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SYNTHESIS, CHARECTERIZATION AND ANTIBACTERIAL ACTIVITY OF SCHIFF BASES OF 3-SUBSTITUTED HYDRAZONO-1,3-DIHYDRO-INDOL-2-ONE

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Abstract

A series of 4 derivatives of novel Schiff bases of 3-substituted hydrazono-1,3-dihydro-indol-2-one have been synthesized in 2 steps by refluxing Isatin and Hydrazine Hydrate in step 1 which were further refluxed with 4 different aldehydes to form the Title compounds. The title compounds were screened for their anti-bacterial activity against both Gram-positive and Gram-Negative strains by Disc-diffusion method for determining zone of inhibition. All the tested compounds at 100µg/disc showed mild to significant activity. Among the synthesized compound, IHNB Was found to be significant active against most of the screened bacteria.

Keywords: SCHIFF Bases, Isatin, 1,3-Dihydro-Indol-2-one, Anti-Bacterial.

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INTRODUCTION

Isatin or 1H-indole-2,3-dione is an indole derivative. Ring system consists of pyrrole ring fused with benzene ring. Pyrrole is a five-member ring containing one nitrogen in the ring system. Several indole derivatives are reported to be antimicrobial activity. Isatin (1H -indole -2,3dione) is well known as pharmacological agent having a range of actions in the brain and to be protective against certain types of infections. A large number of Schiff bases of isatin derivatives have been found to exhibit various biological activities such as anti-inflammatory [1], antifungal, antibacterial [2,3,4] antiviral [8], anticancer [9], and anti HIV activities. Electrophilic carbon atoms of aldehydes and ketones may be targets of nucleophilic attack by amines. This will result in a compound in which the C=O double bond is replaced by a C=N double bond which is known as an **imine**, or **Schiff base**.

The mechanism of formation of an imine involves two steps. First, amine nitrogen acts as a nucleophile, attacking the carbonyl carbon. This is closely analogous to hemiacetal and hemiketal formation. Guanafuracin, which is a known antibiotic, is a hydrazone, and can be prepared easily by combining equimolar amounts of the appropriate aldehyde and hydrazine. Example involves chemistry ofs pyridoxal phosphate (PLP), a derivative of pyridoxine [5,6,7].

METHODOLOGY [1]

STEP-I: ***Synthesis of 3-Hydarzono-1, 3-dihydro-indol-2-one (IHYH)***

0.01mol of Isatin was dissolved in 9ml of ethanol and to this add a mixture of 0.01 mol hydrazine hydrate in 9ml of ethanol and refluxed for appropriate time.

The formation of product was checked by TLC. Then the reaction mixture was kept under refrigeration whole night. The solvent was filtered, washed with ethanol and recrystallized from ethanol.

STEP II: ***Synthesis of SCHIFF Bases Of Hydrazono-1,3-Dihydro-Indol-2-One***

0.01mol of 3-Hydarzono-1, 3-dihydro-indol-2-one which was formed in the step-I was dissolved in 9ml of ethanol and to this add a mixture of 0.01mol of different aldehydes in ethanol and refluxed for appropriate time.

The formation of product was checked by TLC. Then the reaction mixture was kept under refrigeration whole night. The solvent was filtered, washed with ethanol and recrystallized from ethanol.

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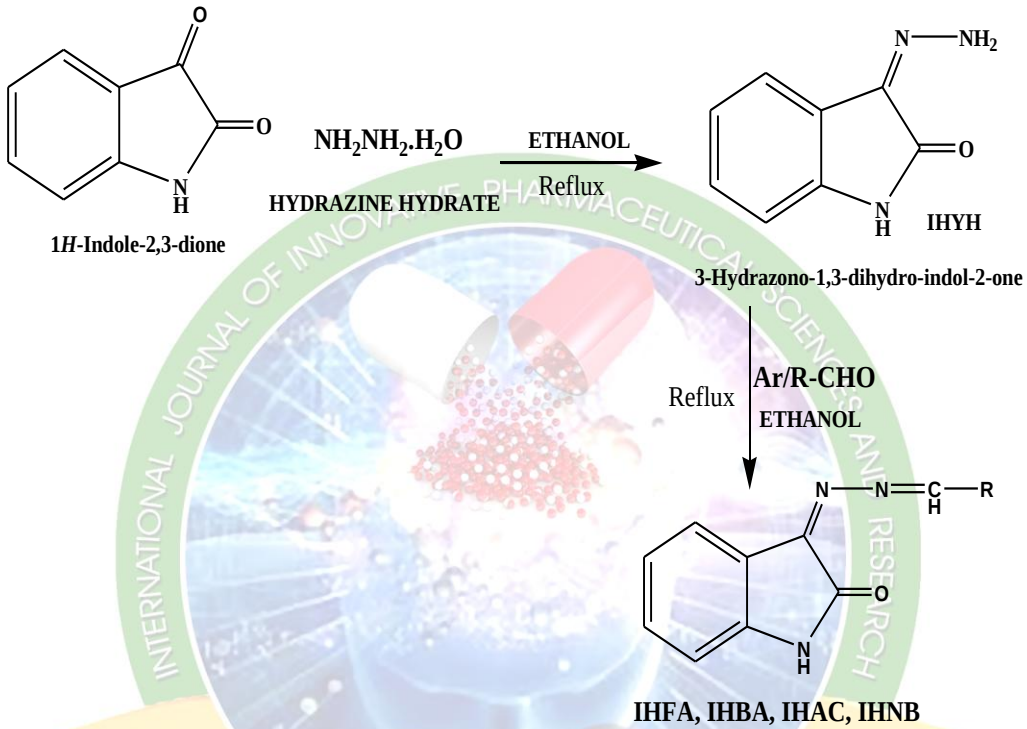
Table 1: List of Aldehydes used

S.No	Compound Code	R
1	IHYH	Hydrazine Hydrate (Intermediate)
2	IHFA	Formaldehyde
3	IHBA	Benzaldehyde
4	IHAC	Acetanilide
5	IHNB	2-Nitro-Benzaldehyde

SCHEME



BIOLOGICAL SCREENING

List of Bacterial strains used:

Two Gram-positive bacteria strain, Staphylococcus aureus, Pseudomonas aeruginosa and two Gram-negative bacteria strain, Escherichia coli, Vibrio cholera were grown in Laboratory for the study, fresh 24hr broth cultures were used.

Table 2: Quantitative Antibacterial screening by Disc diffusion

S.No	Compound Code	Diameter of zone of inhibition(mm)			
		Staphylococcus aureus	Pseudomonas aeruginosa	Escherichia coli	Vibrio cholera
1	IHFA	6	6	1	4
2	IHAC	2	6	2	2
3	IHBA	14	16	3	14
4	IHNB	12	12	6	10

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Antibacterial activity of synthesized compounds by disc diffusion method

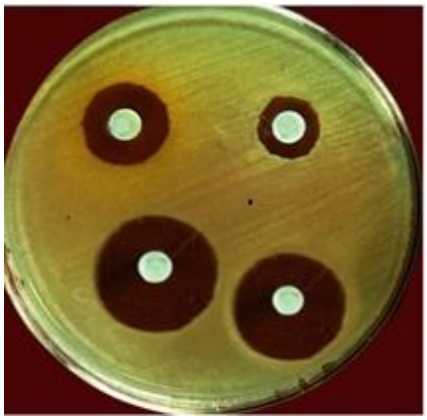

Fig. 1: Antibacterial activity against Staphylococcus aureus

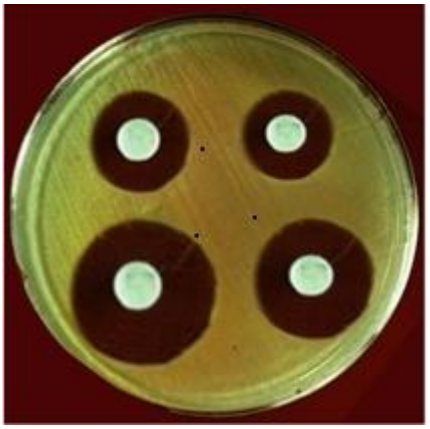

Fig.2: Pseudomonas aeruginosa

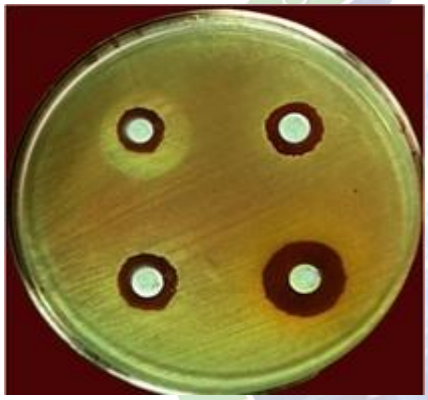

Fig.3: Antibacterial activity against

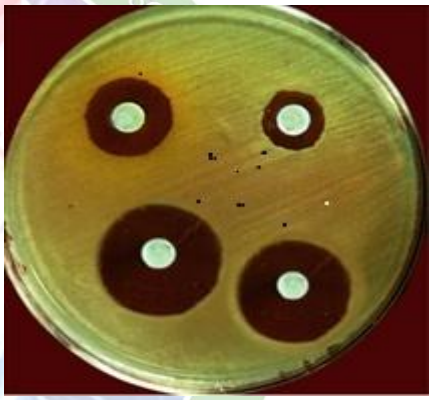

Fig.4: Escherichia Coli Vibrio cholera

RESULTS & DISCUSSION

In the present work 4 different Schiff bases were synthesized in 2 steps.

Step:1

3-Hydrazono-1,3-dihydro Indol-2-one have been prepared from Isatin and Hydrazine Hydrate by Reflux using ethanol as a solvent.

Step: II

4 different Schiff Bases were synthesized by refluxing 3-Hydrazono-1,3-dihydro Indol-2-one with 2 aliphatic and 2 aromatic Aldehydes.

Yield of the derivatives were in the range of 45-73%. Purity of all the newly synthesized compounds was checked by melting point and TLC analysis and their structures were confirmed by Infrared Spectroscopy.

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CHARECTERIZATION

INFRAREDSPCTRAL ANALYSIS

The structures of intermediate (IHYH) was confirmed by infrared spectroscopy. The compound (IHFA) shows the stretching for –C=O, C=N, -C-N in the region 1725.95, 1520.23, 1322.34, respectively. The compound (IHBA) was confirmed by the stretching of C=O, C=N, C-N, Aromatic CH=CH in the region 1738.04, 1540.28, 1306.90, 794.01. The compound (IHAC) shows the stretching of C=O, C=N, C-N, in the region 1741.90, 1518.60, 1392.52. The compound (IHNB) was confirmed by the stretching of aromatic C=O, C=N, and aliphatic C-N in the region 1742.70, 1650.55, 1339.26

BIOLOGICAL EVALUATION

ANTIBACTERIAL STUDIES

- All the newly synthesized compounds were screened for preliminary antibacterial activity against both Gram-positive and Gram-negative bacteria by Disc diffusion method at 100µg/disc concentration level. All the synthesized compounds were shown mild to moderate activity against all the screened microorganisms. All the compounds showed significant activity against Pseudomonas aeruginosa compared to other bacteria. Among the synthesized compounds the aromatic derivatives IHBA and IHNB shown significantly higher activities than aliphatic derivatives.
- All the compounds screened shown better activity against Gram positive bacteria than Gram negative bacteria. All compounds shown more activity against Gram positive bacteria, Pseudomonas aeruginosa. Compound IHNB shown higher activity against all bacterial strains except *Escherichia coli* than other compounds. All compounds shown less activity against Gram Negative bacteria *Escherichia coli* [10].

SUMMARY

EXPERIMENTAL WORK

In the present work totally 4 compounds were synthesized. The title compounds 3-substituted Hydrazono-1,3-dihydro-indol-2-one Schiff derivatives were prepared from 4 different aldehydes by refluxing with compound IHYH which in turn synthesized from Isatin and Hydrazine Hydrate. The yield was found to be in the range of 45-61%. The final compounds were found to be soluble in both polar and non-polar solvents. Thin layer chromatography was used to check the completion of the reaction and purity of the compounds synthesized. Melting points were taken in

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open glass capillary tubes and were uncorrected. The IR spectra of synthesized compounds appeared in the exhibited regions.

ANTI-BACTERIAL ACTIVITY

All the newly synthesized compounds were screened for their preliminary antibacterial activity against Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Vibrio cholera by disc diffusion method at a concentration of 100µg/disc. All the compounds have shown mild to moderate activity against all the screened microorganisms. Among the synthesized compounds, compound IHNB was found to be significant active against most of the screened bacteria. Among the synthesized compounds, compound IHBA demonstrated more zone of inhibition compared to all other compounds.

CONCLUSION

The Schiff bases of aldehyde derivatives of Isatin were already known for different biological studies. In the present investigation an attempt has been made for the synthesis of some novel Isatin Schiff bases combining Hydrazone with different aldehydes by Schiff reaction to get a good Anti-bacterial activity. As per the results of screening it is clearly indicated that the compounds of the scheme have showed good antibacterial activity.

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