International Journal of Advance and Innovative Research
Volume 6, Issue 1 (XVI): January - March, 2019
ISSN 2394 - 7780

EVALUATION OF ANTIMICROBIAL AND ANTIFUNGAL PROPERTIES OF 3-((1H-INDOL-3-YL)(1,3-DIPHENYL-1H-PYRAZOL-4-YL)METHYL)-1H-INDOLE SYNTHESIZED USING NOVEL CLAY CATALYST

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ABSTRACT
This article gives information about study of antibacterial and antifungal properties of synthesized 3-((1H-indol-3-yl)(1,3-diphenyl-1H-pyrazol-4-yl)methyl)-1H-indole using novel clay catalyst.Bis-indolyl pyrazolyl methane has appeared as structurally novel antifungal and antibacterial and activity. Therefore 3-((5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(1H-indol-3-yl)methyl)-1-H-indole was synthesized by addition of 1, 3-diphenyl-1H-pyrazole-4-carboxaldehyde with indole.

Keywords: Novel Clay,Bis indolyl Pyrazolyl methane, antibacterial, antifungal activity, 1, 3-diphenyl-1H-pyrazole-4-carboxaldehyde.

INTRODUCTION
Infectious diseases initiated by microbes such as bacteria and fungi are one of the leading causes of disease and mortality and the major cause for the increase in microbial infections is the resistance developed by these microbial organisms, particularly gram-positive bacteria S. aureus and species of the genus enterococcus towards existing antimicrobial drugs [1]. The appearance and spread of antimicrobial resistance has become one of the most serious public health anxieties across the world. Antimicrobial resistance refers to micro-organism that has developed the ability to inactivate, exclude or block the inhibitory or lethal mechanism of the antimicrobial agents [2]. Vibrindole has been demonstrated for the first time to exhibit antibacterial activity against S. aureus, S. albus and B. subtills. Gentamycin is in use as a standard antibacterial drug [3]. Predominantly bis(indolyl)methanes are the most active cruciferous ingredients, showing a wide array of pharmacological activities [4]. Substituted indole derivatives possess antibacterial activity [5]. S. aureus, the chief culprit, is also a common source of community developed 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 [6]. Bis indolyl methane exhibit antimicrobial and antifungal activities [7]. Analgesic and anti-inflammatory [8].Anticancer [9].Bis(indolyl)methanes were obtained by reactions of indole with various aldehydes in the presence of several bronsted and lewis acid catalysts such as $LiClO_4$ [10], montmorillonite clay K-10 [11-12], NBS [13],$ZrCl_4$ [14], Zeolite [15].But many of these methods have several drawbacks such as use of expensive reagents, longer reaction times, cumbersome workup, and low product yields. But in the present work, we replaced this catalyst by low cost cheaply available Novel clay catalyst.

2. EXPERIMENTAL PROTOCOLS
2.1 Chemistry
All chemicals were acquired 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 methyl acetate in required amount. FT-IR was noted in KBr, HNMR in $CDCl_3$ from Central Instrumentation Facility, Savitribai Phule Pune University, and Pune. X-Ray Powder diffraction (XRD) was noted from department of Physics, Savitribai Phule Pune University. Energy-dispersive X-Ray Spectroscopy (EDS) and Field Emission Scanning Electron Microscope (FESEM) by using device Nova Nano SEM 450 UOP were documented 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, entirely MTCC cultures were confirmed against above mentioned known and unknown drugs. Mueller hinton broth was used as nutrient medium to propagate and dilute the drug suspension for the test bacteria, inoculum size for test strain was adjust to 108cfu [Colony Forming Unit] per milliliter by comparing the turbidity. Subsequent common standard strains were used for screening of antibacterial and antifungal activities. The strains were acquired from Institute of Microbial Technology, Chandigarh.

ISSN 2394 - 7780

The novel clay was assimilated from the field of Bashir Farm (Jatadevale) TqPatahrdi&Dist Ahmednagar. Preparation and characterization of novel clay catalyst such as (XRD, EDS and FESEM) wasreported in our earlier work [16-17].

2.2. Experimental Protocol

2.3. General procedure for Synthesis of Synthesis of 1, 3-diphenyl-1H-pyrazole-4-carbaldehyde

2.3.1. Preparation of Hydrazone derivatives of acetophenone

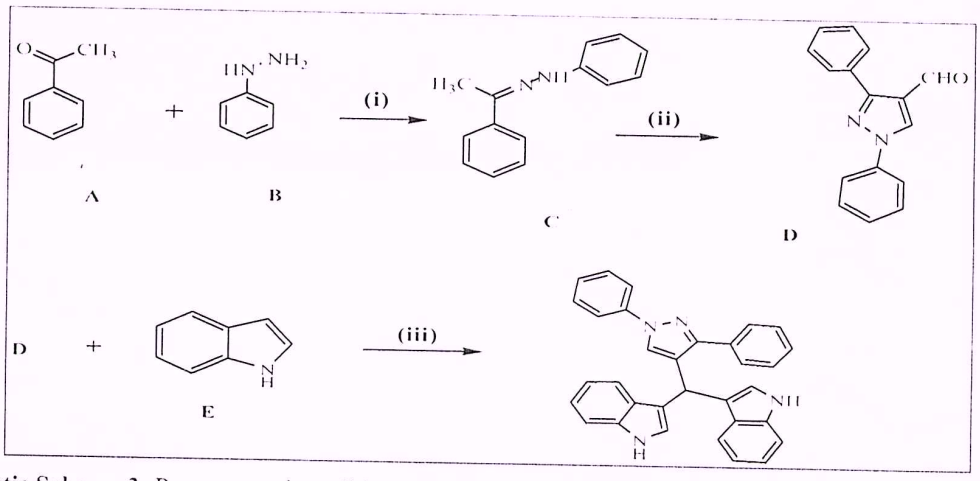
(1.0 mole) of acetophenone and (1.0 mole) of phenyl hydrazine beaker add (2 to 3) drop of acetic acid in conical flask mixed well and heated this mixture in water bath for five minutes solid hydrazone product was separated recrystallized with ethyl alcohol.

3.3.1. Conversion of hydrazone to carboxaldehyde

Take (4 ml) DMF in R.B. Flask and cool it at 0° C in ice bath add it (2 ml) $POCl_3$ drop wise to maintain temperature below 10° C dissolve hydrazone prepared in last stage to minimum amount of DMF in beaker add this mixture to conical Flask drop by drop to maintain temperature below 20° C after thorough of addition stirring well and keep the reaction mixture at room temperature for 30 minute then pour this reaction mixture into ice cold water filter the product recrystallized with ethanol.

2.4. Synthesis of bis(indolyl)methane derivatives

The mixture of (1.0 mole) of 1, 3-diphenyl-1H-pyrazole-4-carboxaldehyde, (2.0 mole) of indole and (0.10 mg) of catalyst in ethyl acetate in conical flask with magnetic needle and stirred this mixture on magnetic stirrer for specific period. The reaction was monitored by TLC. A reaction waschecked by TLC then 10 ml dichloromethane was addedto this mixture and filtered. Catalyst was separated by filtration. This catalyst reused. Then 5 ml of N-hexane was added in filtrate. This mixture was kept in deep freezer pure crystals were separated.



Synthetic Scheme-3: Reagents and conditions: (i) AcOH/EtOH, reflux, 30 minutes; (ii) DMF/$POCl_3$, 0 ^{0}C-30 ^{0}C, 12-14 h; (iii) Novel Clay catalyst, ethylacetate, 12-48Hrs stirring at RT.

3. RESULTS AND DISCUSSION

Sr. no.	Compound name	Antibacterial Activity				Antifungal Activity	
		E.coli	P.aeruginoa	S.aurus	S.pyogenus	Calibicans	A.niger
01	3-((5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(1H-indol-3-yl)methyl)-1H-indole	100	62.5	125	250	500	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

ISSN 2394 - 7780

3-((5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(1H-indol-3-yl)methyl)-1H-indole shows antibacterial activity for bacteria E. coli at 100 mg/ml, P .aeruginosa at 62.5 mg/ml, S. aureus 125 mg/ml and S. pyogenus 250 mg/ml. Amplicillin for E. coli 100 mg/ml, S. aureus 250 mg/ml and S. pyogenus 100 mg/ml. hence it found that amplicillin and this compound shows similar activity for bacteria E. coli and better reactivity than S. Aureus. similar way 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. it is found that 3-((5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(1H-indol-3-yl)methyl)-1H-indole shows less reactivity than all standard drugs.

Antifungal activity of compound 3-((5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(1H-indol-3-yl)methyl)-1H-indole for fungus C. albicans MTCC 227 is 500 mg/ml, A. niger MTCC 282 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. it is detected that this compound shows comparable reactivity as greseofulvin for fungi C. Albicans.

ACKNOWLEDGEMENT

Auther are thankful to**Dr.Mazahar Farooqui** (Principal, RafiqZakaria College for Women, Naukhanda, Aurangabad and Dean, faculty of science& technology, Dr.BabasahebAmbedkarMarathwada University, Aurangabad) for his constant support and guidance.

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