Antimicrobial activity of synthesized3-(1*H*-indol-3-yl)-1, 3 diphenylpropan-1- one derivatives 3(a–j)

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Abstract

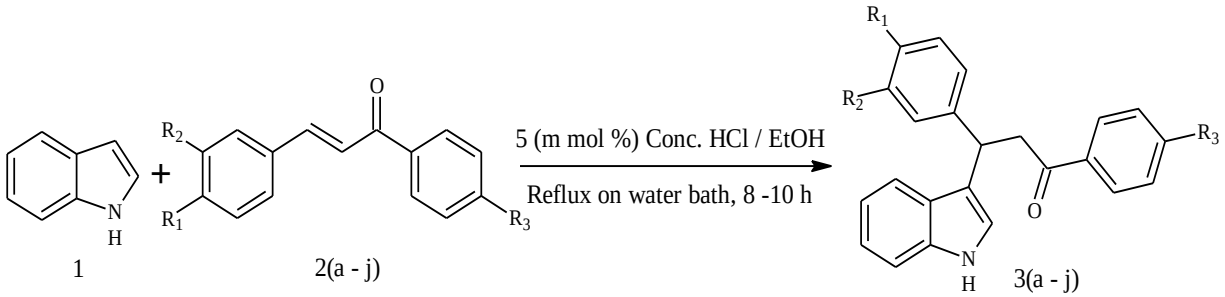
A series of synthesized3-(1*H*-indol-3-yl)-1,3-diphenylpropan-1-one derivatives3a-jwere allowed to evaluated for *in vitro* Antimicrobial screening against various pathogenic bacteria like *P. aureginosa*, *E. coli, V. cholerae*, *S. aureus using amoxicillin* as a standard as well as fungal microorganisms like*Aspergillusniger*, *Penicillin chrysogenum*and *Cladosporiumoxysporum*using flucanazole as standard respectively. Overall the compounds when tested against microorganismsthe results were revealed that the maximum number of synthesized molecules possessed good to moderate activityat 100 µg/ml concentrations, especially the bromine substituted compounds.

Introduction

Indole nucleus has been a structural subunit of many natural and pharmaceuticalagents [1, 2].In addition, several indole derivatives have been found to exhibit anticancer [3, 4], antioxidant [5], antirhemuatiodal and anti-HIV activities [6, 7]. Literature survey reveals that 1,3-Diaryl-2-propen-1-ones (3)display many biological activities *viz.*, antiviral [8],antipicornavirus [8],anti-inflammatory [9],antimicrobial [10],antimitotic [11], antitumor [12] antifungal [13],besides beingsynthons for the construction of diverse heterocycles like isoxazolines [14],isoxazoles [15], quinolinones [16],thienoquinolinones [17], thiadiazines [18], benzofuranones [19], and flavones [20-22].

The importance of chalcones in cell wall synthesis inhibition is well documented in history not only as on microorganism but also in many other cell lines as well. Hence, the present study of *in vitro* antimicrobial activity of the title compounds is to screen randomly on different gram positive and gram negative bacteria. Apart from this the compounds were also screened for *in vitro* antifungal activities as well.

Synthesized Scheme



1 2(a - j) 3(a - j)

R_1, R_3= H, Cl, F. R_2= Cl

The 3-(1H-indol-3-yl)-1, 3-diphenylpropan-1-one derivatives3 (a-j) were synthesized via one pot reaction of indole with differently substituted α, β-unsaturated ketones 2(a–j) inpresence of 5 Mmol% concentrated hydrochloric acid in ethanol solvent.

The advantage of using hydrochloric acid as catalyst in conjugate addition of the α, β-unsaturated ketones in ethanol as compared with indium(III) sulphate, indium(III) chloride and indium(III) bromide is because the indium salts are soluble in solvent media and cannot be easily purified during reaction workup process [23-28].

Antibacterial activity

Material and methods

The antibacterial activity of the synthesized compounds were evaluated by cup-plate method against four different bacterial strains *viz. Staphylococcus aureus, Vibrio cholerae*, *Pseudomonas aureginosa*, and *Escherichia coli*using nutrient agar medium. The test solutions were prepared in DMSO and diluted using distilled water to get concentrations of 100 µg/ml.

The sterilized nutrient media was poured into Petri plates aseptically in a horizontal laminar air flow. The plates were allowed to solidify in the aseptic chamber, followed by inoculating the bacterial strains. In order to determine the antibacterial zone of inhibition, the inoculated Petri plates were divided into quarters and to each quarter a whell was made with the help of cork borer (9 mm). The standard drug amoxicillin and the test compounds were added to the respective labelled whells. Thus, inoculated plates were kept it refrigerator for 10 min. followed by incubation for 24 h at 37 °C [29-31].

Antifungal study

The antifungal screening of the synthesized compounds was evaluated by adopting cup-plate method using potato dextrose agar medium a pH 5.4. Four different fungal strains used in this process were *Aspergillusniger*, *Penicillin chrysogenum* and *Cladosporiumoxysporum.*Three different concentrations of test samples were prepared with DMSO and dilute it with distilled water at the strength was made to 100 µg/ml.

The sterilized PDA media was poured into Petri plates in an aseptic conditioned chamber. The plates were allowed to solidify followed by inoculating the fungal strains. Antifungal zone of inhibition was determined by cup-plate method**.**The inoculated Petri plates were divided into quarters and to each quarter a whell was made with the help of a sterilised cork borer (9 mm). The standard drug and the test compounds were added to the whells so that the volume fills up the whell uniformly. Thus inoculated plates were kept for incubation 28 °C for about 72 hrs [29-31].

Result

Table 1: Antibacterial activity of the synthesised compounds 3(a-j)

SI. No.	Compound	Bacterial zone of inhibition in nm (mean ± SD) n=3			
		PA	EC	VC	SA
1	3a	12.10±0.163	16.17±0.281	14.12±0.321	14.32±0.428
2	3b	17.08±0.365	19.61±0.327	15.10±0.305	18.14±0.264
3	3c	13.62±0.524	18.49±0.491	14.17±0.512	16.37±0.512
4	3d	24.16±0.263	26.37±0.198	24.43±0.162	23.18±0.291
5	3e	22.41±0.435	28.92±0.341	25.83±0.436	24.62±0.321
6	3f	17.84±0.458	22.61±0.194	20.49±0.261	24.45±0.512
7	3g	14.89±0.239	20.16±0.412	12.67±0.267	13.29±0.342
8	3h	19.17±0.375	27.18±0.312	25.68±0.329	20.13±0.268
9	3i	16.19±0.341	22.28±0.271	20.42±0.384	21.64±0.482
10	3j	15.12±0.428	19.36±0.162	19.73±0.403	20.37±0.196
11	Control	--	--	--	
12	Standard	28.43±0.625	34.40±0.452	30.26±0.274	32.48±0.387

PA: Pseudomonas auriginosa, **EC**: Escherichia coli, **VC**: Vibrio cholera**,**

SA: Staphylococcus aureus, **Standard**: Amoxicillin, **Bore Size**: 9 mm,

SD: Standard deviation

Table 2: Antifungal activity of the synthesised compounds 3(a-j)

SI. No.	Compound	Fungal zone of inhibition in nm (mean ± SD) n=3		
		AN	PC	CO
1	3a	20.41±0.284	20.27±0.354	22.16±0.271
2	3b	19.12±0.632	17.31±0.419	15.13±0.124
3	3c	23.17±0.437	20.62±0.356	21.18±0.253
4	3d	18.12±0.324	14.16±0.431	16.28±0.269
5	3e	20.26±0.472	18.15±0.268	22.13±0.534
6	3f	18.64±0.634	15.43±0.243	21.36±0.232
7	3g	16.18±0.436	16.10±0.352	18.43±0.258
8	3h	20.37±0.346	19.87±0.634	20.65±0.376
9	3i	18.37±0.673	18.47±0.732	17.83±0.873
10	3j	25.19±0.387	23.63±0.523	21.51±0.321
11	Control	--	--	--
12	Standard	29.63±0.673	28.42±0.612	30.13±0.625

AN: Aspergillus niger, **PC**: Penicillin chrysogenum, **CO**: Cladosporiumoxysporum

Standard: Flucanazole, **Bore Size**: 9 mm, SD: Standard deviation.

Statistical analysis

Values were expressed as mean ± standard error (SEM). Statistical significance was evaluated by one-way analysis of variance (ANOVA) followed by Student's t-test (⁄p < 0.05) and (⁄⁄p < 0.01)

Discussion

The result tables1 and 2 represent the*in vitro antimicrobial* activity wasdetermined by the cup plate method. The antibacterial result showed that the compounds 5a and 5b showed moderate activity at 100 µg/ml against adopted microbial strains *Pseudomonas aureginosa, Staphylococcus aureus* and *Escherichia coli*,compounds 5c, 5d and 5e showed potent activity at (100 µg/ml) against *Pseudomonas auriginosa, Staphylococcus aureus and Escherichia coli* respectively with standard amoxicillin.

The antifungal results indicated that the compounds 3a, 3b, 3d and 3e showed moderate activity against *Aspergillusniger*, *Cladosporiumoxysporum* and *Penicillin chrysogenum*, whereas the compound 3c showed good activity at 100 µg/ml as flucanazole used as standard.

Indicating the N-substituted indole with halogen functionalities of the aryl ring at 3rd position enhances the antimicrobial property, especially the bromine substituted. The overall conclusion of the compounds when tested against microorganisms, revealed that the maximum number of synthesized molecules possessed both antimicrobial and antifungal activity.

Conclusion

The synthesized 3-(1H-indol-3-yl)-1, 3-diphenylpropan-1-one derivatives 3(a-j)were showed good antibacterial as well as antifungal potency, the tested compounds were resemblance as lead molecules for the development drug candidates in treating pathogenic microbial diseases.

References

1. Kameshwara RV, Bhupender SC, Amir NS, Rakesh T, Keykavous P, Anil K. 3-substitued indoles: One-pot synthesis and evaluation of anticancer and src kinaseinhibitory activities. *Bioorg Med ChemLett*2011, 21:3511-14.
2. Abdel-Rahman F. Synthesis of some new indole derivatives containing pyrazoleswith potential antitumor activity. *Arkivoc*2010, Xi:177-87.
3. Ekhlass N. Synthesis, (*in vitro*) antitumor and antimicrobial activity of somepyrazoline, pyridine, and pyrimidine derivatives linked to indole moiety. *J Am Sci*2010; 6(8):338-47.
4. Chen I, Safe S, Bjeldanes L. Indole-3-carbinol and diindolylmethane as arylhydrocarbon (Ah) receptor agonists and antagonists in T47D human breast cancercells. *BiochemPharmacol*1996, 51:1069-76.
5. Suzen S, Buyukbingol E. Anti-cancer activity studies of indolalthiohydantoin (PIT)on certain cancer cell lines. *Farmaco*2000, 55:246-8.
6. Buyukbingol E, Suzen S, Klopman G. Studies on the synthesis and structure-activity relationships of 5-(3'-indolyl)-2-thiohydantoin derivatives as aldose reductase enzyme inhibitors. *IlFarmaco*1994, 49:443-7.
7. Suzen S, Buyukbingol E. Evaluation of Anti-HIV activity of 5-(2-phenyl-3'-Indolyl)-2-thiohydantoin. *IlFarmaco*1998, 53:525-7.
8. Bauer DJ, Selway JWT, Batchelor JF, Tisdale M, Caldwell IC, Young DAB. 4',6-Dichloroflavan (BW683C), a new anti-rhinovirus compound.*Nature* 1981**,**292:369-70.
9. Cody V, Middleton E, Harborne JB,LissAR.Plant Flavonoids in biology and medicine. *Inc.: New York* 1985, 472.
10. Krishna SV, Rajasekhar A, Reddy TKK, Naidu MSR. Antimicrobial activity of sulphonylchalcones and sulphonylcyclohexenones. *CurrSci*1988, 57:1291-93.
11. Edwards ML, Stemerick DM, Sunkara PS.Chalcones: A new class of antimitotic agents.*J Med Chem*1990**,** 33(7)**:**1948-54.
12. Bilgin AA, Palaska E, Abbabbasoglu U. FABAD.*Farm BilimlerDerg*1991, 16**:** 81.
13. Katritzky AR, Lagowski JH. The Principles of Heterocyclic Chemistry. Chapman and Hall Ltd: London. Elsevier 1971, 140**, eBook ISBN:** 9781483274515.
14. Ciller JA, Seoane C, Soto JL.Synthesis of heterocyclic compounds XLIX. An unexpected synthesis of isoxazolamines.*J Heterocyclic Chem*1985**,** 22(6):1663-5.
15. Donnelly JA, Farrell DF.The chemistry of 2'-amino analogs of 2'-hydroxychalcone and its derivatives.*J Org Chem*1990,55(6):1757-61.
16. Ombetta JE, LyetS, Xicluna A, Robert JF, Panouse J. Preparation and pharmacologic approach of a series of dihydro-4,5 thieno(2,3-c)quinoline-4-ones. *Ann Pharm Fr*1989, 46(6):377.
17. Alberola A, Andres JM, Gonzalez A, Pedrosa R, Vicente M. *Synthesis*1991, 355.
18. Narasimhachari N, Narayanaswami S, Seshadri TR. Synthetic experiments in the benzopyrone series. Part XX. Hydrogen peroxide oxidation of some α-methoxychalkone and synthesis of some partial methyl ethers of quercetin. *Proc Indian AcadSci*1953,37A:104.
19. Algar J, Flynn JP. Alkaline hydrogen peroxide oxidation of *o*-hydroxyphenylstyryl ketones (chalcones) to flavonols *via* the intermediate dihydroflavonols. *Proc Roy Irish Acad*1934,42B:1.
20. Oyamada B. A new general method for the synthesis of flavonol derivatives. *J ChemSoc Japan*1934, 55:1256.
21. Oyamada T. A New general method for the synthesis of the derivatives of flavonol.*Bull ChemSoc Japan*1935, 10(5):182.
22. Arrigo S, Rosaria V, Maria R A. Asymmetric Friedel-Crafts alkylation of indole with chalconescatalyzed by chiral phosphoric acids. *Molecules*2009, 14:3030-6.
23. Xiang J, Haibo T, Yu Y. Facile and efficient Michael addition of indole to nitroolefinscatalyzed by Zn(OAc)2 2H2O. *SynComm* 2011, 41:372-79.
24. Zhi-Liang S, Shun-Jun J, Teck-Peng L. Indium (III) iodide mediated Strecker reaction in water: an efficient and environmentally friendly approach for the synthesis of α-aminonitrile*via* a three-component condensation. *Tetrahedron*2008, 64:8159-63.

25. Marco B, Pier GC, Massimo G, Paolo M, Simona S, Achille UR. Sequential one-pot InBr 3-catalyzed 1, 4-then 1, 3-nucleophilic addition to enones. *J Org Chem* 2002, 67:3700-4.
26. Brindaban CR, Suvendu SD, Sampak S. Indium (III) chloride catalyzed Michael addition of thioles to chalcones: a remarkable solvent effect. *Arkivoc iii* 2005:44-50.
27. Bimal KB, Migue F, Claeissa A. Iodine-catalyzed highly efficient Michael reaction of indoles under solvent-free condition.*Tetrahedron*2005, 46:2479-82.
28. Bei-Yao L, Miao Z, Xin-Min Y, Yan-Qing P. Conjugate addition of indole to α, β -unsaturated ketones catalyzed by Lewis acid immobilized on a bio renewable support. *J Chin ChemSoc* 2010, 57:1243-47.
29. Saundane AR, Rudresh K, Satyanarayan ND, Hiremath SP. Pharmacological screening of 6H, 11H-indole[3,2-c]isoquinolin-5-ones and their derivatives. *Indian J Pharm Sci* 1998, 6:379-83.
30. Laxmi S, Ankit J, Upendra B. Synthesis and antimicrobial activity of some novel schiff base derivatives of 5-nitro isatin. *Asian J Pharm Life Sci* 2011, 1(3):2231-4423.
31. Bhovi MG, Gadaginamath GS. 1, 3-Dipolar cycloaddition reactions: Synthesis and antimicrobial activity of novel 1-triazolylindole and 1-triazolylbenz-[g] indole derivatives. *Indian J Chem* 2005, 44B:1068-73.