Journal home page:
http://www.iajpr.com/index.php/en/

INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH

Computational bioactivity of isatin Schiff base

J.Vinnarasi[1], A.Anto Arockia Raj[1*], Dr.A.Johnson[2], D.Rajamani[3]

[1]*Department of chemistry, St.Xavier's college (Autonomous), Palayamkottai, Tamil Nadu, India.*
[2]*Department of Plant biology and Biotechnology, St.Xavier's college (Autonomous), Palayamkottai, Tamil Nadu, India.*
[3]*Department of chemistry, S.F.R. college for women, Sivakasi, Tamil Nadu, India.*

ARTICLE INFO

Article history
Received 10/06/2013
Available online 30/06/2013

Keywords
Isatin, schiff base, ACD/I lab, Acute Toxicity, Genotoxicity and Median Lethal concentration.

ABSTRACT

Schiff bases derived from isatin plays a vital role in biological and pharmacological activity. The synthesis and characterization of isatin Schiff bases have been reported previously. Our work aims to predict the biological activity of isatin Schiff bases by computational method using ACD/I Lab (Software for biological activity prediction). From this software we predict Acute Toxicity (LD50, mg/kg), Median Lethal Concentration (LC50, mg/L). Isatin Schiff base has more biological activity, our study showed that 2-{[(3Z)-2-oxo-2,3-dihydro- 1H-indol-3-ylidene]amino}benzoic acid , 4-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid, [(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]urea and (3Z)-3-[(pyridin-2-yl)imino]-2,3-dihydro-1H-indol-2-one have more toxic against Mouse/ Intraperitoneal. In oral administration, 2-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid, 4-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid and (3Z)-3-[(pyridin-2-yl)imino]-2,3-dihydro-1H-indol-2- has more activity compared to other schiff base. No hazardous fragments have been found in all the compounds. [(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene] urea shows not reliable and borderline result that indicate this schiff base do not produce toxic to living organism essential for human beings.

Corresponding author

A. Anto Arockia Raj
Department of chemistry,
St.Xavier's college (Autonomous), Palayamkottai,
Tamil Nadu, India.
e.mail: antset.anto.@gmail.com Phone no: +919944274226

Please cite this article in press as J.Vinnarasi et.al. Computational bioactivity of isatin Schiff bas. Indo American Journal of Pharm Research.2013:3(6).

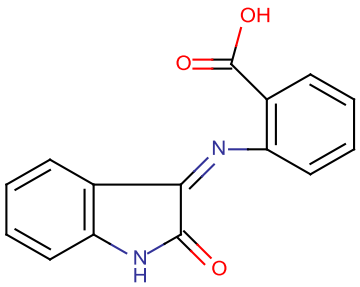
Introduction:

Isatin is an important group of heterocyclic compounds which are biologically active and of significant importance in medicinal chemistry [1]. Isatin is an endogenous compound isolated in 1998 and reported to possess a wide range of central nervous system activities. In the last few years, Isatin derivatives have been discovered which show potential hypnotic, antibacterial and, antihistaminic activity [2]. Isatin was a potent endogenous monoamine oxidase (MAO) inhibitor that is more active against MAO-B than MAO-A. The acute effects of isatin on apomorphine (APO)-induced rotations were evaluated in Parkinsonian rats induced by 6-hydroxydopamine (6-OHDA)lesion[3]. Our aim is to protect the eco system. Knowing the importance of isatin schiff base, predict the bioactivity using computational method, In future identify which functionality is responsible for activity then we design a new drug.

Materials and Methods:

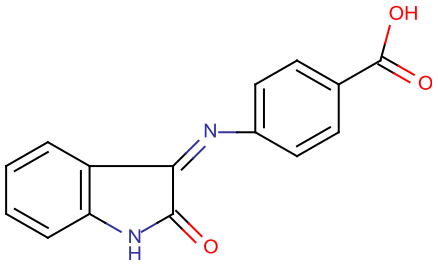
Materials:

Schiff bases derived from isatin with substances like 2-aminobenzoicacid, 4-aminobenzoic acid, urea, thiourea, and pyridin-2-amine. The various Schiff bases **(**A-E**)** given below were chosen for our work [4].



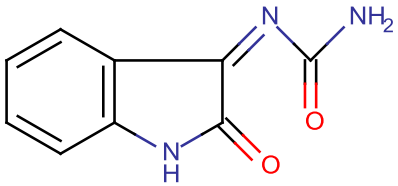
2-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid

A



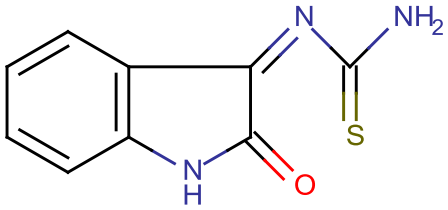
4-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid

B



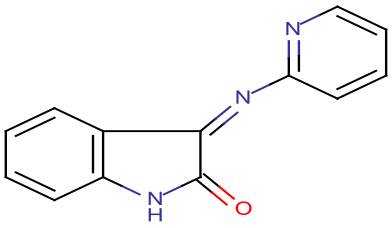
[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]urea

C



[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]thiourea

D

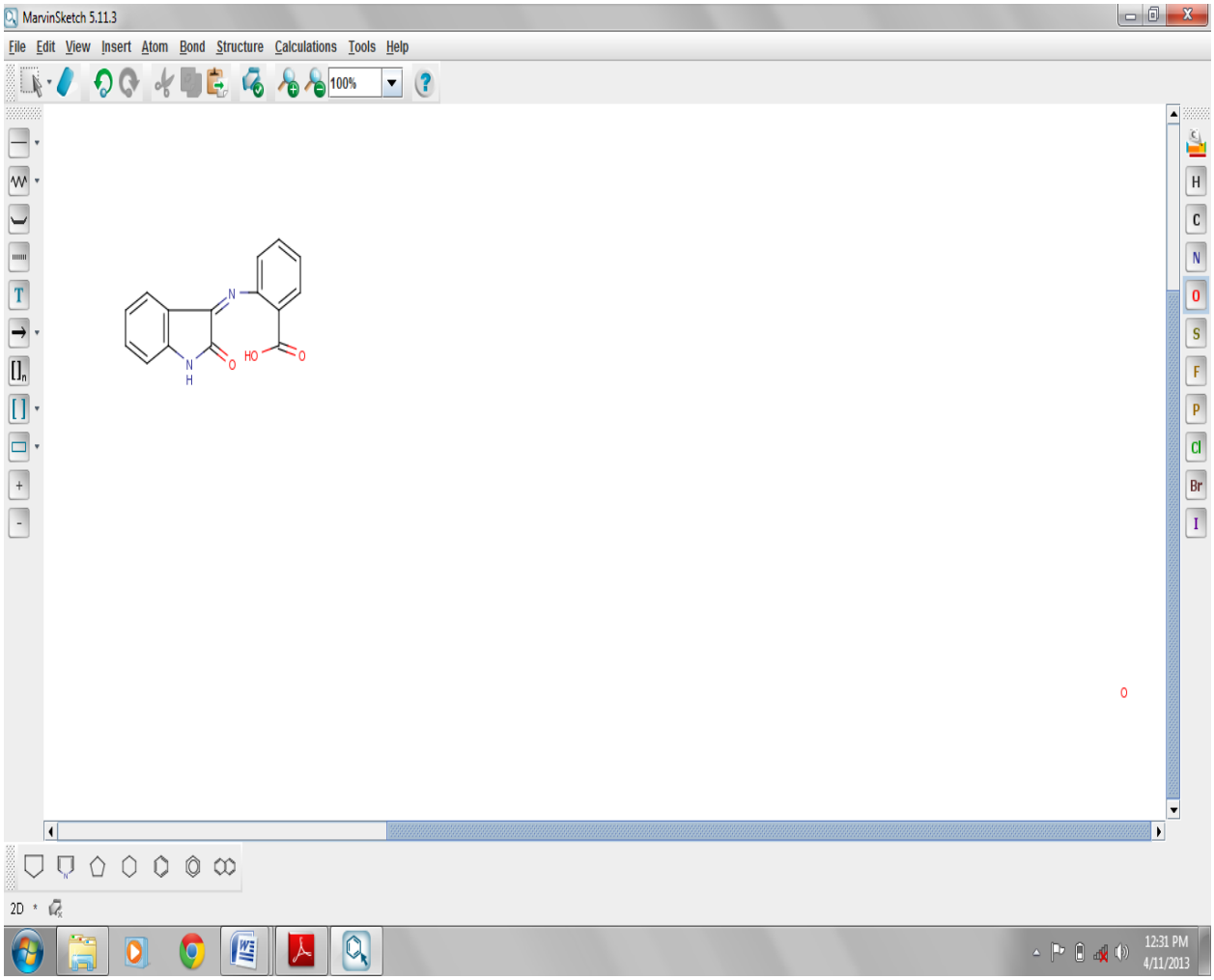


(3Z)-3-[(pyridin-2-yl)imino]-2,3-dihydro-1H-indol-2-one

E

Methods:

The structure of Schiff bases listed **(**A-E**)** were drawn in **Marvin Sketch** and appear as shown in **Fig.1.** and their structures were saved as mol files**(*.mol)**.



ACD/I lab:

Then upload these mol files in ACD/ I lab software from the result we conclude the bio activity of these schiff bases.

Result:

The predicted values for acute toxicity were tabulated in table - 1and the median lethal concentration in table-2.

Table 1: Predicted Values - Acute Toxicity (LD50, mg/kg)

S.No.	Species/ Administration route	A		B		C		D		E	
		LD 50 (mg/ kg)	**RI**	**LD 50 (mg/ kg)**	**RI**	**LD 50 (mg/ kg)**	**RI**	**LD 50 (mg /kg)**	**RI**	**LD 50 (mg /kg)**	**RI**
1.	Mouse/ Intraperitoneal	610	M 0.62	610	M 0.62	720	M 0.54	230	B 0.2	400	M 0.66
2.	Mouse/Oral	1400	M 0.51	1400	M 0.51	940	B 0.41	440	B 0.39	580	M 0.57
3.	Mouse/ Intravenous	530	NR 0.3	530	N R 0.3	260	B 0.43	130	B 0.44	120	B 0.34
4.	Mouse/ Subcutaneous	510	B 0.4	510	B 0.42	510	B 0.3		B 0.45	240	N R 0.29
5.	Rat/ Intraperitoneal	340	N R 0.27	340	NR 0.27	310	B 0.38	280 220	B 0.32	340	B 0.37
6.	Rat/Oral	1600	B 0.44	1600	B 0.44	2100	B 0.48	480	B 0.46	690	NR 0.22

RI – Reliability; B- Borderline; M- Moderate; NR- Not reliable

Genotoxicity Hazards

No hazardous fragments have been found in all the compounds.

Table 2: Predicted Values – Median Lethal Concentration (LC50, mg/L)

S.No	Species	A		B		C		D		E	
		LC 50 (mg/L)	**RI**	**LC50 (mg/L)**	**RI**	**LC50 (mg/L)**	**RI**	**LC 50 (mg/ L)**	**RI**	**LC 50 (mg/L)**	**RI**
1.	Fathead minnow (Pimephales promelas)	3.7	NR 0.13	3.7	NR 0.13	190	NR 0.11	37	NR 0.13	3.2	N R 0.1
2.	Water flea (Daphnia magna)	27	B 0.48	27	B 0.48	57	B 0.37	7.5	M 0.51	4	B 0.48

Discussion:

Rodent acute toxic rat poison is a short-term feeding or feeding several times soon after the poisoning death of a class of rodenticides[4]. Acute toxic rat poison is not only highly toxic to rodents, also highly toxic to humans and animals. Acute toxic rat poison serious ecological damage to the environment, causing secondary poisoning [5].

In Mouse/ Intraperitoneal administration schiff base except thiourea all are showing moderate result and in oral administration thiourea and urea schiff base only shows borderline result, remains showing moderate values. Mouse intravenous /subcutaneous and Rat Intraperitoneal/ oral values are border line and some of them are not reliable.

The genotoxic substances induce damage to the genetic material in the cells through interactions with the DNA sequence and structure. In genetics, genotoxicity describes the property of chemical agents that damages the genetic information within a cell causing mutations, which may lead to cancer[6].

No hazardous fragments have been found in all the compounds.

The fathead species is also important as a biological model in aquatic toxicology studies [7]. Because of its relative hardness and large number of offspring produced, EPA guidelines outline its use for the evaluation of acute and chronic toxicity of samples or chemical species in vertebrate animals [8].The fathead's invasive status in Europe is cited as the main cause for the spread of enteric redmouth disease among trout and eels there [9].

Daphnia magna is widely used as a laboratory animal for testing ecotoxicity starting with Einar Naumann in 1934[10].The use of *Daphnia magna* as an experimental animal for such purposes is advantageous in many respects. Daphnids are small, reaching a size of five mm, so that a great many can be reared in a small space. Daphnids would be affected if there was something toxic added to the water, therefore fish would leave and the Daphnia would die. For these reasons Daphnia prove satisfactory for testing on.

All the schiff base except thiourea shows not reliable and borderline results that indicates our compound not produce toxic to living organism essential for humans.
Our compounds

Conclusion:

Isatin schiff base have more biological activity, our study showed that 2-{[(3Z)-2-oxo-2,3-dihydro- 1H-indol-3-ylidene]amino}benzoic acid , 4-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid, [(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]urea and (3Z)-3-[(pyridin-2-yl)imino]-2,3-dihydro-1H-indol-2-one have more toxic against Mouse/ Intraperitoneal. In oral administration, 2-{[(3Z)-2-oxo-2,3-dihydro- 1H-indol-3-ylidene]amino}benzoic acid , 4-{[(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]amino}benzoic acid and (3Z)-3-[(pyridin-2-yl)imino]-2,3-dihydro-1H-indol-2- have more activity compared to other schiff base. The genotoxic substances induce damage to the genetic material in the cells through interactions with the DNA sequence and structure but No hazardous fragments have been found in all the schiff bases. All the schiff bases except [(3Z)-2-oxo-2,3-dihydro-1H-indol-3-ylidene]thiourea exhibit not reliable and borderline results that indicate our compounds do not produce toxic to living organism essential for human beings. In future identify the functionality which is responsible for that activity then find the structure activity relationship then we design a drug.

References:

1. Bhanupriya Bhrigu, Devender Pathak, Nadeem Siddiqui, M Shamsher Alam, WaquarAhsan, Search for Biological Active Isatins, International Journal of Pharmaceutical Sciences and Drug Research. 2010, 2(4), 229-235.
2. K. Swathi, A. Srinivas and M. Sarangapani, Design, synthesis and biological evaluation of 5-[2(3)-dialkylamino alkoxy] indole 2,3-diones as new antihistamine agents, J. Chem. Pharm. Res. 2010, 2(2),220-225.
3. Yu Zhoua,b, Zhi-Qi Zhaob, Jun-Xia Xie, Effects of isatin on rotational behavior and DA levels in caudate putamen in Parkinsonian rats, Brain Research. 2001, 917 ,127–132.
4. 4. A.AntoArockia Raj, J. Vinnarasi, Dr. M .Johnson, Dr. G.Valli, Synthesis characterization and biological activities of Schiff bases of isatin, BioMedRx. 2013, 1 (2), 217-222.
5. Plunkett, Signe J, Emergency Procedures for the Small Animal Veterinarian. Harcourt Publishers 2001,pp. 289–292, ISBN 0-7020-2487-2.
6. Feller, Roger W, Shawn P, Messonnier, Small Animal Toxicology and Poisonings. Mosby 2004, pp. 321–326, ISBN 0-323-01246-9.
7. Mei, Nan ,Metabolism, Genotoxicity, and Carcinogenicity of Comfrey. Journal of Toxicology and Environmental Health 2010 Retrieved 2013-04-04.
8. Lawrence M. and Brooks M. Burr , Freshwater Fishes, p. 129-130, Houghton Mifflin, New York, NY. 1991,ISBN 0-395-91091-9.
9. Alderton, David, Encyclopedia of Aquarium and Pondfish, Dorling Kindersley, New York, NY.2005, 360,ISBN 0-7566-0941-0.
10. Froese, Rainer and Pauly, Daniel, eds. (2006). Pimephales promelas in FishBase. December 2006 version.
11. Naumann, Einar, Über die Anwendung von Daphnia magnaStraus als Versuchstier zur experimentellen Klarlegung der Lebensverhältnisse im Wasser, International Revue der gesamten Hydrobiologie and Hydrographie 1934, 31 (1), 421–431.

FSDFGHH451001254