Synthesis of Isatin Derivatives as An Antimycobacterial Agents with Antifungal Investigation

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ABSTRACT

Aim: This study focuses on the synthesis and evaluation of novel isatin derivatives as potential antimycobacterial agents with additional antifungal properties. The objective was to explore structural modifications in the isatin scaffold to enhance its biological activity against Mycobacterium species and fungal pathogens.

Experimental Section: A series of isatin derivatives were synthesized through condensation and cyclization reactions involving appropriate aldehydes, amines, and hydrazides. The chemical structures of the synthesized compounds were confirmed using spectroscopic techniques such as NMR, IR, and Mass Spectrometry. Antimycobacterial activity was evaluated using the Resazurin Microtiter Assay against Mycobacterium tuberculosis H37Rv, while antifungal activity was assessed against Candida albicans and Aspergillus niger through the broth microdilution method.

Results & Discussion: Several isatin derivatives exhibited significant antimycobacterial activity, with MIC values ranging between 1.5 and 8 µg/mL, indicating their potential as lead compounds. Derivatives with electron-withdrawing substituents showed enhanced activity, highlighting the importance of electronic effects on biological interactions. Moderate to high antifungal activity was observed, suggesting dual therapeutic potential. Structure-activity relationship (SAR) analysis revealed that substitutions at the 3-position of the isatin ring were crucial for activity.

Conclusion: The synthesized isatin derivatives demonstrated promising antimycobacterial and antifungal properties, establishing them as potential candidates for further pharmacological development. Future studies will focus on molecular docking and in vivo evaluations to elucidate their mechanism of action.

Keywords: Isatin derivatives, antimycobacterial agents, antifungal activity, structure-activity relationship, Mycobacterium tuberculosis.

 https://doi.org/10.5281/zenodo.14633803

INTRODUCTION

The emergence of drug-resistant strains of Mycobacterium tuberculosis and fungal pathogens poses a significant threat to global health.[1, 2] Tuberculosis (TB), caused by M. tuberculosis, remains one of the leading infectious diseases worldwide, with millions of new cases reported annually.[3] Similarly, fungal infections caused by species such as Candida albicans and Aspergillus niger are increasingly becoming a challenge due to limited treatment options and rising resistance to existing antifungal drugs.[4, 5] The urgent need for novel therapeutic agents has driven researchers to explore diverse chemical scaffolds, including heterocyclic compounds, for potential antimicrobial properties.[6, 7]

Isatin, a versatile heterocyclic molecule, has garnered attention due to its structural adaptability and significant pharmacological activities.[8, 9] As a privileged scaffold, isatin derivatives have shown promising results in various therapeutic areas, including anticancer, antiviral, antimicrobial, and antitubercular applications.[10, 11] The presence of both the keto and lactam functionalities in the isatin core allows for extensive structural modifications, enabling researchers to optimize biological activity.[12]

This study aims to synthesize a series of isatin derivatives and evaluate their potential as dual-function antimycobacterial and antifungal agents. By introducing various substituents at strategic positions on the isatin ring, this research seeks to enhance the compounds' interaction with biological targets responsible for mycobacterial and fungal pathogenesis. Additionally, a structure-activity relationship (SAR) analysis will provide insights into the impact of functional group modifications on antimicrobial efficacy. With a dual focus on antimycobacterial and antifungal activities, the synthesized compounds could address the therapeutic gaps in treating co-infections, which are prevalent among immunocompromised patients. This work not only expands the chemical space of isatin derivatives but also contributes to the discovery of novel scaffolds for combating multidrug-resistant pathogens.

OBJECTIVE AND PLAN OF WORK

Objective

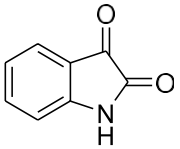
The synthetic versatility of isatin has more importance from the interest in the biological and pharmacological properties of its derivatives. In the field of pharmaceutical chemistry, in plant and animal biochemistry, the importance of the indole nucleus is well known. Therefore, the research interest on isatins has expanded day by day. Keeping this in mind, the present study aims at the synthesis of some isatin derivatives with the help of acetylation of corresponding synthesized Schiff bases and profiling of their pharmacological activities like antimicrobial and anti-inflammatory.

The compound with indole nucleus like isatin derivatives is associated with various pharmacological activities such as analgesic, antipyretic, anticonvulsant, antidepressant, antimicrobial, insecticide, anti-HIV and anticancer. Moreover, isatins are the synthetic precursors of some biologically important compounds such as quinoline 1, 2, 3-thiadiazoline. Besides that, the triazins [5, 6-b] indole-3-thione derivatives have attracted considerable attention in the field of

 https://doi.org/10.5281/zenodo.14633803

medicine due to their antifungal, antimalarial and antiparasitic properties.

The research programme proposed is a continuation of the research work carried out on the synthesis and biological studies of some indole 2, 3-dione derivatives. Promoted by the biological properties of 2, 3-dioxindole derivatives and their Schiff bases derived with the help of acetylation to synthesise different mixed forms of derivatives and to substitute different synthetic procedures in the ring system.



Isatin

Therefore, substitution by various substituent at different positions of aryl ring of isatin is proposed to design newer isatin derivatives.

Plan of work

All the chemicals used in the synthesis of isatin derivatives are of synthetic grade and procured locally. Thin layer chromatography is used for monitoring the progress of reaction and product formation. The thin layer chromatography of the synthesized compounds is carried on precoated TLC (silica gel) plates by using different solvent medium. Identification of spots are done under UV lamp and in iodine chamber. Detection of spots under UV lamp are recorded at both short and long wavelength. Melting points of the synthesized compounds are determined on melting point apparatus.

- Synthesis of isatin derivatives.
- Characterization of synthesized compounds with the help of different analytical method like I.R. Spectroscopy, NMR Spectroscopy.

Screening of synthesized compounds for pharmacological activities (antituberculosis activity and anti-fungal activity).

EXPERIMENTAL SECTION

3-keto group of isatins were substituted by aromatic primary amines (like benzene-1, 4-diamine, etc.) to afford Schiff bases. These Schiff bases were treated with chloroacetylchloride to afford the intermediate compounds. These intermediates treated with amines/phenols and acetonitrile in presence of anhydrous K2CO3 for 12 hours to get desired isatin derivatives.

EXPERIMENTAL PROCEDURES

Scheme-I

1. Synthesis of 3-(4-aminophenylimino)indolin-2-one (3)

Equimolar quantities of isatin (1.47 g) (1) and p-phenylenediamine (1.08 g) (2) were dissolved in 50 ml. ethanol in a 250ml round bottom flask. The glacial acetic acid (2-3 drops) was added and reaction solution was refluxed for 4 hrs. After standing for approximately 24 hr at room

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temperature, the product was obtained by filtration, washed and recrystallized with ethanol.

Yield: 70.09%, m.p. 215-217^{o}C, Rf : 0.49 (n-Hexane: Ethyl acetate; 1:1).

2. N-(4-(2-oxoindolin-3-ylidene-amino) phenyl)-2-chloroacetamide (4)

Equimolar quantities of 3-(4-aminophenylimino) indolin-2-one (2.37 g) (3) and chloroacetylchloride (1.13 ml.) were dissolved in acetonitrile (100 ml) in a 250 ml round bottom flask. The addition of chloroacetylchloride was done in dropwise manner. The anhydrous potassium carbonate was added and reaction mixture was refluxed for 4 hrs. The product was separated by filtration and vacuum dried. Recrystallization was done with ethanol.

Yield: 65.21 %, m.p: 235-237^{o}C, Rf: 0.54 (n-Hexane: Ethyl acetate; 1:1).

3. General procedure for synthesis of isatin derivative (PD1-15)

Equimolar quantities of N-(4-(2-oxoindolin-3-ylidene-amino) phenyl)-2- chloroacetamide (3.13 g) (4) and phenols or primary amines were dissolved in acetonitrile (100 ml) in a 250 ml round bottom flask. The anhydrous potassium carbonate (2 moles) was added and reaction solution was refluxed for 12 hrs. The reaction solution filtered and solvent removed under reduced pressure. The obtained product is washed with excess of water and purified by recrystallization with ethanol.

Scheme-II

1. Synthesis of 3-(4-sulphonamidephenylimino)indolin-2-one (3)

0.01M of isatin (1.47 g) (1) and sulphanilamide (1.72 g) (2) were dissolved in 50 ml ethanol in a 250ml round bottom flask. The glacial acetic acid (2-3 drops) was added and reaction solution was refluxed for 4 hrs. After standing for approximately 24 hr at room temperature, the product was obtained by filtration, washed and recrystallized with ethanol.

Yield: 73.09%, m.p. 210-213^{o}C, Rf : 0.62 (n-Hexane: Ethyl acetate; 1:1).

2. 2-chloro-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl)acetamide (4)

Equimolar quantities of 3-(4-sulphonamidephenylimino)indolin-2-one (3.01g) (3) and chloroacetylchloride (1.13 ml) were dissolved in acetonitrile (100 ml) in a 250 ml round bottom flask. The addition of chloroacetylchloride was done in dropwise manner. The anhydrous potassium carbonate (2 moles) was added and reaction mixture was refluxed for 4 hrs. The product was separated by filtration and vacuum dried. Recrystallization was done with ethanol.

Yield: 66.11 %, m.p: 225-227^{o}C, Rf: 0.62 (n-Hexane: Ethyl acetate; 1:1).

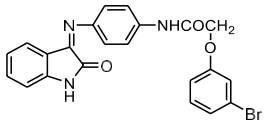
3. General procedure for synthesis of isatin derivative (SD1-15)

Equimolar quantities of 2-chloro-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (3.77 g) (4) and phenols or primary amines were dissolved in acetonitrile (100 ml) in a 250 ml round bottom flask. The anhydrous potassium carbonate (2 moles) was added and reaction solution was refluxed for 12 hrs. The reaction solution was filtered and solvent was removed under reduced pressure. The obtained product washed with excess of water and purified by recrystallization with ethanol.

 https://doi.org/10.5281/zenodo.14633803

Final isatin derivatives (Target compounds)

2-(3-bromophenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD1)



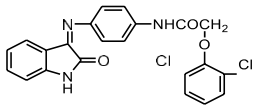
Yield: 60.39 %

Melting Range: 255-257℃

IR (KBr,cm^{-1}): 1641.75 (C=O Str), 2880.09 (C-H Str Ali), 3189.73 (N-H Str).

^{1}H-NMR (512MHz, CDCl3) (PPM): δ 10.37 (s, 1H, N-H), 6.52 (s, 1H, N-H), 6.65 8.13 (m, 12H, Ar-H), 3.82 (m, 2H,), 1.26 (d, J = 3.5 Hz, 1H).
Rf: 0.45 (n-Hexane: Ethyl acetate; 1:1).
Molecular Weight: 450.28

2-(2,6-dichlorophenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD2)



Yield: 58.98 %

Melting Range: 235-237 °C

IR (KBr, cm^{-1}): 1359.12 (C-O-C Str), 1662.55 (C=O Str), 2889.07 (C-H Str Ali).

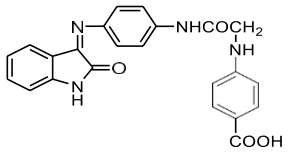
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 10.98 (s, 1H, N-H), 6.61 (s, 1H, N-H), 6.78 (m, 12H, Ar-H), 3.72 (s, 4H), 0.88 (t, J = 6.9 Hz, 1H), 0.84 (s, 1H).
Rf: 0.33 (n-Hexane: Ethyl acetate; 1:1).
Molecular Weight: 440.28

4-((2-oxo-2-((4-((2-oxoindolin-3-ylidene)amino)phenyl)amino)ethyl)amino) benzoic acid (PD3)

Yield: 54.65 %

Melting Range: 215-217 °C

IR (KBr, cm^{-1}): 1374.68 (C-O-C Str), 1638.31 (C=O Str), 2895.87 (C-H Str Ali), 3205.62 (N-H Str), 3736.57 (OH Str).
^{1}H-NMR (512MHz, CDCl3) (PPM): 4.34 (s, 4H, CO), 12.87 (s, OH), 6.99-5.85 (m, 12H, Ar-H).



Rf: 0.71 (n-Hexane: Ethyl acetate; 1:1).

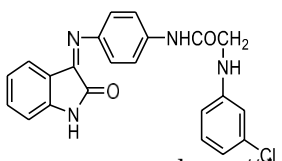
Molecular Weight: 414.41

2-((3-chlorophenyl)amino)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD4)

Yield: 55.95%

Melting Range: 210^{0}-212°C

IR (KBr, cm^{-1}): 697.56 (C-H ben.), 1366.37 (C-O-C Str), 2831.92 (C-H Str Ali), 3011.31 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 7.70-6.91 (m, 12H, Ar-H), 3.51 (s, 4H, CO), 10.70 (s, NH).



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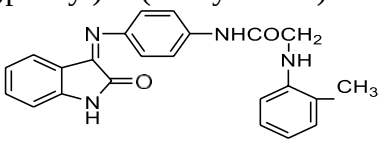
Rf: 0.55 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 404.85

N-(4-((2-oxoindolin-3-ylidene)amino)phenyl)-2-(o-tolylamino)acetamide (PD5)



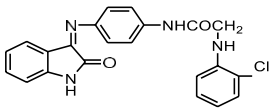
Yield: 63.15%

Melting Range: 245-247 °C

IR (KBr, cm^{-1}): 877.06 (C-H ben.), 1362.97 (C-O-C Str), 1646.01 (C=O Str), 2891.54 (C-H Str Ali), 3007.69 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 3.52 (s, 2H, CO), 10.03 (s, 2H, NH), 7.60-6.39 (m, 12H, Ar-H).
Rf: 0.65 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 384.43

2-((2-chlorophenyl)amino)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD6)



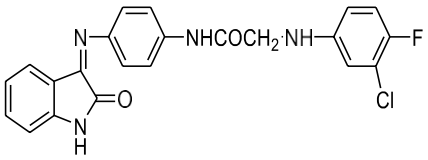
Yield: 67.51%

Melting Range: 210-212 °C

IR (KBr, cm^{-1}): 695.61 (C-H ben.), 1364.63 (C-O-C Str), 1612.09 (C=O Str), 2873.89 (C-H Str Ali), 3177.83 (N-H Str), 3010.53 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 10.52 (s, 1H, N-H), 6.48 (m, 1H, N-H), 6.81 – 7.60 (m, 12H, Ar-H), 3.82 (s, 2H,), 0.84 (s, 1H).
Rf: 0.39 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 404.85

2-((3-chloro-4-fluorophenyl)amino)-N-(4-((2-oxoindolin-3-ylidene)amino) phenyl)acetamide (PD7)



Yield: 63.82%

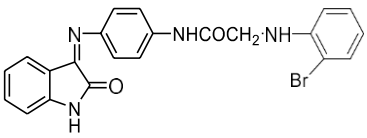
Melting Range: 225-228 °C

IR (KBr, cm^{-1}): 1071.90 (C-H ben.), 1395.44 (C-O-C Str), 1676.31 (C=O Str), 2891.24 (C-H Str Ali), 3344.28 (N-H Str), 3014.81 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 11.07 (s, 2H, 2NH), 7.67-6.89 (m, 12H, Ar-H), 4.01 (s,2H, CO).

Rf: 0.70 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 422.84

2-((2-bromophenyl)amino)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD8)



Yield: 59.52%

Melting Range: 255-257 °C

 https://doi.org/10.5281/zenodo.14633803

ISSN: 0369-8963

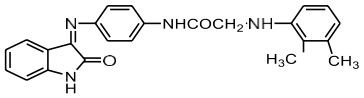
IR (KBr, cm^{-1}): 1075.00 (C-H ben.), 1381.34 (C-O-C Str), 1590.17 (C=O Str), 2887.74 (C-H Str Ali), 3356.63 (N-H Str), 3021.31 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 11.08 (s, 1H, N-H), 6.58 (s, 1H, N-H), 6.81

(m, 12H, Ar-H), 2.95 (s, 2H), 1.25 (m, 1H).

Rf: 0.80 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 449.30

2-((2,3-dimethylphenyl)amino)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl)acetamide (PD9)



Yield:60.56%

Melting Range: 260-263 ºC

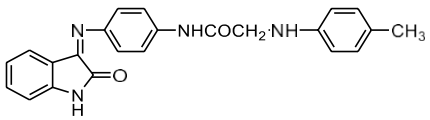
IR (KBr, cm^{-1}): 997.49 (C-H ben.), 1366.80 (C-O-C Str), 1586.28 (C=O Str), 2853.65 (C-H Str Ali), 3253.99 (N-H Str), 3017.06 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 11.07 (s, 2H, 2NH), 7.45-6.46 (m, 11H, Ar-H),

3.44 (s,2H, CO).

Rf: 0.25 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 398.46

N-(4-((2-oxoindolin-3-ylidene)amino)phenyl)-2-(p-tolylamino)acetamide (PD10)



Yield: 51.53 %

Melting Range: 250-252 ºC

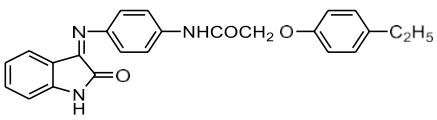
IR (KBr, cm^{-1}): 1001.09 (C-H ben.), 1589.15 (C=O Str), 2824.71 (C-H Str Ali), 3224.62 (N-H Str), 3015.21 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 10.29 (s, 1H, N-H), 6.28 (s, 1H, N-H), 3.57

(s, 2H), 6.71 (m, 12H, Ar-H), 0.83 (s, 4H).

Rf: 0.60 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 384.43

2-(4-ethylphenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl)acetamide (PD11)



Yield: 69.05 %

Melting Range: 230-232 ºC

IR (KBr, cm^{-1}): 981.47 (C-H ben.), 1592.63 (C=O Str), 2888.54 (C-H Str Ali), 3386.63 (N-H Str), 3011.34 (C-H Str. Aro).

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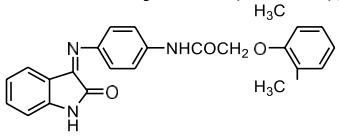
^{1}H-NMR (512MHz, CDCl3) (PPM): 4.24 (s,1H, CO), 10.87 (s, 1H, NH), 7.25-6.85 (m, 12H, Ar-H).
Rf: 0.81 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 399.44

2-(2,6-dimethylphenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD12)

Yield: 52.95 %



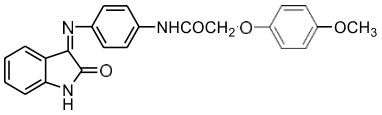
Melting Range: 240-242 ^{o}C

IR (KBr, cm^{-1}): 900.67 (C-H ben.), 1604.14 (C=O Str), 2861.19 (C-H Str Ali), 3261.78 (N-H Str), 3017.67 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 7.94-6.51 (m, 11H, Ar-H), 4.01 (s,2H, CO), 11.07 (s, 2H, NH).
Rf: 0.75 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 399.44

2-(4-methoxyphenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD13)

Yield: 60.43 %



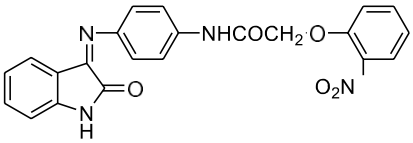
Melting Range: 220-222 ^{o}C

IR (KBr, cm^{-1}): 904.75 (C-H ben.), 1611.43 (C=O Str), 2887.54.15 (C-H Str Ali), 3287.93 (N-H Str), 3005.45 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 3.42 (s,2H, CO), 11.03 (s, 1H, NH), 8.06-6.99 (m, 12H, Ar-H), 3.83-3.89 (s, 11H, Ar-OCH3).
Rf: 0.61 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 401.41

2-(2-nitrophenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl)acetamide (PD14)

Yield: 58.95 %



Melting Range: 215-217 ^{o}C

IR (KBr, cm^{-1}): 999.22 (C-H ben.), 1589.56 (C=O Str), 2716.76 (C-H Str Ali), 3216.07 (N-H Str), 3006.13 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 10.98 (m, 1H, N-H), 6.55 (m, 1H, N-H), 6.80

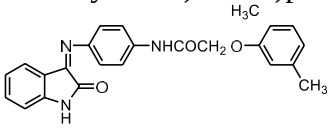
(m, 12H, Ar-H), 3.76 (m, 2H).

Rf: 0.83 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 416.39

2-(2,5-dimethylphenoxy)-N-(4-((2-oxoindolin-3-ylidene)amino)phenyl) acetamide (PD15)

Yield: 55.51 %



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Melting Range: 255-257 ºC

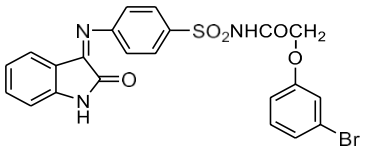
IR (KBr, cm^{-1}): 760.77 (C-H ben.), 1612.09 (C=O Str), 2310.07 (C-H Str Ali), 3177.83 (N-H Str).

^{1}H-NMR (512MHz, CDCl3) (PPM): 10.07 (s, 2H, 2NH), 7.57-6.59 (m, 11H, Ar-H), 4.31 (s,2H, CO).

Rf: 0.77 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 399.44

2-(3-bromophenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD1)



Yield: 55.37 %

Melting Range: 355-357 °C

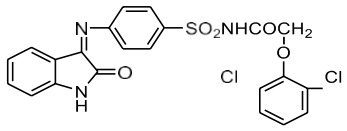
IR (KBr, cm^{-1}): 633.39 (C-H ben.), 1423.82 (C-N Str), 1736.61 (C=O Str), 2771.13 (C-H Str Ali), 3676.90 (N-H Str).

^{1}H-NMR (512MHz, CDCl3) (PPM): 3.91 (s, 2H, 2NH), 6.56 (d, J = 9.2 Hz, 6H), 6.87 (d, J = 6.8 Hz, 4H), 7.47 – 7.59 (m, 7H), 7.41 – 7.51 (m, 7H), 7.52 (d, J = 7.6 Hz, 7H), 7.76 – 8.07 (m, 7H).

Rf: 0.43 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 514.35

2-(2,6-dichlorophenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD2)



Yield: 60.88 %

Melting Range: 335-337 °C

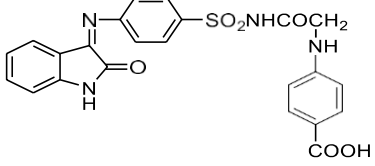
IR (KBr, cm^{-1}): 1145.01 (C-H ben.), 1410.50 (C-N Str), 2835.08 (C-H Str Ali), 3368.92 (N-H Str), 3010.54 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): 4.31 (s, 2H, 2NH), 6.72 – 6.79 (m, 6H), 7.28 – 7.34 (m, 7H), 7.52 – 7.58 (m, 7H), 7.52 (d, J = 7.6 Hz, 7H), 7.76 – 7.74 (m, 7H).

Rf: 0.57 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 504.34

4-((2-oxo-2-(4-((2-oxoindolin-3-ylidene)amino)phenylsulfonamido)ethyl) amino)benzoic acid (SD3)



Yield: 48.76 %

Melting Range: 305-307 °C

IR (KBr, cm^{-1}): 767.93 (C-H ben.), 1416.16 (C-N Str), 1744.77 (C=O Str), 2905.57

 https://doi.org/10.5281/zenodo.14633803

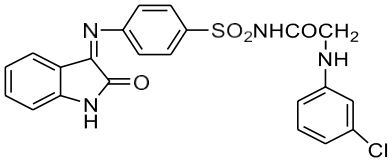
(C-H Str Ali), 3409.96 (N-H Str), 3124.76 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): 3.40 (s, 3H), 3.91 (s, 1H, NH), 6.68 – 6.87 (m, 5H), 7.33 (t, J = 7.9 Hz, 2H), 7.52 (t, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 10.2 Hz, 2H).

Rf: 0.7 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 478.48

2-((3-chlorophenyl)amino)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)- sulfonyl)acetamide (SD4)



Yield: 63.32 %

Melting Range: 295-297 °C

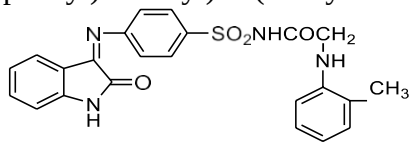
IR (KBr, cm^{-1}): 1071.94 (C-H ben.), 1366.70 (C-O-C Str), 1594.64 (C=O Str), 2765.30 (C-H Str Ali), 3177.89 (N-H Str), 3001.65 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): 3.52 (s, 3H), 4.22 (s, 1H, NH), 6.76 – 6.98 (m, 5H), 7.61 (t, J = 7.9 Hz, 2H), 7.76 (t, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 10.2 Hz, 2H).

Rf: 0.81 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 468.91

N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl)-2-(o-tolylamino) acetamide (SD5)



Yield: 58.39%

Melting Range: 245-247 °C

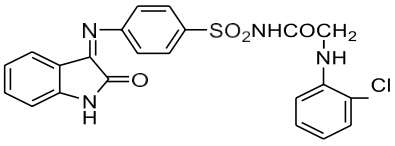
IR (KBr, cm^{-1}): 687.58 (C-H ben.), 1581.49 (C=O Str), 2799.09 (C-H Str Ali), 3344.90 (N-H Str), 3007.70 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): 2.11 (s, 1H, NH), 3.81 (s, 1H, 1NH), 4.61 (s, 2H), 6.66 – 6.68 (m, 5H), 7.33 (t, J = 7.9 Hz, 2H), 7.52 (t, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 8.18 (d, J = 10.2 Hz, 2H).

Rf: 0.49 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 448.49

2-((2-chlorophenyl)amino)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD6)



Yield: 48.19%

Melting Range: 295-298 °C

IR (KBr, cm^{-1}): 1075.57 (C-H ben.), 1411.06 (C-N Str), 1588.53 (C=O Str), 2789.65 (C-H Str Ali), 3366.81 (N-H Str), 3005.47 (C-H Str. Aro).

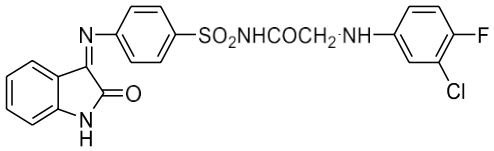
 https://doi.org/10.5281/zenodo.14633803

^{1}H-NMR (512MHz, CDCl3) (PPM): δ 11.04 (s, 1H, N-H), 6.59 (m, 1H, NH), 6.50 (m, 12H, Ar-H), 0.91 – 0.82 (m, 1H).

Rf: 0.69 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 468.91

2-((3-chloro-4-fluorophenyl)amino)-N-((4-((2-oxoindolin-3-ylidene)amino) phenyl)sulfonyl)acetamide (SD7)



Yield: 49.79 %

Melting Range: 325-328 °C

IR (KBr, cm^{-1}): 1006.24 (C-H ben.), 1367.73 (C-O-C Str), 1590.19 (C=O Str), 2758.65 (C-H Str Ali), 3257.57 (N-H Str), 3003.34 (C-H Str. Aro).

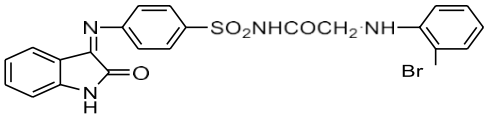
^{1}H-NMR (512MHz, CDCl3) (PPM): 7.97-6.19 (m, 12H, Ar-H), 3.62 (s,2H, CO),

11.03 (s, 2H, 2NH).

Rf: 0.29 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 486.90

2-((2-bromophenyl)amino)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD8)



Yield: 50.09 %

Melting Range: 345-347 °C

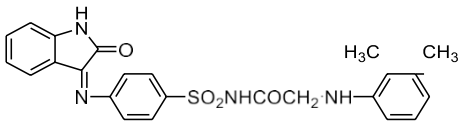
IR (KBr, cm^{-1}): 1077.88 (C-H ben.), 1374.98 (C-O-C Str), 1586.62 (C=O Str), 2758.65 (C-H Str Ali), 3219.63 (N-H Str), 3003.34 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): 4.34 (s, 2H,CO), 09.87 (s, 2H, 2NH), 6.99-5.85 (m, 12H, Ar-H).

Rf : 0.36 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 513.36

2-((2,3-dimethylphenyl)amino)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl)acetamide (SD9)



Yield: 55.67%

Melting Range: 265-267 °C

IR (KBr, cm^{-1}): 1081.18 (C-H ben.), 1376.47 (C-O-C Str), 1590.89 (C=O Str), 2790.13 (C-H Str Ali), 3249.77 (N-H Str), 3001.09 (C-H Str. Aro).

^{1}H-NMR (512MHz, CDCl3) (PPM): δ 11.58 (s, 1H, N-H), 6.47 (m, 1H, NH), 6.75

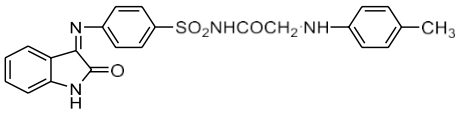
(m, 12H, Ar-H), 2.08 (s, 3H), 1.25 (d, J = 2.1 Hz, 3H), 0.91 – 0.81 (m, 2H).

Rf: 0.85 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 462.52

 https://doi.org/10.5281/zenodo.14633803

N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl)-2-(p-tolylamino) acetamide (SD10)



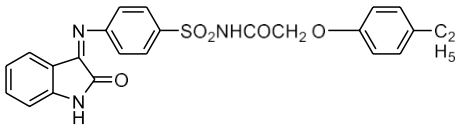
Yield: 54.45%

Melting Range: 245-247 °C

IR (KBr, cm^{-1}): 1003.76 (C-H ben.), 1370.82 (C-O-C Str), 1585.03, 2709.98 (C-H Str Ali), 3227.72 (NH Str), 3003.76 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 3.52 (s,2H, CO), 10.03 (s, 2H, 2NH), 7.60-6.39 (m, 12H, Ar-H).
Rf: 0.55 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 448.49

2-(4-ethylphenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl) acetamide (SD11)



Yield: 53.97%

Melting Range: 275-278 °C

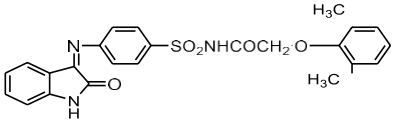
IR (KBr, cm^{-1}): 1079.49 (C-H ben.), 1380.06 (C-O-C Str), 1587.01 (C=O Str), 2819.43 (C-H Str Ali), 3233.65 (N-H Str), 3001.42 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 11.59 (m, 1H, N-H), 6.68 (m, 12H, Ar-H),

1.29 (s, 4H), 1.25 (s, 2H), 0.88 (t, J = 6.9 Hz, 2H).

Rf: 0.67 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 463.51

2-(2,6-dimethylphenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD12)



Yield: 54.76 %

Melting Range: 275-278 ºC

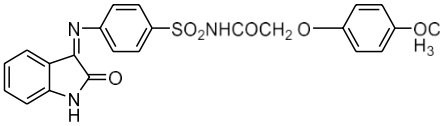
IR (KBr, cm^{-1}): 1077.81 (C-H ben.), 1367.50 (C-O-C Str), 1596.37 (C=O Str), 2898.09 (C-H Str Ali), 3228.97 (N-H Str), 3005.76 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 11.07 (s, 2H, 2NH), 7.67-6.89 (m, 12H, Ar-H),

4.01 (s,2H, CO).

Rf: 0.36 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 463.51

2-(4-methoxyphenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD13)



Yield: 50.80 %

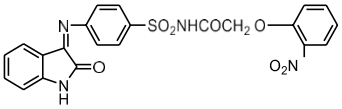
Melting Range: 285-287 ºC

 https://doi.org/10.5281/zenodo.14633803

IR (KBr, cm^{-1}): 695.01 (C-H ben.), 1235.31 (C-O-C Str), 1594.60 (C=O Str), 2765.65 (C-H Str Ali), 3333.39 (N-H Str), 3002.54 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 4.32 (s,2H, CO), 11.03 (s, 2H, 2NH), 7.67-6.09 (m, 12H, Ar-H).
Rf: 0.77 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 465.48

2-(2-nitrophenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl)sulfonyl) acetamide (SD14)



Yield: 49.95 %

Melting Range: 315-317 ^{o}C

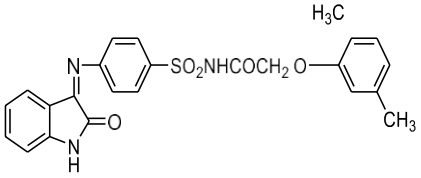
IR (KBr, cm^{-1}): 1149.97 (C-H ben.), 1241.50 (C-O-C Str), 1586.86 (C=O Str), 2870.15 (C-H Str Ali), 3831.91 (N-H Str), 3001.11 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): 11.07 (s, 2H, 2NH), 7.45-6.46 (m, 12H, Ar-H),

3.44 (s,2H, CO).

Rf: 0.51 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 480.45

2-(2,5-dimethylphenoxy)-N-((4-((2-oxoindolin-3-ylidene)amino)phenyl) sulfonyl)acetamide (SD15)



Yield: 60.80%

Melting Range: 275-277 ^{o}C

IR (KBr, cm^{-1}): 1081.61 (C-H ben.), 1390.36 (C-O-C Str), 1592.50 (C=O Str), 2892.84 (C-H Str Ali), 3345.78 (N-H Str), 3005.43 (C-H Str. Aro).
^{1}H-NMR (512MHz, CDCl3) (PPM): δ 11.55 (m, 1H, N-H), 6.44 (m, 1H, NH), 6.79

(m, 12H, Ar-H), 0.91 – 0.81 (m, 5H), 0.87 (s, 3H).

Rf: 0.84 (n-Hexane: Ethyl acetate; 1:1).

Molecular Weight: 463.51

PHARMACOLOGICAL ACTIVITY

1. Antituberculosis Activity

The ongoing emergence or persistence of drug-resistant species and the increasing evolutionary adaptations to widely used Antituberculosiss by pathogenic organisms have decreased the effectiveness of Antituberculosis agents **[Kothari et al., 2011]**. Under standardised conditions, the inhibition of microbial growth can be used to demonstrate the therapeutic efficacy of Antituberculosis agents. A change in Antituberculosis activity will expose any slight change in the molecule that may not be identified by chemical methods, and thus Antituberculosis assays are very critical to solve concerns about potential changes in Antituberculosis agent potency **[Gangwar et al., 2009].** The Antituberculosis assay is based on a comparison of the inhibition of

 https://doi.org/10.5281/zenodo.14633803

micro-organism growth by calculated concentrations of the Antituberculosis agents to be tested by the known concentration of standard antibiotic preparation having a known activity with that procedure **[IP, 1996].**

2. Methods for determining Antituberculosis activity

The Antituberculosis activity of synthesized compounds is tested by several methods:

- Cylinder-plate (or cup-plate) method.
- Poison Food Technique
- Disc Diffusion Method
- Tube Dilution (broth dilution) Method
- Microtitre Technique.

3. The Cylinder-plate (or Cup-plate) Method

The cylinder-plate method (method A) depends upon diffusion of the antibiotic from a vertical cylinder through a solidified agar layer in a Petri dish or plate to an extent such that growth of the added microorganism is prevented entirely in a zone around the cylinder containing a solution of the antibacterial agents. A previously liquefied medium, appropriate to the assay, is inoculated with the requisite quantity of suspension of the microorganism, the suspension is added to the medium at a temperature between 40 to 50°C and the inoculated medium is poured immediately into Petri-dishes to occupy a depth of 3 to 4 mm. The prepared plates or dishes must be stored in such a way that no significant growth or death of the microorganism occurs before use, and the surface of the agar layer is dry at the time of use **[Mohit et al., 2019]**.

4. Poison Food Technique (PFT)

This is a qualitative method for testing. The concentrations of test compound are mixed with agar medium and plated (Petri-dish 90mm diameters). Test bacteria are then streaked on the agar plates and their growth (inhibition) is observed after 24-48 hours incubation (37°C). Sensitivity of several bacterial cultures can be tested in a single plate **[Srivastava et al., 1991]**.

The PFT can also be used for quantitative testing against filamentous fungi because of their radial growth. The test fungus is inoculated (inoculums disc 2mm diameter). Centrally in agar plates supplemented with different concentration of the test compound. Plates are inoculated at 28°C and the linear growth is measured clearly for 7 days. Quantitative assessment can be done by this technique with the help of dose response curves **[Srivastava et al., 1982]**.

5. Disc Diffusion Method

The test compound is impregnated in standard filter discs (6 mm diameter). The media-sabourads dextrose agar or nutrient Agar on Mueller Hinton Agar. 20ml per plate (90 mm diameter) are fooded with 5-10 ml of the test inoculums in broth followed by location method and then drained. The plates are inoculated at 37°C (bacteria), 28°C (fungi) and the zones of inhibition and mm diameter are measured **[Bauer et al., 1966]**.

6. Tube Dilution (Broth Dilution) Method

Tube dilution or broth dilution are twofold serial dilution technique is adopted commonly for in vitro testing of products. The drug is diluted two-fold in a series **[Dhar et al., 1968]**. The test

 https://doi.org/10.5281/zenodo.14633803

samples are usually dissolved in Dimethyl Formamide (DMF) to obtain a 10 µg/ml (natural product) or 1 µg/ml (synthetic product) stock solutions. Appropriate seeded broths i.e., Nutrient Broth (bacteria) and Sabourand's Broth (fungi) are prepared. 0.2 ml solution of the test material is added to 1.8 ml of the seeded broth and this forms the first dilution. 1ml of this is diluted with a further 1 ml of the seeded broth to give second dilution and so on till 10-12 such dilutions are obtained. A set of tubes containing only seeded broth and suitable solvent controls are also maintained under identical conditions. The tubes are inoculated either at 37°C (bacteria) and 28°C (fungi) and the MICs of the products (based upon visual appearance of growth) are noted after 24 hours (for bacteria), 24-48 hours (for yeasts) and 72-96 hours (mycelia fungi) post incubation. The last tube with no apparent growth of the microorganism is taken to represent the MIC of the test compound and is expressed in µg/ml.

7. Microtitre Technique

This method is more modern, sensitive rapid, automated, economical and quantitative compound to two-fold serial dilution technique. Microbroth (270µl per well) with drug dilutions (30µl) are made serially (transferred 150µl) with a multichannel Eppendorf pipette in a microtitre plate with 96 (12×8) wells. The observations are made by optical density (OD at 492nm, matrix 0.2-2). The test inoculum is added (20µl in each well) and suitable controls are separately set accordingly **[Furniss et al., 1989]**.

RESULTS AND DISCUSSION

1. Chemistry

Synthesized derivatives (PD1-PD15)-Scheme-I

The derivatives of isatin (PD1-PD15) were synthesized and presented in **Scheme-I.** Initially, isatin (1) and p-phenylenediamine (2) were dissolved in ethanol. Glacial acetic acid was added and reaction mixture was refluxed for 4 hours. After standing for 24 hours, the compound 3-(4-substituted)indolin-2-one (3) obtained. This 3-(4- substituted)indolin-2-one (3) and chloroacetylchloride were dissolved in acetonitrile in presence of anhydrous carbonate to produce compound N-(4-(2-substituted-3-ylidene- amino) phenyl)-2-chloroacetamide (4). The desired compounds (PD1-PD15) were obtained by refluxing of compounds N-(4-(2-substituted-3-ylidene-amino) phenyl)-2- chloroacetamide (4) and primary amines in acetonitrile with potassium carbonate.

Synthesized derivatives (SD1-SD15)-Scheme-II

The derivatives of isatin (SD1-SD15) were synthesized and presented in **Scheme-II.** Initially, isatin (1) and sulphanilamide (2) were dissolved in ethanol. Glacial acetic acid was added and reaction mixture was refluxed for 4 hours. After standing for 24 hours, the compound 3-(4-sulphonamidesubstituted)indolin-2-one (3) obtained. This 3-(4- sulphonamidesubstituted)indolin-

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2-one (3) and chloroacetylchloride were dissolved in acetonitrile in presence of anhydrous carbonate to produce compound N-(4-(2- substituted-3-ylidene-amino) phenyl)sulfonyl)acetamide (4). The desired compounds (SD1-SD15) were obtained by refluxing of compounds N-(4-(2-substituted-3-ylidene- amino) phenyl)sulfonyl)acetamide (4) and primary amines in acetonitrile with potassium carbonate.

Synthesized compounds were characterized by elemental analysis, FT-IR and ^{1}H- NMR. The FT-IR bands at the 3569-3070, 3105-2670, 1800-1500 and 900-720 cm^{-1} confirmed the presence of NHstr., Ar-CHstr., and other functionalities respectively. The ^{1}H-NMR spectrum showed multiplet at δ 7.01-8.76 confirmed aromatic protons and singlet at δ 3.12-3.89, δ 8.01-10.74 and δ 10.01-11.74 confirms methylene, NH- aromatic protons respectively.

It is evident from the results of synthesized derivatives containing halogen atoms like chloro, bromo and fluoro were showing significant antibacterial and antifungal activity, which depicts that halogen atoms have an important role in Antituberculosis activity. On the other hand, remaining synthesized compounds revealed the variable antibacterial and antifungal activity.

2. Pharmacological Activity

Antituberculosis Activity

The synthesized compounds **(PD1-PD15 & SD1-SD15)** have been screened against different microbial strains, using agar cylinder plate (cup plate method). The test compounds were tested for their antibacterial and antifungal activities against *Bacillus subtillis* (MTCC 441), *Escherichia coli* MTCC (1573), *Klebsiella pneumoniae* (MTCC 618), *Penicillium chrysogenum*, *Bacillus subtilis*, *Candida albicans* and *Aspergillus niger* which were obtained as pure culture from Institute of Microbial Technology, Chandigarh.

Antituberculosis activity was directed by Cylinder-plate (or cup-plate) method or Kirby- Bauer plate dispersion techniques. These strategies were independently used for the antibacterial and antifungal assessment of novel subordinates, utilizing diverse bacterial and parasitic strains and contrasted and distinctive reference standard medications. In cup-plate method, seven unique concentrations of test compounds were taken with determined grouping of bacterial/parasitic strains, and assessed after 24h of incubation. In Kirby-Bauer disc diffusion method, the bacterial/ fungal strains were spread with the nutrient agar media on a petri dish and then the paper disks impregnated with test compounds and disk of standard reference drug were inoculated. The inoculated disks were maintained at 37±0.5°C for 24h/48h. The zone of inhibitions for different test compounds was calculated in mm after the specified inoculation period. The results indicated the bactericidal/ fungicidal capacity of novel derivatives, against tested bacterial/ fungal strains.

 https://doi.org/10.5281/zenodo.14633803

ISSN: 0369-8963

3. Computational studies

A set of molecular parameters were computed for the test compounds as well as two standard drugs ciprofloxacin, fluconazole using Chem 3D Ultra version, 12.0 software. The important molecular parameters of computational study are blood-brain barrier (BBB), log *P* and topological polar surface area etc.

Most of the synthesized derivatives have molar refractivity under 150 as shown in Table

3.1 Topological polar surface area (tPSA) values for the synthesized derivatives were found within 31.20-125.86, which is a surface sum over all polar atoms, primarily oxygen and nitrogen, also their attachment to the hydrogen atoms that helps the compound permeation through the cell. Compounds having a polar surface area of greater than 140 angstroms squared show poor permeating behaviour through cell membranes. The Log P value of synthesized derivatives were 4.00-11.56 within the range of standard drugs which shows that a positive value for Log P indicates a higher concentration in the lipid phase. This indicates that the compounds showed biological potentiality.

Table 1 Molecular properties of the synthesized isatin derivatives (PD1-PD15 & SD1-SD15)

Comp. Code	Molecular Formula	MW[x]	MR[y]	tPSA[z]	Log P	CAA (A^2)[a]	CMA (A^2)[b]	SEV (A^3)[c]	od
PD1	C22H16BrN3O3	450.28	112.99	79.79	3.68	603.16	333.06	298.41	1.54
PD2	C22H15Cl2N3O3	440.28	114.51	79.79	3.97	646.35	344.33	305.46	1.56
PD3	C23H18N4O4	414.41	114.05	119.89	2.03	668.39	354.83	306.29	1.61
PD4	C22H17ClN4O2	404.85	111.84	82.59	3.03	655.84	347.03	299.23	1.60
PD5	C23H20N4O2	384.43	113.14	82.59	2.96	632.19	337.37	298.71	1.56
PD6	C22H17ClN4O2	404.10	111.84	82.59	3.03	630.36	335.70	296.46	1.56
PD7	C22H16ClFN4O2	422.84	112.25	82.59	3.19	634.72	347.49	299.44	1.60
PD8	C22H17BrN4O2	449.30	114.93	82.59	3.30	652.50	347.04	300.81	1.59
PD9	C24H22N4O2	398.46	119.03	82.59	3.45	653.83	360.86	313.70	1.61

https://doi.org/10.5281/zenodo.14633803

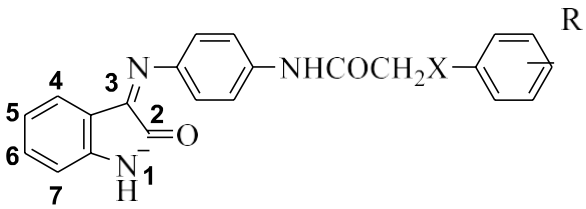
PD10	C23H20N4O2	384.43	113.14	82.59	2.96	636.52	348.11	298.81	1.61
PD11	C24H21N3O3	399.44	115.79	79.79	3.75	676.77	360.28	310.80	1.62
PD12	C24H21N3O3	399.44	117.09	79.79	3.82	644.86	345.95	304.29	1.58
PD13	C23H19N3O4	401.41	112.55	89.02	2.72	661.56	350.10	299.88	1.61
PD14	C22H16N4O5	416.39	NC	131.60	2.45	648.40	346.73	299.45	1.60
PD15	C24H21N3O3	399.44	117.09	79.79	3.82	649.85	346.57	303.82	1.58
SD1	C22H16BrN3O5S	514.35	121.76	113.93	3.23	651.00	361.35	343.96	1.52
SD2	C22H15Cl2N3O5S	505.34	123.28	113.93	3.51	648.83	361.71	341.29	1.53
SD3	C22H18N4O6S	478.48	122.82	154.03	1.58	664.45	373.69	342.87	1.57
SD4	C22H17ClN4O4S	468.91	120.61	116.73	2.58	650.36	363.45	339.00	1.54
SD5	C23H20N4O4S	448.50	121.9	116.73	2.51	635.56	355.63	332.27	1.53
SD6	C22H17ClN4O4S	468.91	120.61	116.73	2.58	633.56	353.98	331.16	1.52
SD7	C22H16ClFN4O4S	486.90	121.02	116.73	2.74	671.37	371.06	337.28	1.58
SD8	C22H17BrN4O4S	513.37	123.7	116.73	2.85	669.29	370.78	338.95	1.57
SD9	C24H22N4O4S	462.52	127.8	116.73	2.99	690.51	384.46	351.56	1.59
SD10	C23H20N4O4S	448.50	121.9	116.73	2.51	672.12	371.73	337.06	1.58
SD11	C24H21N3O5S	463.51	124.56	113.93	3.30	712.60	385.56	343.62	1.62
SD12	C24H21N3O5S	463.51	125.86	113.93	3.37	365.58	337.13	341.67	1.56
SD13	C23H19N3O6S	465.48	121.31	123.16	2.27	658.82	368.55	343.88	1.55
SD14	C22H16N4O7S	480.45	NC	165.74	1.84	369.12	375.59	337.70	1.57
SD15	C24H21N3O5S	463.51	125.86	113.93	3.37	666.38	366.18	336.64	1.56
Ciprofloxacin	C17H18FN3O3	331.34	89.39	72.88	1.32	531.02	281.94	257.63	1.43
Fluconazole	C13H12F2N6O	306.27	78.46	76.15	0.99	429.80	217.72	204.81	1.29

Abbreviations: x-Molecular weight, y-Molar refractivity, z-Topological polar surface area, a-Connolly Accessible Area, b- Connolly Molecular Area, c-Connolly Solvent Excluded Volume, d-Ovality NC-Not calculated

 https://doi.org/10.5281/zenodo.14633803

3.2 Structure Activity Relationship of synthesized isatin derivatives

According to the various synthesized isatin derivatives it was found that the different structural and functional group modification will influence the activity and these are:



X=O or NH
R=Cl, Br, F, -NO_2

- The attachment of any electron-withdrawing group like fluorine, chlorine etc. at position R of the ring system will produce the more potent compounds for Antituberculosis activity. e.g. PD6, PD8
- Addition of primary aromatic amine that may be aromatic or aliphatic at position 3 of the ring system will give compounds with more active against bacterial strains. e.g. PD14.
- Presence of carboxylic group in the ring system shown better results as an anti-inflammatory agent. e.g. PD2
- Nitro group substituted at position R shown prominent Antituberculosis activity.
  e.g. PD14

- Di-alkyl substituted ring at position X shown determinant antifungal activity.
  e.g. SD15
- The derivatives which are substituted at position R of the ring system with halogens like bromine, chlorine etc. will produce more potent antifungal agents.
- If X=NH, it will produce the derivatives with more antibacterial activity. e.g. SD3
- Presence of carboxylic and alkyl groups in the ring system shown better results as an antituberculosis agent. e.g. SD10.

 https://doi.org/10.5281/zenodo.14633803

CONCLUSION

In present study, we synthesized the isatin derivatives with range of pharmacological activities as antituberculosis agents. It has been found that among the synthesized compounds, some of the compounds are potent as compared to the standard, which can be used as lead for novel antituberculosis agents.Most of the synthesized compounds (PD1-PD15 & SD1-SD15) exhibited prominent antibacterial and antifungal. The synthesized compounds found active against Gram negative bacterial strains like Escherichia coli, Pseudomonas aeruginosae, Gram positive bacterial strain Bacillus subtilis and the fungal strains Penicillium chrysogenum and Aspergillus niger. Among all, synthesized derivatives PD6, PD8, PD14, SD3, SD9 and SD11 possess potent antibacterial activity. Whereas PD2, PD7, PD14, SD3. SD9, SD11 and SD15 possess antifungal activity. The significant antituberculosis activity may be attributed to the presence of halogen atoms, direct attachment of aromatic ring with isatin nucleus at position 2 and 3, presence of nitrogen atoms as a ring system may be responsible for potent antituberculosis activity. The synthesized isatin derivatives coded as PD1, PD2, PD5, PD6, PD10, SD6, SD7 and SD10 have shown prominent antituberculosisactivity. The antituberculosisactivity of these derivatives may be possibly due to heterocyclic ring fusion with aromatic ring, alkyl chain between nitrogen atoms at position 1 is unbranched and presence of acidic moiety in the basic isatin ring system. The statistical method was applied i.e. one-way ANOVA and Dennett’s test to get clear picture of synthesized derivatives with their significant differences. This research concluded that synthesized isatin compounds are effective against bacterial strains, fungal strains and also showed prominent antituberculosisactivity. The synthesized isatin derivatives showed prominant activity as antibacterial agents, antifungal agents and antituberculosis agents. These synthesized compounds may further be tested for other pharmacological activities.

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