SYNTHESIS AND CHARACTERIZATION OF NOVEL 3-((2-((5-(4-SUBSTITUTED PHENYL) FURAN-3-YL) METHYLENE) HYDRAZINEYL)METHYL)-2-METHYL-1H-INDOLE AND EVALUATION OF THEIR ANTIMICROBIAL, AMYLASE & PROTEASE ENZYME BINDING ACTIVITY.

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Abstract

Hydra zones are found in many bioactive compounds that are of great interest due to their diverse pharmacological applications. Hydrazones have anticonvulsant, antidepressant, analgesic, anti-inflammatory, antiplatelet, antimicrobial, anticancer, antihypertensive, anthelmintic, antidiabetic, antiparasitic, and other anticipated biological activities. This mode of interest of researchers in synthesising a variety of hydrazone derivatives for various biological activities. As a result, many scientists have created hydrazone derivatives as target structures for their biological activities. This paper focuses on hydrazones' antimicrobial activities.

Keywords: Ester, Hydrazide, Hydrazones

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Introduction

Hydrazones are a significant class of biologically active drug molecules that have piqued the interest of medicinal chemists due to their diverse pharmacological properties. Many researchers are developing these compounds as drugs in order to combat diseases with minimal toxicity and maximum effect. These predictions have paved the way for the development of new biologically active hydrazones. Several hydrazone derivatives have been reported to have significant biological activities.[1][2]

Hydrazones have an azomethine -NHN=CH group and are considered aldehyde and ketone derivatives with the oxygen atom replaced by the $=NNH_2$ group. Hydrazones have a wide range of biological applications, including anticonvulsant, antidepressant, analgesic, anti-inflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, anticancer, vasodilator, antiviral, anti-HIV, anthelmintic, antidiabetic, and trypanocidal properties.[2-10]

Hydrazones are used as hole transporting agents in organic layer photoconductors, as quantitative analytical reagents, particularly in colorimetric and fluorometric metal ion determination.[11-13] Furthermore, some hydrazones have also been used as herbicides, insecticides, nematocides, rodenticides, and plant growth regulators as well as plasticizers and stabilizers for polymers. The metal complexes of hydrazones have potential applications as catalysts, luminescent probes, and molecular sensors.[1,14,15]

Hydrazones are an important class of compounds for new drug development. This created an interest to researchers who have synthesized variety of hydrazone derivatives and screened them for their various biological activities. In the present study, we have made an attempt to collect analgesic, anti-inflammatory, and antiplatelet properties of hydrazone derivatives. Hydrazones are not only intermediates but also very effective organic compounds when they are used as intermediates and coupling products that can be synthesized by using the active hydrozen component of –CONHN=CH– azomethine group. Many effective compounds, such as iproniazid and isocarboxazid, are synthesized by the reduction of hydrazide-hydrazones. Iproniazid, like INH, is used in the treatment of tuberculosis. It has also displayed an antidepressant effect, and patients appear to have a better mood during the treatment. Another clinically effective hydrazide-hydrazones is nifuroxazide, which is used as an intestinal antiseptic. [16-18]

Materials and Methods

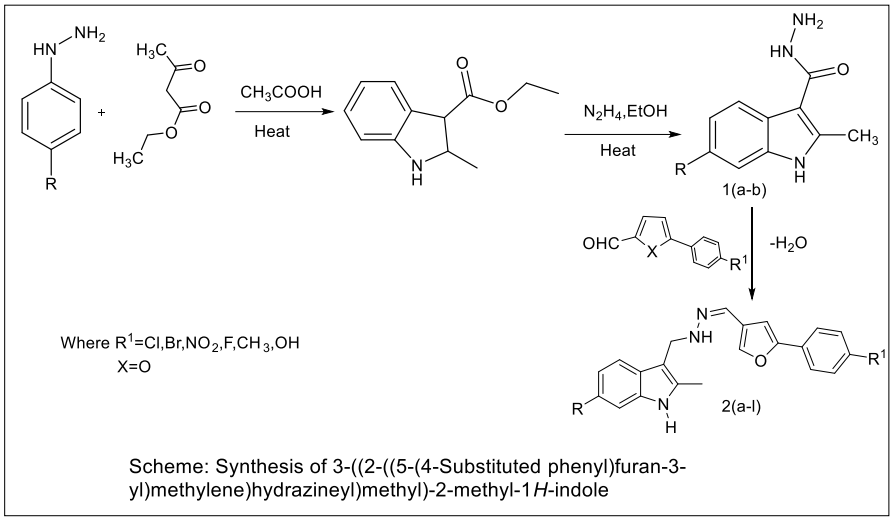
Melting points were determined on an Electrothermal 9100 melting point apparatus (Weiss-Gallenkamp, Loughborough, UK). The purity of the compounds was confirmed by Thin-Layer Chromatography (TLC) using Kieselgel 60 F_{254} (Merck). EI-MS was performed on a JEOL JMS 600 mass spectrometer. ^{1}H-NMR Bruker signals appeared at 300 and 400 MHz in CH_3OH-d_4 and that of ^{13}C-NMR at 75 MHz in $CHCl_3$-d_4. Fourier-transform infrared spectroscopy (FT-IR) spectra were obtained on a Shimadzu, IR Prestige-21 (Shimadzu, Tokyo, Japan).

General procedure for the Synthesis of Ethyl-2-methyl-1H-indole-3-carboxylate.

In a flat bottom glass flask of approximate 250 ml was fitted with a dropping funnel and a reflux condenser, a mixture of ethyl acetoacetate (6.3 ml; 0.05 mole) and glacial acetic acid (3ml, 0.05 mole) was placed in the flat bottom flask and heated under reflux with stirring. Phenyl hydrazine (5 ml; 0.05 mole) was added slowly during first 1hr. The stirring was continued for another hour. The reaction mixture was poured into a 100 ml beaker containing cold water and was stirred vigorously while it solidifies. Filter and dry the crude product, the crude product thus obtained was recrystallized from ethanol.

General procedure for the Synthesis of 2-methyl-1H-indole-3-carbohydrazide.

Ethanolic solution of Ethyl-2-methyl-1H-indole-3-carboxylate (10gm 0.05mol) was refluxed with hydrazine hydrate (2.5 gm; 0.05 mol) for 3 hr at 70°c. The reaction mixture was allowed to cool and poured over crushed ice. The solid thus obtained was filtered and dried. The crude product thus obtained was recrystallized from ethanol.



Scheme: Synthesis of 3-((2-((5-(4-Substituted phenyl)furan-3-yl)methylene)hydrazineyl)methyl)-2-methyl-1*H*-indole

Figure 1: Scheme for synthesis of compounds

Table 1: Compounds melting point, percentage yield and molecular weight.

Compound	*R*	*M.P. in (^{0}c)*	*Yield %*	*M.W*
1a	H	176.7–177.5 °C	67	189.2
1b	NO_2	182-184 °C	58	203.2

Table 2: Compounds melting point, percentage yield and molecular weight

Compound	**R**	**R^1**	***M.P. in (^{0}c)***	***Yield %***
2a	H	Cl	181	80
2b	H	Br	180	90
2c	H	NO_2	181	85
2d	H	F	183	70
2e	H	CH_3	179	60
2f	H	OH	180	75
2g	NO_2	CH_3	179	80
2h	NO_2	OH	180	77
2i	NO_2	F	183	70
2j	NO_2	NO_2	181	69
2k	NO_2	Br	180	78
2l	NO_2	Cl	181	77

Spectral data of Synthesised Compounds

Compound 1a

^{1}H NMR: δ 2.58 (3H, s), 7.00-7.23 (2H, 7.07 (d, *J* = 1.3 Hz), 7.16 (d, *J* = 8.0, 7.8, 1.6 Hz), 7.38 (1H, d, *J* = 8.0, 1.3, 0.5 Hz), 7.73 (1H, d, *J* = 8.3, Hz).

Compound 1b

^{1}H NMR: δ 2.52 (3H, s), 6.25 (1H, d, *J* = 6.8 Hz), 6.71 (1H, d, *J* = 1.5, 0.5 Hz), 7.75 (1H, d, *J* = 6.8, 0.5 Hz).

Compound 2a

^{1}H NMR: δ 2.44 (3H, s), 4.42 (2H, s), 6.89-7.13 (2H, 6.97 (d, *J* = 8.0 Hz), 7.06 (d, *J*= 1.6 Hz), 7.14-7.29 (2H, 7.20 (d, *J* = 7.9 Hz), 7.24 (d, *J* = 0.9 Hz)), 7.39-7.57 (6H, 7.45 (d, *J* = 8.9 Hz), 7.44 (s), 7.46 (d, *J* = 8.9 Hz), 7.50 (d, *J* = 8.0, Hz), 7.89 (1H, d, *J* = 0.9 Hz).

Compound 2b

^{1}H NMR: δ 2.44 (3H, s), 4.42 (2H, s), 6.89-7.13 (2H, 6.97 (d, *J* = 8.0Hz), 7.06 (d, *J* = 7.9 Hz), 7.14-7.60 (8H, 7.20 (d, *J* = 7.9Hz), 7.23 (d, *J* = 0.9 Hz), 7.34 (d, *J* = 8.9Hz), 7.44 (s), 7.50 (d, *J* = 8.0, Hz), 7.54 (d, *J* = 8.9, Hz)), 7.85 (1H, d, *J* = 0.9 Hz).

^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 118.7 (1C, s), 122.3 (1C, s), 125.8 (1C, s), 127.8 (2C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.6 (1C, s), 131.7 (2C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 150.1 (1C, s).
IR (KBr): 1570–1614cm^{-1}(-CH=N-).

Compound 2c

^{1}H NMR: δ 2.44 (3H, s), 4.42 (2H, s), 6.89-7.13 (2H, 6.97 (d, *J* = 8.0, Hz), 7.06 (d, *J* = 7.9, Hz), 7.14-7.57 (8H, 7.20 (d, *J* = 7.9Hz), 7.23 (d, *J* = 0.9 Hz), 7.30 (d, *J* = 8.3Hz), 7.33 (d, *J* = 8.3Hz), 7.44 (s), 7.50 (d, *J* = 8.0, Hz), 7.77 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 117.7 (2C, s), 118.7 (1C, s), 125.8 (1C, s), 127.8 (2C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.6 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 139.5 (1C, s), 150.1 (1C, s).
IR (KBr): 1577.51–1615.26 cm^{-1}(-CH=N-).

Compound 2d

^{1}H NMR: δ 2.44 (3H, s), 4.42 (2H, s), 6.89-7.28 (6H, 6.97 (d, *J* = 8.0, Hz), 7.06 (d, *J* = 7.9Hz), 7.08 (d, *J* = 8.9Hz), 7.20 (d, *J* = 7.9Hz), 7.23 (d, *J* = 0.9 Hz), 7.39-7.67 (4H, 7.44 (s), 7.50 (d, *J* = 8.0Hz), 7.61 (d, *J* = 8.9Hz), 7.85 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 115.4 (2C, s), 118.7 (1C, s), 125.8 (1C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.6 (1C, s), 130.9 (2C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 150.1 (1C, s), 162.5 (1C, s).
IR (KBr): 1560–1600cm^{-1}(-CH=N-).

Compound 2e
^{1}H NMR: δ 2.30 (3H, s), 2.44 (3H, s), 4.45 (2H, s), 6.89-7.29 (6H, 6.97 (d, *J* = 8.0Hz), 7.06 (d, *J* = 7.9 Hz), 7.15 (d, *J* = 8.1Hz), 7.20 (d, *J* = 7.9Hz), 7.24 (d, *J* = 0.9 Hz)), 7.39-7.57 (2H, 7.44 (s), 7.50 (d, *J* = 8.0Hz)), 7.73 (2H, d, *J* = 8.1 Hz), 7.87 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 21.3 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 118.7 (1C, s), 125.8 (1C, s), 126.6 (2C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.1 (2C, s), 129.6 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 141.5 (1C, s), 150.1 (1C, s).
IR (KBr): 1550–1600cm^{-1}(-CH=N-).

Compound 2f
^{1}H NMR: δ 2.44 (3H, s), 4.47 (2H, s), 6.89-7.13 (4H, 6.97 (d, *J* = 8.0, Hz), 7.06 (d, *J* = 7.9Hz), 7.06 (d, *J* = 8.8, Hz)), 7.14-7.27 (2H, 7.20 (d, *J* = 7.9Hz), 7.22 (d, *J* = 0.9 Hz), 7.39-7.57 (4H, 7.44 (s), 7.47 (d, *J* = 8.8Hz), 7.50 (d, *J* = 8.0 Hz), 7.77 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 71.7 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 114.8 (1C, s), 118.7 (1C, s), 125.9 (1C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.6 (1C, s), 130.0 (1C, s), 131.7 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 150.1 (1C, s), 153.2 (1C, s).

Compound 2g
^{1}H NMR: δ 2.25-2.44 (6H, 2.30 (s), 2.39 (s)), 4.29 (2H, s), 7.01 (1H, d, *J* = 2.7, 0.5 Hz), 7.09-7.49 (6H, 7.15 (d, *J* = 8.1, 1.2, 0.5 Hz), 7.24 (d, *J* = 0.9 Hz), 7.35 (dd, *J* = 8.2, 0.5 Hz), 7.43 (dd, *J* = 8.2, 2.7 Hz), 7.44 (s)), 7.73 (2H, ddd, *J* = 8.1, 1.3, 0.5 Hz), 7.87 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 71.7 (1C, s), 104.8 (1C, s), 111.3 (1C, s), 111.9 (1C, s), 114.8 (1C, s), 118.7 (1C, s), 125.9 (1C, s), 128.0-128.3 (2C, 128.1 (s), 128.2 (s)), 128.4 (1C, s), 129.6 (1C, s), 130.0 (1C, s), 131.7 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 136.0 (1C, s), 137.3 (1C, s), 150.1 (1C, s), 153.2 (1C, s).

Compound 2h
^{1}H NMR: δ 2.39 (3H, s), 4.28 (2H, s), 6.96-7.12 (3H, 7.01 (d, *J* = 2.7Hz), 7.06 (d, *J* = 8.8Hz), 7.22 (1H, d, *J* = 0.9 Hz), 7.29-7.53 (5H, 7.35 (d, *J* = 8.2Hz), 7.43 (d, *J* = 8.2Hz), 7.44 (s), 7.47 (d, *J* = 8.8Hz), 7.77 (1H, d, *J* = 0.9 Hz).
13C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 71.7 (1C, s), 104.8 (1C, s), 111.9 (1C, s), 114.8 (1C, s), 115.0 (1C, s), 117.7 (1C, s), 122.6 (1C, s), 125.9 (1C, s), 128.1 (1C, s), 129.6 (1C, s), 130.0 (1C, s), 131.7 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 137.3 (1C, s), 139.5 (1C, s), 140.6 (1C, s), 150.1 (1C, s), 153.2 (1C, s).

Compound 2i
^{1}H NMR: δ 2.39 (3H, s), 4.28 (2H, s), 6.96-7.15 (3H, 7.01 (d, *J* = 2.7, 0.5 Hz), 7.08 (d, *J* = 8.9Hz), 7.23 (1H, d, *J* = 0.9 Hz), 7.29-7.49 (3H, 7.35 (d, *J* = 8.2Hz), 7.43 (d, *J* = 8.2Hz), 7.44 (s), 7.61 (2H, d, *J* = 8.9Hz), 7.85 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.9 (1C, s), 115.0 (1C, s), 115.4 (2C, s), 117.7 (1C, s), 122.6 (1C, s), 125.8 (1C, s), 128.1 (1C, s), 129.6 (1C, s), 130.9 (2C, s), 133.5 (1C, s), 134.8 (1C, s), 137.3 (1C, s), 139.5 (1C, s), 140.6 (1C, s), 150.1 (1C, s), 162.5 (1C, s).

Compound 2j
^{1}H NMR: δ 2.39 (3H, s), 4.28 (2H, s), 7.01 (1H, d, *J* = 2.7Hz), 7.17-7.49 (8H, 7.23 (d, *J* = 0.9 Hz), 7.30 (d, *J* = 8.3Hz), 7.33 (d, *J* = 8.3Hz), 7.35 (d, *J* = 8.2Hz), 7.43 (d, *J* = 8.2 Hz), 7.44 (s), 7.77 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.9 (1C, s), 115.0 (1C, s), 117.7-117.8 (3C, 117.7 (s), 117.7 (s)), 122.6 (1C, s), 125.8 (1C, s), 127.8 (2C, s), 128.1 (1C, s), 129.6 (1C, s), 133.5 (1C, s), 134.8 (1C, s), 137.3 (1C, s), 139.4-139.6 (2C, 139.5 (s), 139.5 (s)), 140.6 (1C, s), 150.1 (1C, s).

Compound 2k
^{1}H NMR: δ 2.39 (3H, s), 4.27 (2H, s), 7.01 (1H, d, *J* = 2.7Hz), 7.18-7.60 (8H, 7.23 (d, *J* = 0.9 Hz), 7.34 (d, *J* = 8.9Hz), 7.35 (d, *J* = 8.2Hz), 7.43 (d, *J* = 8.2Hz), 7.44 (s), 7.54 (d, *J* = 8.9Hz), 7.85 (1H, d, *J* = 0.9 Hz).
^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.9 (1C, s), 115.0 (1C, s), 117.7 (1C, s), 122.3 (1C, s), 122.6 (1C, s), 125.8 (1C, s), 127.8 (2C, s), 128.1 (1C, s), 129.6 (1C, s), 131.7 (2C, s), 133.5

(1C, s), 134.8 (1C, s), 137.3 (1C, s), 139.5 (1C, s), 140.6 (1C, s), 150.1 (1C, s).

Compound 2l

^{1}H NMR: δ 2.39 (3H, s), 4.28 (2H, s), 7.01 (1H, d, *J* = 2.7Hz), 7.19-7.52 (8H, 7.24 (d, *J* = 0.9 Hz), 7.35 (d, *J* = 8.2 Hz), 7.43 (d, *J* = 8.2Hz), 7.45 (d, *J* = 8.9, Hz), 7.44 (s), 7.46 (d, *J* = 8.9Hz), 7.89 (1H, d, *J* = 0.9 Hz).

^{13}C NMR: δ 11.5 (1C, s), 49.1 (1C, s), 104.8 (1C, s), 111.9 (1C, s), 115.0 (1C, s), 117.7 (1C, s), 122.6 (1C, s), 125.8 (1C, s), 128.1 (1C, s), 128.7 (2C, s), 129.5-129.7 (3C, 129.6 (s), 129.6 (s)), 133.5 (1C, s), 133.7 (1C, s), 134.8 (1C, s), 137.3 (1C, s), 139.5 (1C, s), 140.6 (1C, s), 150.1 (1C, s).

Pharmacological activities

Antibacterial activity

All the synthesized compounds were screened for antibacterial activities using minimum inhibitory concentrations (MIC) and zone of inhibitions against Gram positive and Gram Negative bacterial strains. ATCC strains of the test microorganism selected for antibacterial assay were Gram-positive bacteria; *Staphylococcus aureus* ATCC 25923,. The bacterial strains' stock cultures were kept in Nutrient agar (Oxoid, UK) at 4 °C and inocula were prepared by transferring several single colonies of microbes to a sterile Mueller Hinton broth. The bacterial cell suspension was mixed until homogeneity to give a final density of 5 × 10^5 cfu/mL

Disc diffusion method

A loop full of organism i.e. bacillus is taken and it is introduced in a sterile peptone broth and incubated for 6-8 hours. The optical density of the broth is checked until the turbidity reaches 0.5. A sterile swab is taken and dipped in the broth and spread over the petri plate already filled with sterilized and cooled nutrient agar. The disc containing the standard and sample are carefully placed on the media and the plate is incubated for 18-24 hours at 35^0 C. The zone of inhibition is seen as transparent area around the disc.

Micro plate Assay of Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentrations of test microorganisms and reference material were determined using the tetrazolium micro plate assay method. The assay was performed using a 96-well clear microtiter plate. Freshly harvested bacterial cell and fungal cell suspensions were seeded at 5 × 10^5 cfu/mL in each well of the 96-well plate. Different concentrations, 500 to 10 µg/mL, of the test compounds were diluted in series with Muller–Hinton broth. A volume of 200 µL of each concentration was added in triplicate to the wells and the plates were then incubated for 18–24 h at 37 °C ± 0.5. After incubation, in each well, 50 µL of 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl-tetrazolium bromide MTT, having a concentration of 0.2 mg/mL, was added and the plate was incubated at 37 °C for 30 min. An appropriate solvent blank (DMSO) was included as the negative control and the bacterial suspension was included as the positive control. The absorbance was measured at 570 nm with a reference wavelength of 650 nm by adding DMSO using a spectrophotometer and the percentage reduction of the dye (indicating the bacterial growth inhibition) was calculated.

Antibacterial Assay

The antibacterial sensitivities of test compounds were assayed using the paper disc diffusion method using Amikacin for comparison, as shown in Table 1. From the screening, it was concluded that compounds show varied responses against S. *aureus*, *B. subtilis*, and *E. coli*. Against the *S. aureus* compounds 2a and 2e optimum inhibitions of 24 mm and 22 mm, respectively, were found. Against *B. subtilis*, the compound 2e showed a maximum inhibition of 25 mm, while 2d, 2f and 2k presented 23 mm zones of inhibition. In the case of *E. coli*, the compound 2c and 2k was found to have a significant inhibitory effect of 33 mm, while the compounds 2a and 2e showed 25 mm and 24 mm zones of inhibition, respectively.

Table 3: Antibacterial Activity Disc Diffusion Method

Compound	Antibacterial Activity (Paper Disc Diffusion Method) Zone of Inhibition (mm)		
	Staphylococcus aureus (Gram +ve)	Bacillus subtilis ATCC 11774 (Gram +ve)	Escherichia coli ATCC 10536 (Gram −ve)
2a	20	14	25
2b	15	14	14
2c	24	22	33
2d	20	23	21
2e	22	25	24
2f	17	23	22

2g	16	20	24
2h	15	22	22
2i	18	21	21
2j	20	20	23
2k	15	23	33
2l	16	22	22
Amikacin	24	30	38

Determination of Minimum Inhibitory Concentration (MIC)

In order to determine the MIC of synthesized compounds, ceftriaxone were used as standards to compare antibacterial effects. Ceftriaxone was used. The compounds were tested in a concentration range of 25–500 µg/mL and the percent inhibitions were recorded as mentioned in Table 2. Ceftriaxone showed a significant effect with an IC_{50} of 50 µg/mL, inhibiting 55 ± 0.3% of *S. aureus* of the population.

Table 4: Determination of Minimum Inhibitory Concentration

Con. µg/mL	% Inhibition of S. ***aureus*** ATCC 25923												
	Ceftriax-one	2a	2b	2c	2d	2e	2f	2g	2h	2i	2j	2k	2l
25	30 ± 0.8	-	11 ± 1.0	24 ± 0.7	16 ± 0.5	5 ± 0.4	-			5 ± 0.4	11 ± 1.0		24 ± 0.7
50	55 ± 0.3	10±0.6	21 ± 1.2	35 ± 1.2	24 ± 1.0	12± 0.4	5.5± 0.5	-	24 ± 1.0	12± 0.4	21 ± 1.2	10 ± 0.6	35 ± 1.2
100	80 ± 1.2	25 ± 0.7	42 ± 2	44 ± 2.0	38 ± 1.5	35± 0.7	25 ± 0.5	10± 0.6	38 ± 1.5	35± 0.7	42 ± 2	25 ± 0.7	44 ± 2.0
200	96 ± 1.0	55 ± 1	50 ± 2	60 ± 1.5	55 ± 0.9	58± 1.1	52 ± 1.6	25 ± 0.7	55 ± 0.9	58± 1.1	50 ± 2	55 ± 1	60 ± 1.5
300	-	63 ± 1	63 ± 1.5	78 ± 1	71 ± 2.0	77± 1.5	72 ± 1.2	55 ± 1	71 ± 2.0	77± 1.5	63 ± 1.5	63 ± 1	78 ± 1
400	-	69 ± 2	74 ± 2	89 ± 1.5	89 ± 1.5	-	80 ± 1.0	63 ± 1	89 ± 1.5	-	74 ± 2	69 ± 2	89 ± 1.5
500	-	80 ± 1.5	-	-	-	-	-	69 ± 2	-	-	-	80 ± 1.5	-

The synthesized compounds also showed inhibition at various percentages. Among the synthesized compounds (2a-2l), the highest inhibitory effect was presented by 2c and 2l against all bacterial strains. At a dose of 200 µg/mL, it inhibited the growth by 60 ± 1.5% of *S. aureus*.

Result and Discussion

This study reports the synthesis of 3-((2-((5-(4-Substituted phenyl) furan-3-yl) methylene) hydrazineyl) methyl)-2-methyl-1H-indole with isoniazid employing azomethine linkage. The detailed principal peaks are given for each compound. The FTIR spectral analysis supported the presence of the characteristic functional groups present in the synthesized compound. The presence of peaks in proton nmr spectra in the region of 7.22-7.672ppm confirmed the aromatic ring in all the compounds of the series synthesized from (2a-2l), and presence of peaks in Infrared spectroscopy in the region of $\bar{\upsilon}$ = 1577.51–1615.26 cm^{-1} confirms the presence of imine linkage in all the compounds, and In the 13CNMR spectra four key resonance signals were observed. These are δ 143.19-144.02 for azomethine (−CH=N-) and the terminal alkyl groups in all compounds (2a-2l) are in the range from δ 10.49 to 133.11.

Conclusion

The results obtained in this study concluded that the synthesized compounds were of good yields and exhibited appreciable potential due to their antibacterial properties. Amongst the synthesized compounds,2c was found to have promising antibacterial properties,. These hydrazones can be further modified for metal coordination for further investigation of other biological properties.

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