Computer Aided Screening and Evaluation of Drug Likeness Properties of *Kalanchoe pinnata* (Lam.) Pers Phytomolecules

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***Abstract*—The current study focuses on the computational assessment of drug-like characteristics in 56 phytochemicals extracted from *Kalanchoe pinnata* (Lam.) Pers. The MolSoft web server was used to analyse drug-likeness using Lipinski's Rule of Five (LRF), which included parameters such as molecular weight (MW), lipophilicity (CLogP), hydrogen bond donors (HBD), hydrogen bond acceptors (HBA), number of rule violations, and drug-likeness score (DLS). The qualitative and quantitative research found that 27 chemicals had no violations, 24 had one violation, and only 5 had many violations. DLS readings varied from -2.07 to 1.06, with substances like bufalin, thiamine, rutin, and bersaldegenin-3-acetate scoring very positive. The study found flavonoids and phenolic acids to be interesting candidates for medication development and demonstrated the usefulness of computational screening in identifying drug-like compounds.**

***Index Terms*—Computer-Aided Drug Design, Drug Similarity, *Kalanchoe pinnata*, Lipinski's Rule of Five, Phytomolecules.**

I. INTRODUCTION

Natural products have historically made substantial contributions to drug discovery by including structurally diverse and physiologically active molecules. Medicinal plants, especially those utilized in traditional Indian medicine, continue to be an important source of therapeutic compounds. *Kalanchoe pinnata* (Lam.) Pers. is well known for its pharmacological qualities, which include anti-inflammatory, antibacterial, antioxidant, and anticancer activity. Phytochemicals in medicinal plants have a wide range of chemical structures, including flavonoids, phenolic acids, sterols, and glycosides, which all contribute to their biological effects. However, not all bioactive molecules are appropriate for therapeutic development due to physicochemical and pharmacokinetic restrictions. As a result, early evaluation of drug-likeness is vital to identify molecules with favorable features for future development [1,2].

Drug-likeness is a qualitative notion used to determine whether a chemical exhibit features similar to existing medicines. It is determined using molecular descriptors including molecular weight, lipophilicity, hydrogen bonding capability, and structural characteristics [3]. Lipinski's Rule of Five (LRF) is one of the most commonly utilized criteria for determining drug-likeness. Compounds with the following criteria are more likely to have adequate oral bioavailability: molecular weight (MW) ≤500 Da, lipophilicity (CLogP) ≤5, hydrogen bond donors (HBD) ≤5, and hydrogen bond acceptors (HBA) ≤10 [4]. Compounds that violate more than one of these criteria are more likely to have low absorption and permeability. The importance of LRF stems from its capacity to filter huge chemical libraries and identify molecules with desirable drug-like characteristics during the early phases of drug discovery [5].

Advances in computer technologies have transformed drug discovery by allowing for the quick screening of

molecules. Chemical structures and properties can be accessed through databases such as PubChem, while tools such as MolSoft can estimate drug-likeness scores (DLS) using molecular descriptors [6]. These in-silico techniques save time, money, and experimental effort. Recent research has shown that computational analysis of phytochemicals can successfully uncover viable drug candidates in medicinal plants.

In this setting, the current study intends to use computational approaches to assess the drug-like properties of selected phytochemicals from *Kalanchoe pinnata* (Lam.) Pers., thereby selecting possible lead compounds for further exploration.

II. MATERIALS AND METHODS

PubChem Database: It was used to obtain canonical SMILES of phytochemicals. PubChem is a large chemical database that includes structural and biological information on millions of molecules [7].

MolSoft Web Server: This was utilized to calculate the DLS and LRF parameters. It uses fragment-based contributions and physicochemical characteristics to predict [8].

Phyto-molecules

Based on available literature, 56 phytochemicals from *Kalanchoe pinnata* (Lam.) Pers. were chosen for analysis. The chosen phytochemicals are 21-Acetoxypregnenolone, 22,23-Dihydrobrassicasterol, Alpha-Amyrin, Arachidic Acid, Ascorbic Acid, Astragalin, Behenic Acid, Bersaldegenin-3-Acetate, Beta-Amyrin, Beta-Sitosterol, Bryophyllin A, Bryophyllin B, Bryotoxin B, Brytoxin A, Bufalin, Caffeic Acid, Campesterol, Cholesta-3,5-Diene, Cholesterol and Clerosterol etc. Table 1 displays the classification of selected phytomolecules [9].

Table 1: Classification of Selected Phytochemicals

Phyto-molecule	Classification	Phyto-molecule	Classification
21-Acetoxypregnenolone	Steroidal Compound	Glucopyranoside	Carbohydrate Derivative
22,23-Dihydrobrassicasterol	Phytosterol	Glutinol	Triterpenoid
Alpha-Amyrin	Triterpenoid	Glycine	Amino Acid
Arachidic Acid	Fatty Acid	Glycolate Oxidase	Enzyme-Related Compound
Ascorbic Acid	Vitamin (Water-Soluble)	Hentriacontane	Hydrocarbon
Astragalin	Flavonoid Glycoside	Kaempferitrin	Flavonoid Glycoside
Behenic Acid	Fatty Acid	Kaempferol	Flavonoid
Bersaldegenin-3-Acetate	Bufadienolide	Luteolin	Flavonoid
Beta-Amyrin	Triterpenoid	Nicotinamide	Vitamin (B-Complex)
Beta-Sitosterol	Phytosterol	Oxalic Acid	Organic Acid
Bryophyllin A	Bufadienolide	Oxaloacetate	Metabolic Intermediate
Bryophyllin B	Bufadienolide	Palmitic Acid	Fatty Acid
Bryotoxin B	Bufadienolide	Para-Coumaric Acid	Phenolic Acid
Brytoxin A	Bufadienolide	Patuletin	Flavonoid
Bufalin	Bufadienolide	Peposterol	Phytosterol
Caffeic Acid	Phenolic Acid	Phosphoenolpyruvate	Metabolic Intermediate
Campesterol	Phytosterol	Protocatechuic Acid	Phenolic Acid
Cholesta-3,5-Diene	Sterol Derivative	Pseudotaraxasterol	Triterpenoid
Cholesterol	Sterol	Pyridoxine	Vitamin (B6)
Clerosterol	Phytosterol	Pyruvate	Metabolic Intermediate
Clionasterol	Phytosterol	Quercetin	Flavonoid
Codisterol	Phytosterol	P-Hydroxybenzoic Acid	Phenolic Acid
Cysteine	Amino Acid	Rutin	Flavonoid Glycoside
Epigallocatechin	Flavonoid	Stigmasterol	Phytosterol

Ergosta-5,24-Dien-3-Beta Ol	Phytosterol	Syringic Acid	Phenolic Acid
Ferulic Acid	Phenolic Acid	Taraxerol	Triterpenoid
Fridelin	Triterpenoid	Thiamine	Vitamin (B1)
Gallic Acid	Phenolic Acid	Triacontane	Hydrocarbon

Process for Screening and Evaluation of Drug Likeness Properties

The chemical structures of the chosen phytochemicals were gathered from the PubChem database, a comprehensive library of chemical information that includes molecular structures, physicochemical properties, and biological activity [1]. Canonical SMILES for each drug were obtained and utilized as input for the computational study. The MolSoft online server, a popular cheminformatics tool that predicts drug-like features using fragment contributions and molecular descriptors [3], was used to evaluate drug-likeness. The tool computes parameters such as MW, CLogP, HBD, HBA, and DLS [10, 11].

Application of Lipinski's Rule of Five

This rule defines drug-like compounds as those with MW ≤500 Da, CLogP ≤5, HBD ≤5, and HBA ≤10 [4]. The number of violations per compound was recorded. The DLS was estimated with MolSoft. Positive results indicate desirable drug-like qualities, whereas negative values indicate poor drug-likeness [12, 13].

Statistical Analysis

Statistical analysis was used to determine the percentage distribution of chemicals across several categories [14].

III. RESULTS AND DISCUSSION

Drug Likeness

therapeutic-likeness is an important factor in determining which chemicals are acceptable for therapeutic development. LRF characteristics give insight into the physicochemical factors that influence oral bioavailability. Typically, substances with smaller molecular weight have higher permeability. CLogP denotes lipophilicity, and high values reduce solubility. HBD and HBA demonstrate that excessive hydrogen bonding affects membrane permeability, and violations indicate deviation from the ideal drug-like space.

Drug-Likeness Parameters of Selected Phytomolecules

Table 2 highlights the physicochemical parameters and drug-likeness features of 56 phytochemicals assessed using MW, LogP, HBA, HBD, number of Lipinski's rule violations, and DLS.

Table 2: Drug-Likeness Parameters of Selected Phytochemicals

SN.	Phytochemicals	MW	LOGP	HBA	HBD	Violations	DLS
1	21-Acetoxypregnenolone	374.25	3.48	4	1	0	0.71
2	22,23-Dihydrobrassicasterol	257.11	2.68	3	1	0	0.29
3	Alpha-Amyrin	426.39	7.77	1	1	1	0.1
4	Arachidic Acid	312.3	8.66	2	1	1	-0.54
5	Ascorbic Acid	176.03	-1.59	6	4	1	0.74
6	Astragalin	448.1	-0.12	11	7	1	0.67
7	Behenic Acid	340.33	9.67	2	1	1	-0.54
8	Bersaldegenin-3-Acetate	474.23	1.38	8	3	1	1.05
9	Beta- Amyrin	426.39	7.95	1	1	1	-0.22
10	Beta- Sitosterol	414.39	8.45	1	1	1	0.78
11	Bryophyllin A	472.21	2.09	8	2	0	0.67
12	Bryophyllin B	490.22	1.25	9	4	0	0.71

13	Bryotoxin B	488.2	0.51	9	3	0	0.68
14	Brytoxin A	618.3	0.28	12	4	3	1.06
15	Bufalin	386.25	3.54	4	2	0	0.82
16	Caffeic Acid	180.04	1.27	4	3	0	-0.35
17	Campesterol	400.37	7.87	1	1	1	0.59
18	Cholesta-3,5-Diene	368.34	8.31	0	0	1	0.26
19	Cholesterol	386.35	7.44	1	1	1	0.49
20	Clerosterol	412.37	8.58	1	1	1	0.68
21	Clionasterol	414.39	8.45	1	1	1	0.78
22	Codisterol	398.35	7.7	1	1	1	0.43
23	Cysteine	121.02	-2.07	4	4	0	-2.07
24	Epigallocatechin	306.07	0.26	7	6	0	-0.04
25	Ergosta-5-24-Dien-3-Beta-Ol	398.35	7.53	1	1	1	0.76
26	Ferulic Acid	194.06	1.61	4	2	0	-0.61
27	Fridelin	426.39	7.44	1	0	1	-0.43
28	Gallic Acid	170.02	0.78	5	4	0	-0.22
29	Glucopyranoside	180.06	-3.02	6	5	0	-0.12
30	Glutinol	426.39	7.97	1	1	1	-0.41
31	Glycine	75.03	-2.53	3	3	0	-0.16
32	Glycolate Oxidase	232.04	2.83	5	2	0	-0.08
33	Hentriacontane	436.5	16.46	0	0	1	-1.03
34	Kaempferitrin	578.16	-0.71	14	8	2	0.73
35	Kaempferol	257.11	2.68	3	1	0	0.29
36	Luteolin	286.05	2.78	6	4	0	0.38
37	Nicotinamide	122.05	-0.35	2	2	0	0.37
38	Oxalic Acid	90.00	-1.02	4	2	0	-0.97
39	Oxaloacetate	132.01	-1.33	5	2	0	-1.23
40	Palmitic Acid	256.24	6.64	2	1	1	-0.54
41	Para-Coumaric Acid	164.05	1.66	3	2	0	-0.81
42	Patuletin	332.05	1.24	8	5	0	0.5
43	Peposterol	412.37	7.89	1	1	0	0.37
44	Phosphoenolpyruvate	167.98	-0.77	6	3	0	-1.02
45	Protocatechuic Acid	154.03	1.05	4	3	0	0.23
46	Pseudotaraxasterol	426.39	8.15	1	1	1	-0.09
47	Pyridoxin	169.07	-0.5	4	3	0	0.71
48	Pyruvate	87.01	-0.47	3	0	0	-1.77
49	Quercetin	302.04	1.19	7	5	0	0.52
50	P-Hydroxybenzoic Acid	138.03	1.43	3	2	0	-0.37
51	Rutin	610.15	-1.55	16	10	1	0.91
52	Stigmasterol	412.37	7.74	1	1	1	0.62
53	Syringic Acid	198.05	0.82	5	2	0	-0.81
54	Taraxerol	426.39	8.11	1	1	1	-0.9
55	Thiamine	265.11	0.29	4	3	0	0.87
56	Triacontane	422.49	15.95	0	0	1	-1.03

Molecular Weight

The selected chemicals have MW values ranging from 75.03 Da (glycine) to 618.3 Da (brytoxin A). The majority of the phytochemicals were determined to be within the acceptable range of 500 Da, indicating that their molecular size is suitable for membrane permeability.

Lipophilicity

LogP values varied widely among the compounds. Several sterols and triterpenoids had high LogP values (>5), indicating their high lipophilicity. Polar substances, such as ascorbic acid, glycine, and oxaloacetate, had negative LogP values, indicating significant hydrophilicity.

Hydrogen Bonding

It was evaluated using the HBA and HBD values. Most chemicals met acceptable limits (HBA ≤10 and HBD ≤5), indicating positive interactions with biological targets. However, substances like astragalin, kaempferitrin, and rutin had greater values, which could affect their permeability across biological membranes.

Lipinski's Rule Violations

The number of LRF infractions varied across compounds. A large majority of phytochemicals, including 21-acetoxypregnenolone, Bryophyllin A and B, bufalin, quercetin, luteolin, and thiamine, had no violations, showing strict adherence to drug-likeness standards. Several compounds had a single violation, primarily due to increased lipophilicity, whereas only a few compounds, such as brytoxin A and kaempferitrin, had several violations.

Drug-Likeness Score

The DLS ranged from -2.07 to 1.06. Compounds with greater positive ratings included bersaldegenin-3-acetate (1.05), brytoxin A (1.06), thiamine (0.87), bufalin (0.82), and rutin (0.91), indicating a closer match to recognized drug-like compounds. Compounds like cysteine (−2.07), pyruvate (−1.77), and long-chain hydrocarbons like triacontane (−1.03) scored negatively, indicating low drug-likeness.

Drug-Likeness Compliance and Physicochemical Parameter Distribution

Table 3 shows the overall drug-likeness trend and physicochemical features. A significant majority of the compounds fit all of the criteria. Most compounds lie within the acceptable MW range, allowing for effective absorption. However, a significant proportion have increased lipophilicity, particularly sterols and triterpenoids, which may affect solubility. Hydrogen bonding values are frequently within acceptable ranges, indicating a balanced polarity profile.

Table 3: Drug-Likeness Compliance and Physicochemical Parameter Distribution

Parameter	Range	No. of Compounds	Percentage (%)
Drug-Likeness Compliance	Zero violations	27	48.2
	One violation	24	42.8
	≥2 violations	5	8.9
Molecular Weight (MW)	≤500 Da	51	91.1
	>500 Da	5	8.9
CLogP (Lipophilicity)	≤5	34	60.7
	>5	22	39.3
Hydrogen Bond Donors (HBD)	≤5	48	85.7
	>5	8	14.3
Hydrogen Bond Acceptors (HBA)	≤10	50	89.3
	>10	6	10.7

IV. CONCLUSION

The current investigation shows that a large number of phytomolecules from *Kalanchoe pinnata* (Lam.) Pers. have excellent drug-like characteristics. Lipophilicity was discovered as the most significant limiting factor determining drug-likeness, particularly in sterols and fatty acids. Compounds having repeated violations and negative drug-likeness ratings were deemed unsuitable for future development. The study found flavonoids and phenolic acids to be interesting candidates for

medication development and demonstrated the usefulness of computational screening in identifying drug-like compounds.

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ABBREVIATIONS

MW: Molecular Weight; Log P: Partition Coefficient; Clog P: Calculated Partition Coefficient; SMILES: Simplified Molecular Input Line Entry System; SDF: Structure Data File; RO5: Lipinski's Rule of Five; LRF: Lipinski's Rule of Five; CADD: Computer Aided Drug Design; DLS: Drug Likeness Score; HBA, Hydrogen bond acceptor; HBD: Hydrogen bond donor.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Nil

STATEMENT OF ETHICAL APPROVAL

Not Applicable.

REFERENCES

[1] Kim S, et al. PubChem database update. Nucleic Acids Res. 2021;49: D1388–D1395.
[2] Ojewole JA. Anti-inflammatory effects of Kalanchoe pinnata (Lam.) Pers. J Ethnopharmacol. 2005; 99:13–19.
[3] MolSoft LLC. Drug-likeness prediction tool. Available from: https://molsoft.com/mprop/
[4] Lipinski CA. Drug-like properties. Adv Drug Deliv Rev. 2001; 46:3–26.
[5] Veber DF, et al. Molecular properties and bioavailability. J Med Chem. 2002; 45:2615–2623.
[6] Walters WP, Murcko MA. Prediction of drug-likeness. Curr Opin Chem Biol. 2002; 6:540–546.
[7] Patil AA, Suryawanshi SS. Computer-assisted prediction of drug-like properties of selected phytochemicals from Terminalia chebula. Int J Pharm Investig. 2025;15(2).
[8] Patil RS, Khatib NA, Patil VS, Suryawanshi SS. Chlorogenic acid may be a potent inhibitor of dimeric SARS-CoV-2 main protease 3CLpro: an in-silico study. Tradit Med Res. 2021;6(2):20.
[9] https://cb.imsc.res.in/imppat
[10] Sampat G, Suryawanshi SS, Sawant R, Khanal P, Palled MS, Alegaon SG, Kavalapure R. Molecular docking studies and antibacterial activity of leaves of Tabernaemontana divaricata. J Global Trends Pharm Sci. 2020;11(2):7818–7824.
[11] Suryawanshi SS, Jayannache PB, Patil RS, Patil MS, Alegaon SG. Molecular docking studies on screening and assessment of selected bioflavonoids as potential inhibitors of COVID-19 main protease. Asian J Pharm Clin Res. 2020;13(9):174–178.
[12] Dsouza R, Bhingurde T, Patil AA, Suryawanshi SS. Computer-assisted toxicity prediction of selected bioactive compounds from Aloe vera. Int J Pharm Res Dev. 2025;7(1):201–204. doi: 10.33545/26646862.2025.v7.i1c.112
[13] Dsouza R, Maste MM, Suryawanshi SS. Computational insights into Aloe vera phytochemicals: drug-likeness and ADMET prediction for drug discovery. Int J All Res Educ Sci Methods. 2025;13(3):3744–3752.
[14] Bandekar SS, Suryawanshi SS. In silico prediction of physicochemical and drug likeness characteristics of selected phytochemicals from Terminalia bellirica (Gaertn.) Roxb. Int J All Res Educ Sci Methods. 2024;12(3):2585–2590.