ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Molecular Properties and Bioactivity score of the *Aloe vera* antioxidant compounds – in order to lead finding

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ABSTRACT

The objective of this study was to examine antioxidant activity and molecular prediction of the compounds isolated from *Aloe vera* ,and search lead compound through molinspiration software. Ten compounds isolated from aloevera were taken for molecular properties prediction, drug likeness score on the basis of Lipinski's rule, and bioactivity prediction through molinspiration software.The compounds V ,VIII, IX, X fulfill Lipinski's rule and show good drug likeness score. Milog P of these compounds were found below 5 that means these shows good permeability across cell membrane. TPSA below 160 $Å^2$, *n* violatios =1 or <0 it means compound easily bind to receptor, molecular mass <500 ,*n* rotb < 5 [10], No. hydrogen bond donors ≤ 5 (The sum of OHs and NHs),No. hydrogen bond acceptor ≤ 10 (The sum of Os and Ns).Compounds I-X were taken further calculation of bioactivity score by calculating the activity score of GPCR ligand, ion channel modulator, nuclear receptor legend, kinase inhibitor, protease inhibitor, enzyme inhibitor **.**Compound IX (Dihydrocoumarin ethyl ester) showed good drug likeness score and bioactivity score, on comparison with other compounds.

Keywords : *Aloe vera*, Antioxidant activity , Lipinski,s rule

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ISSN: 0975-8585

INTRODUCTION

Aloe species a perennial plant, belonging to the family Liliaceae. *Aloe vera* is undoubtedly one of the most important medicinal plants in the world, providing the raw materials for different uses as medicinal, cosmetic, tonic, drinks, and numerous other uses in the food chemistry [1]. *Aloe vera* possessing functions such as anticancer, anti-inflammatory, antioxidant, antivirus, protecting liver and increase immunity [2]. The *Aloe vera* include anthraquinones, chromones, polysaccharide, enzymes, flavanoids, phenolics etc.

On the basis of literature survey we find many compounds isolated from *Aloe vera* as squalene, α tocopherol, aloin, β carotene, ascorbic acid, dihydrocoumarin, β sterol, limonene, eicosane , carvone etc.

In present study we evaluate compounds for antioxidant activity. Free radical reactions,especially with participation of oxidative radicals, have been shown to be involved in many biological processes that cause damage to lipids, proteins, membranes and nucleic acids, thus giving rise to a variety of diseases. Reactive oxygen species (ROS) have been recognized as playing an important role in the initiation and/or progression of various diseases such as atherosclerosis, inflammatory injury, cancer and cardiovascular disease. Thus, recent studies have investigated the potential of plant products to serve as antioxidants against various diseases induced by free radicals. Additionally, it has been determined that the antioxidant eVect of plant products is mainly due to phenolic compounds, such as flavonoids, phenolic acids, tannins and phenolic diterpenes. There have been numerous studies on the biological activities of phenolics, which are potent antioxidants and free radical scavengers [3].

The objective of our research work was to compare different compounds which are isolated from *Aloe vera.* with standard compound BHT(butylated hydroxy toluene) on the basis of Lipinski,s Rule and physiological interpretation by Molinspiration software.

MATERIALS AND METHODS

Lipinski,s Rule [4,5]

Lipinski's rule of five also known as the Pfizer's rule of five or simply the Rule of five (RO5) is a rule of thumb to evaluate drug likeness or determine if a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in humans. The rule was formulated by Christopher A. Lipinski in 1997.

The rule describes molecular properties important for a drug's pharmacokinetics in the human body, including their absorption, distribution, metabolism, and excretion ("ADME")
Components of the Lipinski's rule:

ISSN: 0975-8585

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 mass less than 500 daltons
- An octanal-water partition coefficient log *P* not greater than 5
- No more than one number of violation .

Molinspiration, web based software was used to obtain parameter such as MiLogP, TPSA, drug likeness. MiLogP, is calculated by the methodology developed by Molinspiration as a sum of fragment based contributions and correction factors [6,7]. MiLog P parameter is used to check good permeability across the cell membrane. TPSA is related to hydrogen bonding potential of compound [8].Calculation 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 bioavailbility of drugs. Through drug likeness datas of molecule, it can be checked molecular properties and structure feature in respect to known drugs .

Bioactivity score [6,7,9]

Bioactivity of the drug can be checked by calculating the activity score of GPCR ligand, ion channel modulator, nuclear receptor legend, kinase inhibitor, protease inhibitor, enzyme inhibitor. All the parameters were checked with the help of software Molinspiration drug-likeness score online (www.molinspiration.com). Calculated druglikeness score of each compounds and compared with the specific activity of each compound, and the results were compared with standard drug.

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.

RESULT

Physiochemical properties

The physicochemical properties as melting point, solubility of the compounds (I-X) are summarized in Table 1.

Drug likeness calculation on the basis of Lipinski rule of five

The drug likeness score was calculated by considering Milog P(partition coefficient), molecular weight, number of heavy atoms, number of hydrogen donor, number of hydrogen acceptor and number of violation, number of rotatable bonds, volume. The drug likeness score and the calculated value of various parameters of the isolated compounds (I-X)are in Table 2.

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Table 1. Physico-chemical properties of the compounds

Compound Code	Compound Name	Molecular formula	M.P(ºC)	Solubility	IUPAC Name
I	α Tocopherol	$C_{25}H_{50}O_2$	2.5	Ethanol	(2R)-2,5,7,8-Tetramethyl-2-(4R,8R)-(4,8,12-trimethyltridecyl)6-chromanol
II	Squalene	$C_{30}H_{50}$	-	Ether	2,6,10,15,19,23-Hexamethylteracosa-2,6,10,14,18,22-Hexaene
III	Aloin A	$C_{21}H_{22}O_9$	148	water	(10S)-10-Glucopyranosyl-1,8-dihydroxy-3-(hydroxymethyl)-9(10H)-anthracenone
IV	β Carotene	$C_{40}H_{56}$	180	Tetra hydrofuran	β Carotene
V	Ascorbic acid	$C_6H_8O_6$	191	Chloroform	(5R)-[(1S)-1,2-Dihydroxyethyl]-3,4-dihydroxyfuran-2(5H)-one
VI	β Sterol	$C_{29}H_{50}O$	136-140	Alcohols	17-(5-Ethyl-6-methylheptan-2-yl)-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-Cyclopenta[9]phenanthren-3-ol
VII	Eicosane	$C_{20}H_{42}$	38	Ether	Icosane
VIII	Carvone	$C_{10}H_{14}O$	25.2	Methanol	2-methyl-5-(1-methyl ethenyl)-2-cyclohexanone
IX	Dihydrocoumarine derivative	C22H18O7	-	Chloroform	Dihydrocoumarine ethyl ester
X	Limonene	$C_{10}H_{16}$	-74.35	Acetone	1-Methyl-4-(1-methyl ethnyl)-cyclohexene
XI	BHT(butylated hydroxyl toluene) (Standard)	C15H24O	71	Ethanol	2,6-bis(1,1-dimethyl ethyl)-4-methyl phenol

Table 2. Drug likeness score for compounds

S.N	Compd.No.	miLogP	TPSA	nAtoms	n ON	nOHNH	*n* violation	n rotb.	volume	MW
1	I	9.043	29.462	31.0	2	1	1	12	474.499	430.717
2	II	9.622	0.0	30.0	0	0	1	15	477.642	410.73
3	III	-0.055	167.901	29.0	9	7	1	2	335.629	404.371
4	IV	9.542	0.0	37.0	0	0	1	10	542.281	494.807
5	V	-1.402	107.217	12.0	6	4	0	2	139.707	176.124
6	VI	8.744	20	31	1	1	0	6	472.754	428.745
7	VII	9.316	0.0	20.0	0	0	1	17	348.189	282.556
8	VIII	2.513	17.07	11	1	0	0	1	159.478	150.221
9	IX	4.681	105.457	32	7	3	0	2	403.493	440.493
10	X	3.615	0.0	10	0	0	0	1	157.296	136.238
11	XI(standard)	5.435	20.228	16	1	1	0	2	240.996	220.356

Bioactivity score of the compounds

The bioactivity scores of the isolated compounds (I-X) are compared with standard drug on the basis of GPCR ligand, ion channel modulator, nuclear receptor legend , kinase inhibitor, protease inhibitor, enzyme inhibitor in Table 3.

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Table 3. Bioactivity score of the compounds.

S.N.	Compound	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1.	I	0.25	0.14	-0.21	0.41	0.28	0.24
2.	II	0.04	0.01	-0.10	0.19	-0.03	0.16
3.	III	0.24	0.13	0.11	0.32	0.19	0.47
4.	IV	-0.04	0.01	-0.01	0.50	-0.06	0.26
5.	V	-0.53	-0.24	-1.09	-1.01	-0.81	-0.20
6.	VI	0.20	0.13	-0.45	0.74	0.12	0.57
7.	VII	-0.04	0.00	-0.14	-0.05	-0.11	0.03
8.	VIII	-1.23	-0.30	-2.51	-0.54	-1.21	-0.45
9.	IX	-0.04	-0.14	-0.43	0.09	-0.01	0.02
10.	X	-0.91	-0.27	-2.01	-0.34	-1.38	-0.21
11.	XI(standard)	-0.34	0.00	-0.48	-0.08	-0.57	-0.07

DISCUSSION

These properties are calculated and discussed on the basis of Lipinski's rule and its component. The compounds V, VIII, IX, X fulfill Lipinski's rule and show good drug likeness score (Table 2.) . Milog P of these compounds was found below 5 that means these shows good permeability across cell membrane. TPSA below 160 Å2, *n* violatios =1 or <0 it means compound easily bind to receptor, molecular mass <500, *n* rotb < 5 [10], No. hydrogen bond donors ≤ 5 (The sum of OHs and NHs),No. hydrogen bond acceptor ≤ 10 (The sum of Os and Ns).

Compound I- X were taken further calculation of bioactivity score. From Table 3 Compounds I, II, III, IV, VI, VII, IX showed good bioactivity score. Compound IX (Dihydrocoumarin ethyl ester) showed good drug likeness score and bioactivity score, on comparison with other compounds.

CONCLUSION

Comparining drug likeness score and bioactivity score of compounds (I-X), Compound IX, in respect of standard BHT (antioxidant compound). Dihydrocoumarine ethyl ester showed good drug likeness score, and bioactivity score. It can be lead compound with antioxidant activity.

ACKNOWLEDGEMENT

We are thankful to Department of Chemistry, Sam Higginbottom Institute of Agriculture Technology and Sciences –Deemed University for providing necessary facilities.

ISSN: 0975-8585

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