IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736.Volume 13, Issue 5 Ser. I (May. 2020), PP 28-31
www.iosrjournals.org

Study of Drug-likeness Properties of Some 6-(2'- Hydroxy-3'/5'-Chloro-5' /3'-Hydroxymethyl Phenyl)-4-Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines

*Santosh V. Agarkar and Suryakant B. Borul[2]
[*]*Indira Gandhi Mahavidyalaya, Ralegaon, Dist Yavatmal, Maharashtra, India.*
Department of Chemistry, Late Ku. Durga K. Banmeru Science College,
Lonar Pin 443302 Dist Buldana, Maharashtra, India.

Abstract: *The prepared 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines were evaluated for their drug-likeness properties by using Data warrior software of Osiris property explorer. The toxicity related risk as tumorogenicity, mutagenicity, irritation, and reproduction effectivity and various physico-chemical properties like clogP, solubility, drug-likeness and drug score were also calculated. The results of this study of drug-likeness properties of synthesized compounds were found encouraging.*

Key Words: *Drug-likeness, OSIRIS property calculator, Thiopyrimidines.*

Date of Submission: 27-04-2020 Date of Acceptance: 10-05-2020

I. Introduction

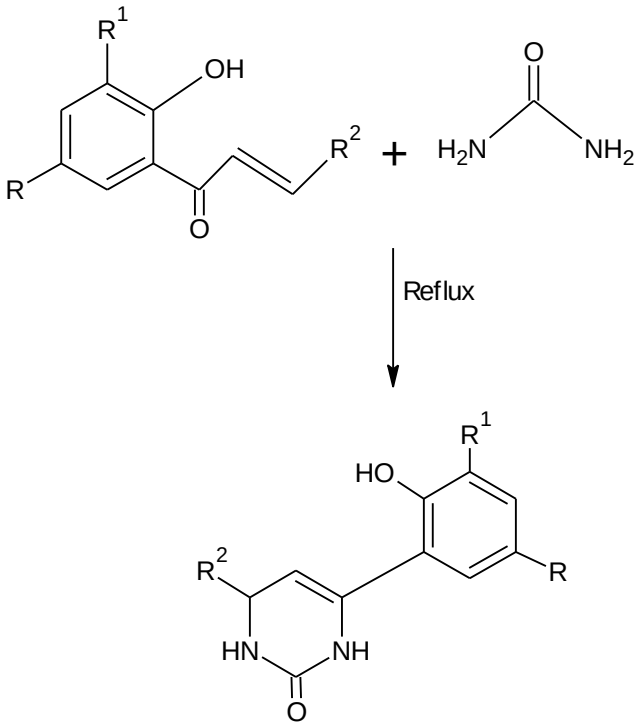
The study of concepts drug-likeness properties are very important for any newly synthesized molecules, because it may leads to drug discovery. The different structural and molecular properties such as hydrophobicity, hydrogen bond character, molecule size etc. are evaluated in order to know whether the newly synthesized compound or predicted compound is exhibiting properties similar to the known drugs or not.

In the present study attempts were made to know the above mentioned properties for the various thiopyrimidines synthesized.

II. Method And Materials

6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines were prepared by refluxing a mixture of 1-(2-hydroxy 3'/ 5'-chloro-5'/3' hydroxymethyl phenyl-3-aryl-2-propern-1-one, thiourea and KOH in methanol for 6 hours. The synthesized compounds were characterized by physical properties and spectral studies. The elemental analysis, Mol. formula, Mol. weight data is given in the table-1 and reaction scheme as shown below (fig.1) and general structure of compound as shown in fig.2.

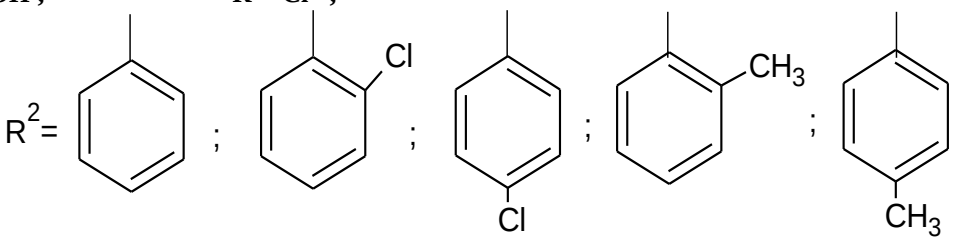
The Drug-likeness properties of compounds were studied by using Data warrior software of Osiris property explorer. The predication of the Osiris calculations is a fragment based approach and the occurrence frequency of each fragment is determined within the collection of traded drug and within collection of the non-drug-like commercially available chemicals. By using the Osiris property explorer the different physico-chemical properties such as clogP, solubility, drug-likeness and drug score were studied. The Osiris property explorer also predicted the toxicity related risks as tumorogenicity, mutagenicity, irritation, and reproduction effectivity of synthesized compound.



6-(2'- Hydroxy-3' (5'-Chloro-5' (3'-Hydroxymethyl phenyl)-
4-Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines

Fig.-1-Synthesis of 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines (Ia-Ie)

R = CH_2-OH ; **R^1 =Cl ;**



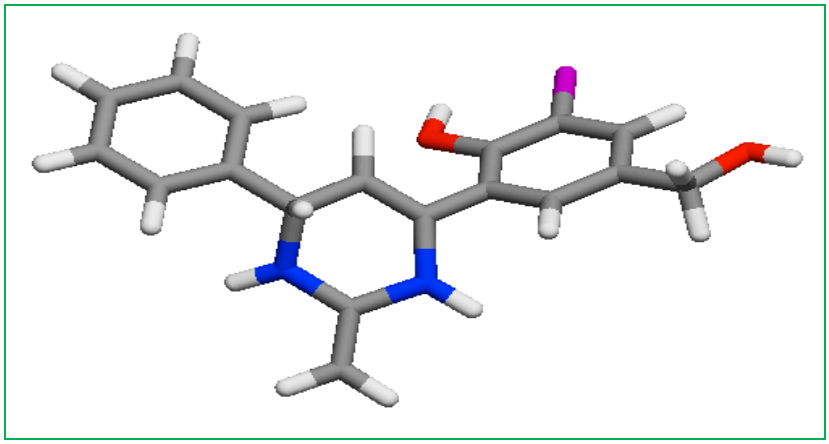


Fig.-2-Structure of 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines (Ia)

Table-1:- Properties of 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines.

Entries	Substituent's	M.P. in ^{0}C	Yield %	Analysis % found(calculated)	
				N	S
Ia	Phenyl	165	72	8.12 (8.34)	9.43(9.53)
Ib	o-chloro Phenyl	105	65	7.43(7.56)	8.52(8.64)
Ic	p-chloro Phenyl	118	67	7.43(7.56)	8.92(8.54)
Id	o-methyl Phenyl	176	60	7.63(8.01)	8.52(9.12)
Ie	p-methyl Phenyl	204	70	7.43(7.66)	8.84(9.12)

III. Results And Discussion

The characteristic data newly synthesized 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines are presented in the table -1. The melting points of these compounds are ranging from 105 to 204^{o}C and percent yield ranging from 60% to 72%. The analysis of nitrogen and sulphur content are ranging from 7.33% (7.56%) to 8.12% (8.34%) and 8. 34% (8.43%) to 9.43% (9.53%) respectively.

The drug-likeness properties of 6-(2'- Hydroxy-3'/5'-Chloro-5'/3'-Hydroxymethyl Phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines are presented in table-2. The molecular weight of these compounds are ranging from 346.83 to 381.28, while cLogp (partition coefficient between n-octanol and water) ranging from -3.86 to 4.59, tSPA (topological surface area) for all the synthesized compound were found to be 96.61 and drug-likeness values ranging from -0.61 to -2.01.

The values of drug-likeness of synthesized compounds phenyl (Ia), o-chloro phenyl (Ib), p-chloro phenyl(Ic), o-methyl phenyl (Id), and p-methyl phenyl (Ie) were calculated as -0.71, -0.61, 0.74, -1.25 and -2.01 respectively. The drug-likeness values of four compounds are negative but the drug-likeness value of p-chloro phenyl(Ic) was 0.74. It was observed that the substituent nature and position in aromatic could significantly affect the predicted value of drug-likeness.

The values of drug score of synthesized compounds phenyl (Ia), o-chloro phenyl (Ib), p-chloro phenyl(Ic), o-methyl phenyl (Id), and p-methyl phenyl (Ie) were calculated as 0.51, -0.44, 0.54, 0.44 and 0.40 respectively.

The Toxicity risks of synthesized compounds are given in table -3. The synthesized compounds were evaluated for their toxicity risk by using Data warrior software of Osiris property explorer. The study revealed that all the newly synthesized compounds were found to have no toxicity risks with respect to mutagenic, tumorogenuc, irritation and reproduction effect (table-3).

Table-2:-Drug likeness properties of 6-(2'- Hydroxy-3' (5'-Chloro-5' (3'-Hydroxymethyl phenyl)-4Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines.

Entry	Molecular Formula	Mol. Wt.	cLogp	Solubility	TPSA	Drug likeliness Value	Drug Score
Ia	$C_{17}H_{15}ClO_2N_2S$	346.83	3.03	-3.86	96.61	-0.71	0.51
Ib	$C_{17}H_{14}Cl_2O_2N_2S$	381.28	3.63	-4.59	96.61	-0.61	0.44
Ic	$C_{17}H_{14}Cl_2O_2N_2S$	381.28	3.63	-4.59	96.61	0.74	0.54
Id	$C_{18}H_{17}ClO_2N_2S$	360.86	3.37	-4.20	96.61	-1.25	0.44
Ie	$C_{18}H_{17}ClO_2N_2S$	360.86	3.37	-4.20	96.61	-2.01	0.40

Table-3:- Toxicity risk of synthesized molecules based on Data warrior software of Osiris property explorer.

Sr. No.	Entry	Mutagenic	Tumorogenic	Irritation	Reproduction effect
1	Ia	None	None	None	None
2	Ib	None	None	None	None
3	Ic	None	None	None	None
4	Id	None	None	None	None

5	Ie	None	None	None	None

IV. Conclusion

The synthesized compounds have shown very good (-2.01 to 0.74) drug-likeness value and the drug scores values are also very good (0.40 to 0.54). This shows that after thorough study of these compounds, these compounds may be used as drug or drug like compounds for the welfare of living organisms. The toxicity risks study also revealed that none of the synthesized compounds have shown toxicity in mutagenic, tumorogenic, irritation and reproductive effect. This is highly encouraging fact of all these newly synthesized 6- (2'- Hydroxy-3' / 5'-Chloro-5' / 3'-Hydroxymethyl Phenyl)- 4 Aryl 3, 4 Dihydro-2 (1H)-Thiopyrimidines.

Reference

[1]. S. M. Sondhi, M. J. Singh, A. Kumar, synthesis, anti-inflammatory and analgesic activities evaluation of some mono, bi, tricyclic pyrimidine derivatives. Bioorganic and medicinal Chemistry. 2005; 13(22):6158-6166.
[2]. C. A. Lipinski, Drug-like properties and the causes of poor solubility and poor permeability. J. Pharmacol. Toxicol. Methods. 2000; 44:235–249.
[3]. B. Torzkoparan, M. Ertan, P. Kelicen, R. Decmirdamar, Farmaco. 1999; 54:588.
[4]. R. S. Vardanyan, V. J. Hruby, G. G. Danagulyan, Isomerization / recyclization of some 5-ethoxycarbonyl-pyrimidines. J. Heterocycl. Chem., 2005;42(4): 557-562.
[5]. Borul, S. B. and Agarkar, S.V. Synthesis and study of Drug likeness property of "(E)-3-Substituted phenyl-1-Piperidino-2-Propen-1-one Cinnamamide. Journal of Emerging Technologies and Innovative Research. 2020; 7(3):46-50.
[6]. S. B. Borul, and S.V. Agarkar, Synthesis and Characterization of Novel Cinnamamide Deriverties and Their Antimicrobial Activities. IOSR Journal of Applied Chemistry (IOSR-JAC). 2014;7(12):52-55.
[7]. A. K. Ghose, V. N. Viswanadhan, J. J. Wendoloski, A Knowledge-Based Approach in Designing Combinatorial or Medicinal Chemistry Libraries for Drug Discovery. 1. A Qualitative and Quantitative Characterization of Known Drug Databases. J. Comb. Chem.1999;1(55):55–68.
[8]. S. Baluja, S. C. Kacchadia, Thiopyrimidine derivatives: synthesis and antibacterial activity, pharmaceutical chemistry journal. 2012;46(2):117-121.
[9]. Seelolla Gangadhara, Cheera Prasad, and Ponneri Venkateswarlu, Indo American Journal of Pharmaceutical Research.2015;5(3).
[10]. P. Maniyan, S. Bernard, D. Yuxiang, C. Jacques, M. Hugues, A.C. Susan, J.C. Darren, N.C. William, S.T. Josefina, S. Christian, W. Sergio, B. Reto, L.V. Jonathan, Bioorg. Med. Chem. Lett. 2006;16:5542-5545

Santosh V. Agarkar. " Study of Drug-likeness Properties of Some 6-(2'- Hydroxy-3'/5'-Chloro-5' /3'-Hydroxymethyl Phenyl)-4-Aryl 3, 4 Dihydro-2(1H)-Thiopyrimidines." *IOSR Journal of Applied Chemistry (IOSR-JAC)*, 13(5), (2020): pp 28-31.