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Theoretical Validation of Medicinal Properties of Ginger

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ABSTRACT

Molecular property and bio-activity scores of ten essential oil constituents present in Ocimum sanctum leaves were predicted using molinspiration software. For all the essential oil compounds, miLog P values were found to be <5 for compound 1-7 indicated their good permeability across the cell membrane and compound 8-10 shows miLog P values > 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 <500, n rotb < 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, Ocimum Sanctum, Bioactivity Score, Lipinski's Rule

I. INTRODUCTION

Zingiber officinale Roscoe (Zingiberaceae) known as adrak or ginger, is significant plant with numerous ethnomedicinal and dietary application. It is a rhizomatous perennial herb reaching up to 90 cm in height. Therhizomes are aromatic, thick lobed, white to yellowish-brown, unevenly branched, annulated and dense with smooth surface. It is initially originate in tropical Asia and now cultivated as a commercial crop in India, China, Australia, America, Africa as well as South East Asia. Ginger is cultivated in tropical and subtropical regions. It is grown by vegetative [1]. Ginger is planted during April-may and harvested about 7-8 months(December-January) after planting when the leaves turn yellow and steadily shrivel. They are washed properly and then dried to improve colour [2]. It is extensively utilized worldwide as a spice, flavoring agent and herbal remedy. In different traditional systems it is taken to cure a variety of diseases such as nausea, vomiting, asthma, palpitation, inflammation, dyspepsia, loss of appetite, constipation, digestion and pain [3,4]. It has been used in both fresh and dried forms for the treatment of cough, rheumatism, asthma, stroke, diabetes[5] and gastrointestinal cancer[6]. Chemical analysis of ginger shows that it contains over 400 different compounds. The major constituents in ginger rhizomes are carbohydrates (50-70%), lipids(3-8%), terpenes and phenolic compounds[7]. Terpene components of ginger include zingiberene, β-bisabolene, α-faresene, β-sesquiphellandrene and α-curcumene, while phenolic compounds include gingerol, paradols and shogaol. These gingerols (23-25%) and shogaol (18-25%) are found in higher quantity than others. Besides these amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g. nicotinic acid and vitamin A) and minerals are also present [8,9]. The aromatic constituents include zingiberene and bisabolene, while the pungent constituents are known as gingerols and shogaols[10]. Other ginerol- or shogaol related compounds (1-10%), which have been reported in ginger rhizome, include 6-paradol, 1-dehydrogingerdione, 6-gingerdione and 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8-gingerdiol and diarylheptanoids[11, 12]. The characteristic odour and flavour of ginger are due to mixture of volatile oils like shogaols and gingerols[13]. Because of remarkable biological activities of this plant, our aim to predict the molecular properties and to evaluate the bioactivity scores using molinspiration [14-16].

II. MATERIALS AND METHODS

Structures of all the ten compounds reported from Ginger were taken from the literature and their structures

were drawn using online molinspiration software (www.molinspiration.com) [14] 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 ten compounds were compared.

Prediction of bio-activity

1. Molecular properties of nine alkoxy derivative of Naringenin were calculated using molinspiration and the values were given in Table 1.
2. Bio-activity scores of the nine alkoxy towards GPCR ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor and enzyme inhibitors were given in Table 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 indentify 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 [5, 6].

Lipinski's rule states:

- ✓ Not more than 5 hydrogen bond donors (nitrogen or oxygen atoms with one or more hydrogen atoms)
- ✓ Not more than 10 hydrogen bond acceptors (nitrogen or oxygen atoms)
- ✓ A molecular weight less than 500
- ✓ An octanol-water partition coefficient log P not greater than 5
- ✓ No more than one number of violation

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.

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.

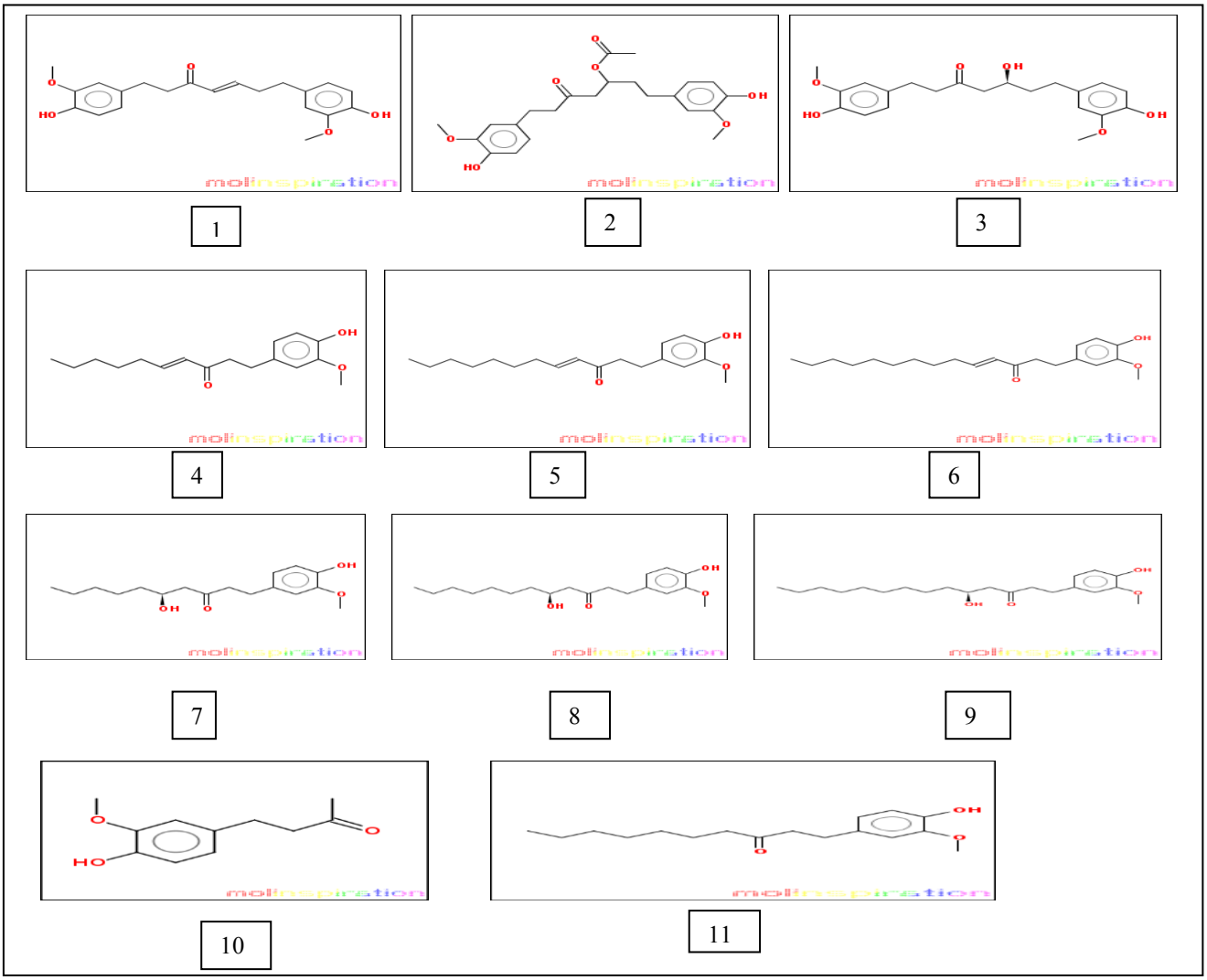

Figure 1

Table 1. Calculation of Molecular properties rttttt

S.N	Compound	miLogP	TPSA	natoms	MW	nON	noHNH	nviolations	nrobt	Volume
1	1	3.32	76.00	26	356.42	5	2	0	9	336.19
2	2	3.13	102.30	30	416.47	7	2	0	12	386.93
3	3	2.43	96.22	27	374.43	6	3	0	10	350.42
4	4	4.35	46.53	20	276.38	3	1	0	9	281.38
5	5	5.36	46.53	22	304.43	3	1	1	11	314.98
6	6	6.37	46.53	24	332.48	3	1	1	13	348.59
7	7	3.22	66.76	21	294.39	4	2	0	10	295.61
8	8	4.23	66.76	23	322.44	4	2	0	12	329.21
9	9	5.24	66.76	25	350.50	4	2	1	14	362.82
10	10	1.52	46.53	14	194.23	3	1	0	4	186.75
11	11	4.60	46.53	20	278.39	3	1	0	10	287.57

Table 2. Bioactivity score

S.No	Compound	GPCR Ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	1	0.13	0.06	-0.25	0.23	0.09	0.23
2	2	0.12	0.06	-0.30	0.13	0.16	0.26
3	3	0.18	0.08	-0.19	0.19	0.21	0.31
4	4	0.06	0.01	-0.50	0.20	-0.05	0.29
5	5	0.11	0.01	-0.39	0.26	0.03	0.27
6	6	0.13	0.01	-0.34	0.26	0.07	0.25
7	7	0.16	0.04	-0.33	0.20	0.15	0.38
8	8	0.18	0.03	-0.27	0.23	0.20	0.34
9	9	0.18	0.03	-0.24	0.22	0.21	0.32
10	10	-0.58	-0.18	-1.15	-0.59	-0.72	-0.07
11	11	-0.01	-0.04	-0.47	0.08	-0.09	0.18

III. RESULTS AND DISCUSSION

a. Molecular property of the Chalcones:

The ten oil constituents obeyed the Lipinski's rule of five and showed good drug likeness scores. MiLog P values of these oily compounds were found to be < 5 (1.07-4.60 for compounds 1 to 4, 7 to 8, 10-11) indicated their good permeability across the cell membrane. All the derivatives were found to have TPSA will be below 160Å^2 (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.

b. Bioactivity scores of the components of Ginger:

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

1. GPCR Ligand: Among the ten compounds were found to be moderately active (≤ 0) and compound no 3, 8 and 9 shows highly active (≥ 0) towards GPCR ligands.
2. Ion channel modulator: Among the ten compounds compound 3 were found to be highly active (≥0). The remaining compounds were to be moderately active (≤ 0).
3. Kinase inhibitor: All ten compounds were found to be inactive (≤ 0) towards Kinase inhibitor.
4. Nuclear receptor ligand: Among the ten compounds, compound no 5-6 were found to be highly active (≥ 0) towards Nuclear receptor ligand. The remaining compounds were to be moderately active (≤ 0).
5. Protease inhibitor: Among the ten compounds, compound no 8- 9 were found to be highly active (≥ 0) towards Protease inhibitor. The remaining compounds were to be moderately active (≤ 0).
6. Enzyme inhibitor: Among the ten compounds, compound no 7-9 were found to be highly active (≥ 0) towards Enzyme inhibitor. The remaining compounds were to be moderately active (≤ 0).

IV. Conclusion

In conclusion, eleven compound show highly active to moderate bioactivity score. All compounds obey Lipinski's rule for Drug Likeness activity of the molecules.

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