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Swiss ADME Predictions of Pharmacokinetics and Drug-Likeness Properties of Chemical Constituents Present in Embelia Ribes

Miss. Tasmeem T. Shaikh, Dr. Rahul S. Adnaik, Miss. Neha B. Patil

Anandi Pharmacy College Kalambe Tarf kale, Kolhapur, India.

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ABSTRACT

Early on in the drug development process, choosing possible candidates can be aided by forecasting the absorption, distribution, metabolism, and excretion (ADME) profiles of drug candidates prior to their synthesis. To aid in the creation of novel medications, it is necessary to obtain reliable data on the pharmacokinetic properties of a molecule as quickly as possible, which ultimately determines the success or failure of the compound. With advances in computer science, in silico methods such as network analysis and screening are increasingly being used to gain insight into the pharmacological mechanisms of action of plants. Embelia ribes Burm. f. known as Vidanga or Baibidanga in Ayurvedic medicine is a rare medicinal plant studied extensively for its diverse medicinal characteristics. The present study aims to predict the in vitro ADME study (Absorption, Distribution, Metabolism, and Excretion) properties of Embelia Ribes Burm using the freely available web tool Swiss ADME. The results of these studies can be used by researchers to conduct in vitro and in vivo studies to uncover the pharmacological mechanisms of action of traditional medicinal herbs. A straightforward, reliable, and precise technique for comprehending the ADME characteristics of the substances found in Embelia ribes is Swiss ADME.

Keywords: Embeila Ribes, Vilangin, Anti- Inflammatory, Swiss ADME, Lipinki's rule of five.

1. INTRODUCTION:

Embelia ribes Burm. f. also known as Vidanga or Baibidanga[25] in Ayurvedic medicine, is a member of the Myrsinaceae family, which grows in hilly areas of India up to 1500 meters in elevation, from the outer Himalayas to the Western Ghats[1]. Embelia ribes Burm F. is a large scandent shrub, commonly known as false black pepper and White flowered[26]. Embelia Leaves are obtusely acuminate, base cuneate or rhomboid about 7.5 by 3 cm in size, nerve slender flowers are 0.2 cm long and are white ovary ovoid not conic upward. Fruits are globular of different colours from dull red to nearly black warty or wrinkled, and about 2-4 mm in diameter[2]. The stem is 45-72cm whitish grey, stubbed with lenticels, and the roots are brownish gray[3]. The Medicinal Board, Government of India, New Delhi, has determined that E. ribes is significant for large-scale cultivation due to its commercial application [3,25]. Vidanga is reported to be used in Unani (Baobarang), Siddha (Vaivilangam), Folk, Tibetan (Byi dan ga), and Homeopathic (Embelia ribes) systems of medicines and the major system employing E.ribes and its constituents is the ancient Ayurveda[4]. E. ribes has many traditional uses in health care purposes as useful in a wide range of skin diseases as it detoxifies the blood, is used to treat vomiting, bloating, indigestion, gastritis, and constipation, to relieve dental caries and bad breath, has contraceptive effects and widely used in weight loss process[4]. Carminative, anti-malignant, diuretic (fruit, for example), anthelmintic (seeds, for example), antibacterial, and neuroprotective (leaves, root bark) are some of the most often reported effects from traditional applications [5]. E. ribes demonstrate a range of biological effects, some of which include its anti-tumor, antioxidation, and anti-inflammatory capabilities, according to pharmacological examinations[5]. The whole plant diagnoses rheumatism, fever, abdominal and lung illnesses, constipation, indigestion, fungal infections, mouth ulcers, sore throats, pneumonia, heart disease, and obesity. The fruit is a good appetizer to cure tumors, ascites, bronchitis, jaundice, and mental illnesses[1]. The leaves of E. ribes possess properties like astringent, demulcent, and depurative, and are used to cure pruritus, sore throats, mouth ulcers, skin disorders, and leprosy[1]. *Embelia ribes* fruits contain various chemical constituents like a quinone derivative embelin (3-undecyl 2, 5- dihydroxy, 1,4-benzoquinone), an alkaloid christembine and a volatile oil vilangin; its chemical constituents 2,5-dihydroxy-4-undecyl-3,6-benzoquinone. The major fruit constituents are embelic acid, tannins, christembine, embelin, vilangin, 2, 5-isobutylamine salts, quercetol, and volatile oil[2]. SwissADME is one of the newest and largest websites managed by the Swiss Institute of Bioinformatics (SIB), aiming to promote bioinformatics services and resources to scientists around the world[21]. It promotes the evaluation of ADME parameters of drug applicants and molecules and gives records that acquiesce antecedent uncertainty dedication with inside the drug discovery process, it's far the podium to decide Lipinski`s rule of five[27].

2.1 Material and Methods:

Swiss ADME: The Swiss Institute Bioinformatics, developed the Swiss ADME software which was assessed by the website www.swissadme.ch on Google, which was to estimate the individual ADME behaviors of the compounds derived from the Embelia Ribes plant[6]. A simplified molecular input line entry system (SMILES) defines the input list, which consists of many inputs with one input molecule per line. The results for each molecule are shown as tables, graphs, and an Excel spreadsheet[6,28].

2.2 Structure and bioavailability radar: The two-dimensional chemical structure with canonical SMILES is present in the first section to assess the drug-likeness of the molecules of interest. The six different physicochemical properties like lipophilicity. (LIPO), size (SIZE), polarity (POLAR), insolubility (INSOLU), insaturation (INSATU), and flexibility (FLEX) were taken into consideration by the bioavailability rader[29]. The following criteria were considered: polarity should have a topological polar surface area (TPSA) between 20 and 130 0A2, solubility: log S not greater than 6, saturation: fraction of carbons in the sp hybridization not less than 0.25, flexibility: no more than 9 rotatable bonds, and lipophilicity should have an XLOGP3 value between -0.7 and +5.0 [7].

2.3 Physicochemical properties: The following criteria were considered: polarity should have a topological polar surface area (TPSA) between 20 and 130 0A2, solubility: log S not greater than 6, saturation: fraction of carbons in the sp hybridization not less than 0.25, flexibility: no more than 9 rotatable bonds, and lipophilicity should have an XLOGP3 value between -0.7 and +5.0 [7,30,10].

2.4 Lipophilicity: As it complements the most informative and instructive physicochemical property in medicinal chemistry[16], Lipophilicity is considered an Important parameter in drug discovery and design [11]. It is experimentally demonstrated as partition coefficients (log P) or distribution coefficients (log D). The partition equilibrium of an un-ionized solute between water and an immiscible organic solvent is represented as Log P[31]. Higher log P values correspond to greater lipophilicity [19]. Swiss ADME provides Five freely available models such as XLOGP3, WLOGP, MLOGP, SILICOS-IT, and iLOGP to evaluate the lipophilicity of the compound[32]. XLOGP3 is an atomistic approach that includes corrective factors and a knowledge-based library[8]. WLOGP relies on an atomistic method using a fragmental system[18]. MLOGP is a topological method built on a linear relationship with 13 implemented molecular descriptors [12,13]. SILICOS-IT is a hybrid method based on 27 fragments and 7 topological descriptors. iLOGP is a physics-based method that depends on the free energies of solvation in n-octanol and water calculated by the generalized-born and solvent-accessible surface area (GB/SA) model[7,33]. The arithmetic mean of the data is the consensus log P o/w that the five suggested approaches anticipate [7].

2.5 Solubility: The solvent used, ambient temperature, and pressure have a significant effect on the solubility of a compound[31]. The saturation concentration is the measurement of solubility, which is the point where adding more solute does not affect its concentration[14]. Upon dissolving in 250 mL or less of aqueous media within the pH range of 1 to 7.5, a drug is considered highly soluble. Two topological approaches are used by Swiss ADME to predict water solubility. The initial approach involves utilizing the ESOL model which classifies solubility based on the logarithmic scale (Insoluble<-10, Poorly soluble<-6, Moderately soluble<-4, Soluble<-2, Very soluble<0). Both approaches differ from the fundamental general solubility equation[17] as they do not take into account the melting point parameter. However, the predicted and experimental values have a significant linear correlation (R2=0.69 and 0.81 respectively). SILICOS- IT developed the third predictor for Swiss ADME, which also classifies solubility based on the logarithmic scale (Insoluble<-10, Poorly soluble<- 6, Moderately soluble<-4, Soluble<-2, Very soluble<0), with the linear coefficient being corrected by molecular weight (R2=0.75)[31,32]. Predicted values are displayed in the decimal logarithm of the molar solubility in water (log S). The Swiss ADME offers solubility values in mol/l and mg/ml, as well as qualitative solubility classes[34].

2.6 Pharmacokinetics: A graph depicting two computed descriptors, ALOGP versus PSA, shows a region with favorable properties for gastrointestinal (GI) absorption, which is where the distinction lies. The circular region with the highest concentration of well-absorbed molecules is known as the Egan egg. The egg is utilized to assess the model's ability to predict passive GI absorption and brain[35] access through passive diffusion resulting in the creation of the BOILED-Egg (Brain or Intestina L Estimate D permeation predictive model). Drug research and discovery benefit from the BOILED-Egg model's ability to predict passive GI absorption quickly, spontaneously, effectively, and robustly[15]. The yellow region (the yolk) indicates the space that has the highest chance of penetrating to the brain, while the white region reflects the space filled by molecules that absorb more by the GI tract [7]. More than 50%-90% of therapeutic molecules are biotransformed by CYP isoenzymes, which have five major isoforms (CYP1A2, CYP3A4, CYP2C9, CYP2C 19, CYP2D6). In the intestinal epithelium, P-gp is a major contributor to the pulling of xenobiotics back into the intestinal lumen and back into the capillaries from the capillary endothelial cells of the brain[20,21]. Swiss ADME utilizes the support vector machine algorithm to analyze datasets that have identified substrates /non-substrates or inhibitors / non-inhibitors for bilinary classification. The molecule that emerges will be classified as either 'Yes' or 'No' depending on whether it has the potential to be both P-gp and CYP substrates, as specified. The SVM model designed for P- gp substrates was developed utilizing a training set comprising 1,033 molecules and evaluated on a test set of 415 molecules. The model achieved a 10-fold cross-validation accuracy

of 0.72 and an area under the curve (AUC) of 0.77. The external accuracy and AUCAUC=0.94 respectively. By using a diverse training and test set, Support Vector Machine (SVM) models were created to inhibit Cytochrome P-450 1A2, 2C19, 2C9, 2D6, and 3A4 molecules. The SVM model for the Cytochrome P-450 1A2 inhibitor was created by training on 9145 molecules and then tested on 3000 molecules. An accuracy (ACC) of 0.83 and an area under the curve (AUC) of 0.90 were obtained during the 10-fold cross-validation, and an accuracy of 0.84 and an AUC of 0.9 were obtained during external validation. An SVM model for the Cytochrome P-450 2C19 inhibitor molecule was created by constructing a training set of 9272 molecules and testing it on 3000 molecules. The cross-validation for 10 folds resulted in an ACC of 0.80 and an AUC of 0.86, while the external validation also resulted in an ACC of 0.80 and an AUC of 0.87[36]. A training set of 5940 molecules was used to develop the SVM model for the Cytochrome P- 450 2C9 inhibitor molecule and 2075 molecules were tested on it. The external validation resulted in an ACC of 0.71 and an AUC of 0.81. A 3664 training set and 1068 experiments were used to construct the SVM model for the Cytochrome P-450 2D6 inhibitor molecule. The 10-fold cross-validation revealed that the ACC was 0.79 and the AUC was 0.85. The external validation exhibited an ACC of 0.81 and an AUC of 0.87[36]. Finally, the SVM model was built for the Cytochrome P-450 3A4 inhibitor molecule using a training set of 7518 molecules and tested on 2579 molecules. The cross-validation with 10 folds resulted in an ACC of 0.77 and an AUC of 0.85, while the external validation resulted in an ACC of 0.78 and an AUC of 0.86 [36].

2.7 Medicinal chemistry: This section aims to provide support to medical chemists who strive to discover new drugs daily. PAINS(Pan Assay Interference Compounds or frequent hitters or promiscuous compounds) are molecules that respond strongly to assays, regardless of the protein targets[37]. In different assays, these compounds are active, which makes them a potential starting point for further investigation. The Swiss ADME warns when such moieties are present in the molecule being evaluated[24]. In another approach, Brenk focuses on smaller, less hydrophobic compounds than those identified by the "Lipinski rule of 5," to expand the possibilities for lead optimization. The process involves excluding compounds that have potential mutagenic, reactive, and unfavorable groups like nitro groups, sulfates, phosphates, 2-halo-pyridines, and thiols. The Brenk model restricts the ClogP/ClogD values to between 0 and 4, the number of hydrogen-bond donors to fewer than 4, the number of hydrogen-bond acceptors to fewer than 7, and the number of heavy atoms to between 10 and 27[38]. Furthermore only compounds of limited complexity, defined as having fewer than 8 rotatable bonds, fewer than 5 ring systems, and no ring system with more than 2 fused rings, were considered as drugs[38]. The concept of lead affinity is intended to provide high-affinity leads in high-throughput screening (HTS), thus enabling the investigation of additional interactions during the lead optimization phase[37]. The lead affinity concept is intended to ensure high lead affinity in high- throughput screening (HTS) and to enable the exploration of additional interactions during the lead optimization phase. Lead optimization is usually carried out using a rule-based method Molecules with a molecular weight of 100 to 350 Da and a C log P of 1 to 3.0 are considered superior to drug-like compounds and therefore lead-l.

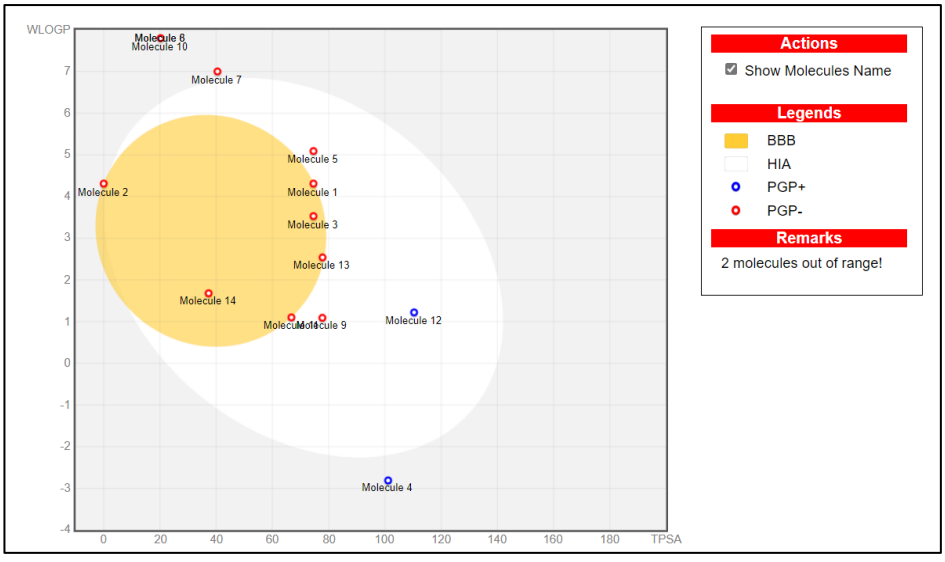

Fig 1: Boiled Egg Model of the Phytoconstituents of *Embelia Ribes Burm.*

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3. Results:

Table 1: General Characteristics of Phytoconstituents of *Embelia Ribes Burm.*

Sr No	Small molecule	Pub chem ID	Molecular formula	Canonical SMILES	Molecular weight (g/mol)
1	Embelin	3218	$C_{17}H_{26}O_4$	CCCCCCCCCCCC1=C(C(=O)C=C(C1=O)O)O	294.4
2	Vilangin	417182	$C_{35}H_{52}O_8$	CCCCCCCCCCCC1=C(C(=O)C(=C(C1=O)O)CC2=C(C(=O)C(=C(C2=O)O)CCCCCCCCCCC)O)O	600.8
3	Daucosterol	5742590	$C_{35}H_{60}O_6$	CC[C@H](CC[C@@H](C)[C@H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CC=C4[C@@]3(CC[C@@H](C4)O[C@H]5[C@@H]([C@H]([C@@H]([C@H](O5)CO)O)O)O)C)C)C(C)C	576.8
4	Homoembelin	4460091	$C_{15}H_{22}O_4$	CCCCCCCCCC1=C(C(=O)C=C(C1=O)O)O	266.33
5	Quercitol	441437	$C_6H_{12}O_5$	C1[C@H]([C@@H](C([C@H]([C@@H]1O)O)O)O)O	164.16
6	Rapanone	100659	$C_{19}H_{30}O_4$	CCCCCCCCCCCCCC1=C(C(=O)C=C(C1=O)O)O	322.4
7	Sitosterol	222284	$C_{29}H_{50}O$	CC[C@H](CC[C@@H](C)[C@H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CC=C4[C@@]3(CC[C@@H](C4)O)C)C)C(C)C	414.7
8	Betulin	72326	$C_{30}H_{50}O_2$	CC(=C)[C@@H]1CC[C@]2([C@H]1[C@H]3CC[C@@H]4[C@]5(CC[C@@H](C([C@@H]5CC[C@]4([C@@]3(CC2)C)C)(C)C)O)C)CO	442.7
9	Taraxasterol	115250	$C_{30}H_{50}O$	C[C@H]1[C@@H]2[C@H]3CC[C@@H]4[C@]5(CC[C@@H](C([C@@H]5CC[C@]4([C@@]3(CC[C@]2(CCC1=C)C)C)C)(C)C)O)C	426.7
10	Caffeic acid	689043	$C_9H_8O_4$	C1=CC(=C(C=C1/C=C/C(=O)O)O)O	180.16
11	Stigmasterol	5280794	$C_{29}H_{48}O$	CC[C@H](/C=C/[C@@H](C)[C@H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CC=C4[C@@]3(CC[C@@H](C4)O)C)C)C(C)C	412.7
12	Vanillic acid	8468	$C_8H_8O_4$	COC1=C(C=CC(=C1)C(=O)O)O	168.15
13	Catechin	9064	$C_{15}H_{14}O_6$	C1[C@@H]([C@H](OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O	290.27
14	Daraprim	4993	$C_{12}H_{13}ClN_4$	CCC1=C(C(=NC(=N1)N)N)C2=CC=C(C=C2)Cl	248.71
15	Cinnamic acid	444539	$C_9H_8O_2$	C1=CC=C(C=C1)/C=C/C(=O)O	148.16

Table 2: Lipophilicity of the Phytoconstituents of *Emelia Ribes Burm*

Sr No	Small Molecules	iLOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	Consensus Log $P_{o/w}$
1	Embelin	3.28	5.42	4.31	1.21	4.15	3.68
2	Vilangin	5.88	10.86	8.77	1.34	9.21	7.21
3	Daucosterol	5.17	7.74	5.85	3.96	5.02	5.55
4	Homoembelin	2.88	4.34	3.53	0.71	3.34	2.96
5	Quercitol	0.77	-2.73	-2.81	-2.35	-2.08	-1.84
6	Rapanone	3.88	6.50	5.09	1.68	4.98	4.43
7	Sitosterol	5.05	9.34	8.02	6.73	7.04	7.24
8	Betulin	4.47	8.28	7.00	6.00	6.21	6.39
9	Taraxasterol	4.68	9.13	8.02	6.92	6.81	7.11
10	Caffeic acid	0.97	1.15	1.09	0.70	0.75	0.93
11	Stigmasterol	5.08	8.56	7.80	6.62	6.86	6.98
12	Vanillic acid	1.40	1.43	1.10	0.74	0.73	1.08
13	Catechin	1.33	0.36	1.22	0.24	0.98	0.83
14	Daraprim	2.15	2.69	2.54	1.64	2.44	2.29
15	Cinnamic acid	1.55	2.13	1.68	1.90	1.70	1.79

Table 3: Water solubility of the phytoconstituents of *Embelia Ribes Burm*

Small Molecules	ESOL				Ali				SILICOS-IT			
	LogS (ESOL)	Solubility		Class	LogS (ALI)	Solubility		Class	LogS (SILICOS-IT)	Solubility		Class
		mg/mL	mol/L			mg/mL	mol/L			mg/mL	mol/L	
Embelin	-4.42	1.12e-02	3.80e-05	Moderately soluble	-6.74	5.33e-05 -	1.81e-07	Poorly soluble	-4.32	1.40e-02	4.75e-05	Moderately soluble
Vilangin	-8.95	6.67e-07	1.11e-09	Poorly soluble	-13.95	6.68e-12	1.11e-14	Insoluble	-9.32	2.86e-07	4.76e-10	Poorly soluble
Daucosterol	-7.70	1.15e-05	2.00e-08	Poorly soluble	-9.67	1.23e-07	2.14e-10	Poorly soluble	-4.40	2.28e-02	3.94e-05	Moderately soluble
Homoembelin	-3.70	5.35e-02	2.01e-04	Soluble	-5.62	6.37e-04	2.39e-06	Moderately soluble	-3.52	7.99e-02	3.00e-04	Soluble
Quercitol	0.86	1.20e+03	7.28e+00	Highly soluble	1.16	2.36e+03	1.44e+01	Highly soluble	2.49	5.06e+04	3.08e+02	Soluble
Rapanone	-5.14	2.32e-03	7.21e-06	Moderately soluble	-7.86	4.42e-06	1.37e-08	Poorly soluble	-5.12	2.45e-03	7.60e-06	Moderately soluble
Sitosterol	-7.90	5.23e-06	1.26e-08	Poorly soluble	-9.67	8.90e-08	2.15e-10	Poorly soluble	-6.19	2.69e-04	6.49e-07	Poorly soluble
Betulin	-7.67	9.48e-06	2.14e-08	Poorly soluble	-8.99	4.50e-07	1.02e-09	Poorly soluble	-6.17	2.99e-04	6.75e-07	Poorly soluble
Taraxasterol	-8.24	2.47e-06	5.79e-09	Poorly soluble	-9.45	1.51e-07	3.55e-10	Poorly soluble	-6.96	4.65e-05	1.09e-07	Poorly soluble
Caffeic acid	-1.89	2.32e+00	1.29e-02	Very soluble	-2.38	7.55e-01	4.19e-03	Soluble	-0.71	3.51e+01	1.95e-01	Soluble
Stigmasterol	-7.46	1.43e-05	3.46e-08	Poorly soluble	-8.86	5.71e-07	1.38e-09	Poorly soluble	-5.47	1.40e-03	3.39e-06	Moderately soluble
Vanillic acid	-2.02	1.60e+00	9.52e-03	Soluble	-2.44	6.15e-01	3.66e-03	Soluble	-1.32	8.10e+00	4.82e-02	Soluble
Catechin	-2.22	1.74e+00	5.98e-03	Soluble	-2.24	1.66e+00	5.72e-03	Soluble	-2.14	2.09e+00	7.19e-03	Soluble
Daraprim	-3.47	8.48e-02	3.41e-04	Soluble	-3.98	2.62e-02	1.05e-04	Soluble	-4.87	3.39e-03	1.36e-05	Moderately soluble
Cinnamic acid	-2.37	6.29e-01	4.25e-03	Soluble	-2.54	4.23e-01	2.85e-03	Soluble	-1.84	2.14e+00	1.45e-02	Soluble

Table 4: Pharmacokinetic Parameters of the Phytoconstituents of *Embelia Ribes Burm*

Molecules	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp (skin permeation)
Embelin	High	Yes	No	No	Yes	Yes	Yes	No	-4.25 cm/s
Vilangin	Low	No	Yes	No	No	No	No	No	-2.25 cm/s
Daucosterol	Low	No	No	No	No	No	No	No	-4.32 cm/s
Homoembelin	High	Yes	No	No	Yes	No	Yes	No	-4.84 cm/s
Quercitol	Low	No	Yes	No	No	No	No	No	-9.24 cm/s
Rapanone	High	No	No	No	Yes	Yes	Yes	No	-3.65 cm/s
Sitosterol	Low	No	No	No	No	No	No	No	-2.20 cm/s
Betulin	Low	No	No	No	No	No	No	No	-3.12 cm/s
Taraxasterol	Low	No	No	No	No	No	No	No	-2.42 cm/s
Caffeic acid	High	No	No	No	No	No	No	No	-6.58 cm/s
Stigmasterol	Low	No	No	No	No	Yes	No	No	-2.74 cm/s
Vanillic acid	High	No	No	No	No	No	No	No	-6.31 cm/s
Catechin	High	No	Yes	No	No	No	No	No	-7.82 cm/s
Daraprim	High	Yes	No	Yes	Yes	No	No	Yes	-5.91 cm/s
Cinnamic acid	High	Yes	No	No	No	No	No	No	-5.69 cm/s

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Table 5: Drug likeness of the Phytoconstituents of *Embelia Ribes Burm*

Molecules	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability score
Embelin	Yes; 0 violation	Yes	Yes	Yes	No; 1 violation: XLOGP3>5	0.85
Vilangin	Yes; 1 violation: MW>500	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70	No; 2 violations: Rotors>10, TPSA>140	No; 2 violations: WLOGP>5.88, TPSA>131.6	No; 3 violations: MW>600, XLOGP3>5, Rotors>15	0.56
Daucosterol	Yes; 1 violation: MW>500	No; 4 violations: MW>480, WLOGP>5.6, MR>130, #atoms>70	Yes	Yes	No; 1 violation: XLOGP3>5	0.55
Homoembelin	Yes; 0 violation	Yes	Yes	Yes	Yes	0.85
Quercitol	Yes; 0 violation	No; 2 violations: WLOGP<-0.4, MR<40	Yes	Yes	No; 2 violations: MW<200, XLOGP3<-2	0.55
Rapanone	Yes; 0 violation	Yes	No; 1 violation: Rotors>10	Yes	No; 1 violation: XLOGP3>5	0.85
Sitosterol	Yes; 1 violation: MLOGP>4.15	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Betulin	Yes; 1 violation: MLOGP>4.15	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70	Yes	No; 1 violation: WLOGP>5.88	No; 1 violation: XLOGP3>5	0.55
Taraxasterol	Yes; 1 violation: MLOGP>4.15	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Caffeic acid	Yes; 0 violation	Yes	Yes	Yes	No; 1 violation: MW<200	0.56
Stigmasterol	Yes; 1 violation: MLOGP>4.15	No; 3 violations: WLOGP>5.6, MR>130, #atoms>70	Yes	No; 1 violation: WLOGP>5.88	No; 2 violations: XLOGP3>5, Heteroatoms<2	0.55
Vanillic acid	Yes; 0 violation	Yes	Yes	Yes	No; 1 violation: MW<200	0.85
Catechin	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Daraprim	Yes; 0 violation	Yes	Yes	Yes	Yes	0.55
Cinnamic acid	Yes; 0 violation	No; 2 violations: MW<160, #atoms<20	Yes	Yes	No; 1 violation: MW<200	0.85

Table 6: Medicinal Chemistry Properties of Phytoconstituents of *Embelia Ribes Burm*

Molecules	Pains	Brenk	Leadlikeness	Synthetic accessibility
Embelin	1 alert: quinone_A	1 alert: chinone_1	No; 2 violations: Rotors>7, XLOGP3>3.5	3.66
Vilangin	1 alert: quinone_A	1 alert: chinone_1	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	5.78
Daucosterol	0 alert	1 alert: isolated_alkene	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5	8.02
Homoembelin	1 alert: quinone_A	1 alert: chinone_1	No; 2 violations: Rotors>7, XLOGP3>3.5	3.44
Quercitol	0 alert	0 alert	No; 1 violation: MW<250	3.39
Rapanone	1 alert: quinone_A	1 alert: chinone_1	No; 2 violations: Rotors>7, XLOGP3>3.5	3.88
Sitosterol	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	6.30
Betulin	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	5.68

Taraxasterol	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	5.40
Caffeic acid	1 alert: catechol_A	2 alerts: catechol, michael_acceptor_1	No; 1 violation: MW<250	1.81
Stigmasterol	0 alert	1 alert: isolated_alkene	No; 2 violations: MW>350, XLOGP3>3.5	6.21
Vanillic acid	0 alert	0 alert	No; 1 violation: MW<250	1.42
Catechin	1 alert: catechol_A	1 alert: catechol	Yes	3.50
Daraprim	0 alert	0 alert	No; 1 violation: MW<250	2.43
Cinnamic acid	0 alert	1 alert: michael_acceptor_1	No; 1 violation: MW<250	1.67

4. Discussion:

Embelia ribes Burm. f. is a rare medicinal plant that has been studied extensively for its diverse medicinal characteristics. The use of medicinal plants in therapeutics is perhaps as old as recorded history. Embelia ribes are one of the most significant medicinal plants. Embelia ribes also has the following properties: Antihelminthic, antibacterial, antioxidant, anti-diabetic, anticonvulsant, anti-cancer, antihyperlipidemic, Antifungal, Antihyperhomocysteinemic, Mollusicidal, Wound healing, Antifertility, Antihyperglycemic, Antitumor, and anti- inflammatory, Chemotherapeutic, Contraceptive, Anxiolytic, Antidepressant, Antimitotic, Cardioprotective effect, Antiobesity, and Antihyperlipidemic are all treated with it. Embelia ribes was studied for its hepatoprotective and analgesic properties. *Embelia ribes* fruits contain a quinone derivative embelin (3-undecyl 2, 5- dihydroxy, 1,4-benzoquinone), an alkaloid christembine, and a volatile oil vilangin; its chemical constituents 2,5-dihydroxy-4-undecyl- 3,6-benzoquinone. The fruit contains embelic acid, tannins, christembine, and embelin as major constituents. Vilangin, 2, 5-isobutylamine salts, quercetol, and volatile oil are also present.

Ayurveda is one of the earliest systems of medicine and offers vast opportunities for the discovery of effective and therapeutically useful compounds for the development of herbal medicines. Today, the use of herbal medicines is widespread in both developing and developed countries due to their proven side effects and natural origin.

The World Health Organization reports that more than 30% of all plant species have been used for medical purposes. Currently, thanks to constant advances in the field of informatics, many successful drug discoveries from natural products using computer-aided drug design methods, for example, the development of dazamide, imatinib, dasatinib ponatinib, etc. Computational drug design was used to predict ADMET properties of drugs, leading to early drug discovery. The rationale for these in silico approaches is the relatively lower time required compared to standard ADMET profiling. For example, it takes one minute to screen 20,000 molecules in an in silico model, but it takes 20 weeks to perform the same exercise in a wet lab. Thanks to the accumulation of ADMET data in the late 1990s, many pharmaceutical companies now use computational models that in some cases replace wet screenings. Therefore, this paradigm shift has driven the development of several theoretical methods to predict ADMET parameters. Many of these theoretical models have been implemented in several programs currently available for drug development protocols, although some predictions often disappoint.

Software tools currently used to predict the ADME properties of potential drug candidates often utilize quantitative structure-activity relationships, QSAR, or knowledge-base methods. In the present study, we used the online software tool Swiss ADME, which is available free of charge to users, to evaluate the ADME properties of *Emelia Ribes Burm*. The plant phytoconstituents included using the software include such as Embelin, Vilangin, Daucosterol, Homoembelin, Quercitol, Rapanone, Sitosterol, Betulin, Taraxasterol, Caffeic acid, Stigmasterol, Vanillic acid, Catechin, Daraprim, Cinnamic acid. Accordingly, phytoconstituents were analyzed for ADME properties and displayed respectfully with tables and figures. Moreover, the values can be used as monographs by researchers and scientists to develop potential semi-synthetic and synthetic drugs for multiple purposes.

5. CONCLUSION:

Plant-derived small molecules that interfere with metabolic changes are considered potential therapeutics in drug discovery and development. Based on the exponential growth of biological and chemical data, computer-aided drug design (CADD) has dramatically changed the way research and development work to identify potential drugs. The use of computational methods in the drug discovery and development process is recognized for its effectiveness in terms of implementation, time, and cost. This study presents the freely available Swiss ADME web tool for assessing the ADME properties of phytoconstituents in the plant *Embelia ribes*. These results can serve as a fundamental tool for further evaluation of the biological and pharmacological properties of the plant. Preliminary in silico studies suggest that several compounds, including Embelin, Vilangin, Betulin, Daucosterol, Quercitol,

etc, have properties that could be further investigated and tested as potential drug candidates for diagnosis of various diseases. However, these bioactive substances need to be confirmed and further tested before they can be considered for clinical trials.

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