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2, 3-Dioxoindoline Derivatives: Synthesis, Reactions and Exploring Pharmacological Activities

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ABSTRACT

Heterocyclic compounds represent an important class of organic compounds having vivid biological and pharmacological properties. These heterocyclic moieties, either individually or in fused form, are continuously used by researchers for the creation of new drugs due to their extensive biological profile. Isatin (1 H - indole-2,3-dione), also known as (2,3-dioxoindoline, indole quinine and indenedione), exhibits a broad range of biological activity and is therefore regarded as a bio-active heterocyclic moiety. Isatin derivatives are synthesized by using two common methods such as Sandmeyer's and Stolle process. The isatin moiety also shows important chemical reactions such as oxidation, ring expansion, Friedel–Crafts reaction and aldol condensation. The advances in the use of isatins for organic synthesis during the last twenty-five years, as well as a survey of its biological and pharmacological properties are reported in this review.

Keywords: 2,3-dioxoindoline, Spectral characterization, Novel 2,3dioxoindoline, Tautomerization, SARS-CoV-2

INTRODUCTION

Heterocyclic compounds are a significant class of chemical molecules with distinct biological and pharmacological characteristics. These heterocyclic moieties, either individually or in fused form, are continuously used by researchers for the creation of new drugs due to their extensive biological profile.[1]

In 1841, Erdmann and Laurent discovered isatin (1 H - indole-2,3-dione), also known as (2,3- dioxoindoline, indole quinine and indenedione), as a by-product of the oxidation of indigo using nitric and chromic acids. Isatin is a privileged moiety that exhibits a broad range of biological activity and is therefore regarded as a bio-active heterocyclic moiety.[2]

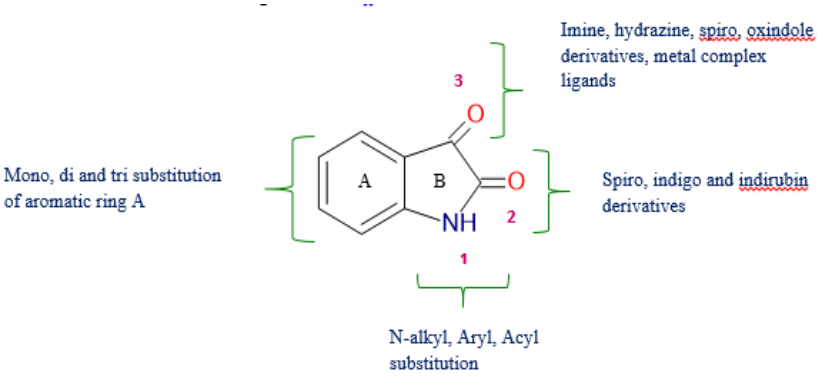
Isatin and its derivatives show various biological activities like anti-cancer, anti-bacterial, anti-fungal, antidiabetic, anti convulsant, anti-tubercular, anti-HIV, neuroprotective, anti-oxidant, anti glycation, anti-malarial, anti-inflammatory, analgesic, and anti-anxiety activities. Naturally, isatin is also found in plants of genus Isatis in Calanthe discolor Lindl. In human beings, it is found as a metabolic derivative of the adrenaline hormone and is also a component of secretion from the parotid gland of Bufo frogs.[3]

Isatin, commonly referred to as tribulin, is an orange-red monoclinic prism crystal that is produced from the indole molecule and has the chemical formula $C_8H_5NO_2$, bitter taste, its molecular mass is 147.13. Melting point: 203.5 °C (Part sublimation). Dissolved in water, hot ethanol, benzene, acetone, ether-soluble. Soluble in boiling alcohol, soluble in ether and boiling water and it is reddish brown, soluble in caustic and solution is purple, it changes to yellow after placement. Its alcohol solution has a very unpleasant odor. Weakly alkaline and also it can salify with a perchlorate.

Isatin has a nitrogen atom at position 1 and two carbonyl groups at positions 2 and 3. It comprises two cyclic rings, one of which is six-membered and the other is five-membered. Both of the rings are planar. The six membered ring has an aromatic character, whereas the five membered ring possesses an anti-aromatic character. isatin can be represented in two tautomeric forms, either as the lactam or the lactim structure.[4] In this review article, design strategies for the synthesis of isatin containing heterocyclic through their different approaches have been represented. It also provides structural insights and important account of structure-activity relationships and docking studies of isatin derivatives for the potent pharmacological profile.[5,6]

ISATIN: A VITAL COMPOUND

A series of multi-substituted isatin (2,3-dioxoindoline) derivatives were synthesized using the Sandmeyer reaction, Several other synthetic methods such as Martinet, Stolle, Gassman, reviewed earlier. However, there is a problem of low yields and inseparable mixtures of regioisomeric products are formed using substrates containing m-substituted or electron-withdrawing substituents.[7]



The substitution of aryl ring (A) with EWD groups, Alkylation of nitrogen atom in ring (B), and also modification at C2 and C3 carbonyl functionalities, which leads to the formation of vivid biologically important derivatives (EWD- Electron withdrawing groups).

SYNTHESIS OF 2,3-DIOXOINDOLINE: (Sandmeyer's process.)

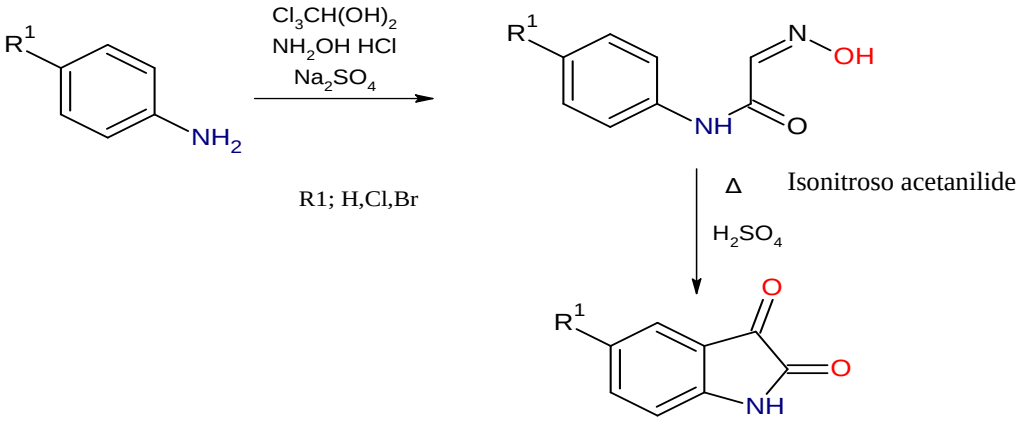
STEP 1

Isonitrosoacetanilides: In a 5 lit. RB flask, chloralhydrate (0.54 mol) and 1200mL of water were placed. To this solution, crystallized sodium sulphate (1300 g) was then added followed by a solution of an appropriate aromatic amine in 300mL of water and concentrated hydrochloric acid (0.52mol). Finally, a solution of hydroxylamine HCl (1.58mol) in 500mL of water was added. The contents of the flask were heated over a wire-gauge by a Mecker burner so that vigorous boiling begins in about 45 minutes. After 1 to 2 minutes of vigorous boiling the reaction was completed. During the heating period itself the crystals of isonitrosoacetanilides started separating out. On cooling under the current of water, the entire product was solidified. It was filtered under suction, air dried, and purified by recrystallization from suitable solvent(s).

STEP 2

2,3-dioxo indoline: Sulphuric acid (600 g, d, 1.84, 326 mL) were warmed at 50∘C in a one liter RB flask fitted with an efficient mechanical stirrer and to this, finely powdered appropriate isonitroso acetanilide (0.46mol) was added at such a rate so as to maintain the temperature between 60∘C and 70∘C but not higher. External cooling was

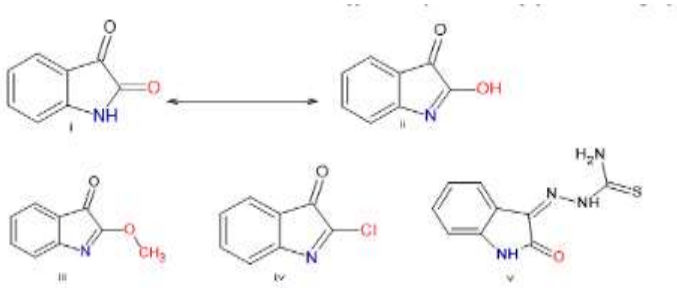
applied at this stage so that the reaction could be carried out more rapidly. After the addition of isonitroso compound was completed the temperature of the solution was raised to 80∘C and maintained at that temperature for 10 minutes, to complete the reaction. Then the reaction mixture was cooled to room temperature and poured on crushed ice (2.5 kg) while stirring. After standing for about half-an-hour, the product separated was filtered, washed several times with small portions of cold water, and dried. Purification of the compound was affected by the recrystallization from methanol. [8]



STRUCTURAL CHARACTERISTICS

Tautomerization

Initially postulated by Baeyer in 1882, Lactam(i) and Lactim(ii) are two tautomeric forms of isatin in which a proton transfer between the nitrogen atom and the oxygen atom located at the second carbon takes place. Isatin is primarily found in the lactam structure in the solid form. The synthesis of O-alkyl ethers (iii) and isatin-chloride (iv) provides evidence for the lactim form's existence. Additionally, only the lactam form's signal can be seen in the 1H NMR spectrum of isatin in CD3OD, whereas only the lactim form's signal can be seen in DMSO-d6. A theoretical analysis of the stability of several conformers and tautomers of isatin-3-thiosemicarbazone in the gas phase and the aqueous phase was described in one of our earlier works. It was found that tautomer (v) is the key tautomer and one of its conformer's accounts for approximately 87% of the population in the gas phase. [9]



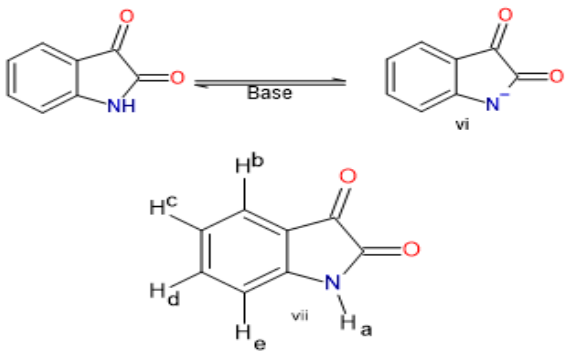
Spectral studies

The UV-visible spectrum of isatin exhibits an absorption maxima in the range of 260 nm to 350 nm, which corresponds to a π-π* transition. This is because of the aromatic ring. The aromatic ring's donor/acceptor ability determines the absorption maximum and band intensity in this region, and when the ring's donor ability rises, the maxima band shifts batho chromically. The free electron pair transitions of nitrogen and oxygen, known as the n-π* and intra

molecular charge transfer (ICT) transitions, are represented by a rather faint absorption band in the range of 350 nm to 600 nm. The long-wavelength absorption bands in the 350–600 nm range vanish in basic media, and a new batho chromically shifted band in the 400–750 nm range replaces them. This new band arises due to the formation of an azanion (vi).[10]

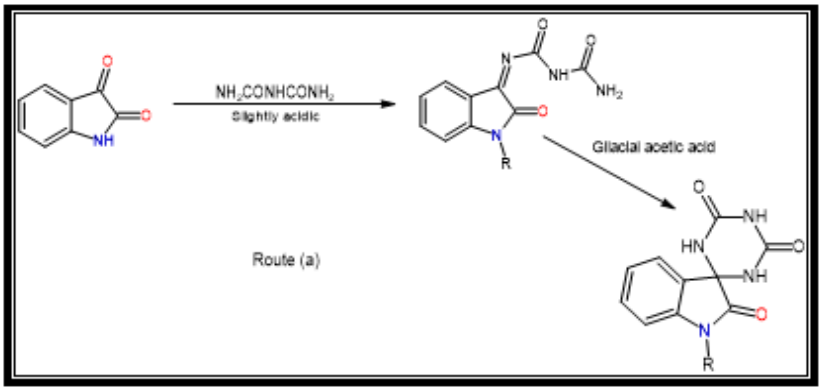
The 1H-NMR spectrum of isatin (vii) shows a doublet at δ 7.47 ppm and 6.86 ppm corresponding to Hb and He respectively. The hydrogen atom (Ha) attached to nitrogen appears as a singlet at approximately δ 11.03 ppm. The protons Hc and Hd show triplets at δ 7.05 ppm and 7.57 ppm, respectively. Deprotonation of NH in the isatin moiety leads to a downfield shift for the azanion's protons (Hb, Hc, Hd, and He) in the 1H-NMR spectrum.[11]

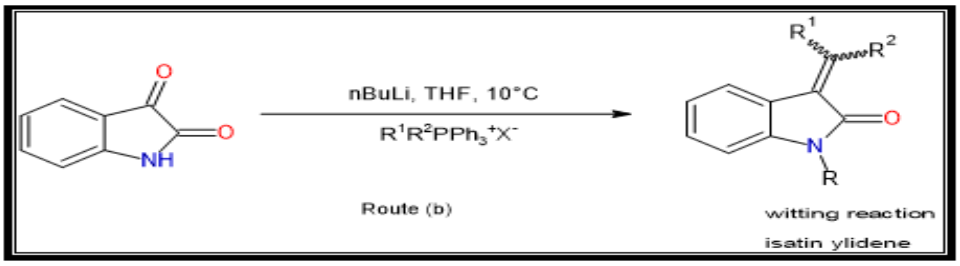
The IR spectrum of isatin shows two strong bands at 1740 and 1620 cm^{-1}, representing the carbonyl stretching vibrations. A broad band accompanied by some sub bands occurs at 3188 cm^{-1} corresponding to N–H stretching, which moves to 2370 cm^{-1} on deuteration of N–H.[12]

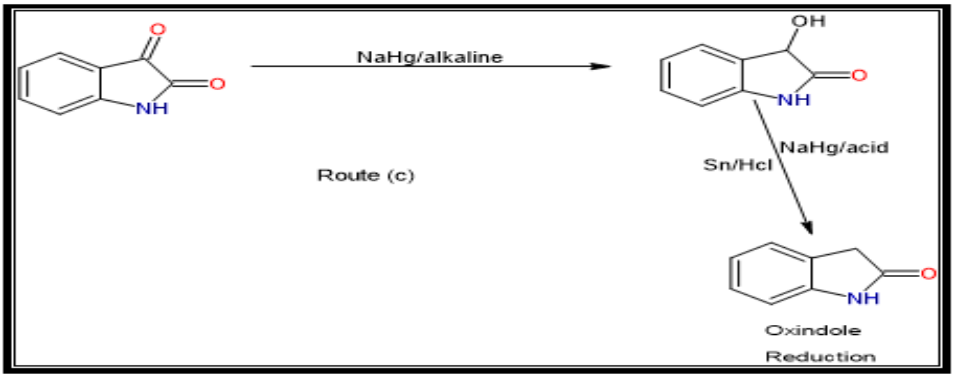


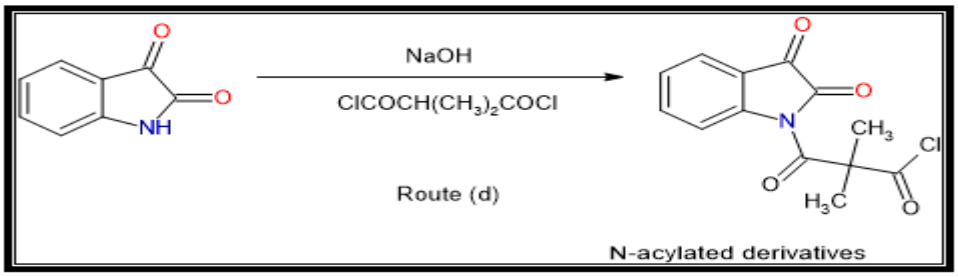
Chemical properties

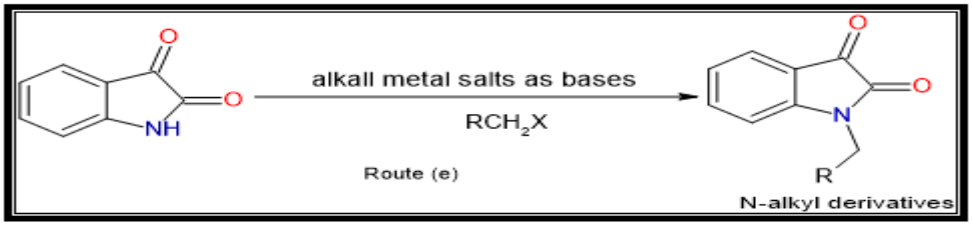
Isatin itself has versatile positions, on which many reactions can occur and thus able to form hybrid molecules. In isatin, the NH group can undergo *N* -alkylation, *N* -arylation, *N* -acylation where as the reactivity of carbonyl group at C2 can be explored for the synthesis of spirocyclic compounds, indigo and indirubins. On the other hand, the carbonyl group at C3 can be converted into corresponding imine or hydrazone derivatives as well as used in the synthesis of spirocyclic compounds and oxindoles. The imine formation takes place very easily with some free amino containing compounds in the presence of glacial acetic acid **Route (a)**. Another is alkene formation using phosphonium ylide at the 3rd position of isatin (Wittig reaction) **Route (b)**. Using the 3rd position carbonyl, isatin may be converted into oxindole by first converting isatin to 3-hydroxy isatin and then reduction **Route (c)**. The first NH position may be alkylated or acetylated with the help of base in DMF solvent **Route (d)** & **Route (e)**. The 2nd position can be converted into *O*-alkylated regioisomers with an alkyl halide in the presence of silver salts **Route (f)**. Isatin may be prepared from anthranilic acid as but it can also be converted back into anthranilic acid either by oxidation in presence of chromium trioxide/acetic acid or hydrogen peroxide **Route (g)**. Reactions of indole with an alkyl halide in the presence of sodium hydride, borane in THF gives *N*- alkylated indole, whereas it gives 3-alkyl indole in the presence of alkyl lithium in the presence of lithium aluminum hydride **Route (h)**. The general electrophilic substitution reaction like halogenation, nitration or sulphonation occurs at 5th position **Route (i)**. [13]

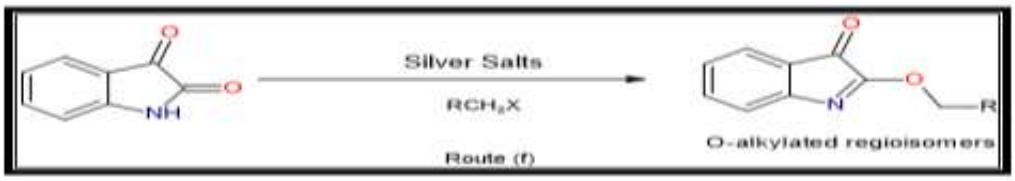

NH2CONHCONH2
Slightly acidic
Glacial acetic acid
Route (a)

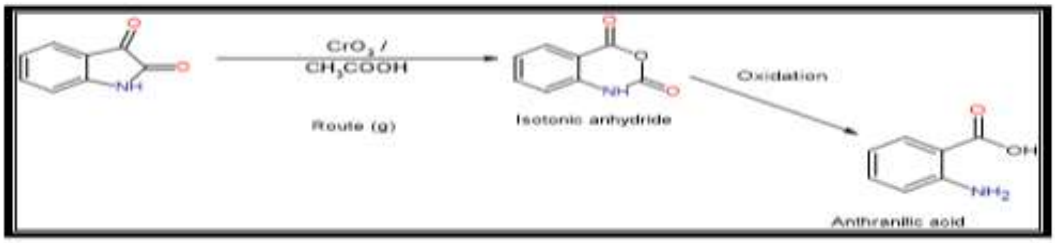

nBuLi, THF, 10°C
R1R2PPh3+X-
Route (b)
witting reaction
isatin ylidene

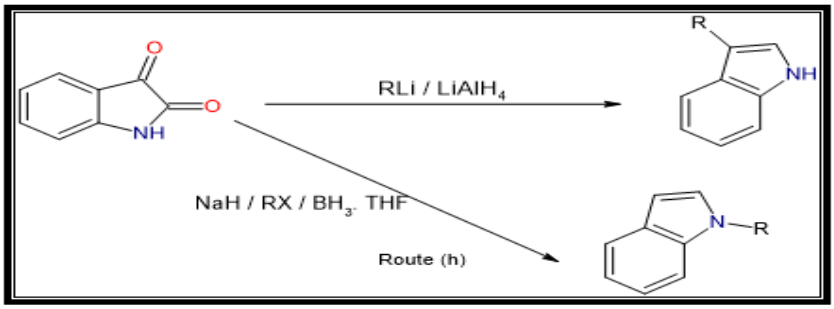

NaHg/alkaline
Route (c)
NaHg/acid
Sn/Hcl
Oxindole
Reduction

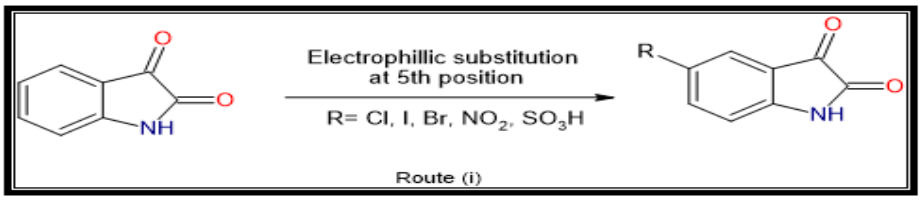

NaOH
ClCOCH(CH3)2COCl
Route (d)
N-acylated derivatives


alkali metal salts as bases
RCH2X
Route (e)
N-alkyl derivatives







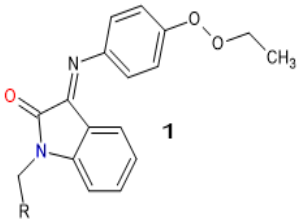


PHARMACOLOGICAL ACTIVITIES:

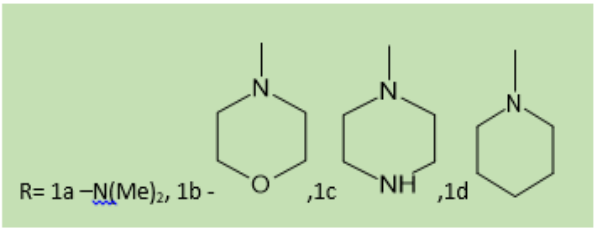
1. Anti-bacterial activity

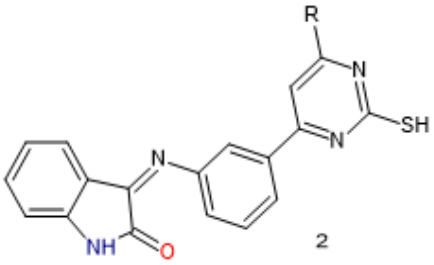
Researchers are thoroughly examining isatin derivatives for their antibacterial activity as they show therapeutic potential against a number of harmful microorganisms. It has been shown in numerous investigations that the Schiff bases and Mannich bases of isatin and its derivatives have potent antibacterial properties. 5 Halogenation, N-alkylation, and N-Mannich bases are also useful in producing a notable improvement in the antibacterial activity, according to SAR investigations of several isatin derivatives.

In vitro anti-bacterial and antifungal properties of Schiff bases of isatin (1 and 2) against Gram positive (Staphylococcus aureus and Bacillus subtilis) and Gram negative (Escherichia coli and Proteus vulgaris) bacteria and fungi were examined (Candida albicans and Aspergillus niger). Results demonstrated that these compounds significantly inhibited the growth of B. subtilis, S. aureus, and E. coli bacteria. In addition to its antibacterial properties, compound (2a) demonstrated strong antifungal properties on par with those of the widely used medication clotrimazole.[14]



1





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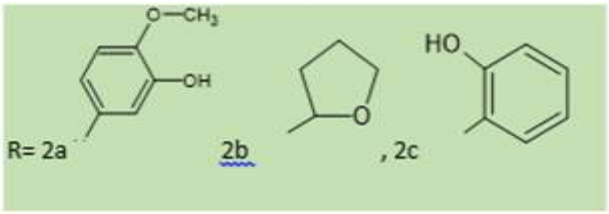
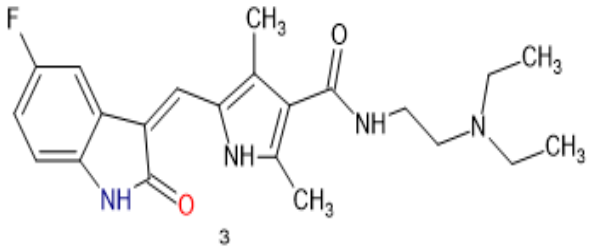
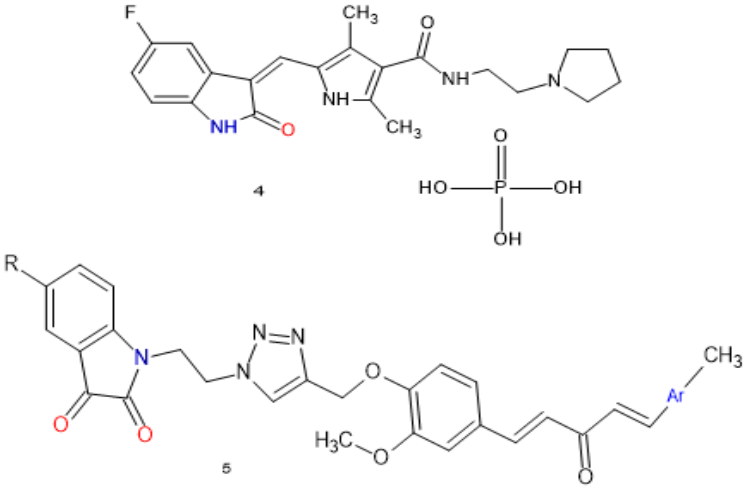


2. Anti-cancer activity

According to the 2015 WHO Global Health Survey Report, cancer claimed the lives of 8.8 million people worldwide. Therefore, it is extremely difficult for researchers to create new, powerful anti-cancer drugs that give selectivity while also having decreased toxicity. Researchers have looked at the anti-cancer properties of isatin and its derivatives in great detail. Figures indicate that the commercially available anticancer drugs Sunitinib V (3) and Toceranib phosphate (4) both contain isatin as a significant pharmacophore unit.[15] Microtubules, the essential cytoskeletal fibers, are engaged with various cell capabilities, including cell arrangement and structure support, as well as mitosis and cell division. Antimitotic drugs work by slowing down microtubule elements by going after tubulin, a significant protein piece of microtubules and subsequently one of the most basic vital focuses for making new anticancer medications. So far, six tubulin families have been identified: α-, β-, γ-, δ-, ε-, and ζ-tubulin. Microtubules, on the other hand, are made up entirely of α- and β-tubulin, so developing inhibitors for them could improve cancer treatment.[16] The synthesis of series of molecular hybrids of isatin and mono carbonyl curcumin tethered by triazole ring as shown in (5) and evaluated their tubulin inhibition activity. One compound was found to significantly inhibit the tubulin polymerization (IC50 = 1.2 μM against HCT-116). Moreover, another compound was led to the disruption of microtubules as confirmed by immunofluorescence technique.[17]



3

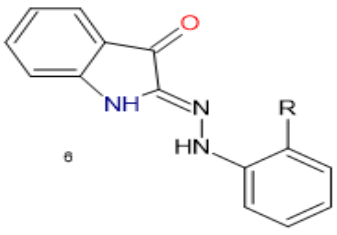


R= H, Cl, Br
Ar = Furan, p-chlorophenyl, p-methoxyphenyl, phenyl, p-nitrophenyl, thiofuran

(5.i)

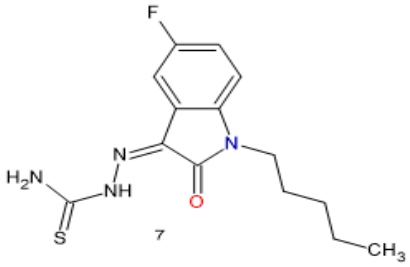
3. Anticonvulsant Activity

A nervous condition known as epilepsy, commonly referred to as convulsions, is characterised by unexplained seizures. *In vivo* studies were performed in mice using the maximum electric shock and pentylenetetrazol models of epilepsy. This showed that most drugs provided substantial protection against electrically triggered seizures at a dose of 5 mg/kg. In addition, in silico studies were used to confirm the results obtained from In vivo and In vitro studies compound (6) shows the structure of isatin derivatives that have anticonvulsant activity.[18]



4. Anti- Alzheimer

One clinical strategy for treating the disease that continues to spark attention among doctors is the inhibition of amyloid β-peptide accumulation in Alzheimer's disease. In the search for substances that interact with Amyloid -peptide A and obstruct its typical aggregation path towards oligomeric or polymeric hazardous assemblies, tiny natural chemical molecules with low molecular weight and low toxicity are greatly wanted. A wide variety of neuro pharmacological and chemotherapeutic activities can be found in isatin, a naturally occurring indole, and several of its derivatives. As potent inhibitors of amyloid –Aβ-peptide aggregation, the two created novel isatin thiosemicarbazone derivatives. Isatin thiosemicarbazones have the capacity to change the pathway of Aβ-aggregation, as revealed by thioflavin T-fluorescence, circular dichroism assays, and transmission electron microscopy. Two of the produced derivatives demonstrated excellent inhibition of aggregation and entirely ceased the generation of amyloid fibrils. In addition, research undertaken in vitro on primary neuronal cell cultures revealed that isatin thiosemicarbazones inhibited Aβ-induced neurotoxicity and the production of reactive oxygen species at concentrations as low as 1 μM. The Isatin derivatives as anti-Alzheimer showed in compound (7, 8).[19]



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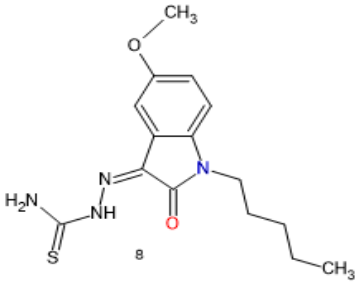
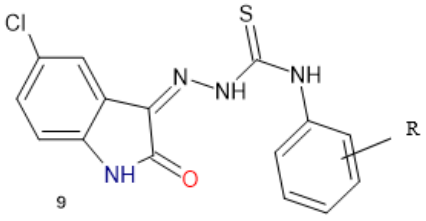


8

5. Inhibitor of α-glucosidase Enzyme

The small intestine's brush-border surface is home to the membrane-bound enzyme known as α-glucosidase, which breaks down carbs. It causes a polysaccharide chain's 1-4 bonded glycosidic link to cleave, releasing D-glucose that helps maintain normal bodily function. Aziospermia, diabetes, viral infection, and pomp illness have all been linked to an increase in α-glucosidase in humans, which causes blood glucose levels to rise. [20,21,22] Glucosidase has thus been recognised as a crucial target in medication development. The 1H-NMR, 13C-NMR, and HR-EIMS techniques were used to synthesis and analyse a new series of isatin-based thiosemicarbazide derivatives. The potential of the synthesised compounds to inhibit α-glucosidase was examined. The α glucosidase inhibitors of all compounds are excellent. Isatin derivatives (9) as inhibitor of α-glucosidase enzyme.[23]

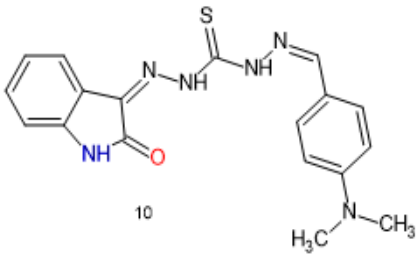


9

R= 4-CH3, 2-Br, 2,3-diChloro, 2,6-dimethyl

6. Anti-diabetic activity

Diabetes, often abbreviated as diabetes mellitus (DM), is an illness that is marked by a disturbed metabolism and abnormally elevated blood sugar (hyperglycemia), which can be brought on by either low levels of the hormone insulin or an abnormal resistance to its effects. The new chemical 1-(4-(dimethylamino)benzylidene)-5-(2-oxoindolin-3-ylidene) thiocarbohydrazone (10) has been shown to have anti-diabetic properties. Blood glucose levels reduced dramatically after the compound was given to diabetic rats in single doses of 50 and 100 mg kg1 in a dose-dependent manner. More million individuals have type 2 diabetes, which makes up around 90% of all cases A therapeutic target for type 2 diabetes is α-glucosidase, a carbohydrate enzyme secreted from the intestinal chorionic epithelium. Certain compounds of chromone and isatin have been identified as α-glucosidase inhibitors. Because of this, combining these two scaffolds into a single molecule can enhance its pharmacological action. To test their in vitro -glucosidase inhibitory action, a novel series of chromone-isatin derivatives (11) were produced in this direction. Although all of the compounds displayed outstanding inhibitory activity, compound (11a), which included hydroxyl groups at the 7-position of the chromone and a 4-bromobenzyl group at the N1-position of the isatin, was the most potent. Furthermore, to understand the binding interaction of these compounds with α-glucosidase, a molecular docking study was performed.[24]



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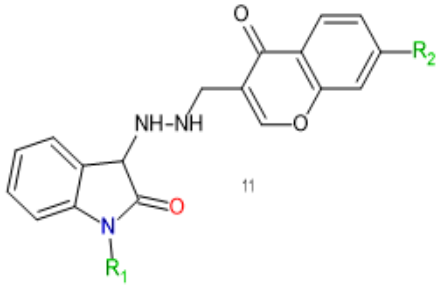


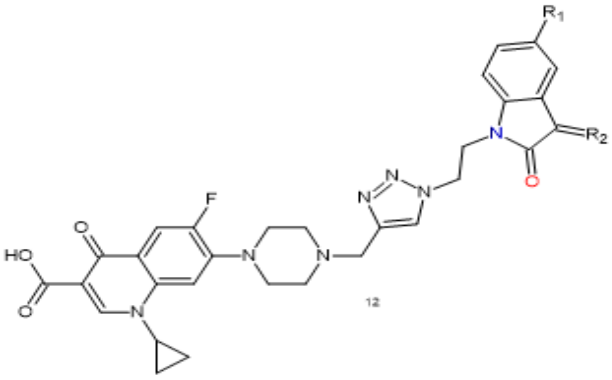
11

R_1
a= 4-bromobenzyl
b= 4-chlorobenzyl
c=3-fluorobenzyl
d= 4-fluorobenzyl

R2
a = OH
b= H
c= H
d= OH

7. Anti-tuberculosis activity

The fatal disease tuberculosis (TB), which is mostly caused by Mycobacterium tuberculosis (MTB), is the second greatest cause of infectious disease-related mortality globally. Unfortunately, the effectiveness of the currently available medications is declining as cases of extensively and multi-drug resistant TB (MDR-TB) rise. A breakthrough anti-TB medicine that can actually more effective against the disease's difficult-to-kill MDR and other latent forms is therefore urgently needed.[25] Numerous novel anti-tubercular medicines have been discovered recently attributable to the isatin scaffold. The synthesis and in vitro anti-mycobacterial activity of a series of 1H-1,2,3-triazoletethered ciprofloxacin (CPFX) isatin conjugates (12) against Mycobacterium smegmatis and Mycobacterium tuberculosis (MTB) H37Rv have been described for several isatin derivatives. According to the preliminary findings, all hybrids demonstrated good activity against the MTB H37Rv strain and significant activity against M. smegmatis. Additionally, the hybrids with the carbonyl group (12a-d) were more effective against MTB H37Rv than the comparable methyloximehybrids (12e-h).[26]

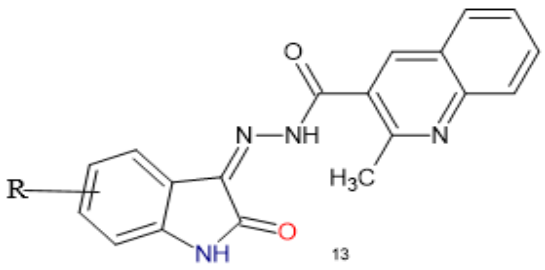


12

R1
a = H
b = Me
c = Cl
d = F
e = H
f = Me
g = Cl
h = F

R2
a = O
b = O
c = O
d = F
e = NOMe
f = NOMe
g = NOMe
h = NOMe

As possible anti-tubercular drugs, docking investigations of isatin-quinoline hybrids (13) against the enoyl-ACP reductase enzyme (PDB ID: 4TZK) have been published. The results demonstrated that compound (13b) has the maximum binding affinity and fits well in the enzyme's active site. The key residues in charge of the enzyme activity, Tyr158 and the cofactor NAD 500, exhibit strong hydrophobic interactions with this substance.[27]

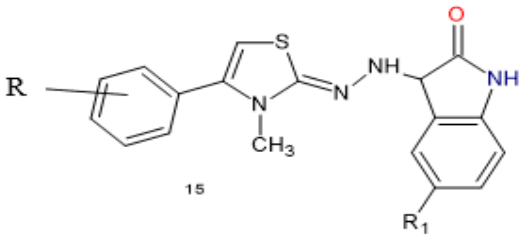


13

a = H
b = 5-F
c = 5-NO_2
d = 4,5-dichloro
e = 7-Br

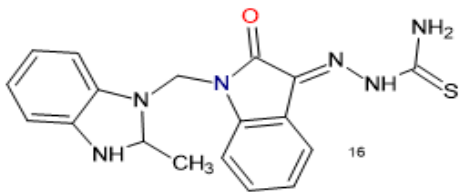
8. Anti-viral activity

The most common virus is the type 1 human immunodeficiency virus. Highly active anti-retroviral therapy (HAART), which combines a number of antiviral drugs to target various stages of the viral replication cycle, is the currently accepted treatment for this illness.[28] HIV-RT, sometimes known as HIV-RT, is a crucial component of the HIV-1 replication cycle. It is linked to two crucial enzymatic activities: ribonuclease H and DNA/RNA dependent polymerase (DDDP and RDDP) (RNase H). Therefore, creating HIV-RT inhibitors can aid in addressing the two targets. It has been found that isatin-based molecular hybrids act as dual inhibitors of RT-related enzymatic activities. Isatin-thiazoline hybrids (15) have been identified as dual inhibitors of HIV-1 reverse transcriptase in a recent investigation (RT). [29]



15

In another study, the anti-viral activities of isatin-β- thiosemicarbazone hybrids with an imidazole derivative against the chikungunya virus (CHIKV) have been reported. In this investigation,1-[{1-[(2-methylbenzimidazol-1-yl)methyl]-2-oxo-indolin ylidene} amino] thiourea (MBZM-N-IBT) (16) emerged as a potent anti-viral molecule against CHIKV.[30]



16

The anti-viral activities of isatin derivatives against the pox virus, vaccinia virus, rhinovirus, Moloney leukemia virus, and SARS virus, have also been reported.

In SARS-COV-2, the brand-new coronavirus that was the cause of the global pandemic COVID-19 posed a serious threat to everyone's health. The search for potential inhibitors of the viral proteins increased due to the lack of effective treatments. Its recently discovered crystal structure, crucial function in viral replication, and lack of similarity to any human protease make SARS-CoV-2 major protease (Mpro) the ideal target for inhibitor research. Comparing 118 compounds with 16 different heterocyclic moieties to 5

natural products and 7 repurposed medicines using a computer-aided drug design (CADD) technique. The best docking scores for isatin coupled with oxidiazoles (A2 and A4) derivatives were -11.22 kcal/mol and -11.15 kcal/mol, respectively, according to a molecular docking analysis against the Mpro protein. Studies on the link between structure and activity revealed favourable comparisons with the repurposed medication ebselen, an active Mpro inhibitor with an IC50 value of -0.67 lM. A2 and A4 underwent Molecular Dynamics (MD) simulations for 50 ns, demonstrating their stability within the binding pocket, particularly at the S1, S2, and S4 domains, where high binding energies indicate their eligibility as possible Mpro inhibitors for SARS-CoV-2.[31]

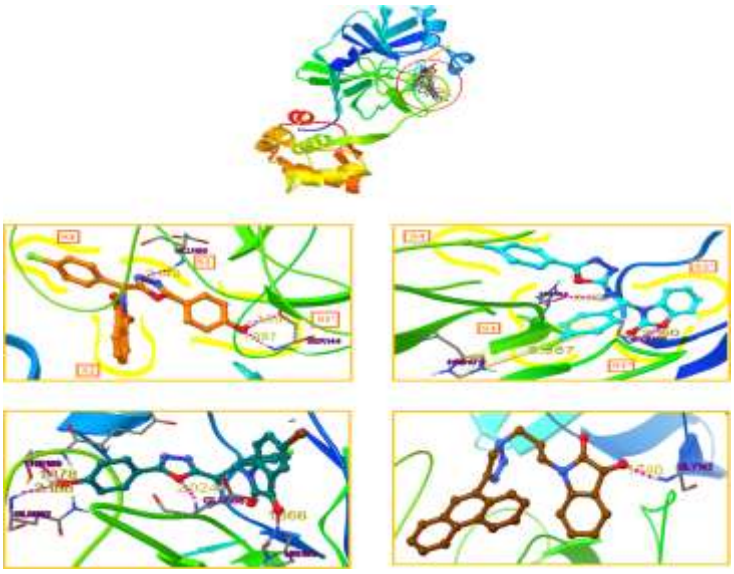
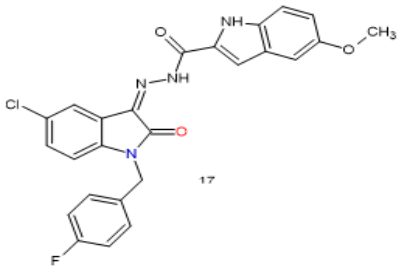
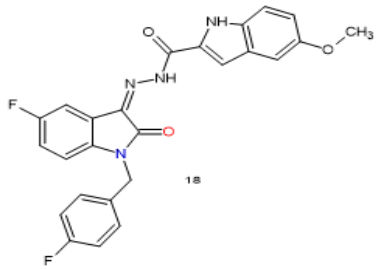


Figure 1. The binding mode of the four best docked compounds in the active site of the SARS-CoV-2 virus Mpro (PDB ID: 6LU7). The interacted amino acid residues and the distances in Å are given in yellow. Top, the ligands are shown together in the binding pocket. At bottom, 4 panels, individual compounds docked into the binding site of SARS CoV-2 virus Mpro. A2: Saffron; A4: Sky; A8: Ocean blue; A20: Dark brown.

9. ANTIFUNGAL ACTIVITY:

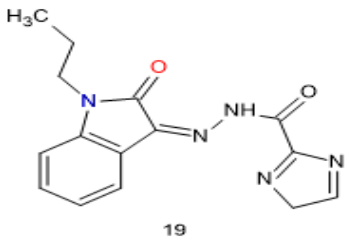
A unique set of indole-isatin hybrids were tested for their antifungal efficacy against Penicillium notatum, Aspergillus niger, and Candida albicans. In order to create the compounds, indole acetic acid was first converted to an ester in an acidic environment, and then, in the presence of hydrazine hydrate, to a hydrazide. Later, the hydrazide's free amino group was condensed with isatin through the Schiff reaction. Compound (17) was discovered to be the most effective against all species of fungi, whereas compound (18) shown good efficacy against Aspergillus niger and Candida albicans.[32]



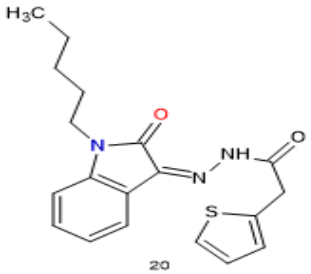


10. ANTI-INFLAMMATORY ACTIVITY

The newly created hydrazide derivatives N-pyrazolyl hydrazone of isatin (PHI) (19) and N-thiopheneacetyl hydrazone of isatin (THI) (20) were tested for their anti-inflammatory properties in both acute and chronic inflammatory pain models brought on by carrageenan and the full Freud's adjuvant (CFA). The compounds demonstrated a dosage-dependent decrease in inflammation, with the highest degree of action occurring at a dose of 10 mg/Kg. The pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) and the CFA-induced NF- Kb and MAPK signalling pathways were found to be suppressed by the substances. Likewise, the chemicals did not demonstrate any toxicity in the mice when it came to the liver, kidney, muscle strength, or motor coordination. Isatin exhibits strong anti-inflammatory properties when combined with N-pyrazolyl hydrazone and N-thiopheneacetyl hydrazone .[33]



19



20

CONCLUTION

Drug research has made significant use of isatin. Plenty of other naturally occurring compounds contain the ring, which is also used to create compounds with a variety of biological activities. These heterocycles possessing isatin are active and have shown a diverse range of properties, including anti-tubercular, anti-tumor, anti-inflammatory, antiviral, anticonvulsant, and anticancer properties. Different techniques are used to create isatin derivatives, but the Sandmeyer process is a popular one. Many researchers have taken use of the isatin moiety by utilising NH in the first position, C2 and C3 carbonyl positions to generate diverse derivatives with various biological activities. Despite the fact that many isatin medications are in clinical use, they have tremendous toxicity and resistance problems. Therefore, new research is essential in order to create more selective inhibitors and minimize undesirable consequences. The ability of isatin derivatives to perform various actions depends on its substitution at three places (N1, C2, and C3) and electrophilic substitution at position five. The potential anticancer, antiviral, antitubercular, anti-inflammatory, and antifungal activity of some of the derivatives has been described, demonstrating that isatin conjugated compounds can develop into therapeutic candidates with improved efficacy and reduced toxicity. Some derivatives' molecular docking investigations against diverse targets are described in order to confirm their biological activity. It is safe to conclude that isatin plays a vital and active part in the pharmaceutical sector. Isatin is an essential nucleus owing to all of these characteristics, which further offer new opportunities for research.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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