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Druglikeness Evaluation of Sanguinarine by Lipinski Filters

KEYWORDS: sanguinarine, druglikeness, anticancer alkaloid, Lipinski filters.

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ABSTRACT *Sanguinarine is a budding anticancer plant alkaloid. We have calculated the druglikeness of sanguinarine by Lipinski filters. The evaluation suggested that sanguinarine alkaloid fulfills all the five rules of Lipinski and can prove to be an excellent drug molecule*

Introduction:
Druglikeness literary means how "druglike" a substance is with respect to factors like bioavailability. It can be calculated from the molecular structure before the substance is even synthesized and tested. A traditional method to evaluate druglikeness is to check compliance of Lipinski's Rule of Five [1]. 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 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, based on the observation that most medication drugs are relatively small and lipophilic molecules . The rule describes molecular properties important for a drug›s pharmacokinetics in the human body, including their absorption, distribution, metabolism, and excretion («ADME"). However, the rule does not predict if a compound is pharmacologically active [2]. The rule is important to keep in mind during drug discovery when a pharmacologically active lead structure is optimized stepwise to increase the activity and selectivity of the compound as well as to insure drug-like physicochemical properties are maintained as described by Lipinski›s rule. Candidate drugs that conform to the RO5 tend to have lower attrition rates during clinical trials and hence have an increased chance of reaching the market [3].

Lipinski's rule states that, in general, an orally active drug has no more than one violation of the following criteria:

- Not more than 5 hydrogen bond donors.
- Not more than 10 hydrogen bond acceptors (nitrogen or oxygen atoms)
- A molecular mass less than 500 daltons.
- An octanol-water partition coefficient log P not greater than 5.
- Molar refractivity values should be 40-130.

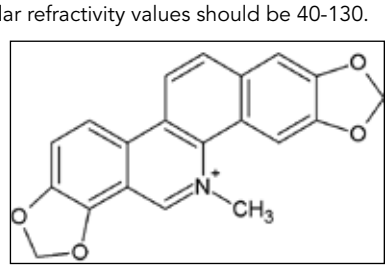

Figure 1 structure of sanguinarine

Sanguinarine (13-methyl benzodioxolo{5, 6-c}-1,3-dioxolo{4, 5-i}phenanthridinium) (Figure 1 above), is derived from the root of Sanguinaria canadenis and other poppy-fumaria species that has been used in folk medicine since ancient times [5].Additionally, it is also extracted from many other plants, including Agremone mexicana, Chelidonium majus, Macleaya cordata, and Herba chelidonii [6]. The diverse pharmacological, photochemical, and photobiological properties of sanguinarine include antimicrobial, antiinflammatory, antioxidant, antitumor activities, and singlet oxygen generation potential. FDA has approved the usage of sanguinarine as antibacterial and antiplaque agents in toothpastes. Sanguinarine can inhibit proliferation of different types of cancer cells. On the other hand, sanguinarine was found to be less toxic toward normal cells, such as normal human epidermal keratinocytes[7-11].We have evaluated the drug likeness of the sanguinarine alkaloid by Lipinski rule of five.

Methodology: The chemical structure of sanguinarine was drawn and converted to pdb file with Marwin Sketch 5.12.1 (http://www.chemaxon.com). The pdb file was uploaded on the scfbioiitd web server [12] for calculating the drug like properties using Lipinski drug filters.

Results & Discussions
Table1: sanguinarine values of RO5

Lipinski filters(RO5)	Druglikeness	Sanguinarine
Molecular weight	less than 500 daltons	332 daltons
Hydrogen Bond Donor	Less than5	0
H Bond Acceptor	Less than 10	5
LogP	Less than 5	4.230
Molar Refractivity	40 - 130	94.584

Comparison in Table 1 above shows that Sanguinarine follows all the five Lipinski filters and can prove to be an excellent therapeutic drug. Its therapeutic potential is supported by many experimental studies in literature.

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