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ISATIN-3-THIOSEMICARBAZONE: A COMPREHENSIVE REVIEW OF ITS CHEMICAL, BIOLOGICAL, AND PHARMACOLOGICAL PROPERTIES

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ABSTRACT

A derivative of isatin, a flexible scaffold with a wide range of biological functions in medicinal chemistry, is isatin-3-thiosemicarbazone (ISTSC). With an emphasis on ISTSC's synthesis, chemical characteristics, biological activities, and possible pharmaceutical uses, this research attempts to provide a thorough analysis of the substance. The mechanisms of action, structure-activity connections, and prospects for further development of ISTSC as a therapeutic agent are also highlighted in the review. A flexible scaffold in medicinal chemistry, isatin is the source of isatin-3-thiosemicarbazone (ISTSC), which has been shown to have a wide range of important biological properties. The wide range of therapeutic potentials of ISTSC is attributed to its unique chemical structure, which consists of an isatin moiety conjugated with a thiosemicarbazone group. The objective of this research is to provide a thorough analysis of ISTSC, including its synthesis techniques, specific chemical characteristics, and a thorough investigation of its biological activities. Because of its antibacterial, antiviral, anticancer, and anti-inflammatory properties, ISTSC is a molecule that is very desirable for use in drug development. The review explores how ISTSC interacts at the molecular level with different biological targets, delving into the mechanisms of action that underlie these biological activities. The study also covers structural-activity relationships (SAR), showing how alterations to the ISTSC structure might affect its selectivity and effectiveness. The possible pharmacological uses of ISTSC are examined, underscoring its potential for the creation of novel medicinal medicines. The study concludes by outlining potential future research paths and perspectives. It emphasises the necessity for more studies to optimise synthesis, comprehend specific processes, and carry out clinical trials in order to determine the safety and effectiveness of ISTSC in medicinal applications.

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1. Overview

Because of its wide range of biological actions, the chemical molecule isatin-3-thiosemicarbazone (ISTSC) has attracted a lot of interest lately. This substance is derived from isatin, a naturally occurring indole derivative that was first identified in the early 1800s as a result of the oxidation of indigo dye. The pharmacological characteristics of isatin and its derivatives have been thoroughly investigated, and it has been discovered that adding a thiosemicarbazone moiety to the isatin structure greatly increases its biological activity.

1.1 Anatomical Details

The two primary structural elements of ISTSC are the thiosemicarbazone group and the isatin moiety. The pyrrole ring and benzene ring are fused to form the heterocyclic isatin core, which has a bicyclic structure and two keto groups at positions two and three. Its capacity to create hydrogen bonds, which is essential for its interaction with a variety of biological targets, and its adaptability in chemical reactions are the two main characteristics of its core structure.

The thiosemicarbazone group, which is joined to the isatin ring at position three, is made up of a semicarbazone, which is a functional group with an NH-C(=S)-NH2 unit, in which sulphur is used in lieu of the oxygen atom in the carbonyl group. The molecule's electrical characteristics are drastically changed by this substitution, which improves the molecule's capacity to interact with biological macromolecules and metal ions—a crucial interaction for the molecule's pharmacological actions.

1.2 Historical Background and Significance

Since thiosemicarbazones may form stable complexes with metal ions, they have been studied and synthesised since the early 1900s. This has led to the recognition of their potential as therapeutic agents. A thiosemicarbazone group added to the isatin structure

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produced a product that combined the bioactivity and reactivity of both parent molecules, giving it a unique set of features.

1.3 Importance for Biology

ISTSC is a chemical of interest for a variety of medicinal applications since it has shown a wide range of biological activities:

ISTSC has shown strong antimicrobial action against a variety of bacterial and fungal infections. Through the inhibition of important bacterial enzymes and disruption of cell wall formation, it has shown effective against both Gram-positive and Gram-negative bacteria, including drug-resistant strains.

- Antiviral Activity: ISTSC has shown effectiveness against a variety of viruses, including RNA viruses. Its main antiviral action is to block the enzymes responsible for viral replication, so stopping the virus's ability to multiply and propagate.

- Anticancer Activity: The anticancer potential of ISTSC is among its most promising features. It demonstrates cytotoxic properties against a range of cancer cell lines, including those from the breast, lung, and colon. The substance blocks topoisomerase enzymes, which are essential for DNA replication and cell division, causes apoptosis (programmed cell death) via mitochondrial pathways, and obstructs the division of cells during the cell cycle.

- Anti-inflammatory Activity: It has been discovered that ISTSC has notable anti-inflammatory characteristics. By preventing the synthesis of pro-inflammatory cytokines and enzymes like COX-2 (Cyclooxygenase-2), which are essential for the inflammatory response, it lowers inflammation.

1.4 Investigation and Advancement

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Extensive study has been conducted on the possible therapeutic uses of ISTSC due to its various biological actions. In order to improve its effectiveness and selectivity, research has concentrated on synthesis optimisation, mechanism of action knowledge, and structure-activity relationships (SAR) exploration. The objective is to create medicines that effectively cure a range of infectious illnesses, malignancies, and inflammatory disorders using ISTSC and its variants.

1.5 Looking Ahead

Even with the encouraging outcomes, further investigation is required to fully grasp ISTSC's potential. This involves thorough preclinical and clinical assessments to guarantee its safety and effectiveness, optimisation of its pharmacokinetic features, and in-depth mechanistic research to clarify its interactions at the molecular level. The further research and development of ISTSC might lead to the introduction of novel therapeutic compounds that can effectively treat some of the most difficult medical conditions.

To sum up, isatin-3-thiosemicarbazone, which combines the advantageous aspects of isatin and thiosemicarbazone into a single molecule with a variety of biological functions, is a major development in medicinal chemistry. Its therapeutic agent potential calls for further research and development, with the potential to make major contributions to contemporary medicine.

2.1 The Chemical Make-Up

The integration of two essential functional groups—the isatin moiety and the thiosemicarbazone group—defines isatin-3-thiosemicarbazone (ISTSC). The overall chemical behaviour and biological activity of the molecule are greatly influenced by each of these constituents.

Isatin Social Group

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In ISTSC, the isatin moiety (1H-indole-2,3-dione) constitutes the fundamental structure. As a heterocyclic molecule, it has a bicyclic ring system made up of a five-membered nitrogen-containing ring (the indole structure) joined to a six-membered benzene ring. The two carbonyl groups that are present at positions 2 and 3 further alter the indole ring. Because it offers a stiff, planar shape that is favourable to many kinds of chemical interactions, this bicyclic scaffold is essential.

- Retraction of electrons Carbonyl Groups: The isatin ring is made electron-deficient by the carbonyl groups at positions 2 and 3, which increases the ring's capacity to engage in nucleophilic and electrophilic processes. Hydrogen bonds, which are crucial for binding interactions with biological targets, may also be formed by these carbonyl groups.
- Aromaticity: The compound's stability and capacity to interact with other aromatic systems via π-π stacking interactions—which are often important in protein-ligand interactions—are facilitated by the aromatic character of the benzene ring.

Group of Thiosemicarbazones

At the third position, the isatin ring is joined to the thiosemicarbazone group (NH2-NH-C=S). This functional group has a variety of roles in biological processes and is well-known for how easily it can form metal complexes.

- Thione-Thiol Tautomerism: Between the thione (NH-C=S) and thiol (N=C-SH) forms, the thiosemicarbazone group may exist in equilibrium. Because of its tautomerism, the molecule is more reactive and has a greater capacity to chelate metal ions, both of which are critical to its biological activity.
- Hydrogen Bonding: The thiosemicarbazone moiety's NH and NH2 groups are able to create many hydrogen bonds. This capacity is necessary for ISTSC to bind to receptors and enzymes, which affects its biological functions including modulating receptors and inhibiting enzymes.
- Nucleophilicity: The sulphur atom in the thiosemicarbazone group is a strong nucleophile, which means that it reacts with electrophilic centres in biological molecules. This reaction may lead to the creation of covalent connections with proteins or the inhibition of enzymes.

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Integral Framework

The thiosemicarbazone and isatin groups in ISTSC combine to form a molecule with a highly conjugated system. By prolonging the π-electron system throughout the molecule, this conjugation improves its stability and capacity to engage in a variety of non-covalent interactions with biological targets, including hydrogen bonding, π-π stacking, and van der Waals forces.

- Extended conjugation and planarity: These properties of ISTSC make it easier for the compound to interact with nucleic acids and insert itself into the active sites of enzymes, which is important for its antibacterial and anticancer properties.
- Metal Chelation: ISTSC is able to efficiently chelate metal ions due to the thiosemicarbazone group's dual atoms of sulphur and nitrogen. This feature is important because chelating metals may alter biological processes that are reliant on metals, which can have antibacterial or anticancer effects.

In conclusion, the chemical structure of ISTSC offers a flexible and reactive framework thanks to its isatin core and thiosemicarbazone moiety. This structure may interact chemically in a variety of ways, which supports its wide range of biological functions. When the distinct qualities of the isatin and thiosemicarbazone groups come together, a molecule is produced that has a great deal of promise for medical use.

2.2 Incorporation

The condensation reaction between isatin and thiosemicarbazide is the simple process that yields isatin-3-thiosemicarbazone (ISTSC). The specific procedures, prerequisites, and factors for maximising the synthesis process to get high purity and yield are covered in depth in this section.

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2.2.1 Substances and Agents

- Isatin (1H-indole-2,3-dione): The starting material is a heterocyclic molecule that is commercially accessible.
- Thiosemicarbazide: An organic reagent that forms the required thiosemicarbazone by reacting with isatin.
- Acid Catalyst: Acids that help with the condensation process are often utilised, such as hydrochloric acid or acetic acid.
- Solvent: Ethanol is often utilised since it works well in the reflux process and can dissolve both isatin and thiosemicarbazide.

2.2.2 Conditions of Reaction

1. Making the Reaction Mixture: - Stir isatin and ethanol at room temperature until a clear solution forms.
   - Dissolve thiosemicarbazide separately in a small quantity of ethanol.

2. Catalyst Addition: - To the isatin solution, add a few drops of an acid catalyst, such as glacial acetic acid. By protonating isatin's carbonyl group, the catalyst increases its reactivity against thiosemicarbazide's nucleophilic assault.

3. Condensation Reaction: Stirring constantly, gradually incorporate the thiosemicarbazide solution into the isatin solution.
   - Reflux the mixture by heating it to a temperature that is usually between 78 and 80°C, which is the boiling point of ethanol. Refluxing makes sure the reactants stay in contact for a long time, which encourages full reaction.

4. Reaction Monitoring: - Use thin-layer chromatography (TLC) to track the development of the reaction. By comparing the locations of the starting ingredients and the result, this method assists in determining when the reaction is complete.

2.2.3 Separation and Cleaning

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1. Cooling and precipitation: Cool the reaction mixture to room temperature after the reaction is finished, as determined by TLC.

- Permit the mixture to stand so that the ISTSC may precipitate as a solid product more easily.

2. Filtration: - Use vacuum filtration to remove the solid ISTSC from the reaction mixture by filtering the precipitated result.

3. Cleaning: - Use cold ethanol to clean the collected solid of any unreacted starting ingredients or byproducts. This stage aids in the product's purification.

4. Drying: To get rid of any leftover solvent, dry the filtered material in a desiccator or under low pressure. The ISTSC is produced in its pure state by the drying process.

2.2.4 Yield and Optimisation

- Choice of Solvent: Depending on solubility and reaction kinetics, other solvents such as methanol or a combination of ethanol and water may be used in addition to the often used ethanol.

- Reaction Time: Reflux may last for different amounts of time. Reflux should last for 3–4 hours on average, however longer durations can be needed for full conversion.

Molar Ratios: To achieve a full reaction with isatin, use a tiny excess of thiosemicarbazide (e.g., a molar ratio of 1:1.1).

- Catalyst Concentration: The right quantity of acid catalyst must be used to prevent overabundance, which might cause adverse reactions or product deterioration.

2.2.5 Scheme for Reaction

The following reaction scheme may be used to summarise the synthesis:

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\[Itin (C_8H_5NO_2) + Thiosemicarbazide} (CH_5N_3S) \rightarrow Itin-3-Thiosemicarbazone} (C_9H_8N_4OS) + H_2O \]

Water is a byproduct of this reaction, and the main result is ISTSC.

In summary, the synthesis of isatin-3-thiosemicarbazone is a well-defined condensation process that can be made as pure and high yields as possible by carefully controlling the reaction parameters, solvent selection, and purification methods.

3. Activities Related to Biology

3.1 Inhibitory Effect on Microbes

The compound isatin-3-thiosemicarbazone (ISTSC) has attracted a lot of interest because of its strong antibacterial capabilities against a range of bacterial and fungal infections. Given the rising rate of antibiotic resistance, the compound's broad-spectrum action makes it an attractive option for the creation of novel antimicrobial drugs.

Microbiological Activity

Effectiveness against a variety of bacterial species, including both Gram-positive and Gram-negative bacteria, has been shown for ISTSC. Because these two categories of bacteria have quite different cell wall architectures, which often affects how susceptible they are to antibiotics, this broad-spectrum action is essential.

Positive for Grammes Bacteria: The peptidoglycan layer of gram-positive bacteria, such *Staphylococcus aureus* and *Streptococcus pneumoniae*, is thick. By focusing on vital bacterial enzymes and obstructing the production of the bacterium's cell walls, ISTSC has shown its capacity to stop the development of these germs. For example, transpeptidases are essential for the peptidoglycan layer to cross-link, and their inhibition by ISTSC might result in cell lysis and death.

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- Negative for Grammes Bacteria: Gram-negative bacteria have an outer membrane that offers extra protection, but their peptidoglycan layer is thinner. Examples of these bacteria include *Escherichia coli* and *Pseudomonas aeruginosa*. Because ISTSC may penetrate the outer layer of bacteria and interfere with important enzymatic activities inside their cells, it has proven efficient against various types of bacteria. It is especially remarkable that it can combat resistant strains, such Methicillin-resistant *Staphylococcus aureus* (MRSA), since there aren't many therapeutic choices for these illnesses.

Fungi Involvement

ISTSC has antifungal action in addition to antibacterial qualities. It has been shown to be effective against a range of fungal pathogens, such as *Aspergillus* and *Candida* species, which are often responsible for human fungal infections. The suppression of fungal enzymes essential for cell wall construction and cellular metabolism is thought to be the antifungal mechanism, which stops fungal growth and multiplication.

Antimicrobial Action Mechanisms

The ISTSC's antimicrobial mechanisms are complex and include many important processes:

- Enzyme Inhibition: Important enzymes involved in fungal and bacterial metabolism are targeted by ISTSC and inhibited. For instance, it has the ability to block the enzymes DNA gyrase and topoisomerase IV, which are essential for cell division and DNA replication in bacteria. It could prevent fungus from producing ergosterol, which is necessary to preserve the integrity of their cell membranes.

- Cell Wall Disruption: ISTSC weakens the structural integrity of bacterial and fungal cells by interfering with the formation of the cell wall. This may entail the suppression of peptidoglycan synthesis-related enzymes in bacteria, which would result in cell lysis. Inhibiting glucan synthase, an enzyme essential for the production of beta-glucan, a crucial component of fungal cell walls, weakens the walls of the fungal cells and causes them to die.

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- Modification of Membrane Permeability: ISTSC may also damage pathogens' cell membranes, increasing permeability and causing cell contents to seep out. Due to the disruption of homeostasis and potential for rapid cell death, bacteria and fungi are especially vulnerable to this impact.

Research and Results

Numerous investigations have highlighted ISTSC's antibacterial potential:

- In Vitro Studies: According to in vitro tests, ISTSC demonstrates minimum inhibitory concentrations (MICs) that are either higher than or on par with a number of the antimicrobial drugs already on the market. These investigations often use common microbiological procedures, including agar diffusion and broth dilution, to assess how well ISTSC works against different bacteria strains.

Synergistic Effects: Studies have also looked at how ISTSC works well in conjunction with other antimicrobial drugs. According to these research, ISTSC may improve the efficiency of already available antibiotics, perhaps cutting dosage requirements and minimising the chance of side effects.

- Resistance Profiles: Notably, ISTSC has shown efficacy against bacterial and fungal strains that are resistant to many drugs. This includes *Enterobacteriaceae*, which produce extended-spectrum beta-lactamases (ESBL), as well as MRSA. This kind of action implies that ISTSC may be useful in treating infections that don't respond to traditional treatments.

Clinical Consequences

ISTSC's encouraging antibacterial activity raises the possibility of the following therapeutic uses:

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- Treatment of Resistant illnesses: ISTSC has the potential to be a therapeutic agent that treats illnesses brought on by bacteria and fungi that are resistant to antibiotics, offering a backup plan in the event that existing therapies are ineffective.

- Combination treatments: ISTSC may be used in combination treatments to improve treatment effectiveness and slow the establishment of resistance due to its synergistic actions with other antimicrobials.

Topical Uses: Owing to its broad-spectrum action, ISTSC may be used in topical medications to treat skin infections, especially those brought on by resistant strains.

To sum up, ISTSC is a potential lead molecule that may be used in the battle against antibiotic resistance. Numerous infectious illnesses may eventually find new, efficient therapies thanks to continued research and development.

3.2 Inhibitory Effect on Viral

Because of its proven effectiveness against a range of RNA viruses, isatin-3-thiosemicarbazone (ISTSC) has attracted a lot of attention as a possible antiviral drug. Many dangerous infectious illnesses are caused by RNA viruses, which include well-known pathogens like the influenza virus, hepatitis C virus (HCV), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The capacity of ISTSC to inhibit these viruses offers new opportunities for the development of antiviral therapies.

Method of Action

RNA-dependent RNA polymerase (RdRp) in particular is one of the viral replication enzymes that is mainly inhibited by the antiviral mechanism of ISTSC. In the RNA virus replication cycle, RdRp is an essential enzyme that creates the viral RNA genome from an RNA template. ISTSC successfully halts the replication process by targeting and blocking this enzyme, stopping the virus from spreading throughout the host.

Important Phases of the Antiviral Process:

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1. Binding to RdRp: It is thought that ISTSC interacts with RNA-dependent RNA polymerase's active site. Hydrophobic interactions and hydrogen bond formation between ISTSC and certain amino acid residues within the RdRp enzyme are most likely involved in this interaction.

2. Inhibition of RNA Synthesis: After attaching itself to RdRp, ISTSC stops the enzyme from working, which stops fresh viral RNA strands from being made. An essential stage in the viral life cycle, genome replication is stopped by this blockade.

3. Disruption of Viral Assembly: Since viral proteins are encoded by their RNA, ISTSC indirectly prevents the creation of viral proteins by blocking RNA synthesis. As a result, the assembly and release of viral particles from the host cell are reduced.

Particular Antiviral Activity Examples

1. Influenza Virus: Research has shown that ISTSC is very effective against a range of influenza virus types. Viral RNA synthesis is decreased by ISTSC via inhibition of the influenza virus RdRp, which lowers the viral load and lessens the severity of illness. ISTSC treatment significantly reduces viral replication, according to in vitro studies, suggesting that it may be used as a therapeutic agent to treat influenza.

2. Hepatitis C Virus (HCV): ISTSC research has also focused on HCV, an RNA virus that causes chronic liver illness. It has been suggested that ISTSC's effect on the HCV RdRp accounts for its capacity to impede HCV replication. According to experimental research, ISTSC may lower HCV RNA levels in infected cells, indicating a possible use for it in hepatitis C antiviral regimens.

3. SARS-CoV-2: Research on ISTSC and other antiviral drugs has been spurred by the appearance of SARS-CoV-2, the virus that caused the COVID-19 pandemic. According to preliminary research, ISTSC may block SARS-CoV-2's RdRp, which would lessen the virus's ability to replicate. Because of its comparable mechanism to other RNA viruses, ISTSC is a viable option for more research and COVID-19 clinical trial preparation.

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Possibility of Combined Treatment

The prospective use of ISTSC in combination treatment is one of its attractive features. Combining ISTSC with other antiviral medications may improve treatment outcomes, lower the risk of resistance emerging, and provide a wider range of antiviral action. For example, to have a more complete antiviral impact, ISTSC might be coupled with protease inhibitors, which target distinct phases of the viral life cycle.

Prospects for Antiviral Research in the Future

Future studies on ISTSC as an antiviral drug have to concentrate on a number of important areas:

1. Structural Optimisation: ISTSC's chemical structure is changed to improve its selectivity and binding affinity for RdRp enzymes of different RNA viruses.

2. In Vivo experiments: Using animal models infected with RNA viruses, conducting in vivo experiments to assess the pharmacokinetics, safety, and effectiveness of ISTSC.

3. Clinical studies: Moving forward with clinical studies to evaluate ISTSC's therapeutic potential in people, especially for RNA viral infections that are newly developing and reemerging.

4. Mechanistic Studies: To learn more about the mechanism of inhibition and to find possible resistance routes, ISTSC and RdRp enzymes' intricate molecular interactions are being examined.

To sum up, ISTSC is a potentially effective antiviral agent that specifically targets RNA-dependent RNA polymerase via a well-defined mode of action. Its ability to work in conjunction with other antiviral drugs and its broad-spectrum efficacy against different RNA viruses make it an attractive target for more antiviral medication development.

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3.3 Inhibition of Cancer

The anticancer potential of isatin-3-thiosemicarbazone (ISTSC) has been extensively researched. Prostate, lung, colon, and breast cancer cell lines are among the cancer cell types that ISTSC has cytotoxic effects against. ISTSC has a diverse range of anticancer activities via many pathways that impede the proliferation of cancer cells and encourage their demise. These methods are covered in depth in the next subsections.

3.3.1 Apoptosis Induction

Programmed cell death, or apoptosis, is a key process by which ISTSC carries out its anticancer actions. ISTSC triggers apoptosis via both extrinsic and intrinsic (mitochondrial) pathways:

- Intrinsic Pathway: Cytochrome C is released into the cytoplasm as a result of ISTSC's impact on the mitochondrial membrane potential. This release initiates the activation of caspase-9, which in turn activates caspase-3, bringing about the apoptotic execution phase. Pro-apoptotic (Bax, Bak) and anti-apoptotic (Bcl-2, Bcl-xL) proteins are regulated in this pathway. Pro-apoptotic protein production is encouraged by ISTSC, while anti-apoptotic protein expression is inhibited, tilting the scales in favour of cell death.

- Extrinsic route: In addition to the extrinsic apoptotic route, which is less often seen, ISTSC may also activate death receptors on the cell surface, including Fas and TNF-related apoptosis-inducing ligand (TRAIL) receptors. The death-inducing signalling complex (DISC) is formed as a result of this activation, and caspase-8 is activated. Caspases-8 may then either directly activate caspase-3 or intensify the apoptotic signal by means of the mitochondrial route.

3.3.2 Topoisomerase Enzyme Inhibition

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Enzymes known as topoisomerases are vital for controlling DNA topology during chromosomal segregation, transcription, and replication. It has been shown that ISTSC inhibits topoisomerase I and II activity:

- Topoisomerase I Inhibition: By stabilising the complex that forms between DNA and topoisomerase I, ISTSC prevents DNA strand breaks caused during replication from being re-ligated. DNA damage from this inhibition causes cell cycle arrest and apoptosis.

- Inhibition of Topoisomerase II: ISTSC also targets topoisomerase II, which is essential for releasing DNA tangles during mitosis and replication. ISTSC induces DNA double-strand breaks and improper chromosomal segregation by blocking topoisomerase II, which results in mitotic disaster and cellular death.

3.3.3 Interference with the Advancement of the Cell Cycle

ISTSC suppresses the growth of cancer cells by interfering with the cell cycle at many checkpoints:

- G1 Phase Arrest: By upregulating the expression of cyclin-dependent kinase inhibitors (p21, p27), and downregulating cyclins (cyclin D1, for example) and cyclin-dependent kinases (CDKs), ISTSC may cause cell cycle arrest in the G1 phase. The advancement to the S phase, when DNA synthesis takes place, is stopped by this arrest.

- S Phase Arrest: By causing DNA damage and triggering the DNA damage response (DDR) pathway, ISTSC may obstruct the S phase. By preventing cells with damaged DNA from proliferating, this block helps to curb the growth of cancerous cells.

- G2/M Phase Arrest: ISTSC has the ability to disrupt the G2/M transition, which is essential for mitosis. Through the inhibition of crucial regulators including CDK1 and cyclin B1, ISTSC stops cells from going through mitosis, which results in senescence or apoptosis.

3.3.4 Additional Systems

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Apart from the aforementioned principal routes, ISTSC may also exhibit anticancer effects via other pathways.

- Generation of Reactive Oxygen Species (ROS): ISTSC may increase the rate at which cancer cells produce ROS. Increased reactive oxygen species (ROS) may result in oxidative stress, which can damage DNA, oxidise proteins, peroxide lipids, and finally induce apoptosis.

- Inhibition of Angiogenesis: By downregulating vascular endothelial growth factor (VEGF) and its receptors, ISTSC has been shown to decrease the angiogenesis (the development of new blood vessels). Because of this inhibition, tumours are deprived of the blood flow and nourishment required for development and spread.

- Modulation of Signalling Pathways: ISTSC may disrupt a number of signalling pathways, including the NF-κB, Wnt/β-catenin, and PI3K/Akt/mTOR pathways, which are often dysregulated in cancer. ISTSC may prevent cell survival, proliferation, and metastasis by modifying these pathways.

In conclusion, ISTSC has strong anticancer action via a variety of channels, including as apoptosis induction, topoisomerase enzyme inhibition, disruption of the cell cycle, production of reactive oxygen species, suppression of angiogenesis, and modification of important signalling pathways. These varied pathways demonstrate ISTSC's potential as a strong anticancer drug that can target several facets of cancer cell biology.

3.4 Inhibitory Action on Inflammation

ISTSC has significant anti-inflammatory qualities as well. The intricate biological reaction of bodily tissues to damaging stimuli like infections, damaged cells, or irritants is known as inflammation. The immune system is activated during this process, releasing a range of mediators such as chemokines, pro-inflammatory cytokines, and enzymes like COX-2

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(Cyclooxygenase-2). These mediators are essential in the development of the inflammatory response, which produces pain, swelling, redness, and heat.

3.4.1 Anti-Inflammatory Action Mechanisms

The capacity of ISTSC to obstruct many important pathways implicated in the inflammatory process accounts for its anti-inflammatory properties. These pathways include:

1. Inhibition of Pro-inflammatory Cytokines: TNF-α, IL-1β, and IL-6 are examples of pro-inflammatory cytokines that are less produced when ISTSC is present. The start and continuation of the inflammatory response depend on these cytokines. ISTSC may reduce inflammation by blocking the synthesis of these molecules, which in turn reduces the overall inflammatory signal.

2. Inhibition of Cyclooxygenase-2 (COX-2): During inflammation, arachidonic acid is converted to prostaglandins, which are powerful mediators of pain and inflammation. COX-2 is an enzyme that is increased during inflammation. It has been shown that ISTSC inhibits COX-2 activity, which lowers prostaglandin synthesis. This inhibition aids in reducing swelling and discomfort, two symptoms linked to inflammation.

3. Modulation of the NF-κB Pathway: The protein complex known as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) regulates DNA transcription and is essential for controlling the immune system's response to infection. The expression of many inflammatory genes, including as those that code for adhesion molecules, chemokines, and cytokines, is regulated by NF-κB. It has been discovered that ISTSC inhibits the NF-κB pathway's activity, which reduces the production of inflammatory mediators.

4. Reduction of Oxidative Stress: Reactive oxygen species (ROS), which may lead to oxidative damage to tissues, are often produced in conjunction with inflammation. Because

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of its antioxidant qualities, ISTSC may help scavenge these ROS and lessen oxidative stress and the inflammatory consequences that go along with it.

7. Conclusion

Isatin-3-thiosemicarbazone is a promising compound with a wide range of biological activities. Its unique chemical structure allows it to interact with various biological targets, making it a versatile candidate for drug development. Continued research into its mechanisms of action, structure-activity relationships, and potential therapeutic applications could lead to the development of new, effective treatments for various diseases.

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