

Study of antimicrobial activity of novel Isatin derivatives

Sravanthi Chirra ^{1,*}, S Neelufar Shama ², D Pranitha ³, Ch Madhav Reddy ¹ and Venkateshwar Rao Jupally ⁴

¹ Department of pharmaceutical chemistry, Scient Institute of Pharmacy, Ibrahimpatnam, Hyderabad, Telangana, India-501506.

² Department of Pharmacognosy, Scient Institute of Pharmacy, Ibrahimpatnam, Hyderabad, Telangana, India-501506.

³ Department of pharmaceuticals, Scient Institute of Pharmacy, Ibrahimpatnam, Hyderabad, Telangana, India-501506.

⁴ Department of pharmaceutical chemistry, Talla Padmavathi College of Pharmacy, Orus, Warangal, India-506002.

World Journal of Biology Pharmacy and Health Sciences, 2023, 13(01), 039–043

Publication history: Received on 03 November 2022; revised on 29 December 2022; accepted on 31 December 2022

Article DOI: <https://doi.org/10.30574/wjbphs.2023.13.1.0285>

Abstract

Objective: The aim of this study to synthesize, characterize and screen some new isatin derivatives for their antimicrobial activities.

Method: A library of isatin derivatives were synthesized, structures of newly synthesized compounds were deduced based on spectral data and elemental analysis.

Results: Antibacterial activity was screened against gram positive and gram negative bacterial strains.

Conclusion: The novel isatin derivatives produce significant antimicrobial activities.

Keywords: Isatin; Antibacterial; Antifungal; Analgesic; Anticonvulsant activity

1. Introduction

The field of medicinal chemistry is devoted to the discovery and development of new molecules for treating many diseases. The process of establishing a new molecule is exceedingly complex and involves the talents of people from the field of heterocyclic chemistry. The biological and pharmacological properties shown by the many pharmaceutical industries and as a result of this, the synthesis of heterocyclic compounds emerged as powerful techniques for generating lead molecule.

Isatin derivatives have been an area of intensive research due to their applicability in the prevention and treatment of various disorders. The isatins are fundamental constituents of a number of natural and synthetic products with biological activity. Isatin is a versatile compound isolated in 1988 and reported to possess a wide range of biological activities. It is also a synthetically versatile substrate that can be used to prepare a large variety of heterocyclic compounds, and acts as a raw material for synthesis of drugs. Schiff bases of isatin are known to possess a wide range of pharmacological properties, that are anticonvulsant [1], antibacterial [2], antifungal [2], anti-inflammatory [3], analgesic [3], antioxidant [4] and anti cancer [5] activities. In view of the biological importance of these isatins, it was planned to synthesize a new series of isatin analogues and were evaluated for antimicrobial, analgesic and anticonvulsant activity.

*Corresponding author: Sravanthi Chirra

2. Material and methods

2.1. Chemicals

All reagents were obtained from Sigma Aldrich. All the solvents used in these studies were dried and distilled before use. Melting points were determined by open capillary tube method and are uncorrected. Purity of the compounds checked by TLC using glass plates coated with Silica gel-G as adsorbent, and spots were detected by iodine vapor.

2.2. Biological activities

2.2.1. Anti-bacterial activity

The compounds were tested in vitro for their antibacterial activity against two gram positive bacteria viz *Bacillus subtilis* and *Staphylococcus Aureus* and two gram negative bacteria viz *Escherichia coli* and *Plasmodium vulgaris* are pathogenic in human beings.

2.2.2. Method

Cup plate agar diffusion method using Muller Hinton agar [6].

2.2.3. Materials

Nutrient agar, 18-24h growth culture in nutrient agar, sterile petridishes, sterile micropipettes, and sterile cotton swabs sterile cork borer (8mm) and sterile test tubes.

2.2.4. Preparation of nutrient agar

Peptone 0.6g, yeast extracts 0.15g, dipotassium dehydrogenate phosphate 0.13g was dissolved in 100ml distilled water and pH was adjusted to 7.2. This solution was sterilized by autoclaving at 15 p.s.i for 20 min.

2.2.5. Preparation of subculture

One day prior to these testing's, inoculation of the above bacterial cultures were made in the nutrient agar and incubated at 37°C for 18-24h.

2.2.6. Preparation of medium (Muller-Hinton Agar)

The 3.8g of agar was dissolved into 100ml of distilled water and the pH was adjusted to 7.4 ±0.2. It was sterilized by autoclaving at 15 p.s.i for 20 minutes.

2.2.7. Preparation of test solutions

Each test compound (5g) was dissolved in diethyl formamide (5ml) to give stock solution of concentration 1000µg/ml. Then 0.1ml of this solution was used for testing.

2.2.8. Preparation of standard solution

Standard drug norfloxacin was used. The concentration was 100µg/ml

2.2.9. Method of testing [7]

Muller – Hinton agar plates were prepared by pouring 10-15ml of the medium into each sterilized Petridis and were allowed to set at room temperature. The cell suspension was standardized to the density of 530nm using spectrophotometer and was inoculated over the surface of agar medium using sterile cotton swab. The eight cups were scooped in each plate using a sterile cork borer of 8mm diameter the solution of test compounds (0.10ml) were added in cups by using micropipettes and these were incubated at 37°C for 48h. The zone of inhibition was measured in mm of each organism.

2.3. Anti-fungal activity

2.3.1. Method

Cup-plate agar diffusion method using Sabourand Dextrose agar [8].

2.3.2. Materials used

Subourand-Dextrose agar, 18-24h growth culture on sabourand dextrose agar, sterile petridishes, sterile micropipettes, and sterile cotton swabs sterile cork borer (8mm) and sterile test tubes.

2.3.3. Preparation of Sabouraud-Dextrose Agar

Dextrose (40g), neopeptone (10g), agar (15g) was dissolved in distilled water (1000ml) and p^H adjusted to 5.5-6. This solution was sterilized by autoclaving at 120°C for 10 min.

2.3.4. Preparation of sub-cultures

One day prior to these testing's, inoculation of the above fungal cultures were made in the Sabourand Dextrose agar and incubated at 37°C for 18-24h. A suspension of cell from this culture was made in sterile distilled water. Five colonies more than 1mm diameter were mixed with 5ml of normal saline and vortexes for 15s. The cell density was adjusted using spectrophotometer at 530nm with addition of normal saline.

2.3.5. Preparation of test solutions

Each test compound (5g) was dissolved in dimethyl formamide (5ml) to give stock solution of concentration 1000µg/ml, then 0.1ml of this solution was used for testing.

2.3.6. Preparation of standard solution

Standard drug norfloxacin was used. The concentration was 100µg/ml

2.3.7. Method of testing [8]

Sabouraud-Dextrose agar plates were prepared by pouring 10-15ml of the medium into each sterilized Petridis and were allowed to set at room temperature. The cell suspension was standardized to the density of 530nm using spectrophotometer and was inoculated over the surface of agar medium using sterile cotton swab. The eight cups were scooped in each plate using a sterile corn borer of 8mm diameter, corresponding to control, standard and test solution.

Then the solution of test compounds (0.10ml) were added in cups by using micropipettes and these were incubated at 37°C for 48h. The zone of inhibition was measured in mm of each organism.

3. Results and discussion

In present study, the compounds were synthesized as depicted in scheme. The fourteen different novel isatin 3- [N-(4-substituted)-hydrazinyl-3-oxo prop 1-en-2yl] benzamides were prepared.

3.1. Antibacterial activity

Table 1 Inhibitory zone (diameter) mm of synthesized compounds against tested bacterial strains by cup plate agar diffusion method:

Sr. No	Compounds	Zone of inhibition (in mm)			
		<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. vulgaris</i>
1	B ₁	13	16	15	14
2	B ₂	19	18	17	18
3	B ₃	18	19	17	18
4	B ₄	13	12	14	11
5	B ₅	20	19	16	10
6	B ₆	22	22	20	19
7	B ₇	20	23	20	18
8	B ₈	21	20	19	16

9	B ₉	17	13	14	14
10	B ₁₀	13	17	16	13
11	B ₁₁	18	18	17	18
12	B ₁₂	15	17	15	14
13	B ₁₃	18	19	18	19
14	B ₁₄	20	21	18	13
Standard	Norfloxacin	23	25	21	20

Compounds B₂, B₃, B₁₁ and B₁₃ have shown promising antibacterial activity. However B₅, B₆, B₈ and B₁₄ compounds have shown excellent activity.

3.2. Antifungal activity

Compounds B₇, B₈, and B₁₃ are have shown greater zone of inhibition as compared with griseofulvin. The compounds B₂, B₆ and B₁ have shown excellent activity.

Table 2 Inhibitory zone (diameter) mm of synthesized compounds against tested fungal strains by cup plate agar diffusion method

S.NO	Compounds	Zone of inhibition (in mm)			
		<i>C. albicans</i>	<i>A. niger</i>	<i>C. verticulate</i>	<i>A. flavus</i>
1	B ₁	15	16	15	13
2	B ₂	18	22	20	14
3	B ₃	17	16	18	13
4	B ₄	18	19	16	12
5	B ₅	15	18	13	10
6	B ₆	21	22	20	17
7	B ₇	24	25	22	18
8	B ₈	22	26	20	19
9	B ₉	14	17	19	12
10	B ₁₀	13	15	17	11
11	B ₁₁	17	20	18	15
12	B ₁₂	14	16	18	16
13	B ₁₃	23	22	19	17
14	B ₁₄	15	13	16	10
Standard	Griseofulvin	25	26	24	20

4. Conclusion

Here, we concluded that novel isatin derivatives produce significant antimicrobial. It has been necessary from the results of preliminary investigations that there is a need further advanced studies, at least on a few of synthesized compounds.

Compliance with ethical standards

Acknowledgments

The authors are thankful to Shri. K. C. Shekar Reddy, Chairman Scient Institute of Pharmacy, Ibrahimpatnam, Rangareddy & Talla Mallesham Secretary & Correspondent of LS educational society, Warangal to provide necessary facilities to carry out this work.

Disclosure of conflict of interest

No conflict of interest.

References

- [1] Pandey S, Sriram D, Nath G, Declercq E. Synthesis, antibacterial, antifungal and anti HIV activities of schiff and mannich bases derived from isatin derivatives and N-[4-(4'-chloro phenyl) thiazol-2yl] thiosemicarbazide. *Eur J of Pharma Sci* 1999; 9(1): 25-31.
- [2] Ragavendran JV, Sriram D, Patel SK, Reddy TV, BharathwajanN, Stables J, et al. Design and Synthesis of anticonvulsants from a combined pthaimide-GABA-anilide and hydrazone pharmacophore. *Eur J of med chem.* 2007;42(2): 146-51.
- [3] Pannerselvam P, Ravi Sankar R, Kumaraswamy M, Ramesh Kumar N. Synthesis, antiinflammatory and antimicrobial activites of some novel schiff's bases of 5-substituted Isatin. *Der Pharma Chem.*2010; 2(1):28-37
- [4] Andreani A, Burnelli S, Granaiola M, LeoniaA, Locatelli A, Morigi R, et al, New Isatin derivatives with antioxidant activity. *Eur J of med chem.* 2010;45(4):1374-8.
- [5] Rajyalakshmi G, Ram Narsimha reddy A, Sarangapani M, Synthesis, characterization and anticancer activity of certain 3-[4-(5-mercapto-1,3,4-oxadiazole-2-yl)phenylimino]indolin-2-one derivatives. *Sudi Pharma J.* 2011;19:153-158.
- [6] HW Seely and Van Denmark PK *Microbes in action, Laboratory manual of microbiology, IInd Edn, 1975 (55).*
- [7] J Barbara, Howard, *Clinical and Pathogenic microbiology, IInd Edn, CV Mosby company, Toranto, 1987(914).*
- [8] CJ Van, H Kurata, *Antifungal susceptibility testing, J Med Vet Mycol, 32, 1994 (267).* SM Sondhi, Nidhi Singhod and RP Verma, *Synthesis anti-inflammatory and analgesic activity evaluation of some 2-(9-acridinyl amino)-pyridines and 2-(9-acridinyl amino/imino) thiazoles, Indian J Chem, 36B, 1997.*