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In Silico ADME/ Tox profile of tetrasubstitutedazadipyrrins

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Abstract

We have explored the ADME (Absorption, Distribution, Metabolism and Excretion) profile of eight different derivatives of tetrasubstitutedaza-dipyrrins. Compound 1-9 are screened with the help of online webtoolSwissADME. Studies were performed for pharmacokinetic, lipophilicity, water solubility, bioavailability and drug likeness properties. Compound 9 found to a optimum among all the compounds under investigation.

Key words : Aza- Dipyrrins, Pyrrole, ADME, SwissADME.

Introduction

Aza Dipyrrins are heterocyclic compounds with two pyrrole rings connected with a azomethane group. They are versatile compounds wild applications in the field of electronic materials such dye sensitized solar cells, polymers and medicine[1]. Recently azaazadipyrrin attracted much attention due to their various biological activities and applications in nanomedicine[4]. Recently dong and co-workers reported use of azadiprrin dyes in cancer phototheronotics[2]. Koca *et. al.* explore the properties of poly florinatedphthalocyanine derivatives as potential theranosticagents[3,4]. Use as PH activatable BODIPY are reported and their use in photodynamic therapy and bioimaging have discussed[5]. Recently Thomson et al reported the reactivity of sodium, lithium and potassium salts of aza-dipyrrins. In our pursuit to explore ADME properties and drug likeness of azadipyrrin we have screened the several tetra substituted azadipyrrin derivatives. (Fig 1).

Experimental

The in silico ADME studied were performed by online webserver Swiss ADME, the canonical smiles were generated from CHEMCD website and pub chem website.

Result and Discussion

To begin with the canonical smiles were inserted in online webserver window of SwissADME, the calculations were run and results obtained were interpreted. ADME properties are vital in the drug development, a decent drug candidate must own suitable ADME properties besides excellent bioactivity.

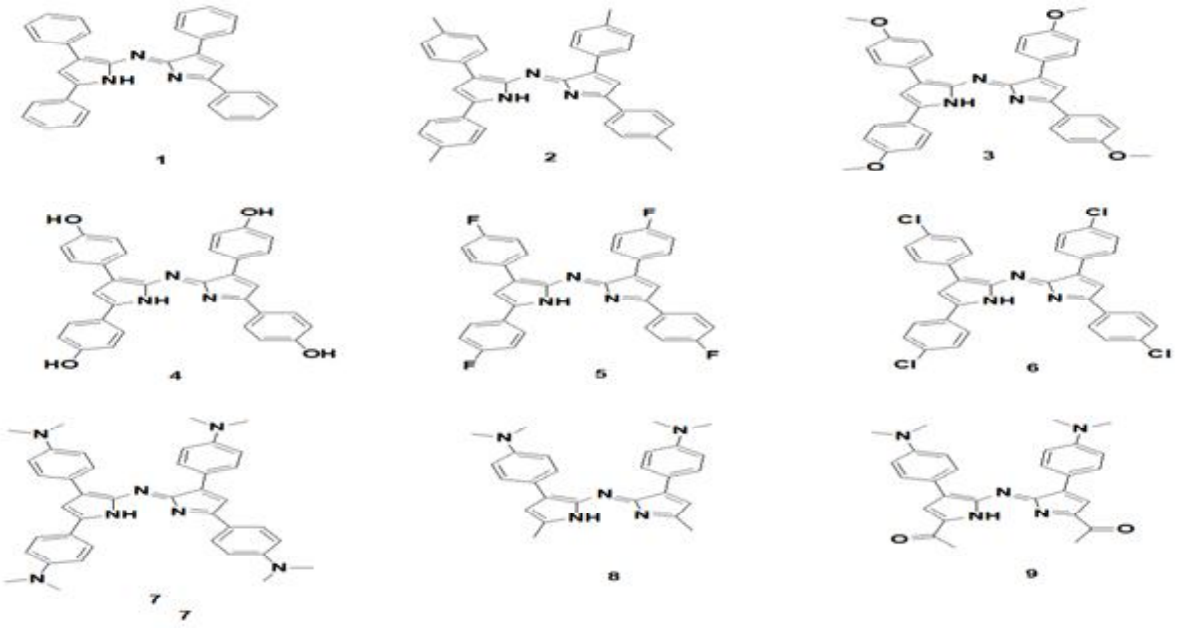

Fig 1: Structures of aza-Dipyrrins

Table 1. ADME properties of Compounds 1-9

Molecule	iLOGP	ESOL Log S	GI absorption	BBB permeant	Pgp substrate	Lipinski violations	Bio availability Score
1.	4.11	-7.58	Low	No	No	1	0.55
2.	4.97	-8.78	Low	No	No	2	0.17
3.	5.05	-7.88	Low	No	No	2	0.17
4.	2.94	-7.02	Low	No	No	1	0.55
5.	4.33	-8.22	Low	No	No	2	0.17
6.	4.95	-9.96	Low	No	Yes	2	0.17
7.	4.91	-8.54	Low	No	No	2	0.17
8.	3.43	-5.45	High	Yes	Yes	1	0.55
9.	**2.68**	**-5.1**	**High**	**No**	**No**	**0**	**0.55**

ADME properties of compounds under investigation are summarized in Table 1. Drug candidates need the balance between lipophilicity and water solubility for effectively reach to its target. **Compound 9** have moderate values of Log P (2.68) and Log S (-5.1) indicates its modest probability to reach to target. Among the compounds 1-9, compounds 8 and 9 have high Gastrointestinal absorption with good absorption profile. When we compare compound 8 and 9 for their Blood Brain Barrier permeation compound 9 is safe and does not permeant for Blood Brain Barrier makes it a desirable candidate. In addition, it is not a P-Glycoprotein (P-gp) substrate making more innocuous as a drug candidate. Furthermore, for drug likeness compound 9 does not violate any Lipinski rule and have 0.55 bioavailability score.

Conclusion

We have done in silico ADME screening of nine derivatives of Aza dipyrrins. The ADME profile revealed that compound 9 have good pharmacokinetic properties and drug likeness with no violation of Lipinski rule and 0.55 bioavailability score. Compound 9 had a good ADME profile and need future investigation on its drug target to be a lead compound.

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