Swiss ADME Predictions of Phytoconstituents Present in Ocimum sanctum Linn

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Article

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Abstract: The utilization of medicinal herbs has been steadily increasing globally since the Pandemic. The use of these medicinal plants helps minimize side effects and adverse consequences. As technology evolves, insilico analysis, such as screening, is often employed to figure out the mechanism of action of these medicinal plants. This method takes into account the pharmacokinetics and screening of medicinal plants. The main emphasis is on the profile of Ocimum sanctum Linn using insilico techniques like Swiss ADME. The results of these studies can be utilized to future studies involving in vivo and in vitro studies for establishing the particular activity of medicinal plants.

Keywords: *Ocimum sanctum*; Swiss ADME; Phytoconstituents

1. Introduction

Ocimum sanctum L. (also known as Tulsi) has been used for thousands of years in Ayurveda for its diverse healing properties. Tulsi, the Queen of herbs, the legendary 'Incomparable one' of India, is one of the holiest and most cherished of the many healing and healthy giving herbs of the orient (Priyabrata Pattanayak *et al.*, 2010) [1]. *Ocimum sanctum* L. also known as "*Tulsi*," is an aromatic plant in the basil family Lamiaceae (tribe ocimeae), which is native throughout the eastern world tropics. It is an erect, much branched subshrub, 30–60 cm tall with hairy stems and simple, opposite, green leaves that are strongly scented. Leaves have petioles and are ovate up-to 5 cm long, usually slightly toothed (Felix Bast *et al.*, 2014) [2].

Tulsi has been used traditionally in Ayurveda and Siddha systems of medicine for prevention and cure of common cold, headache, cough, influenza, earache, fever, colic pain, sore throat, bronchitis, asthma, hepatic diseases, malarial fever, as an antidote for snake bite and scorpion sting, flatulence, migraine headaches, fatigue, skin diseases, wound, insomnia, arthritis, digestive disorders, night blindness and diarrhoea (Rakesh Kumar Joshi *etal.*, 2017)[3]. It is one of the holiest and most sacred herbs grown widely in India. It is a herb that is bestowed with enormous antimicrobial substances and is used to treat a variety of illnesses ranging from diabetes mellitus, arthritis, bronchitis, skin diseases, etc. (Prakash P *et al.*, 2005 & Viyoch J *et al.*, 2006 & Magesh V *et al.*, 2009) [4–6].

The Plant has many medicinal properties like Antimalarial, Insecticidal activity, Treating Hepatic disorders, Antiemetic and Anti helminthic action, Antidiabetic, Animal bite antidote, Antiulcer activity, Heart tonic activity, Antifertility effect, Anti stress activity and other Pharmacological Activity (Harish Chandra Andola *et al.*, 2011 & Amit Kumar *et al.*, 2013 & Nipun Mahajan *et al.*, 2013) [7–9]. One such website that supports drug development is Swiss ADME. It allows individuals to compute physicochemical characteristics as well as predict ADME parameters, pharmacokinetic features, drug-like nature, and medicinal chemistry compatibility of one or more small compounds. The aim of the present study was to investigate the individual ADME behaviour of the bioactive substances found in Ocimum sanctum and interpret the findings using the Swiss ADME website (www.swissadme.ch).

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2. Materials and Methods

2.1. Swiss ADME

The Swiss Institute of Bioinformatics' Swiss ADME software (www.swissadme.ch) was accessed using a web server that shows the Swiss ADME submission page in Google to estimate the individual ADME behaviours of the constituents from Ocimum sanctum. The findings have been presented for each input molecule in tables, graphs, and an excel spreadsheet. The list was created to handle one input molecule per line that contains several inputs, described by the simplified molecular input line entry system (SMILES).

2.2. Physicochemical properties

The two-dimensional chemical structure was described in the first section using canonical SMILES. A preliminary assessment of the pharmacological similarity of the compounds of interest is given by the bioavailability radar, which considers six physicochemical parameters: LIPO (Lipophilicity), SIZE, POLAR (Polarity), INSOLU (Insolubility), INSATU (Insaturation), and FLEX (Flexibility). These sections include clean molecular and physicochemical properties like molar refractivity, TPSA, number of rotatable bonds, number of H-bond acceptors, number of H-bond donors, number of heavy atoms, number of aromatic heavy atoms, and fraction csp^3.

2.3. Solubility

The solvent used, along with the temperature and pressure of the surrounding environment, have a significant impact on a compound's solubility. The range of solubility is defined as the saturation concentration, at which the concentration of the solute in the solution does not rise as more solute is added (Lachman *et al.*, 1986) [10]. When the maximum dose strength of the drug dissolves in 250 mL or less of aqueous media with a pH range of 1 to 7.5, that drug is considered to be extremely soluble. 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 (Solubility class: Log S Scale: Insoluble<-10 poorly<-6, moderately<-4 soluble<-2, very<0<highly). Both differ from the fundamental general solubility equation (Yalkowsky *et al.,*1980) [11]. 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). The fractional logarithm of the molar solubility in water (log S) represents all expected values. Along with qualitative solubility classes, Swiss ADME also offers solubility in mol/l and mg/ml.

2.4. Lipophilicity

Lipophilicity is a crucial molecular characteristic that frequently has a positive correlation with the bioactivity of substances (Melanie Kah *et al.,* 2008) [12]. It is demonstrated experimentally using either distribution coefficients (log D) or partition coefficients (log P). The representation of P illustrates the partition equilibrium of a unionized solute between water and an immiscible organic solvent. One of the key physicochemical characteristics, lipophilicity has connections to both pharmacodynamic and pharmacokinetic properties. It establishes how medications are absorbed, metabolized, distributed, excreted, and toxic (ADMET) (Lungu *et al*., 2019 & Giaginis *et al*., 2018 & Kamel M.S *et al*., 2022 & Erckes V *et al*., 2022) [13–16].

A crucial element in the transport of molecules through membranes is lipophilicity. Additionally, it affects how they bind to receptors at the drug's action site and to plasma proteins. Lipophilicity is therefore regarded as a reference measure for the estimation of a drug's biological activity. In terms of biology, lipophillicity is the logarithm of a chemical's n-octanol to water partition (logP). This parameter has been used in studies on the quantitative relationship between the structure

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and the activity (QSAR) (Ginex T *et al.*, 2019 & Kempinska D *et al.*, 2019 & Dolowy M *et al.*, 2021) [17–19]. Swiss ADME presents five accessible models, namely XLOGP3, WLOGP, MLOGP, SILICOS-IT, and iLOGP, for analysing the lipophilicity character in a molecule. XLOGP3, an atomistic accost including corrective factors and knowledge based library (Cheng T *et al.*, 2007) [20]; WLOGP, application of purely atomistic method stationed on fragmental system (Wildman SA *et al.*, 1999) [21]; MLOGP, 13 molecular descriptors were implemented in an archetype of topological technique indicated on a linear relationship (Moriguchi *et al.*, 1994) [22]; SILICOS-IT, 7 topological descriptors and 27 fragments are used in a mongrel technique; iLOGP, a physics-based technique that relies on the generalized-born and solvent accessible surface area (GB/SA) model to compute the free energies of solvation in n-Octanol and water; An arithmetic average of the values predicted by the five suggested approaches is called consensus log P o/w. (Daina Antoine *et al.*,2017) [23].

2.5. Drug likeness

Swiss ADME filters chemical libraries using five different rule-based filters from major pharmaceutical companies in an attempt to enhance the quality of proprietary chemical groups by eliminating molecules with characteristics that are not compatible with an acceptable pharmacokinetics profile (Daina Antoine *et al.*,2017) [23].

The Muegge filter (also known as the Bayer filter) distinguishes molecules that are identical to drugs from substances that are different. These models illustrate molecules as drugs, such as those with molecular weights of 200 to 600 Da, XLOGP values within -2 and 5, TPSA values of 150, etc. Number of rings is 7, number of carbon atoms is greater than 4, number of heteroatoms is greater than 1, number of rotatable bonds is 15, and H-bond acceptor and donor are 10 and 5 respectively.

Egan filter (Pharmacia filter) predicts that mechanisms involved in a small molecule's membrane permeability will influence drug absorption. These models illustrate a drug's molecule assuming it were given a WLOGP value of 5.88 and a TPSA value of 131.6, respectively. Because it takes into consideration active transport and efflux mechanisms, the Egan computational model for human passive intestinal absorption (HIA) of small molecules is accurate in predicting drug absorption (Egan WJ *et al.*, 2000) [24].

According to physicochemical properties, the presence of functional groups, and substructures, the Ghose filter (Amgen) determines small molecules. The qualifying range for small molecules is between 20 and 70 atoms, whereas the qualifying range for large molecules is between 160 and 480 Da, WlogP is between -0.4 and 5.6, and molar refractivity (MR) is between 40 and 130 (Ghose AK *et al.*, 1998) [25].

Veber filter (GSK filter) model classifies compounds as drug-like if they have 12 or less H-bond donors and acceptors, a TPSA of 140 or less, and fewer than 10 rotatable bonds. Reduced TPSA correlates with increased permeation rate, increased rotatable bond counts correlate to lower permeation rate, and compounds having these characteristics will have good oral bioavailability (Veber DF *et al.*, 2002) [26].

Molecular weight (MW) less than 500, MLOGP ≤ 4.15, N or O ≤ 10, NH or OH ≤ 5, and the Lipinski filter (Pfizer) are the pioneer rules of five that describe tiny compounds based on physicochemical property profiles. All nitrogen and oxygen are strictly considered by Lipinski as H-bond acceptors, while all nitrogen and oxygen that contain at least one hydrogen are regarded as H-bond donors. In addition, neither nitrogen nor aliphatic fluorine are donors or acceptors (Lipinski CA *et al.*, 2001) [27].

The Abbott bioavailability score is intended to predict the probability that a substance will have at least 10% oral bioavailability in rodents or measurable Caco-2 permeability, which predicts the probability that a compound would have F>10% based on the predominant charge at biological pH in a rat model. It involves rapid chemical libraries screening to identify the optimum compounds for synthesis (Martin YC, 2005) [28].

2.6. Medicinal Chemistry

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These areas of study are intended to assist medicinal chemistry investigators in their ongoing seek for new medications. In particular, these substances have been shown to be active in a number of tests, which could be considered as prospective beginning points for additional research. Frequent hits or promiscuous compounds, often known as PAINS (Pan Assay Interference Compounds), are chemicals that exhibit a robust reaction in assays regardless of the protein Targets. SwissADME returns warnings if such moieties are found in the molecule under evaluation (Baell *et al.*, 2010) [29].

To allow leads through high throughput screening (HTS) with exceptional affinity the chance to be utilized for more interactions throughout the lead optimization phase, the concept of a lead likeness was developed. Leads are exposed to chemical changes that will most likely cause them to shrink and become more lipophilic in nature which is less hydrophobic than molecules similar to drugs 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 (Teague.S *et al.*,1999 & Hann MM *et al.*,2012) [30,31].

2.7. Pharmacokinetics

A plot between WLOGP and TPSA is drawn to indicate the estimated amounts for gastrointestinal absorption and brain penetration of compounds. The Egan egg, which is used to evaluate the predictive efficacy of the model for GI passive absorption and prediction for brain access by passive diffusion to ultimately lay the BOILED-Egg (Brain Or IntestinaL EstimateD permeation model), is an elliptical region that is most populated by easily absorbed molecules.

For the purpose of drug discovery and research, the BOILED-Egg model generates a rapid, spontaneously accurately mimicked, yet lively way to forecast passive GI absorption (Brito Sanchez *et al.*, 2015 & Di LP et al., 2012) [32,33].

The molecules in the white region are those that are more likely to get absorbed by the GI tract, while the molecules in the yellow region (the yolk) are those that are most likely to reach the brain. The knowledge about compounds being substrate or non-substrate of the permeability glycoprotein (P-gp, suggested the most important member among ATP-binding cassette transporters or ABC-transporters) is key to appraise active efflux through biological membranes, for instance from the gastrointestinal wall to the lumen or from the brain (Montanari et al.,2015) [34]. Through metabolic biotransformation, Cytochromes P450 (CYP), a superfamily of isoenzymes, is an essential component of drug elimination (Testa *et al.*, 2007) [35].

One can estimate that 50 to 90% (depending on the authors) of therapeutic molecules are substrate of five major isoforms (CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4) (Di, L.,2014) [36]. SwissADME provides it possible to determine whether a compound is a P-gp substrate or an inhibitor of the most significant CYP isoenzymes. On thoroughly cleaned, large databases of known substrates/non-substrates or inhibitors/non-inhibitors, we employ the support vector machine algorithm (SVM) (Cortes et al.,1995) [37].

SVM was found to perform better than other machine-learning algorithms for binary classification. The models return "Yes" or "No" if the molecule under investigation has higher probability to be substrate or non-substrate of P-gp (respectively inhibitor or non-inhibitor of a given CYP) (Mishra *et al.*,2010) [38].

3. Results

Table 1. General Characteristics of Phytoconstituents of Ocimum sanctum.

Sl.No	Molecules	Formula	Molecular Weight (in g/mol)	Canonical SMILES
1	MethylEugenol	$C_{11}H_{14}O_2$	178.23	C=CCc1ccc(c(c1)OC)OC
2	Eugenol	$C_{10}H_{12}O_2$	164.2	C=CCc1ccc(c(c1)OC)O
3	δ-Caryophyllene	$C_{15}H_{24}$	204.35	C/C/1=C\CCC(=C)[C@@H]2

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				[C@@H](CC1)C(C2)(C)C
4	Caryophyllene oxide	$C_{17}H_{30}O$	250.42	C[C@]12CC[C@@]3(C)O[C@]3 (CCC[C@@]2(CC1(C)C)C)C
5	β-Elemene	$C_{15}H_{24}$	204.35	C=C[C@]1(C)CC[C@H] (C[C@H]1C(=C)C)C(=C)C
6	MethylChavicol	$C_{10}H_{12}O$	148.2	COc1ccc(cc1)CC=C
7	Linalool	$C_{10}H_{18}O$	154.25	C=C[C@](CCC=C(C)C)(O)C
8	δ-Cardinene	$C_{15}H_{24}$	204.35	CC1=C[C@H]2C(=C(C) CC[C@@H]2C(C)C)CC1
9	β-Bisabolene	$C_{15}H_{24}$	204.35	CC(=CCCC(=C)[C@H] 1CCC(=CC1)C)C
10	1,8-Cineole	$C_{10}H_{16}$	154.25	CC12CCC(CC1)C(O2)(C)C
11	Camphor	$C_{10}H_{16}O$	152.23	O=C1CC2C(C1(C)CC2)(C)C
12	Isocaryophyllene	$C_{10}H_{16}$	136.23	CC1=CCC2C(C1)C2(C)C
13	Apigenin-7-O-glucuronide	$C_{21}H_{18}O_{11}$	446.36	OC(=O)[C@H]1O[C@H](Oc2cc(O)c3c(c2)oc(cc3=O) c2ccc(cc2)O)[C@@H]([C@H]([C@@H]1O)O)O
14	Carvacrol	$C_{10}H_{14}O$	150.22	CC(c1ccc(c(c1)O)C)C
15	Circimaritin	$C_{17}H_{14}O_6$	314.29	COc1cc2oc(cc(=O)c2c (c1OC)O)c1ccc(cc1)O
16	Isothymusin	$C_{17}H_{14}O_7$	330.29	COc1c(O)c2oc(cc(=O)c 2c(c1OC)O)c1ccc(cc1)O
17	Pinene	$C_{11}H_{16}$	148.24	CC1=CCC23C1C(C)(C)C2C3
18	Molludistin	$C_{21}H_{20}O_9$	416.38	COc1cc(O)c2c(c1[C@@H]1OC[C@@H] ([C@@H](C1O)O)O)oc(cc2=O)c1ccc(cc1)O
19	Rosameric acid	$C_{18}H_{16}O_8$	360.31	O=C(O[C@@H](C(=O)O)Cc1ccc(c(c1) O)O)/C=C/c1ccc(c(c1)O)O
20	Orientin	$C_{21}H_{22}O_{11}$	450.39	OC[C@H]1O[C@@H]([C@@H]([C@H]([C@@H] 1O)O)O)c1c(O)cc(c2c1OC(=CC2O)c1ccc(c(c1)O)O)O
21	Vicenin	$C_{27}H_{30}O_{15}$	594.52	OC[C@H]1O[C@H]([C@@H]([C@H]([C@@H]1O) O)O)c1c(O)c([C@@H]2O[C@H](CO)[C@H]([C@@H] ([C@H]2O)O)O)c(c2c1oc(cc2=O)c1ccc(cc1)O)O
22	Urosolic acid	$C_{30}H_{48}O_3$	456.7	C[C@@H]1CC[C@]2([C@@H]([C@H]1C) C1=CC[C@H]3[C@@]([C@@]1(CC2)C)(C)CC [C@@H]1[C@]3(C)CC[C@@H](C1(C)C)O)C(=O)O
23	Luteolin	$C_{15}H_{10}O_6$	286.24	Oc1cc(O)c2c(c1)oc(cc2=O)c1ccc(c(c1)O)O
24	Luteolin-7-O-glucuronide	$C_{21}H_{20}O_{12}$	464.38	OC(=O)[C@H]1O[C@@H](Oc2cc3OC(=CC(c3c(c2)O) O)c2ccc(c(c2)O)O)[C@@H]([C@H]([C@@H]1O)O)O
25	3-Carene	$C_{10}H_{16}$	136.23	CC1=CC[C@@H]2[C@H](C1)C2(C)C
26	Citral	$C_{10}H_{16}O$	152.23	O=C/C=C(\CCC=C(C)C)/C
27	Geraniol	$C_{10}H_{18}O$	154.25	OC/C=C(/CCC=C(C)C)\C
28	Methyl Cinnamate	$C_{11}H_{12}O_2$	176.21	CC(=O)OC/C=C/c1ccccc1
29	β-Ocimene	$C_{10}H_{16}$	136.23	C=C/C(=C\CC=C(C)C)/C
30	λ-Terpineol	$C_{10}H_{18}O$	154.25	CC1=CCC(CC1)C(O)(C)C
31	PhenylPropanoids	$C_9H_{11}NO_2$	165.19	N[C@H](C(=O)O)Cc1ccccc1
32	Germacrene-D	$C_{15}H_{24}$	204.35	C/C/1=C/CCC(=C)/C=C\[C@@H](CC1)C(C)C
33	λ-Humulene	$C_{15}H_{24}$	204.35	C/C/1=C\CC(C)(C)/C=C/C/C(=C/CC1)/C
34	Camphene	$C_{10}H_{16}$	136.23	C=C1C2CCC(C1(C)C)C2
35	Myrcene	$C_{10}H_{16}$	136.23	C=CC(=C)CCC=C(C)C
36	Thymol	$C_{10}H_{14}O$	150.22	Cc1ccc(c(c1)O)C(C)C
37	λ-Linolenic acid	$C_{18}H_{30}O_2$		CC/C=C\C/C=C\C/C=C\CCCCCCCC(=O)O

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								278.43	

Table 2. Physicochemical Properties of the Phytoconstituents of Ocimum sanctum Linn.

Sl.No	Molecules	Heavy atoms	Aromatic heavy atoms	Fraction Csp3	Rotatable bonds	H-bond acceptors	H-bond donors	Molar Refractivity	TPSA
1	MethylEugenol	13	6	0.27	4	2	0	53.53	18.46
2	Eugenol	12	6	0.2	3	2	1	49.06	29.46
3	δ-Caryophyllene	15	0	0.73	0	0	0	68.78	0
4	Caryophyllene oxide	18	0	1	0	1	0	77.87	12.53
5	β-Elemene	15	0	0.6	3	0	0	70.42	0
6	MethylChavicol	11	6	0.2	3	1	0	47.04	9.23
7	Linalool	11	0	0.6	4	1	1	50.44	20.23
8	δ-Cardinene	15	0	0.73	1	0	0	69.04	0
9	β-Bisabolene	15	0	0.6	4	0	0	70.68	0
10	1,8-Cineole	11	0	1	0	1	0	47.12	9.23
11	Camphor	11	0	0.9	0	1	0	45.64	17.07
12	Isocaryophyllene	10	0	0.8	0	0	0	45.22	0
13	Apigenin-7-O-glucuronide	32	16	0.24	4	11	6	106.72	187.12
14	Carvacrol	11	6	0.4	1	1	1	48.01	20.23
15	Circimaritin	23	16	0.12	3	6	2	84.95	89.13
16	Isothymusin	24	16	0.12	3	7	3	86.97	109.36
17	Pinene	11	0	0.82	0	0	0	47.66	0
18	Molludistin	30	16	0.29	3	9	5	105.11	149.82
19	Rosameric acid	26	12	0.11	7	8	5	91.4	144.52
20	Orientin	32	12	0.33	3	11	9	107.27	200.53
21	Vicenin	42	16	0.44	5	15	11	139.23	271.2
22	Urosolic acid	33	0	0.9	1	3	2	136.91	57.53
23	Luteolin	21	16	0	1	6	4	76.01	111.13
24	Luteolin-7-O-glucuronide	33	12	0.29	4	12	8	107.38	206.6
25	3-Carene	10	0	0.8	0	0	0	45.22	0
26	Citral	11	0	0.5	4	1	0	49.44	17.07
27	Geraniol	11	0	0.6	4	1	1	50.4	20.23
28	Methyl Cinnamate	13	6	0.18	4	2	0	52.24	26.3
29	β-Ocimene	10	0	0.4	3	0	0	48.76	0
30	λ-Terpineol	11	0	0.8	1	1	1	48.8	20.23
31	PhenylPropanoids	12	6	0.22	3	3	2	45.5	63.32
32	Germacrene-D	15	0	0.6	1	0	0	70.68	0
33	λ-Humulene	15	0	0.6	0	0	0	70.42	0
34	Camphene	10	0	0.8	0	0	0	45.22	0
35	Myrcene	10	0	0.4	4	0	0	48.76	0
36	Thymol	11	6	0.4	1	1	1	48.01	20.23
37	λ-Linolenic acid	20	0	0.61	13	2	1	88.99	37.3

Table 3. Solubility of the Phytoconstituents of Ocimum sanctum Linn.

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Molecules	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	
MethylEugenol	-2.61	4.37E-01	2.45E-03	Soluble	-2.55	4.98E-01	2.79E-03	Soluble	-3.5	5.62E-02	3.16E-04	Soluble
Eugenol	-2.46	5.69E-01	3.47E-03	Soluble	-2.53	4.90E-01	2.98E-03	Soluble	-2.79	2.65E-01	1.61E-03	Soluble
δ-Caryophyllene	-3.87	2.78E-02	1.36E-04	Soluble	-4.1	1.64E-02	8.01E-05	Moderately soluble	-3.77	3.49E-02	1.71E-04	Soluble
Caryophyllene oxide	-4.49	8.18E-03	3.27E-05	Moderately soluble	-4.91	3.08E-03	1.23E-05	Moderately soluble	-4.94	2.88E-03	1.15E-05	Moderately soluble
β-Elemene	-4.76	3.57E-03	1.74E-05	Moderately soluble	-5.89	2.62E-04	1.28E-06	Moderately soluble	-3.58	5.36E-02	2.62E-04	Soluble
MethylChavicol	-3.09	1.21E-01	8.17E-04	Soluble	-3.24	8.49E-02	5.73E-04	Soluble	-3.35	6.54E-02	4.42E-04	Soluble
Linalool	-2.4	6.09E-01	3.95E-03	Soluble	-3.06	1.35E-01	8.75E-04	Soluble	-1.84	2.20E+00	1.43E-02	Soluble
δ-Cardinene	-3.43	7.51E-02	3.67E-04	Soluble	-3.49	6.55E-02	3.20E-04	Soluble	-3.52	6.19E-02	3.03E-04	Soluble
β-Bisabolene	-4.89	2.61E-03	1.28E-05	Moderately soluble	-6.22	1.22E-04	5.98E-07	Poorly soluble	-3.58	5.36E-02	2.62E-04	Soluble
1,8-Cineole	-2.52	4.63E-01	3.00E-03	Soluble	-2.59	3.98E-01	2.58E-03	Soluble	-2.45	5.45E-01	3.53E-03	Soluble
Camphor	-2.16	1.04E+00	6.86E-03	Soluble	-2.18	1.00E+00	6.57E-03	Soluble	-2.6	3.83E-01	2.52E-03	Soluble
Iso - caryophyllene	-3.44	4.90E-02	3.60E-04	Soluble	-4.1	1.09E-02	8.01E-05	Moderately soluble	-2.23	8.06E-01	5.92E-03	Soluble
Apigenin-7-O-glucuronide	-3.63	1.04E-01	2.33E-04	Soluble	-5	4.51E-03	1.01E-05	Moderately soluble	-2.22	2.67E+00	5.98E-03	Soluble
Carvacrol	-3.31	7.40E-02	4.92E-04	Soluble	-3.6	3.79E-02	2.53E-04	Soluble	-3.01	1.46E-01	9.71E-04	Soluble
Circimaritin	-4.2	2.00E-02	6.35E-05	Moderately soluble	-4.87	4.26E-03	1.35E-05	Moderately soluble	-5.22	1.91E-03	6.08E-06	Moderately soluble
Isothymusin	-3.83	4.91E-02	1.49E-04	Soluble	-4.56	9.18E-03	2.78E-05	Moderately soluble	-4.63	7.71E-03	2.33E-05	Moderately soluble
Pinene	-2.49	4.85E-01	3.27E-03	Soluble	-2.39	5.98E-01	4.03E-03	Soluble	-2.5	4.70E-01	3.17E-03	Soluble
Molludistin	-3	4.20E-01	1.01E-03	Soluble	-3.32	1.99E-01	4.79E-04	Soluble	-3.5	1.33E-01	3.19E-04	Soluble
Rosameric acid	-3.44	1.31E-01	3.63E-04	Soluble	-5.04	3.32E-03	9.22E-06	Moderately soluble	-2.17	2.41E+00	6.70E-03	Soluble
Orientin	-2.06	3.90E+00	8.65E-03	Soluble	-2.69	9.12E-01	2.03E-03	Soluble	-0.09	3.69E+02	8.18E-01	Soluble

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Vicenin	-2.05	5.25E+00	8.83E-03	Soluble	-2.9	7.46E-01	1.26E-03	Soluble	-0.27	3.19E+02	5.36E-01	Soluble
Urosolic acid	-7.23	2.69E-05	5.89E-08	Poorly soluble	-8.38	1.92E-06	4.21E-09	Poorly soluble	-5.67	9.72E-04	2.13E-06	Moderately soluble
Luteolin	-3.71	5.63E-02	1.97E-04	Soluble	-4.51	8.84E-03	3.09E-05	Moderately soluble	-3.82	4.29E-02	1.50E-04	Soluble
Luteolin-7-O-glucuronide	-2.64	1.06E+00	2.28E-03	Soluble	-3.75	8.17E-02	1.76E-04	Soluble	0.07	5.43E+02	1.17E+00	Soluble
3-Carene	-3.44	4.90E-02	3.60E-04	Soluble	-4.1	1.09E-02	8.01E-05	Moderately soluble	-2.23	8.06E-01	5.92E-03	Soluble
Citral	-2.43	5.67E-01	3.73E-03	Soluble	-3.05	1.34E-01	8.83E-04	Soluble	-1.96	1.66E+00	1.09E-02	Soluble
Geraniol	-2.78	2.59E-01	1.68E-03	Soluble	-3.67	3.30E-02	2.14E-04	Soluble	-1.84	2.20E+00	1.43E-02	Soluble
Methyl Cinnamate	-2.43	6.58E-01	3.74E-03	Soluble	-2.44	6.42E-01	3.64E-03	Soluble	-2.96	1.91E-01	1.08E-03	Soluble
β-Ocimene	-3.17	9.20E-02	6.75E-04	Soluble	-3.97	1.45E-02	1.07E-04	Soluble	-2.04	1.24E+00	9.10E-03	Soluble
λ-Terpineol	-2.87	2.10E-01	1.36E-03	Soluble	-3.49	4.95E-02	3.21E-04	Soluble	-1.69	3.17E+00	2.06E-02	Soluble
Phenyl Propanoids	-0.08	1.38E+02	8.35E-01	Very soluble	0.7	8.21E+02	4.97E+00	Highly soluble	-1.86	2.30E+00	1.39E-02	Soluble
Germacrene-D	-4.03	1.92E-02	9.39E-05	Moderately soluble	-4.47	6.93E-03	3.39E-05	Moderately soluble	-3.32	9.83E-02	4.81E-04	Soluble
λ-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
Camphene	-3.34	6.18E-02	4.54E-04	Soluble	-3.93	1.60E-02	1.17E-04	Soluble	-2.48	4.55E-01	3.34E-03	Soluble
Myrcene	-3.05	1.22E-01	8.96E-04	Soluble	-3.88	1.80E-02	1.32E-04	Soluble	-2.42	5.24E-01	3.85E-03	Soluble
Thymol	-3.19	9.74E-02	6.49E-04	Soluble	-3.4	5.97E-02	3.98E-04	Soluble	-3.01	1.46E-01	9.71E-04	Soluble
λ-Linolenic acid	-3.19	9.74E-02	6.49E-04	Soluble	-3.4	5.97E-02	3.98E-04	Soluble	-3.01	1.46E-01	9.71E-04	Soluble

Table 3. Lipophilicity of the Phytoconstituents of Ocimum sanctum Linn.

Sl.No	Molecules	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P
1	MethylEugenol	2.65	2.52	2.43	2.3	3	2.58
2	Eugenol	2.37	2.27	2.13	2.01	2.48	2.25
3	δ-Caryophyllene	3.25	4.38	4.73	4.63	4.19	4.24
4	Caryophyllene oxide	3.53	4.91	4.94	4.31	5.15	4.57
5	β-Elemene	3.37	6.11	4.75	4.53	4.5	4.65
6	MethylChavicol	2.47	3.37	2.42	2.67	2.96	2.78
7	Linalool	2.7	2.97	2.67	2.59	2.35	2.66
8	δ-Cardinene	3.41	3.8	4.73	4.63	4.12	4.14
9	β-Bisabolene	3.67	6.43	5.04	4.53	4.5	4.83
10	1,8-Cineole	2.58	2.74	2.74	2.45	2.86	2.67
11	Camphor	2.12	2.19	2.4	2.3	2.85	2.37
12	Isocaryophyllene	2.63	4.38	3	4.29	2.79	3.42

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13	Apigenin-7-O-glucuronide	1	1.46	0.14	-1.63	-0.1	0.17
14	Carvacrol	2.24	3.49	2.82	2.76	2.79	2.82
15	Circimaritin	2.56	3.32	2.89	0.47	3.07	2.46
16	Isothymusin	2.58	2.61	2.59	-0.07	2.59	2.06
17	Pinene	2.66	2.74	3	4.58	3.06	3.21
18	Molludistin	2.21	0.6	0.71	-1.25	1.37	0.73
19	Rosameric acid	1.48	2.36	1.65	0.9	1.5	1.58
20	Orientin	1.02	-1.03	-1.16	-2.32	-1.21	-0.94
21	Vicenin	1.73	-2.26	-3.04	-4.51	-1.8	-1.98
22	Urosolic acid	3.95	7.34	7.09	5.82	5.46	5.93
23	Luteolin	1.86	2.53	2.28	-0.03	2.03	1.73
24	Luteolin-7-O-glucuronide	1.79	-0.13	-0.78	-1.94	-1.64	-0.54
25	3-Carene	2.63	4.38	3	4.29	2.79	3.42
26	Citral	2.47	3.03	2.88	2.49	2.65	2.71
27	Geraniol	2.52	3.56	2.67	2.59	2.35	2.74
28	Methyl Cinnamate	2.17	2.25	2.15	2.49	2.57	2.33
29	β-Ocimene	2.91	4.26	3.48	3.56	2.88	3.42
30	λ-Terpineol	2.51	3.39	2.5	2.3	2.17	2.58
31	PhenylPropanoids	1.08	-1.52	0.64	-1.11	0.86	-0.01
32	Germacrene-D	3.14	4.74	4.89	4.53	4.01	4.26
33	λ-Humulene	3.29	4.55	5.04	4.53	3.91	4.26
34	Camphene	2.58	4.22	3	4.29	3.08	3.43
35	Myrcene	2.89	4.17	3.48	3.56	3.05	3.43
36	Thymol	2.32	3.3	2.82	2.76	2.79	2.8
37	λ-Linolenic acid	2.32	3.3	5.66	2.76	2.79	2.8

Table 4. Drug likeness of the Phytoconstituents of Ocimum sanctum Linn.

Sl.No	Molecules	Lipinski violations	Ghose violations	Veber violations	Egan violations	Muegge violations	Bioavailability Score
1	MethylEugenol	0	0	0	0	1	0.55
2	Eugenol	0	0	0	0	1	0.55
3	δ-Caryophyllene	1	0	0	0	1	0.55
4	Caryophyllene oxide	1	0	0	0	1	0.55
5	β-Elemene	1	0	0	0	2	0.55
6	MethylChavicol	0	1	0	0	2	0.55
7	Linalool	0	1	0	0	2	0.55
8	δ-Cardinene	1	0	0	0	1	0.55
9	β-Bisabolene	1	0	0	0	2	0.55
10	1,8-Cineole	0	1	0	0	2	0.55
11	Camphor	0	1	0	0	2	0.55
12	Isocaryophyllene	1	1	0	0	2	0.55
13	Apigenin-7-O-glucuronide	2	0	1	1	3	0.11
14	Carvacrol	0	1	0	0	2	0.55
15	Circimaritin	0	0	0	0	0	0.55
16	Isothymusin	0	0	0	0	0	0.55
17	Pinene	1	1	0	0	2	0.55

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18	Molludistin	0	0	1	1	0	0.55
19	Rosameric acid	0	0	1	1	0	0.56
20	Orientin	2	1	1	1	3	0.17
21	Vicenin	3	4	1	1	4	0.17
22	Urosolic acid	1	3	0	1	1	0.85
23	Luteolin	0	0	0	0	0	0.55
24	Luteolin-7-O-glucuronide	2	1	1	1	3	0.11
25	3-Carene	1	1	0	0	2	0.55
26	Citral	0	1	0	0	2	0.55
27	Geraniol	0	1	0	0	2	0.55
28	Methyl Cinnamate	0	0	0	0	1	0.55
29	β-Ocimene	0	1	0	0	2	0.55
30	λ-Terpineol	0	1	0	0	2	0.55
31	PhenylPropanoids	0	0	0	0	1	0.55
32	Germacrene-D	1	0	0	0	1	0.55
33	λ-Humulene	1	0	0	0	1	0.55
34	Camphene	1	1	0	0	2	0.55
35	Myrcene	0	1	0	0	2	0.55
36	Thymol	0	1	0	0	2	0.55
37	λ-Linolenic acid	0	1	0	0	2	0.55

Table 5. Medicinal Chemistry Properties of Phytoconstituents of Ocimum sanctum Linn.

Sl.No	Molecules	PAINS	Brenk	Leadlikeness	Synthetic Accessibility
1	MethylEugenol	0	1	1	1.71
2	Eugenol	0	1	1	1.58
3	δ-Caryophyllene	0	1	2	4.51
4	Caryophyllene oxide	0	1	1	4.46
5	β-Elemene	0	1	2	3.63
6	MethylChavicol	0	1	1	1.28
7	Linalool	0	1	1	2.74
8	δ-Cardinene	0	1	2	4.14
9	β-Bisabolene	0	1	2	3.9
10	1,8-Cineole	0	0	1	3.65
11	Camphor	0	0	1	3.22
12	Isocaryophyllene	0	1	2	3.84
13	Apigenin-7-O-glucuronide	0	0	1	5.06
14	Carvacrol	0	0	1	1
15	Circimaritin	0	0	0	3.27
16	Isothymusin	0	1	0	3.38
17	Pinene	0	1	1	4.81
18	Molludistin	0	0	1	4.91
19	Rosameric acid	1	2	1	3.38
20	Orientin	1	1	1	5.34
21	Vicenin	0	0	1	6.4
22	Urosolic acid	0	1	2	6.21
23	Luteolin	1	1	0	3.02
24	Luteolin-7-O-glucuronide	1	1	1	5.32

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25	3-Carene	0	1	2	3.84
26	Citral	0	3	1	2.49
27	Geraniol	0	1	2	2.58
28	Methyl Cinnamate	0	0	1	1.98
29	β-Ocimene	0	2	2	3.63
30	λ-Terpineol	0	1	1	3.24
31	PhenylPropanoids	0	0	1	1.46
32	Germacrene-D	0	1	2	4.55
33	λ-Humulene	0	1	2	3.66
34	Camphene	0	1	2	3.5
35	Myrcene	0	2	2	2.85
36	Thymol	0	0	1	1
37	λ-Linolenic acid	0	0	1	1

Table 6. Pharmacokinetic Parameters of the Phytoconstituents of Ocimum sanctum.

Sl.No	Molecules	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)
1	MethylEugenol	High	Yes	No	Yes	No	No	No	No	-5.6
2	Eugenol	High	Yes	No	Yes	No	No	No	No	-5.69
3	δ-Caryophyllene	Low	No	No	No	Yes	Yes	No	No	-4.44
4	Caryophyllene oxide	High	Yes	No	No	No	Yes	No	No	-4.34
5	β-Elemene	Low	No	No	No	Yes	Yes	No	No	-3.21
6	MethylChavicol	High	Yes	No	Yes	No	No	No	No	-4.81
7	Linalool	High	Yes	No	No	No	No	No	No	-5.13
8	δ-Cardinene	Low	No	No	No	Yes	Yes	No	No	-4.85
9	β-Bisabolene	Low	No	No	No	No	Yes	No	No	-2.98
10	1,8-Cineole	High	Yes	No	No	No	No	No	No	-5.3
11	Camphor	High	Yes	No	No	No	No	No	No	-5.67
12	Isocaryophyllene	Low	Yes	No	No	No	Yes	No	No	-4.02
13	Apigenin-7-O-glucuronide	Low	No	Yes	No	No	No	No	No	-7.99
14	Carvacrol	High	Yes	No	Yes	No	No	No	No	-4.74
15	Circimaritin	High	No	No	Yes	No	Yes	Yes	Yes	-5.86
16	Isothymusin	High	No	No	Yes	No	Yes	Yes	Yes	-6.46
17	Pinene	Low	Yes	No	No	No	Yes	No	No	-5.26
18	Molludistin	Low	No	No	No	No	No	No	No	-8.41
19	Rosamericacid	Low	No	No	No	No	No	No	No	-6.82
20	Orientin	Low	No	No	No	No	No	No	No	-9.78
21	Vicenin	Low	No	Yes	No	No	No	No	No	-11.53

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22	Urosolic acid	Low	No	No	No	No	No	No	No	-3.87
23	Luteolin	High	No	No	Yes	No	No	Yes	Yes	-6.25
24	Luteolin-7-O-glucuronide	Low	No	Yes	No	No	No	No	No	-9.22
25	3-Carene	Low	Yes	No	No	No	Yes	No	No	-4.02
26	Citral	High	Yes	No	No	No	No	No	No	-5.08
27	Geraniol	High	Yes	No	No	No	No	No	No	-4.71
28	Methyl Cinnamate	High	Yes	No	No	No	No	No	No	-5.78
29	β-Ocimene	Low	Yes	No	No	No	No	No	No	-4.11
30	λ-Terpineol	High	Yes	No	No	No	No	No	No	-4.83
31	PhenylPropanoids	High	No	No	No	No	No	No	No	-8.39
32	Germacrene-D	Low	No	No	No	No	Yes	No	No	-4.18
33	λ-Humulene	Low	No	No	No	No	Yes	No	No	-4.32
34	Camphene	Low	Yes	No	No	No	Yes	No	No	-4.13
35	Myrcene	Low	Yes	No	No	No	No	No	No	-4.17
36	Thymol	High	Yes	No	Yes	No	No	No	No	-4.87
37	λ-Linolenic acid	High	Yes	No	Yes	No	No	No	No	-4.87

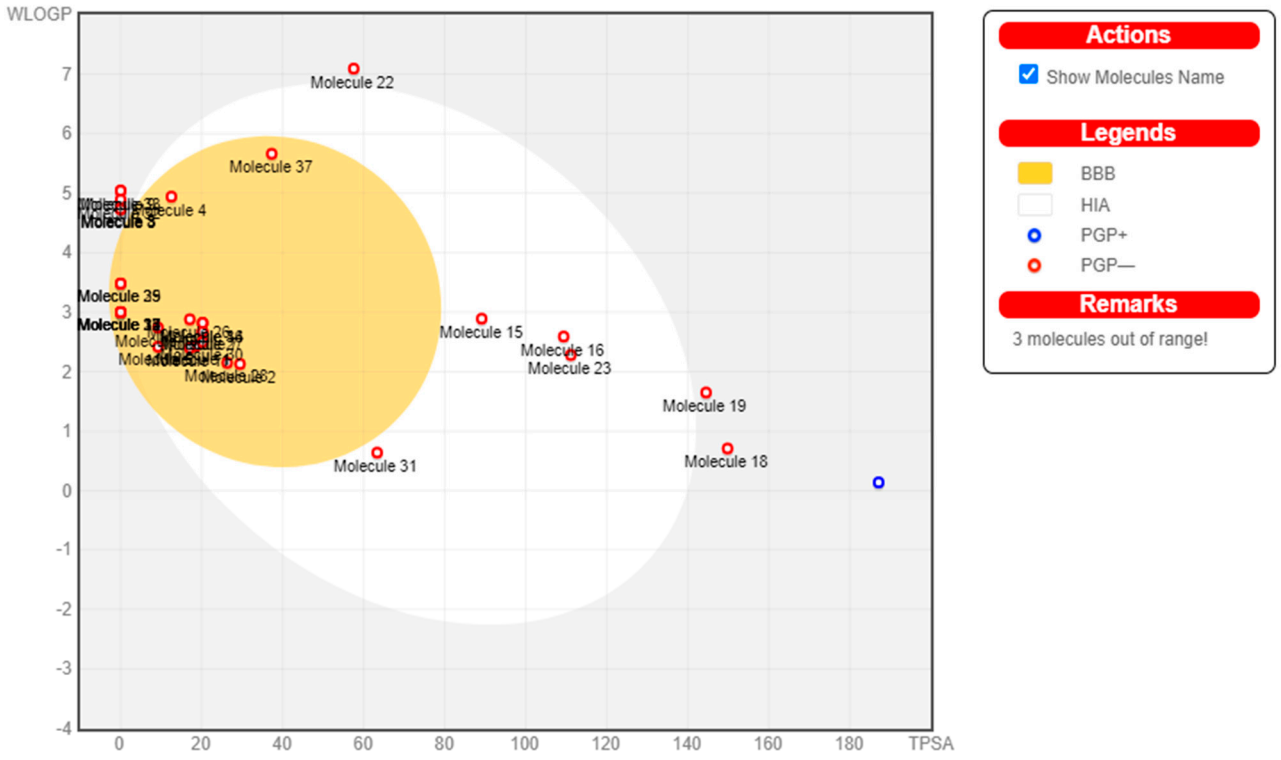

Figure 1. Boiled Egg Model of the Phytoconstituents of Ocimumsanctum Linn.

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4. Discussion

For the purpose of the current study, we evaluated the ADME properties of Ocimum sanctum Linn using the free online SwissADME software application. Through the software, the phytoconstituents of the plants were identified, they are Methyl Eugenol, Eugenol, β-Caryophyllene, Caryophyllene oxide, β-Elemene, Methyl Chavicol, Linalool, δ-Cadinene, β-Bisabolene, 1,8-Cineole, Camphor, Isocaryophyllene, Apigenin-7-O-glucuronide, Carvacrol, Circimaritin, Isothymusin, Pinene, Molludistin, Rosameric acid, Orientin, Vicenin, Urosolic acid, Luteolin, Luteolin-7-O-glucuronide, 3-Carene, Citral, Geraniol, Methyl Cinnamate, β-Ocimene, α-Terpineol, PhenylPropanoids, Germacrene-D, α-Humulene, Camphene, Myrcene, Thymol, α-Linolenic acid (Roshan Kumar *et al.*,2022 & Bhattacharya AK *et al.*,1996 & Kothari SK *et al.*,2005 & Awasthi PK *et al.*,2007 & Kicel A *et al.*,2005 & Khan A *et al.*,2010 & Machado MIL *et al.*,1999 & Pino JA *et al.*,1988 & Brophy JJ *et al.*,1993 & Kashyap C *et al.*,2011)[39–48].

As a result, the phytoconstituents ADME characteristics were examined, and the results were presented in appropriate tables and figures. Researchers and scientists can also utilize the values as monographs to generate future research semi- and synthetic pharmaceuticals for a wide range of applications.

5. Conclusion

CADD (Computer Aided Drug Design) has significantly changed research and development routes in drug concept exploration as an outcome of rapid growth in biological and chemical information. In terms of application, time, and cost, the use of computational techniques in the drug discovery and development process is often acclaimed. Modern chemistry relies extensively on computers, which are essential for both drug discovery and development. CADD is used in the pharmaceutical industry to develop and improve novel, safe, and effective pharmaceuticals. In these studies, a free web-based tool called SwissADME is presented to evaluate the ADME characteristics of Phytoconstituents found in the Ocimum sanctum Linn plant. This information could be used as a starting point for a more comprehensive evaluation of the plant's biological and pharmacological properties.

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