IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

ADME Properties Of Halophenyl Analogues Of Pyrrole - A Theoretical Prediction

Rani Suryawanshi Patil and Kalpana Padmanaban
Department of Chemistry, K.L.E. Society's Science and Commerce College, Kalamboli,
Navi Mumbai - 410 218, India.

ABSTRACT

Pyrrole (**I**), fluorophenyl (**II**), chlorophenyl (**III**), bromophenyl (**IV**) and iodophenyl (**V**) analogues of pyrrole were selected and modelled by SwissADME database and physicochemical, pharmacokinetics, drug-likeness and medicinal properties were screened. The results indicate that all studied molecules obey Lipinski rule and possess positive gastrointestinal (GI) absorption with blood brain barrier (BBB) permeation. **I-V** exhibit good bioavailability score and remarkable synthetic accessibility.

KEYWORDS: Pyrrole, Halo compounds, Theoretical study, SwissADME database and ADME properties

I. INTRODUCTION

Heterocyclic compounds are ring-shaped molecules in which one or more carbon atoms are substituted by atoms other than carbon, known as heteroatoms. The most commonly found heteroatoms are nitrogen, oxygen, and sulfur, although other elements can also be part of the ring. These compounds represent a significant class of organic chemistry due to their wide range of applications in medicinal and synthetic fields. Heterocyclic structures are commonly found in numerous drugs, vitamins, natural products, biomolecules, and other biologically active compounds [1].

Pyrrole and their derivatives have great significant role as important intermediates, natural products, synthetic materials, pigments, pharmaceuticals and in drug development [2] Many pyrrole derivatives show antibacterial, antiviral, anti-inflammatory, antitumoral, and antioxidant activity for example, lipitor (cholesterol-lowering drug) and amtolmetin (anti- inflammatory agent) pharmaceuticals agents [3].

Furthermore, pyrroles are found in many naturally occurring compounds like heme, chlorophyll and vitamin B12. Moreover, many natural products containing the pyrrole ring display a wide range of agrochemical activities, including compounds such as ryanodine, pyrrolomycin, and dioxapyrrolomycin [4,5]. In addition, several commercially available pesticides also incorporate pyrrolyl groups in their structures, for example, the fungicides fludioxonil and fenpiclonil. Therefore, pyrrole derivatives play a significant role in pest control.

In medicinal chemistry, finding new synthetic molecules with characteristics similar to drugs is a constant problem. The synthesis of pharmacological molecules, the majority of which are based on N-heterocyclic motifs, has been influenced by natural products. The large number of pyrrole-based medications that are on the market attests to the fact that the pyrrole ring is one of the most investigated heterocycles in drug development programs for a number of therapeutic areas. Medicinal chemists continue to recognize the strong pharmacological and pharmaceutical potential of the pyrrole nucleus, which serves as a key pharmacophore in many drugs [6].

Efforts have been undertaken to present various strategic methods for synthesizing pyrrole and pyrrole-containing analogues. Structure–activity relationship studies, along with their therapeutic applications reported over the past decade, have been reviewed. Additionally, certain molecules that are key components in the market and in clinical trials have also been highlighted [7].

An environmentally friendly method has been developed for synthesizing pyrroles in aqueous media, using tetrahydrofuran and aniline derivatives as reactants, with β-cyclodextrin-SO_3H serving as the catalyst [8].

To the best of our knowledge, no theoretical research has been documented on the selected halophenyl pyrrole compounds (**I-V**) so far. Therefore, this work focuses on the medicinal properties of **I-V** by utilizing SwissADME web tool [9].

II. METHODOLOGY

In this present work, physicochemical properties, pharmacokinetics, drug-likeness and medicinal chemistry of the selected pyrrole analogues (**I-V**) have been analysed by SwissADME web tool. The 2D structure of the selected molecules were first modelled (shown in Figure 1.) and converted into corresponding SMILES (Simplified Molecular Input Line Entry System) which have been mentioned in Table 1 and the program was further simulated to study the ADME properties of the molecules.

III. RESULTS AND DISCUSSION

Analysis of Physicochemical properties

The physicochemical properties of **I-V** screened by SwissADME server have been recorded in Table 1. From the result it is inferred that all have one rotatable bond (RB) except **V** which has two RB. No studied molecule has either hydrogen bond donor (NHD) or acceptor (NHA) but **II** has one NHA. Molar refractivity (MR) increases from **I** to **V** and topological polar surface area (TPSA) of all the chosen compounds are showing positive results for a suitable drug and more solubility nature of the compounds offer the notable point towards the drug development.

Table 1. Physicochemical descriptors of I-VI by SwissADME web tool

Descriptor	I	II	III	IV	V
SMILES	c1ccc(cc1)n1cccc1	Fc1ccc(cc1)n1cccc1	Clc1ccc(cc1)n1cccc1	Brc1ccc(cc1)n1cccc1	Ic1ccc(cc1)n1cccc1
MF	$C_{10}H_9N$	$C_{10}H_8FN$	$C_{10}H_8ClN$	$C_{10}H_8BrN$	$C_{10}H_8IN$
MW (g/mol)	143.19	161.18	177.63	222.08	269.08
NRB	1	1	1	1	1
NHA	0	1	0	0	0
NHD	0	0	0	0	0
MR	45.77	45.73	50.78	53.47	58.49
TPSA (Å²)	4.93	4.93	4.93	4.93	4.93
Log $P_{o/w}$	2.41	2.71	2.94	3.03	3.07
Log S (ESOL)	-3.34	-3.46	-3.89	-4.20	-4.47

Table 2. ADME descriptors of I-VI by SwissADME web tool

Descriptor	I	II	III	IV	V
GI absorption	High	High	High	High	High
BBB permeant	Yes	Yes	Yes	Yes	Yes
Log K_p (skin permeation) cm/s	-4.99	-5.03	-4.75	-4.98	-5.29
Lipinski Rule	Yes	Yes	Yes	Yes	Yes
Bio-availability Score	0.55	0.55	0.55	0.55	0.55
Leadlikeness	1	1	2	2	2
Synthetic accessibility	1	1.17	1.29	1.32	1.78

Screening of Pharmacokinetics

The selected compounds were examined for pharmacokinetics and drug-likeness properties and shown in **Table 2**.

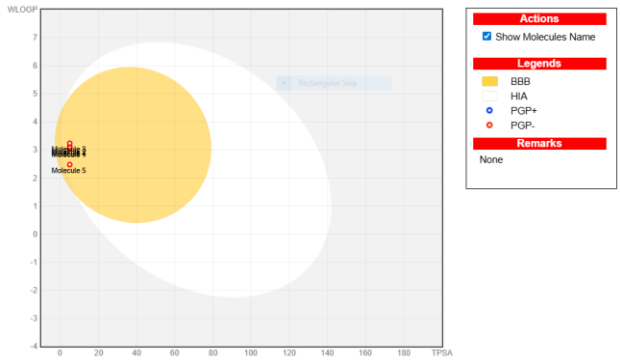


Figure 1. BOILED egg of I-V by SwissADME server

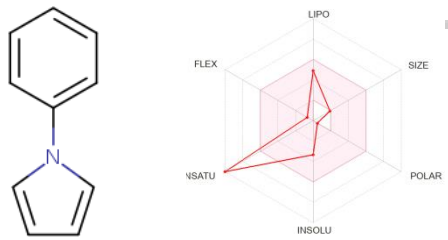
From the results, it is inferred that the gastrointestinal (GI) absorption is high with blood brain barrier (BBB) permeation for all the studied molecules and it is exhibited in the yellow portion of the BOILED egg (**Figure 1**.) It is good indication of **I-V** to efficiently act on central nervous system. All (**I-V**) have good skin permeation also.

Lipinski's rule

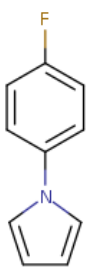
Lipinski rule of 5 helps to distinguish between drug-like and non-drug-like molecules [10,11]. It predicts high probability of success or failure due to drug likeness for molecules complying with 2 or more of the following rules.

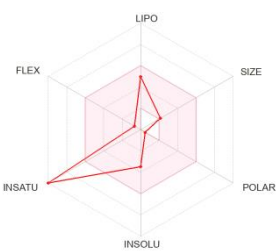
- Molecular mass less than 500 Dalton
- High lipophilicity (expressed as LogP less than 5)
- Less than 5 hydrogen bond donors
- Less than 10 hydrogen bond acceptors
- Molar refractivity should be between 40-130

I-**V** are obeying Lipinski's rule thereby eligible for being an oral drug at the preliminary stage of drug discovery.

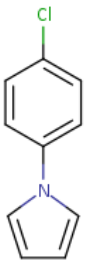


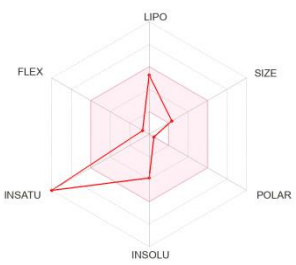
I



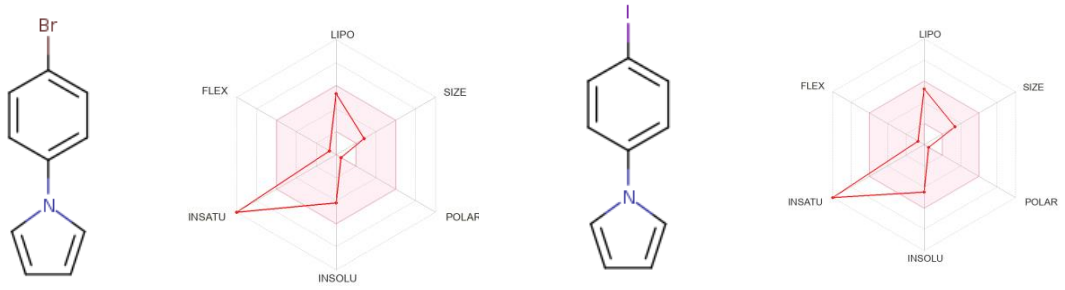


II





III



IV **V**

Figure 2. Modelled structure and bioavailability radar of I-V by SwissADME server

Bio-availability Radar

The modelled structure and bio-availability radar of the studied compounds (**I-V**) have been exhibited in **Figure 2**. In bio-availability radar of the compounds Pink / Red area is shown in the plot which reflects the maximum range of Lipophilicity, Size, Polarity, Insolubility, Instauration and Flexibility. By analysing the radar of **I-V**, it is showing promising results for all the characteristics which provide the hopeful pathway.

Medicinal chemistry

Bio-availability score is also notable for all the molecules under study. Affirmative result of lead-likeness with remarkable synthetic accessibility score makes **I-V** as suitable candidates to experimentalists.

IV. CONCLUSION

Pyrrole nucleus is one of the most valid heterocycles in drug development. This theoretical predictions on ADME properties of halophenyl derivatives of pyrrole (**I-V)** are possessing positive therapeutic properties and showing favourable chances for the experimentalists to step ahead in the drug development.

V. REFERENCES

1. Komal S., Neelam S., Dinesh K., Rajni T., Sunita D. and Puja G. (2024). Review On Heterocyclic Compounds Synthesis And Evaluation, International Journal of Pharmaceutical Sciences and Research. 15(12), 3416-3429.
2. A. Furstner (2003). Chemistry and biology of roseophiline and prodigiosine alkaloids: 2500 years in overview, Angew. Chem. 115, 3706–3728.
3. Meir B., Boris Y.,Raphael M., Yechiel B. (1980) Structure–activity relationships of pyrrole amidine antiviral antibiotics III: Preparation of distamycin and congocidine derivatives based on 2,5-disubstituted pyrroles, J Pharm Sci. 69(11) 1334-1338.
4. Pepper, B. P.; Carruth, L. A.(1945) A new plant insecticide for control of the european corn borer. J. Econ. Entomol. 38, 59– 66.
5. Charan, R. D.; Schlingmann, G.; Bernan, V. S.; Feng, X.; Carter, G. T. (2006) Dioxapyrrolomycin biosynthesis in streptomyces fumanus. J. Nat. Prod., 69, 29– 33.
6. Valeria R., et.al., (2020). Bioactive pyrrole-based compounds with target selectivity, European Journal of Medicinal Chemistry. 208 (15), 112783.
7. Varun B., et.al., (2015). Pyrrole: a resourceful small molecule in key medicinal hetero-aromatics, RSC Adv. 5, 15233.
8. Patil R. N., Kumar A. V. et.al., (2018). Biomimetic Clauson-Kass and Paal-Knorr pyrrole synthesis using β-cyclodextrin-SO_3H under aqueous and neat conditions-application to formal synthesis of polygonatine, Chemistry Select. 3(34), 9812.
9. Daina. A., Michielin. O., & Zortr. V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports. 7, 42717.
10. Lipinski. C. A., Lombardo. F., Dominy. B.W., & Feeney. P.J, (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings 1 PII of original article: S0169-409X(96)00423-1. The article was originally published in Advanced Drug Delivery Reviews 23 (1997) 3–25. 1 Advanced Drug Delivery Reviews. 46 (1), 3.

11. Kalpana P. and Rani P. (2025). Swissadme Analysis Of Some Selected Analogues Of Pyrrole, IJCRT, 3(4), k925-k929.