EJPMR, 2026, 13(1), 482-485 **Review Article** **Impact Factor 7.065**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

SYNTHESIS OF INDOLES WITH THIAZOLIDINONE DERIVATIVES AND BIOLOGICAL ACTIVITY

Indu Singh*[1], Arun Kumar[2], Abha Awasthi[3], Bhopal Singh[4] and Pragya Patel[5]

[1]Associate Professor, Department of Chemistry, Meerut College Meerut, UP, India.
[2]Principal & Dean, GMC Badaum, UP, India.
[3]Professor, Department of Chemistry, Meerut College Meerut, UP, India.
[4]Assistant Professor, Department of Chemistry, Meerut College Meerut, UP, India.
[5]Department of Chemistry, Meerut College Meerut, UP, India.

***Corresponding Author: Dr. Indu Singh**

Associate Professor, Department of Chemistry, Meerut College Meerut, UP, India.

https://doi.org/10.5281/zenodo.18205787

How to cite this Article: Indu Singh*[1], Arun Kumar[2], Abha Awasthi[3], Bhopal Singh[4] and Pragya Patel[5] (2026). Synthesis Of Indoles With Thiazolidinone Derivatives And Biological Activity. European Journal of Pharmaceutical and Medical Research, 13(1), 482–485.

Article Received on 05/12/2025 **Article Revised on 25/12/2025** **Article Published on 10/01/2026**

ABSTRACT

Ethyl 2-methyl-1H-indole-3-carboxylate (1) was obtained by reaction with phenylhydrazine and ethyl-3-oxobutanoate. Compound 1 reacted with hydrated hydrazine and furnished compound 2. Compound 3-5 were synthesized by reaction of substituted aromatic aldehydes with compound 2 and then compounds 3-5 were converted in to compounds 6-8 by interaction with triethylamine in presence of dioxane. All the synthesized compounds were characterized by their spectral and elemental analysis data. Antifungal activity of the synthesized compounds have been evaluated and compared with standard drug fluconazole.

KEYWORDS: Indole, thiazolidinone, antifungal activity, fluconazole.

INTRODUCTION

Indole, which is aromatic heterocyclic compound has attracted in the interest of different researchers. From the literatures it has been found that it possesses a wide range of biological activity like antifungal[1-4], antioxidant[5], antimicrobial[6-9] activities. In this paper another important core is thiazolidinone. The derivative of thiazolidinone neucleus has been founded to possess different pharmacological properties like antifungal[10-11], antitubercular[12], antimicrobial[13-18], antioxidant[19] activity. On approach in drug design, the combination of two pharmacophores of various biological active present in one single molecule. The aim of this approach is focus on improve the activity and reduce side effects.

MATERIAL AND METHOD

In this work different kinds of reagent were used and dissolved in proper solvents and melting points were noted down by melting point apparatus using ordinary glass capillary tube. The purity of reaction was recorded by TLC plate method on silica gel. Perkin Erlmer 2400 was used to confirm various portion of elemental part. Becman and Brucker spectrometer were used to check different value of IR and ^{1}HNMR respectively.

EXPERIMENTAL

Synthesis of Ethyl 2-methyl-1H-indole-3-carboxylate (1)
This compound was prepared according to the method of Kumar. Phenyl hydrazine (0.01 mol) was treated with ethyl 3-oxobutanoate (0.01 mol) in the presence of glacial acetic acid and reflux for 7 h. The reaction mixture was poured onto ice. The product was filtered, washed, dried and recrystallized with ethanol to give compound 1.

Yield: 76%. m.p 84^{0}C. IR (KBr) ν_{max} in cm^{-1} 1604 C=C, 1645 C=O, 1650 C-N, 3046 C-H, 3480 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 2.87 (m, 2H, CH_2), 3.21 (s, 3H, indole-CH_3), 3.84 (t, 3H, CH_3), 6.21 (d, 1H, C-NH), 7.12-7.81 (m, 4x1H, C-H indole), $C_{12}H_{13}NO_2$; Calcd; C: 70.92.; H: 6.45; N : 6.89%; Found C: 70.94; H: 6.49; N: 6.48%.

Preparation of 2-methyl-1H-indole-3-carbohydrazide (2)
Ethanolic solution of compound 1 (0.01 mol) was refluxed with hydrated hydrazine (0.01 mol). The product was filtered off, washed with ethanol and crystallized from appropriate solvent to give compound 2.
Yield: 67%. m.p 92^{0}C. IR (KBr) ν_{max} in cm^{-1} 1610 C=C, 1649 C=O, 1658 C-N, 3041 C-H, 3485 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.40 (d, 2H, NH_2), 3.87 (s, 3H, CH_3), 5.97 (t, 1H, CO-NH), 6.25 (d, 1H, C-NH), 7.11-7.85 (m, 4x1H, C-H indole); $C_{10}H_{11}N_3O$; Cald ; C: 63.48.; H: 5.86; N : 22.21%; Found C: 63.44; H: 5.89; N: 22.24%.

Preparation of N'-benzylidene-2-methyl-1H-indole-3-carbohydrazide 3
A mixture of compound 2 (0.01 mol) and substituted aromatic aldehyde (0.01 mol) in 20 ml of DMF and few drops of acetic acid was added and refluxed for 5h. The reaction mixture was allow to cool, the product was filtered and crystallized from ethanol to obtained compounds 3.
Yield: 67%. m.p 124^{0}C.IR (KBr) ν_{max} in cm^{-1} 1556 CH=N, 1614 C=C, 1642 C=O, 1651 C-N, 3044 C-H, 3489 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.84 (s, 3H, CH_3), 6.28 (s, 2x1H, C-NH), 7.11-7.85 (m, 4x1H, C-H indole); 7.87-8.12 (m, 5x1H, CH-Ar), 8.45 (d, 1H, CH=N), $C_{17}H_{15}N_3O$,: Cald ; C: 73.63.; H: 5.45; N : 15.15%; Found C: 73.65; H: 5.49; N: 15.18%.

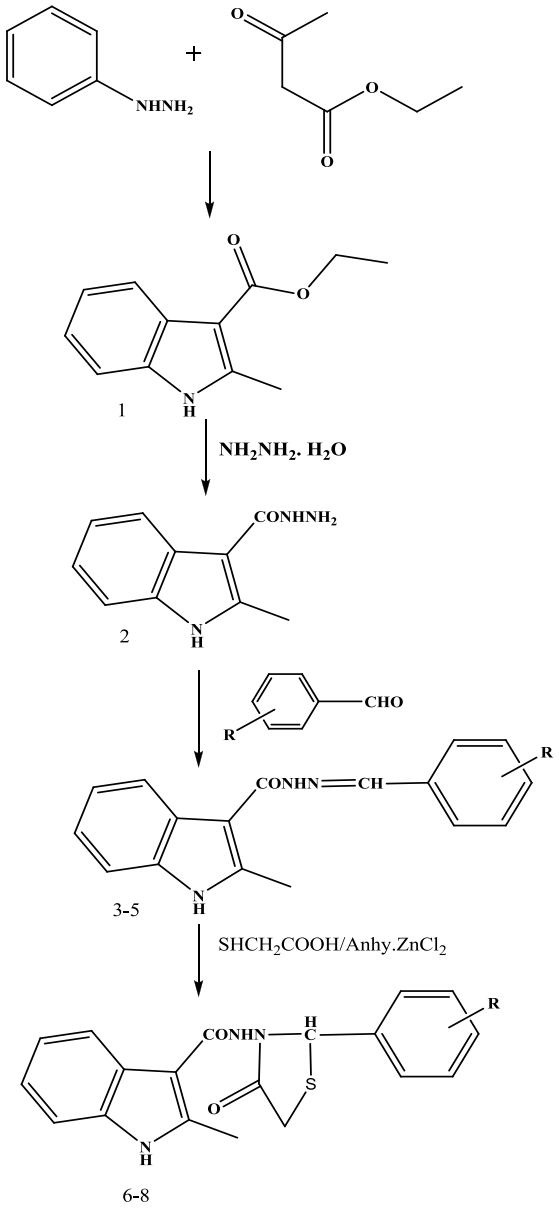
The compounds 4 and 5 were prepared using a similar method of compound 3. Elemental and spectral analyses of compounds 4 and 5 have given below.
N'-(4-hydroxybenzylidene)-2-methyl-1H-indole-3-carbohydrazide (4)
Yield: 67%. m.p 132^{0}C. IR (KBr) ν_{max} in cm^{-1} 1550 CH=N, 1617 C=C, 1645 C=O, 1661 C-N, 3041 C-H, 3483 N-H, 3498 OH. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.83 (s, 3H, CH_3), 6.24 (s, 2x1H, C-NH), 7.11-7.75 (m, 4x1H, C-H indole); 7.87-8.12 (m, 4x1H, CH-Ar), 8.45 (d, 1H, CH=N), 12.11 (s, 1H, OH), $C_{17}H_{15}N_3O_2$; Cald ; C: 69.61.; H: 5.15; N : 14.33%; Found C: 69.65; H: 5.18; N: 14.68%.

N'-(4-chlorobenzylidene)-2-methyl-1H-indole-3-carbohydrazide (5)
Yield 67%. m.p 149^{0}C. IR (KBr) ν_{max} in cm^{-1} 745 C-Cl, 1556 CH=N, 1611 C=C, 1647 C=O, 1668 C-N, 3041 C-H, 3485 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.84 (s, 3H, CH_3), 6.28 (s, 2x1H, C-NH), 7.11-7.85 (m, 4x1H, C-H indole); 7.87-8.12 (m, 4x1H, CH-Ar), 8.45 (d, 1H, CH=N), $C_{17}H_{14}ClN_3O$; Cald ; C: 65.49.; H: 4.53; N : 13.48%; Found C: 65.45; H: 4.50; N: 13.45%.

(R)-2-methyl N'-(4-oxo-2-phenylthiazolidin-3-yl)-2-methyl-1H-indole-3-carboxamide (6)
A mixture of compound 3a (0.01 mol) in dry dioxane (10 ml) and triethyamine (0.005 mol) was take in round bottom flask. The reaction mixture was stirred on an ice bath and when temperature dropped below 0-5^0 C, then chloroacetylchloride (0.01mol) was added drop wise with stirring. The reaction mixture was then kept a side for 48 h and cool with ice water. The product was dried and recrystallized from appropriate solvent to give compound 6.
Yield: 67%. m.p 168^{0}C. IR (KBr) ν_{max} in cm^{-1} 787 C-S-C, 1559 CH=N, 1616 C=C, 1649 C=O, 1665 C-N, 3045 C-H, 3481 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.21 (s, 2H, CH_2), 3.82 (s, 3H, CH_3), 6.23 (s, 2x1H, C-NH), 7.13-7.82 (m, 4x1H, C-H indole); 7.89-8.14 (m, 5x1H, CH-Ar), 8.56 (s, 1H, CH-N), $C_{19}H_{17}N_3O_2S$, 351.42; : Cald ; C: 64.94.; H: 4.88; N : 11.96%; Found C: 64.97; H: 4.85; N: 11.99%.

The compounds 7 and 8 were prepared using a similar method of compound 6. Elemental and spectral analyses of compounds 7 and 8 have given below.
(R)- N-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-2-methyl-1H-indole-3-carboxamide (7)
Yield: 67%. m.p187^{0}C. IR (KBr) ν_{max} in cm^{-1} 789 C-S-C, 1556 CH=N, 1616 C=C, 1651 C=O, 1670 C-N, 3044 C-H, 3473 N-H, 3498 OH; . ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.26 (s, 2H, CH_2), 3.88 (s, 3H, CH_3), 6.29 (s, 2x1H, C-NH), 7.14-7.86 (m, 4x1H, C-H indole); 7.85-8.10 (m, 4x1H, CH-Ar), 8.54 (s, 1H, CH-N), 12.40 (s, 1H, OH-Ar), $C_{19}H_{17}N_3O_3S$, 367.42; : Cald ; C: 62.11.; H: 4.66; N : 11.44%; Found C: 62.14; H: 4.67; N: 11.48%.

(R)- N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-2-methyl-1H-indole-3-carboxamide (8)
Yield 67%. m.p 206^{0}C. IR (KBr) ν_{max} in cm^{-1} 763 C-Cl, 783 C-S-C, 1555 CH=N, 1618 C=C, 1647 C=O, 1651 C-N, 3045 C-H, 3485 N-H. ^{1}HNMR ($CDCl_3$ + DMSO-d_6) □ in ppm: 3.24 (s, 2H, CH_2), 3.86 (s, 3H, CH_3), 6.28 (s, 2x1H, C-NH), 7.10-7.82 (m, 4x1H, C-H indole); 7.87-8.18 (m, 4x1H, CH-Ar), 8.59 (s, 1H, CH-N), $C_{19}H_{16}ClN_3O_2S$, 385.87; : Cald ; C: 59.14.; H: 4.18; N : 10.89%; Found C: 59.18; H: 4.15; N: 10.86%.



R = H, 4-OH, 4-Cl
Scheme 1

Table 1: Antifungal activity of compounds 1-8.

Compounds	R group	Fungal Inhibition Zone /mm		
		C. albicans	C. albicans ATCC	C. krudei
1	-	6	-	-
2	-	10	8	7
3	H	13	10	9
4	4-OH	17	14	12
5	4-Cl	21	18	15
6	H	25	21	16
7	4-OH	28	23	18
8	4-Cl	30	24	19
Fluconazole		29	25	19

ANTIFUNGAL ACTIVITY

All the synthesized derivatives of indole with thiazolidinone moiety were screened for their in vitro antifungal activity against fungal strain c. albicans, c. albicans ATCC and c. krusei by disc diffusion method.[20] Standard drug, fluconazole was used against fungal strain. Inhibition nature of strains was checked and recorded in mm. Compounds 2, 3, 4, 5 have shown mild to moderate antifungal activity against all these fungal strains. Incorporating thiazolidinone moiety in indole derivatives, compuounds 6, 7 and 8 were proved to be most active antifungal against fungal strains. Compound 8 showed good antifungal activity as compared standard drug fluconazole.

CONCLUSION

A new series of indole derivatives with thiazolidinone moiety were prepared and characterized by elemental and spectral analysis. The newly synthesized drugs were screened for their in vitro antifungal activity. Some of the compounds of this series exhibited significant antifungal activity.

ACKNOWLEDMENT

Authors would like to thank the Higher Education Department Uttar Pradesh, India for providing financial support in the form of a minor research project under the research and department scheme.

REFERENCES

1. Ryu, C.K.; Lee, J.Y.; Park, R.E.; Ma, M.Y.; Synthesis and antifungal activity of 1H- indole-4,7-diones. Bioorganic & Medicinal Chemistry. Letters, 2007; 17(1): 127-31.
2. Ryu, C.H.; Yoon, J.H.; Song, A.L.; Im, H.A.; Kim, J.Y. and Kim, A. Synthesis and antifungal evaluation of pyrido[1,2-a]indole-1,4-diones and benzo[f]pyrido[1,2-a]indole-6,11-diones. Bioorganic & Medicinal Chemistry Letters, 2012; 22(1): 497-499.
3. Kulkarni, S.D.; Tankar, A.N.; Ram, B.G.; Ghongade, D.B.; Chandak, B.G. and Tiwari, R.N. Synthesis and evaluation of antifungal activity of novel indole derivatives. International Journal of Chemical Science, 2009; 7(3): 2203-2207.
4. Wu, Y.; Sun, A.; Chen, F.; Zhao, Y.; Zhu, X.; Zhang, T.; Ni, G. and Wang, R. Synthesis, structure-activity relationship and biological evaluation of indole derivatives as anti-candida albicans agents. Bioorganic Chemistry, 2024; 146: doi:107293.
5. Saundane, A.R.; Walmik, P; Synthesis, antioxidant, antimicrobial, antimycobacterial, and cytotoxic activities of azetidinone and thiazolidinone moieties linked to indole nucleus. Journal of Chemistry, 2013; doi.org/10.1155/2013/543815.
6. Salman, A.; Mahmoud, N.; Abdel-Aziem, A.; Mohamed, M. and Elsisi, D. Synthesis, reactions and antimicrobial activity of some new 3-substituted indole derivatives. International Journal of Organic Chemistry, 2015; 5(2): 81-99.

7. Quazi, I.; Sastry, V.G. and Ansari, J.A. Synthesis and antimicrobial activity of indole derivative bearing the pyrazole moiety. International Journal of Pharmaceutical Sciences and Research, 2016; doi: 10.13040/IJPSR.0975-8232.8(3).1145-52.
8. Simakov, S.; Kartsev, V.; Petrou, A.; Nicolaou, L.; Geronikaki,; Ivanov, M.; Kostic, M.; Glamoclija, J.; Sokovic, M; Talea, D. and Vizirianakis, I.S. 4-(indol-3-yl)thiazole-2-amines and 4-indol-3-yl)thiazole Acylamines as novel as novel antimicrobial agents: synthesis, in silico and in vitro evaluation. Pharmaceuticals; 2021; 14(11): doi 10.3390/ph14111096.
9. Nimbalkar, D.; Maske, P.P.; Lokapure, S.G.; Heralagi, R.V. and Kalyane, N.V. Synthesis and antimicrobial activity of some indole derivatives. Asian Journal of Research in Chemistry, 2012; 5(7): 837-842.
10. Belwai, C.K. and Joshi, K.A. Synthesis and antifungal activity of some novel thiazolidinone derivatives of 4-(4-oxo-2-phenylthiazolidin-3-yl)benzoic acid. International Journal of ChemTech Research, 2012; 4(4): 1758-1764.
11. Pawar, S.; Karan, R.; Rawal, R.K. and Gupta, P.K. Antimicrobial and antifungal evaluation of some novel thiazolidin-4-one scaffold bearing compounds. Letters in Applied NanoBioScience, 2024; 13(4): doi.org/10.33263/LIANBS134.166.
12. Sreedevi, A. and Usha Rani, U. Synthesis and biological evaluation of 3-(2-benzoyl-4-chlorophenyl)-4H-spiro[indole-3,2-[1,3]thiazolidine]-2,4(1H)-dione derivatives for anti-tubercular and antimicrobial activities. Indian Journal of Science and Technology, 2024; 17(20): 2101-2109.
13. Sankar, P.S.; Divya, K.; Reddy, G.D.; Padmavathi, V. and Zyryanov, G.V. Synthesis, characterization and antimicrobial activity of azetidinone and thiazolidinone derivatives. AIP Conf. Proc, 2019; doi.org/10.1063/1.5087379.
14. Kamala, L.; Veena, B.S.; Anantha, P.V.; Lakshmi, Vasantha, P. and Sujatha, E. Synthesis and antimicrobial activity of novel 5-[(1H-indol-3-yl)methylene]thiazolidine-2,4-dione-[1,2,3]triazole hybrids. Russian Journal of General Chemistry, 2017; 87: 316-321.
15. Evren, A.E.; Yurttas, L. and Gencer, H.K. Synthesis of new thiazole derivatives bearing thiazolidin-4(5)-one structure and evaluation of their antimicrobial activity. Brazilian Journal of Pharmaceutical Sciences, 2022; doi.org/10.1590/s2175-97902022e19248.
16. Abo-Ashour, M.H.; Eldehna, W.M.; George, R.F.; Abdel-Aziz.; Elaasser, M.M.; Gawad, N.M.A.; Gupta, A; Bhakta, S. and Abou-Seri, S.M. Novel indole-thiazolidinone conjugates: Design, synthesis and whole-cell phenotypic evaluation as a novel class of antimicrobial agents. European Journal of Medicinal Chemistry, 2018; 160: 49-60.
17. Shih, M.H.; Xu, Y-Y.; Yang, Y-S and Lin, G.L. A facile synthesis and antimicrobial activity evaluation of sydnonyl-substituted thiazolidine derivatives. Molecules, 2015; 20(4): 6520-6532.
18. Asghar, B.H. and Arshad, M. Synthesis, characterization, antimicrobial, and molecular docking studies of thiazolidin-4-one derivatives fused with indole and pyrimidine moieties. Russian Journal of Bioorganic Chemistry, 2023; 49: 1438-1451.
19. Buvana, C.; Sukumar, M.; Ravi, T.K. and Rajan, N. Synthesis, characterization and study of antifungal and antioxidant activities of some thiazolidinone derivatives. Internationa Journal of Pharm Tech Research, 2013; 5(1): 171-176.
20. Pai, S.T. and Platt, M.W. Antifungal effect of allium sativum extract against the aspergillus species involved in otomycosis, Letters in applied microbiology, 1995; 20: 14-18.