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Research Article

Theoretical Validation of Medicinal Properties of *Curcuma longa Linn* - Part-2.

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ABSTRACT

Molecular property and bio-activity scores of ten terpenoids derivative of *Curcuma longa Linn* present in Curcuma longa Linn were predicted using molinspiration software. For all the essential oil compounds, miLog P values were found to be 5 this shows these compounds were not easily permeable across the cell membrane. TPSA in the range of 0.00 -66.76 (well below 160Å2) and n violations= 1 or 0, molecular mass < 5 [10], N0 of hydrogen bond donors ≤ 5 (the sum of OHs and NHs), No of hydrogen bond acceptor ≤ 10 (The sum of Os and Ns) were observed for these compounds. This indicate that these compounds were found to obey Lipinski's rule and can easily bind to receptor and were taken further for the calculation of bioactivity score by calculating the activity score of GPCR ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor and enzyme inhibitor.

KEYWORDS

Molinspiration, Curcuma longa Linn, Bioactivity Score, Lipinski's Rule

1. INTRODUCTION

Curcuma, belonging to the family Zingiberaceae, is an economically significant genus having both medicinal and food values. According to Xia et. al [1] the genus Curcuma includes 70 perennial rhizomatous species, which are disseminated extensively all over tropical and subtropical regions of the world. The rhizome of Curcuma is a source of a yellow dye and has been historically used as spices, food preservatives, flavoring agent, and household remedy for treatment of many diseases [2]. They have been used as traditional medicines for the treatment of enlarged liver, spleen, stomach ulcer, diabetes, cough, hepatic disorders, chest pain, skin diseases, boils, blood purifier and rheumatism [3-6]. Curcuma longa is a tropical rhizomatous cultivated most extensively in India, followed by Bangladesh, China, Thailand, Cambodia, Malaysia, Indonesia and the Philippines. In India, the main turmeric growing states are Tamil Nadu, Andhra Pradesh, Maharashtra, Orissa, Karnataka and Kerala. India accounts more than 90% of total output of world [7]. Many principal active ingredients have been found in *C. longa*, including diarylheptanoids, sesquiterpenoids, diterpenoids, polysaccharides and phenolic acids [8]. Essential oil is the main component of turmeric and also one of the main active components. The aromatic flavor of turmeric is because of its essential oil. Terpenoids are the major components in volatile oil of turmeric. Phytochemical researches elucidated about 62 sesquiterpenoids, 1 monoterpene, 4 norsesquiterpenoids and 1 norditerpene isolated from turmeric [9]. In this research paper we validated the biological activity of terpenoids.

2. MATERIALS AND METHODS

Structures of all the ten compounds reported from *Curcuma longa Linn* were taken from the literature and their structures were drawn using online molinspiration software (www.molinspiration.com) [10] for calculation of molecular properties (Log P, Total polar surface area, number of hydrogen bond donors and acceptors, molecular weight, number of atoms, number of rotatable bonds etc.) and prediction of bioactivity score for drug targets (GPCR ligands, kinase inhibitors, ion channel modulators, enzymes and nuclear receptors). The bioactivity score and drug likeness properties of the all the seven compounds were compared.

2.1. Prediction of bio-activity

1. Molecular properties of ten terpenoids derivative of *Curcuma longa Linn* were calculated using molinspiration and the values were given in Table 1.

2. Bio-activity scores of ten terpenoids derivative of *Curcuma longa Linn* towards GPCR ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor and enzyme inhibitors were given in Table 2.

2.2. Lipinski's Rule

Lipinski's rule of five commonly known as the Pfizer's rule of five or simply the Rule of five is a regulation of thumb to estimate drug likeness or to identify a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in man. The principle was designed by Christopher A. Lipinski in 1997. The rule expresses molecular properties vital for a drug's pharmacokinetics in the human body, including their absorption, distribution, metabolism and elimination (ADME) Components of the Lipinski's rule [11, 12].

2.2.1. Lipinski's rule states

a. Not more than 5 hydrogen bond donors (nitrogen or oxygen atoms with one or more hydrogen atoms).

b. Not more than 10 hydrogen bond acceptors (nitrogen or oxygen atoms).

c. A molecular weight less than 500.

d. An octanol-water partition coefficient log P not greater than 5.

e. No more than one number of violation

2.3. Molinspiration

Molinspiration, web based software was used to obtain parameter such as MiLogP, TPSA, drug likeness. MiLogP, is estimated by the methodology developed by Molinspiration as a sum of fragment based contributions and correction factors. MiLog P parameter is applied to check good permeability across the cell membrane. TPSA is related to the hydrogen bonding potential of the compound. Computation of volume developed at Molinspiration is based on group contributors. Number of rotatable bonds measures molecular flexibility. It is a very good descriptor of absorption and bioavailability of drugs. Through drug likeness data's of a particle, it can be checked molecular properties and structure feature with regard to known drugs.

2.4. Bioactivity score

Bioactivity of the drug can be found out by estimating the activity score of GPCR ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor, enzyme inhibitor. All the parameters were determined with the aid of software Molinspiration drug-likeness score online (www.molinspiration.com). Calculated drug likeness score of each

compound and compared with the specific bodily process of each compound. For organic molecules the probability is if the bioactivity score is (>0), then it is active, if (-5.0-0.0) then moderately active, if (< -5.0) then inactive.

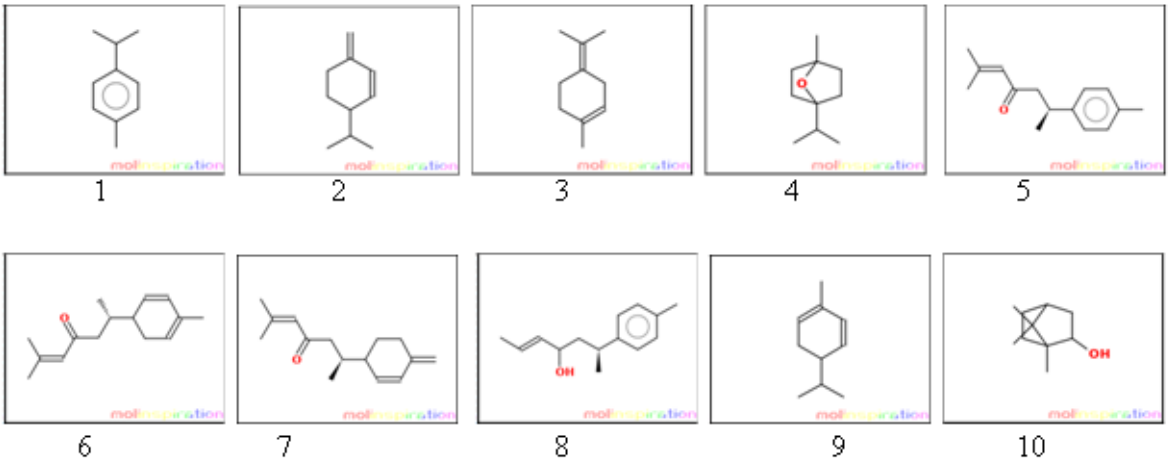

Figure 1. Structures of ten terpenoids isolated from *Curcuma longa Linn.*

Table 1. Calculation of Molecular properties.

S. N.	Compound	miLogP	TPSA	natoms	MW	nON	noHNH	nviolations	nrobt	Volume
1	1	3.90	0.00	10	134.22	0	0	0	1	150.55
2	2	3.58	0.00	10	136.24	0	0	0	1	157.32
3	3	3.67	0.00	10	136.24	0	0	0	0	156.72
4	4	2.72	9.23	11	154.25	1	0	0	1	166.66
5	5	4.48	17.07	15	216.32	1	0	0	4	230.32
6	6	3.78	17.07	16	218.34	1	0	0	4	236.53
7	7	3.56	17.07	16	218.34	1	0	0	4	237.09
8	8	3.88	20.23	15	204.31	1	1	0	4	219.62
9	9	3.79	0.00	10	136.24	0	0	0	1	156.77
10	10	2.35	20.23	11	154.25	1	1	0	0	165.72

Table 2. Bioactivity score.

S. N.	Compound	GPCR Ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	1	-1.18	-0.61	-1.40	-1.21	-1.42	-0.78

2	2	-0.99	-0.48	-1.55	-0.28	-1.31	-0.27
3	3	-0.88	-0.41	-1.61	-0.50	-1.74	-0.26
4	4	-0.52	-0.08	-1.15	-0.33	-0.59	-0.32
5	5	-0.68	-0.46	-1.36	-0.14	-0.80	-0.25
6	6	-0.48	-0.20	-1.31	0.51	-0.55	0.39
7	7	-0.47	-0.23	-1.42	0.58	-0.50	0.35
8	8	-0.15	0.16	-0.82	-0.14	-0.40	0.04
9	9	-1.00	-0.40	-1.40	-0.32	-1.38	-0.15
10	10	-0.47	-0.51	-1.57	-0.84	-0.80	-0.23

Table 3. Drug-likeness model score.

Sr. No.	Compound No	Drug-likeness Score
1	1	-1.62
2	2	-1.37
3	3	-1.42
4	4	-1.20
5	5	-0.56
6	6	-1.06
7	7	-1.02
8	8	-0.40
9	9	-1.24
10	10	-0.44

3. RESULTS AND DISCUSSIONS

3.1. Molecular property of the curcuminoids

The seven curcuminoids derivative of *Curcuma longa Linn* obeyed the Lipinski's rule of five and showed good drug likeness scores. MiLog P values of these curcuminoids compounds were found to be < 5 (1.69-2.67 for compounds 1 to 7) indicated their good permeability across the cell membrane. All the derivatives were found to have TPSA will be below 160Å2 (100.13), molecular weight < 500, No. of hydrogen bond donors ≤ 5, No. of hydrogen acceptor ≤ 10, n-violations 0, number of rotatable flexible bonds >5.

3.2. Bioactivity scores of the components of Curcuma longa Linn

The bioactivity scores of the seven compounds have shown the following observations.

1. GPCR Ligand: All ten compounds were found to be inactive (≤ 0).
2. Ion channel modulator: All the ten compounds were found to be inactive (≤ 0).
3. Kinase inhibitor: All ten compounds were found to be inactive (≤ 0) towards Kinase inhibitor.
4. Nuclear receptor ligand: All the ten compounds, were found to be inactive (≤ 0) towards Nuclear receptor ligand.
5. Protease inhibitor: Among the ten compounds, were to be inactive (≤ 0) towards Protease inhibitor.
6. Enzyme inhibitor: All the ten compounds, were found to be inactive (≤ 0) towards Enzyme inhibitor.

3.3. Drug-likeness model score

Drug-likeness model score indicates that all ten compounds shows moderately drug like activity.

4. CONCLUSION

In conclusion, ten terpenoids derivative of *Curcuma longa Linn* show inactive to moderate bioactivity score. All compounds obey Lipinski's rule for Drug Likeness activity of the molecules.

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