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Molecular Properties and Bio-Activity Score of Alkaloids in Erythna Varigata Leaves to find Lead Compound

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A B S T R A C T

Molecular properties and Bio-Activity score of alkaloids present in erythrina varigata leaves were calculated using molinspiration software. MiLog P values of these compounds were found to be below 5 that means these alkaloids showed good permeability across cell membrane. TPSA in the range of 38.777 to 72.711 (well below 160 Á2) and molecular mass <500. Number of violations =0 and rotb < 7. Number of hydrogen bond donors < 5 (The sum of OHs and NHs) and hydrogen bond acceptor <7 (The sum of Os and Ns) .These observation showed that alkaloids can easily bind to receptor and were taken further for the calculation of bioactivity score. The result of bioactivity score of GPCR ligand, ion channel modulator, nuclear receptor ligand, inhibitor activities towards kinase, protease and enzymes indicated that the alkaloids I exhibited the highest score (0.48) towards GPCR ligand, II, VI and XII exhibited ion channel modulator (0.02-0.30), kinase inhibitor (0.03-0.41) and enzyme inhibitor (0.41-0.38) activities. Alkaloids I, II and VI may be a good lead compounds as protease inhibitor, enzyme inhibitor and kinase inhibitor respectively as per the comparative scores of fifteen alkaloids chosen for our work.

Keywords: Bio-Activity, Alkaloids, GPCR ligand, Enzyme Inhibitor.

A R T I C L E I N F O

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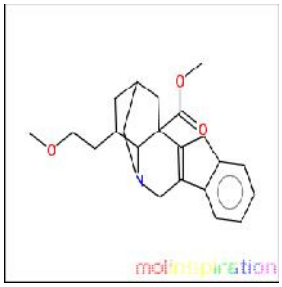
1. Introduction

Erythrina variegata (belongs to the Family, Fabaceae) is a medium-sized deciduous small tree with prickly stems and branches, leaves with triangular leaflets and large coral red flowers. The bark of the plant is astringent, febrifuge, anti-bilious and anthelmentic. It is also useful in opthalmia and skin diseases. The leaves are used in fever, inflammation and joint pain. The juice of the leaves is used to relieve earache and toothache (1). It has the reputation to stimulate lactation and menstruation and is used as laxative, diuretic and expectorant (2). It has potential effects for the treatment of diseases like convulsion, bacterial infection, insomnia, helminthiasis, cough, malarial fever, venereal disease, asthma, cuts and wounds. [5, 6, 7]. The erythrina-alkaloids showed leishmanicidal activity [8] and spirocyclic alkaloids were found to exhibit various pharmacological activities like anxiolytic, sedative and central nervous system depressant [9–18]. Tetrahydroprotoberberine-type alkaloids showed important central nervous system actions in addition to anti-malarial effects [19, 20]. Knowing the various pharmacological activities as revealed above, our present work deals with the molecular properties and bioactivity score evaluation using molinspiration software.

2. Materials and Methods

Structures of alkaloids present in erythrina varigata were selected from reported literature [21] for our work as given in fig.I-XV were drawn using online molinspiration software (www.molinspiration.com) 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 fifteen alkaloids were compared to identify lead compound.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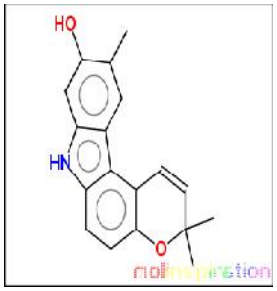

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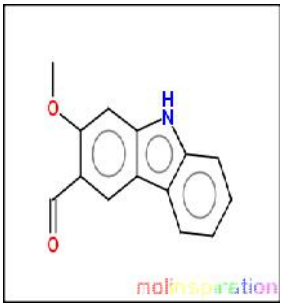

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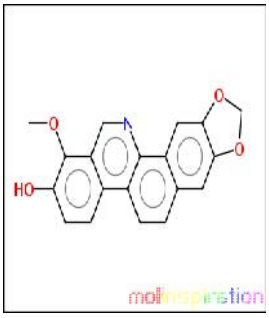

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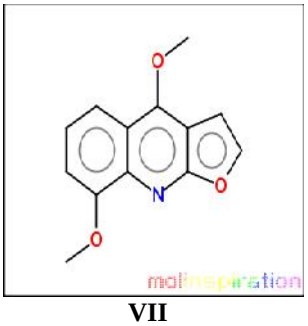

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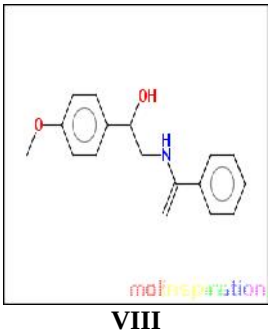

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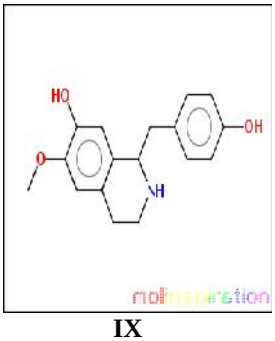

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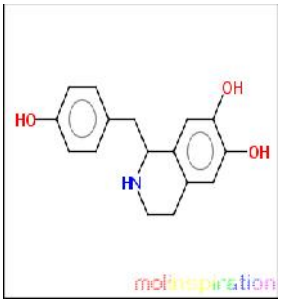

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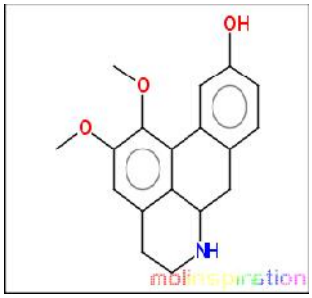

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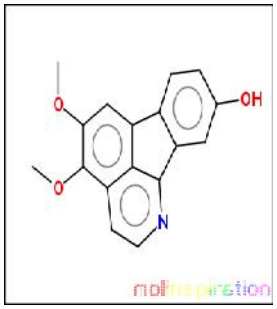

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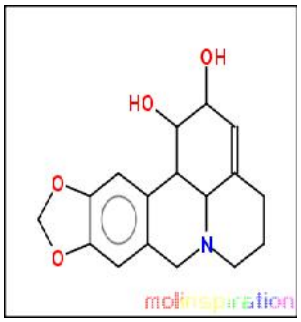

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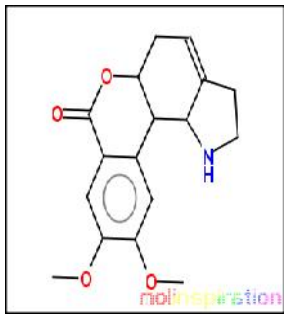

XV

Molinspiration software

Molinspiration, software was used to obtain parameter such as MiLogP, TPSA, and drug likeness. Log P measure molecular hydrophobicity, that affects drug absorption, bioavailability, drug-receptor interactions, metabolism of molecules, as well as their toxicity**.** Molecular Polar Surface Area (TPSA) are calculated based as a sum of fragment contributions of O- and N- centered polar fragments and related to the hydrogen bonding potential of a molecule. TPSA is a very good predictor of drug transport properties such as intestinal absorption, bioavailability, blood brain barrier penetration etc. The molecular properties and structure features of a drug can be checked by drug likeness data of a molecule. The calculated value for the drug likeness score and the various parameters of the all the alkaloids were given in Table 1. The bioactivity scores of these alkaloids were given in Table 2.

Table 1: Drug likeness score for alkaloids

S.NO	ALKALOIDS	miLogP	TPSA	natoms	n ON	n OHNH	n violation	Nrot bond	volume	MW
1	I	3.169	38.777	26.0	4	0	0	5	335.551	353.462
2	II	4.986	45.253	21.0	3	2	0	0	256.777	279.339
3	III	3.218	42.096	17.0	3	1	0	2	201.542	225.247
4	IV	3.098	43.493	19.0	4	1	0	3	233.65	257.289
5	V	2.976	71.558	20.0	5	2	0	3	235.105	271.272
6	VI	4.113	60.822	24.0	5	1	0	1	269.355	319.316
7	VII	2.882	44.5	17.0	4	0	0	2	200.53	229.235
8	VIII	2.936	41.489	20.0	3	2	0	6	262.779	269.344
9	IX	2.312	61.717	21.0	4	3	0	3	265.827	285.343
10	X	2.005	72.711	20.0	4	4	0	2	248.299	271.316
11	XI	2.705	50.723	22.0	4	2	0	2	272.513	297.354
12	XII	3.197	51.588	21.0	4	1	0	2	243.555	279.295
13	XIII	1.914	57.245	27.0	6	0	0	4	334.952	369.417
14	XIV	0.809	62.162	22.0	5	2	0	0	266.202	301.342
15	XV	1.656	56.8	22.0	5	1	0	2	271.285	301.342

Table 2: Bioactivity score of the compounds

S.No	ALKALOIDS	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	I	**0.46**	0.02	-0.14	0.21	**0.18**	0.23
2	II	0.02	0.03	0.27	**0.41**	-0.19	**0.38**
3	III	-0.34	-0.07	0.03	-0.30	-0.74	-0.06
4	IV	0.01	0.04	0.25	-0.11	-0.45	0.14
5	V	-0.02	0.06	0.21	0.09	-0.29	0.18
6	VI	0.13	0.22	**0.41**	0.02	-0.07	0.33
7	VII	-0.37	0.24	-0.14	-0.99	-0.74	0.10
8	VIII	-0.01	-0.49	-0.46	-0.42	-0.50	-0.12
9	IX	0.21	0.13	-0.23	-0.19	-0.09	0.09
10	X	0.25	0.23	-0.24	-0.15	-0.04	0.16
11	XI	0.39	**0.30**	-0.12	0.02	-0.13	0.24
12	XII	0.23	0.16	0.31	0.09	-0.26	0.28
13	XIII	0.17	-0.05	-0.33	-0.32	-0.15	-0.08
14	XIV	0.39	0.11	-0.25	0.13	0.07	0.37
15	XV	0.25	0.27	-0.08	-0.05	-0.02	0.39

>0- active, -5.0-0.0- moderately active, < -5.0- inactive

3. Results and Discussion

I . Drug likeness calculation

The alkaloids (I to XV) obeyed the Lipinski's rule and showed good drug likeness score (Table1). MiLog P values were found below 5 which indicated good permeability of these alkaloids. All alkaloids were found to have TPSA in the range of 38.777 to 72.711 (well below 160) and their molecular weights less than 500. Number of hydrogen bond donors (< 5) and hydrogen bond acceptors (<7) were found to be within Lipinski's limit i.e. less than 5 and 10respectively.All the above compounds were flexible (< 7 rotatable bonds) and found to have n violations =0

II. Bioactivity score of the compounds

The bioactivity scores of the fifteen alkaloids selected for the calculation of the bio activity score on the basis of GPCR ligand, ion channel modulator, nuclear receptor ligand , kinase inhibitor, protease inhibitor, enzyme inhibitor were given in Table-2 showed the following observations as per the rule.

a) GPCR ligand: Alkaloids I, VI, IX, X, XI, XII, XIII, XIV and XV were found to be highly bioactive (>0) towards GPCR ligands. The compounds II and IV were found to be moderately active (≤0).

b) Ion channel modulator

The Ion channel modulator properties of alkaloid VI , VII, IX, X, XI, XII, XIV and XV were highly bioactive (>0) whereas I, II, IV, V were found to be moderately bioactive(≤0).

c) Kinase inhibitor

Alkaloids II, IV, V, VI and XII were found to be highly bioactive (>0) as inhibitor towards Kinase and others were found to be moderately bioactive(<0).

d) Nuclear receptor ligand

The Nuclear receptor ligand activities (0.02-0.41) of I, II and XIV were found to be higher than other alkaloids.

e) Protease inhibitor

Alkaloids I and XIV were found to be active as Protease inhibitor (>0).

f) Enzyme inhibitor

Alkaloids I,II, IV, V, VI, VII, X, XI, XII, XIV and XV were highly bioactive(>0) as Enzyme inhibitors, whereas other compounds were found to be moderately active (<0) .

Among the fifteen alkaloids chosen for our work

a. Activity towards GPCR ligands and protease inhibition of the compound **I** were found to be highest(0.46) among others.
b. Compound II bio activity as nuclear receptor ligand and enzyme inhibitor were found to be highest (0.41and 0.38) among other alkaloids.
c. Alkaloid IV plays a vital role as kinase inhibitor (0.41).

4. Conclusion

Among the fifteen alkaloids selected from erythrina varigata plant for the calculation of the molecular propreties and bio activity score showed the following observation:

a. Alkaloids (I – XV) were found to obey the Lipinski's rule and showed good drug likeness score. (MiLog P below 5).
b. All compounds were found to have TPSA in the range of **38.777 to 72.711** (well below 160) and their molecular weights less than 50038.777 to 72.711 and were well below 160.
c. Number of hydrogen bond donors (< 5) ,hydrogen bond acceptors (<7) and n violation = 0 of these alkaloids proved their drug likeness nature.
d. The compound I was found to exhibit the highest score as 0.48 towards GPCR ligand

e. The compounds II, VI and XII were found to exhibit higher bio activity as ion channel modulator (0.02-0.30), kinase inhibitor (0.03-0.41) and enzyme inhibitor (0.41-0.38).

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