



Review on hydrazone and it's biological activities

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Abstract

The main traits and attributes of hydrazone are enumerated in its abstract. The chemical compound hydrazone is composed of a particular functional group known as the hydrazone group ($-NHN=$). Numerous biological activities, such as antibacterial, antiviral, antioxidant, and anticancer properties, are well-known for it. Because of these properties, hydrazone molecules are attractive options for a range of medical and pharmaceutical applications. However, hydrazones' particular biological activity can differ based on their chemical makeup and alterations. To completely comprehend their methods of action and their therapeutic applications, more research is required.

Keywords: Healthcare, Chemical Compound, Biological Activities.

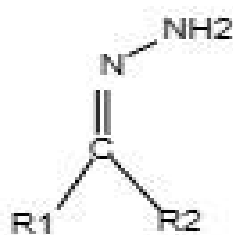
1. Introduction

Medicinal chemistry has paid a great deal of attention to hydrazones, which are chemical molecules that contain a $C=N-NH_2$ functional group present. Of the hydrazone, the nitrogen atom is both electrophilic and nucleophilic, whereas the carbon atom is both. Inherently nucleophilic. Compounds having distinct physical and chemical properties that are thought to be crucial for their synthesis are produced when hydrazone is combined with other functional groups. chemicals that are heterocyclic. From antibacterial and antiviral characteristics to anticancer and anti-inflammatory actions, this diverse class of chemicals has a wide range of biological activity. Hydroxides are intriguing prospects for medication development due to

their special chemical structure and reversible reactivity. This review article contains. Our investigation delves into the diverse biological functions of hydrazones, examining their modes of operation and possible uses in different medical domains. This study attempts to provide a thorough grasp of the present state of hydrazone research by looking at the most recent research findings and consolidating previous information. We examine the intricate interactions that highlight the pharmaceutical potential of hydrazones, ranging from their involvement in fighting infectious diseases to their impact on cancer treatment and anti-inflammatory pathways. The structural variety of the hydrazone class is also covered in this review, with an emphasis on how little changes can have a big impact on bioactivity. Our goal is to provide important insights that will help shape future approaches to drug creation by clarifying the structure-activity correlations of hydrazones. Since with the goal of providing a thorough overview of the most recent developments and viable paths for using hydrazones in the creation of new therapeutic agents, this review aims to be a useful tool for researchers, physicians, and pharmaceutical scientists as they navigate the complex field of hydrazone chemistry and biology. Since their numerous uses in organic synthesis and medicinal chemistry, hydrazones—which date back to the late 1800s—have grown in prominence. Since Emil Fischer synthesized hydrazones in 1895 and further investigated them in a variety of processes, these compounds have been used as intermediates in the synthesis of agrochemicals and medications. The condensation reaction of ketones with aldehydes and hydrazine derivatives produces hydrazones. These molecules are highly versatile and find use in medical chemistry, organic synthesis, and as intermediates in the synthesis of many drugs. Because of their distinctive reactivity, hydrazones are useful tools for chemists and researchers who are developing agrochemicals, medicines, and other organic molecules. The scientific world has paid considerable attention to hydrazones, a class of organic molecules, because of their flexible reactivity and unique structural features.

$R_1R_2C=NNH_2$ is the generic formula for the molecule that is produced during the synthesis of hydrazones, which is the condensation of ketones or aldehydes with hydrazine or its derivatives. Hydrazones are essential intermediates in organic synthesis that find use in materials research, pharmaceutical chemistry, and the production of agrochemicals. Because of their unusual features, hydrazones are useful building blocks for a variety of chemical transformations due to their unique molecular architecture, which is characterized by the azomethine bond. Hydrazones are widely used in the production of pharmacological drugs, agrochemicals, and functional materials. Researchers have taken advantage of this reactivity to access a wide range of structurally varied molecules. With relation to hydrazones, the review attempts to give a thorough summary of the present state of knowledge, covering their structural variety, synthetic methods, and numerous uses. We aim to shed light on the possible future paths and problems in the investigation of this fascinating class of substances by exploring recent advancements and upcoming trends. This study aims to provide insights that further our understanding of hydrazones and their crucial significance in modern organic chemistry by methodically analyzing the body of existing literature.

2. Hydrazone's structural makeup



A. C=N Double Bond: During the condensation reaction, a C=N double bond is created, which is a component of the core structure of hydrazones. This characteristic is essential to their biological processes.

B. Variable substituents: The kind and location of substituents on the aromatic or aliphatic rings frequently affect the biological activities of hydrazones.

C. Electronic impacts: The electronic characteristics of hydrazones might affect their reactivity and biological impacts. These features can be influenced by groups on the aromatic ring that donate or withdraw electrons.

D. Steric Considerations: The accessibility of the active site can be impacted by steric hindrance brought on by large substituents, which can change how hydrazones interact with biological targets.

E. Hydrazone Tautomerism: The balance between the various tautomeric forms that hydrazones can take on influences the hydrazones' biological activity.

Chemists can customize hydrazone structures by comprehending the synthesis, and an understanding of the structure offers insights into potential effects on biological interactions. In order to design hydrazones with particular and desired biological activity for applications in medicinal chemistry, the interaction between synthesis and structure is essential.

3. Creation of Hydrazone

A. Condensation Reaction: Carbonyl compounds (aldehydes or ketones) react with hydrazine or its derivatives to produce the majority of hydrazones. The C=N bond that hydrazones are known for is formed by this reaction.

B. Acyl Hydrazone Formation: Acyl compounds, such as acyl chlorides, react with hydrazine or hydrazine derivatives to form acyl hydrazones.

C. Cyclization events: Cyclic hydrazone derivatives can be created by synthesizing hydrazones via intramolecular cyclization events.

D. Reactions that include cross-coupling: Hydrazones have the ability to engage in Heck or Suzuki reactions, which allow for the addition of a variety of substituents.

E. Hydrazones and their byproducts Compounds known as hydrazones are defined by the functional group $R_1R_2C=NNH_2$. They are created when ketones or aldehydes combine

condensationally with hydrazine or its derivatives. The resultant derivatives of hydrazone show a variety of characteristics and uses. Aspects of hydrazones and their derivatives include the following:

1. Structural Diversity: The synthesis of hydrazine derivatives and carbonyl compounds results in a variety of structural configurations for hydrazone derivatives.

2. Synthesis: The usual method for creating hydrazones is to condense a carbonyl molecule with hydrazine or one of its derivatives. In organic synthesis, this adaptable reaction has been thoroughly studied.

3. Medicinal chemistry: Because of their possible pharmacological actions, hydrazone derivatives have gained interest in this field. A few have antimicrobial, anti-inflammatory, and anti-cancer qualities.

4. Catalysis: Compounds containing hydrazone are used as catalysts in a variety of organic reactions, which helps to create synthetic processes that are more effective and environmentally friendly.

5. Material sciences: Materials based on hydrazone find use in this field, helping to create functional materials for optoelectronics, sensors, and electronics.

6. Bioconjugation: Strategies involving the selective linking of biomolecules are made possible by the application of hydrazone chemistry. This has consequences for medication delivery, chemical biology, and diagnostics.

7. Ligands in Coordination Chemistry: Hydrazone derivatives interact with metal ions to form complexes, acting as ligands in coordination chemistry. The electrical and magnetic characteristic of these compounds are intriguing.

8. Photochromic compounds: A few derivatives of hydrazone display photochromic activity, which involves color changes in response to light. Applications such as sensors and smart materials are being investigated for this characteristic.

Hydrazone derivatives are useful instruments in many scientific fields, such as organic chemistry, pharmaceutical chemistry, materials science, and catalysis, due to their diverse character. Scholars persist in investigating and uncovering novel uses for these substances.

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4. Amplification of hydrazone

Resonance, which is the delocalization of electrons inside the molecule, is commonly observed in hydrazones. The azomethine group's resonance form ($R_1R_2C=NNH_2$) can be used to depict the resonance structures for a hydrazone. The double bond between the nitrogen and carbon atoms can alternately be found in the resonance structures. The general stability of hydrazone compounds is aided by this resonance stabilization. According to the resonance forms, the carbon and nitrogen atoms are not able to create a clean double bond since the electrons are dispersed among them. Resonance delocalization frequently affects the reactivity and characteristics of hydrazone derivatives, making them adaptable substances for a range of chemical reactions and uses.

5. Hydrazone's consistency

The substituents' nature, the surrounding environment, and the resonance stabilization occurring within the molecule all have an impact on how stable hydrazone is.

A. Replacements: The stability of the hydrazone can be affected by substituents that donate or remove electrons. By promoting resonance, for example, electron-withdrawing groups can stabilize the hydrazone.

B. Resonance stabilization: Hydrazones' azomethine group facilitates resonance stabilization by dividing the electron density between the nitrogen and carbon atoms. The stability of hydrazone compounds is enhanced by this resonance.

C. Steric effects: Bulky substituents can produce steric hindrance, which can impact hydrazone stability. Depending on the particular reaction conditions, bulky groups may prevent hydrazones from forming or from becoming stable.

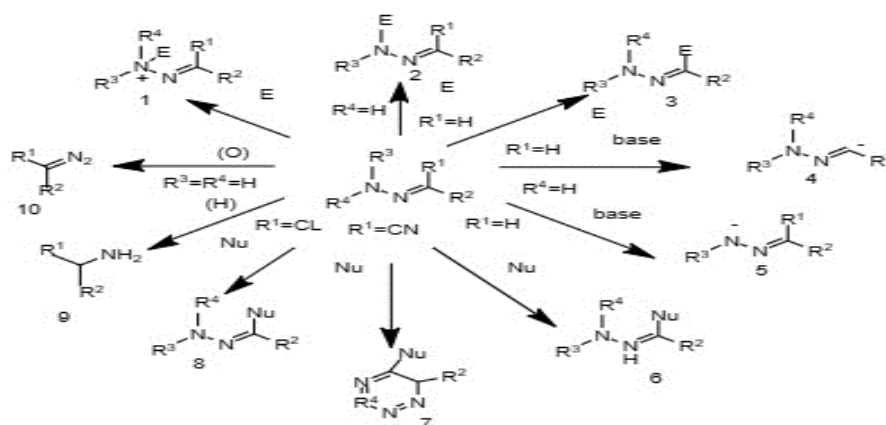
D. Environmental Factors: Hydrazone stability can be impacted by reaction circumstances including temperature and pH. Hydrazones can occasionally hydrolyze in basic or acidic environments.

E. Conjugation: Hydrazone compounds' stability may be affected by conjugation with adjacent functional groups or π -systems. Additional conjugation may improve stability.

F. Metal complexation: Hydrazones' overall stability may be impacted by the formation of stable complexes with metal ions. A factor is the coordinating environment and the type of metal.

Comprehending these elements is essential for forecasting and monitoring the stability of hydrazones in diverse applications, such as their employment as ligands in coordination chemistry, intermediates in organic synthesis, or in medicinal chemistry for drug development.

6. Variations In Hydrazone Reactions



Because they are complex molecules, hydrazones can undergo a variety of reactions that enhance their synthetic value. The following are some significant hydrazone reactions:

1. **The formation reaction** is the first step in the process, when hydrazine or its derivatives are combined with an aldehyde or ketone carbonyl molecule to generate hydrazone.
2. **Oxidation:** Hydrazones have the ability to react with other oxidants to produce azo compounds or other oxidation products. Oxidizing agents are frequently used, such as metal oxidants or peroxides.
3. **Reduction:** Hydrazones can be reduced in order to produce hydrazine. Sodium borohydride and lithium aluminum hydride are examples of common reducing agents.
4. **Cyclization:** Hydrazones can create cyclic hydrazone derivatives through intramolecular cyclization processes. Reaction circumstances that are suitable can help with this.
5. **Hydrolysis:** Hydrazones can hydrolyze, especially in acidic or basic environments. This process causes the C=N bond to split, releasing hydrazine or its derivatives and the associated carbonyl compounds.
6. **Addition Reaction:** The hydrazone may introduce different functional groups by addition reactions with electrophiles or nucleophiles, depending on its nature.

7. **Formation of Metal Complexes:** Hydrazones are frequently used in coordination chemistry because of their ability to coordinate with metal ions to generate metal complexes.
8. **Cross-coupling reactions:** Hydrazones can create new C-C bonds by taking part in cross-coupling reactions like Heck or Suzuki reactions.
9. **Aldol-Type Reactions:** Hydrazones have the ability to engage in aldol-type reactions, which include the formation of carbon-carbon bonds.
10. **Amination:** By reacting with amines, hydrazones can become aminated, which adds amino groups to the hydrazone structure.

Chemists can modify hydrazone structures for use in organic synthesis, medicinal chemistry, and materials research by comprehending these processes. Hydrazone Types Based on the characteristics of their structures and the types of reactants used in their synthesis, hydrazones are a broad class of chemicals.

7. These are a few varieties of hydrazones.

1. **Hydrazones Aldehyde:** They are a frequent class of hydrazones, formed by the condensation of aldehydes with hydrazine or hydrazine derivatives.
2. **Ketone Hydrazones:** These chemicals are created when ketones react with hydrazine or its derivatives; they are comparable to aldehyde hydrazones but originated from ketones.
3. **Aromatic Hydrazones:** Because they contain aromatic moieties, these hydrazones, which can include aromatic aldehydes or ketones, are frequently linked to particular biological functions.

4. Acyl hydrazone: Created when hydrazine or hydrazine derivatives react with acyl compounds (such as acyl chlorides or anhydrides), resulting in the inclusion of an acyl group.

5. Schiff Bases: A larger family of substances that also includes hydrazones, Schiff bases are often created when a primary amine condenses with a carbonyl molecule.

6. Pyrazole Hydrazones: These hydrazones, which are produced when pyrazole derivatives combine with hydrazine, frequently show intriguing pharmacological properties.

7. Imine Hydrazones: These hydrazones are produced when hydrazine or its derivatives combine with imines, which are molecules with a C=N double bond.

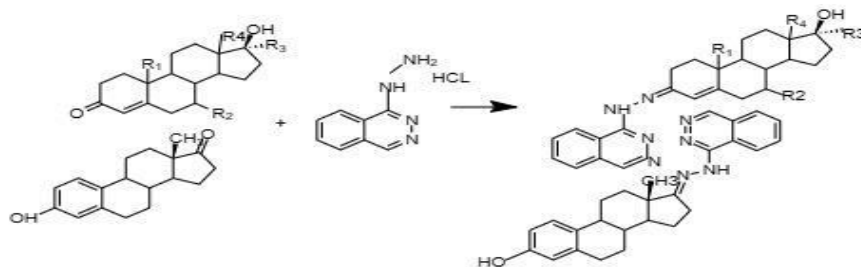
8. Diazine Hydrazones: These are created when hydrazine or its derivatives condense with diazines, such as pyridazine or pyrimidine.

Hydrazones are a flexible class of compounds with a wide range of uses in medicinal chemistry due to the variety of substituents present in their structure and the specific type on which their biological activities depend.

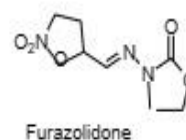
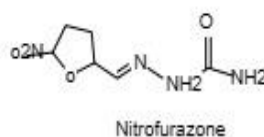
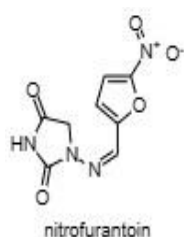
8. Hydrazone's biological actions

Compounds with a C=N-NH₂ moiety, known as hydrazones, have demonstrated a variety of biological functions. Antimicrobial, antiviral, anticancer, and anti-inflammatory qualities are displayed by certain. Drug development researchers are investigating the potential of hydrazones in medical chemistry, as they have demonstrated a variety of biological functions. They are looked into regarding their:

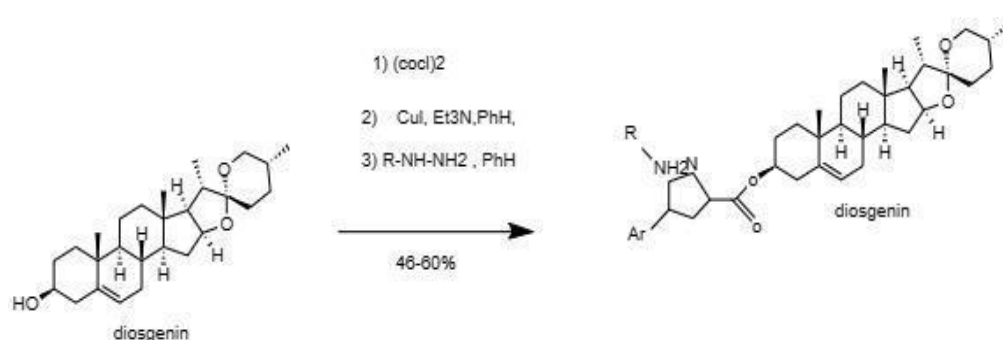
1. **Antimicrobial Properties:** A number of hydrazones have the potential to be developed into antimicrobial agents due to their antibacterial and antifungal properties.



2. **Antiviral activity:** A number of hydrazones have shown antiviral properties, indicating their potential for use in the creation of antiviral medications. Research has demonstrated that certain hydrazones have anticancer potential, which means that they can stop the proliferation of cancer cells and may be useful in the treatment of cancer.

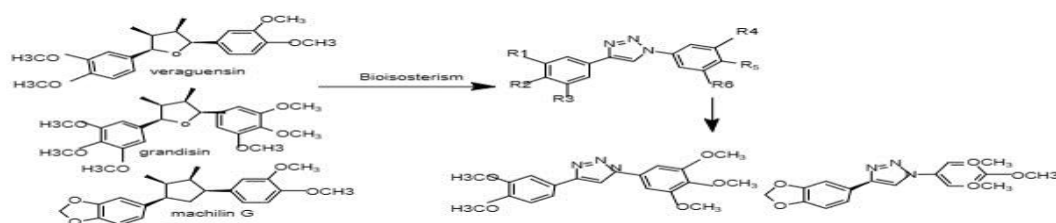


3. **Anti-inflammatory effects:** Hydrazones may possess anti-inflammatory properties, which makes them pertinent in inflammatory disorders. Certain hydrazones exhibit antioxidant qualities that are advantageous in the treatment of illnesses linked to oxidative stress.

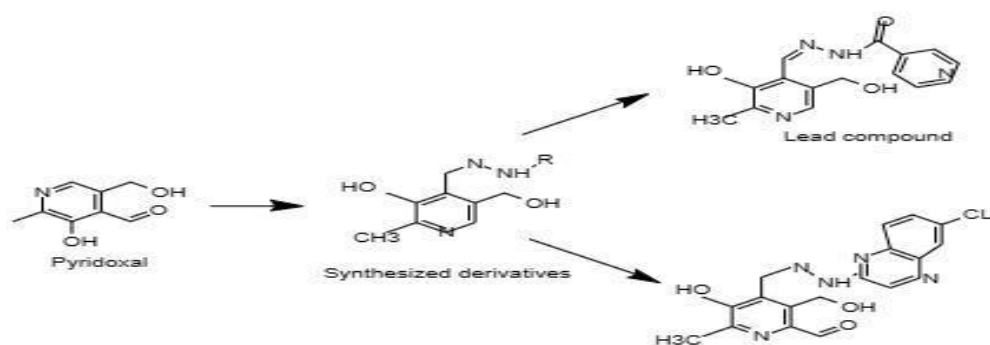


4. **Antileishmanial activity:** Antileishmanial hydrazones have demonstrated a number of advantageous actions in the fight against leishmaniasis. By interfering with crucial metabolic pathways in *Leishmania* parasites, they frequently exhibit strong antiparasitic actions. The minimal toxicity that certain hydrazones have demonstrated to mammalian

cells further increases their potential as therapeutic agents. Part of what makes certain hydrazones effective is their capacity to specifically target particular parasite enzymes or structures. A more comprehensive comprehension of the advantageous actions of antileishmanial hydrazones would result from a thorough investigation of these facets.

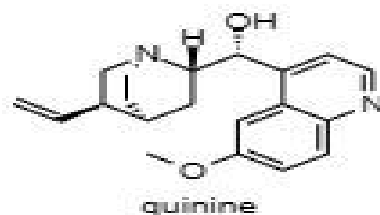
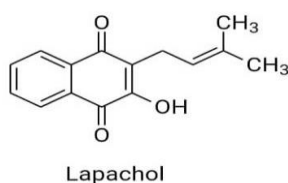


5. **Antitubercular action:** Numerous investigations have indicated that hydrazones have promise antitubercular activity. The primary agent of tuberculosis, *Mycobacterium tuberculosis*, is frequently inhibited by these substances. Because hydrazones can interfere with important bacterial biological functions such cell wall formation and metabolic pathways, they are thought to have antitubercular activity. For a thorough knowledge of hydrazones as possible medicines against tuberculosis, it would be imperative to investigate the precise mechanisms and structural aspects responsible for this activity.

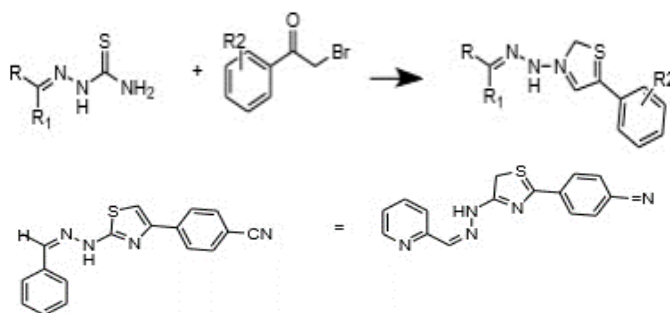


6. **Antimalarial action:** Hydrazones have proven to be efficient against the *Plasmodium* parasites that cause malaria, exhibiting noteworthy antimalarial activity. Possible modes of action involve interfering with vital biological functions of the parasites, like blocking

heme detoxification or interfering with protein synthesis. A few hydrazones are also less harmful to mammalian cells, which makes them more appealing as antimalarial drugs. Understanding these pathways and the structural elements influencing antimalarial action might be helpful in determining how well hydrazones work against malaria.



7. **Anti-HIV activity:** Studies indicate that hydrazones may have anti-HIV action. Possible mechanisms for this activity include suppression of viral replication or disruption of viral enzymes. Certain hydrazones may focus on particular phases of the HIV life cycle, so qualifying them for treatment with antiretrovirals. Evaluating the potential of hydrazones in the creation of novel HIV therapeutic approaches would require examining the structural features and molecular interactions underlying their anti-HIV effects.



8. **Antiplatelet activity:** Research on hydrazones' antiplatelet activity is being done. A critical stage in the production of blood clots, platelet aggregation, has been shown to be inhibited by some hydrazones. Researching hydrazones' potential as antiplatelet agents and comprehending the precise mechanisms by which they impact platelet function may have consequences for the creation of medications for disorders involving aberrant blood

clotting, such as cardiovascular illnesses. Understanding their antiplatelet function might be aided by more research into the molecular connections and mechanisms involved.



9. Vitality Of Hydrazone

Because of their many uses and varied features, hydrazones are important in several scientific fields:

1. Medicinal chemistry: Hydrazones are useful in medication development because they show a wide range of biological actions. Their significance in pharmaceutical chemistry is attributed to their antibacterial, anticancer, and anti-inflammatory characteristics.

2. Drug Design and Discovery: Researchers can create compounds with certain biological activity by altering the structure of hydrazones. This adaptability is essential for finding novel medications with improved therapeutic outcomes.

3. Coordination Chemistry: Hydrazones have the ability to combine with metal ions to form complexes, which advances the study of coordination chemistry. The material sciences and catalysis can both benefit from these complexes.

4. Synthetic Chemistry: Hydrazones are useful in synthetic chemistry due to their simplicity in synthesis and adaptability in functional group changes. They act as transitional materials for making different kinds of organic compounds.

5. Biomedical Research: Because hydrazones are useful in the development of probes and imaging agents, they are used in biomedical research. Their capacity to engage with particular biological targets in a selective manner advances the development of diagnostic instruments.

6. Antioxidant and Neuroprotective Agents: Antioxidant qualities in several hydrazones make them promising agents to combat problems associated with oxidative stress. Further investigation into their neuroprotective properties is under underway.

7. Polymer Chemistry: The use of hydrazones in polymer chemistry aids in the creation of functional polymers that are used in medication delivery systems, adhesives, and coatings.

8. Hydrazone-based Sensors: Hydrazones can be used in sensor designs to identify particular analytes, which advances the development of chemical and biosensors alike.

9. Dye Chemistry: Hydrazones are employed in the color chemistry sector to synthesize pigments and dyes.

10. Photodynamic Therapy: A method of treating cancer that entails activating photosensitizers to cause cell death has been demonstrated to be effective with certain hydrazones.

Hydrazones are versatile chemicals that can be used in a wide range of chemical reactions. This versatility highlights how important they are to the advancement of science and technology in many fields.

REFERENCES

- [1]. Synth. React, Inorg. Met, Org. Chem., 30(6), 1159, 2000; R. M. Patil and N. V. Thakkar.
- [2]. Tada, R., Chavda, Naimish, and Shah, Manish K. J. Chem. Pharm. Res., 3(2), 290, 2011.
- [3]. Main Group Metal Chemistry, 32(6), 297, 2009; J. B. Biswal, S. S. Garje, and B. L. Jadhav.
- [4]. Mhadaye, M. E., and Patil, R. M. Indian Journal of Research, 5(4), 63 (2016).
- [5]. Furnis BS, Tatchell AR, Hannaford AJ, Smith PWG, and ELBS Longman London, 1989. Vogel Textbook of Practical Organic Chemistry, Fifth Edition.
- [6]. International Journal of Advanced Chemistry, 2(1), 20 (2014); M. Emayavaramban, K. Kumar, P. Mani, B. Prabhakaran, and A. Muthuvel.
- [7]. Modh KM, Sen DJ, Soni JP. Studies of the structure-activity connection of pyrazolone derivatives with the imidazole, benzimidazole, and benztriazole moiety produced for anti-inflammatory properties.2011; J Appl Pharm Sci; 1: 115–120.
- [8]. Passi NA, Anand IS, Sen DJ, Prajapati MK. Pharmacological study of biotransformation of substituted and unsubstituted indanone acetic acid adduct with pyrazolone ring for analgesic efficacy.2010; 2: 182-189 in Int J Drug Dev Res.

- [9]. Ismail MMF, Khalifa NM, Fahmy HH, Nossier EH, Abdulla MM. As anti-inflammatory agents, some new pyrazoline and pyranopyrazole derivatives have been designed, docked, and synthesized. *J Heterocyclic Chem.* 2014; 51:450-458.
- [10]. Suthakaran R, Satish K, and Rivelli T. Synthesis, characterization, and assessment of several pyrazolone derivatives' analgesic properties. 2011; 2: 172–174 in *IJIPR*.
- [11]. Mariappan G, Sutharson L, Haldar A, Saha BP. Synthesis and assessment of pyrazolone derivatives' bioactivity. (2010) *Indian J. Chem.* 49: 1671–1674.
- [12]. Arandelovic S, Todorovic N, Trifunovic S, Manojlovic N, Jelic R, Joksovic MD, Markovic V, Eric S, Stanojkovic T, Gligorijevic N. Studies on the antiproliferative properties and QSAR of many novel 4-aminomethylidene derivatives of pyrazol-5-ones. 21: 4416–4421 in *Bioorg Med Chem Lett.* (2011).
- [13]. Shivananda KN, Shyma PC, Arulmoli T, Isloor AM, Isloor S, and Vijesh AM. Creation of novel pyrazolone compounds that exhibit strong antibacterial properties. (2011) *Der Pharma Chemica* 3: 454–463.
- [14]. Schuetha KN, Vijayakumar V, Ragavan RV. New bioactive 4-oxy/thio substituted-1H-pyrazol-5(4H)-ones are synthesized by an effective cross-Claisen condensation process. 2009. *Eur J Med Chem* 44: 3852–3857.
- [15]. Shrivastava PK, Shrivastava SK, Verma A, Das N. Synthesis and biological assessment of novel compounds of aryl pyrazole-3-one as possible hypoglycemic agents. (2008) *Ind J Chem.* 47: 1555–1558.
- [16]. Sriram D, Yogeewari P, Perumal S, Gunasekaran P. A simple four-step sequential procedure for the rapid synthesis of new 2-aryl-5-methyl-2, 3-dihydro-(1H)-3-pyrazolones in water and assessment of their antitubercular properties. 2011. *Eur J Med Chem* 46: 4530–4536.
- [17]. Jones LH, Barba O. Pyrazole derivatives as inhibitors of reverse transcriptase. 8 April 2004; WO Patent 029042 A1. Nakagawa H, Ohyama R, Suzuki T, Kimata A, and Miyata
- [18]. Edaravone derivatives effectively scavenge hydroxyl radicals through 3-methyl-1-(pyridine-2-yl)-5-pyrazolone, which has an intramolecular base. 2006; 16: 5939–5942 in *Bioorg Med Chem Lett*.
- [19]. Heng MP, Teoh WY, Sim KS, Tan KW, Lee SK, Lo KM, Chew ST. 2014. Topoisomerase inhibition and cytotoxicity studies of copper complexes with phosphonium-containing hydrazone ligand. 76:397–407, *European Journal of Medicinal Chemistry*.
- [20]. Senkardes S, Atalay R, Kucukguzel SG, Basu NK, Durmaz I, Manvar D, Basu A, and Durmaz I. 2016. Create New Diflunisal Hydrazone Hydrazones as Hepatocellular Carcinoma Inhibitors and Anti-Hepatitis C Virus Agents. 108:301-308, *European Journal of Medicinal Chemistry*.
- [21]. Popiolek L, Malm A, Stefanska J, Musik I, Biernasiuk A, Kielczykowska M, Wujec M. (2016). Dissociation constants, antibacterial activity, and synthesis of new compounds of 2,3-disubstituted-1,3-thiazolidin-4-one. 53:393–402 in *Journal of Heterocyclic Chemistry*.
- [22]. Popiolek L, Malm A, Biernasiuk A. (2016). New Furan/Thiophene-1,3-Benzothiazin-4-one hybrids: design, synthesis, and in vitro antibacterial efficacy. 53:479–486 in *Journal of Heterocyclic Chemistry*.
- [23]. Munoz-Davila MJ. (2014). Antibiotic Resistance and the Use of Antiquated Antibiotics. Emphasized the Use of Nitrofurantoin to Treat Infections in the Lower Urinary Tract. *Medicines*, 3:39–48.
- [24]. Nasr T, Bondock S, Youns M, Eur J. 2014. New coumarin substituted hydrazone-hydrazone derivatives: anticancer activity. 76:539–548 in the *European Journal of Medicinal Chemistry*.