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Application Of Lipinski's Rule ^{4} (Predictive Adme) Of Marine Cardioactive Biomolecules

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Abstract:
Lipinski,s rule has predictive value for calculating drug likeness, We made a pioneer attempt to apply this rule to marine cardioactive biomolecules (MCBs).

1.Iroduction

The pharmacokinetic suitability of drug depends on absorption, distribution, metabolism and elimination (ADME). Drug likeness can be calculated by predictive ADME based on Lipinski's rule of five. This is the basic concept of drug design. The best possible absorption and bioavailability are very important, despite of good potency, efficacy etc.

Lipinski's rule states that poor ADME and bioavailability occur if –

- Molecular weight (MW) > 500 (should not exceed 500)
- Computed log P should not be greater than 5.
- Pc value (octanol/ H2O) should not exceed 5.
- There should be less than 5 H-donors expressed as the sum of OH and NH groups.
- There should be less than 10H-bond acceptors expressed as sum of N and O atoms (heteroatoms).

Veber et.al correlated oral bioavailability to molecular flexibility (rotatable bonds= 10 or fewer) and low polar surface which is characterized by aromatic density (numbers of aryl rings) and H-bond donors. The total H- bond count should be less than or equal to twelve including both donors and acceptors, independent of molecular weight .The reduced polar surface has better membrane permeation.

Predictive ADME of Marine cardioactive biomolecules[1-15] neglected log P and Pc values in this study because lipophilicity is not so relevant for natural products. They can be carried to the site of action by active transporters.

Therefore MWs, H-donors, H-acceptors and number of aryl rings were consider for theoretical predictivity. They are given in table - one.

No.	Names	Molecular weights	Hydrogen donors	Hydrogen acceptors	Number of aryl rings
1.	Aaptamine	228.2	one	two	Two
2.	Autonomium chloride	337.0	one	one	One
3.	Dieckol	328.5	eleven	seven	Six
4.	Doridosine	297.2	five	two	None
5.	Eckol	372.2	six	three	Three
6.	Eledosine	1188.4	eleven	fifteen	One
7.	Halenaquinol	334.3	two	five	One
8.	Hymenin	389.0	three	two	None
9.	Laminin	182.4	two	three	None
10.	1-methyl isoguanosine	298.2	Five	four	None
11.	Octopamine	153.1	three	three	One
12.	Phlorofucofuroeckol	602.4	nine	five	Five
13.	Saxitoxin	299.3	five	two	None
14.	Spongosine	300.2	three	seven	None
15.	Spongouridine	244.2	four	six	None
16.	Tetrodotoxin	319.2	six	three	None
17.	Xestoquinone	318.2	none	four	One

Table 1: Parameters of Lipinski's rule for Marine cardioactive biomolecules

The compliance of Lipinski's rule is analysed for seventeen Marine cardioactive biomolecules .Their interpretation is below:-

- Except six and twelve, all comply with molecular weight limitations.
- Except three, five, six, ten, twelve, thirteen, and sixteen, all have less than five H- bond donors.
- Except six, all have less than ten H-bond acceptors.

The interesting finding is related to aryl density equivalent to number of aryl rings. It was low profiled in all the Marine cardioactive biomolecules except three, five, and twelve. It is assumed that three, five, and twelve have strong anionic character which is balanced by hydrophobic aryl rings for membrane permeability.

The application of this rule to Marine cardioactive biomolecules is a pioneer step in drug design.

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