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A Review on Isatin and Its Derivatives Activity for Antimicrobial and Antioxidant

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ABSTRACT
Isatin (1H-indole-2,3-dione) is a naturally occurring eight-carbon compound that undergoes diverse chemical reactions. The isatin nucleus exhibits a wide range of biological activities, including antimicrobial, anti-inflammatory, anticonvulsant, antiviral, anti-HIV, antioxidant, and CNS depressant effects. Substituted isatin derivatives also retain these pharmacological properties. This review highlights common synthetic methods, physical properties, and antimicrobial and antioxidant activities of isatin and its derivatives[1]. Novel isatin-based imidazolone derivatives were synthesized by condensing various isatinhydrazones with a substituted imidazolone compound. Antimicrobial activity was evaluated using the disk diffusion method, and among the tested compounds, the 5-bromo–substituted derivative showed the highest antimicrobial efficacy[2].

I. Introduction

Organic molecules with a variety of biological and pharmacological properties are known as heterocyclic compounds. Isatin, or 1H-indole-2,3-dione, also referred to as indole quinone or indene dione, is one such biologically active heterocyclic molecule. It has two carbonyl groups in locations two and three, as well as a nitrogen atom in position one. It is made up of two cyclic rings, one having five members and the other with six. (figure 1).Both of the rings are flat. Six-member rings are aromatic, while five-member rings are anti-aromatic.[3].

Fig.1 Isatin Structure

The isatin moiety is abundant in nature, and its derivatives exhibit a range of pharmacological properties. The isatin moiety can be moved to almost any position since they are "privileged building blocks." Because of isatins' wide range of biological roles and structural modifications, more researchers have been inspired to investigate them and create an enormous number of structurally different derivatives. In recent years, a number of isatin compounds have been studied for their antibacterial qualities, and some of them demonstrated promising in vitro results[4].

Because of its capacity to produce Researchers from all over the world are paying attention to isatin, a very versatile nucleus that is a significant and varied anticancer agent that is safer than other anti-cancer medications. As dual inhibitors of VEGFR and carbonic anhydrases, indolinone-based benzene sulfonamides and N-substituted isatin hybrids have recently been demonstrated to have important anticancer effects[5].

Isatin (1H-indole-2,3-dione) is a promising new class of heterocyclic molecules with a range of biological profiles, including antituberculosis, antibacterial, antifungal, antiviral, antitumor, anti-HIV, anti-inflammatory, anti-plasmodial, and anti-malarial activities, as well as good tolerance in humans. Other pharmacores can be added to the unique natural product scaffold known as the isatin unit. Therefore, joining isatin and quinoline moieties with various linkers may enhance the anti-plasmodial and anti-malarial qualities[6].

Most hospital-acquired and community-acquired bacterial infections are caused by Gram-positive (like S. aureus, Staphylococcus pneumoniae/S. epidermidis, Streptococcus pneumoniae/S. pneumoniae, Bacillus subtilis/B. subtilis, E. faecalis, and Enterococcus faecium/E. faecium) and Gram-negative (like Escherichia coli/E. coli and Pseudomonas aeruginosa/P. aeruginosa).

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Furthermore, because of the widespread, long-term, improper, and even abusive use of antibiotics, bacteria have already acquired resistance to nearly all currently used antibiotics, which has made the issue worse. Drug-resistant infections are responsible for about 0.7 million deaths worldwide each year; if current trends continue, that number might rise to 10 million by 2050.

Additionally, certain isatin-based medications, such semaxanib and indirubin, have previously been used in clinical settings or are undergoing clinical studies to treat a variety of illnesses. More researchers have been motivated to explore isatins and produce a huge number of structurally diverse derivatives due to their vast variety of biological functions, numerous structural alterations, and successful therapeutic applications.

Several isatin derivatives have been tested for their antibacterial properties in recent years, and some of them showed encouraging in vitro and in vivo potency. The recent developments of isatin derivatives as possible antimicrobial agents were compiled in this study, and the structure-activity relationship (SAR) was also covered to offer guidance for future logical designs of more potent candidates[7].

As an alternative to their inorganic counterparts, organic molecules—whether commercially available or synthesised through experimentation—have garnered a lot of attention in recent decades.Most organic compounds exhibit a push-pull behaviour with elevated polarisability and dipole moment values.As a result, it is discovered that organic molecules have exceptional nonlinear optical (NLO) characteristics with several uses.These include white light sources, photovoltaic devices, effective transistors, and organic light-emitting diodes (OLEDs).

Among these molecules, isatin, also known as 1H-indole-2, 3-dione, has two different kinds of carbonyl groups (keto and lactam groups) as a ring structure made up of a benzene fused pyrrole ring. It has been determined that isatin and its derivatives are an advantageous precursor for the synthesis and design of various medications. These molecules are crucial for obtaining compounds with potential optoelectronic properties, according to a number of papers. For example, Kasi et al. reported on the polymerisation and electrochemical analysis of an isatin molecule and found that these modified molecules exhibit good optoelectronic properties suitable for optoelectronic applications[8].

Here, research was done to look at the different developments in the synthesis of isatin and its derivatives. This review specifically covered the Sandmeyer synthesis, Stolle synthesis, and Gassman synthesis for the synthesis of isatin. Isatin and its derivatives were essential in biomedical applications. Applications for isatin and its derivatives are numerous and include fungicide, bactericide, anti-HIV, anti-epileptic, and anti-instigative. The isatin derivatives reduce the risk of diabetes, gastrointestinal problems, and pyelonephritis by inhibiting the urease and α-glucosidase enzymes. This review covered the synthetic pathways for isatin production as well as the benefits of isatin and its derivatives in the biomedical industry[9].

II. BACKGROUND

Isatin (1H-indole-2,3-dione) is a versatile heterocyclic compound that serves as a key intermediate in the synthesis of numerous biologically active molecules. It exhibits a wide range of pharmacological properties, including antimicrobial, antiviral, anticancer, anticonvulsant, anti-inflammatory, and antioxidant activities. Because of its diverse reactivity, isatin derivatives have gained significant attention in medicinal and synthetic chemistry.

PHYSICAL PROPERTIES

Isatin is a naturally occurring orange solid with a molecular weight of 147.13g/mol. Its melting point is between 202 and 203°C. It is insoluble in non-polar organic solvents like hexane, toluene, and benzene, somewhat soluble in CH2 Cl2 and CHCl3, and soluble in polar organic solvents like methanol, acetone, acetonitrile, DMSO, DMF, and ethyl acetate.

REACTIVITY OF ISATIN

Isatin mainly reacts at three locations: N-alkylation and carbonyl reactions at C-3, aromatic substitution at C-5 that boosts biological activity, and chemoselective reductions, oxidations, ring expansions, and spiro annulations at C-2. If the system has electron-withdrawing groups at the nitrogen or benzene rings, an attack at C-2 may also take place. (Fig.2)

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Fig. 2 REACTIVITY OF ISATIN

SYNTHESIS OF ISATIN

The Sandmeyer Isatin Synthesis

In 1919, Sandmeyer was the first to document this response. Chloral (i.e., trichloroacetaldehyde), hydroxylamine, and a primary aryl amine condense to isonitroso acetanilide, which is then electrophilically cyclized in the presence of a strong acid, such as concentrated sulphuric acid, to yield an isatin derivative (Scheme 1). This reaction is known as the Sandmeyer isatin synthesis, or Sandmeyer synthesis. The isatin derivatives generated by this reaction have been used to make quinolines, acridines, and indophenazines. The synthesis of isonitroso acetanilides using the Sandmeyer method is less successful with aniline derivatives that are poorly soluble in aqueous sodium sulphate media, but it is also ineffective with anilines that contain electron-rich ortho [10].

Scheme 1 Sandmeyer Isatin Synthesis

Schiff reaction

By condensing the keto group of isatin with various aromatic primary amines 3, schiff bases of isatin 4 can be produced (Scheme 2). By reacting with aromatic diamines in the presence of catalytic quantities of glacial acetic acid in EtOH under reflux conditions, bis-Schiff bases of isatin can be produced[11].

Scheme 2 Schiff reaction

Antimicrobial activity

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The three series of isatin derivatives [3 hydrazino, 3-thiosemicarbazino, and 3-imino carboxylic acid derivatives] were created by microwave irradiation. A range of bacteria and fungi were used to assess the synthetic chemicals' antibacterial properties. The results demonstrated the biological activity of N-alkyl isatin derivatives across a range of activity spectrums. The active derivatives of 3-hydrazino and 3-thiosemicarbazino isatin exhibited mild to moderate activity against Gram-positive bacteria, while the bulk of these derivatives were found to be biologically inactive [12].

Anti-bacterial activity

The compounds were tested in vitro for their antibacterial activity against two gram positive bacteria viz bacillus subtilis and stephalococcus. Aureus and two gram negative bacteria viz. Eschericia coli and plasmodium vulgaris are pathogenic in human beings[13].

Antioxidant Activity

Free radicals are extremely unstable atoms or molecules that have an odd electron in their outermost shell. They constantly look for an electron from any species to complete their outermost shell so they can become stable. Free radicals are produced in the mitochondria of our bodies during the oxygen metabolism process. Therefore, it is crucial to eliminate these free radicals because failing to do so will result in a number of illnesses, including malignant neoplastic disease, diseases of the brain and blood vessels, diabetes, heart disease, ulceration, mucoviscidosis, ageing, gastrointestinal ulcers, and acquired immune deficiency syndrome.

Antioxidants are therefore utilised to solve this issue since their primary purpose is to change these extremely unstable free radicals into stable compounds. Many medications that treat illnesses brought on by free radicals contain antioxidants[14].

III. Conclusions

In summary, the high prevalence of diseases caused by bacterial infection increasing antibiotic resistance is the reason for more urgent for medicinal research. In this study, we presented different biological properties of eight compounds of chemicals combined with isatin-β-thiosemicarbazones that were re-synthesized. They were used to investigate antimicrobial activity against 21 different types of Gram-positive and Gram-negative bacteria, DNA protection, and DNA interactions.Isatin derivatives possess a variety of pharmacological properties including anti-bacterial activity, and some of isatin-based compounds have already used for clinical deployment in the control and eradication of various diseases.

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