Available online at www.pharmaresearchlibrary.com/ijcps ISSN: 2321-3132

Research Article

International Journal of Chemistry and Pharmaceutical Sciences
IJCPS, 2013: Vol.1(5): 365-369
www.pharmaresearchlibrary.com/ijcps

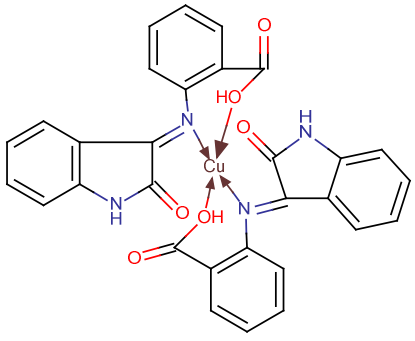
Insilico Drug Activities of Some Isatin Metal Complexes

A. Anto Arockia Raj[1]*, J.Vinnarasi[1], M.Johnson[2]
[1]Department of Chemistry, St.Xavier's College, Palayamkottai-627002, Tamil Nadu, India.
[2] Centre for Plant Biotechnology, Dept. of Botany, St.Xavier's College, Palayamkottai-627002, Tamil Nadu, India.
*E-mail:antset.anto@gmail.com

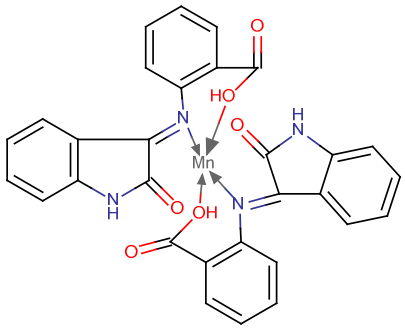
Abstract
Isatin schiff bases complexes were found to have anti-HIV activity. Hence our aim is to correlate the biological activity of isatin complexes against the HIV by *Insilico* method. The target molecule (virus) was taken from Protein data bank. Various softwares were used to find out the drug likeness properties of these schiff bases. We have selected Maraviroc, Darunavir, Nelfinavir, Zidovudine and Zalcitabine as standard drugs among the available drugs for correlating the drug activities against our Isatin transition metal complexes. We observed that some of our complexes were found to have higher drug activities compared to standard drugs.
Keywords. Isatin complexes, Hex 6.3, Marvin sketch, ACD /I Lab.

Introduction
Drug discovery has its beginning the root of mankind (1). Medicinal chemistry is an interdisciplinary science that by its very nature encompasses the sciences of chemistry, biochemistry, physiology, pharmacology and molecular modelling. It has been stated that medicinal chemistry concern with the discovery, development, identification and interpretation of the mode of action of biologically active compounds at molecular level (2). The synthetic compounds offered an opportunity to medicinal screening. The inventions of new lead molecules are used to design effective and safe drugs and also to reduce drug toxicities (3).Isatin (indol-2,3-dione) is a resourceful endogenous heterocyclic molecule identified in human being and rat tissues. Several of its derivatives were reported to exhibit a wide range of promising pharmacodynamic profile like anticonvulsant (4, 5), anti-HIV (6) cytotoxic (7), tuberculostatic (8), anti-microbial (9). At millimolar concentrations isatin has been found to inhibit different enzymes, an effect that may contribute to its anti infective actions (10).A significant rising interest in the design of metal compounds as drugs and our aim to dock a metal complexes with HIV and compare with standard drugs.

Experimental
Materials
Schiff base derived from isatin and 2-aminobenzoic acid. The prepared schiff base complex with transition metals (Cu, Mn, Cd, Zn, Co, Ni).The various Schiff bases **(**A-E**)** given below were chosen for our work (11).

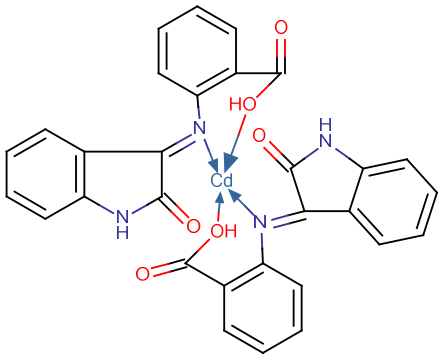


A
1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)-4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-cupracyclohexane]-4,4'-dione



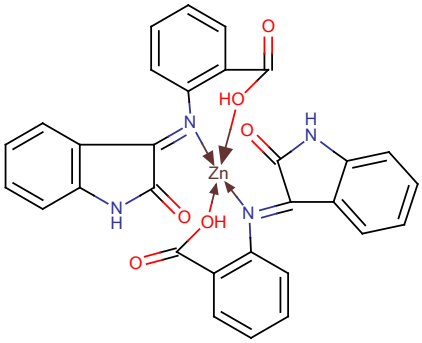
B

1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)- 4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-manganacyclohexane]-4,4'-dione



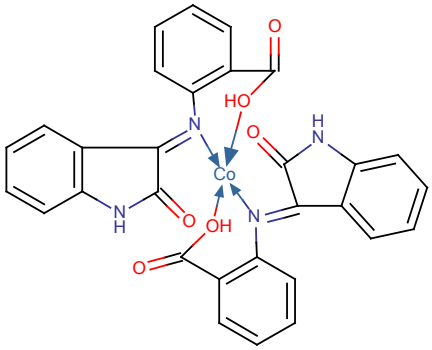
C

1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)-4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-cadmacyclohexane]4,4'-dione



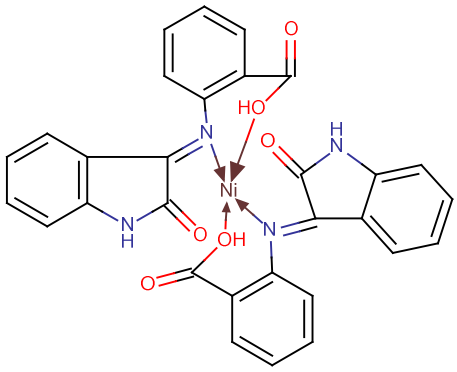
D

1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)- 4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-zincacyclohexane]-4,4'-dione



E

1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)-4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-cobaltacyclohexane] 4,4'-dione



F

1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)-4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-nickelacyclohexane]-4,4'-dione

Methods

The structure of isatin metal complexes listed **(**A-F**)** were drawn in **Marvin Sketch** and appear as shown in **Fig.1.** and their structures were saved as pdb **(*.pdb)**. The following five antibiotics were taken as the standard drugs from the drug bank.

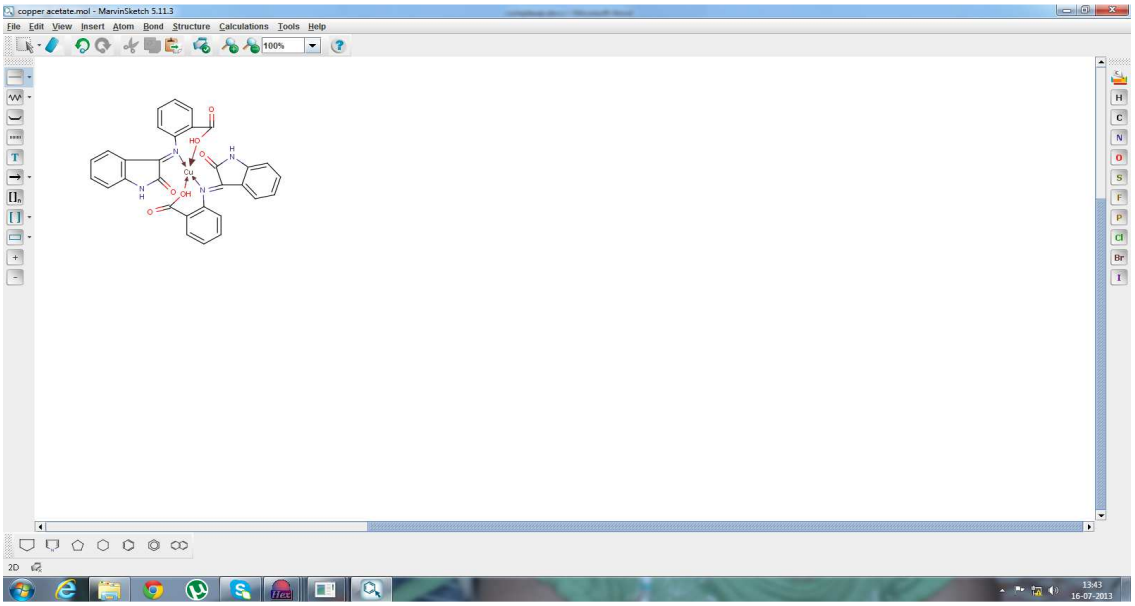


Figure.1 The Marvin sketch window

Maraviroc

Maraviroc is a chemokine receptor antagonist drug developed by the drug company Pfizer that is designed to act against HIV by interfering with the interaction between HIV and CCR5. Maraviroc is an entry inhibitor and works by blocking HIV from entering human cells. Specifically maraviroc is a selective, slowly reversible, small molecule antagonist of the interaction between human CCR5 and HIV-1 gp120.

Darunavir

Darunavir is an inhibitor of the human immunodeficiency virus (HIV) protease. In studies, the drug, co-administered with ritonavir in combination therapy, significantly reduced viral load and increased CD4 cell counts in this treatment-experienced patient population (Tibotec, 2006, Product Monograph, Prezista 2006). Darunavir is used as an adjunct therapy with low dose ritonavir, which inhibits cytochrome P_{450} 3A (CYP3A) which increases the bioavailability and half life of darunavir.

Nelfinavir

Nelfinavir is a protease inhibitor with activity against Human Immunodeficiency Virus Type 1 (HIV-1). Protease inhibitors block the part of HIV called protease. HIV-1 protease is an enzyme required for the proteolytic cleavage of the viral polyprotein precursors into the individual functional proteins found in infectious HIV-1. Nelfinavir binds to the protease active site and inhibits the activity of the enzyme. This inhibition prevents cleavage of the viral

polyproteins resulting in the formation of immature non-infectious viral particles. Protease inhibitors are almost always used in combination with at least two other anti-HIV drugs.

Zidovudine

Zidovudine is a nucleoside reverse transcriptase inhibitor (NRTI) with activity against Human Immunodeficiency Virus Type 1 (HIV-1). Zidovudine is phosphorylated to active metabolites that compete for incorporation into viral DNA. They inhibit the HIV reverse transcriptase enzyme competitively and act as a chain terminator of DNA synthesis. The lack of a 3'-OH group in the incorporated nucleoside analogue prevents the formation of the 5' to 3' phosphodiester linkage essential for DNA chain elongation, and therefore, the viral DNA growth is terminated.

Zalcitabine

Zalcitabine is an analog of 2'-deoxycytidine that is pharmacologically related to but structurally different from other nucleotide reverse transcriptase inhibitors (NRTIs). Zalcitabine inhibits the activity of HIV-1 reverse transcriptase (RT) both by competing with the natural substrate dGTP and by its incorporation into viral DNA.

HEX 6.3

Macromolecular Docking was done using HEX 6.3 – software using Spherical Polar Fourier Correlations. In Hex's docking calculations, each molecule is modeled using 3D parametric functions, which are used to encode both surface shape and electrostatic charge and potential distributions. With suitable scaling factors, this docking score can be interpreted as interaction energy. Hex reads protein and DNA molecular structures from PDB- format files These are treated as receptor.

Result and Discussion

We calculated the E-Total value of isatin metal complexes (A-F) against HIV virus using Hex 6.3 docking software The results obtained after docking gets completed were shown in Fig. 2 and the complexes docking values are listed in table 1 and the standard drugs are tabulated in table 2.

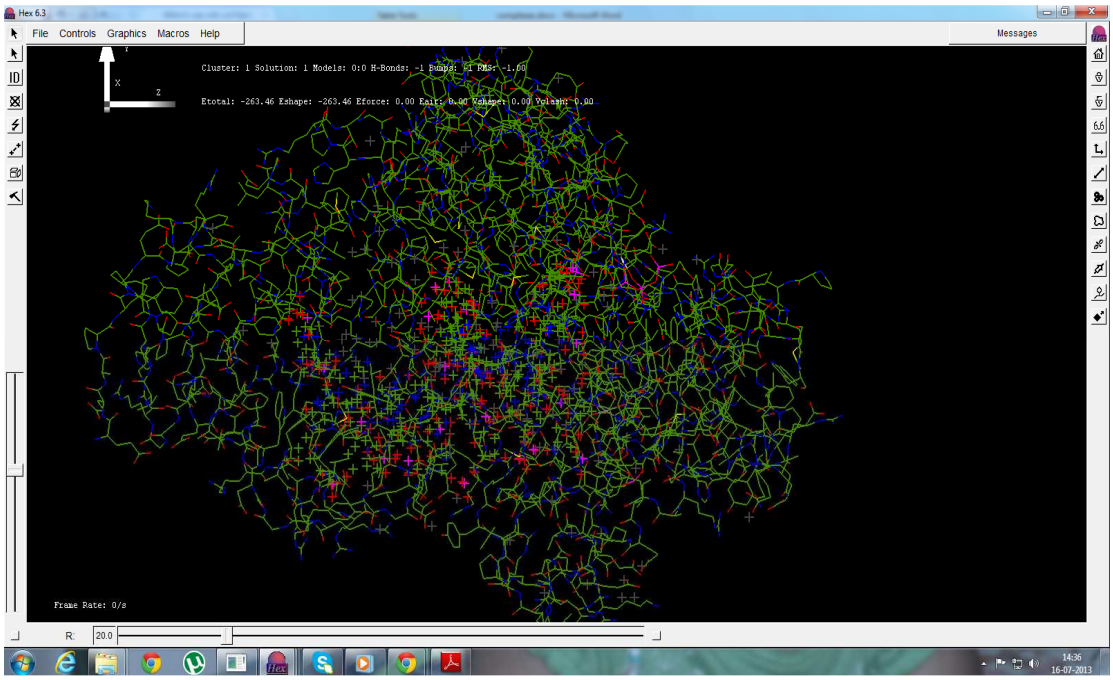


Figure.2. Docking Window

Table 1. E total values for isatin metal complexes binding with HIV

S.No	Complexes	E total value
1.	Cu	-258.21
2.	Mn	-258.82
3.	Cd	-265.12
4.	Zn	-263.46
5.	Co	-269.39
6.	Ni	-262.84

Table.2 E total values for standard drugs binding with HIV

S.No	Drug	E total value
1.	Maraviroc	-258.20
2.	Darunavir	-289.26
3.	Nelfinavir	-293.95
4.	Zidovudine	-173.40
5.	Zalcitabine	-157.44

By comparing the E total values of our isatin metal complexes with the standard drugs taken from drug bank, we found that the chosen metal complexes having higher E total value than Maraviroc, Zidovudine and Zalcitabine. 1,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)- 4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2-cobaltacyclohexane]-4,4'-dione shows higher value than other metal complexes.

Conclusion

On the basis of results, we conclude that, our complexes have showed the E total values as greater than -250. All metal complexes having higher E total value compared to Maraviroc, Zidovudine and Zalcitabine. ,1'-bis(2-oxo-2,3-dihydro-1H-indol-3-ylidene)- 4H,4'H-2,2'-spirobi[benzo[d]1-oxa-3-aza-2- cobaltacyclohexane]-4,4'-dione shows higher value than other metal complexes.

References

1. Alfred Burger. Medicinal Chemistry, Part I. 5th Edition, Wiley Inter Science ltd, New York, 1**970;** pp.1-3.
2. Graham Patrick. Medicinal Chemistry, Viva Books Pvt. ltd, pp.1.
3. Wilson and Gisvold's .Text book of Organic Medicinal and Pharmaceutical Chemistry, 9th edition, Jaime.A.Delgade, William .A.Remers, J.B Lippincott, pp.1.
4. A Gursoy; N Karali, *Farmaco.* **1996,** *51*, 437-442.
5. M Verma;SN Pandeya; KN Singh ; J P Stables, *Acta Pharm*, **2004**, *54*, 49-56.
6. SN Pandeya; D Sriram; EDE Clercq; C Pannecouque ; M Witvrouw, *Indian Journal of pharmaceutical Sciences*, **1998** ,*60*, 207-212
7. LV Kara; M.L Julie; R Marie; GP Stephen; BB John, *Journal of Medicinal Chemistry*, **2007**, *50*, 5109-5117.
8. D Sriram; P Yogeeswari ; K Meena, *Pharmazie*, **2006**, *61*, 274- 277.
9. A Patel; S Baria; G Talele; J Patel; M Sarangapani, *Iranian Journal of Pharmaceutical Research*, **2006**, *4*, 249-254.
10. V Glover; SK Bhattacharya, *Ind. J. Exp. Biol,*. **1991**, *29*, 1.
11. G Valli; J Vinnarasi, *International Journal of Pure and Applied Chemistry*, **2011**, *6(3).*