Properties and Functions of Isoindoline: A Short Review

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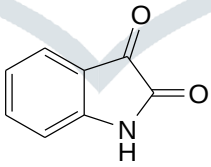
Increase in rapid growth of cancer is a major health concern all over the world. Prevention and treatment of cancer with several anti-cancer drugs have decreased the health immunity and damage cells growth, but the number of new diagnosis continues to increase. Therefore, new and more efficient anticancer agents are required against different cancer diseases. Indolinone and Isoindolinone derivatives are the biologically active heterocyclic compounds and represents many important classes of therapeutically agents in medicinal chemistry such as- anticonvulsant[1-3], anticancer[4-6], antioxidant[7-9], anti-rheumatoid arthristis[10,11], anti-HIV.[12,13].

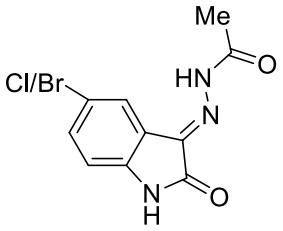
Some studies have revealed that a group of 3-substituted indolinone sulfamat[14] is steroid sulfatase inhibitors and act as an anti-proliferative inhibitor against breast cancer and some of these show *in-vivo* anti-neoplastic and anti-estrogenic activity. These derivatives act as pharmalogical agents used in the treatment of epileptic seizures[14]. They inhibit bipolar disorder and suppress the rapid and excessive firing of neurons in brain. Isoindolinone derivatives are also bioactive natural products and frequently used as anti-inflammatory and anti-bacterial drug.

Isatin[1] is a heterocyclic compound, synthesized as an oxidized product of indigo dye, nitric acid, and chromic acid.

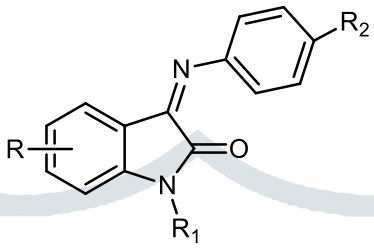


CNS activity of isatin compounds depend on substitution of benzene ring of isatin. The medicinal role of isatin is to regulate acetylcholine levels in the brain and striatum DA levels. Isatin inhibits function of large number of enzymes (phosphatase, xanthine oxidase, hyaluronidase).

Isatin-3-hydrazone[3] is a series of substituted isatin semicarbazones and bioisosteric hydrazones are designed and synthesized for anticonvulsant activity.

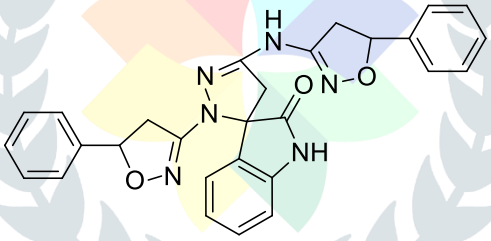


A series of compound synthesized by reacting 5-substituted N-methyl/acetyl isatin and aromatic amine. These derivatives have been evaluated for anticonvulsant activities [4].

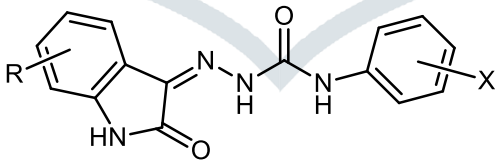


R= Br, Cl, R1= Me, Et, H, R2= NO2, F

Pyrazolinyl/isoxarolinyl indol-2-ones[5] derivative is a series of 3-spiro [1', 3', 4'-oxa/thiadiazolyl-2'-{5'-(substitutedphenyl-3"-amino)-4'-{5"-(substitutedphenylisoxazo vinyl)}]-5'-indol-2-ones synthesized, having thiadiazole ring show higher antipsychotic activity and anticonvulsant activity than the oxadiazole containing compounds.

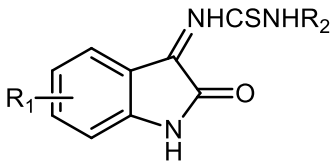


A series of N-substituted isatin-3-semicarbazones were synthesized and evaluated for their anticonvulsant activity[6].

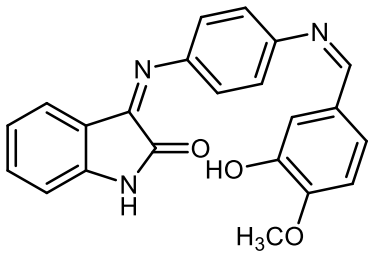


X =Br, NO2, R = Me, Isopropyl

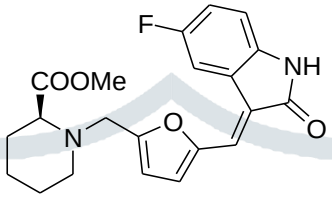
3-aryloxyl, arylthioxy acetyl hydrazone-2-indolinones were synthesized which acts as anticonvulsant agent and anti-cancer drug[7].



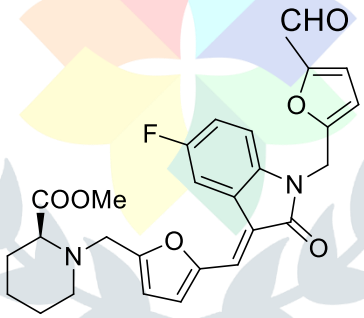
R_1 = Me, Chlorophenyl, R_2 =Ph



Indolinone[8] as protein Tyrosine Phosphate 1B inhibitor is a novel series of heterocyclic derivatives identified as PTP1B inhibitors on the basis of molecular docking phenomenon.

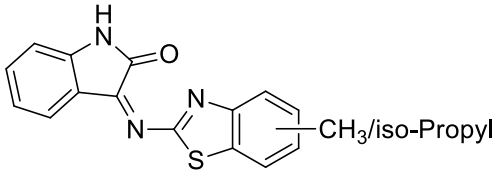


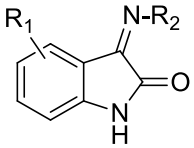
In 3-substituted indolinone[8] found that all three components (indolinone, furan, pipyridine) have same type interaction with PTP1B but slightly deviated from binding site i.e only one N-H….O hydrogen bonding interaction could observed for indolinone moiety. This hydrogen bonding played an important role to the binding between the inhibitor and active site of cell.



(PTP1B inhibitor)

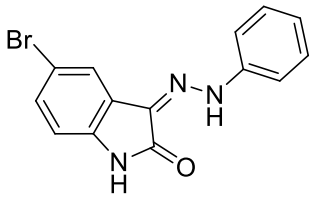
N-substituted indolinone[8] has two hydrogen bonding interaction i.e N site of indolinone moiety and another is aldehyde site and through this site it binding with damage cells can takes place.[9, 10]



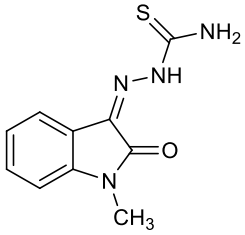


R_1 = Cl, $N(Me)_3$, R_2 = Chlorophenyl, m-bromobenzene

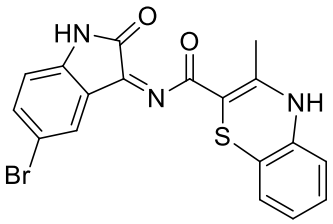
Some of the significant indolinone compounds with pharmacological activities can be identified as



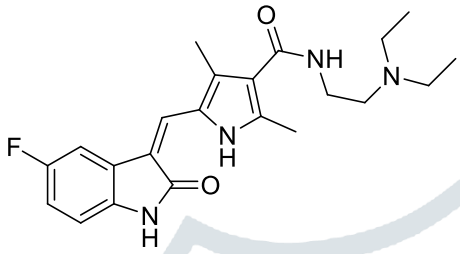
Tuberculostatic agent



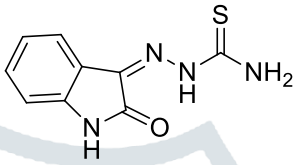
Anti-viral Methisazone



Anti-fungal agent

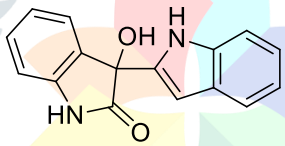


Anti cancer drug



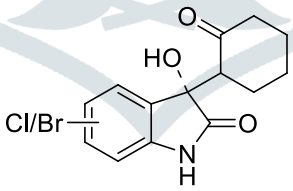
Anti HIV

Some isatin derivatives[17] are selectively synthesized at selective pH. N-substituted isatin[18] have been used as intermediate for different heterocyclic compounds.



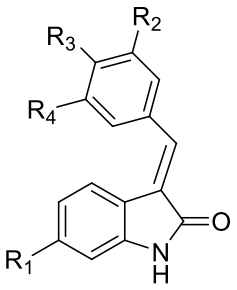
Anticancer drug

A series of hydroxy-2-oxindoles[19] derivatives are synthesized which shows MES and PTZ test (MES- Maximal Electro Shock, PTZ- Pentylenetetrazol infusion).



Anticonvulsant

Some 2-indolinone derivatives act as Tubulin inhibitors[20, 21]. They bind with active tubulin cells and destroy them. Inhibition of microtunle formation leads to mitotic arrest and leads vascular disruption.



	R_1	R_2	R_3	R_4
a =	OH	H	OH	H
b =	OCH3	OCH3	OCH3	OCH3

Some amino acid based indolinones act as a class of ATP competative receptor tyrosine kinase inhibitors which reduce epidunal growth factor and effect on glioma. Some derivatives have anti proliferative activity in cancer cells by inhibiting various kinase families.

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