Evaluation of Antibacterial and Antifungal Properties of the Bis-indole Derivatives Synthesized by using Novel Clay Catalyst

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Received: 20.03.2018 ***Accepted: 23.04.2018*** ***Published Online 15.06.2018***
https://doi.org/10.30731/ijcps.7.3.2018.10-16

Abstract

The present article represent the evaluation of Antibacterial & Antifungal properties of Bis-indole derivatives synthesized by using local clay material obtained from Bashir farm at Jatadevale, Tq. Pathardi, Dist. Ahmednagar gives very clean and good product.Compound 3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole shows good antibacterial activity than standard drug Ampicillin for bacteria S. aureus and similar activity for bacteria E. coli. Compound 3-((1H-indol-3-yl)(2-nitrophenyl)methyl)-1H-indole shows good antibacterial activity than standard drug Ampicillin for bacteria E. coli & S. aureus

Keywords: S. Aureus, E. coli, Clay, P. aeruginosa, EDS, FESEM, bis-indole, substituted aldehydes, nanomaterial.

Introduction

Most current bactericidal compounds inhibit DNA, RNA, cell walls and protein synthesis. In the case of S. aureus, infection occurs by inhibition of cell wall synthesis by non-lytic cell death. Staphylococcus Aureus, a gram-positive coccal bacterium, infects tissues when the skin or mucosal barriers are breached. Its infections spread through contact with pus from an infected wound, skin to skin contact with an infected person by producing hyaluronidase that destroys tissues and contact through the objects used by an infected person. It is estimated that 20% of human population are long term carriers of S. aureus. It remains still as one of the five most common causes of nosocomial infections and is often the cause of post-surgical wound infections. S. aureus, the chief culprit, is also a common source of community acquired infections, and causes illnesses that range from minor skin infections and abscesses to life-threatening diseases such as severe pneumonia, meningitis, joint infections and heart and blood stream infections. Drug resistant bacterial infections are becoming more prevalent and are a major challenging health issue faced today. This rise of drug-resistance has limited our repertoire of effective antimicrobials that could combat overcome the problem of drug-resistance. Inflammation is a complex biological response of vascular tissues to harmful stimuli like pathogens, cells and irritant [1]. Indole and its derivatives have wide range of applications in biological and medicinal activities [2]. Bis-indole derivatives not only increase the natural metabolism of hormones in the body but also used as anticancer

drug [3]. Such as anti-bacterial antitumor, Bis-indole derivatives are members of promising new drug class these are diarylamidine derivatives that target DNA synthesis, providing a broad-spectrum antibacterial activity [4]. Man is closely influenced by the activities if microorganisms. Microorganisms are a part of our lives in more ways than most of us understand. They have shaped our present environment and their activities will greatly influence our future. Microorganisms should not be considered separate from human beings, but profound beneficial influence as a part of our life. They are employed in the manufacture of dairy products, certain foods, min processing of certain medicines and therapeutic agents, in manufacture of certain chemicals and in numerous other ways. Despite the established useful functions and potentially valuable activities of microorganism, these microscopic dorms of life may be best known as agents of food spoilage and causal agents of human beings Viz. Acquired immune deficiency syndrome[Aids], Herpes, Legionnaires Disease, Influenza, Jaundice, Tuberculosis, Typhoid, Dermatomycoses, Dysentery, Malaria Etc. In human being animals [infected with brucellosis, tularemia etc...] and plants [infected with mildews, rusts, smuts, cankers, leaf spots, etc...] have also been known to be victims of microbial pathogens. So far as is known, all primitive and civilized societies have experienced diseases caused by microbes, frequently with disastrous results. Moreover, microorganisms have played profound roles in warfare, religion and the migration of populations. Control of microbial population is necessary to prevent transmission of disease, infection,
decomposition, contamination and spoilage caused by them man's personal comforts and convenience depend to a large extent on the control of microbial population[9-13]

Experimental

Chemistry

All chemicals were purchased from major chemical suppliers as high or highest purity grade and without further purification. The melting points are uncorrected TLC is run in n- hexane and ethyl acetate in required amount. FT-IR is recorded in KBr, HNMR in $CDCl_3$ from Central Instrumentation Facility, Savitribai Phule Pune University, Pune. X-Ray Powder diffraction (XRD) is recorded from department of Physics, Savitribai Phule Pune University. Energy-dispersive X-Ray Spectroscopy (EDS) and Field Emission Scanning Electron Microscope (FESEM) by using instrument Nova Nano SEM 450 UOP were recorded from Central Instrumentation Facility, Savitribai Phule Pune University, and Maharashtra

All the synthesized drugs were used for antibacterial test procedures, All necessary controls like drug control, vehicle control, agar control, organism control, known antibacterial drugs control, all MTCC cultures were tested against above mentioned known and unknown drugs, muellerhinton broth was used as nutrient medium to grow and dilute the drug suspension for the test bacteria, inoculum size for test strain was adjust to 10^8cfu [Colony Forming Unit] per milliliter by comparing the turbidity, Following common standard strains were used for screening of antibacterial and antifungal activities: The strains were procured from Institute of Microbial Technology, Chandigarh.

E. coli	**P. aeruginosa**	**S. aureus**	**S. pyogenus**	**C. albicans**	**A. niger**	**A. clavatus**
MTCC 443	MTCC 1688	MTCC 96	MTCC 442	MTCC 227	MTCC 282	MTCC 1323

DMSO was used as diluents / vehicle to get desired concentration of drugs to test upon Standard bacterial strains. Minimal Inhibition Concentration [mic] the main advantage of the 'Broth Dilution Method' for MIC determination lies in the fact that it can readily be converted to determine the MIC as well. Serial dilutions were prepared in primary and secondary screening. The control tube

containing no antibiotic is immediately sub cultured [before inoculation] by spreading a loopful evenly over a quarter of plate of medium suitable for the growth of the test organism and put for incubation at 37 ^{0}C overnight. The tubes are then incubated overnight. The MIC of the control organism is read to check the accuracy of the drug concentrations. The lowest concentration inhibiting growth of the organism is recorded as the MIC. The amount of growth from the control tube before incubation [which represents the original inoculum] is compared.

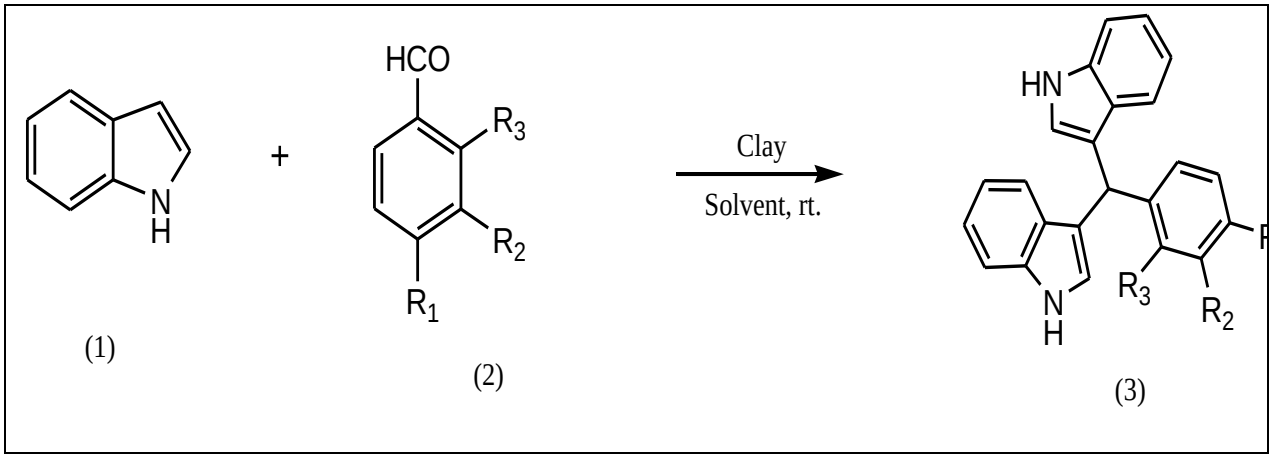
Methods used for primary and secondary screening, each synthesized drug were diluted obtaining 2000 microgram /ml concentration, as a stock solution. In primary screening 1000 micro/ml, 500 micro/ml, and 250 micro/ml concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms. Secondary screen the drugs found active in primary screening were similarly diluted to obtain 200 micro/ml 100 micro/ml, 50 micro/ml, 25 micro/ml, 12.5 micro/ml, 6.250 micro/ml, and concentrations. Reading result the highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculum. The test mixture should contain 10^8 organism/ml.

Preparation of catalyst

Clay collected from the hilly areas of Bashir farm Jatadevala, Tq Pathardi Dist. Ahmednagar Maharashtra, India was treated and characterized as per work published earlier [8 & 14].

General procedure for the synthesis of bis-indole derivatives

The mixture of one mole of aldehyde of two mole of indole and 0.10 mg of catalyst in ethyl acetate in mortar and pestle grind this reaction mixture well for specific period. The reaction was monitored by TLC.Reactions checked by TLC then add 10ml dichloromethane then reaction mixture was filtered. Catalyst is separated by filtration. This catalyst reused. Then some amount of N-hexane is added in solvent.This mixture was kept in deep freezer pure crystals are separated. As a part of our study of the chemistry indole [biological active moiety] we have synthesized bis-indole by using novel Clay catalyst.



Result and Discussion

Table 1

Sr.no.	Compound name	Antibacterial Activity				Antifungal Activity	
		E. coli	*P. aeruginosa*	***S. aurus***	***S. pyogenus***	***C. alibicans***	***A. niger***
01	3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole	100	100	100	125	500	1000
02	3-((4-chlorophenyl)(1H-indol-3-yl)methyl)-1H-indole	200	250	500	500	500	500
03	3-((1H-indol-3-yl)(2-nitrophenyl)methyl)-1H-indole	62.5	100	200	200	1000	1000
04	3-((1H-indol-3-yl)(phenyl)methyl)-1H-indole	125	100	500	250	1000	≥ 1000
05	3-((1H-indol-3-yl)(3-nitrophenyl)methyl)-1H-indole	200	250	500	500	≥1000	1000
06	Gentamycin	0.05	1	0.25	0.5	-	-
07	Ampicillin	100	-	250	100	-	-
08	Chloramphenicol	50	50	50	50	-	-
09	Ciprofloxin	25	25	50	50	-	-
10	Norfloxacin	10	10	10	10	-	-
11	Nystatin	-	-	-	-	100	100
12	Greseofulvin	-	-	-	-	500	100

It is found that the bis-indole derivatives we have synthesized are biological active. The compound 3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole shows minimal inhibition concentration for antibacterial activity for bacteria S. Aureus at 100 mg/ml. while minimal inhibition concentration for the standard drugs ampicillin is 250 mg/ml. while antibacterial activity for bacteria E.coli at 100 mg/ml and minimal inhibition concentration for standard drug amplicillin is 100 mg/ml this shows that compound first is more reactive than standard drug amplicillin. At the same time it is found that the antibacterial activity for the bacteria S. pyogenus is 125 mg/ml and the standard drug amplicillin shows

at100 mg/ml. For these bacteria it shows less reactivity for antibacterial activity. Antifungal activity of compound for fungus C. albicans is 500 mg/ml, A. nigeris 1000 mg/ml and minimal fungicidal concentration for standard drug Nystatin 100 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. Standard drug Nystatin 500 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. This concludes that the compound first shows similar antifungal activity as standard drug greseofulvin for fungus C. Albicans.

The compound 3-((4-chlorophenyl)(1H-indol-3-yl)methyl)-1H-indole shows antibacterial activity for bacteria E.coli at 200 mg/ml, P.aeruginosa at 250 mg/ml, S. aureus 500 mg/ml and S. pyogenus 500 mg/ml. Standard drug Gentamycin for E. coli 0.05 mg/ml, P. aeruginosa 1 mg/ml, S. aureus 0.25 mg/ml and S. pyogenus 0.5 mg/ml. Standard drug Ampicillin for E. coli 100 mg/ml, S. aureus 250 mg/ml and S. pyogenus 100 mg/ml. Standard drug Chloramphenicol for E. coli 50 mg/ml, P. aeruginosa 50 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Ciprofloxacin for E. coli 25 mg/ml, P. aeruginosa 25 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Norfloxacin for E. coli 10 mg/ml, P. aeruginosa 10 mg/ml, S. aureus 10 mg/ml and S. pyogenus 10 mg/ml. Hence the compound second shows less reactivity than all standard drugs.Antifungal activity of compound second for fungus C. albicans is 500, A. niger is 500 mg/ml and minimal fungicidal concentration for standard drug Nystatin 100 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. Standard drug Nystatin 500 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. here it is observed that compound second shows similar antifungal activity as standard drug greseofulvin for fungus C. Albicans.

The compound 3-((1H-indol-3-yl)(2nitrophenyl)methyl)-1H-indole shows antibacterial activity for bacteria E.coli at 62.5 mg/ml, P. aeruginosa at 100 mg/ml, S. aureus 200 mg/ml and S. pyogenus 200 mg/ml. Standard drug Ampicillin for E. coli 100 mg/ml, S. aureus 250 mg/ml and S. pyogenus 100 mg/ml. here it is observed that this shows better reactivity than the standard drug ampicillin for E. coli and S. aureus. While the Standard drug Gentamycin for E. coli 0.05 mg/ml, P. aeruginosa 1 mg/ml, S. aureus 0.25 mg/ml and S. pyogenus 0.5 mg/ml. Standard drug Chloramphenicol for E. coli 50 mg/ml, P. aeruginosa 50 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Ciprofloxacin for E. coli 25 mg/ml, P. aeruginosa 25 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Norfloxacin for E. coli 10 mg/ml, P. aeruginosa 10 mg/ml, S. aureus 10 mg/ml and S. pyogenus 10 mg/ml. Hence the compound third shows more reactivity than all standard drugs.Antifungal activity of compound third for fungus C. albicans is 1000, A. niger, is 1000 mg/ml and minimal fungicidal concentration for standard drug Nystatin 100 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. Standard drug Nystatin 500 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. here it is conclude that this compound shows less antifungal activity than these all standard drugs.

The compound 3-((1H-indol-3-yl)(phenyl)methyl)-1H-indole shows antibacterial activity for bacteria E.coli at 125 mg/ml, P.aeruginosa at 100 mg/ml, S. aureus 500 mg/ml and S. pyogenus 250 mg/ml. Standard drug gentamycin for E. coli 0.05 mg/ml, P. aeruginosa 1 mg/ml, S. aureus 0.25 mg/ml and S. pyogenus 0.5 mg/ml. Standard drug Ampicillin for E. coli 100 mg/ml, S. aureus 250 mg/ml and S. pyogenus 100 mg/ml. Standard drug Chloramphenicol for E. coli 50 mg/ml, P. aeruginosa 50 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Ciprofloxacin for E. coli 25 mg/ml, P. aeruginosa 25 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Norfloxacin for E. coli 10 mg/ml, P. aeruginosa 10 mg/ml, S. aureus 10 mg/ml and S. pyogenus 10 mg/ml. Hence the compound fourth shows less reactivity than all standard drugs.Antifungal activity of compound fourth for fungus C. albicans is less than 1000 mg/ml, A. niger is 1000 mg/ml and minimal fungicidal concentration for standard drug Nystatin 100 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. Standard drug

Nystatin 500 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. hence it is found that this compound shows less antifungal activity than standard drug Nystatin and greseofulvin.

The compound 3-((1H-indol-3-yl)(3-nitrophenyl)methyl)-1H-indoleshows antibacterial activity for bacteria E. coli at 200 mg/ml, P. aeruginosa at 250 mg/ml, S. aureus 500 mg/ml and S. pyogenus 500 mg/ml. Standard drug Gentamycin for E. coli 0.05 mg/ml, P. aeruginosa 1 mg/ml, S. aureus 0.25 mg/ml and S. pyogenus 0.5 mg/ml. Standard drug Amplicilin for E. coli 100 mg/ml, S. aureus 250 mg/ml and S. pyogenus 100 mg/ml. Standard drug Chloramphenicol for E. coli 50 mg/ml, P. aeruginosa 50 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Ciprofloxacin for E. coli 25 mg/ml, P. aeruginosa 25 mg/ml, S. aureus 50 mg/ml and S. pyogenus 50 mg/ml. Standard drug Norfloxacin for E. coli 10 mg/ml, P. aeruginosa 10 mg/ml, S. aureus 10 mg/ml and S. pyogenus 10 mg/ml. Hence the compound fifth shows less reactivity than all standard drugs.Antifungal activity of compound fifth for fungus C. albicans is less than 1000 mg/ml, A. niger is 1000 mg/ml and minimal fungicidal concentration for standard drug Nystatin 100 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. Standard drug Nystatin 500 mg/ml, A. niger 100 mg/ml, A. clavatus 100 mg/ml. the standard Nystatin and greseofulvin shows better antifungal activity than this compound.

Conclusion

Compound 3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole shows good antibacterial activity than standard drug Ampicillin for bacteria S. aureus and similar activity for bacteria E. coli. Compound 3-((1H-indol-3-yl)(2-nitrophenyl)methyl)-1H-indole shows good antibacterial activity than standard drug Ampicillin for bacteria E. coli & S. aureus.

Compound 3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole and 3-((4-chlorophenyl)(1H-indol-3-yl)methyl)-1H-indole shows similar antifungal activity like standard drug Greseofulvin for fungi C. albicans.

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