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Azo Compounds and their Potential Applications: Article Review

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Keywords: Azo Dyes, Diazo Coupling Reactions, Anti-Bacterial, Anti-Cancer, Anti-Tuberculosis, Anti-Viral, Material Science.

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Abstract:

A review of the existing body of literature about azo compounds and their practical applications. Azo compounds, which include a (-N=N-) group, serve as the fundamental structure for several produced compounds in different fields of chemistry, particularly coordination chemistry. These compounds are extensively utilized as coloring agents, as they account for around fifty percent of synthetic colors. Azo compounds are a significant class of chemicals with different applications in various fields of life. Due to the wide variety of their applications, it is essential to possess different synthesis techniques in order to get new azo derivatives with high yields. The main viable techniques for synthesizing azo compounds are diazotization and azo coupling reactions. Azo compounds have diverse uses in areas including anticancer, antifungal, antioxidant, anti-inflammatory, and anti-bacterial activities. In addition, it has several additional uses such as coloring fiber, printing systems, photo-electronics, polymer additives, and storage, and providing resistance to solvents, water, light, and weather.

Keywords: Azo Dyes, Diazo Coupling Reactions, Anti-Bacterial, Anti-Cancer, Anti-Tuberculosis, Anti-Viral, Material Science.

مركبات الآزو وتطبيقاتها المحتملة: مقالة مراجعة

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الخلاصة:

تتضمن هذهِ المقالة مراجعة للأدبيات الموجودة حول مركبات الآزو واستخداماتها العملية. تعمل مركبات الآزو، والتي تتضمن مجموعة *(-N=N-)*، بمثابة البنية الأساسية للعديد من المركبات المنتجة في مجالات مختلفة من الكيمياء، وخاصة الكيمياء التناسقية. وتستخدم هذه المركبات على نطاق واسع كعوامل تلوين، حيث إنها تمثل حوالي خمسين بالمائة من الألوان الاصطناعية. مركبات الآزو هي فئة مهمة من المواد الكيميائية ذات تطبيقات مختلفة في مختلف مجالات الحياة. ونظرًا للتنوع الكبير في التطبيقات، فمن الضروري امتلاك تقنيات تركيبية مختلفة للحصول على مشتقات آزو جديدة ذات إنتاجية عالية. التقنيات الرئيسية القابلة للتطبيق لتصنيع مركبات الآزو هي تفاعلات اقتران الآزو. تتمتع مركبات الآزو باستخدامات متنوعة في مجالات تشمل الأنشطة المضادة للسرطان والفطريات ومضادات الأكسدة والمضادة للالتهابات والمضادة للبكتريا بالإضافة إلى ذلك، له عدة استخدامات إضافية مثل تلوين الألياف، وأنظمة الطباعة، والإلكترونيات الضوئية، وإضافات البوليمر، والتخزين، وتوفير مقاومة للمذيبات، والماء والضوء والطقس.

الكلمات المفتاحية: أصباغ الآزو، تفاعلات اقتران داي ازو، مضاد للبكتيريا، مضاد للسرطان، مضاد للسل، مضاد للفيروسات، علم المواد.

1. Introduction:

Azo compounds exhibit distinct color features because they have a chromophore group (-N=N-) attached to aromatic or heterocyclic systems. [1]. Azo days contain at least one nitrogen-nitrogen double bond, and they can exist in various structural forms [2]. Azo dyes, being widely used in numerous industries, are the oldest and broadest category of industrially manufactured organic dyes [3]. Their applications in coloring fabrics, leather, paper, food, and cosmetic items [4], [5], as well as their applications in biomedical research as well as studies [6]. Furthermore, it found use in the most advanced fields including laser technology photodynamic treatment [7], and dye-sensitized solar cells [8]. Diazotization and coupling reactions are two easy methods for producing these dyes. To increase the dispersibility of the dye, several approaches and modifications are utilized to achieve the required color properties, income, and particle dimensions [9]. Azo dyes are the most prevalent category of dyes, comprising almost 60% of the overall dye composition [10]. Azo dyes constitute nearly 70 percent of the dyes used in the industrial sector [11]. The azo group, represented by the chemical

formula N=N-, is a chromophore group that gives color to azo dyes. Azo dyes can include a single or several auxochromic groups, which are functional groups [12]. Azo dyes could exhibit an enormous variety of colors, including yellow, orange, red, blue, and green. The two nitrogen atoms have a double bond that allows light in the visible spectrum to be absorbed, which is what gives the color, namely wavelengths ranging from 400 to 750 nm [13].

2- Material and Methods:

2.1 General Properties of Azo Compounds: The presence of the -N=N- functional group is indicative of the presence of azo compounds [14]:

- The structures of aromatic azo compounds are more stable than those of compounds with alkyl groups because the R groups in these compounds are arene rings.
- This occurs because the arene groups and the (-N=N-) group form an extended delocalized system.
- The aromatic azo groups are typically employed as dyes due to their high color intensity.
- A diazonium salt and a coupling agent undergo a coupling reaction to produce aromatic azo compounds.

2.2 Types of Azo Compounds: Azo chromophores are a distinct category of organic substances that function as colorants. Their basic structural framework is characterized by the absence of azo groups. The presence of two azo groups is referred to (bis-azo). Compound 2, specifically known as 6-hydroxy-1,4-dimethyl-2-oxo-5-((4 (phenyldiazenyl) phenyl) diazenyl)-1,2-dihydropyridine-3-carbonitrile, has two fundamental azo structures. Occasionally, there might be three groups (tris-azo), four groups (tetrakis-azo), or even more (poly-azo) under certain circumstances, but this occurrence is rare. See (**Figure 1**) [15].

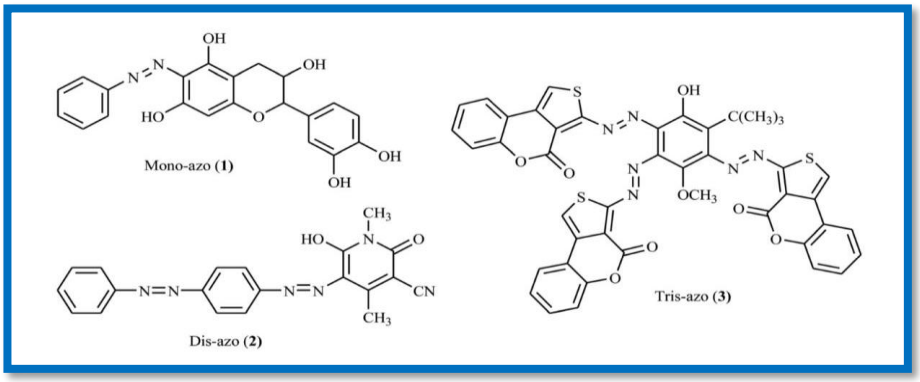
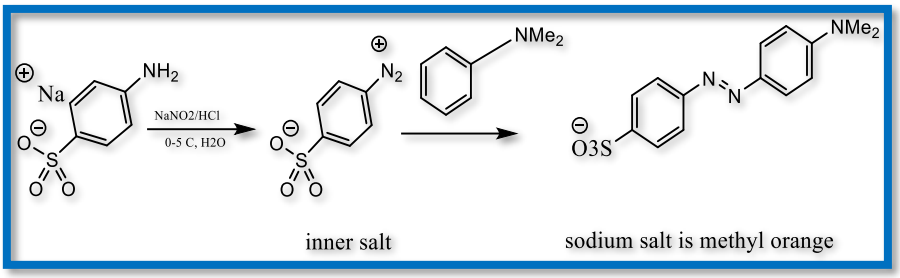


Figure 1: Chemical structures of azo dyes with different numbers of azo groups [15]

2.3 Diazo Coupling Reactions:

- In a diazo coupling reaction, the doazonium salt reacts with an additional arene to form a coupling agent.
- The coupling agent's benzene ring undergoes a reaction with the diazonium salt, which functions as an electrophile.

- When a frigid solution of diazonium salt is added to a solution containing the coupling agent, a colored precipitate of an azo compound is generated; several of these compounds are used as dyes.
- Usually, the coupling agent works in one of the Benzene Ring's two or four locations (the functional group is located in position four).
- The color of the chemical produced is contingent upon the coupling agent that is being reacted with the diazonium salt, **Scheme1 [16]**.



Scheme 1: Diazo coupling reaction

2.4: Applications for Azo Dyes: Azo dyes are commonly utilized in several sectors like textile, fiber, cosmetics, leather, paint, and printing. Azo compounds have been shown to possess antibacterial, antiviral, anti-fungal, and cytotoxic properties, in addition to their involvement in coloring (**Figure 2**) **[17]**.

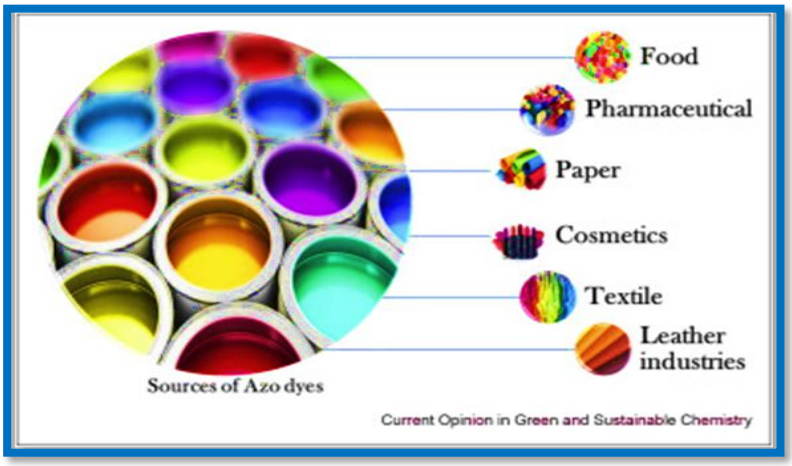


Figure 2: Applications of azo dyes [17]

They possess the ability to act as drug carriers **[18]**. (**Figure 3**) may function as a carrier that captures therapeutic substances or can use a prodrug approach. The administration of the medication is triggered by either internal or external stimuli specifically inside the area of interest, as shown in colon-targeted drug delivery. Furthermore, certain azo dyes are used in cellular staining to examine cellular components and metabolic processes, in addition to their drug-like qualities and the ability to act as drug carriers (**Figure 4**) **[19]**.

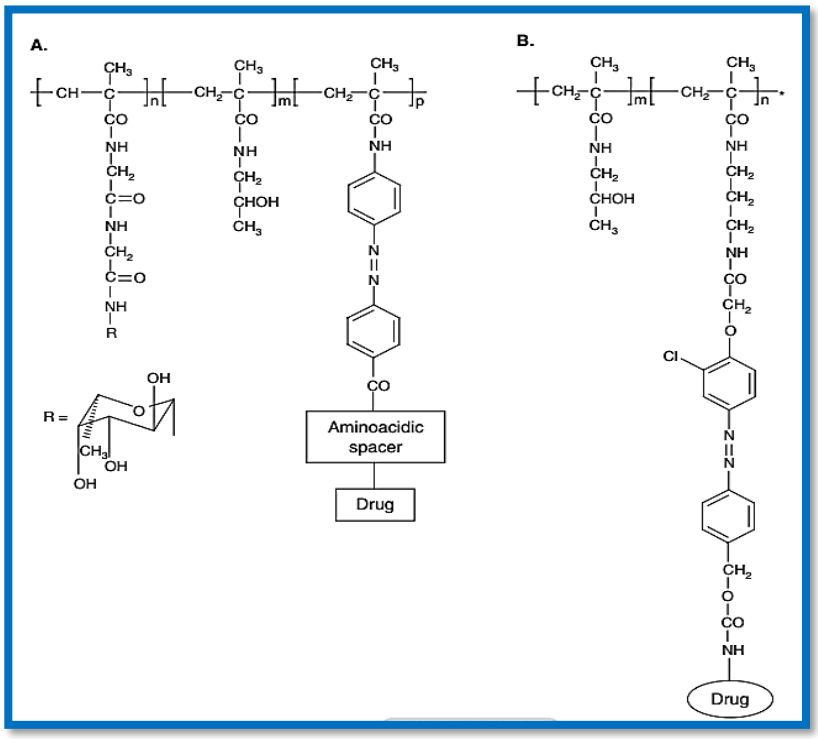


Figure 3: Structures Of Bioadhesive, Colon-Specifi C Hydroxypropyl Ethacrylamide Copolymers Containing: A.An Aminoacid Spacer, And B.A Self-Eliminating Group [18]

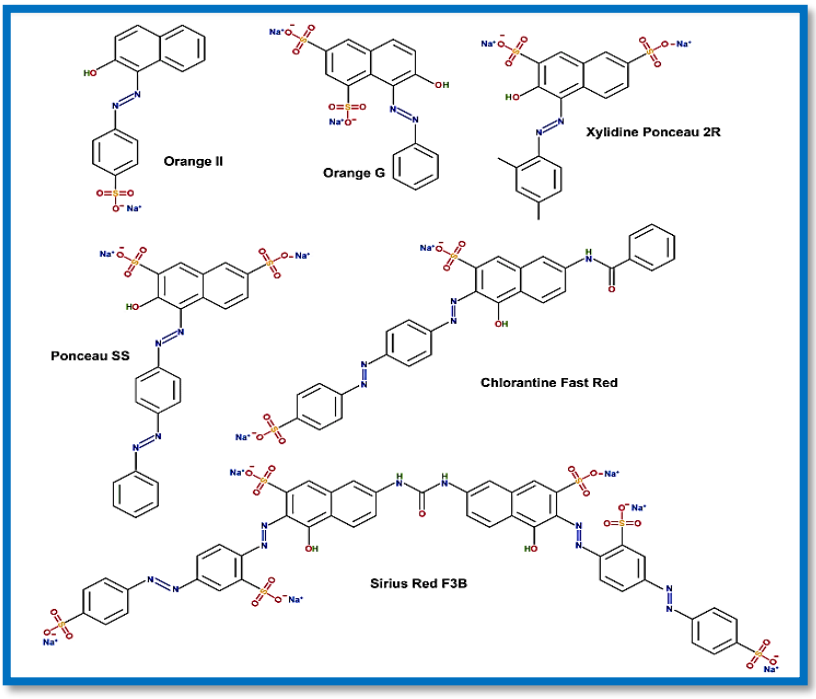


Figure 4: Examples Of Sulfonated Azo Dyes That Are Frequently Used to Stain Proteins [19]

Nevertheless, the biological role of azo compounds, specifically in the field of chemotherapy for cancer, is still in its early stage of development. These findings may be linked to the first discovery that revealed azo compounds as possible factors in the development of cancer and mutagenesis. Presently, scientists are investigating aromatic azo compounds to evaluate their

potential in the realm of biomedicine, namely for the purposes of cancer diagnostics and treatment [20]. Generally, due to the extensive potential of heterocycle-containing azo dye bk derivatives in pharmaceutical and drug research, there is still a lack of sufficient information on their usage [21]. Currently, there is a significant focus on the generation of azo dyes and their derived compounds that include heterocycles. The reason for this is that these compounds have shown potent biological activity, like chemosensing properties, analgesic properties, antibacterial, antifungal, antiviral, anticonvulsant, anti-diabetic, anti-inflammatory, anti-tubercular, and anticancer DNA binding properties. Herein, we show an overview of the production of several azo dyes and their by-products including heterocycles. Additionally, we discuss their potential medicinal characteristics (Figure 5) [22].

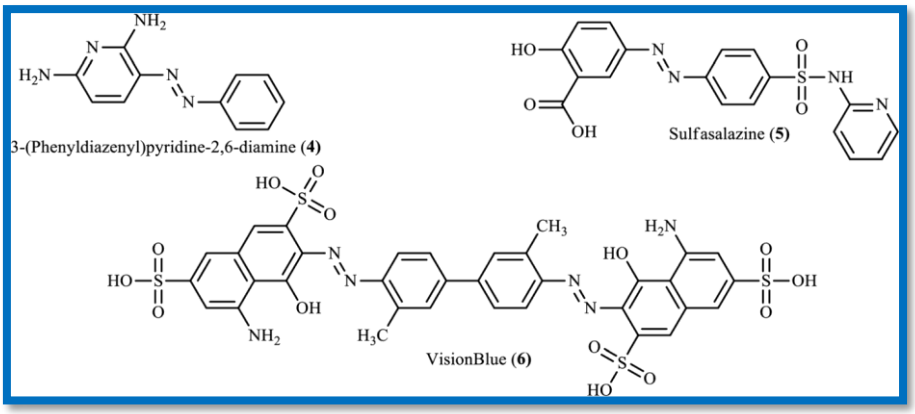


Figure 5: Chemical structures of azo-based drugs [22]

2.5 Food Industries: Azo dyes provide around seventy percent of all organic dyes produced worldwide, making them the biggest class of synthetic food colors [23, 24]. Furthermore, it has been shown that the yellow dyes (tartrazine and sunset yellow) and red dyes (azorubine, ponceau, amaranth, and Allura red) are the most widely used azo dyes in the food business. They are often added to jams, candies, confections, ice cream, jellies, alcoholic beverages, soft drinks, and other goods of a similar kind to provide color. Although widely used, several investigations have identified specific adverse effects on human health. There is sufficient evidence indicating that the decomposition of azo dyes produces toxic and carcinogenic compounds, such as aromatic amines. The relationships between azo dyes, hemoglobin, and human serum albumin have been verified by recent studies [25, 26]. According to some studies, youngsters who use artificial food coloring may become more stimulated and active, particularly if they use it often. Moreover, they could have the potential to lead to the development of asthma and allergy conditions. Therefore, it is crucial to regulate the levels of azo compounds in food products (Figure 6) [27].

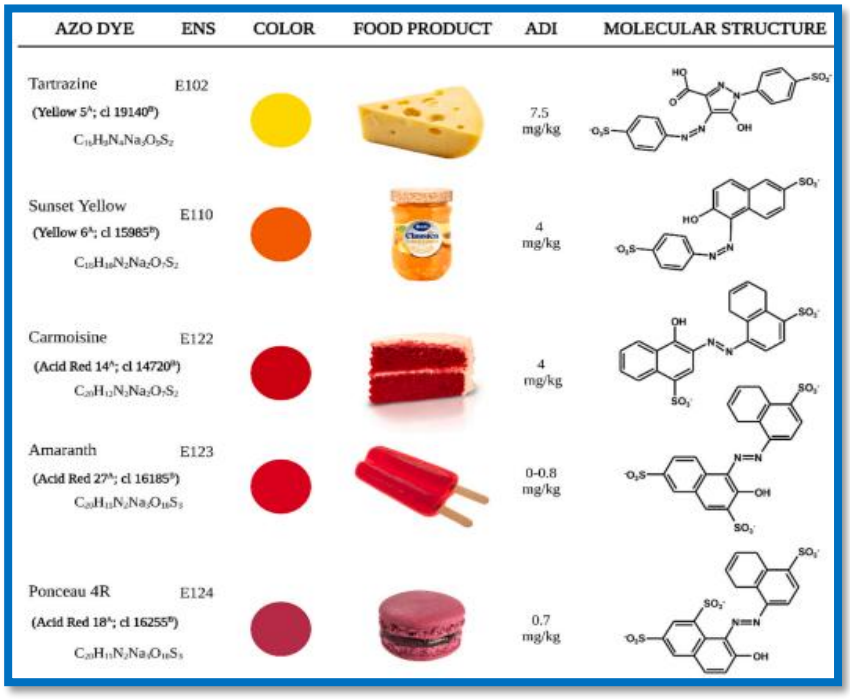


Figure 6: Features Of the Azo Compounds Most Utilized in The Food Industrial [27]

2.6 Textile of Azo Dyes: Approximately four decades ago, the pigment known as indigo was discovered under the wrappings of mummified bodies within Egyptian tombs, marking the first occurrence of an organic colorant. Every year, the globe produces more than 7,107 tons of dyestuff, and there are over 100,000 dyes that are available for purchase. Among the many uses for these dyes, the textile sector accounts for the lion's share, followed by the food and cosmetics industries, and paper printing **[28]**. Synthetic organic dyes, including processing dyes, reactive dyes, and direct dyes, are now the mainstay of the textile industry. The term "natural dye" encompasses any colorant derived from elements found in nature, including but not limited to plants, animals, and minerals. In order to apply non-substantive natural dyes to textiles, it is necessary to utilize mordants, which are usually metallic salts. These mordants exhibit a strong attraction to both the dye and the fiber **[29]**. The textile processing industries are the primary users of synthetic dyes, which are widely employed in other sectors. (**Figure 7**) **[30]**.

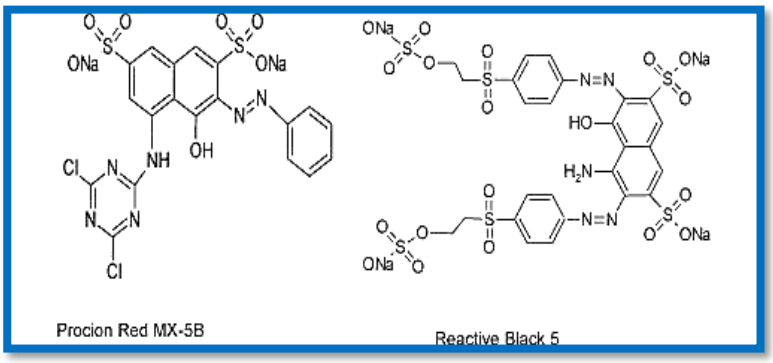


Figure 7: Azo Dyes in Textile Industry [30]

Perkin was a trailblazer in the production of synthetic organic dye, namely mauve, as far back as 1856. In 1871, Wolfe created the first synthetic organic dye by using nitric acid to process the natural color indigo, resulting in the production of picric acid. Since then, a plethora of other chemical dyes have been included in the ever-growing collection of dyes [31]. The textile sector utilizes around 70 percent of all dyestuffs. When dying or printing on cotton, you must use reactive dyes, vat dyes, or azo dyes. At approximately 21% of the total, disperse dyes make up the biggest category in the industry. There is a 16 percent share for direct dyes and an 11 percent share for reactive dyes in the market. One common way to categorize textile dyes is by the chemicals they contain, but another is by the many purposes they have in the textile industry (**Figure 8**) [32].

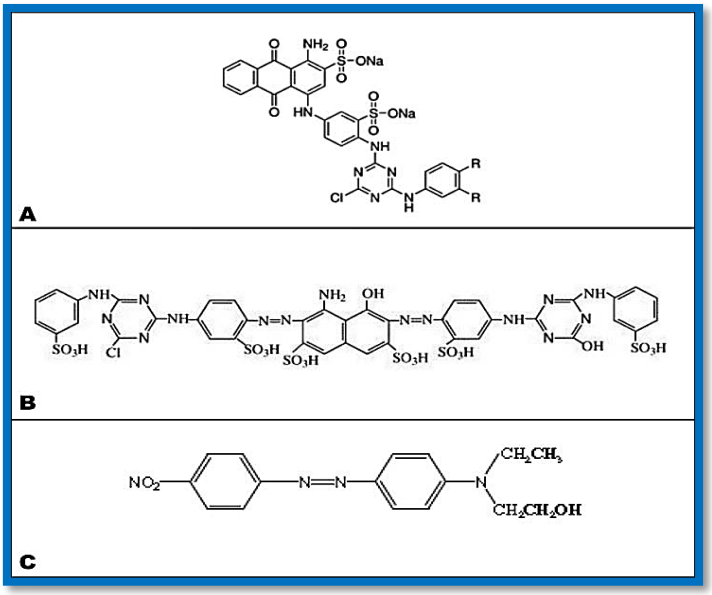


Figure 8: The chemical compositions of the textile dyes that were investigated are as follows: (A) reactive blue 2 (anthraquinone dye); (B) reactive green 19 (azo dye); (C) diffuse red 1 (azo dye) [32]

2.7 Azo Dyes in Material Science: Azo dyes possess high photosensitivity and demonstrate both linear and nonlinear optical characteristics. These properties are utilized in the development of optical storage devices, semiconductors, photovoltaic cells [33], holographic recording using azo dye-doped polymers [34], optical computing [35], and dye-sensitized solar cells [36]. Researchers Asif et al, conducted a study on five azo dyes, namely Direct Red 111, Acid Orange 5, Food Yellow 6, Metanil Yellow, and Acid Orange 61. Their electrical and nonlinear optical characteristics were determined using DFT. They exhibited three clearly differentiated categories of azo dye: two with an acidic nature and one with an alkaline nature. The introduction of a proton to the dye greatly amplifies the nonlinear optical response. It is crucial that optical characteristics not be linear for optical data processing devices, modulators, ultra-fast optical switches, sensors, and high-density optical storage systems [37]. The great

optical and thermal properties, together with the excellent photosensitivity and photo-isomerization capabilities, of azo dyes have led to their usage in recording devices and high-density optical storage [38]. Azo dyes possess desirable optical, thermal, and electrical characteristics, making them appealing for use in dye-sensitized solar cells (DSSCs). Additionally, they exhibit robust chemical stability. Azo DSSCs have higher priority over standard semiconductor photovoltaic cells because they are more cost-effective, readily accessible, and exhibit greater efficiency. When an azo dye molecule is excited, it undergoes oxidation, which increases its conductivity by bringing one electron into the conduction band. The electrolyte's iodide content makes it easier for electrons to get through, which oxidizes the dye molecule. The oxidized dye molecule is then restored to its initial form by reduction by triiodide [39]. Louis et al, have examined C.I. Disperse Yellow 56 (DA, DB, DC), a commercially available dye, and two mono azo dyes derived from 1-nitroso-2- and 2-nitroso-1-naphthol (**Figure 9**). The optical properties, energy band gaps, and charge transfer electron excitation of these dyes were the primary areas of investigation in the research. According to the findings, the excited state of the dyes resides above TiO_2's conduction band and has the potential to swiftly introduce electrons into the semiconductor. To get the best possible photocurrent response, the chosen molecules must have high light-harvesting efficiency (LHE). The best result (0.7308 for dye DC) is shown by acetone. The results of this study, the dyes exhibit favorable characteristics and might potentially be used as photosensitizers in DSSC [40]. In DSSC devices, azo dyes have shown very high conversion efficiencies. Because of their high molar extinction coefficient, ease of synthesis, and lack of environmental effect, these dyes have various benefits over other photosensitive compounds. They also include an azo (-N = N-) chromophore [40].

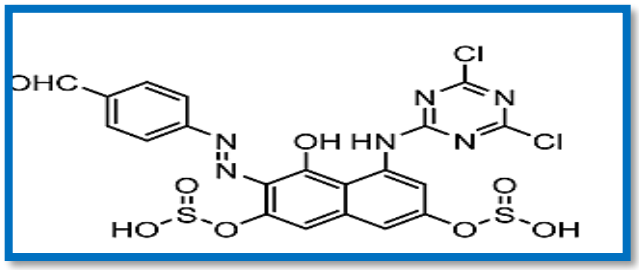


Figure 9: Azonitrobenzaldehyde Derivatives [40]

2.8 Antibacterial Azo Dyes: Antimicrobial efficacy, which involves combating microorganisms and inhibiting their growth, depends entirely on the presence of chemicals that accomplish this discreetly and without causing substantial harm to surrounding tissues. Antimicrobial compounds may be classified as either bactericidal or bacteriostatic, based on whether they have the ability to kill bacteria or only inhibit their growth. The increasing

resistance of germs to antibacterial treatments is causing significant health consequences. This problem motivates research aimed at identifying new chemicals that can efficiently inhibit bacterial growth. Azo dyes exhibit strong antibacterial efficacy and can either kill or prevent the growth of microorganisms, making them bactericidal or bacteriostatic, respectively, through their specific mechanisms of action **[41]**. Studying the in-vitro antibacterial properties of oxazolone azo dyes against certain gram-negative and gram-positive bacteria, Fawzia et al, examined Streptococcus pneumoniae, Bacillus subtilis, Pseudomonas aeruginosa, and Escherichia coli. As standards, Ampicillin and Gentamicin were used in the agar diffusion technique to determine various amounts. When contrasted with the reference medications, the findings demonstrated that the dyes showed encouraging promise. The investigation revealed that the oxazolone azo chromophore derivatives were effective against both gram-positive and gram-negative bacteria, with moderate to high efficiency against Streptococcus pneumonia and Bacillus subtilis, respectively. On the other hand, gram-negative bacteria, such as Pseudomonas aeruginosa, were not effectively combatted by them **[42]**. These creative azo dyes, namely 3-[(E)-(4-hydroxyquinolin-5-yl) diazenyl], were developed by Shoukat et al. Its molecular formula is 4-[(E)-(4-hydroxyquinolin-5-yl) diazenyl]-4-methylbenzoic acid-(a).6-Methoxybenzoic acid-(b) is the name of the chemical. Diazenyl, 4-[(E)-(4-hydroxyquinolin-5-yl)] \ Trimethylbenzoic acid-(c),5-[(E)-(4-hydroxyquinolin-5-yl) diazenyl is the chemical name of the substance. A combination of amino-methylbenzoic acid and 8-hydroxy quinoline is used to create 2-methylbenzoic acid-(d). Using the disk diffusion technique and Amoxycillin as the reference medication, the antibacterial activity of the azo dyes is next evaluated against Pseudomonas Aureus and Streptococcus Aureus. Furthermore, their ability to inhibit the growth of Fusareum Oxyporum is assessed by means of the cup plate technique, with fluconazole serving as the reference antifungal medication. The outstanding antimicrobial capabilities and accessible availability of azo dyes make them a preferred ingredient in compounds with antibacterial and antifungal properties. On top of that, they are inexpensive and easy to prepare (**Figure 10**) **[43]**.

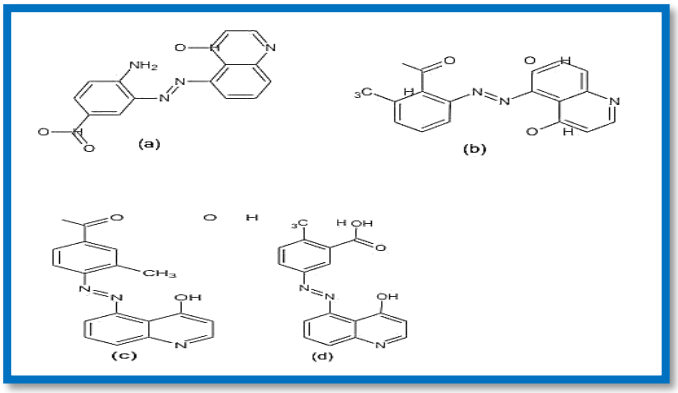


Figure 10: Amino-Methyl Benzoic Acid Derived Azo Dyes [43]

2.9 Antiviral Azo Dyes: The development of antiviral treatment is challenging due to the fact that viruses are intracellular parasites that depend on their hosts for energy, machinery for macromolecular synthesis, and workstations for genome replication and particle assembly **[44]**. There are two main methods for developing antiviral drugs: one is to focus on the elements of the host cell, while the other is to directly target the viruses. Antiviral drugs that specifically target viruses include uncoating inhibitors, polymerase inhibitors, protease inhibitors, nucleoside and nucleotide reverse transcriptase inhibitors, and integrase inhibitors. A plethora of therapies have been devised to counteract herpes viruses, and influenza, as well as innovative antiviral drugs for the control of hepatitis C infection and HIV. Experimental research has shown that azo dye has promise as a prospective antiviral treatment. Its mechanism of action involves the suppression of pathogen proliferation, interference with protein production, and prevention of viral attachment to host cells (**Figure 11**) **[45]**.

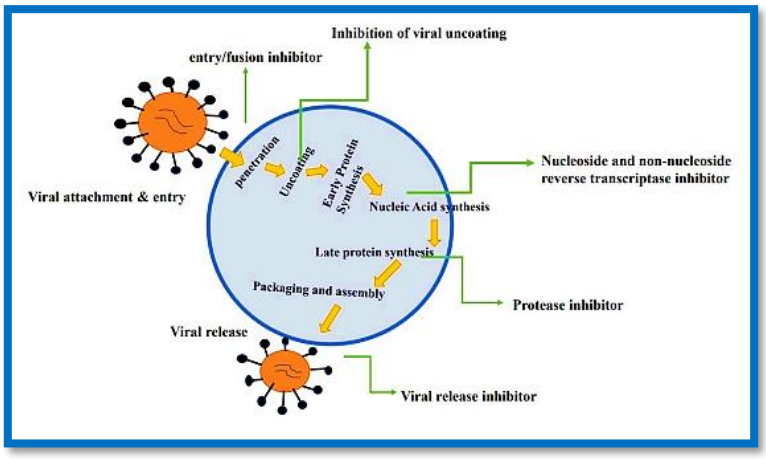
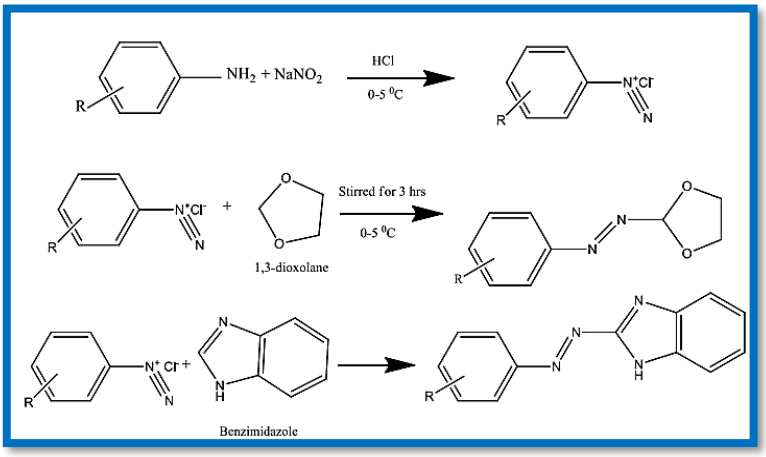


Figure 11: General Antiviral Action of Mechanism [45]

Research on human enteroviruses, including EV71, CVA16, and CVA6, was carried out by Meng et al. The primary focus of the research was to determine whether or not brilliant black bn, a sulfonated food azo dye, might limit the infection of these viruses in both laboratory and in vivo conditions. Among children in particular, these human viruses are very contagious and cause hand, foot, and mouth illness. Scientists have discovered that several sulfonated azo dyes, which are often added to food, have potent antiviral properties when tested against human enteroviruses. The capacity to efficiently inhibit all tested strains of CVA16, CVA6, and EV71 was proven by brilliant black BN (E151) and others. E151 and other azo dyes used in food prevented the virus from entering. The release of related viruses was dose-dependent, and dye E151 reduced the binding of EV71. An essential component of the virus's uncoating process, E151 blocked the interaction between EV71 and cyclophilin A. Animal studies shown that AG129 mice were protected against EV71 isolates 10 times the fatal dose when given E151 at

a dosage of 200 mg/kg body weight daily during the first four days of the trial. Taken as a whole, these findings suggest that E151 may effectively combat EV71 infections. The study focused on the synthesis compounds of the azo series (**Scheme 2**) **[46]**.

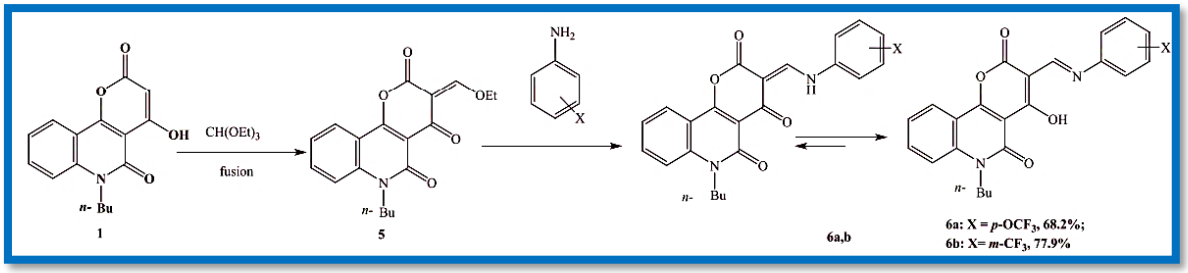


Scheme 2. Synthesis scheme of azo compounds A1-A5

Diazonium salt solutions were coupled with active methylene compounds (1,3-dioxolane and benzimidazole) to produce the compounds listed in the title. This reaction resulted in the formation of [(E)-1-(1,3-dioxolan-2-yl)-2-phenyldiazene] (A1), [(E)-1-(1,3-dioxolan-2-yl)-2-(4-methyl-phenyl)diazene](A2), 2-[(E)-phenyldiazenyl]-1H-benzimidazole](A3), [(E)-1-(1,3-dioxolan-2-yl)-2-(4-ethylphenyl) diazene](A4), and [(E)-1-(1,3-dioxolan-2-yl)-2-(2 methylphenyl)diazene] (A5). Utilizing spectroscopic methods, particularly electron ionization mass spectrometry (EI-MS) and Fourier transform infrared spectroscopy (FT-IR), the molecular structures of the recently produced substances were ascertained. In vivo techniques were used to test compounds against the H9N2 strain of avian influenza and the Lasota strain of Newcastle disease. At a concentration of 0.1 mg/100 µL, the assessment results showed that azo dyes A5 had the strongest anti-NDV and anti-AIV action. Alternatively, when tested at the same doses, the other azo compounds showed reduced activity **[47]**.

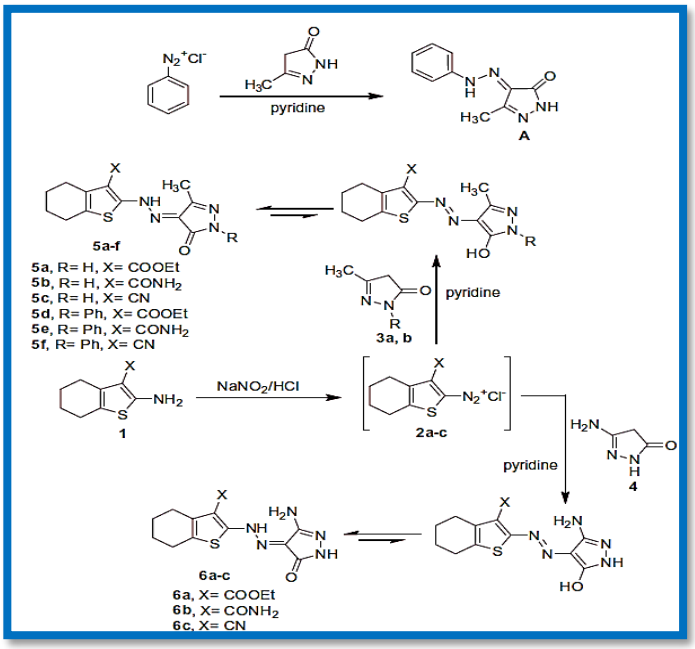
2.10 Antitumoral and Anticancer Azo Dyes: Cancer and tumors arise due to abnormal proliferation of cells. Chemotherapy, a commonly used cancer therapy, is cytotoxic and works by inhibiting the growth of cancer cells. Azo dyes have been shown to exhibit cytotoxicity and possess anticancer effects. In vitro, assays are performed to evaluate the antitumoral properties of azo dyes and determine their effectiveness and potential in suppressing tumor growth. This is achieved by reducing the synthesis of DNA, RNA, and proteins inside the cells **[48]**. Conventional procedures were used to synthesize a set of novel azo dye derivatives (**Scheme 3**) using pyrano-quinolinone as the initial substance. The synthesized compounds underwent spectral analysis to determine their chemical properties and were then tested for their anticancer

effects on many human tumor cell lines, examples of cancer cell lines are HepG2 for liver cancer, HCT-116 for colon carcinoma, and MCF-7 for breast cancer. 5-fluorouracil served as a reference medication. The in vitro cytotoxicity screening findings showed that all of the substances tested had significant action against MCF-7 cells. Compounds 6a and 6b have shown exceptional efficacy against three different types of human tumor cell lines **[49]**.



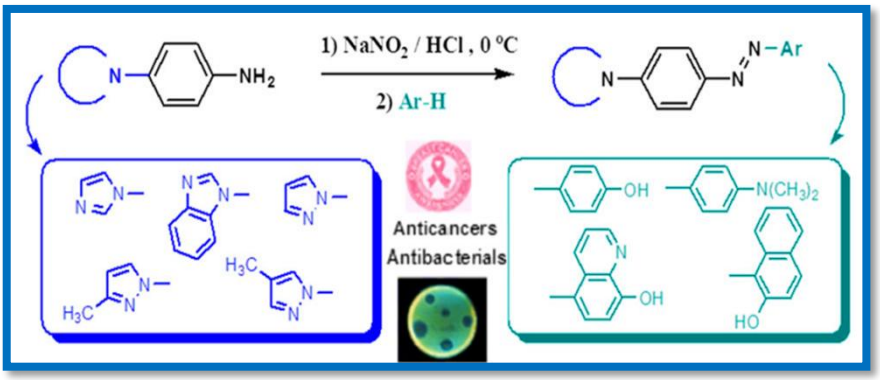
Scheme 3: Synthesis of Compounds 6a, b

The diazo coupling of diazonium salts of 3-substituted-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophenes 1a-c with 3-methyl-1H pyrazol-5(4H)-one, 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one, or 3-amino-1H-pyrazol-5(4H)-one, respectively, was used to synthesize a series of thiophenes 5a-f and 6a-c that incorporate pyrazolone moieties. The color measurements and fastness qualities of recently synthesized dyes were evaluated when applied as dispersion dyes on polyester fabric. When compared to aniline-based azo dyes, they have a high extinction coefficient and a color shift from red to blue. The synthesized colors were tested for their anticancer effects. Compounds 5c and 5d exhibited a moderate degree of activity, whereas the bulk of them showed good activity, according to the data. (**Scheme 4**) **[50]**.



Scheme 4: Preparation of substituted-4- {2- [(or 3-phenyl-)4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl] hydrazono} Derivatives 5 and 6 of -1H-pyrazol-5(4H)-one

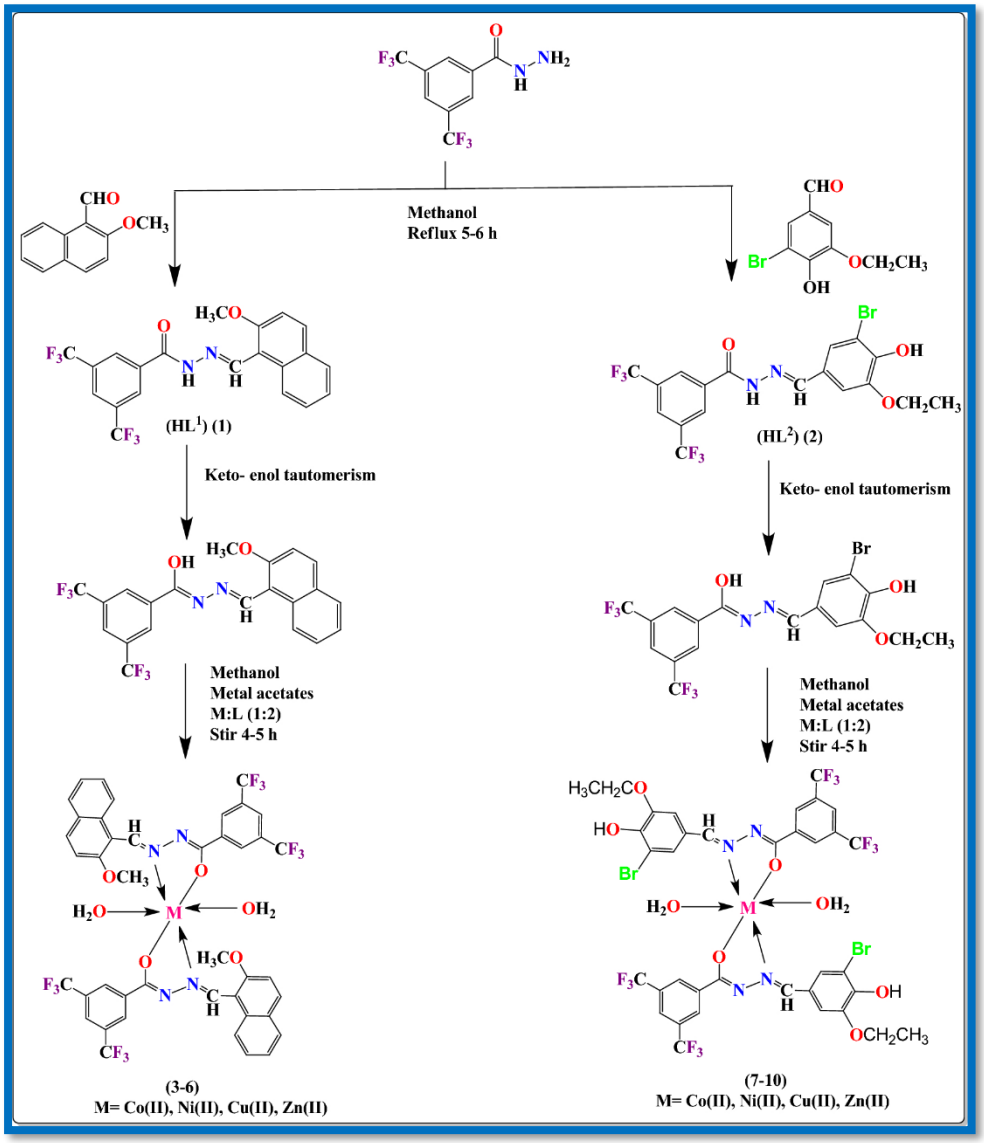
Abdalla et al, achieved research on the biological activity of new chelates made from sulfamerazine-resorcinol azo-dye. These chelates were either mono- or homo-bi-nuclear in structure. The chelates were produced by the reaction between sulfamerazine diazonium salt and resorcinol. The investigation revealed that these compounds had potent antibacterial and antitumoral properties, particularly when they formed complexes with anticancer drugs. Out of all the produced complexes, the Ni (II) molecule showed notable promise in suppressing the development of human liver cancer, as assessed in the study **[51]**. By using $NaNO_2$/HCl, a diazotization procedure was carried out on a series of 4-(1-azolyl) aniline derivatives that included azole groups such as benzimidazole, 3-methylpyrazole,4-methylpyrazole, pyrazole, and imidazole. A series of aromatic molecules, including N, N-dimethylaniline, 2-naphthol, 8-hydroxyquinoline, and phenol, were further reacted with the diazonium salts to get the related azo compounds. Some of the items were tested for their antibacterial activity against both Gram-positive (Staphylococcus aureus, ATCC 25923) and Gram-negative (Escherichia coli, ATCC 25922) bacteria. Additionally, they exhibited anticancer characteristics against MCF7 breast cancer cells in laboratory tests performed on a variety of items (**Scheme 5**) **[52]**.



Scheme 5: Steps For Preparation of Azo Derivatives

2.11 Antituberculosis Azo Dye: Tuberculosis is an extremely perilous illness that presents a significant global challenge. Thus, in order to identify a potent medication, the process of synthesizing hydrazone ligands and forming metal complexes with Co (II), Ni (II), Cu (II), and Zn (II) were conducted. These compounds were extensively examined utilizing a variety of spectroscopic and analytical methods. The confirmation of the geometry octahedral of the complexes was achieved via spectrum analysis. In addition, the compounds (1-10) were tested for their effectiveness in controlling tuberculosis (TB) formation in a laboratory setting. The results showed that complexes (6), (9), and (10) had the highest potency, with a MIC value ranging from 0.0028 ± 0.0013 to 0.0063 ± 0.0013 µmol/mL. Among these complexes, the Zn(II) complex (10) was particularly effective, with a MIC value of 0.0028 ± 0.0013 µmol/mL.

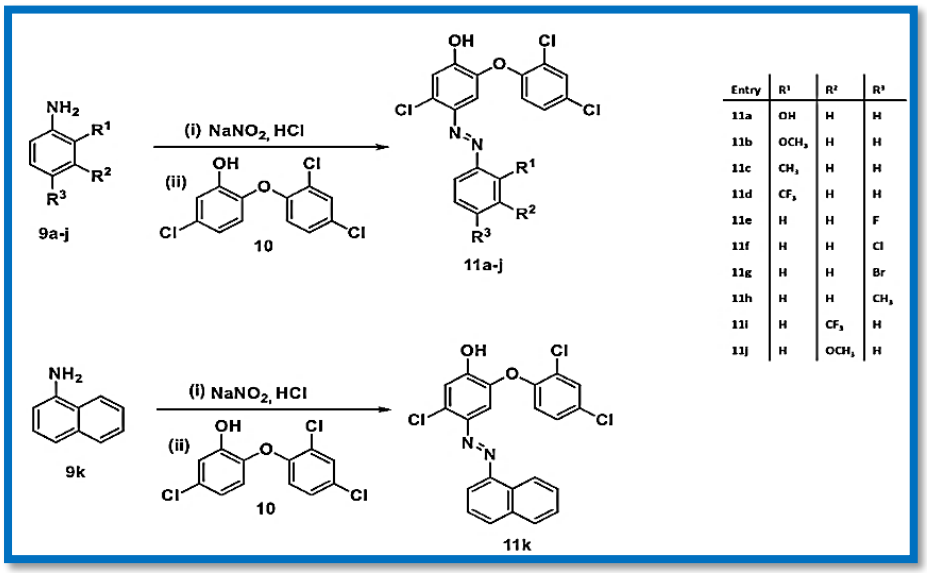
In fact, it was nearly four times more effective in suppressing TB disease compared to streptomycin, which had a MIC value of 0.0107 ± 0.0011 µmol/mL. The antibacterial and anti-inflammatory evaluations demonstrated that the complex (10) exhibited higher activity, as shown by its lowest MIC (0.0057–0.0114 µmol/mL) and IC50 (7.14 ± 0.05 µM) values, which are equivalent to those of the standard medicines (**Scheme 6**) **[53]**.



Scheme 6: Synthesis of (HL^1–HL^2) hydrazone ligands (1–2) and their transition metal complexes (3–10)

A study was done to evaluate the connections among the structure and activity of several triclosan azo-adducts against both Mycobacterium TB and non-tuberculous mycobacteria. The most potent molecule in the series had activity that was fourfold higher than triclosan and sixteenfold higher than rifabutin against drug-resistant Mycobacterium abscessus. Furthermore, this chemical exhibited lower toxicity towards human macrophages compared to triclosan on the first day. Furthermore, one of the azo-adducts demonstrated a twofold increase in potency

against M. tuberculosis in comparison to triclosan, and a twofold increase in efficiency against Mycobacterium marinum in comparison to isoniazid. Furthermore, the synthesized azo-adducts have shown comparable efficacy against M. abscessus strains that exhibit overexpression of InhA. This implies that these chemicals operate via a distinct mechanism, as shown in **Scheme 7 [54]**.



Scheme 7: Synthesis of TCS azo-adducts 11a-k

The pharmacological activity of a set of azo dyes (C1-C5) generated from benzothiazole was evaluated against Mycobacterium TB. The efficacy of colors (C1-C5) against Mycobacterium TB (H37 RV strain) was assessed using the microplate Alamar Blue Assay (MABA) technique. The findings were compared to those obtained with the conventional therapy of streptomycin. The results of the anti-TB activity tests show that compounds C1, C2, C3, and C5 showed comparable sensitivity to the standard streptomycin (MIC = 6.24 g/mL) and also showed significant sensitivity (MIC = 1.6 g/mL). Compound C4, a chemically synthesized dye, stands out due to the presence of an ethoxy group at the 6th position of the benzothiazole molecule. The minimal inhibitory concentration (MIC) is 3.2 grams per milliliter (g/mL) (**Figure 12**) **[55]**.

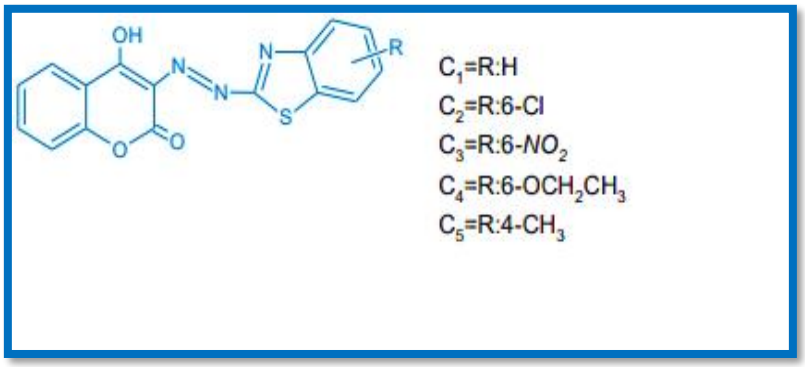


Figure 12: Coumarin-Benzothiazole Based Azo Dyes [55]

3. Conclusions

Azo dyes are now the most produced dye chemistry, and they may become much more significant in the future. Azo dyes are often employed in a wide range of industries, such as the textile, leather, food, pharmaceutical, paper, and cosmetics sectors. They make up around half of all synthetic dyes. Additionally, azo dyes have found the widest use, as seen by the findings in this research, since they are simple to synthesize via the reaction of an azo coupling component that contains atom-active hydrogen bonded to a carbon atom. This reaction is explained by the electron-rich electrophilic aromatic substitution mechanism. About 60% of the synthetic hues created are produced using this method. Azo dyes are substances with intense colors that result from the azo coupling reaction of aromatic amines, phenols, or naphthols with diazonium ions.

4. References

[1] Ferreira I, et al. Seawater as an alternative to dye cotton fiber with reactive dyes. Textile Research Journal, 2020; 91, (9-10): 1184–1193.

[2] Helal T, Abbas J, Mohammed F. Synthesis and Identification of new 4-Amino phenazone derivatives containing azo group. Chemistry, 2014; 2(7).

[3] Mohamed S, Soumaya B, et al. Synthesis, characterization and antimicrobial activity of some new azo dyes derived from 4-hydroxy-6-methyl-2H-pyran-2-one and its dihydro derivative. Dyes and Pigments, 2021; 188: 109073.

[4] Zhi-gang Y, et al. Monoazo dyes based on 5, 10-dihydrophenophosphazine, Part 2: Azo acid dyes. Dyes and Pigments, 2009; (81)2: 137-143.

[5] Zhi-gang, Y, et al. Monoazo dyes based on 5, 10-dihydrophenophosphazine, Part 2: Azo acid dyes. Dyes and Pigments, 2009; (81)2: 137-143.

[6] Chung K. Azo dyes and human health: A review. Journal of Environmental Science and Health, Part C, 2016; (34)4: 233-261.

[7] Piao W, et al. Development of an azo-based photosensitizer activated under mild hypoxia for photodynamic therapy. Journal of the American Chemical Society, 2017; (139)39: 13713-13719.

[8] EL mekkawi D. Abdel-mottaleb M. The interaction and photostability of some xanthenes and selected azo sensitizing dyes with TiO2 nanoparticles. International Journal of Photoenergy, 2005; (7)2: 95-101.

[9] Shankarling G, Deshmukh P, Joglekar A. Process intensification in azo dyes. Journal of environmental chemical engineering, 2017; (5)4: 3302-3308.

[10] Gürses A, et al. Classification of dye and pigments. Dyes and pigments, 2016; 31-45.

[11] Berradi M, et al. Textile finishing dyes and their impact on aquatic environs. Heliyon, 2019; 5(11).

[12] Alsantali R, et al. Miscellaneous azo dyes: a comprehensive review on recent advancements in biological and industrial applications. Dyes and pigments, 2022; 199: 110050.

[13] Fei Na, Sauter B, Gillingham D. The pK a of Brønsted acids controls their reactivity with diazo compounds. Chemical Communications, 2016; 52(47): 7501-7504.

[14] Aljamali N, Rahi D. New Formazan Compounds (Synthesis, Identification, Physical Properties). Journal of Chemical and Pharmaceutical Sciences, 2017; (10)3: 1461-1472.

[15] Benkhaya S, M'rabet S, EL harfi A. Classifications, properties, recent synthesis and applications of azo dyes. Heliyon, 2020; (6)1.

[16] Aljamali, N. Review in azo compounds and its biological activity. Biochem Anal Biochem, 2015; (4)2: 1-4.

[17] Aljamali N. Review in azo compounds and its biological activity. Biochem Anal Biochem, 2015; (4)2: 1-4.

[18] Roldo M, et al. Azo compounds in colon-specific drug delivery. Expert opinion on drug delivery, 2007; (4)5: 547-560.

[19] Mello M, Dos anjos E, De campos B. Usefulness of sulfonated azo dyes to evaluate macromolecularly oriented protein substrates. Acta Histochemica, 2024; (126)3: 152154.

[20] Udoikono A, et al. Reactive azo compounds as a potential chemotherapy drugs in the treatment of malignant glioblastoma (GBM): Experimental and theoretical studies. Journal of Photochemistry and Photobiology, 2022; 10: 100116.

[21] Benkhaya S, M'rabet S, EL harfi A. Classifications, properties, recent synthesis and applications of azo dyes. Heliyon, 2020; (6)1.

[22] Singh K, et al. Insights into the structure activity relationship of nitrogen-containing heterocyclics for the development of antidepressant compounds: An updated review. Journal of Molecular Structure, 2021; 1237: 130369.

[23] Popli S., Patel U. Destruction of azo dyes by anaerobic–aerobic sequential biological treatment: a review. International Journal of Environmental Science and Technology, 2015; (12): 405-420.

[24] Singh P, Singh R. Bio-removal of azo dyes: a review. International Journal of Applied Sciences and Biotechnology, 2017; (5)2: 108-126.

[25] Lipskikh O, et al. Sensors for voltammetric determination of food azo dyes-A critical review. Electrochimica Acta, 2018; 260: 974-985.

[26] Puvaneswari N, Muthukrishnan J, Gunasekaran P. Toxicity assessment and microbial degradation of azo dyes. 2006.

[27] Barciela P, Perez-vazquez A, Prieto M. Azo dyes in the food industry: Features, classification, toxicity, alternatives, and regulation. Food and Chemical Toxicology, 2023; 178: 113935.

[28] Silveira E, et al. Selection of Pseudomonas for industrial textile dyes decolourization. International Biodeterioration & Biodegradation, 2009; (63)2: 230-235.

[29] Samanta A, Agarwal P. Application of natural dyes on textiles. 2009.

[30] Benkhaya S, M'rabet S, EL harfi A. Classifications, properties, recent synthesis and applications of azo dyes. Heliyon, 2020; (6)1.

[31] Mathur N, Bhatnagar P, Bakre P. Assessing mutagenicity of textile dyes from Pali(Rajasthan) using Ames bioassay. Applied ecology and environmental research, 2006; (4)1: 111-118.

[32] Leme D, et al. Genotoxicity assessment of reactive and disperse textile dyes using human dermal equivalent (3D cell culture system). Journal of Toxicology and Environmental Health, Part A, 2015; 7(8)7: 466-480.

[33] Aljamali N, Hassen H. Review on azo-compounds and their applications. Journal of Catalyst & Catalysis, 2021; (8)2: 8-16.

[34] Rahmouni A, et al. Photoassisted holography in azo dye doped polymer films. The Journal of Physical Chemistry B, 2016; (120)43: 11317-11322.

[35] Guru prasad L. Azo dye doped polymer films for nonlinear optical applications. Chinese Journal of Polymer Science, 2014; 32: 650-657.

[36] Derkowska-zielinska B, et al. Photovoltaic cells with various azo dyes as components of the active layer. Solar Energy, 2020; 203: 19-24.

[37] Asif M, et al. Shedding light on the second order nonlinear optical responses of commercially available acidic azo dyes for laser applications. Dyes and Pigments, 2022; 202: 110284.

[38] Madiahlagan E, et al. Synthesis, liquid crystalline properties and photo switching properties of coumarin-azo bearing aliphatic chains: Application in optical storage devices. Journal of Molecular Liquids, 2019; 292: 111328.

[39] Behera A, Sen A. Pyrrole–Best additional spacers for azo based dye sensitized solar cells: A computational study. Journal of Photochemistry and Photobiology A: Chemistry, 2022; 433: 114146.

[40] Odey J, et al. Experimental and theoretical studies of the electrochemical properties of mono azo dyes derived from 2-nitroso-1-naphthol, 1-nitroso-2-naphthol, and CI disperse yellow 56 commercial dye in dye-sensitized solar cell. Journal of Molecular Structure, 2021; 1241: 130615.

[41] Singh K, et al. Antiviral and antimicrobial potentiality of nano drugs. In: Applications of targeted nano drugs and delivery systems. Elsevier, 2019; 343-356.

[42] Albelwi F, et al. Novel oxazolones incorporated azo dye: Design, synthesis photophysical-DFT aspects and antimicrobial assessments with In-silico and In-vitro surveys. Journal of Photochemistry and Photobiology, 2021; 7: 100032.

[43] Prashantha A, Ali R, Keshavayya J. Synthesis, spectral characterization, DFT studies and antimicrobial activities of amino-methylbenzoic acid based azo dyes. Inorganic Chemistry Communications, 2021; 127: 108392.

[44] Khanum R, et al. Recent review on Synthesis, spectral Studies, versatile applications of azo dyes and its metal complexes. Results in Chemistry, 2023; 5: 100890.

[45] Meng T, et al. In vitro and in vivo inhibition of the infectivity of human enterovirus 71 by a sulfonated food azo dye, brilliant black BN. Journal of Virology, 2019; (93)17: 10.1128/jvi. 00061-19.

[46] Meng T, et al. In vitro and in vivo inhibition of the infectivity of human enterovirus 71 by a sulfonated food azo dye, brilliant black BN. Journal of Virology, 2019; (93)17: 10.1128/jvi. 00061-19.

[47] Tahir T, et al. Antiviral evaluation of bioactive azo derivatives to treat endemic poultry viruses. The Thai Journal of Veterinary Medicine, 2020; (50)3: 435-443.

[48] Mbeunkui F, Johann D. Cancer and the tumor microenvironment: a review of an essential relationship. Cancer chemotherapy and pharmacology, 2009; 63: 571-582.

[49] Saeed A, Alneyadi S, Abdou I. Anticancer activity of novel Schiff bases and azo dyes derived from 3-amino-4-hydroxy-2H-pyrano [3, 2-c] quinoline-2, 5 (6H)-dione. Heterocyclic Communications, 2020; (26)1: 192-205.

[50] Gouda M, et al. Synthesis and antitumor evaluation of thiophene based azo dyes incorporating pyrazolone moiety. Journal of Saudi Chemical Society, 2016; (20)2: 151-157.

[51] Khedr A, Gouda A, El-ghamry H. Nano-synthesis approach, elaborated spectral, biological activity and in silico assessment of novel nano-metal complexes based on sulfamerazine azo dye. Journal of Molecular Liquids, 2022; 352: 118737.

[52] GHASEMI, Zarrin, et al. Synthesis of azo dyes possessing N-heterocycles and evaluation of their anticancer and antibacterial properties. *Monatshefte für Chemie-Chemical Monthly*, 2018, 149: 149-157.

[53] Kumar B, et al. Investigation of antituberculosis, antimicrobial, anti-inflammatory efficacies of newly synthesized transition metal (II) complexes of hydrazone ligands: structural elucidation and theoretical studies. Scientific Reports, 2023; (13)1: 15906.

[54] Alcaraz M, et al. Tailoring selective triclosan azo-adducts: Design, synthesis, and anti-mycobacterial evaluation. Heliyon, 2023; (9)11.

[55] Manjunatha B, et al. Coumarin-benzothiazole based azo dyes: synthesis, characterization, computational, photophysical and biological studies. Journal of Molecular Structure, 2021; 1246: 131170.