Int. J. Pharm. Investigation, 2025; 15(2):614-630.
https://www.jpionline.org

Original Article

Computer-Assisted Prediction of Drug-Like Properties of Selected Phytochemicals from *Terminalia chebula*

Adarsh Arun Patil, Shailendra Sanjay Suryawanshi*

Department of Pharmaceutical Chemistry, KLE College of Pharmacy, Belagavi, KLE Academy of Higher Education and Research, Belagavi, Karnataka, INDIA.

ABSTRACT

Introduction: The growing focus on natural products in drug discovery has led to a deeper investigation of phytochemicals from traditional medicinal plants. *Terminalia chebula*, known for its broad range of therapeutic uses, is a rich source of bioactive compounds. **Materials and Methods:** This study employs computer-aided techniques to predict the drug-like properties of selected phytochemicals from *Terminalia chebula*. By utilizing sophisticated computational tools, we assessed crucial drug-like features such as adherence to Lipinski's Rule of Five. The results reveal that several phytochemicals from *Terminalia chebula* exhibit promising drug-like qualities, including good bioavailability and minimal toxicity. **Results and Discussion:** This study highlights the potential of *Terminalia chebula*'s phytochemicals as strong candidates for drug development and establishes a basis for further experimental research and refinement. The use of computational approaches in evaluating natural products underscores their crucial role in contemporary drug discovery.

Keywords: Computer-aided technique, Drug-like Properties, Lipinski's Rule of Five, Phytochemicals, *Terminalia chebula*.

Correspondence:
Dr. Shailendra Sanjay Suryawanshi
Department of Pharmaceutical Chemistry, KLE College of Pharmacy, Belagavi, KLE Academy of Higher Education and Research, Belagavi, Karnataka, INDIA.
Email: shailendrasuryawanshi@klepharm.edu

Received: 24-08-2024;
Revised: 22-10-2024;
Accepted: 14-12-2024.

INTRODUCTION

Terminalia chebula, commonly known as Haritaki, is a medicinal plant widely used in traditional medicine systems such as Ayurveda, Unani and traditional Chinese medicine. The fruit of *Terminalia chebula* is revered for its wide range of therapeutic properties, including antioxidant, anti-inflammatory, antimicrobial, anticancer and hepatoprotective effects. These effects are attributed to its rich phytochemical content, which includes tannins, flavonoids, glycosides and triterpenoids (Kumar *et al*., 2016; Sharma *et al*., 2017). For a compound to be considered a viable drug candidate, it must exhibit favorable drug-like properties such as solubility, permeability and bioavailability. These properties are crucial for ensuring that the compound can reach the target site in the body at therapeutic concentrations. Lipinski's Rule of Five is commonly used to predict drug-likeness, taking into account factors such as molecular weight, hydrogen bond donors and acceptors and the octanol-water partition coefficient (logP) (Lipinski *et al*., 1997). Compounds that violate more than one of these criteria are generally considered less likely to be orally active drugs. The integration of computational tools in drug discovery, known as Computer-Aided Drug Design (CADD), has significantly enhanced the efficiency of the drug development process. Techniques such as molecular docking, Quantitative Structure-Activity Relationship (QSAR) modeling and pharmacophore modeling allow researchers to rapidly screen and optimize potential drug candidates (Kitchen *et al*., 2004; Sliwoski *et al*., 2014). These computational methods not only expedite the drug discovery process but also improve the accuracy of predicting a compound's drug-like properties and potential therapeutic efficacy. Phytochemicals such as chebulagic acid, chebulinic acid, gallic acid, ellagic acid and quercetin have been identified in *Terminalia chebula*. These compounds have demonstrated various biological activities, including anti-inflammatory, antioxidant and anticancer effects, making them potential candidates for drug development (Singh *et al*., 2020). However, their viability as drug candidates must be assessed through the evaluation of their drug-like properties using computational methods. Several computational tools and databases are available for predicting the drug-like properties of phytochemicals. SwissADME, Molinspiration and PreADMET are commonly used to predict properties such as molecular weight, logP, Topological Polar Surface Area (TPSA) and bioavailability (Daina *et al*., 2017). Molecular docking studies can predict the binding affinity of phytochemicals to specific target proteins, while QSAR modeling can estimate the biological

DOI: 10.5530/ijpi.20250067

activity of these compounds based on their chemical structure (Cherkasov *et al*., 2014).

Recent research has focused on the *in silico* analysis of *Terminalia chebula* phytochemicals to predict their drug-like properties and therapeutic potential. For instance, molecular docking studies have shown that chebulagic acid has a strong binding affinity toward cancer-related proteins, suggesting its potential as an anticancer agent (Kumar *et al*., 2021). Similarly, QSAR studies have been utilized to predict the antioxidant and anti-inflammatory activities of various *Terminalia chebula* phytochemicals (Patil *et al*., 2019). While computational methods offer significant advantages in predicting drug-like properties, they also have limitations. The accuracy of these predictions is highly dependent on the quality of the input data and the computational algorithms used. Additionally, *in silico* predictions need to be validated through *in vitro* and *in vivo* studies to confirm their relevance and applicability (Ekins *et al*., 2007). Future research should focus on integrating computational predictions with experimental validation to advance the drug discovery process for *Terminalia chebula* phytochemicals. The application of computational methods to predict the drug-like properties of phytochemicals from *Terminalia chebula* holds great potential for drug discovery. These methods allow for the rapid screening and optimization of potential drug candidates, offering valuable insights into their therapeutic potential. However, further research is necessary to validate these predictions and translate them into effective therapeutic agents.

In this study, we employ advanced computational techniques to predict the drug-like properties of selected phytochemicals derived from *Terminalia chebula*. This approach provides valuable insights into the potential of these compounds as drug candidates, highlighting their suitability for further development and optimization. The integration of computational methods in evaluating *Terminalia chebula* phytochemicals underscores the growing importance of *in silico* tools in modern drug discovery. By bridging traditional knowledge with cutting-edge technology, this research seeks to identify promising drug-like candidates from *Terminalia chebula*, paving the way for new therapeutic developments and contributing to the field of natural product-based drug discovery.

MATERIALS AND METHODS

Software's and Servers used

Pubchem database is used for collection of canonical smiles and downloading SDF files. Molsoft software is used for determination of drug likeness (Kim *et al*., 2016; Totrov and Abagyan, 2008).

List of Phytochemicals

The list of selected phytochemicals included in the study are, 1, 16-Hexadecanediol, 1, 19-Eicosadiene, 1, 2-Benzenedicarboxylic acid, 1,2,3,6-Tetrakis-o-galloyl-beta-D-glucose, 10-Nonadecanone, 1-Decanol, 1H-Indene, 1-Octanol, 1-Tricosene, 2-Alpha-Hydroxyursolic acid, 2-Undecanone, 3, 4-Dimethoxy quercetin [5, 7-Dihydroxy-2-(3-hydroxy-4- met hoxyphenyl)-3-Methoxy-4H-chromen-4-one] 3'-Methoxy quercetin 4-o-methylgallic acid, 8-Pentadecanone, 9, 12, 15-Octadecatrienoic acid 9-Eicosene, 9-Heptadecanone, 9-Octadecene, 9-Octadecenoic acid ethyl ester, 9-Tricosene, Acetic acid, Alpha-Phellandrene, Arachidic acid [icosanoic acid], Arjunetin, Arjungenin, Arjunglucoside I, Arjunglucoside II, Arjunic acid, Arjunolic acid, Ascorbic acid, Behenic acid [Docosanoic acid], Bellericoside, Beta-caryophyllene, Beta-Sitosterol, Caffeic acids, Casuarinin, Chebulagic acid, Chebulanin, Chebulinic acid, Chebuloside II, Corilagin Cyclododecane, Cyclooctacosane, Cylohexane, Daucosterol, Eicosyl trifluoroacetate, Ellagic acid, Ethanedioic acid, Ethyl gallate, Eugenol, Ferulic acid, Gallic acid, Heptacosanoic acid, Heptafluorobutyric acid, Heptylcyclohexane, Hexacosanoic acid, Hexacosyl pentafluoropropionate, Hexadecane, Ibogamin-9(17H)-ol [(9α)-12-Methoxy-16, 17-didehydro-9, 17-dihydroibogamin9-ol], Isoquercetin, Kaempferol-3-rutinoside, Linoleic acid, Linoleic acid ethyl ester, Luteolin, Maslinic Acid, Melilotic acid, Methyl gallate, Octacosanoic acid, Octatriacontyl pentafluoropropionate, Oleic acid, Oxirane, Palmitic acid, p-Coumaric acid, Pelargonidin, Pentatriacontane, Phloroglucinol, Phthalic acid, Punicalagin, Punicalin, Pyrogallol, Quercetin, Ricinoleic acid, Rutin, Shikimic acid, Squalene, Stearic acid, Sulfurous acid, Terchebin, Terchebulin, Terflavin A, Terflavin B, Terminolic acid, Terpinen-4-ol, Terpinolene, Tetracosanoate, Tetracosanoic acid [Lignoceric acid], Tetracosyl heptafluorobutyrate, Tetradecane, Tetratetracontane, Tetratriacontane, Tetratriacontyl heptafluorobutyrate, Tetratriacontyl pentafluoropropionate, Triacontane, Triacontanoic acid, Tricosyl pentafluoropropionate, Tritetracontane, Vanillic acid and Vitamin E (Saleem *et al*., 2002; Sabu and Kuttan, 2002; Bag *et al*., 2013; Wang *et al*., 2015).

Collection of Canonical SMILES of selected Phytochemicals from PubChem Database

In order to collect canonical SMILES for selected phytochemicals, we have accessed the PubChem website and searched for each phytochemical by entering its name in the search bar. After locating the compound in the search results, we clicked on it to open its compound summary page on that page, we scrolled down to the "Chemical and Physical Properties" section and found the "Canonical SMILES" field, usually located under "Molecular Descriptors." Then we copied the canonical SMILES string and repeated this process for each phytochemical.

Chemical structures of selected phytochemicals

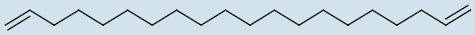
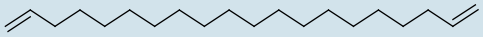
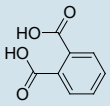
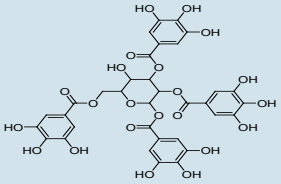
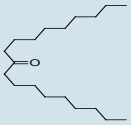
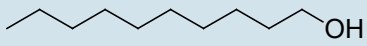
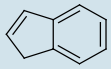
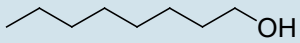
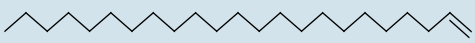
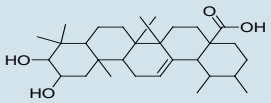
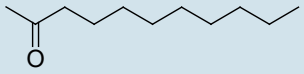
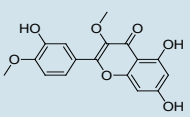
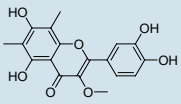
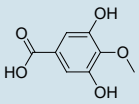
In order to draw the chemicals structures of selected phytochemicals in ChemDraw using a canonical SMILES string, we have accessed the "Structure" menu in ChemDraw. From

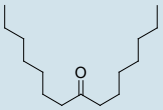
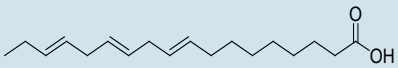
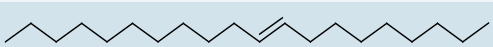
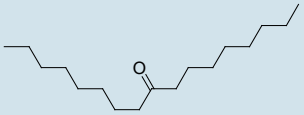
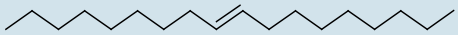
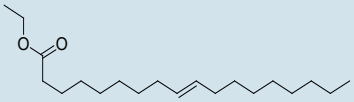
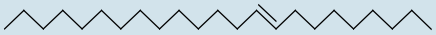
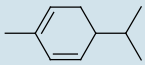
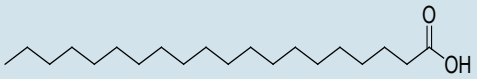
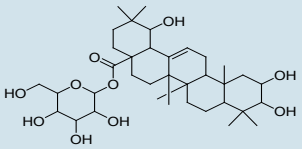
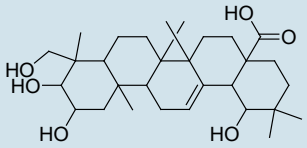
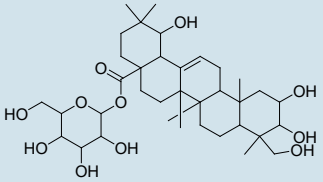
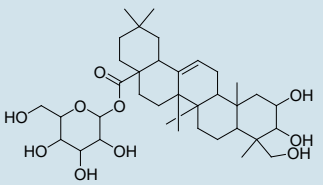
there, we have selected "Convert SMILES to Structure" and then inserted canonical SMILES string into the input box that appears and click "OK". ChemDraw automatically generated structure then adjusted using ChemDraw's tools, such as the bond and atom tools. Table 1 represents the chemical structure of selected phytochemicals.

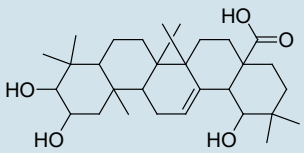
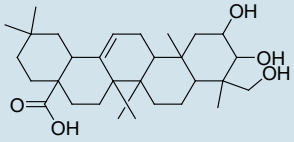
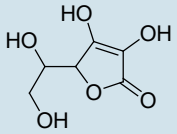
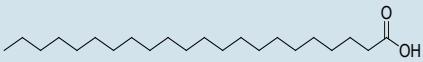
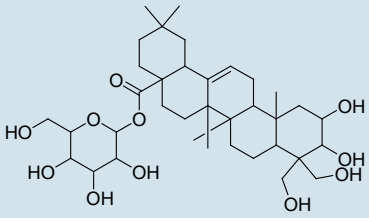
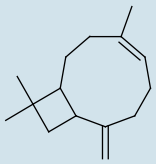
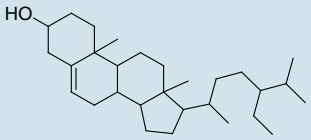
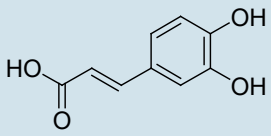
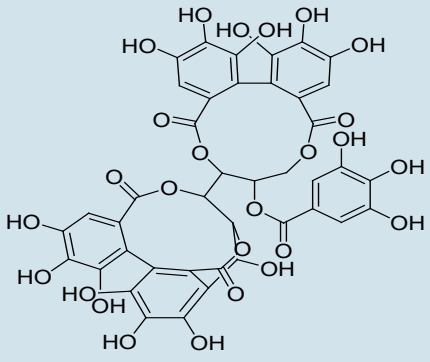
Determination of Drug Likeness Score

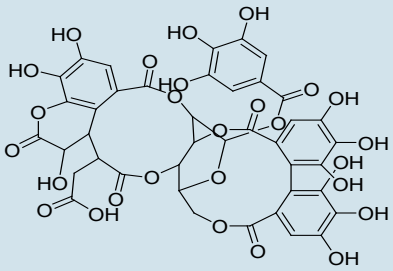
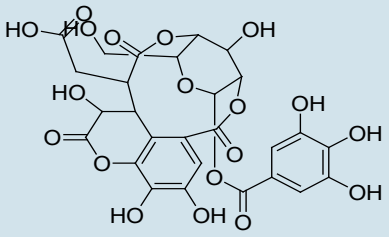
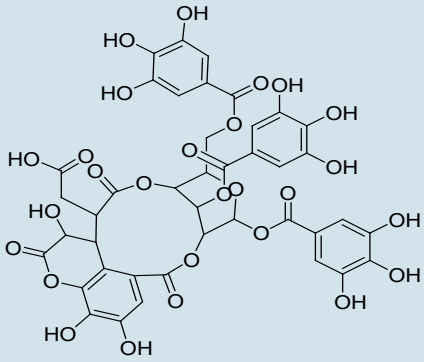
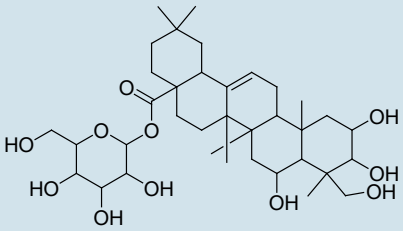
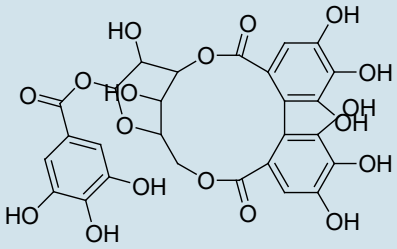
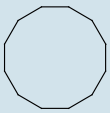
MolSoft web servers (https://molsoft.com/mprop/) were used to forecast the drug-like characteristics of phytocompounds. Lipinski's rule of five was used to compute drug-like qualities, which states that molecules should have a molecular weight of 500, a C logP of 5, less than 10 hydrogen bond acceptors and less

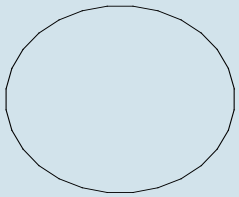
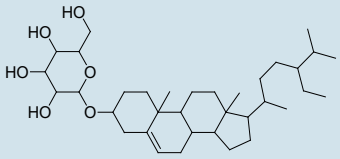
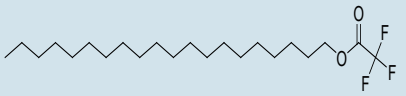
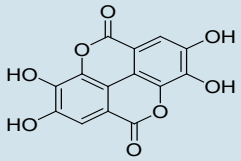
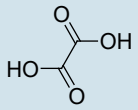
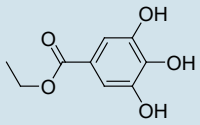
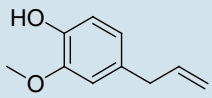
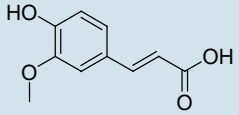
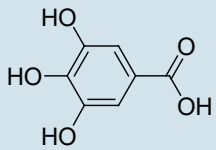
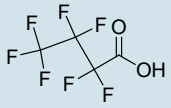
Table 1: Chemical structure of selected phytochemicals.

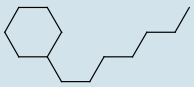
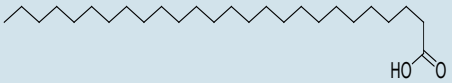
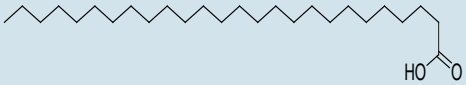
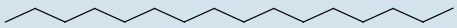
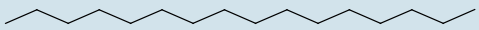
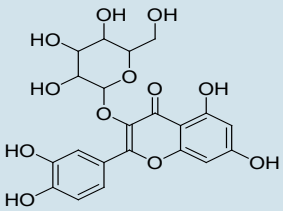
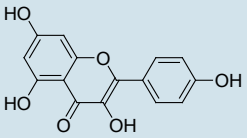
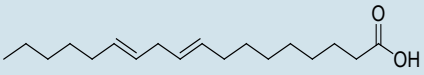
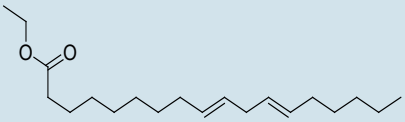
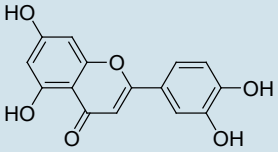
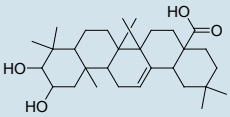
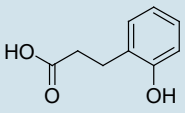
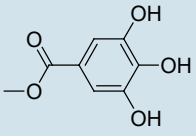
Sl. No.	Phytochemicals	Chem Draw Structure
1	1, 16-Hexadecanediol	
2	1, 19-Eicosadiene	
3	1, 2-Benzenedicarboxylic acid	
4	1,2,3,6-Tetrakis-O-galloyl-beta-D-glucose	
5	10-Nonadecanone	
6	1-Decanol	
7	1H-Indene	
8	1-Octanol	
9	1-Tricosene	
10	2-Alpha-Hydroxyursolic acid	
11	2-Undecanone	
12	3, 4-Dimethoxy quercetin [5, 7-Dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3-Methox y-4H-chromen-4-one]	
13	3'-Methoxy quercetin	
14	4-O-methylgallic acid	

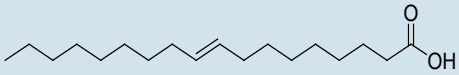
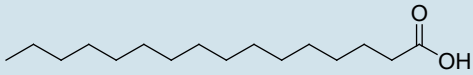
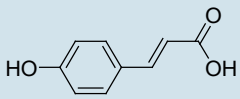
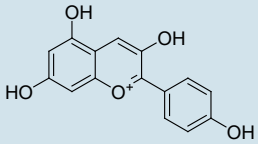
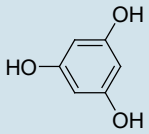
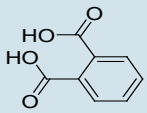
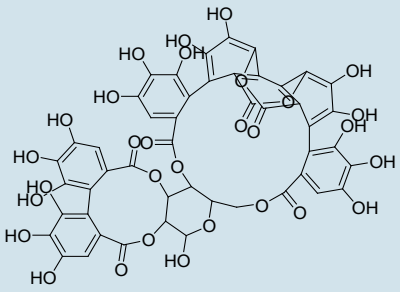
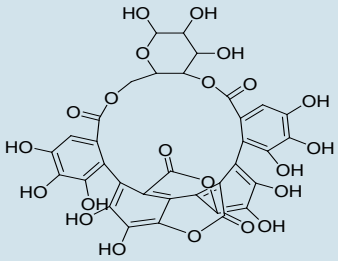
Sl. No.	Phytochemicals	Chem Draw Structure
15	8-Pentadecanone	
16	9, 12, 15-Octadecatrienoic acid	
17	9-Eicosene	
18	9-Heptadecanone	
19	9-Octadecene	
20	9-Octadecenoic acid ethyl ester	
21	9-Tricosene	
22	Acetic acid	
23	Alpha-Phellandrene	
24	Arachidic acid [icosanoic acid]	
25	Arjunetin	
26	Arjungenin	
27	Arjunglucoside I	
28	Arjunglucoside II	

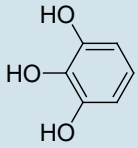
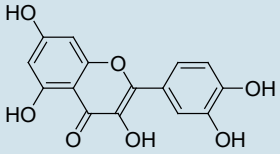
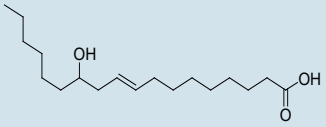
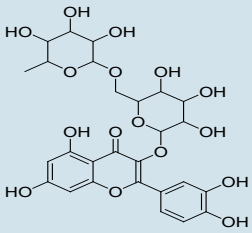
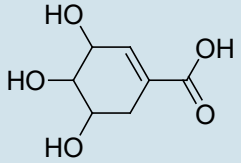
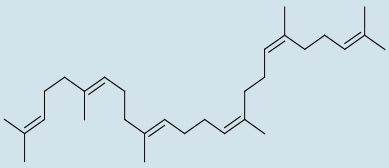
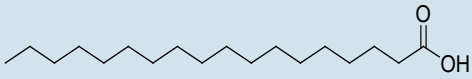
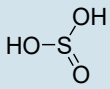
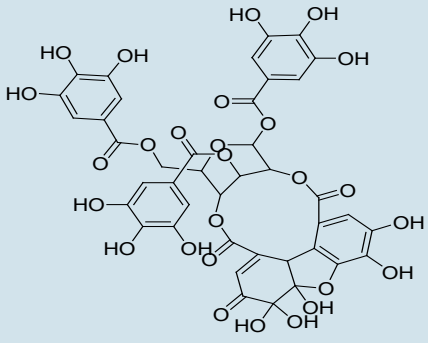
Sl. No.	Phytochemicals	Chem Draw Structure
29	Arjunic acid	
30	Arjunolic acid	
31	Ascorbic acid	
32	Behenic acid [Docosanoic acid]	
33	Bellericoside	
34	Beta-caryophyllene	
35	Beta-Sitosterol	
36	Caffeic acids	
37	Casuarinin	

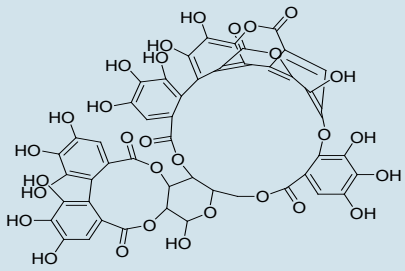
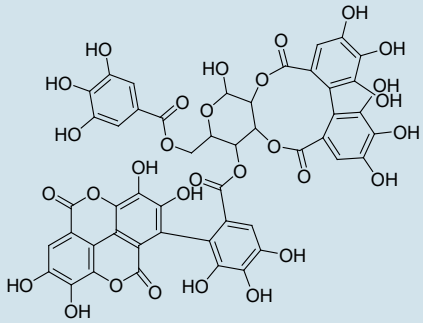
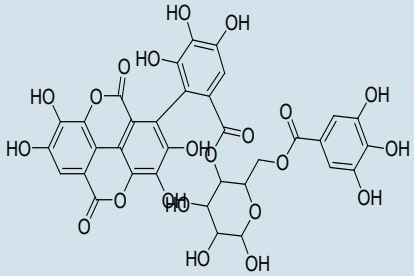
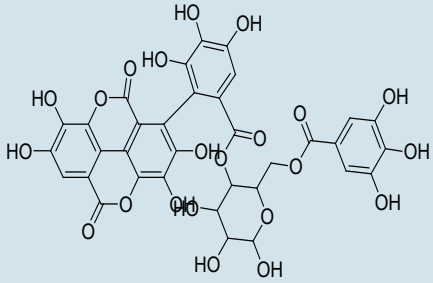
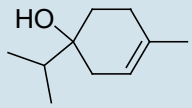
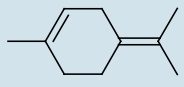
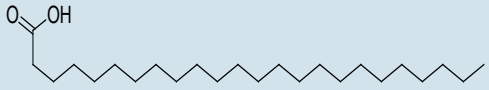
Sl. No.	Phytochemicals	Chem Draw Structure
38	Chebulagic acid	
39	Chebulanin	
40	Chebulinic acid	
41	Chebuloside II	
42	Corilagin	
43	Cyclododecane	

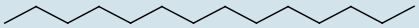
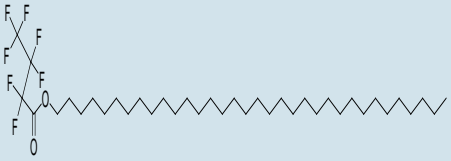
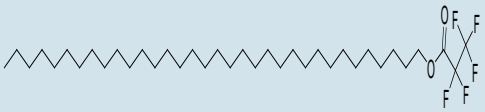
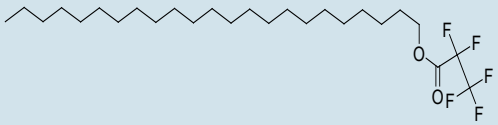
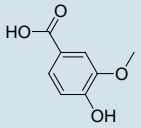
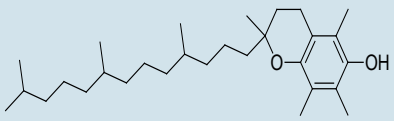
Sl. No.	Phytochemicals	Chem Draw Structure
44	Cyclooctacosane	
45	Cylohexane	
46	Daucosterol	
47	Eicosyl trifluoroacetate	
48	Ellagic acid	
49	Ethanedioic acid	
50	Ethyl gallate	
51	Eugenol	
52	Ferulic acid	
53	Gallic acid	
54	Heptacosanoic acid	
55	Heptafluorobutyric acid	

Sl. No.	Phytochemicals	Chem Draw Structure
56	Heptylcyclohexane	
57	Hexacosanoic acid	
58	Hexacosyl pentafluoropropionate	
59	Hexadecane	
60	Ibogamin-9(17H)-ol [(9α)-12-Methoxy-16, 17-didehydro-9, 17-dihydroibogamin9-ol]	
61	Isoquercetin	
62	Kaempferol-3-rutinoside	
63	Linoleic acid	
64	Linoleic acid ethyl ester	
65	Luteolin	
66	Maslinic Acid	
67	Melilotic acid	
68	Methyl gallate	

Sl. No.	Phytochemicals	Chem Draw Structure
69	Octacosanoic acid	
70	Octatriacontyl pentafluoropropionate	
71	Oleic acid	
72	Oxirane	
73	Palmitic acid	
74	p-Coumaric acid	
75	Pelargonidin	
76	Pentatriacontane	
77	Phloroglucinol	
78	Phthalic acid	
79	punicalagin	
80	Punicalin	

Sl. No.	Phytochemicals	Chem Draw Structure
81	Pyrogallol	
82	Quercetin	
83	Ricinoleic acid	
84	Rutin	
85	Shikimic acid	
86	Squalene	
87	Stearic acid	
88	Sulfurous acid	
89	Terchebin	

Sl. No.	Phytochemicals	Chem Draw Structure
90	Terchebulin	
91	Terflavin A	
92	Terflavin B	
93	Terminolic acid	
94	Terpinen-4-ol	
95	Terpinolene	
96	Tetracosanoate	
97	Tetracosanoic acid [Lignoceric acid]	

Sl. No.	Phytochemicals	Chem Draw Structure
98	Tetracosyl heptafluorobutyrate	
99	Tetradecane	
100	Tetratetracontane	
101	Tetratriacontane	
102	Tetratriacontyl heptafluorobutyrate	
103	Tetratriacontyl pentafluoropropionate	
104	Triacontane	
105	Triacontanoic acid	
106	Tricosyl pentafluoropropionate	
107	Tritetracontane	
108	Vanillic acid	
109	Vitamin E	

than 5 hydrogen bond donors. To anticipate drug-like features of compounds, the canonical Simplified Molecular Line-Entry Systems (SMILES) were retrieved from PubChem and entered into the MolSoft online server (Hatano *et al*., 2005; MolSoft, 2024; Daina *et al*., 2017; Egan *et al*., 2000; Muegge *et al*., 2001; Patil *et al*., 2020; Suryawanshi *et al*., 2020; Suryawanshi *et al*., 2020; Sampat *et al*., 2020).

RESULTS

The concept of drug likeness is crucial in drug design, indicating how closely a substance aligns with the characteristics of a typical drug, particularly in terms of bioavailability. In this study, various parameters related to drug similarity were computed for selected phytochemicals to gain insights into their bioavailability in the human body. The study focused on determining whether these

Table 2: Drug Likness Profile of Phytochemicals from *Terminalia chebula*.

Sl. No.	Phytochemicals	MW (> 500)	Clog *P* (> 5)	HBA (> 10)	HBD (> 5)	Number of Violations	DLS
1	1, 16-Hexadecanediol	257.11	2.68	3	1	0	0.29
2	1, 19-Eicosadiene	278.3	10.39	0	0	1	-1.03
3	1, 2-Benzenedicarboxylic acid	166.03	0.8	4	2	0	-1.34
4	1,2,3,6-Tetrakis-O-galloyl-beta-D-glucose	788.11	0.74	22	13	3	0.92
5	10-Nonadecanone	257.11	2.68	3	1	0	0.29
6	1-Decanol	158.17	4.11	1	1	0	-0.92
7	1H-Indene	116.06	2.79	0	0	0	-1.82
8	1-Octanol	130.14	3.10	1	1	0	-0.92
9	1-Tricosene	322.36	12.16	0	0	1	-1.25
10	2-Alpha-Hydroxyursolic acid	472.36	5.3	4	3	1	0.06
11	2-Undecanone	170.17	3.99	1	0	0	-1.28
12	3, 4-Dimethoxy quercetin [5, 7-Dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3-Methoxy-4H-chromen-4-one]	330.07	2.42	7	3	0	0.07
13	3'-Methoxy quercetin	344.09	3.35	7	4	0	0.29
14	4-O-methylgallic acid	184.04	0.95	5	3	0	-0.7
15	8-Pentadecanone	226.23	6.1	1	0	1	-1.20
16	9, 12, 15-Octadecatrienoic acid	278.22	5.88	2	1	1	0.09
17	9-Eicosene	280.31	10.35	0	0	1	-1.12
18	9-Heptadecanone	254.26	7.11	1	0	1	-1.2
19	9-Octadecene	252.28	9.34	0	0	1	-1.12
20	9-Octadecenoic acid ethyl ester	310.29	8.31	2	0	1	-0.84
21	9-Tricosene	322.36	11.87	0	0	1	-1.12
22	Acetic acid	60.02	-0.10	2	1	0	0.55
23	Alpha-Phellandrene	136.13	4.01	0	0	0	-1.23
24	Arachidic acid [icosanoic acid]	312.3	8.66	2	1	1	-0.54
25	Arjunetin	650.4	2.60	10	7	2	0.58
26	Arjungenin	504.35	2.97	6	5	1	0.64
27	Arjunglucoside I	666.40	0.93	11	8	3	0.63
28	Arjunglucoside II	650.4	1.80	10	7	2	0.65
29	Arjunic acid	488.35	4.64	5	4	0	0.54
30	Arjunolic acid	488.35	3.84	5	6	0	0.64
31	Ascorbic acid	176.03	-1.59	6	4	0	0.74
32	Behenic acid [Docosanoic acid]	340.33	9.67	2	1	1	-0.54
33	Bellericoside	666.40	0.74	11	8	3	0.66
34	Beta-caryophyllene	204.19	5.35	0	0	1	-1.74
35	Beta-Sitosterol	414.39	8.45	1	1	1	0.78
36	Caffeic acids	180.04	1.27	4	3	0	-0.35
37	Casuarinin	936.09	2.78	26	16	3	0.32
38	Chebulagic acid	954.1	0.22	27	13	3	0.58

Sl. No.	Phytochemicals	MW (> 500)	Clog *P* (> 5)	HBA (> 10)	HBD (> 5)	Number of Violations	DLS
39	Chebulanin	652.09	-1.91	19	9	3	0.55
40	Chebulinic acid	956.11	-0.36	27	13	3	0.70
41	Chebuloside II	666.4	1.02	11	8	3	0.66
42	Corilagin	634.08	0.51	18	11	3	0.64
43	Cyclododecane	168.19	6.28	0	0	1	-1.16
44	Cyclooctacosane	392.44	14.37	0	0	1	-1.16
45	Cylohexane	84.09	3.25	0	0	0	-1.01
46	Daucosterol	576.44	6.31	6	4	2	0.5
47	Eicosyl trifluoroacetate	394.31	10.45	2	0	1	-1.44
48	Ellagic acid	302.01	1.53	8	4	0	-1.11
49	Ethanedioic acid	90	-1.02	4	2	0	-0.97
50	Ethyl gallate	198.05	1.4	5	3	0	-0.39
51	Eugenol	164.08	2.21	2	1	0	-0.74
52	Ferulic acid	194.06	1.61	4	2	0	-0.61
53	Gallic acid	257.11	2.68	3	1	0	0.29
54	Heptacosanoic acid	410.41	12.2	2	1	1	-0.54
55	Heptafluorobutyric acid	213.99	2.01	2	1	0	-1.55
56	Heptylcyclohexane	182.2	6.44	0	0	1	-1.19
57	Hexacosanoic acid	396.4	11.7	2	1	1	-0.54
58	Hexacosyl pentafluoropropionate	528.4	14.37	2	0	2	-1.47
59	Hexadecane	226.27	8.87	0	0	1	-1.03
60	Ibogamin-9(17H)-ol [(9α)-12-Methoxy-16, 17-didehydro-9, 17-dihydroibogamin9-ol]	326.2	3.28	4	1	0	1.17
61	Isoquercetin	464.1	-0.54	12	8	2	0.68
62	Kaempferol-3-rutinoside	286.05	1.61	6	4	0	0.5
63	Linoleic acid	280.24	6.6	2	1	1	-0.3
64	Linoleic acid ethyl ester	308.27	7.8	2	0	1	-0.84
65	Luteolin	286.05	2.78	6	4	0	0.38
66	Maslinic Acid	472.36	5.51	4	3	1	0.55
67	Melilotic acid	166.06	1.19	3	2	0	-0.92
68	Methyl gallate	184.04	0.9	5	3	1	-0.65
69	Octacosanoic acid	424.43	12.71	2	1	1	-0.54
70	Octatriacontyl pentafluoropropionate	696.58	20.44	2	0	2	-1.47
71	Oleic acid	282.26	7.11	2	1	1	-0.30
72	Oxirane	44.03	-0.41	1	0	0	-1.15
73	Palmitic acid	256.24	6.64	2	1	1	-0.54
74	p-Coumaric acid	164.05	1.66	3	2	0	-0.81
75	Pelargonidin	271.06	1.97	5	4	0	-0.57
76	Pentatriacontane	257.11	2.68	3	1	0	0.29
77	Phloroglucinol	126.03	0.31	3	3	0	-1.05
78	Phthalic acid	166.03	0.8	4	2	0	-1.34

Sl. No.	Phytochemicals	MW (> 500)	Clog *P* *(> 5)*	HBA (> 10)	HBD (> 5)	Number of Violations	DLS
79	Punicalagin	1084.07	3.29	30	17	3	-0.29
80	Punicalin	782.06	0.94	22	13	3	-0.09
81	Pyrogallol	126.03	0.93	3	3	0	-1.36
82	Quercetin	302.04	1.19	7	5	0	0.52
83	Ricinoleic acid	298.25	5.67	3	2	1	-0.36
84	Rutin	610.15	-1.55	16	10	3	0.91
85	Shikimic acid	174.05	-1.38	5	4	0	-1.06
86	Squalene	410.39	12.91	0	0	1	-0.9
87	Stearic acid	284.27	7.65	2	1	1	-0.54
88	Sulfurous acid	81.97	-1.24	4	2	0	-1.09
89	Terchebin	954.1	0.26	27	14	3	0.57
90	Terchebulin	1084.07	3.61	30	16	3	-0.31
91	Terflavin A	1086.08	2.98	30	17	3	0.19
92	Terflavin B	784.08	0.63	22	13	3	0.45
93	Terminolic acid	504.35	3.06	6	5	1	0.61
94	Terpinen-4-ol	154.14	3.39	0	0	0	-0.11
95	Terpinolene	136.13	4.42	0	0	0	-1.43
96	Tetracosanoate	367.36	10.91	2	0	1	-0.97
97	Tetracosanoic acid [Lignoceric acid]	368.37	10.68	2	1	1	-0.54
98	Tetracosyl heptafluorobutyrate	550.36	14.16	2	0	2	-1.47
99	Tetradecane	198.23	7.86	0	0	1	-1.03
100	Tetratetracontane	618.70	23.03	0	0	2	-1.03
101	Tetratriacontane	478.55	17.98	0	0	1	-1.03
102	Tetratriacontyl heptafluorobutyrate	690.52	19.21	2	0	2	-1.47
103	Tetratriacontyl pentafluoropropionate	640.52	18.42	2	0	2	-1.47
104	Triacontane	422.49	15.95	0	0	1	-1.03
105	Triacontanoic acid	452.46	13.72	2	1	1	-0.54
106	Tricosyl pentafluoropropionate	486.35	12.86	2	0	1	-1.47
107	Tritetracontane	604.69	22.53	0	0	2	-1.03
108	Vanillic acid	168.04	1.2	4	2	0	-0.18
109	Vitamin E	430.38	10.08	2	1	1	0.48

phytoconstituents possess properties that make them suitable candidates for drug development. To evaluate the drug likeness of the compounds, several physicochemical parameters were considered, including Molecular Weight (MW), Hydrogen Bond Acceptors (HBA), Hydrogen Bond Donors (HBD), partition coefficient (Log P) and adherence to Lipinski's rule of five (RO5). The permissible ranges for these parameters, indicative of good oral bioavailability, were defined as follows: MW<500 Daltons, HBA≤10, HBD≤5, Log P≤5 and RO5 violations≤1. Utilizing the MolSoft web server, the draggability of the specified medicines and phytoconstituents was assessed. The results, as presented in Table 1, indicate that the majority of the selected antibiotic medicines exhibited satisfactory levels of Hydrogen Bond Donors (HBD) and partition coefficients (Log P) within the acceptable ranges. However, some compounds did not meet the typical values for key parameters such as Molecular Weight (MW) and the number of Hydrogen Bond Acceptors (HBA). Table 2 represents the drug Likness Profile of Phytochemicals from *Terminalia Chebula.*

Data Analysis: Drug-Likeness Evaluation of Selected Phytochemicals

In this study, the drug-likeness of selected phytochemicals from *Terminalia chebula* was evaluated using key physicochemical parameters that influence bioavailability in the human body.

These parameters include Molecular Weight (MW), Hydrogen Bond Acceptors (HBA), Hydrogen Bond Donors (HBD), partition coefficient (Log P) and adherence to Lipinski's rule of five (RO5). The evaluation was conducted using the MolSoft web server to determine the suitability of these phytochemicals as drug candidates.

Molecular Weight (MW)

Molecular weight is a critical factor in drug design as it influences the ability of a compound to be absorbed, distributed, metabolized and excreted. Lower molecular weight compounds are generally more likely to be absorbed and to penetrate cell membranes. (For good oral bioavailability, MW should be less than 500 Daltons.) We observed that most selected compounds adhered to the molecular weight criterion; however, a few exceeded the 500 Daltons threshold, which may impact their bioavailability negatively.

Hydrogen Bond Acceptors (HBA)

The number of hydrogen bond acceptors in a molecule influences its solubility and permeability. A higher number of HBAs can enhance the solubility but may reduce membrane permeability. (A good drug candidate should have no more than 10 hydrogen bond acceptors). The analysis revealed that while most compounds met the HBA criterion, a subset exceeded this limit, which might impede their permeability and, consequently, their bioavailability.

Hydrogen Bond Donors (HBD)

Hydrogen bond donors are crucial for drug-receptor interactions. However, an excessive number of HBDs can reduce the ability of a compound to cross cell membranes. An ideal drug candidate should have no more than 5 hydrogen bond donors. The majority of the compounds exhibited acceptable levels of HBDs, falling within the permissible range, which suggests they have a good balance between solubility and membrane permeability.

Partition Coefficient (Log P)

Log P is the measure of a compound's hydrophobicity and indicates its ability to pass through the lipid bilayer of cell membranes. It also affects the solubility of the compound in water versus organic solvents. A Log P value of ≤ 5 is indicative of good membrane permeability and solubility balance. Most of the selected phytochemicals showed Log P values within the desirable range, suggesting good permeability and bioavailability. However, compounds with Log P values higher than 5 may have issues with excessive hydrophobicity, potentially leading to poor solubility in aqueous environments.

Lipinski's Rule of Five (RO5)

Lipinski's Rule of Five provides a set of guidelines to evaluate whether a compound has properties consistent with good oral bioavailability. Compounds that violate more than one of these rules are generally considered less likely to be orally active drugs. The compound should have RO5 violations≤1. The analysis showed that most of the selected compounds adhered to Lipinski's rules, indicating their potential as orally active drugs. However, a few phytochemicals violated more than one of these rules, suggesting that they might require modification to improve their drug-likeness.

The results of this study highlight that most of the selected phytochemicals from *Terminalia chebula* possess favorable drug-likeness properties based on the evaluated parameters. The majority of these compounds met the criteria for molecular weight, hydrogen bond donors and acceptors and partition coefficient, making them suitable candidates for further drug development. However, certain compounds that did not fully comply with the typical values, particularly in terms of molecular weight and the number of hydrogen bond acceptors, may require structural modification to enhance their drug-likeness. Further studies, including *in vitro* and *in vivo* testing, are recommended to validate these findings and explore the therapeutic potential of these phytochemicals. The findings underscore the importance of computational tools in the early stages of drug discovery, providing valuable insights that can guide experimental studies.

DISCUSSION

Lipinski's Rule of Five serves as a well-established framework in drug design, assessing the drug-likeness of a compound based on its physicochemical characteristics. Typically, compounds that breach more than one of these rules are viewed as less likely to be orally active drugs. The study's analysis revealed that most of the selected phytochemicals from *Terminalia chebula* complied with Lipinski's guidelines, suggesting their potential as promising drug candidates. Nonetheless, a few phytochemicals exhibited multiple violations of these rules, indicating that they may need further optimization to improve their oral bioavailability and overall drug-likeness. The outcomes of this study have important implications for the development of new drugs derived from natural products, especially phytochemicals from *Terminalia chebula*. Utilizing computational tools to predict drug-likeness offers an effective and economical method for identifying potential drug candidates, reducing the need for more costly experimental procedures in the initial stages. The fact that many of the evaluated phytochemicals met the drug-likeness criteria highlights their potential for further exploration as therapeutic agents.

CONCLUSION

A thorough analysis was conducted on 109 phytoconstituents extracted from *Terminalia chebula* to assess their drug similarity and physicochemical properties. The findings indicated that a significant majority of these phytoconstituents complied

with Lipinski's rule of five, suggesting favorable drug likeness. Additionally, their physicochemical characteristics aligned within the recommended ranges, indicating optimal membrane permeability and bioavailability. These results strongly suggest that the phytoconstituents from *Terminalia chebula* exhibit considerable potential as therapeutic candidates. Their adherence to Lipinski's rule of five and favorable physicochemical properties highlight their suitability for further exploration and development in pharmaceutical research, emphasizing their promising prospects for effectively addressing various health conditions.

ACKNOWLEDGEMENT

The authors express heartfelt gratitude to KLE College of Pharmacy, Belagavi and KLE Academy of Higher Education and Research, Belagavi for providing financial support and basic computational facilities required for completion of proposed research work. Authors express special thanks to Ramu Patil, Traditional Healer from Kalkundri village, Chandgad Taluka, Kolhapur District, Maharashtra for providing key information regarding traditional applications of Haritaki. Authors are also thankful to Mr. Arun Ningappa Patil and Ms. Alka Arun Patil for their constant support, valuable guidance and motivation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This project is funded with amount of RS 10,000/- by KLE Academy of Higher Education and Research, Belagavi under the seed money project for undergraduate research.

ABBREVIATIONS

CADD: Computer Aided Drug Design; **DLS:** Drug Likeness Score; **HBA:** Hydrogen bond acceptor; **HBD:** Hydrogen bond donor.

REFERENCES

Bag, A., Bhattacharyya, S. K., Pal, N. K., & Chattopadhyay, R. R. (2013). *In vitro* antimicrobial potential of *Terminalia chebula* fruit extracts against multidrug-resistant uropathogens. Asian Pacific Journal of Tropical Biomedicine, 3(9), 732–736.

Cherkasov, A., Muratov, E. N., Fourches, D., Varnek, A., Baskin, I. I., Cronin, M., Dearden, J., Gramatica, P., Martin, Y. C., Todeschini, R., Consonni, V., Kuz'min, V. E., Cramer, R., Benigni, R., Yang, C., Rathman, J., Terfloth, L., Gasteiger, J., Richard, A., & Tropsha, A. (2014). QSAR modeling: Where have you been? Where are you going to? Journal of Medicinal Chemistry, 57(12), 4977–5010. https://doi.org/10.1021/jm4004285

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports, 7(1), Article 42717. https://doi.org/10.1038/srep42717

Egan, W. J., Merz, K. M., & Baldwin, J. J. (2000). Prediction of drug-likeness via molecular property distributions. Journal of Medicinal Chemistry, 43(20), 3867–3877.

Ekins, S., Mestres, J., & Testa, B. (2007). *In silico* pharmacology for drug discovery: Methods for virtual ligand screening and profiling. British Journal of Pharmacology, 152(1), 9–20. https://doi.org/10.1038/sj.bjp.0707305

Hatano, T., Shintani, Y., Aga, Y., Shiota, S., Tsuchiya, T., & Yoshida, T. (2005). *Terminalia chebula* Retz. phenolic compounds inhibit the growth of methicillin-resistant Staphylococcus aureus. Phytotherapy Research, 19(7), 599–604.

Kim, S., Thiessen, P. A., Bolton, E. E., Chen, J., Fu, G., Gindulyte, A., Han, L., He, J., He, S., Shoemaker, B. A., Wang, J., Yu, B., Zhang, J., & Bryant, S. H. (2016). PubChem Substance and Compound databases. Nucleic Acids Research, 44(D1), D1202–D1213. https://doi.org/10.1093/nar/gkv951

Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening for drug discovery: Methods and applications. Nature Reviews. Drug Discovery, 3(11), 935–949. https://doi.org/10.1038/nrd1549

Kumar, A., Rajput, S. K., Sharma, A., & Kumar, P. (2021). *In silico* screening of bioactive compounds of *Terminalia chebula* against breast cancer using molecular docking. Journal of Applied Pharmaceutical Sciences, 11(4), 99–106.

Kumar, S., Pandey, A. K., & Sharma, M. (2016). Medicinal attributes of *Terminalia chebula*: A comprehensive review on ethnomedicinal, phytochemical and pharmacological aspects. Asian Pacific Journal of Tropical Biomedicine, 6(6), 457–468.

Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (1997). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews, 23 (1–3), 3–26.

MolSoft. (2024). Molecular properties prediction: MolSoft web servers [Internet]. https://molsoft.com/mprop/MaltarolloVG.

Muegge, I., Heald, S. L., & Brittelli, D. (2001). Simple selection criteria for drug-like chemical matter. Journal of Medicinal Chemistry, 44(12), 1841–1846. https://doi.org/10.1021/jm015507e

Oliveira, P. R., Honorio, K. M., & da Silva, A. B. (2013). Applications of machine learning techniques in drug discovery: Current status and future perspectives. European Journal of Medicinal Chemistry, 70, 287–299

Patil, R. S., Khatib, N. A., Patil, V. S., & Suryawanshi, S. S. (2020). Cholonergic acid may be a potent inhibitor of dimeric SARS-CoV-2 main protease 3CLpro: An in-silico study. Traditional Medicinal Research, 1–14.

Patil, V. M., Nandave, M., Rane, R. A., & Thakur, P. P. (2019). QSAR and docking studies of phytochemicals of *Terminalia chebula* as potential inhibitors of angiotensin-converting enzyme. Journal of Biomolecular Structure and Dynamics, 37(9), 2298–2311.

Sabu, M. C., & Kuttan, R. (2002). Antidiabetic activity of medicinal plants and its relationship with their antioxidant property. Journal of Ethnopharmacology, 81(2), 155–160. https://doi.org/10.1016/s0378-8741(02)00034-x

Saleem, A., Husheem, M., Härkönen, P., & Pihlaja, K. (2002). Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* Retz. fruit. Journal of Ethnopharmacology, 81(3), 327–336. https://doi.org/10.1016/s0378-8741(02)00099-5

Sampat, G., Suryawanshi, S. S., Sawant, R., Khanal, P., Palled, M. S., Alegaon, S. G., & Kavalapure, R. (2020). Molecular docking studies and antibacterial activity of leaves of *Taberna montana* divaricate. Journal of Global Trends in Pharmaceutical Sciences, 11(2), 7818–7824.

Sharma, R., Sharma, P., & Sharma, A. (2017). *Terminalia chebula*: Review on pharmacological activities and chemical constituents. Journal of Medicinal Plants Studies, 5(3), 169–174.

Singh, G., Kumar, A., & Sharma, P. (2020). Therapeutic potential of chebulagic acid from *Terminalia chebula* in anticancer drug discovery. Current Pharmaceutical Design, 26(43), 5666–5680.

Sliwoski, G., Kothiwale, S., Meiler, J., & Lowe, E. W. (2014). Computational methods in drug discovery. Pharmacological Reviews, 66(1), 334–395. https://doi.org/10.1124/pr.112.007336

Suryawanshi, S. S., Jayannache, P. B., Patil, R. S., Ms, P., & Sg, A. (2020). Molecular docking studies on screening and assessment of selected bioflavonoids as potential inhibitors of COVID-19 main protease. Asian Journal of Pharmaceutical and Clinical Research, 31, 174–178. https://doi.org/10.22159/ajpcr.2020.v13i9.38485

Suryawanshi, S. S., Maruche, S., Patil, P., Palled, M. S., & Pancham, Y. (2020). Comparative *in vitro* antioxidant activity of fruit extracts of *Embelica officinalis* Gaertn. and drug likeness profile of selected phytoconstituents. International Journal of Botany Studies, 5(6), 704–709.

Totrov, M., & Abagyan, R. (2008). MOLSOFT: A new software suite for structure-based drug design. Journal of Computer-Aided Molecular Design, 22(1), 47–55.

Wang, M., Yang, J., Chen, L., Ding, Y., Kong, Y., Sun, X. *et al.* (2015). Antioxidant and immunomodulatory activities of phenolic compounds from *Terminalia chebula* fruits. Food Chemistry, 173, 591–599.

Cite this article: Patil AA, Suryawanshi SS. Computer-Assisted Prediction of Drug-Like Properties of Selected Phytochemicals from *Terminalia chebula*. Int. J. Pharm. Investigation. 2025;15(2):614-30.