Amgen) describes small molecules stationed on the physicochemical property, existence of functional groups and substructures. The qualifying range includes of molecular weight is between 160 and 480 Da, WlogP is between -0.4 to 5.6, molar refractivity (MR) is between 40 to 130 for a total number of atom; the qualifying range is between 20 and 70 atoms in a small molecule (Ghose *et al.*, 1998 & Ghose *et al.*, 1999) [34, 35]. Veber filter (GSK filter) model symbolizes molecules as a drug like if they have ≤ 10 rotatable bonds and a TPSA equal to or less than 140 Å2 with 12 or fewer H-bond donors and acceptors. Compounds with these properties will have good oral bioavailability, reduced TPSA correlates increased permeation rate, increased rotatable bonds counts has a negative effect on the permeation rate (Veber *et al.*, 2002) [36]. Egan filter (Pharmacia filter) anticipates that drug absorption depends on processes involved in the membrane permeability of the small molecule. These models symbolize molecules as a drug like if they have WLOGP ≤ 5.88 and TPSA ≤ 131.6 respectively. The Egan computational model for human passive intestinal absorption (HIA) of small molecules accounted for active transport and efflux mechanisms and will be therefore robust in predicting absorption of drugs (Egan *et al.*, 2000) [37]. Muegge filter (Bayer filter) is a self-reliant Pharmacophore point filter that segregates drug-like and non-drug-like molecules. These models symbolize molecules as a drug like if they have a molecular weight between 200 to 600 Da, TPSA ≤ 150, Number of rings ≤ 7, XLOGP between -2 and 5, Number of carbon atoms > 4, number of heteroatoms > 1, number of rotatable bonds ≤ 15, H-bond acceptor ≤ 10, H- bond donor ≤ 5 respectively. Abbott bioavailability score seeks to predicts the probability of a compound to have at least 10% oral bioavailability in rat or measurable Caco-2 permeability which predicts the probability of a compound to have F>10% based on the predominant charge at biological pH in a rat model. It focuses on fast screening of chemical libraries to select the best molecules to be synthesized (Martin, 2005) [38].

Medicinal chemistry

This section aims to bolster medicinal chemists in their daily drug discovery endeavors. PAINS (Pan Assay Interference Compounds or frequent hitters or promiscuous compounds) are the molecules that show potent response in assays irrespective of the protein targets, notably such compounds are reported to be active in many different assays, which can be considered as potential starting points for further exploration. Swiss ADME returns warnings if such moieties are found in the molecule under evaluation (Baell & Holloway, 2010) [39]. In other models, Brenk considers compounds that are smaller and less hydrophobic and not those defined by "Lipinski's rule of 5" is to widen opportunities for lead optimization. This was after the exclusion of compounds with potentially mutagenic, reactive and unfavorable groups such as nitro groups, sulfates, phosphates, 2-halopyridines and thiols. Brenk model restricts the ClogP/ClogD to between 0 and 4, the number of hydrogen-bond donors and acceptors to fewer than 4 and 7, respectively, and the number of heavy atoms to between 10 and 27 respectively. Additionally, only compounds with limited complexity defined as fewer than 8 rotatable bonds, fewer than 5 ring systems and no ring systems with more than 2 fused rings are considered medicinal (Brenk *et al.*, 2008). The concept of lead likeness is designed to provide leads with tremendous affinity in high throughput screening (HTS) that allows for the exploitation of additional interactions in the lead optimization phase. Leads are exposed to chemical modifications that will most likely decrease size and increase lipophilicity which is less hydrophobic than drug-like molecules. Lead optimization has been done by a rule-based method consisting of molecules with molecular weight in between 100 and 350 Da, ClogP between 1 and 3.0 and are greatly considered as superior to those of drug-like compounds and therefore lead like (Hann & Keseru, 2012 and Teague *et al.*, 1999) [40, 41].

Experimental Results with Tables/Figures

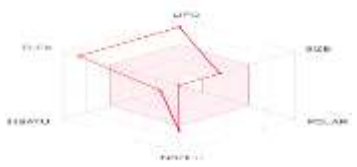
Table 1: General characteristics of Phyto-constituents of *Bauhinia acuminata*.

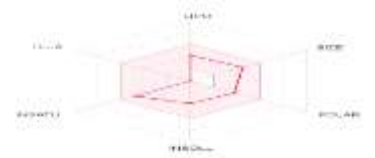
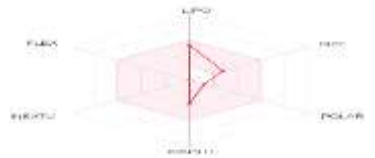
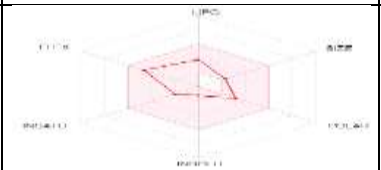
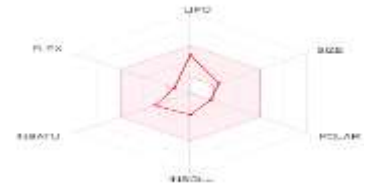
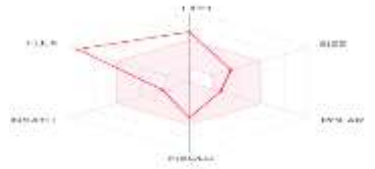
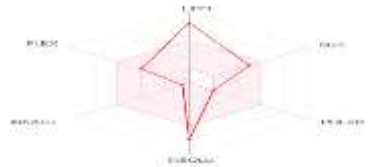
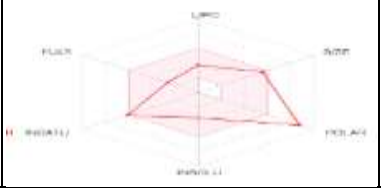
Phyto-constituents	Mol. Weight	Mol formula	Smile notation	Structure
Quercetin	302.04	$C_{15}H_{10}O_7$	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O	
Neophytadiene	280.31	$C_{20}H_{40}$	CC(C)CCCC(C)CCCC(C)CCCC(=C)C=C	
Rhoeagenine	355.11	$C_{19}H_{17}NO_6$	CN1CCC2=CC3=C(C=C2C4C1C5=C(C(O4)O)C6=C(C=C5)OCO6)OCO3	
Alpha humulene	204.19	$C_{15}H_{24}$	CC1=CCC(C=CCC(=CCC1)C)(C)C	
Isoaromadendrene epoxide	220.18	$C_{15}H_{24}O$	CC1CCC2C1C3C(C3(C)C)CC4C2(O4)C	
Butanedioic acid diethyl ester	174.09	$C_8H_{14}O_4$	CCOC(=O)CCC(=O)OCC	
9,12,15-octadecatrienoic acid	276.41	$C_{18}H_{28}O_2$	CCCCCC=CCC=CCCC=CCCCC(=O)O	
Beta-ionone	192.15	$C_{13}H_{20}O$	CC1=C(C(CCC1)(C)C)C=CC(=O)C	
9,12-octadecadienoic acid	286.24	$C_{18}H_{32}O_2$	CCCCCC=CCC=CCCCCCCCC(=O)O	
Alpha muurolol	222.20	$C_{15}H_{26}O$	CC1=CC2C(CCC(C2CC1)(C)O)C(C)C	
Bauhinione	284.10	$C_{17}H_{16}O_4$	COC1=CC=C2C(CCC3=C2C(=O)C(C)=C(OC)C3=O)=C1	
Beta-sitosterol	414.718	$C_{29}H_{50}O$	CCC(CCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)O)C)C)C(C)C	
Kaempferol-3-glucoside	448.38	$C_{21}H_{20}O_{11}$	C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)OC4C(C(C(C(O4)C(=O)O)O)O)O)O	

Bioavailability Radar

The pink area represents the optimal range for each property. Lipophilicity: XLOGP3 between −0.7 and +5.0, Size: MW between 150 and 500 g/mol, Polarity: TPSA between 20 and 130 Å^2, Solubility: log *S* not higher than 6, Saturation: fraction of carbons in the sp3 hybridization not less than 0.25, Flexibility: no more than 9 rotatable bonds.

Table 2: Bioavailability Radar & Results

Phyto-constituent	Bioavailability radar	Results
Quercetin		In this example, the compound is predicted to be not orally bioavailable, because of high instauration.
Neophytadiene		In this example, the compound is predicted to be not orally bioavailable, because it is too flexible, in saturation and Lipophilicity.

Rhoeagenine		In this example, the compound is predicted to be **orally bioavailable**.
Alpha humulene		In this example, the compound is predicted to be **orally bioavailable**.
Isoaromadendrene epoxide		In this example, the compound is predicted to be **orally bioavailable**.
Butanedioic acid diethyl ester		In this example, the compound is predicted to be **orally bioavailable**.
9,12,15-octadecatrienoic acid		In this example, the compound is predicted to be not orally bioavailable, because it is too flexible and lipophilic.
Beta-ionone		In this example, the compound is predicted to be **orally bioavailable**.
9,12-octadecadienoic acid		In this example, the compound is predicted to be not orally bioavailable, because it is too flexible and lipophilic
Alpha muurolol		In this example, the compound is predicted to be **orally bioavailable**.
Bauhinione		In this example, the compound is predicted to be **orally bioavailable**.
Beta-sitosterol		In this example, the compound is predicted to be not orally bioavailable, because it is lipophilic and insoluble.
Kaempferol-3-glucoside		In this example, the compound is predicted to be not orally bioavailable, because it is polar.

Rhoeagenine, Alpha humulene, Isoaromadendrene epoxide, Butanedioic acid diethyl ester, Beta-ionone, Alpha muurolol, Bauhinione are the phytoconsitutents of *Bauhinia acuminata* are having oral bioavailability.

Table 3: Computed Lipophilicity of the Phytoconstituents of *Bauhinia acuminata*

Phyto-constituent	ILOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log Po/w
Quercetin	0.00	1.59	1.99	-0.56	1.54	0.91
Neophytadiene	5.05	9.62	7.17	6.2	7.30	7.07
Rhoeagenine	3.16	1.85	1.08	1.85	2.06	2.00
Alpha humulene	0.00	4.55	5.04	4.53	3.91	3.61
Isoaromadendrene epoxide	0.00	3.76	3.48	3.81	3.39	2.89
Butanedioic acid diethyl ester	0.00	1.20	0.89	0.93	1.17	0.84
9,12,15-octadecatrienoic acid	3.94	6.34	5.66	4.38	5.59	5.18
Beta-ionone	2.77	2.91	3.66	2.94	3.81	3.22
9,12-octadecadienoic acid	4.14	5.98	5.88	4.47	5.77	5.45
Alpha muurolol	2.77	2.91	3.66	2.94	3.81	3.22
Bauhinione	4.14	6.98	5.88	4.47	5.77	5.45
Beta-sitosterol	0.00	3.34	3.78	3.67	3.22	2.80
Kaempferol-3-glucoside	2.75	2.50	2.47	1.23	3.70	2.53

Table 4: Computed Water solubility of the Phytoconstituents of *Bauhinia acuminata*

Phyto-constituent	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	
Quercetin	-3.19	1.96e-0.1	6.49e-04	soluble	-3.96	3.32e-02	1.10e-04	soluble	-3.24	1.73e-01	5.73e-04	soluble
Neophytadiene	-6.77	4.74e-05	1.70e-07	Poorly soluble	-9.53	8.15e-08	2.93e-10	Poorly soluble	-6.11	2.18e-04	7.82e-07	Poorly soluble
Rhoeagenine	-3.62	8.77e-02	2.37e-04	soluble	-2.93	4.31e-01	1.17e03	soluble	-3.95	4.18e-02	1.13e-04	soluble
Alpha humulene	-3.97	2.17e-02	1,06e-04	soluble	-4.27	1.09e-02	5.34e-05	Moderately soluble	-3.52	6.19e-02	3.03e-04	soluble
Isoaromadendrene epoxide	-3.57	5.86e-02	2.66e-04	soluble	-3.72	4.24e-02	1.92e-04	soluble	-2.81	3.40e-01	1.54e-03	soluble
Butanedioic acid diethyl ester	-1.21	1.06e+01	6.11e-02	Very soluble	-1.90	2.19e+00	1.26e-02	Very soluble	-1.65	3.92e+00	2.25e-02	soluble
9,12,15-octadecatrienoic acid	-4.70	5.52e-03	1.98e-05	Moderately soluble	-6.91	3.40e-02	1.22e-07	Poorly soluble	-3.96	3.08e02	1.11e-04	Soluble
Beta-ionone	-2.73	3.55e-01	1.85e-03	Soluble	-2.93	2.26e-01	1.18e-03	soluble	-3.10	1.54e-01	8.02e-04	soluble
9,12-octadecadienoic acid	-5.05	2.49e-03	8.87e-06	Moderately soluble	-7.58	7.42e-06	2.64e08	Poorly soluble	-4.67	5.93e-03	2.11e-05	Moderately soluble
Alpha muurolol	-2.73	3.55e-01	1.85e-03	soluble	-2.93	2.26e-01	1.18e-03	soluble	-3.10	1.54e-01	8.02e-04	Soluble
Bauhinione	-5.05	2.49e-03	8.87e-06	Moderately soluble	-7.58	7.42e-06	2.64e-08	Poorly soluble	-4.67	5.93e-03	2.11e-05	Moderately soluble
Beta-sitosterol	-3.26	1.23e-01	5.54e-04	soluble	-3.44	8.04e-02	3.61e-04	soluble	-2.73	4.10e-01	1.85e-03	soluble
Kaempferol-3-glucoside	-3.26	1.57e-01	5.53e-04	soluble	-3.25	1.60e-01	5.62e-04	soluble	-4.97	3.03e-03	1.07e-05	Moderately soluble

BOILED-Egg for Prediction of GI Absorption and Brain Penetration

The analysis predicts that the phytochemicals show poor GI absorption, with nearly 80% of the molecules exhibiting BBB penetration, and all of them are predicted as the nonsubstrates of P-gp (PGP−); only one phytochemical is P-gp substrates.

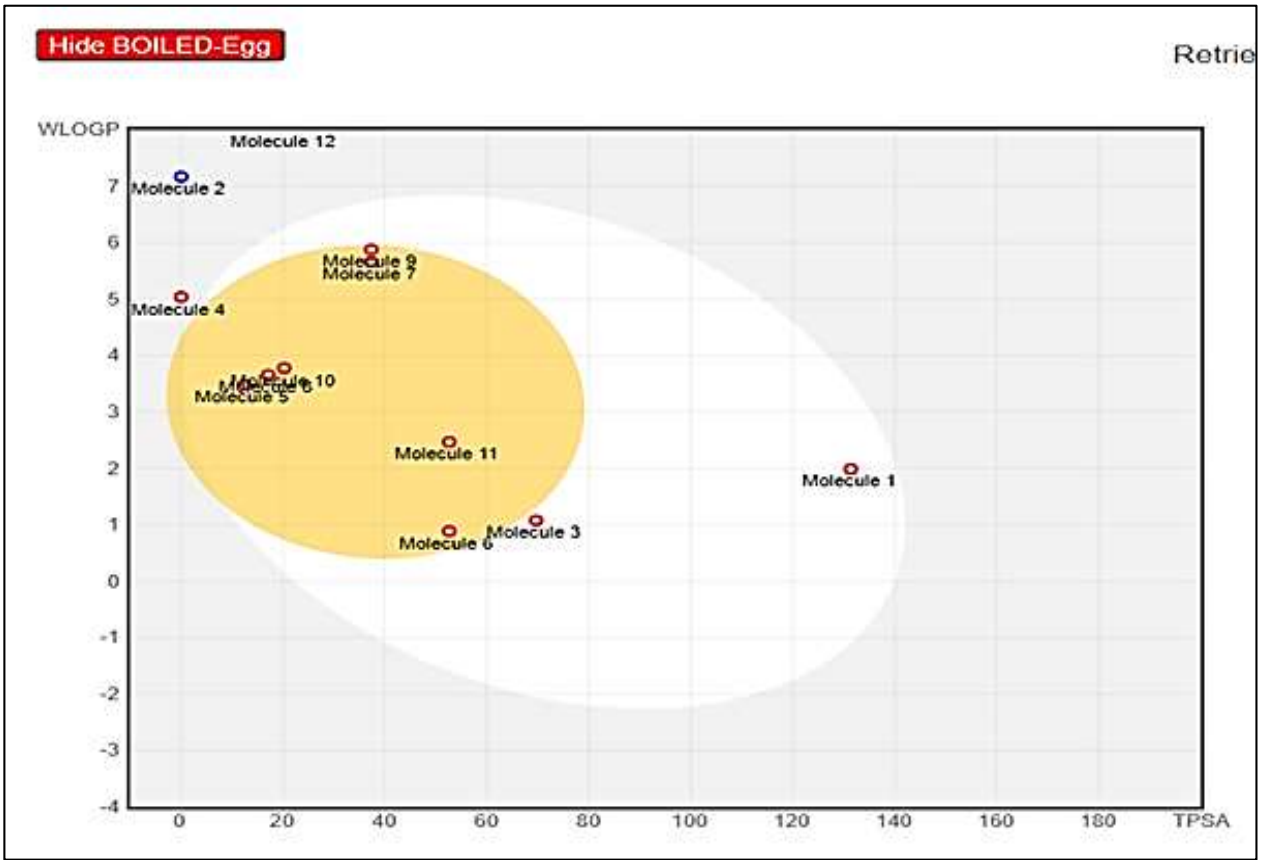


Fig 1: The BOILED egg Model prediction of GI absorption and BBB penetration of the Phyto-constituents of *Bauhinia acuminata* by using swiss ADME

Quercetin**,** Rhoeagenine are having GI or intestinal absorption Neophytadiene, Alpha humulene, Isoaromadendrene epoxide, Butanedioic acid diethyl ester, Beta-ionone, 9, 12-octadecadienoic acid, Alpha muurolol, Bauhinione, Kaempferol-3-glucoside are having BBB penetration.

Beta-sitosterol is not absorbed and not penetrated
9, 12, 15-octadecatrienoic acid is effluated from CNS by the P-glycoprotein.

Table 5: Computed Pharmacokinetic Parameters of the Phyto-constituents of *Bauhinia acuminata*

Phyto-constituent	GI Absorption	BBB permeantt	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp (cm/s)
Quercetin	High	No	No	yes	No	No	yes	yes	-7.01
Neophytadiene	Low	No	yes	No	No	Yes	No	Yes	-1.17
Rhoeagenine	High	No	No	Yes	No	No	Yes	No	-7.24
Alpha humulene	Low	No	No	No	No	No	No	No	-4.32
Isoaromadendrene epoxide	High	Yes	No	No	No	No	No	No	-4.97
Butanedioic acid diethyl ester	High	Yes	No	No	No	No	No	No	-6.51
9,12,15-octadecatrienoic acid	High	Yes	No	Yes	No	Yes	No	No	-3.50
Beta-ionone	High	Yes	No	No	No	No	No	No	-5.41
9,12-octadecadienoic acid	High	Yes	No	Yes	No	Yes	No	No	-3.05
Alpha muurolol	High	Yes	No	No	No	No	No	No	-5.41
Bauhinione	High	Yes	No	Yes	No	Yes	No	No	-3.05
Beta-sitosterol	High	Yes	No	No	No	No	No	No	-5.29
Kaempferol-3-glucoside	High	Yes	No	Yes	Yes	Yes	No	Yes	-6.26

Table 6: Computed Drug likeness of the Phyto-constituents of *Bauhinia acuminata*

Phyto-constituent	Lipinski	Veber	Egan	Muegge	Bioavailability score
Quercetin	Yes	Yes	Yes	Yes	0.55
Neophytadiene	Yes	No	No	No	0.55
Rhoeagenine	Yes	Yes	Yes	Yes	0.55
Alpha humulene	Yes	Yes	Yes	No	0.55
Isoaromadendrene epoxide	Yes	Yes	Yes	No	0.55
Butanedioic acid diethyl ester	Yes	Yes	Yes	No	0.55
9,12,15-octadecatrienoic acid	Yes	No	Yes	No	0.85
Beta-ionone	Yes	Yes	Yes	No	0.55
9,12-octadecadienoic acid	Yes	No	No	No	0.85

Alpha muurolol	Yes	Yes	Yes	No	0.55
Bauhinione	Yes	No	No	No	0.85
Beta-sitosterol	Yes	Yes	Yes	No	0.55
Kaempferol-3-glucoside	Yes	Yes	Yes	Yes	0.85

Table 7: Computed Medicinal Chemistry Properties of Phytoconstituents of *Bauhinia acuminata*

Phyto-constituent	Pains	Brenk	Lead likeness	Synthetic accessibility
Quercetin	1 alert: catechol_A	1 alert: catechol	Yes	3.23
Neophytadiene	0 alert	1 alert: polyene	No; 2 violations: Rotors>7, XLOGP3>3.5	4.08
Rhoeagenine	0 alert	0 alert	No; 1 violation: MW>350	4.29
Alpha humulene	0 alert	1 alert: isolated_alkene	No; 2 violations: MW<250, XLOGP3>3.5	3.66
Isoaromadendrene epoxide	0 alert	1 alert: Three membered_heterocycle	No; 2 violations: MW<250, XLOGP3>3.5	3.96
Butanedioic acid diethyl ester	0 alert	1 alert: more_than_2_esters	No; 1 violation: MW<250	1.96
9,12,15-octadecatrienoic acid	0 alert	1 alert: isolated_alkene	No; 2 violations: Rotors>7, XLOGP3>3.5	3.23
Beta-ionone	0 alert	1 alert: michael_acceptor_1	No; 1 violation: MW<250	3.38
9,12-octadecadienoic acid	0 alert	1 alert: isolated_alkene	No; 2 violations: Rotors>7, XLOGP3>3.5	3.1
Alpha muurolol	0 alert	1 alert: isolated_alkene	No; 1 violation: MW<250	4.92
Bauhinione	1 alert: quinone_A	1 alert: chinone_1	Yes	3.21
Beta-sitosterol	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	6.3
Kaempferol-3-glucoside	0 alert	0 alert	No; 1 violation: MW>350	5.22

Discussion

Computer-based drug designing has been employed very much widely in the prediction of ADMET properties of the drugs now as days which leads to budding stage drug discovery. The rationale behind these Insilco approaches is due to the relatively lower cost time factor involved compared to standard ADMET profiling. As an example, it will take a minute in an Insilco model to screen 20,000 and more molecules but will take 20 weeks in the "wet" laboratory to do the same exercise. Due to the accumulated ADME data available with this software in the late 1990s, many pharmaceutical companies are now using computational models that, in some cases, are replacing the "wet" screens. This paradigm shift has now, therefore, spurred up in the development of several theoretical methods for the prediction of ADMET parameters.

In the present study, we used Swiss ADME online software tool which is available free for the users to evaluate the ADME properties of *Bauhinia acuminata* respectively.

Conclusion

With the rapid increase in chemical and biological information, CADD has been dramatically reshaping the research and development pathways in drug candidate identification. The use of computational techniques in the drug discovery and development process is widely appreciated in terms of implementation, money and time. A freely available Swiss ADME, a web-based tool is presented in this study to evaluate the ADME properties of phytoconstituents present in *Bauhinia acuminata*. The phytoconstituents of the plants were enlisted through the software includes Quercetin, Neophytadiene, Rhoeagenine, Alpha humulene, Butanedioic acid diethyl ester, 9,12,15-octadecatrienoic acid, Beta-ionone, 9,12-octadecadienoic acid, Alpha muurolol, Bauhinione, Kaempferol-3-glucoside. Accordingly, the phytoconstituents were analyzed for Physicochemical and Pharmacokinetic properties and depicted in respected tables and figures. Further, the values can be used as monographs by researchers and scientists for the development of potential Semisynthetic and synthetic drugs for multifarious usage.

Acknowledgement

Not applicable

Conflicts of Interest

There are no conflicts of interest.

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