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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL DERIVATIVES OF AZO-SALICYLIC ACIDDERIVATIVES FOR ANTI-BACTERIAL AND ANTI-FUNGAL ACTIVITIES"

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ABSTRACT:
Azo compounds, characterized by their distinctive azo moiety and aromatic systems, play pivotal roles across various industries due to their versatile applications. Their prevalence in food, cosmetics, pharmaceuticals, dyes, and textiles underscores their significance in modern chemistry. Notably, azo compounds exhibit diverse biological activities, contributing significantly to medicinal and therapeutic advancements.Recent research explores compounds like Congo Red and Evans Blue for their potential as HIV replication inhibitors, highlighting ongoing efforts in disease treatment. Additionally, their antibacterial and pesticidal properties make them promising candidates for industrial and medical applications. Synthesis of azo compounds offers pathways for exploring novel functionalities and derivatives, further enhancing their utility. Commonly referred to as chromogens, azo compounds find extensive use as synthetic dyes, with broad applications from textiles to photoconductive materials. Their role as chemotherapeutic agents and enzyme inhibitors underscores their broad utility. MIC assays provide valuable insights into their antimicrobial efficacy, aiding in combating infectious diseases. In summary, the multifaceted properties of azo compounds drive ongoing research and innovation, showcasing their significance in both industrial and medicinal realms.

Keywords: Azo-moiety, acetyl salicylic acid, anti-bacterial, anti-fungal

INTRODUCTION

The azo moiety (-N=N-) and two unique or related monocyclic, polycyclic, or heterocyclic aromatic systems distinguish azo compounds from other colours. They have numerous uses in the food, cosmetic, pharmaceutical, and dyeing industries and textile industries as well as

analytical chemistry due to their distinctive biological activities and physico-chemical properties. However, its colouring option continues to be the most popular and widely used one. The most substantial and diverse family of dyes is the azo dye family.[1,2]

The biological activity of the azo compounds makes them appropriate for treating textiles with biocide.Azo compounds are used as anti-diabetic, antiseptic, antineoplastic, antibacterial, and anti-tumour medicines and are extensively recognised for their medicinal efficacy[29]. They are involved in a wide range of biological functions, such as nitrogen fixation, carcinogenesis, protein synthesis, and DNA and RNA inhibition.[1,23,32] It's likely that some of the Schiff bases' alleged biological activity is due to the azo-imide relationship, as azo compounds are helpful in the medical and pharmaceutical industries.[1,6,7,34]

Congo Red and evans blue, two azo chemicals, are currently being researched as HIV viral replication inhibitors. Antibacterial and pesticidal properties are demonstrated by the presence of the azo moiety. A recent study on the use of compounds containing the azo group as antibacterial agents was published. The bulk of azo compounds are created by diazotizing a primary aromatic amine, followed by nucleophilic coupling. As a result, chemicals such as benzoic, phenolic, salicylic, and naphthol undergo diazotization reactions. It is intriguing to examine the production of those salicylic azo compounds and their derivatives in order to research the newer potentials of such compounds because to the range of applications for azo compounds.[3,11,39]

In the literature, azo compounds are occasionally referred to as chromogens. The coupling elements amino- and hydroxy-groups are frequently employed[42,49]. As a result of ongoing efforts to identify a particular dye for use in a variety of industrially significant materials, including including but not restricted to paper, leather, inkjet printers, and aluminium sheet varied classes of synthetic dyes, including azo dyes, have emerged. Additionally, azo compounds are the most common organic photoconductive compounds and have numerous uses in the photo industry, including photodynamic therapy, photographic, or electro-photographic systems.[3,8,9]

Some of the azo dyes can be used as chemotherapeutic agents and have antiseptic and antiprotozoal effects. Compared to anionic dyes, cationic dyes are more active in acidic media and prefer to attack gramme-positive bacteria. Scarlet red and diamazon are the two most popular azo dyes used as antiseptics. We are encouraged to synthesize azo compounds because of their biological activity and industrial use as colourants. [4]

A white, crystalline substance with a slight acidity called aspirin has analgesic and anti-inflammatory actions.[24,25,42] Cancer and cardiovascular disease are also prevented by using it. By preventing the development of thromboxane, a substance that normally binds platelet molecules to form a patch across injured blood vessels, the substance has an antiplatelet effect.[5,12,28]

Azo chemicals can also be used to suppress the action of certain enzymes, including chymotrypsin and tyrosinase. Azo compounds, such as azo-oxyresveratrol and 1,3-indandione, as well as their derivatives, have shown strongtyrosinase inhibitory, antifungal, and antibacterial effects. Azo-salicylic acid derivatives showed that the compounds prepared and after diagnosis are not used only as dyes but can also be used in the field of medicines because of its have the

biological activity against different type of bacteria and fungi and also found through the diagnosis that these compounds prepared have high melting point that lead to high expire date.[10]

Anti-susceptibility test-The disk diffusion method is among the most flexible susceptibility testing methods in terms of antimicrobial agents that can be tested. The method consists of placing paper disks saturated with antimicrobial agents on a lawn of bacteria seeded on the surface of an agar medium, incubating the plate overnight, and measuring the presence or absence of a zone of inhibition around the disks.[13,17]

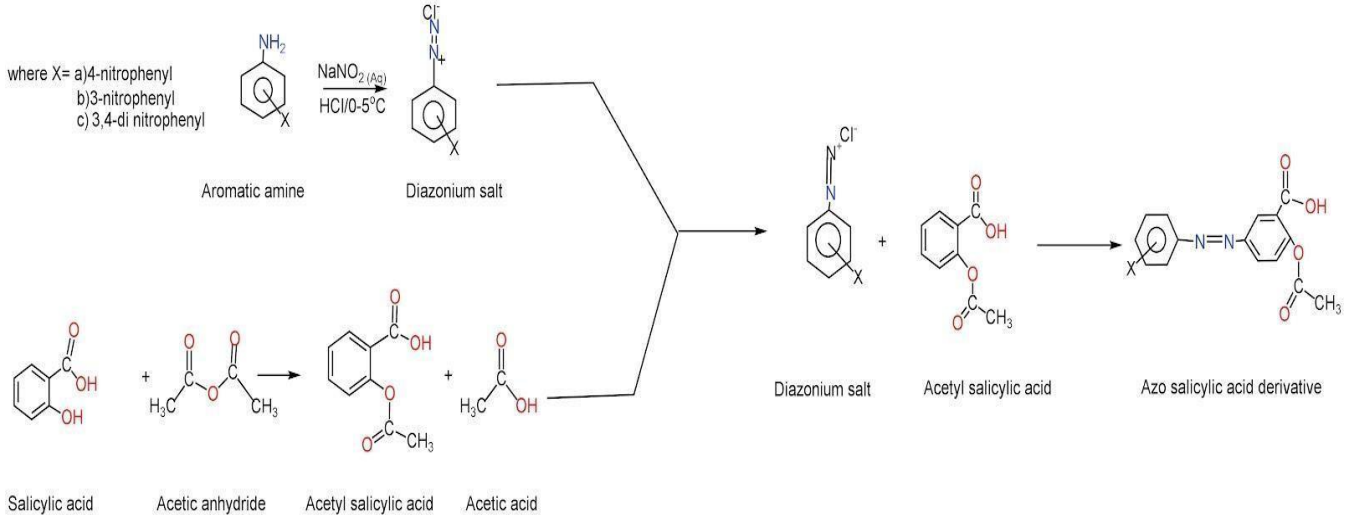
To conduct a Minimum Inhibitory Concentration (MIC) test, one introduces a substantial but imperceptible quantity of microorganisms into the sample, then observes whether the mixture of microorganisms and sample transitions from transparent to turbid. If turbidity occurs, it indicates that microorganisms have proliferated significantly, suggesting that the sample, at that specific dilution, does not inhibit their growth.[13,14,15]Clear test wells following incubation may harbor either the initial low-level microorganism inoculation or indicate that the antimicrobial agent has effectively eradicated all microorganisms. Distinguishing between these outcomes visually is not feasible.[50,51] Therefore, scientists employ MIC assays primarily to gauge the inhibitory efficacy of an antimicrobial agent rather than its biocidal properties.[16]

MATERIALS AND METHODS

p- Nitroaniline, m-Nitroaniline, 3,4-Dinitroaniline, salicylic acid, acetic anhydride and solvents will be used in the synthesis of azo-salicylic acid derivatives. Thin layer Chromatography will be used to check the purity of the prepared compounds. Gallenkamp equipment will be used to record melting points. Shimadzu spectrometer analysis of the synthesized compounds' FT-IR spectra (KBr). The Bruker-NMR spectrometer was used to determine the proton nuclear magnetic resonance (1H-NMR) spectra.[18]

Synthesis of Azo salicylic acid derivatives:

Scheme: Coupling reaction of diazonium salt derivatives with acetyl salicylic acid .



Step.1 Formation of diazonium salt:

To (5 mmol) aromatic amine solution, water(1.5ml) and conc.HCl (1.5 ml) is taken in ice-salt bath (0°C) and is kept cooled.The sodium nitrite solution (5.5 mmol) is added slowly by stirring to (1.5 ml) of water. At 0°C, the mixture is kept for further step. Similar steps were taken to synthesize the other diazonium salts.[3]

Step.2 Coupling reaction with salicylic acid derivative:

To (5.4mmol) salicylic acid derivatives solution and 2.5 M aq. sodium hydroxide (10 ml), the diazonium salt solution was added in portions. For 3–5 hours, the mixture was held at 0–5 C^{o} while being stirred. The liquid was then brought to pH 3 by adding conc. HCl (1.5 ml). The compound precipitated, separated and rinsed with water. With the help of glacial acetic acid, the required product dried and crystallized again.[3]

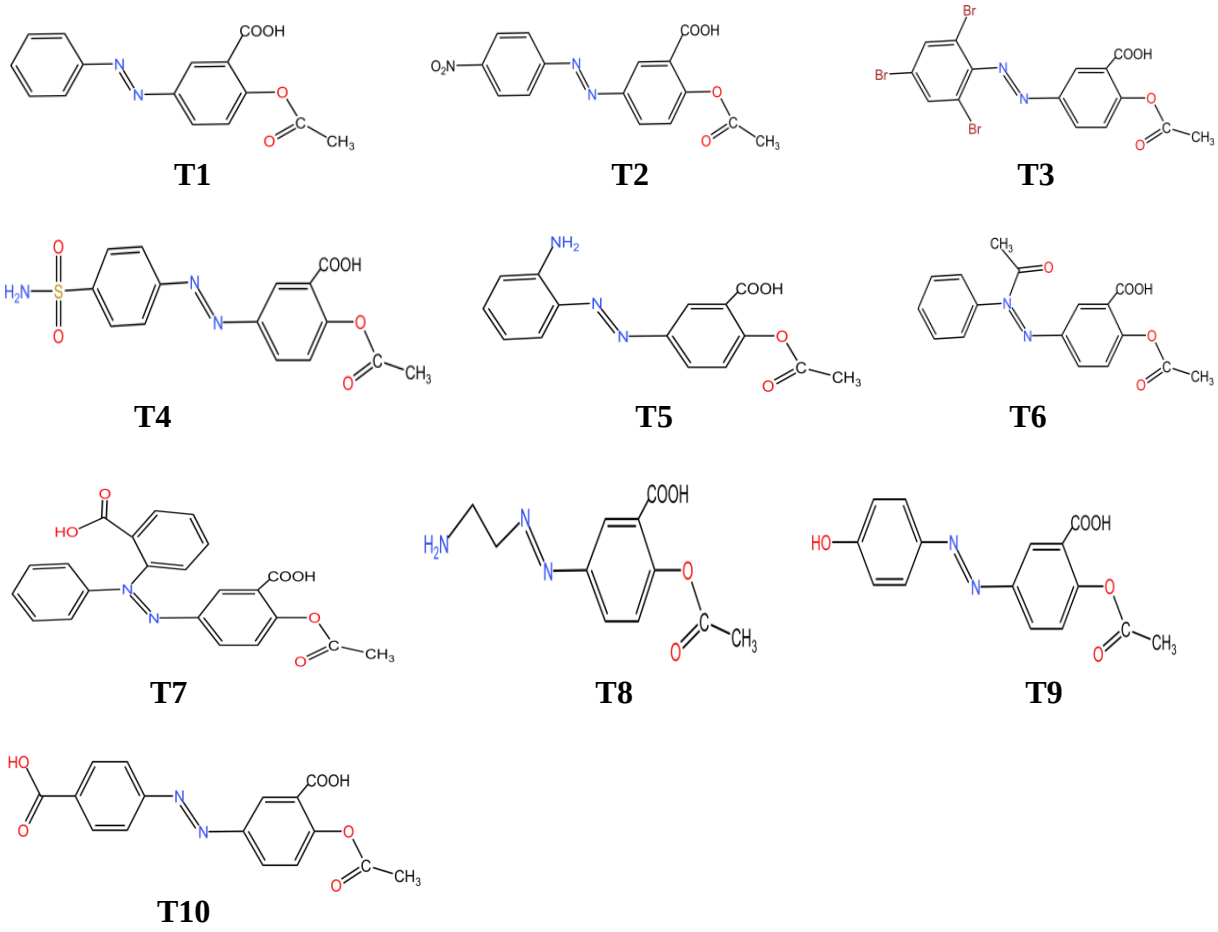


Fig.1 : Chemical structure of azo-salicylic acid derivatives

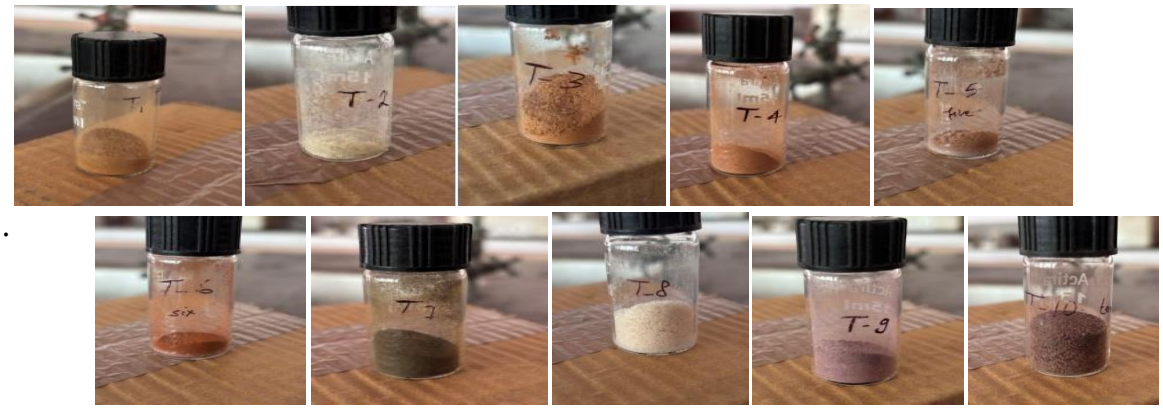


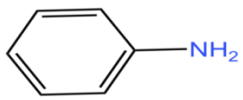
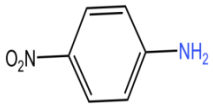
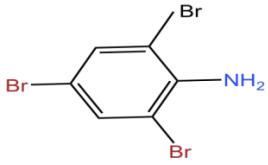
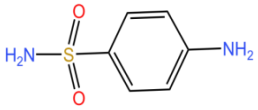
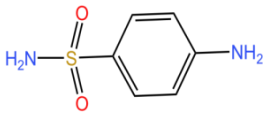
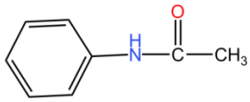
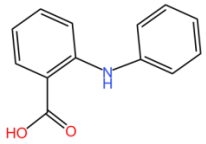
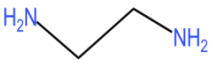
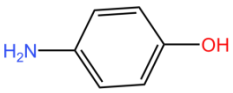
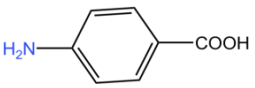
Fig.2 : The color of synthesized derivatives.

Table 1: Physical properties of synthesized derivatives.

Comp. name	Color	Melting point	Solubility in water	Solubility in 1-butanol	Solubility in ethanol	Solubility in methanol
T1	cider orange	220 ^{o}C	insoluble	highly Soluble	highly Soluble	highly Soluble
T2	light cider orange	176 ^{o}C	insoluble	highly soluble	highly soluble	highly soluble
T3	clay orange	200 ^{o}C	insoluble	highly soluble	highly soluble	highly soluble
T4	rust orange	205 ^{o}C	insoluble	highly soluble	highly soluble	highly soluble
T5	cider orange	160 ^{o}C	insoluble	sparingly soluble	highly soluble	highly soluble
T6	ginger orange	180 ^{o}C	insoluble	highly soluble	highly soluble	highly soluble
T7	spice orange	183 ^{o}C	insoluble	highly soluble	highly soluble	highly soluble
T8	cider orange	179 ^{o}C	insoluble	sparingly soluble	highly soluble	highly soluble
T9	rust orange	124 ^{o}C	insoluble	sparingly soluble	slightly soluble	slightly soluble
T10	clay orange	221 ^{o}C	insoluble	sparingly soluble	slightly soluble	slightly soluble

Table 2: FT-IR absorptions of synthesized azo-salicylic acid derivatives.

Compound code	MOLECULAR FORMULA	R1	R2	Mol. weight	m.p	Yield (%)	R_F Value

	(R)						
T1	$C_{15}H_{12}O_4N_2$		$C_9H_8O_4$	284.3 g/mol	220°C	32.7%	0.327
T2	$C_{15}H_{11}O_6N_3$		$C_9H_8O_4$	329.27 g/mol	176 °C	54.61%	O.272
T3	$C_{16}H_{12}O_4Br_3N_2$		$C_9H_8O_4$	535.99 g/mol	200 °C	75.6%	0.4375
T4	$C_{16}H_{16}O_6N_3S$		$C_9H_8O_4$	378.38 g/mol	205 °C	74.4%	0.375
T5	$C_{16}H_{16}O_4N_3$		$C_9H_8O_4$	314.11 g/mol	160 °C	39.31%	0.685
T6	$C_{19}H_{21}O_5N_2$		$C_9H_8O_4$	357.39 g/mol	180 °C	43.18%	0.555
T7	$C_{24}H_{24}O_6N_2$		$C_9H_8O_4$	436.46 g/mol	183 °C	55.88%	0.621
T8	$C_{12}H_{16}O_4N_3$		$C_9H_8O_4$	266.28 g/mol	179 °C	25.73%	0.59
T9	$C_{16}H_{15}O_5N_2$		$C_9H_8O_4$	315.3 g/mol	124 °C	39.58%	0.635
T10	$C_{17}H_{15}O_6N_2$		$C_9H_8O_4$	343.32 g/mol	221 °C	45.6%	0.596

RESULTS AND DISCUSSION

The new azo dye compounds were synthesized by coupling a diazonium salt with salicylic acid, as illustrated in Scheme (1). The reaction was conducted under ice-cold conditions (0-5°C).The structures assigned were confirmed by consistent results from FTIR, 13CNMR, LCMS, UV, and Elemental analysis.[19]

COMPOUND T1: (E)-2-acetoxy-5-(phenyldiazenyl)benzoic acid

Yield: % (Cider Orange); M.P: 220-224 °C; R_f : 0.327(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 370nm; IR spectrum(cm^{-1}):3775.29 cm^{-1}(NH stretching), 3912.56 cm^{-1} (OH stretching), 2930.81 cm^{-1} (CH stretching), 2348.90 cm^{-1} asymmetrical stretching (CN stretching), 1845.65 cm^{-1} (CO stretching), 836.46 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 40.94(s),102(s),113, 146.53, 154(s),165.87(s); Mass spectrum (m/z): 284 (M+),224,114; UV(λ_{max}): 342nm; CHN calculated for $C_{15}H_{12}O_4N_2$ (284.3): C:63.38% ,H:4.26%,O:22.51% ,N:9.85%

Compound T2: (E)-2-acetoxy-5-((4-nitrophenyl)diazenyl)benzoic acid

Yield: % (Light cider Orange); M.P: 176°C; R_f : 0.272(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 224nm; IR spectrum(cm^{-1}):3775.29 cm^{-FE1}(NH stretching), 3912.56 cm^{-1} (OH stretching), 2930.81 cm^{-1} (CH stretching), 2423.70 cm^{-1} asymmetrical stretching (CN stretching), 1845.65 cm^{-1} (CO stretching), 764 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 42(s),114,132,138(s),141, 150(d),156(s); Mass spectrum (m/z): 329 (M+),248,102,48; UV(λ_{max}): 342nm; CHN calculated for $C_{15}H_{11}O_6N_3$ (329.27): C:54.72% ,H:3.37%,O:29.15% ,N:12.76%

COMPOUND T3: (E)-2-acetoxy-5-((2,4,6-tribromophenyl)diazenyl)benzoic acid

Yield: % (Clay Orange); M.P: 200 °C; R_f : 0.4375(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 214nm; IR spectrum(cm^{-1}): 3912.75 cm^{-1} (OH stretching), 3403.61 cm^{-1}(NH stretching), 2860.54 cm^{-1} (CH stretching), 2341.65 cm^{-1} asymmetrical stretching (CN stretching), 1845.65 cm^{-1} (CO stretching),756.12 (C-Br stretching)826.3cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 51(s),118, 121,128(s), 137(d),142(d),165(s); Mass spectrum (m/z): 534(M+),224,156,48; UV(λ_{max}): 342nm; CHN calculated for $C_{16}H_{12}O_4Br_3N_2$ (535.99): C:35.85% ,H:2.26%,O:11.94% ,N:5.23,Br:44.72%

COMPOUND T4: (E)-2-acetoxy-5-((4-sulfamoy|phenyl)diazenyl)benzoic acid

Yield: % (Rust Orange); M.P: 205 °C; R_f : 0.375(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 352nm; IR spectrum(cm^{-1}): 3912.75 cm^{-1} (OH stretching),3403.61 cm^{-1}(NH stretching), 2921.71 cm^{-1} (CH stretching), 2596.69 (SH stretching) , 2356.80cm^{-1} asymmetrical stretching (CN stretching), 1662.34 cm^{-1} (CO stretching), 756.77 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 47(s),115,129,131,138,142(d),166(s); Mass spectrum (m/z): 378 (M+),248,114,48; UV(λ_{max}): 342nm; CHN calculated for $C_{16}H_{16}O_6N_3S$ (378.38): C:50.79% ,H:4.26%,O:25.37% ,N:11.11%,S:8.47%

COMPOUND T5: (E)-2-acetoxy-5-((2-aminophenyl)diazenyl)benzoic acid

Yield: % (Cider Orange); M.P: 160 °C; R_f : 0.685(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 364nm; IR spectrum(cm^{-1}): 3320.22 cm^{-1} (OH stretching), 2917.60 cm^{-1} (CH stretching), 1748.09 cm^{-1} (CO stretching), 3513.12cm^{-1}(NH stretching), 2350.38 cm^{-1} asymmetrical stretching (CN stretching), 528.87 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 52(s),114,125(d),129(s),139,146,161(s); Mass spectrum (m/z): 314 (M+),224,114; UV(λ_{max}): 342nm; CHN calculated for $C_{16}H_{16}O_4N_3$ (314.32): C:61.14% ,H:5.13%,O:20.36% ,N:13.37%

COMPOUND T6: HO-(Z)-2-acetoxy-5-(2-acetyl-2-pheny1-2λ^4-diazenyI)benzoic acid

Yield: % (Ginger Orange); M.P: 180 °C; R_f : 0.555(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 205nm; IR spectrum(cm^{-1}):3351.12 cm^{-1}(NH stretching), 3502.12cm^{-1} (OH stretching), 2881.3 cm^{-1} (CH stretching), 2347.30cm^{-1} asymmetrical stretching (CN stretching), 1810 cm^{-1} (CO stretching), 882.5 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 44(s),118,121,134(s),136,153(d),162(s); Mass spectrum (m/z): 357 (M+),241,102,48; UV(λ_{max}): 342nm; CHN calculated for $C_{19}H_{21}O_5N_2$ (357.39): C:63.86% ,H:5.92%,O:22.38% ,N:7.84%

COMPOUND T7: (2)-2-acetoxy-5-12-12-carboxyphenyl)-2-pheny1-2λ⁴-diazenyl)benzoic acid

Yield: % (Spice Orange); M.P: 183°C; R_f : 0.621(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 224nm; IR spectrum(cm^{-1}) : 2812.33 cm^{-1} (CH stretching), 3697.14cm^{-1}(NH stretching), 3596.15cm^{-1} (OH stretching), 2323.64cm^{-1} asymmetrical stretching (CN stretching), 1804.21 cm^{-1} (CO stretching), 821.8cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 51(s),119,125,133(d),138,139(s),148,166(s); Mass spectrum (m/z): 436 (M+),284,114,48; UV(λ_{max}): 342nm; CHN calculated for $C_{24}H_{24}O_6N_2$ (436.46): C:66.05% ,H:5.54%,O:21.99% ,N:6.42%

COMPOUND T8: (E)-2-acetoxy-5-((2-aminoethyl)diazenyl)benzoic acid

Yield: % (Cider Orange); M.P: 179 °C; R_f : 0.590(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 305nm; IR spectrum(cm^{-1}): 3912.41 cm^{-1} (OH stretching), 3233.88 cm^{-1}(NH stretching), 2919.82 cm^{-1} (CH stretching), 2303.29 cm^{-1} asymmetrical stretching (CN stretching), 1751.37 cm^{-1} (CO stretching), 882.13 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 55(s),119(d),122(s),136,139,145(d),161(s),165(s); Mass spectrum (m/z): 266 (M+),214,48; UV(λ_{max}): 342nm; CHN calculated for $C_{12}H_{16}O_4N_3$ (266.28): C:54.13% ,H:6.06%,O:24.03% ,N:15.78%

COMPOUND T9: (E)-2-acetoxy-5-((4-hydroxyphenyl)diazenyl)benzoic acid

Yield: % (Rust Orange); M.P: 124 °C; R_f : 0.635(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 242nm; IR spectrum(cm^{-1}): 37743.81cm^{-1} (OH stretching), 3775.29 cm^{-1}(NH stretching), 2922.13 cm^{-1} (CH stretching), 2348.90 cm^{-1} asymmetrical stretching (CN stretching), 1664.23cm^{-1} (CO stretching), 813.66 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 48(s),112,119(d),127,135,144(d),161(s),164(s); Mass spectrum (m/z): 315 (M+),224,48; UV(λ_{max}): 342nm; CHN calculated for $C_{16}H_{15}O_5N_2$ (315.3): C:60.95% ,H:4.8%,O:25.37% ,N:8.88%

COMPOUND T10: (E)-2-acetoxy-5-((4-carboxyphenyl)diazenyl)benzoic acid

Yield: % (Clay Orange); M.P: 221 °C; R_f : 0.596(Chloroform : acetone : n-butanol : 88% Formic acid 4:1:1:1); UV(λmax): 352nm; IR spectrum(cm^{-1}): 3720.58 cm^{-1} (OH stretching), 3238.46 cm^{-1}(NH stretching), 2921.71 cm^{-1} (CH stretching), 2348.90 cm^{-1} asymmetrical stretching (CN stretching), 1635.49 cm^{-1} (CO stretching), 786.46 cm^{-1} (Aro); ^{13}CNMR (500MHz, Methanol): 50(s),116(s),118,134,139,142,165,169(s); Mass spectrum (m/z): 344 (M+),248,114; UV(λ_{max}): 342nm; CHN calculated for $C_{17}H_{15}O_6N_2$ (343.32): C:59.48% ,H:4.4%,O:27.96% ,N:8.16%

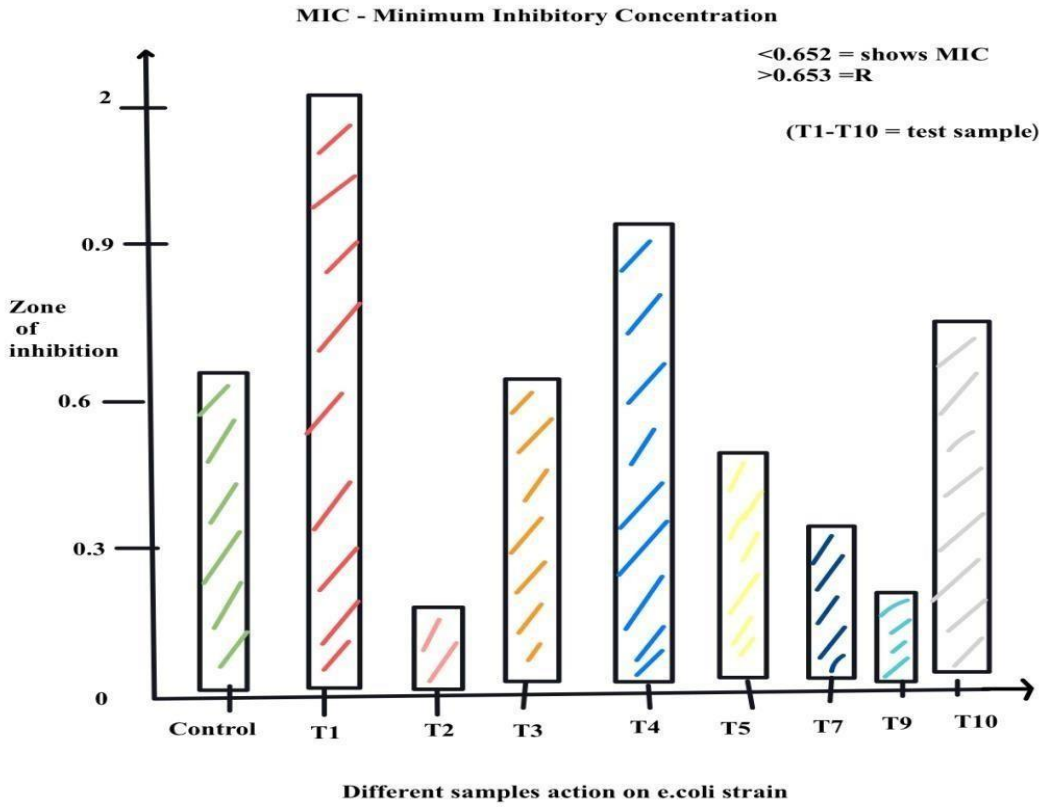
Table 3: Biological activity of synthesized azo-salicylic acid derivatives with gentamicin as standard.

Azo dye compounds	Escherichia Coli	Candida Albicans	klebsiella Sp.
T1	R	13mm	13mm
T2	16mm	24mm	17mm
T3	16mm	28mm	24mm
T4	11mm	15mm	11mm
T5	10mm	10mm	12mm
T6	12mm	12mm	13mm
T7	14mm	R	17mm
T8	R	12mm	32mm
T9	18mm	15mm	12mm
T10	10mm	R	R
Gentamicin	23mm	12mm	18mm

Table 4: Minimum Inhibitory Concentration

S.No.	CONTROL	TEST(O.D)	MIC
T1	0.652 nm	2.990 nm	R
T2	0.652 nm	0.093 nm	MIC
T3	0.652 nm	0.641 nm	MIC
T4	0.652 nm	1.0889 nm	R
T5	0.652 nm	0.546 nm	MIC
T7	0.652 nm	0.36 nm	MIC
T9	0.652 nm	0.151 nm	MIC
T10	0.652 nm	0.713 nm	R

R= Resistance, MIC=Minimum Iinhibitory Concentration, O.D= Optimum Density



Biological activity Anti-microbial activity: Anti-bacterial activity will be carried out by Agar diffusion method of prepared azo dye compounds. Biological activity of prepared azo dye compounds were determined with gentamicin as standard, by agar diffusion method, all azo dye compounds were tested and the plates were incubated at 370C for 24 hours, the inhibition zone measured in (mm). Azo dye compound were evaluated for antibacterial activity against different bacterial strain, (Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Klebsiella sp.) and fungi such as (Candida albicans).[3]

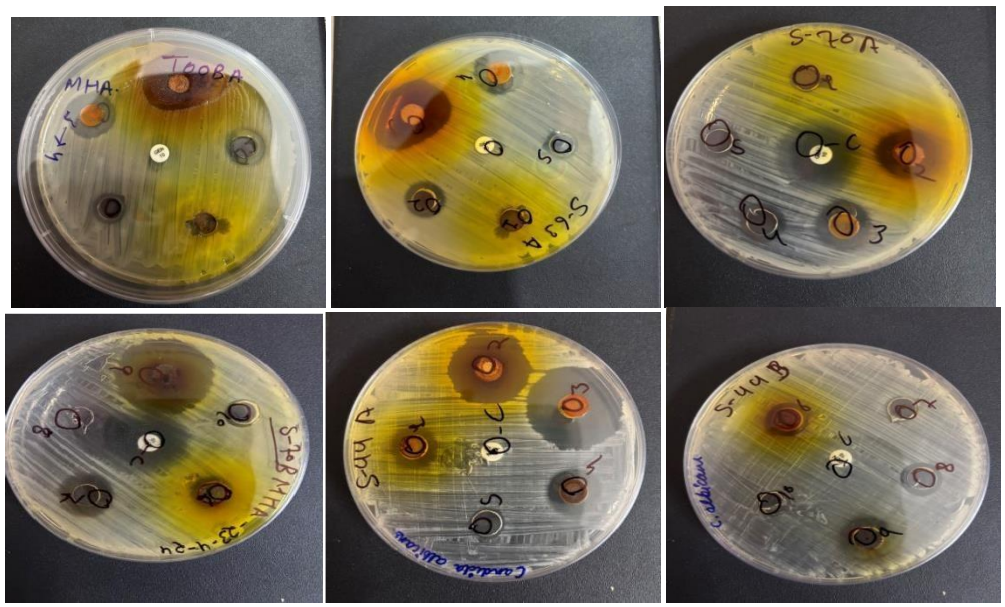


Fig.6 : Agar diffusion method of synthesized azo-salicylic acid derivatives.

The results presented in Tables 3 and 4 indicate that several azo dye compounds (T2, T3, and T8) exhibit higher biological activity compared to others, approaching the effectiveness of the standard antibiotic Gentamicin. Conversely, compounds T1 and T10 demonstrate lower biological activity relative to the rest. Specifically, compound T1 shows activity against yeast and gram-negative bacteria such as Candida Albicans and Klebsiella sp., while compound T10 is effective only against Escherichia coli. Compound T7 is resistant to yeast (Candida Albicans) but shows biological activity against both gram-negative bacteria. Compounds T2,T3, T5, T7, and T9 demonstrate minimum inhibitory concentrations (MIC).

CONCLUSION

Based on the antimicrobial evaluation of azo dye compounds through agar diffusion and Minimum Inhibitory Concentration (MIC) assays, significant findings have emerged regarding their biological activity. The compounds T2, T3, and T8 displayed notable antibacterial efficacy, comparable to the standard antibiotic Gentamicin, against a range of bacterial strains including Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, and Klebsiella species. Moreover, these compounds exhibited varying degrees of effectiveness against the yeast Candida albicans, underscoring their potential as broad-spectrum antimicrobial agents.Conversely, compounds T1 and T10 demonstrated lower biological activity, with T1 showing effectiveness primarily against Candida albicans and Klebsiella species, while T10 exhibited activity solely against Escherichia coli. Compound T7 displayed resistance against Candida albicans but demonstrated biological activity against gram-negative bacteria. Notably, compounds T2, T3, T5, T7, and T9 revealed specific Minimum Inhibitory Concentrations (MIC), indicating their potency in inhibiting microbial growth.

Overall, the observed antimicrobial properties of these azo dye compounds highlight their potential for diverse industrial and medical applications. Further research into their structure-activity relationships and pharmacological profiles could pave the way for their development as novel therapeutic agents against infectious diseases.

CONFLICT OF INTEREST: There are no conflicts of interest declared by the authors.

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