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Swiss ADME prediction of phytochemicals present in *Butea monosperma* (Lam.) Taub

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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 developed, in silico approaches like network analysis and screening been extensively utilized to enlighten pharmacological basis of the functions of traditional medicinal plants. In these approach, network pharmacology, insilico screening and pharmacokinetic screening can augment active compounds among the candidates and indicate mechanism of action of medicinal plants. The present focus on the use of insilico ADME tool called SwissADME for pharmacological and pharmacognostic profiling of Butea monosperma Lam. The results of these study 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, *Butea monosperma*, phytochemicals

1. Introduction
The ancient mankind has a rich awareness of the usage of medicinal plants as herbal medicines. In the world, more than 80% of the living in slighter developed countries confide on traditional medicine and humans are reliant on herbs for their elemental obligations such as food stuffs, shelters, clothing, flavour, fragrance and medicines (Divya and Mini, 2011 & Manoj Kumar Mishra, 2016, Gurib-Fakim, 2006 and Brijesh & Madhusudan, 2015) [1, 2, 3, 4]. The drug discovery in medicinal plants affords improved and imperative leads against multifarious pharmacological targets including for diseases like cancer, malaria, cardiovascular diseases, diabetes and neurological disorders.

Ayurveda recommends number of medicinal plants for treatment of different disorders, one of them being *Butea Monosperma* (Lam) Taub, frequently known as flame tree, belongs to family *Fabaceae*, distributed throughout India and south Asian peninsula (Shah GM, 1959) [5]. It is medium sized deciduous tree with 10-15 meter height, flowers are odorless and looks reddish and leaves are trifoliate. The plants has numerous medicinal properties like laxative, anthelmintics, aphrodisiac, appetizer etc. (Burli and Khade, 2007, Upadhyay B, 2011, Gaikwad SR, 2008, Katewa SS, 2004, Aher RK, 2004, Sikarwar RL and Kumar V, 2005, Tambekar DH and Khante BS, 2010, Jain A, 2004, Brijesh & Madhusudan, 2015) [6, 7, 8, 9, 10, 11, 12, 13, 4]. Specifically they are used as Anti-stress (Soman *et al*, 2004) [14], Noortropic /Cognitive activity (Zafar *et al*, 1989) [15], Anti-bacterial (Ambersing *et al*, 2014. Bharathirajan and Prakash, 2014) [16, 17], Anti-filarial (Deshmukh *et al*, 2014) [18], Sunscreen activity (More *et al*, 2013) [19], Anti-convulsant (Sangale *et al*, 2015) [20], Anti-anthelmintic (Borkar *et al*, 2011, Bibhilesh *et al*, 2000) [21, 22], Anti-oxidant (Raqibul *et al*, 2009. Singh *et al*, 2015. Sharma *et al*, 2009. Vijay *et al*, 2008) [23, 24, 25, 26], Anti-diabetic (Harish *et al*, 2014. Samad *et al*, 2014) [27, 28], Anti-nociceptive/ Ameliorative potential (Venkata *et al*, 2013, Venkata *et al*, 2012) [29, 30] respectively.

Analyzing and anticipating the pharmacological basis of the therapeutic activity of traditional medicinal plants are decisive for the goal of modernizing their use, considering the complicated and diverse phytoconstituents of the medicinal plants, defining the specific chemical components in such plants and their major biological functions (Koutsoukas A *et al*, 2011, Fan Yi *et al*, 2018) [31, 32].

If quick and convenient pathway has been established to predict huge number of chemical constituents and then based on these if we perform *in vivo* and *in vitro* pharmacological experiments for verification, there will be significant improvement in the efficiency for evaluating the chemical activities of medicinal plants (Yi F *et al*, 2016) [33].

Swiss ADME is one such website which allows to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, drug-like nature and

medicinal chemistry friendliness of one or multiple small molecules to support drug discovery. The present study was designed to submit the bioactive compounds present in *Butea monosperma* for insilico ADMET screening using Swiss ADME website (http://www.swissadme.ch/index.php) to evaluate the individual ADME behaviour and interpret the results.

2. Materials and Methods

2.1 Swiss ADME

Swiss ADME software (www.swissadme.ch) 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 compounds from Butea monosperma. The list is made to contain one input molecule per line with several inputs, defined by simplified molecular input line entry system (SMILES) and the results are presented for each molecule in tables, graphs and also an excel spreadsheet (Egan *et al*., 2000) [34].

2.2 Structure and bioavailability radar

The two dimensional chemical structure with canonical SMILES were shown in the first section. The bioavailability radar empowers preliminary glimpse at the drug likeness of the molecules of interest which considers six physicochemical properties are taken in to 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) [35].

2.3 Physicochemical properties

These section comprises of clean molecular and physicochemical characteristics like molecular formula, molecular weight, number of heavy atoms, number of aromatic heavy atoms, fraction csp3, number of rotatable bonds, number of H-bond acceptors, number of H-bond donors, molar refractivity, TPSA respectively. The values were computed with open babel version 2.3.0 (O'Boyle, 2011 & Daina *et al*., 2017) [36, 35].

2.4 Lipophilicity

Lipophilicity is a paramount parameter in drug discovery and design (Leeson & Springthorpe, 2007) [37] on the grounds that it complements the single most informational and successful physicochemical property in medicinal chemistry (Testa *et al*., 2000) [38]. It is experimentally demonstrated as partition coefficients (log P) or as distribution coefficients (log D). Log P portrays 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) [39]. 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) [40]; WLOGP, application of purely atomistic method stationed on fragmental system (Wildman and Crippen, 1999) [41]; MLOGP, an archetype of topological method suggested on a linear relationship with implemented 13 molecular descriptors (Moriguchi *et al*., 1992 & Moriguchi *et al*., 1994) [42, 43]; SILICOS-IT, an 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) [35].

2.5 Solubility

Solubility of a compound radically confide on the solvent used, ambient temperature and pressure. The breadth of solubility measured as the saturation concentration where upon adding more solute does not increase its concentration in the solution (Lachman *et al*., 1986 & Savjani *et al*., 2012) [44]. A drug is considered highly soluble when the highest dose strength is soluble in 250 mL or less of aqueous media over the pH range of 1 to 7.5. 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 (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) [45] 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.

2.6 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 Intestina L Estimate D permeation predictive model). The BOILED-Egg model produces a rapid, spontaneous, efficiently 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) [46]. The white region is the space of the molecules with greater extent of absorption by GI tract, the yellow region (yolk) is the space with highest probability to permeate to the brain (Daina *et al*., 2017, Daina *et al*., 2016 & Montanari and Ecker, 2015) [35]. Cytochrome p450 (CYP) isoenzymes biotransforms more than 50-90% of therapeutic molecules from its five major isoforms (CYP1A2, CYP3A4, CYP2C9, CYP2C19, CYP2D6). P-gp is broadly dispersed in intestinal epithelium which pumps xenobiotic back in to the intestinal lumen and from the capillary endothelial cells of the brain back in to the capillaries (Ogu & Maxa, 2000 and Ndombera *et al*., 2019) [49, 50]. 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 expected to be 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.

2.7 Drug likeness

Swiss ADME performs filtering of chemical libraries to exclude molecules with peculiarities incompatible with an acceptable pharmacokinetics 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) [35]. The Lipinski filter (Pfizer) is the pioneer rule of five that characterize small molecules based on physicochemical property profiles which includes Molecular Weight (MW) less than 500, MLOGP ≤ 4.15, N or O ≤ 10, NH or OH ≤ 5. Lipinski considers stringently that all nitrogens and oxygen as H-bond acceptor and all nitrogens and oxygens with at least one hydrogen as H-bond donors. Besides, aliphatic fluorines are acceptors and alinine nitrogen are neither donors nor acceptors (Lipinski *et al*., 2001). The Ghose filter (Amgen) describes small molecules stationed on 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 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) [52, 53]. Veber filter (GSK filter) model symbolize molecules as 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) [54]. Egan filter (Pharmacia filter) anticipates drug absorption depend on processes involved in membrane permeability of a small molecule. These model symbolizes molecule 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 molecule accounts for active transport and efflux mechanisms and is therefore robust in predicting absorption of drugs (Egan *et al*., 2000) [34]. Muegge filter (Bayer filter) is a self-reliant Pharmacophore point filter that segregates drug like and non-drug like molecules. These model symbolizes molecule as a drug like if they have molecular weight between 200 to 600 Da, XLOGP between -2 and 5, TPSA ≤ 150, Number of rings ≤ 7, 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 probability of a compound to have F>10% based on the predominant charge at biological pH in a rat model. It focusses on fast screening of chemical libraries to select best molecules to be synthesized (Martin, 2005) [56].

2.8 Medicinal chemistry

The aim of these section is to bolster medicinal chemists in their daily drug discovery endeavours. PAINS (Pan Assay Interference Compounds or frequent hitters or promiscuous compounds) are the molecules which shows 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. SwissADME returns warnings if such moieties are found in the molecule under evaluation (Baell & Holloway, 2010) [57]. In other model, Brenk considers compounds that are smaller and less hydrophobic and not those defined by "Lipinski's rule of 5" to widen opportunities for lead optimization. This was after 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 designed to provide leads with tremendous affinity in high throughput screening (HTS) that avow for 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 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) [58, 59].

3. Results

Table 1: General Characteristics of Phytoconstituents of *Butea Monosperma* Lam.

Sl. No	Small molecule	Pubchem ID	Molecular formula	Canonical SMILES	Molecular weight (in g/mol)
1	Butrin	164630	$C_{27}H_{32}O_{15}$	C1C(OC2=C(C1=O)C=CC(=C2)OC3C(C(C(C(O3)CO)O)O)O)C4=CC(=C(C=C4)O)OC5C(C(C(C(O5)CO)O)O)O	596.53

2	Isobutrin	5281256	$C_{27}H_{32}O_{15}$	C1=CC(=C(C=C1C=CC(=O)C2=C(C=C(C=C2)OC3C(C(C(O3)CO)O)O)O)O)OC4C(C(C(C(O4)CO)O)O)O)O	596.53
3	Coreopsin	12303942	$C_{21}H_{22}O_{10}$	C1=CC(=C(C=C1C=CC(=O)C2=C(C=C(C=C2)OC3C(C(C(O3)CO)O)O)O)O)O)O	434.39
4	Isocoreopsin	12309899	$C_{21}H_{22}O_{10}$	C1C(OC2=C(C1=O)C=CC(=C2)OC3C(C(C(O3)CO)O)O)O)C4=CC(=C(C=C4)O)O	434.39
5	Monospermoside	42607524	$C_{21}H_{22}O_{10}$	C1=CC(=C(C=C1C=CC(=O)C2=C(C=C(C=C2)O)O)OC3C(C(C(O3)CO)O)O)O)O	434.39
6	Isomonospermoside	42607822	$C_{21}H_{22}O_{10}$	C1C(OC2=C(C1=O)C=CC(=C2)O)C3=CC(=C(C=C3)O)OC4C(C(C(O4)CO)O)O)O	434.39
7	Palasitrin	42607742	$C_{27}H_{30}O_{15}$	C1=CC(=C(C=C1C=C2C(=O)C3=C(O2)C=C(C=C3)OC4C(C(C(O4)CO)O)O)O)OC5C(C(C(C(O5)CO)O)O)O)O	594.52
8	Myricyl alcohol	68972	$C_{30}H_{62}O$	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCO	438.81
9	Pyrocatechin	289	$C_6H_6O_2$	C1=CC=C(C(=C1)O)O	110.11
10	Jalaric ester I	101277336	$C_{31}H_{48}O_7$	CC1(C2CCC(C23CC1C(=CC3OC(=O)CCCCCCCC=CCCCCCCO)C(=O)O)C=O)CO	532.71
11	Jalaric ester II	102239795	$C_{31}H_{50}O_9$	CC1(C2CCC(C23CC1C(=CC3OC(=O)CCCCCCCC(C(CCCCCCO)O)O)C(=O)O)C=O)CO	566.72
12	α-amyrin	73170	$C_{30}H_{50}O$	CC1CCC2(CCC3(C(=CCC4C3(CCC5C4(CCC(C5(C)C)O)C)C)C2C1C)C)C	426.72
13	Nonacosanoic acid	20245	$C_{29}H_{58}O_2$	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCC(=O)O	438.77
14	Stearic acid	5281	$C_{18}H_{36}O_2$	CCCCCCCCCCCCCCCCCC(=O)O	284.48
15	Palmitic acid	985	$C_{16}H_{32}O_2$	CCCCCCCCCCCCCCCC(=O)O	256.42
16	Arachidic acid	10467	$C_{20}H_{40}O_2$	CCCCCCCCCCCCCCCCCCCC(=O)O	312.53
17	Lignoceric acid	11197	$C_{24}H_{48}O_2$	CCCCCCCCCCCCCCCCCCCCCCCC(=O)O	368.64
18	Oleic acid	445639	$C_{18}H_{34}O_2$	CCCCCCCCC=CCCCCCCCC(=O)O	282.46
19	Linoleic acid	5280450	$C_{18}H_{32}O_2$	CCCCCC=CCC=CCCCCCCCC(=O)O	280.45
20	Allophanic acid	150833	$C_2H_4N_2O_3$	C(=O)(N)NC(=O)O	104.07
21	Butolic acid	5312870	$C_{14}H_{28}O_3$	CCCCCCCCC(CCCCC(=O)O)O	244.37
22	Shellolic acid	20055026	$C_{15}H_{20}O_6$	CC1(C2CCC(C23CC1C(=CC3O)C(=O)O)C(=O)O)CO	296.31
23	Gallic acid	370	$C_7H_6O_5$	C1=C(C=C(C(=C1O)O)O)C(=O)O	170.12
24	Cyanidin	128861	$C_{15}H_{11}O_6^+$	C1=CC(=C(C=C1C2=[O+]C3=CC(=CC(=C3C=C2O)O)O)O)O	287.24
25	Lupenone	92158	$C_{30}H_{48}O$	CC(=C)C1CCC2(C1C3CCC4C5(CCC(=O)C(C5CCC4(C3(CC2)C)C)(C)C)C)C	424.70
26	Lupeol	259846	$C_{30}H_{50}O$	CC(=C)C1CCC2(C1C3CCC4C5(CCC(C(C5CCC4(C3(CC2)C)C)(C)C)O)C)C	426.72
27	(-) -Medicarpin	336327	$C_{16}H_{14}O_4$	COC1=CC2=C(C=C1)C3COC4=C(C3O2)C=CC(=C4)O	270.28
28	Miroestrol	165001	$C_{20}H_{22}O_6$	CC1(C2CC3(CC(=O)C(C2C3O)(C4=COC5=C(C41)C=CC(=C5)O)O)O)O)C	358.39
29	3,9-dimethoxypterocarpan	101795	$C_{17}H_{16}O_4$	COC1=CC2=C(C=C1)C3COC4=C(C3O2)C=CC(=C4)OC	284.31
30	β-Sitosterone	9801811	$C_{29}H_{48}O$	CCC(CCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(=O)C4)C)C)C(C)C	412.69
31	n-heneicosanoic acid	16898	$C_{21}H_{42}O_2$	CCCCCCCCCCCCCCCCCCCCC(=O)O	326.56

Table 2: Lipophilicity of the Phytoconstituents of *Butea monosperma* Lam.

Sl. No.	Small molecule	iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log $P_{o/w}$
1	Butrin	1.72	-1.67	-2.87	-3.50	-2.23	-1.71
2	Isobutrin	1.88	-0.79	-2.76	-3.58	-2.11	-1.47
3	Coreopsin	1.83	1.02	-0.23	-1.50	-0.05	0.21
4	Isocoreopsin	2.08	0.14	-0.34	-1.42	-0.11	0.07
5	Monospermoside	1.66	1.02	-0.23	-1.50	-0.05	0.18
6	Isomonospermoside	1.77	0.14	-0.34	-1.42	-0.11	0.01
7	Palasitrin	2.14	-1.08	-2.74	-3.58	-1.96	-1.44
8	Myricyl alcohol	7.67	14.70	10.92	7.46	11.84	10.52
9	Pyrocatechin	1.13	0.88	1.10	0.79	0.94	0.97
10	Jalaric esters I	4.38	5.30	5.38	3.26	6.51	4.97
11	Jalaric esters II	4.08	3.17	3.55	1.78	5.17	3.55
12	α-amyrin	4.77	9.01	8.02	6.92	6.52	7.05
13	Nonacosanoic acid	6.87	14.16	10.62	7.01	10.98	9.93
14	Stearic acid	4.30	8.23	6.33	4.67	6.13	5.93
15	Palmitic acid	3.85	7.17	5.55	4.19	5.25	5.20
16	Arachidic acid	4.56	9.29	7.11	5.13	7.01	6.62
17	Lignoceric acid	5.62	11.46	8.67	6.00	8.77	8.10
18	Oleic acid	4.27	7.64	6.11	4.57	5.95	5.71
19	Linoleic acid	4.14	6.98	5.88	4.47	5.77	5.45
20	Allophanic acid	-0.63	-0.07	-0.67	-1.53	-1.71	-0.92
21	Butolic acid	3.31	4.14	3.74	2.81	3.65	3.53
22	Shellolic acid	0.98	-0.02	0.49	0.79	0.23	0.49

23	Gallic acid	0.21	0.70	0.50	-0.16	-0.20	0.21
24	Cyanidin	-2.59	1.94	2.91	0.32	0.24	0.56
25	Lupenone	4.54	9.56	8.23	6.82	7.41	7.31
26	Lupeol	4.89	9.87	8.02	6.92	6.82	7.31
27	(-)- medicarpin	2.54	2.77	2.69	1.87	2.75	2.52
28	Miroestrol	1.66	0.19	1.22	0.71	1.42	1.04
29	3,9-dimethoxypterocarpan	3.25	3.09	2.99	2.11	3.27	2.94
30	β-Sitosterone	4.70	8.98	8.23	6.62	7.63	7.23
31	n-heneicosanoic acid	4.78	9.83	7.50	5.36	7.45	6.98

Table 3: Water solubility of the Phytoconstituents of *Butea monosperma* Lam

Small molecule	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	
Butrin	-2.24	3.47e+00	5.81e-03	Soluble	-2.97	6.40e-01	1.07e-03	Soluble	0.09	7.27e+02	1.22e+00	Soluble
Isobutrin	-2.66	1.31e+00	2.20e-03	Soluble	-4.11	4.59e-02	7.70e-05	Moderately soluble	0.85	4.23e+03	7.10e+00	Soluble
Coreopsin	-3.07	3.73e-01	8.58e-04	Soluble	-4.33	2.03e-02	4.68e-05	Moderately soluble	-0.94	4.98e+01	1.15e-01	Soluble
Isocoreopsin	-2.64	9.86e-01	2.27e-03	Soluble	-3.19	2.83e-01	6.53e-04	Soluble	-1.71	8.55e+00	1.97e-02	Soluble
Monospermoside	-3.07	3.73e-01	8.58e-04	Soluble	-4.33	2.03e-02	4.68e-05	Moderately soluble	-0.94	4.98e+01	1.15e-01	Soluble
Isomonospermoside	-2.64	9.86e-01	2.27e-03	Soluble	-3.19	2.83e-01	6.53e-04	Soluble	-1.71	8.55e+00	1.97e-02	Soluble
Palasitrin	-2.60	1.51e+00	2.54e-03	Soluble	-3.58	1.56e-01	2.62e-04	Soluble	0.10	7.52e+02	1.26e+00	Soluble
Myricyl alcohol	-9.97	4.66e-08	1.06e-10	Poorly soluble	-15.23	2.58e-13	5.89e-16	Insoluble	-11.32	2.11e-09	4.82e-12	Insoluble
Pyrocatechin	-1.63	2.57e+00	2.33e-02	Very soluble	-1.31	5.34e+00	4.85e-02	Very soluble	-1.18	7.21e+00	6.55e-02	Soluble
Jalaric esters I	-5.23	3.15e-03	5.92e-06	Moderately soluble	-7.59	1.35e-05	2.54e-08	Poorly soluble	-5.52	1.59e-03	2.99e-06	Moderately soluble
Jalaric esters II	-4.03	5.28e-02	9.32e-05	Moderately soluble	-6.23	3.31e-04	5.83e-07	Poorly soluble	-4.34	2.60e-02	4.58e-05	Moderately soluble
α-amyrin	-8.16	2.94e-06	6.89e-09	Poorly soluble	-9.33	2.02e-07	4.72e-10	Poorly soluble	-6.71	8.23e-05	1.93e-07	Poorly soluble
Nonacosanoic acid	-9.70	8.77e-08	2.00e-10	Poorly soluble	-15.03	4.11e-13	9.37e-16	Insoluble	-10.46	1.54e-08	3.50e-11	Insoluble
Stearic acid	-5.73	5.26e-04	1.85e-06	Moderately soluble	-8.87	3.80e-07	1.33e-09	Poorly soluble	-6.11	2.19e-04	7.71e-07	Poorly soluble
Palmitic acid	-5.02	2.43e-03	9.49e-06	Moderately soluble	-7.77	4.31e-06	1.68e-08	Poorly soluble	-5.31	1.25e-03	4.88e-06	Moderately soluble
Arachidic acid	-6.44	1.13e-04	3.61e-07	Poorly soluble	-9.97	3.31e-08	1.06e-10	Poorly soluble	-6.91	3.84e-05	1.23e-07	Poorly soluble
Lignoceric acid	-7.89	4.71e-06	1.28e-08	Poorly soluble	-12.23	2.19e-10	5.94e-13	Insoluble	-8.49	1.18e-06	3.21e-09	Poorly soluble
Oleic acid	-5.41	1.09e-03	3.85e-06	Moderately soluble	-8.26	1.54e-06	5.46e-09	Poorly soluble	-5.39	1.14e-03	4.04e-06	Moderately soluble
Linoleic acid	-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
Allophanic acid	-0.31	5.11e+01	4.91e-01	Very soluble	-1.42	3.96e+00	3.81e-02	Very soluble	1.18	1.56e+03	1.50e+01	Soluble
Butolic acid	-3.17	1.65e-01	6.74e-04	Soluble	-5.06	2.15e-03	8.80e-06	Moderately soluble	-3.57	6.53e-02	2.67e-04	Soluble
Shellolic acid	-1.47	1.01e+01	3.42e-02	Very soluble	-1.95	3.35e+00	1.13e-02	Very soluble	-0.12	2.27e+02	7.67e-01	Soluble
Gallic acid	-1.64	3.90e+00	2.29e-02	Very soluble	-2.34	7.86e-01	4.62e-03	Soluble	-0.04	1.55e+02	9.10e-01	Soluble
Cyanidin	-3.34	1.31e-01	4.56e-04	Soluble	-3.96	3.12e-02	1.09e-04	Soluble	-2.66	6.34e-01	2.21e-03	Soluble
Lupenone	-8.43	1.58e-06	3.72e-09	Poorly soluble	-9.83	6.28e-08	1.48e-10	Poorly soluble	-7.44	1.54e-05	3.63e-08	Poorly soluble
Lupeol	-8.64	9.83e-07	2.30e-09	Poorly soluble	-10.22	2.58e-08	6.05e-11	Insoluble	-6.74	7.69e-05	1.80e-07	Poorly soluble
(-)- medicarpin	-3.64	6.21e-02	2.30e-04	Soluble	-3.43	1.00e-01	3.70e-04	Soluble	-4.31	1.32e-02	4.90e-05	Moderately soluble
Miroestrol	-2.35	1.59e+00	4.44e-03	Soluble	-2.00	3.58e+00	1.00e-02	Very soluble	-2.57	9.62e-01	2.69e-03	Soluble
3,9-dimethoxypterocarpan	-3.84	4.11e-02	1.44e-04	Soluble	-3.53	8.33e-02	2.93e-04	Soluble	-5.01	2.79e-03	9.82e-06	Moderately soluble
β-Sitosterone	-7.66	9.03e-06	2.19e-08	Poorly soluble	-9.23	2.44e-07	5.91e-10	Poorly soluble	-6.88	5.39e-05	1.31e-07	Poorly soluble
n-heneicosanoic acid	-6.80	5.13e-05	1.57e-07	Poorly soluble	-10.54	9.53e-09	2.92e-11	Insoluble	-7.31	1.61e-05	4.93e-08	Poorly soluble

Table 4: Pharmacokinetic Parameters of the Phytoconstituents of *Butea monosperma* Lam

Small molecule	GI absorption	BBB permeantt	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log K_p (cm/s)
Butrin	Low	No	No	No	No	No	No	No	-11.12
Isobutrin	Low	No	No	No	No	No	No	No	-10.50
Coreopsin	Low	No	Yes	No	No	No	No	No	-8.23
Isocoreopsin	Low	No	Yes	No	No	No	No	No	-8.85
Monospermoside	Low	No	Yes	No	No	No	No	No	-8.23
Isomonospermoside	Low	No	Yes	No	No	No	No	No	-8.85
Palasitrin	Low	No	Yes	No	No	No	No	No	-10.69
Myricyl alcohol	Low	No	Yes	No	No	No	No	No	1.46
Pyrocatechin	High	Yes	No	No	No	No	No	Yes	-6.35
Jalaric esters I	Low	No	Yes	No	Yes	No	No	Yes	-5.79
Jalaric esters II	Low	No	No	No	Yes	No	No	Yes	-7.51
α-amyrin	Low	No	No	No	No	No	No	No	-2.51
Nonacosanoic acid	Low	No	Yes	No	No	No	No	No	1.08
Stearic acid	High	No	No	Yes	No	No	No	No	-2.19
Palmitic acid	High	Yes	No	Yes	No	Yes	No	No	-2.77
Arachidic acid	Low	No	No	Yes	No	No	No	No	-1.61
Lignoceric acid	Low	No	No	Yes	No	No	No	No	-0.41
Oleic acid	High	No	No	Yes	No	Yes	No	No	-2.60
Linoleic acid	High	Yes	No	Yes	No	Yes	No	No	-3.05
Allophanic acid	High	No	No	No	No	No	No	No	-6.98
Butolic acid	High	Yes	No	No	No	No	Yes	No	-4.85
Shellolic acid	High	No	Yes	No	No	No	Yes	No	-8.12
Gallic acid	High	No	No	No	No	No	No	Yes	-6.84
Cyanidin	High	No	Yes	Yes	No	No	No	No	-6.67
Lupenone	Low	No	No	No	No	No	No	No	-2.10
Lupeol	Low	No	No	No	No	No	No	No	-2.10
(-)- medicarpin	High	Yes	Yes	Yes	Yes	No	Yes	Yes	-5.98
Miroestrol	High	No	Yes	No	No	No	No	No	-8.35
3,9-dimethoxypterocarpan	High	Yes	Yes	Yes	Yes	No	Yes	Yes	-5.84
β-Sitosterone	Low	No	No	No	No	No	No	No	-2.44
n-heneicosanoic acid	Low	No	No	Yes	No	No	No	No	-1.31

Table 5: Drug likeness of the Phytoconstituents of *Butea monosperma* Lam

Small molecule	Lipinski	Veber	Egan	Muegge	Bioavailability score
Butrin	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: TPSA>150, H-acc>10, H-don>5	0.17
Isobutrin	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: TPSA>150, H-acc>10, H-don>5	0.17
Coreopsin	Yes; 1 violation: NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, H-don>5	0.55
Isocoreopsin	Yes; 1 violation: NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, H-don>5	0.55
Monospermoside	Yes; 1 violation: NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, H-don>5	0.55
Isomonospermoside	Yes; 1 violation: NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, H-don>5	0.55
Palasitrin	No; 3 violations: MW>500, NorO>10, NHorOH>5	No; 1 violation: TPSA>140	No; 1 violation: TPSA>131.6	No; 3 violations: TPSA>150, H-acc>10, H-don>5	0.17
Myricyl alcohol	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 3 violations: XLOGP3>5, Heteroatoms<2, Rotors>15	0.55
Pyrocatechin	Yes; 0 violation	Yes	Yes	No; 1 violation: MW<200	0.55
Jalaric esters I	Yes; 1 violation: MW>500	No; 1 violation: Rotors>10	Yes	No; 2 violations: XLOGP3>5, Rotors>15	0.56
Jalaric esters II	Yes; 1 violation: MW>500	No; 2 violations: Rotors>10, TPSA>140	No; 1 violation: TPSA>131.6	No; 2 violations: TPSA>150, Rotors>15	0.11
α-amyrin	Yes; 1 violation: MLOGP>4.15	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Nonacosanoic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Rotors>15	0.56
Stearic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Rotors>15	0.56
Palmitic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	Yes	No; 1 violation: XLOGP3>5	0.56

Arachidic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Rotors>15	0.56
Lignoceric acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Rotors>15	0.56
Oleic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 1 violation: XLOGP3>5	0.56
Linoleic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 1 violation: XLOGP3>5	0.56
Allophanic acid	Yes; 0 violation	Yes	Yes	No; 2 violations: MW<200, #C<5	0.56
Butolic acid	Yes; 0 violation	No; 1 violation: Rotors>10	Yes	Yes	0.56
Shellolic acid	Yes; 0 violation	Yes	Yes	Yes	0.56
Gallic acid	Yes; 0 violation	Yes	Yes	No; 1 violation: MW<200	0.56
Cyanidin	Yes; 0 violation	Yes	Yes	Yes	0.55
Lupenone	Yes; 1 violation: MLOGP>4.15	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Lupeol	Yes; 1 violation: MLOGP>4.15	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
(-)- medicarpin	Yes; 0 violation	Yes	Yes	Yes	0.55
Miroestrol	Yes; 0 violation	Yes	Yes	Yes	0.55
3,9-dimethoxypterocarpan	Yes; 0 violation	Yes	Yes	Yes	0.55
β-Sitosterone	Yes; 1 violation: MLOGP>4.15	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
n-heneicosanoic acid	Yes; 1 violation: MLOGP>4.15	No; 1 violation: Rotors>10	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Rotors>15	0.56

Table 6: Medicinal Chemistry Properties of Phytoconstituents of *Butea monosperma* Lam

Sl. No.	Small molecule	Pains	Brenk	Leadlikeness	Synthetic accessibility
1	Butrin	0 alert	0 alert	No; 1 violation: MW>350	6.22
2	Isobutrin	0 alert	1 alert: michael_acceptor_1	No; 2 violations: MW>350, Rotors>7	6.23
3	Coreopsin	1 alert: catechol_A	2 alerts: catechol, michael_acceptor_1	No; 1 violation: MW>350	4.98
4	Isocoreopsin	1 alert: catechol_A	1 alert: catechol	No; 1 violation: MW>350	5.00
5	Monospermoside	0 alert	1 alert: michael_acceptor_1	No; 1 violation: MW>350	4.96
6	Isomonospermoside	0 alert	0 alert	No; 1 violation: MW>350	5.03
7	Palasitrin	0 alert	1 alert: michael_acceptor_1	No; 1 violation: MW>350	6.29
8	Myricyl alcohol	0 alert	0 alert	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	3.97
9	Pyrocatechin	1 alert: catechol_A	1 alert: catechol	No; 1 violation: MW<250	1.00
10	Jalaric esters I	0 alert	2 alerts: aldehyde, isolated_alkene	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	7.42
11	Jalaric esters II	0 alert	1 alert: aldehyde	No; 2 violations: MW>350, Rotors>7	7.76
12	α-amyrin	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	6.17
13	Nonacosanoic acid	0 alert	0 alert	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	3.86
14	Stearic acid	0 alert	0 alert	No; 2 violations: Rotors>7, XLOGP3>3.5	2.54
15	Palmitic acid	0 alert	0 alert	No; 2 violations: Rotors>7, XLOGP3>3.5	2.31
16	Arachidic acid	0 alert	0 alert	No; 2 violations: Rotors>7, XLOGP3>3.5	2.77
17	Lignoceric acid	0 alert	0 alert	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	3.24
18	Oleic acid	0 alert	1 alert: isolated_alkene	No; 2 violations: Rotors>7, XLOGP3>3.5	3.07
19	Linoleic acid	0 alert	1 alert: isolated_alkene	No; 2 violations: Rotors>7, XLOGP3>3.5	3.10
20	Allophanic acid	0 alert	0 alert	No; 1 violation: MW<250	1.27
21	Butolic acid	0 alert	0 alert	No; 3 violations: MW<250, Rotors>7, XLOGP3>3.5	2.58
22	Shellolic acid	0 alert	0 alert	Yes	5.72
23	Gallic acid	1 alert: catechol_A	1 alert: catechol	No; 1 violation: MW<250	1.22
24	Cyanidin	1 alert:	2 alerts: catechol,	Yes	3.15

		catechol_A	charged_oxygen_sulfur		
25	Lupenone	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	5.38
26	Lupeol	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	5.49
27	(-)- medicarpin	0 alert	0 alert	Yes	3.54
28	Miroestrol	0 alert	0 alert	No; 1 violation: MW>350	5.29
29	3,9-dimethoxypterocarpan	0 alert	0 alert	Yes	3.64
30	β-Sitosterone	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	6.33
31	n-heneicosanoic acid	0 alert	0 alert	No; 2 violations: Rotors>7, XLOGP3>3.5	2.88

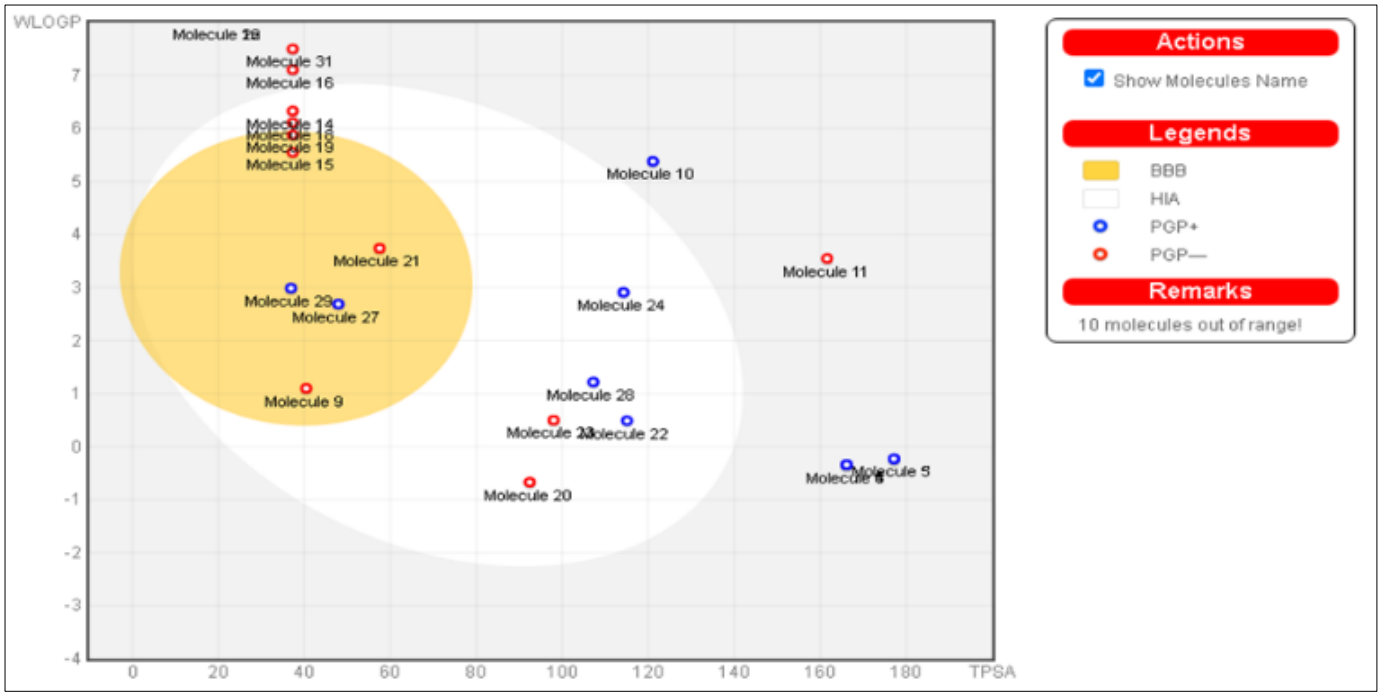

Fig 1: Boiled Egg Model of the Phytoconstituents of *Butea monosperma* Lam

4. Discussion

Ayurveda is one of the earliest system of medicine providing extensive leads to discover the effective and therapeutically useful compounds for drug development from herbs, currently the use of herbal medicine is widespread in both developing and developed countries due to its checked adverse effects and from its natural source (Ekor, 2013) [60]. World Health Organization reports over 30% of all plant species have at one time or another used for medicinal purposes (Schippmann *et al*, 2002) [61]. Currently, due to continuous advancement in computer science, lot of successful findings drugs from natural products using computer aided drug design methods for example the development of Dazamide, Imatinib, Dasatinib and Ponatinib etc. (Ghosh AK, Gemma, 2015) [62].

Computer based drug designing has been employed in the prediction of ADMET properties of the drugs which leads to budding stage drug discovery (Lipinski *et al*. 1997; Lombardo *et al*, 2003; Gleeson *et al*, 2011) [63, 64, 65]. The rationale behind these insilico approaches are due to relatively lower cost time factor involved compared to standard ADMET profiling (DiMasi *et al*. 2003; Darvas *et al*, 2002) [66, 67]. As an example, it takes a minute in an in silico model to screen 20,000 molecules, but takes 20 weeks in the "wet" laboratory to do the same exercise (Hodgson 2001) [68]. Due to the accumulated ADMET data in the late 1990s, many pharmaceutical companies are now using computational models that, in some cases, are replacing the "wet" screens (Hodgson 2001) [68]. This paradigm shift has therefore spurred up the development of several theoretical methods for the prediction of ADMET parameters. A host of these theoretical models have been implemented in a number of software programs currently available for drug discovery protocols (OCHEM platform 2009; Lhasa 2010; Schrodinger 2011a; Cruciani *et al*, 2000) [69, 70, 71, 72], even though some of the predictions are often disappointing (Tetko *et al*, 2006) [73]. The software tools currently used to predict the ADMET properties of potential drug candidates often make use of quantitative structure-activity relationships, QSAR (Tetko *et al*, 2006; Hansch *et al*, 2004) [73, 74] or knowledge-base methods (Greene *et al*. 1999; Button *et al*. 2003; Cronin 2003) [75, 76, 77].

In the present study we used SwissADME online software tool which is available free for the users to evaluate the ADME properties of Butea monosperma Lam respectively. The phytoconstituents of the plants were enlisted through the software includes, Isobutrin, Coreopsin, Isocoreopsin, Monospermoside, Isomonospermoside, Jalaric ester I, Jalaric ester II, α-amyrin, β-Sitosterone, n-heneicosanoic acid, Pyrocatechin, Gallic acid, 3,9-dimethoxypterocarpan, Stearic acid, Arachidic acid, Myricyl alcohol, Palmitic acid, Lignoceric acid, Oleic acid, Linoleic acid, Allophanic acid, Butolic acid, Shellolic acid, Butrin, Cyanidin, Lupenone, Lupeol, (-)- medicarpin, Miroestrol, Palasitrin and Nonacosanoic acid (Gupta *et al*, 1970, Rastogi and Mehrotra,

1979; Singh *et al*, 1974, Nadkarni, 2002, Shukla *et al*, 2002, Murti *et al*, 1940 and Mishra *et al*, 2000, Barua *et al*, 1970, Ghosh *et al*, 1981, Guha *et al*, 1990, Gunakkunru *et al*, 2005, Gupta *et al*, 1970a, Gupta *et al*, 1970b, Mehta and Bokadia, 1981) [78]. Accordingly the phytoconstituents were analyzed for ADME properties and depicted in respected tables and figures. Further, the values can be used as monographs by researchers and scientists for development of potential semisynthetic and synthetic drugs for multifarious usage.

5. Conclusion

With the rapid increase in biological and chemical information, CADD has been dramatically reshaping research and development pathways in drug candidate identification. Use of computational techniques in drug discovery and development process is widely appreciated in terms of implementation, time and money. A freely available SwissADME, a web based tool is presented in these study to evaluate the ADME properties of phytoconstituents present in Butea monosperma Lam plant. These information can be used as a primary tool for further evaluating the biological and pharmacological properties of the plant.

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