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ACCELERATED DISCOVERY OF BIOACTIVE 3-CHLORO-2-HYDRAZINYLPYRIDINE DERIVATIVES VIA CONTINUOUS FLOW SYNTHESIS IN A ROTOR-STATOR SPINNING DISC REACTOR

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ABSTRACT
Creating heterocyclic compounds that can be used for medicine is an important area of study in medicinal chemistry. This study shows how to create new 3-chloro-2-hydrazinylpyridine compounds in a special machine called a rotor-stator spinning disc reactor (RS-SDR). The special design of the RS-SDR allows for better mixing, efficient heat transfer, and accurate control of reaction conditions, making it easier and quicker to produce hydrazinylpyridine compounds in larger amounts. By carefully designing molecules and adjusting the process conditions, we were able to produce a lot of high-quality products in a safe and eco-friendly way. Our method is much faster and works better than traditional batch processes, even when solid materials are involved. Testing of certain compounds showed that they have good abilities to fight germs and reduce inflammation. This suggests they could be important starting points for creating new medicines. These results show how combining continuous flow chemistry with designing ring-shaped chemical structures can create useful molecules more sustainably and efficiently. This work shows how the RS-SDR is a useful tool for speeding up the process of finding new drugs by allowing for environmentally friendly and larger-scale production.
Keywords: 3-Chloro-2-hydrazinylpyridine, Continuous Flow Chemistry, Rotor-Stator Spinning Disc Reactor, Heterocyclic Compounds, Bioactive Derivatives, Process Intensification, Antimicrobial and Anti-inflammatory Activity.

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INTRODUCTION

As the need for quicker, cleaner, and safer ways to make chemicals grows, the old method of batch synthesis is being replaced more and more by continuous flow chemistry. Recent studies show that continuous manufacturing can cut production times by as much as 80%, while also lowering waste and energy use. This is an important step toward making chemical production more sustainable. This change is particularly important in the pharmaceutical and fine chemical industries, where accuracy, the ability to scale up production, and caring for the environment are very important.[1] Batch processes are common but have some major issues. They often have bad heat transfer, uneven mixing, and difficulties in dealing with mixed reactions, especially those that include solids or slurries.[2] These problems make it hard to scale up the process and achieve consistent results, which are important for developing drugs. Continuous flow systems provide better temperature control, improved movement of materials, and steadier reaction conditions.[3] However, using solid-liquid systems or slurry reactions in these continuous flow setups is still very difficult.[4] This research focuses on solving that problem. One important area in medicine is creating nitrogen-rich ring compounds, especially pyridine types, because they have many different health benefits. Compounds like 3-chloro-2-hydrazinylpyridine could be useful for making medicines that fight germs, malaria, and inflammation.[5-6] However, the usual method for making these compounds often needs tough conditions, takes a long time, and isn't good for producing large amounts. To solve these problems, our study looks at using a rotor-stator spinning disc reactor (RS-SDR). This is a very efficient system that mixes well, heats up and spreads materials quickly, and works well with different types of substances.[7] RS-SDR technology uses a fast-spinning disc located between fixed parts to create strong forces. This helps mix liquids and solids better.

Because of this, it is great for complex chemical reactions that involve mixtures. Its small size also makes it easier to manage the conditions of the reactions.[8] This method matches Sustainable Development Goal (SDG) 12, which is about using resources responsibly and making products in a better way. It helps to create things in an eco-friendly way, using less energy and producing less waste. In this study, we describe a method for making 3-chloro-2-hydrazinylpyridine compounds using a new technology called RS-SDR. We focus on how well the reaction works, how easy it is to make larger amounts, and its importance for biological use. By improving the flow and reaction settings, we got high amounts of product using gentle and easy-to-scale methods. Also, the compounds that were made were tested to see if they could fight germs and malaria, especially against Plasmodium falciparum and various harmful bacteria and fungi.[9] This research shows a better and more eco-friendly way to create complicated chemical compounds and also provides new active molecules that could help in finding new drugs. The results show that RS-SDR technology is useful for improving drug manufacturing. It also has the potential to connect research done in labs with larger industrial production.[10]

EXPERIMENTAL

Overview of Continuous Flow Processing

Summary of Continuous Flow Processing. Continuous flow processing is becoming more popular in the chemical industry because it is safer, can be scaled up easily, allows for better control of reactions, and works more efficiently compared to traditional batch methods. One type of flow reactor that stands out is the rotor-stator spinning disc reactor (RS-SDR), which is very good at speeding up chemical reactions, especially those with different phases.[11-12]

Spinning Disc Reactor (SDR) Technology

An SDR is a type of reactor that constantly moves materials to mix them well and allow heat and mass to move quickly. It has three main parts: a moving disc (rotor), a still disc (stator), and a reaction chamber that can change height. When you add reactants to the system, the spinning action creates strong mixing and movement, which helps mix everything better. This is particularly useful for reactions that involve both solids and liquids. This process makes things work better, speeds up reactions, and allows for bigger production.[13]

Experimental Setup

All chemicals and solvents used were of laboratory reagent (LR) grade, purchased from Avra Synthesis, Spectrochem, and SD Fine Chemicals, and used without further purification. All substrates were commercially available. The synthesis of 3-chloro-2-hydrazinylpyridine derivatives was carried out using a Kinetichem Synthetron RS-SDR (Fig.-1). Reactants were introduced using the Holmarc SPLF syringe pump system (Fig.-2), allowing precise control over flow rate and residence time. The RS-SDR featured an adjustable gap size ranging from 50 µm to 2.5 inches, enabling adaptation to various reaction viscosities and mixing requirements. For this study, a 200 µm gap was employed, corresponding to a reactor volume of 0.63 millilitre. Holmarc's syringe pumps support syringe sizes from 5 mL to 60 mL, with flow rates ranging from 15.63 µL/hr to 36.2 mL/min, depending on the syringe used.

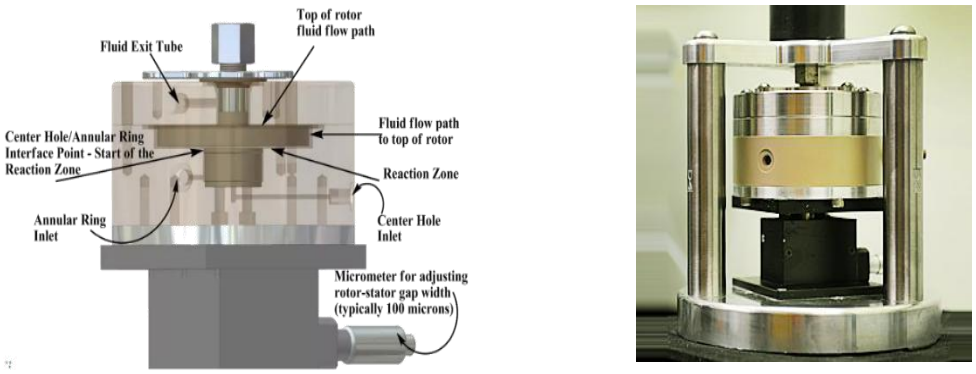


Fig.-1: RS-SDR System used for Continuous Flow Synthesis, Showing Rotor-Stator Configuration

Fig.-2: Holmarc Syringe Pump Setup for Controlled Reagent Delivery

Reaction Procedure

The reactions were done at normal pressure and the best temperature. We mixed 3-chloro-2-hydrazinylpyridine with a suitable aromatic aldehyde in ethanol, using acetic acid as a simple and affordable catalyst. The reaction solution was added to the SDR at different flow rates to find the best time for staying in the system and how well it worked. We improved the flow conditions by looking at how much product we got and using TLC tests. Each test was done three times to make sure the results were consistent.

Analytical Techniques and Monitoring

We checked the reaction using thin-layer chromatography (TLC) with Merck silica gel 60 F254 plates. The final product was analysed using a type of machine called a 400 MHz NMR spectrometer from Agilent, which helps identify its structure based on its hydrogen atoms. All the created compounds were shown to be new based on their different NMR patterns. A comparison was made between the SDR method and regular batch processes that use different types of catalysts. The results showed that the SDR method had faster reaction times, easier conditions, and better results (Table-1).

Table-1: Comparative Yields and Reaction Times of SDR Vs Batch Processes

Entry	Catalyst	Condition	Time	Yield (%)	Ref.
1	Acetic Acid	Ethanol / Temp 40℃ / SDR	3-6 Seconds	95%	This Work
2	H3CO3	Ethanol: Water (1:1)/ RT	15 min	95%	14
3	Acetic Acid	Ethanol / Temp 78℃	60 min	-	15
4	MFA	Ethanol / RT	10-30 min	89%	16
5	TFA	Ethanol / 80℃	10 min	90%	17
6	Zeolite	Ethanol / Ultrasound Method	40 min	88%	18

Reaction Scheme: Schematic Representation of the Continuous-Flow Synthesis of Bioactive 3-Chloro-2-hydrazinylpyridine Derivatives with Aromatic Aldehydes in a Rotor–Stator Reactor.

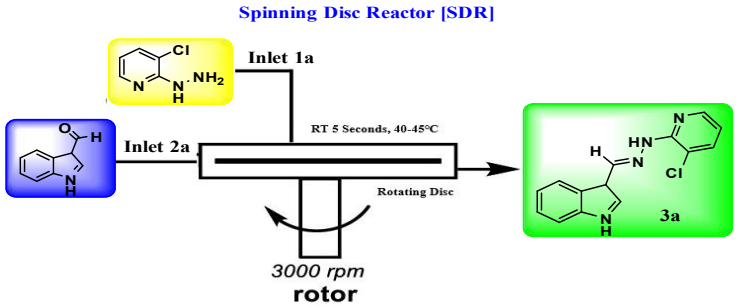


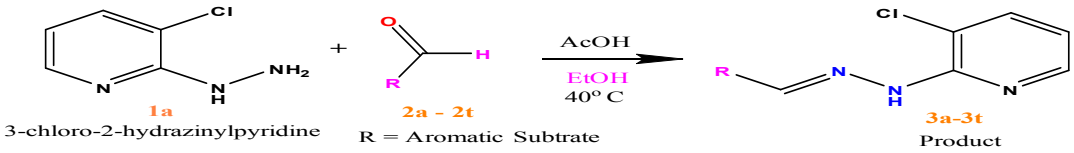
Fig.-3: Continuous Flow Synthesis of Compound 3a. [3-((2-(3-chloropyridin-2-yl) hydrazono) methyl)-1H-indole

Referring to Fig.-3, the flow reactor described is a Spinning Disc Reactor (SDR) with a single reaction vessel having a 0.63 mL capacity. The reaction vessel is jacketed to maintain the required temperature and pressure based on the reaction conditions. The heating medium is passed through the jacket surrounding the reaction vessel to provide the necessary temperature. Feed containers at inlets **1a** and **2a**

are connected to pumps that feed the reactor with the respective reactants. The reaction mixture is then continuously collected in a collection vessel, from which the final product is removed and taken out. A set of screening experiments using SDR equipment was conducted with a 10% ethanol solution of Reagent **1a** (3-Chloro-2-hydrazinyl Pyridine) and a second inlet stream of a 20% ethanol solution of Reagent **2a** (1H-indole-3-carbaldehyde). The screening experiments quickly revealed that a residence time (RT) of only 5 seconds and a molar ratio of **1a:2a** of 1:1 was sufficient to achieve complete conversion (Table-2). The flow reactor temperature was maintained at 40-45°C, with a residence time of **5 seconds**, to ensure complete conversion of product **3a** (Table-2, entries 1-20).

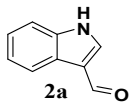
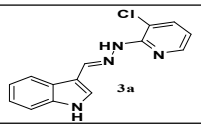
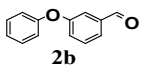
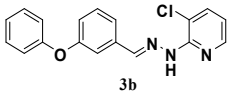
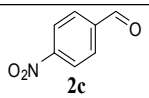
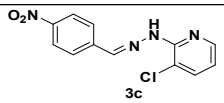
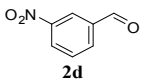
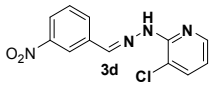
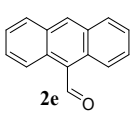
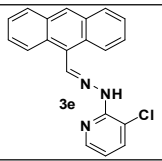
General Procedure

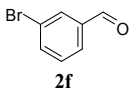
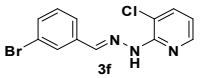
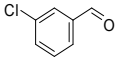
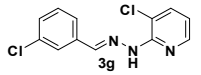
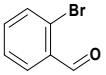
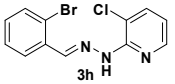
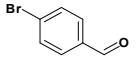
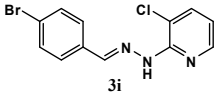
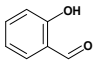
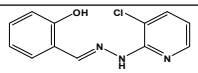
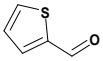
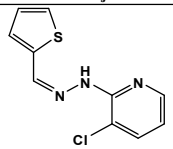
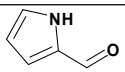
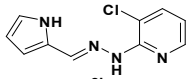
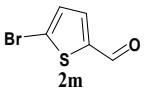
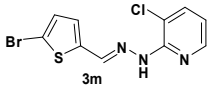
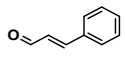
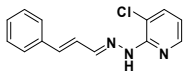
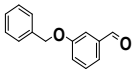
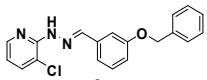
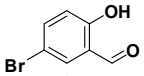
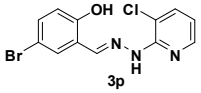
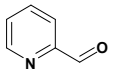
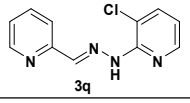
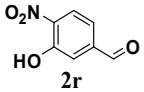
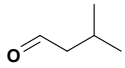
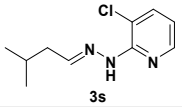
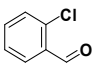
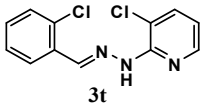
An Efficient Continuous-Flow Approach for the Synthesis of Novel 3-Chloro-2-hydrazinylpyridine Derivatives Using a Rotor–Stator Spinning Disc Reactor



A 10% solution of 3-Chloro-2-hydrazinyl Pyridine. **(1a)** was prepared by dissolving 3.55 g of 3-Chloro-2-hydrazinyl Pyridine. **(1a)** (99 % purity) Solid into 31.5g of ethanol at room temperature. Similarly, a 20% solution of 1H-indole-3-carbaldehyde **(2a)** was prepared by dissolving 3.65g of 1H-indol-3-carbaldehyde **(2a)** (96% purity) solid into 13.85g of ethanol and 0.15g of acetic acid (99% purity), allowing it to dissolve completely at room temperature. A two-line inlet Spin Disc Reactor (volume = 0.63 mL) was used to perform the continuous reaction. The 10% solution 3-Chloro-2-hydrazinyl Pyridine. **(1a)** was fed into the reactor through the first dosing line using pump (P1) at a rate of 5.29 mL/min (4.76 g/min, 0.0033 moles/min). The 20% solution of 1H-indole-3-carbaldehyde **(2a)** and acetic acid was fed through the second dosing line using pump (P2) at a rate of 2.3 mL/min (2.42 g/min, 0.0033 moles/min). The flow rate was adjusted to maintain a mole equivalent ratio of 3-Chloro-2-hydrazinyl Pyridine. **(1a)**: 1H-indole-3-carbaldehyde **(2a)**: Acetic acid of 1:1:0.15. Both dosing lines discharged their contents into the reaction region, which was maintained at 40°C. The desired product, 3-((2-(3-chloropyridin-2-yl) hydrazono) methyl)-1H-indole. **(3a)** was formed within a residence time of 5 Seconds. The results of the reaction setup are highlighted in Table-2.

Table-2: Summary of Hydrazone Derivatives Synthesised under Continuous Flow Conditions using Rotor-Stator Spinning Disc Reactor

Entry	Aldehydes (R)	Products	Time (Sec.)	Yield (%)
1	 2a	 3a	5	95
2	 2b	 3b	4	90
3	 2c	 3c	3	92
4	 2d	 3d	5	90
5	 2e	 3e	4	95

6	 **2f**	 **3f**	5	93
7	 **2g**	 **3g**	4	93
8	 **2h**	 **3h**	5	94
9	 **2i**	 **3i**	4	92
10	 **2j**	 **3j**	6	89
11	 **2k**	 **3k**	5	88
12	 **2l**	 **3l**	4	92
13	 **2m**	 **3m**	6	87
14	 **2n**	 **3n**	4	91
15	 **2o**	 **3o**	5	90
16	 **2p**	 **3p**	5	92
17	 **2q**	 **3q**	4	94
18	 **2r**	 **3r**	6	88
19	 **2s**	 **3s**	5	89
20	 **2t**	 **3t**	5	93

The completion of the reaction was monitored by Thin-Layer Chromatography (TLC). The reaction mixture collected for 5 min was quenched in cold water, and the solid was filtered to obtain the final product. The final solid was purified by crystallisation and column chromatography for NMR analysis.

The product obtained was a novel compound identified by 1H NMR spectroscopy. For a 55-minute collection, substrate (1a) is taken (23.81 g, 0.0166 moles/5 min) and produced (4.272 g, 0.0158 moles/5 min), 95% yield as a yellow crystalline solid product. (3a) (Similarly, compounds 3b–3t were prepared by following the same experimental flow process as described above.)

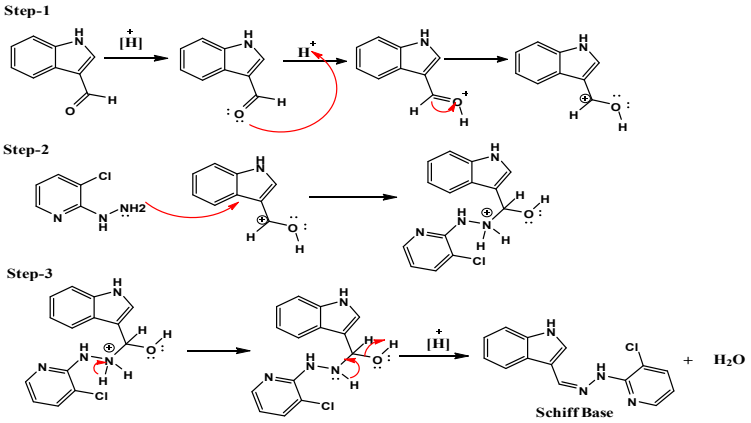


Fig.-4: Proposed Mechanism of 3-((2-(3-chloropyridin-2-yl) hydrazono) methyl)-1H-indole

Detection Method

Spectroscopic Characterisations and Physical Properties of Synthesised Derivatives

(E)-3-((2-(3-chloropyridin-2-yl) hydrazono) methyl)-1H-indole (3a)

^{1}H NMR (500 MHz, DMSO) δ 11.43 (s, 1H, (Ar-NH-N)), 9.98 (s, 1H, (Ar-NH)), 8.57 (s, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 8.19 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.17 (ddd, *J* = 25.2, 11.3, 4.0 Hz, 2H), 6.75 (dd, *J* = 7.7, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 151.08 (s), 146.69 (s), 140.81 (s), 137.10 (s), 136.93 (s), 128.25 (s), 124.45 (s), 122.37 (s), 122.05 (s), 120.02 (s), 114.65 (s), 112.58 (s), 112.40 (s), 111.61 (s). LC-MS m/z calculated $C_{14}H_{11}ClN_4$: Exact Mass: 270.07.

(E)-3-chloro-2-(2-(3-phenoxybenzylidene) hydrazinyl) pyridine (3b)

1H NMR (500 MHz, DMSO) δ 10.47 (s, 1H), 8.34 (s, 1H), 8.13 (dd, J = 4.8, 1.3 Hz, 1H), 7.72 (dd, J = 7.7, 1.5 Hz, 1H), 7.41 (dt, J = 13.0, 7.6 Hz, 4H), 7.29 (s, 1H), 7.14 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 7.7 Hz, 2H), 7.00 – 6.97 (m, 1H), 6.81 (dd, J = 7.7, 4.8 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 157.05 (s), 156.58 (s), 150.49 (s), 146.57 (s), 142.14 (s), 137.72 (s), 137.36 (s), 136.55 (s), 130.44 (s), 130.13 (s), 129.91 (s), 123.61 (s), 122.05 (s), 119.24 (s), 118.69 (s), 116.13 (s), 115.52 (s), 113.87 (s). LC-MS m/z calculated $C_{18}H_{14}ClN_3O$: Exact Mass: 323.08.

(E)-3-chloro-2-(2-(4-nitrobenzylidene) hydrazinyl) pyridine (3c)

1H NMR (500 MHz, DMSO) δ 10.89 (s, 1H), 8.47 (s, 1H), 8.27 (d, J = 8.8 Hz, 2H), 8.22 (dd, J = 4.7, 1.4 Hz, 1H), 7.91 (d, J = 8.8 Hz, 2H), 7.80 (dd, J = 7.8, 1.5 Hz, 1H), 6.91 (dd, J = 7.8, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.19 (s), 146.96 (s), 146.71 (s), 141.84 (s), 140.46 (s), 140.06 (s), 137.98 (s), 129.43 (s), 127.02 (s), 124.09 (s), 116.95 (s), 114.39 (s). LC-MS m/z calculated $C_{12}H_9ClN_4O_2$: Exact Mass: 276.04.

(E)-3-chloro-2-(2-(3-nitrobenzylidene) hydrazinyl) pyridine (3d)

1H NMR (500 MHz, DMSO) δ 10.76 (s, 1H), 8.48 (s, 2H), 8.22 (d, J = 3.8 Hz, 1H), 8.20 – 8.15 (m, 1H), 8.06 (d, J = 7.7 Hz, 1H), 7.82 – 7.76 (m, 1H), 7.71 (t, J = 8.0 Hz, 1H), 6.89 (dd, J = 7.7, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.33 (s), 148.29 (s), 146.66 (s), 140.24 (s), 137.85 (s), 137.21 (s), 132.65 (s), 130.33 (s), 123.02 (s), 119.92 (s), 116.60 (s), 114.13 (s). LC-MS m/z calculated $C_{12}H_9ClN_4O_2$: Exact Mass: 276.04.

2-(2-(anthracen-9-ylmethylene) hydrazinyl)-3-chloropyridine (3e)

1H NMR (500 MHz, dmso) δ 10.68 (s, 1H), 9.55 (s, 1H), 8.79 (d, J = 5.7 Hz, 2H), 8.56 (s, 1H), 8.09 (dd, J = 45.2, 2.5 Hz, 3H), 7.73 (d, J = 4.0 Hz, 1H), 7.50 (d, J = 25.5 Hz, 4H), 6.79 (s, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.76 (s), 146.85 (s), 146.68 (s), 142.28 (s), 138.27 (s), 137.72 (s), 134.57 (s), 131.09 (s),

129.49 (s), 129.25 (s), 128.93 (s), 128.63 (s), 126.80 (d, *J* = 5.3 Hz), 126.21 (s), 126.02 (s), 125.46 (d, *J* = 12.7 Hz), 125.17 (s), 124.47 (s), 116.16 (s), 113.87 (s). LC-MS m/z calculated $C_{20}H_{14}ClN_3$: Exact Mass: 331.09

(E)-2-(2-(3-bromobenzylidene) hydrazinyl)-3-chloropyridine (3f)
1H NMR (500 MHz, dmso) δ 9.97 (s, 1H), 7.83 (s, 1H), 7.27 (dd, J = 4.7, 1.5 Hz, 1H), 7.10 (dd, J = 7.9, 1.6 Hz, 1H), 6.85 (dd, J = 7.8, 1.5 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.50 (t, J = 7.5 Hz, 1H), 6.36 (td, J = 7.8, 1.6 Hz, 1H), 5.95 (dd, J = 7.7, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.47 (s), 146.66 (s), 141.05 (s), 137.84 (s), 134.14 (s), 133.05 (s), 130.55 (s), 127.93 (s), 126.90 (s), 122.73 (s), 116.45 (s), 114.06 (s). LC-MS m/z calculated $C_{12}H_9BrClN_3$: Exact Mass: 308.97

(E)-3-chloro-2-(2-(3-chlorobenzylidene) hydrazinyl) pyridine (3g)
1H NMR (500 MHz, dmso) δ 9.68 (s, 1H), 7.43 (s, 1H), 7.26 (dd, J = 4.7, 1.4 Hz, 1H), 6.85 – 6.77 (m, 2H), 6.67 (d, J = 7.6 Hz, 1H), 6.53 – 6.43 (m, 2H), 5.92 (dd, J = 7.7, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.47 (s), 146.67 (s), 141.13 (s), 137.80 (s), 137.60 (s), 133.63 (s), 130.67 (s), 128.54 (s), 125.32 (d, *J* = 19.8 Hz), 124.99 (s), 116.36 (s), 114.02 (s). LC-MS m/z calculated $C_{12}H_9Cl_2N_3$: Exact Mass: 265.02

(E)-2-(2-(2-bromobenzylidene) hydrazinyl)-3-chloropyridine (3h)
1H NMR (500 MHz, dmso) δ 9.69 (s, 1H), 7.42 (s, 1H), 7.27 (dd, J = 4.7, 1.5 Hz, 1H), 6.95 (t, J = 1.6 Hz, 1H), 6.83 (dd, J = 7.7, 1.5 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 6.60 (ddd, J = 8.0, 1.9, 0.9 Hz, 1H), 6.45 (t, J = 7.8 Hz, 1H), 5.93 (dd, J = 7.8, 4.7 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.46 (s), 146.67 (s), 141.02 (s), 137.82 (d, *J* = 4.5 Hz), 131.42 (s), 131.15 (s), 130.96 (s), 128.22 (s), 125.68 (s), 122.21 (s), 116.36 (s), 114.01 (s). LC-MS m/z calculated $C_{12}H_9BrClN_3$: Exact Mass: 308.97.

(E)-2-(2-(4-bromobenzylidene) hydrazinyl)-3-chloropyridine (3i)
1H NMR (500 MHz, dmso) δ 9.62 (s, 1H), 7.43 (s, 1H), 7.26 (dd, J = 4.7, 1.5 Hz, 1H), 6.83 (dd, J = 7.7, 1.6 Hz, 1H), 6.73 – 6.65 (m, 4H), 5.92 (dd, J = 7.7, 4.7 Hz, 1H) ^{13}C NMR (126 MHz, dmso) δ 150.50 (s), 146.65 (s), 141.61 (s), 137.74 (s), 134.62 (s), 132.06 (s), 131.74 (s), 131.46 (s), 128.26 (s), 121.96 (s), 116.21 (s), 113.91 (s). LC-MS m/z calculated $C_{12}H_9BrClN_3$: Exact Mass: 308.97

(E)-2-((2-(3-chloropyridin-2-yl) hydrazono) methyl) phenol (3j)
1H NMR (500 MHz, dmso) δ 11.81 (s, 1H), 10.74 (s, 1H, Ar-OH), 8.47 (s, 1H, -CH), 8.10 (dd, J = 4.8, 1.5 Hz, 1H), 7.68 (dd, J = 7.7, 1.5 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.13 (td, J = 8.1, 1.6 Hz, 1H), 6.82 – 6.74 (m, 3H). ^{13}C NMR (126 MHz, dmso) δ 157.21 (s), 150.04 (s), 146.85 (s), 144.72 (s), 144.53 (s), 137.75 (s), 130.40 (s), 130.18 (s), 129.62 (s), 119.10 (d, *J* = 15.6 Hz), 116.38 (d, *J* = 5.9 Hz), 113.77 (s). LC-MS m/z calculated $C_{12}H_{10}ClN_3O$: Exact Mass: 247.05.

(E)-3-chloro-2-(2-(thiophen-2-ylmethylene) hydrazinyl) pyridine (3k)
1H NMR (500 MHz, dmso) δ 10.30 (s, 1H), 8.51 (s, 1H), 8.07 (dd, J = 4.7, 1.4 Hz, 1H), 7.63 (dd, J = 7.7, 1.5 Hz, 1H), 7.46 (d, J = 5.0 Hz, 1H), 7.20 (d, J = 3.0 Hz, 1H), 7.00 (dd, J = 5.0, 3.6 Hz, 1H), 6.72 (dd, J = 7.7, 4.8 Hz, 1H). 13C NMR (126 MHz, dmso) δ 150.44 (s), 146.63 (s), 140.20 (s), 138.49 (s), 137.58 (s), 128.73 (s), 127.72 (s), 127.37 (s), 115.91 (s), 113.72 (s). LC-MS m/z calculated $C_{10}H_8ClN_3S$: Exact Mass: 237.01.

(E)-2-(2-((1H-pyrrol-2-yl) methylene) hydrazinyl)-3-chloropyridine (3l)
1H NMR (500 MHz, dmso) δ 11.25 (s, 1H), 9.95 (s, 1H, Ar-NH), 8.10 (s, 1H), 7.94 (dd, J = 4.8, 1.4 Hz, 1H), 7.55 (dd, J = 7.6, 1.3 Hz, 1H), 6.71 (d, J = 1.5 Hz, 1H), 6.60 (dd, J = 7.7, 4.8 Hz, 1H), 6.20 (dd, J = 4.2, 2.8 Hz, 1H), 5.95 (dd, J = 5.5, 2.6 Hz, 1H). 13C NMR (126 MHz, dmso) δ 150.80 (s), 146.29 (s), 137.32 (s), 136.93 (s), 128.02 (s), 121.42 (s), 114.99 (s), 113.28 (s), 111.61 (s), 108.96 (s). LC-MS m/z calculated $C_{10}H_9ClN_4$: Exact Mass: 220.05

(E)-2-(2-((5-bromothiophen-2-yl) methylene) hydrazinyl)-3-chloropyridine (3m)
1H NMR (500 MHz, dmso) δ 10.44 (s, 1H), 8.42 (s, 1H), 8.08 (dd, J = 4.7, 1.5 Hz, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.13 (d, J = 3.9 Hz, 1H), 7.05 (d, J = 3.9 Hz, 1H), 6.75 (dd, J = 7.7, 4.7 Hz, 1H). 13C NMR (126

MHz, dmso) δ 150.26 (s), 146.65 (s), 142.18 (s), 137.70 (s), 137.46 (s), 131.08 (s), 129.01 (s), 116.21 (s), 113.88 (s), 112.88 (s). LC-MS m/z calculated $C_{10}H_7BrClN_3S$: Exact Mass: 314.92

(E)-3-chloro-2-(2-((1E,2E)-3-phenylallylidene) hydrazinyl) pyridine (3n)
1H NMR (500 MHz, dmso) δ 10.29 (s, 1H), 8.12 (d, J = 9.3 Hz, 1H), 8.03 (dd, J = 4.7, 1.5 Hz, 1H), 7.62 (dd, J = 7.7, 1.6 Hz, 1H), 7.47 (d, J = 7.4 Hz, 2H), 7.26 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.3 Hz, 1H), 6.95 (dd, J = 16.1, 9.3 Hz, 1H), 6.80 – 6.67 (m, 2H). ^{13}C NMR (126 MHz, dmso) δ 150.43 (s), 146.62 (s), 146.44 (s), 145.42 (s), 137.55 (s), 136.38 (s), 135.79 (s), 128.86 (s), 128.34 (s), 127.57 (s), 126.78 (s), 126.44 (s), 115.96 (s), 113.74 (s). LC-MS m/z calculated $C_{14}H_{12}ClN_3$: Exact Mass: 257.07

(E)-2-(2-(3-(benzyloxy) benzylidene) hydrazinyl)-3-chloropyridine (3o)
^{1}H NMR (500 MHz, dmso) δ 10.37 (s, 1H), 8.25 (s, 1H), 8.07 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.63 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.19 (m, 3H), 7.15 (d, *J* = 7.7 Hz, 1H), 6.90 (dd, *J* = 7.9, 2.2 Hz, 1H), 6.72 (dd, *J* = 7.7, 4.7 Hz, 1H), 5.02 (s, 2H). ^{13}C NMR (126 MHz, dmso) δ 158.70 (s), 150.62 (s), 146.62 (s), 142.86 (d, *J* = 7.6 Hz), 137.72 (s), 137.03 (s), 136.81 (s), 129.90 (s), 128.49 (s), 128.31 (s), 127.84 (d, *J* = 16.4 Hz), 119.47 (s), 116.05 (s), 115.60 (s), 113.86 (s), 112.08 (s), 69.30 (s). LC-MS m/z calculated $C_{19}H_{16}ClN_3O$: Exact Mass: 337.10

(E)-4-bromo-2-((2-(3-chloropyridin-2-yl) hydrazono) methyl) phenol (3p)
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.89 (d, *J* = 10.0 Hz, 1H), 10.98 (d, *J* = 4.7 Hz, 1H, Ar-OH), 8.52 (s, 1H), 8.21 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.80 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.63 (d, *J* = 2.5 Hz, 1H), 7.36 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.92 – 6.83 (m, 2H). ^{13}C NMR (126 MHz, dmso) δ 150.23 (s), 146.58 (s), 146.44 (s), 142.17 (s), 137.65 (s), 137.42 (s), 137.18 (s), 131.03 (s), 128.96 (s), 116.14 (s), 113.85 (s), 112.84 (s). LC-MS m/z calculated $C_{12}H_9BrClN_3O$: Exact Mass: 324.96

(E)-3-chloro-2-(2-(pyridin-2-ylmethylene) hydrazinyl) pyridine (3q)
^{1}H NMR (500 MHz, DMSO-d_6) δ 10.80 (s, 1H), 8.56 (d, *J* = 4.6 Hz, 1H), 8.44 (s, 1H), 8.20 (d, *J* = 3.6 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.87 – 7.69 (m, 2H), 7.37 – 7.27 (m, 1H), 6.89 (ddd, *J* = 12.3, 7.6, 4.8 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 154.31 (s), 150.36 (s), 149.29 (s), 146.64 (s), 143.10 (s), 137.91 (s), 136.58 (s), 125.26 (s), 123.35 (s), 119.31 (s), 116.59 (s). LC-MS m/z calculated $C_{11}H_9ClN_4$: Exact Mass: 232.05

(E)-5-((2-(3-chloropyridin-2-yl) hydrazono) methyl)-2-nitrophenol (3r)
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.30 (s, 1H), 10.61 – 10.32 (m, 1H), 8.35 (s, 1H), 8.21 – 8.08 (m, 2H), 7.87 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.83 (s, 1H). ^{13}C NMR (126 MHz, dmso) δ 152.55 (s), 150.52 (s), 146.52 (s), 140.98 (s), 137.65 (s), 137.02 (s), 132.59 (s), 126.96 (s), 122.73 (s), 119.65 (s), 115.91 (s), 113.85 (s). LC-MS m/z calculated $C_{12}H_9ClN_4O_3$: Exact Mass: 292.04

(E)-3-chloro-2-(2-(3-methylbutylidene) hydrazinyl) pyridine (3s)
^{1}H NMR (600 MHz, DMSO-d_6) δ 9.85 (s, 1H), 8.06 (d, *J* = 4.4 Hz, 1H), 7.72 – 7.61 (m, 3H), 6.73 (dd, *J* = 7.5, 4.9 Hz, 1H), 2.13 (t, *J* = 6.4 Hz, 2H), 1.81 (hept, *J* = 6.7 Hz, 1H), 0.93 (d, *J* = 6.7 Hz, 5H). ^{13}C NMR (126 MHz, dmso) δ 150.92 (s), 146.80 (s), 146.35 (s), 137.20 (s), 115.01 (s), 112.93 (s), 40.85 (s), 26.63 (s), 22.36 (s), 22.31 (s). LC-MS m/z calculated $C_{10}H_{14}ClN_3$: Exact Mass: 211.09

(E)-3-chloro-2-(2-(2-chlorobenzylidene) hydrazinyl) pyridine (3t)
^{1}H NMR (600 MHz, DMSO-d_6) δ 10.82 (s, 1H), 8.79 (s, 1H), 8.19 (d, *J* = 4.1 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.34 (m, 2H), 6.87 (dd, *J* = 7.3, 4.9 Hz, 1H). ^{13}C NMR (126 MHz, dmso) δ 150.43 (s), 146.62 (s), 138.66 (s), 137.79 (s), 132.62 (s), 132.28 (s), 130.20 (s), 129.77 (s), 127.39 (s), 126.44 (s), 116.39 (s), 114.02 (s).
LC-MS m/z calculated $C_{12}HCl_2N_3$: Exact Mass: 265.02

RESULTS AND DISCUSSION

1. Continuous Synthesis of Hydrazone Derivatives Using Spinning Disc Reactor (SDR)

We continuously made hydrazone derivatives **(3a–3t)** using a Spinning Disc Reactor (SDR), which provided a fast, effective, and eco-friendly way to produce useful biological molecules. The change in

conversion was finished in 5 seconds at a temperature of 40–45°C when using equal amounts of 3-chloro-2-hydrazinylpyridine **(1a)** and 1H-indole-3-carbaldehyde **(2a)** in ethanol. These improved conditions regularly produced consistent results in many tests (Table-2, Entries 1–20), showing that the SDR works well and can be used on a larger scale for hydrazone condensation reactions. The SDR mixes things well and helps transfer materials easily, making operations simpler and better for the environment. It supports cleaner, energy-saving processes that produce less waste and need less cleaning. The hydrazone compounds **(3a-3t)** that were created were then studied and tested for their biological activities, as explained in the method section.

Antibacterial Activity

All synthesised derivatives (3a–3t) were evaluated in vitro against four bacterial strains: Escherichia coli (MTCC 443), Pseudomonas aeruginosa (MTCC 1688), Staphylococcus aureus (MTCC 96), and Streptococcus pyogenes (MTCC 442), using the microbroth dilution method. Minimum Inhibitory Concentration (MIC) values are presented in Table-3.

Table-3: *In-vitro* Antimicrobial and Antimalarial Activities of Synthesised 3-chloro-2-hydrazinyl Pyridine Derivatives

Compounds	Antibacterial activity MIC (µg/mL) [S.D. = ± 5]				Antifungal activity MIC (µg/mL) [S.D. = ± 10]			Antimalarial activity IC_{50} in µg/mL [S.D. = ± 0.005]
	E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenus*	*C. albicans*	*A. niger*	*A. clavatus*	*P. falciparum*
3a	125	125	62.5	100	500	1000	1000	0.81
3b	250	200	100	62.5	1000	>1000	>1000	1.03
3c	100	125	250	62.5	500	1000	1000	0.64
3d	125	200	250	100	250	500	500	0.71
3e	62.5	100	100	100	1000	250	250	0.87
3f	125	100	125	125	1000	500	500	0.68
3g	200	62.5	200	250	>1000	500	500	0.62
3h	62.5	100	100	200	500	1000	>1000	0.84
3i	50	100	100	125	1000	500	500	0.81
3j	100	62.5	125	250	250	500	500	1.07
3k	125	200	62.5	100	1000	250	250	0.68
3l	100	200	100	125	1000	1000	1000	1.05
3m	62.5	100	125	200	250	500	500	0.64
3n	62.5	125	125	125	1000	1000	1000	0.92
3o	100	62.5	100	100	250	1000	1000	0.86
3p	125	100	125	125	500	500	500	0.95
3q	100	62.5	200	200	1000	500	500	0.79
3r	62.5	100	250	100	500	250	250	0.86
3s	125	125	100	125	1000	1000	1000	0.68
3t	62.5	100	125	250	1000	500	500	0.75
Gentamycin	0.05	1	0.25	0.5	-	-	-	-
Ampicillin	30	-	40	25	-	-	-	-
Chloramphenicol	50	50	50	50	-	-	-	-
Ciprofloxacin	25	25	50	50	-	-	-	-
Norfloxacin	10	10	10	10	-	-	-	-
Nystatin	-	-	-	-	100	100	100	-
Griseofulvin	-	-	-	-	500	100	100	-
Chloroquine	-	-	-	-	-	-	-	0.020
Quinine	-	-	-	-	-	-	-	0.268

Table-4: Comparative antibacterial activity (ZOI, mm) of hydrazone derivatives (3a–3t) against *E. coli, P.aeruginosa, S. aureus,* and *S. pyogenes*

Antibacterial Activity [Zone of Inhibition] Microgramme / mm																
Compounds	*E. Coli* F. MTCC 443				P. *Aeruginosa* Q. MTCC 1688				R. *Aureus* S. MTCC 96				T. *Pyogenus* U. MTCC 442			
	25	50	100	250	25	50	100	250	25	50	100	250	25	50	100	250
3a	9	11	12	14	7	8	10	11	10	11	14	17	9	10	12	13
3b	8	10	11	12	9	10	11	12	8	10	11	12	10	11	12	13
3c	9	10	11	12	9	11	12	13	9	10	12	13	8	9	11	12
3d	9	11	13	14	9	10	11	12	10	11	12	14	10	11	13	14
3e	10	13	16	18	8	11	12	14	9	10	11	13	10	11	12	13
3f	10	11	12	14	8	10	11	12	10	12	13	15	8	10	11	14
3g	10	11	12	13	10	11	13	16	9	10	12	13	9	11	12	13
3h	9	12	15	16	9	10	12	14	8	10	11	13	9	12	13	15
3i	10	12	15	19	9	10	13	15	10	12	13	15	10	11	14	15
3j	10	11	12	14	10	12	13	16	9	10	11	13	9	10	11	13
3k	10	12	13	14	9	10	12	14	10	11	12	14	10	11	13	15
3l	9	11	13	15	10	11	12	14	9	10	11	13	10	11	12	14
3m	9	11	13	16	9	11	12	13	10	11	13	14	9	12	13	14
3n	10	12	13	15	8	10	12	13	10	11	13	15	10	11	12	15
3o	10	11	13	14	10	12	14	16	8	10	12	14	9	11	13	14
3p	9	10	12	13	9	10	12	13	8	9	11	12	9	10	11	13
3q	9	11	13	14	9	10	12	13	10	11	12	14	10	11	12	13
3r	9	10	12	14	9	11	13	14	9	10	11	12	9	10	11	12
3s	10	12	14	15	9	10	13	14	10	12	13	14	9	12	13	14
3t	9	11	12	13	10	11	12	13	8	10	11	13	10	11	12	13
Standard Drugs																
Ampicillin	15	16	19	20	NA				14	16	18	19	13	14	16	18
Chloramphenicol	17	23	23	23	17	18	19	21	13	19	20	20	14	19	20	21
Ciprofloxacin	23	28	28	28	23	24	26	27	19	21	21	22	19	21	22	22
Norfloxacin	25	26	27	29	19	21	23	23	19	20	21	21	22	25	26	28

These results suggest that certain derivatives serve as promising leads for developing antibacterial agents, particularly against Gram-negative pathogens.\

Several Compounds Exhibited Significant Antibacterial Activity

Compounds 3e, 3h, 3i, 3m, 3n, 3r, and 3t showed MICs ranging from 50–125 µg/mL against E. coli. 3g, 3j, 3o, and 3q showed moderate activity against P. aeruginosa. 3a and 3k were active against S. aureus. 3b and 3c demonstrated comparable activity to standard antibiotics against S. pyogenes.

Compound	*E. coli*	*P.aeruginosa*	*S.aureus*	*S.pyogenes*	*C.albicans*	*A.niger*	*A.clavatus*
3a	125	125	62.5	100	500	1000	1000
3b	250	200	100	62.5	1000	1200	1200
3c	100	125	250	62.5	500	1000	1000
3d	125	200	250	100	250	500	500
3e	62.5	100	100	100	1000	250	250
3f	125	100	125	125	1000	500	500
3g	200	62.5	200	250	1200	500	500
3h	62.5	100	100	200	500	1000	1200

3i	50	100	100	125	1000	500	500
3j	100	62.5	125	250	250	500	500
3k	125	200	62.5	100	1000	250	250
3l	100	200	100	125	1000	1000	1000
3m	62.5	100	125	200	250	500	500
3n	62.5	125	125	125	1000	1000	1000
3o	100	62.5	100	100	250	1000	1000
3p	125	100	125	125	500	500	500
3q	100	62.5	200	200	1000	500	500
3r	62.5	100	250	100	500	250	250
3s	125	125	100	125	1000	1000	1000
3t	62.5	100	125	250	1000	500	500

Fig.-5: Heat Map or Bar Chart Comparing ZOI of Synthesized Compounds vs Standard Antibiotics
A color-scale heatmap (green → strong, yellow → medium, red → weak activity)

Green-highlighted cells for the lowest MIC (best compound) in each organism column

Zone of Inhibition (ZOI)
Assays (Table-4) further supported these findings. Compounds 3e, 3h, and 3i showed the largest ZOI (up to 19mm against *E. coli* and *S. aureus* at 250 µg/mL), approaching or exceeding the activity of Chloramphenicol and Ampicillin.

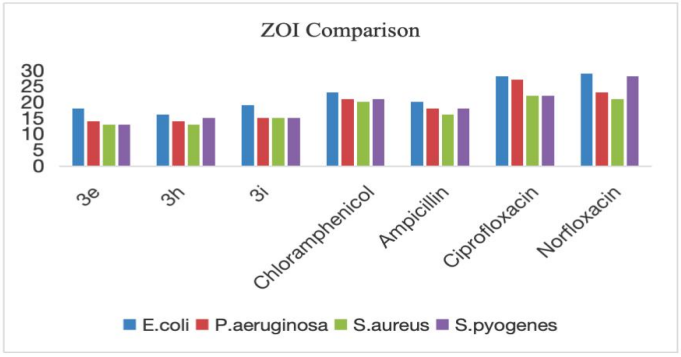


Fig.-6: Comparison of Zone of Inhibition (ZOI) of Compounds 3e, 3h, and 3i with Standard Antibiotics

The promising activity of compounds **3e, 3h**, and **3i**, further testing and optimisation of these compounds could yield potential alternatives or adjuncts to standard antibiotic therapies. Additionally, exploring their mechanisms of action could provide insights into novel therapeutic approaches for treating infections caused by resistant bacterial strains. Compounds 3e, 3h, and 3i exhibited the largest inhibition zones (up to 19 mm), comparable to those observed for standard antibiotics (Chloramphenicol and Ampicillin). The antifungal potential of compounds 3a–3t was assessed against Candida albicans (MTCC 227) and Aspergillus niger (MTCC 282), using the ZOI method. Results are detailed in **Table-5.** Compounds 3n, 3s, and 3o demonstrated superior antifungal activity, with inhibition zones reaching 12–14 mm at 250 µg/mL, particularly against A. niger. Compounds 3f, 3d, and 3k also showed good inhibition, though slightly lower than Nystatin, the standard drug.

Table-5: Zone of Inhibition Activity Table of Synthesised 3-chloro-2-hydrazinyl Pyridine Derivatives

Antifungal Activity [Zone of Inhibition] Micrograms/mm								
Compounds	C. ALBICANS MTCC 227				A. NIZER MTCC 282			
	25	50	100	250	25	50	100	250
3a	7	8	9	11	7	9	10	11
3b	8	9	10	11	8	9	10	11
3c	7	8	11	12	7	8	9	10
3d	8	10	11	12	8	10	11	12
3e	7	8	10	11	9	10	11	12

3f	8	10	11	12	9	10	12	13
3g	9	10	12	13	8	9	10	12
3h	8	10	11	13	7	8	9	11
3i	8	9	10	11	8	9	11	12
3j	8	9	10	12	8	10	11	12
3k	9	10	12	13	7	8	10	11
3l	9	10	11	12	8	9	10	12
3m	8	9	10	11	9	11	12	13
3n	9	10	11	12	9	11	12	14
3o	9	11	12	13	9	10	12	13
3p	8	10	11	12	8	9	10	12
3q	8	9	10	11	8	9	10	11
3r	8	9	10	12	8	10	11	12
3s	9	10	12	13	9	11	12	14
3t	9	10	11	12	9	10	11	13
Nystatin	19	24	29	29	19	24	29	29

Although the overall activity was lower than that of Nystatin, some derivatives displayed promising activity at higher concentrations, indicating their potential for further antifungal development.

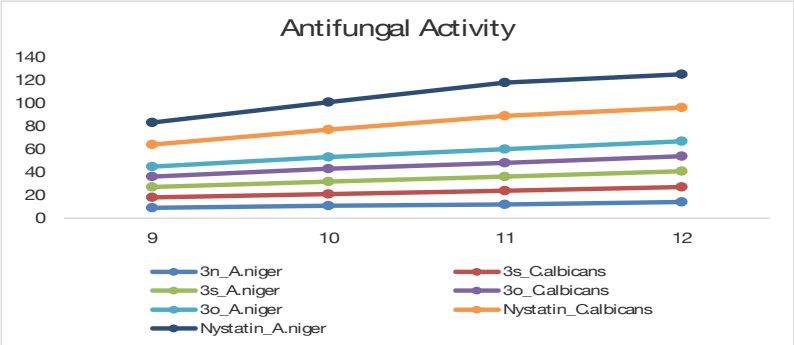


Fig.-7: Antifungal Activity of Synthesised Hydrazone Derivatives 3n, 3s, and 3o

Antimalarial Activity

In vitro antimalarial activity against *Plasmodium falciparum* was measured by IC_{50} values (Table-6). All derivatives showed varying degrees of activity: The most active compounds were 3g (0.62 µg/mL), 3c (0.64 µg/mL), and 3m (0.64 µg/mL). Compounds 3j, 3b, and 3l had the highest IC_{50} values (≥1 µg/mL), indicating lower potency. While none of the derivatives matched the potency of standard drugs Chloroquine (IC_{50} = 0.020 µg/mL) or Quinine (IC_{50} = 0.268 µg/mL), several showed moderate activity and could be structurally optimized to enhance efficacy.

Table-6: Antimalarial Activity (*Plasmodium falciparum*) Minimal Inhibition Concentration

Compounds	Mean IC50 Values
3a	0.81 µg/ml
3b	1.03 µg/ml
3c	0.64 µg/ml
3d	0.71 µg/ml
3e	0.87 µg/ml
3f	0.68 µg/ml
3g	0.62 µg/ml
3h	0.84 µg/ml
3i	0.81 µg/ml
3j	1.07 µg/ml
3k	0.68 µg/ml
3l	1.05 µg/ml
3m	0.64 µg/ml

3n	0.92 µg/ml
3o	0.86 µg/ml
3p	0.95 µg/ml
3q	0.79 µg/ml
3r	0.86 µg/ml
3s	0.68 µg/ml
3t	0.75 µg/ml

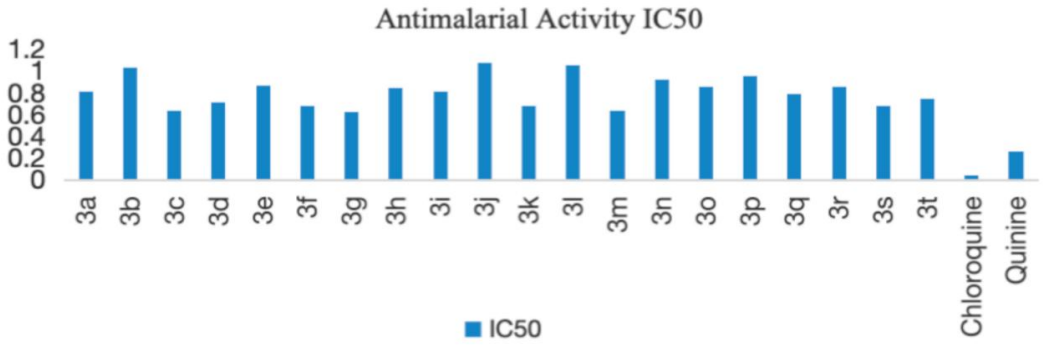


Fig.-8: IC_{50} Values for Synthesised Hydrazone Derivatives Against Plasmodium Falciparum

CONCLUSION

The continuous synthesis of hydrazone derivatives (3a–3t) using a Spinning Disc Reactor (SDR) demonstrated a rapid, efficient, and environmentally sustainable method for generating bioactive compounds. The SDR's ability to achieve complete conversion within 5 seconds at mild temperatures (40–45°C) under equimolar conditions highlights its potential for scalable and green chemical manufacturing, minimising waste and purification requirements. The synthesised hydrazone derivatives exhibited broad-spectrum biological activity. Among them, compounds 3e, 3h, and 3i showed significant antibacterial effects against *E. coli* and *S. aureus*, comparable to standard antibiotics. Compounds 3n, 3s, and 3o demonstrated notable antifungal activity against *A. niger*, while 3g, 3c, and 3m displayed promising antimalarial activity with IC_{50} values below 0.7 µg/mL. These findings underscore the potential of hydrazone scaffolds as multifunctional bioactive agents suitable for further optimisation. Future work should focus on (i) detailed mechanistic and structure–activity relationship (SAR) studies to identify pharmacophoric features driving bioactivity; (ii) in vivo biological evaluation to confirm therapeutic relevance; and (iii) process intensification studies to enable continuous, large-scale production. This research directly supports SDG 3 (Good Health and Well-Being) by contributing to the discovery of novel antibacterial, antifungal, and antimalarial candidates addressing the growing challenge of antimicrobial resistance. It also aligns with SDG 12 (Responsible Consumption and Production) through the implementation of a green, energy-efficient continuous synthesis process that reduces chemical waste and enhances process sustainability.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

This research directly supports *SDG-3: Good Health and Well-Being*. All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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REFERENCES

1. A. Domokos, B. Nagy, B. Szilágyi, G. Marosi, and Z. K. Nagy, *Organic Process Research and Development*, **25(4)**, 721(2021), https://doi.org/10.1021/acs.oprd.0c00504
2. Marek Trojanowicz, *Molecules,* **25(6)**, 1434(2020), https://doi.org/10.3390/molecules25061434
3. B. Gutmann, and C. O. Kappe, *Journal of Flow Chemistry,* **7(3-4)**, 65(2017), https://doi.org/10.1556/1846.2017.00009
4. P. Brandão, M. Pineiro, and T. M. Pinho e Melo, *European Journal of Organic Chemistry*, **43**, 7188(2019), https://doi.org/10.1002/ejoc.201901335
5. S. D. Pask, O. Nuyken, and Z. Cai, *Polymer Chemistry,* **3(10)**, 2698(2012), https://doi.org/10.1039/C2PY20237A
6. P. Oxley, C. Brechtelsbauer, F. Ricard, N. Lewis, and C. Ramshaw, *Industrial and Engineering Chemistry Research*, **39(7),** 2175(2000), https://doi.org/10.1021/ie990869u
7. K. Boodhoo, and A. Harvey(Eds.), *Process intensification technologies for green chemistry: engineering solutions for sustainable chemical processing,* John Wiley and Sons, p.59, 90(2013), https://doi.org/10.1002/9781118498521.ch3
8. M. Meeuwse, J. Van der Schaaf, and J. C. Schouten, *AIChE Journal*, **58(1)**, 247(2012), https://doi.org/10.1002/aic.12586
9. S. Goel, M. Khulbe, A. Aggarwal, and A. Kathuria, *Molecular Diversity*, **26(5)**, 2939(2022), https://doi.org/10.1007/s11030-021-10338-9
10. D. Ghiasy, M. T. Tham, and K. V. Boodhoo,*Industrial and Engineering Chemistry Research*, **52(47)**, 16832(2013), https://doi.org/10.1021/ie4020149
11. M. Vicevic, K. Novakovic, and K. Boodhoo, *Frontiers in Chemical Engineering*, **3**, 661498(2021), https://doi.org/10.3389/fceng.2021.661498
12. A. N. Manzano Martí nez, K. M. Van Eeten, J. C. Schouten, and J. Van der Schaaf, *Industrial and Engineering Chemistry Research*, **59(36)**, 16095(2020), https://dx.doi.org/10.1021/acs.iecr.0c03157
13. A. Chaudhuri, S. D. Zondag, J. H. Schuurmans, J. Van der Schaaf, and T. Noël, *Organic Process Research and Development*, **26(4)**, 1279(2022), https://doi.org/10.1021/acs.oprd.2c00012
14. N. B. Patil, P. Bandiwadekar, and G. U. Chaturbhuj, *Results in Chemistry*, **7,** 101423(2024), https://doi.org/10.1016/j.rechem.2024.101423
15. V. S. Padalkar, B. N. Borse, V. D. Gupta, K. R. Phatangare, V. S. Patil, and N. Sekar, *Journal of Heterocyclic Chemistry*, **53(5)**, 1347(2016), https://doi.org/10.1002/jhet.1506
16. D. S. Raghuvanshi, P. P. Mahulikar, and J. S. Meshram, *RSC Advances*, **5(59)**, 48071(2015), https://doi.org/10.1039/C5RA03528G
17. D. J. Van Dijken, P. Kovaricek, S. P. Ihrig, and S. Hecht, *Journal of the American Chemical Society*, **137(47)**, 14982(2015), https://doi.org/10.1021/jacs.5b09519
18. V. Jetti, P. Chidurala, R. Pagadala, J. S. Meshram, and C. Ramakrishna, *Journal of Heterocyclic Chemistry*, **51(S1)**, E183(2014), https://doi.org/10.1002/jhet.1922

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