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SYNTHESIS AND ANTIMICROBIAL EVALUATION OF O-MANNICH BASES OF DIHYDROPYRIMIDINES BEARING BENZIMIDAZOLE

Hanmanthu Guguloth
Department of Chemistry, Kakatiya University, Warangal, Telangana

Abstract:
*The present study aims at the synthesis of Mannich Bases of dihydropyrimidinesbearing benzoimidazoleand their evaluation as antimicrobial agents. A new series of benzoimidazole-dihydropyrimidine hybrids (**3a-p**) were synthesized from condensation reaction of chalcones by cyclizing with urea which offered intermediatedihydropyrimidines (**2a-p**).TheMannich reaction of dihydropyrimidines, formaldehyde and benimidazole offered the title hybrids (**3a-p**) and then structures of these compounds were confirmedby IR, NMR, and mass spectroscopy.The compounds were tested for their antimicrobial activity against Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Aspergillus nigerandCunninghamellaverticulata. The data obtained from cup plate method indicated that the compound **3e** and **3o** shows most active antibacterial activity against two Gram (+) veand one Gram (-) ve bacteria.The compound **3a** have produced a maximum inhibition and **3d**show minimum zone of inhibition against A. niger and C.vericulataat.*

Key Words:*Dihydropyrimidines; Benzimidazole; Mannich Bases; Antimicrobial*

Corresponding Author:
Hanmanthu Guguloth,
Department of Chemistry,
Kakatiya University,
Warangal, Telangana
Mail: hanmanthu.guguloth@yahoo.com;
Mobile: +91 9849395880

QR code

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INTRODUCTION:

In the past two decades, there has been extraordinary activity in the discovery and development of new antimicrobial agents. One need only reflect upon the long list of new penicillin's, cephalosporin's and quinolones that were not available in the past to form the opinion that such activity was the result of unrelated research and discovery efforts in many different chemical areas. The development procedure for a new antimicrobial agent involves studies that characterize its mechanism of action and extensively assess its safety and efficacy in both humans and other animals [1].

Antimicrobial drugs have caused a dramatic change not only in the treatment of infectious diseases, but also in the fate of mankind. Antimicrobial chemotherapy made remarkable advances, resulting in the overly optimistic view that infectious diseases would be conquered in the near future [2].However, in reality, emerging and re-emerging infectious diseases have left us facing a counter charge from infections. Infections with drug resistant organisms remain an important problem in clinical practice that is difficult to solve. If an improper antimicrobial agent happens to be chosen for the treatment of infection with drug resistant microorganisms, the therapy may not achieve beneficial effect, and moreover, may lead to a worse prognosis. In addition, in a situation where multidrug-resistant organisms have spread widely, there may be quite a limited choice of agents for antimicrobial therapy [3].At present, fewer brand new antimicrobial agents are coming onto the market. Considering this situation together with the increasing awareness of drug safety, we are now facing a situation of severely limited options among antimicrobial agents [1].

Dihydropyrimidines and their derivatives occupy an important role in the realm of natural and synthetic organic chemistry because of their therapeutic and pharmacological properties. They have emerged as integral backbone of several calcium channel blockers, antihypertensive agents, a- 1α-antagonistsand neuropeptide Y(NPY) antagonists [4]. Similarly, various spiro-derivativesbased on heterocyclics have antibacterial, anticonvulsant, antitumor and anticancer activities[5]. The pyrimidine ring forms an integral part of the structure of a number of important natural products. The biodynamic property of the ring system prompted us to design pyrimidine derivatives stimulating pharmachore and substituents responsible for diverse pharmacological activities [6]. As the pyrimidine ring system is highly biologically active, therefore, it was thought of interest to construct it alone as well as condensed with the same moiety *i.e.* the creation of pyrimidopyrimidine to see the additive effect of these rings towards antifungal activities. Further, a considerable amount of work has been done on the synthesis and pharmacological activities like analgesic, antispasmodic, anaesthetic and antimicrobial activity of various N- Mannichbases derived from these dihydropyrimidines as well as intermediates obtained during such drug synthesis [7, 8].

The fusion of benzene and imidazole forms a heterocyclic aromatic organic compound called benzimidazole which is bicyclic in nature. It is an important pharmacophore and a privileged structure in medicinal chemistry. Heterocyclic compounds are more biologicaly active as compared to others [9].Benzimidazole is one such compound which attracts the attention of synthetic chemists for the designing more potent benzimidazole derivatives having wide diverse of biological activity [10]. Literature reveals that benzimidazole-containing compounds show biological activities as PARP inhibitors as anticancer agents[11], cytomegalovirus (HCMV) inhibitors [12],ulcers, anti-inflammatory agents and as anti-histaminics [13] .Mannich reaction has been studied by several groups of workers in the field of medicinal chemistry, mainly because of the various pharmacological properties of the Mannich Bases so formed. A variety of Mannich Bases have been reported to possess analgesic [14], anti-inflammatory [15],local anaesthetic, anticancer [16], antibacterial [17], antifungal [18]and several other activities.

EXPERIMENTAL:

Chemistry

Melting points were determined using Thermonik Melting Point Apparatus (Campbell electronics, India) by capillary method and are uncorrected. Infrared (IR) spectra were taken on a Fourier Transform Infrared Spectrophotometer IR-Prestige 21 (Shimatzu Corporation, Japan) from 4000-400 cm^{-1} using KBr discs. ^1H NMR spectra were recorded at 400 MHz in DMSO-d_6 using a Bruker Avance 400 instrument (Bruker Instruments Inc., USA). Chemical shifts were measured at δ units (ppm) relative to tetramethylsilane (TMS). Fast-atom bombardment (FAB) mass spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer (Jeol Ltd Akishima, Tokyo, Japan) using argon/xenon (6 kV, 10 mA) as FAB gas, m-nitrobenzyl alcohol as matrix, and 10 kV as accelerating voltage at room temperature. Elemental analysis was performed on a Vario EL III Elemental Analyser (Elementar, Germany) using sulfanilamide as standard. All chemicals were purchased from Merck, Spectrochem or CDH, India. Solvents were of reagent grade and were purified and

dried by standard procedure. Reactions were monitored by thin-layer chromatography on silica gel plates in either iodine or UV chambers. Intermediates were characterized by IR spectroscopic analysis and elemental analysis for CHN. In the elemental analysis, the observed values were within ±0.4% of the calculated values. Final compounds were characterized by ^{1}H NMR and FAB mass spectrometry (MS). The final yields and the physicochemical data of the compounds **3a-p** are presented in **Table 1.**

General synthesis of Chalcones (1a-p)

To a solution of suitably benzaldehyde (0.01 M) and substituted acetophenone (0.01 M) in ethanol (10 ml) was added aqueous solution of potassium hydroxide (60%) drop wise with continuous stirring at 0 °C over a period of 15 minutes. The reaction mixture was kept at room temperature for about 48 h with occasional shaking. After 48 h it was poured into ice-cold water, and then neutralized to pH 2 using 6 N hydrochloric acid. The yellow precipitate obtained was filtered, washed, dried, and recrystallized from dry methanol. The intermediates **1a-p** wereobtained.

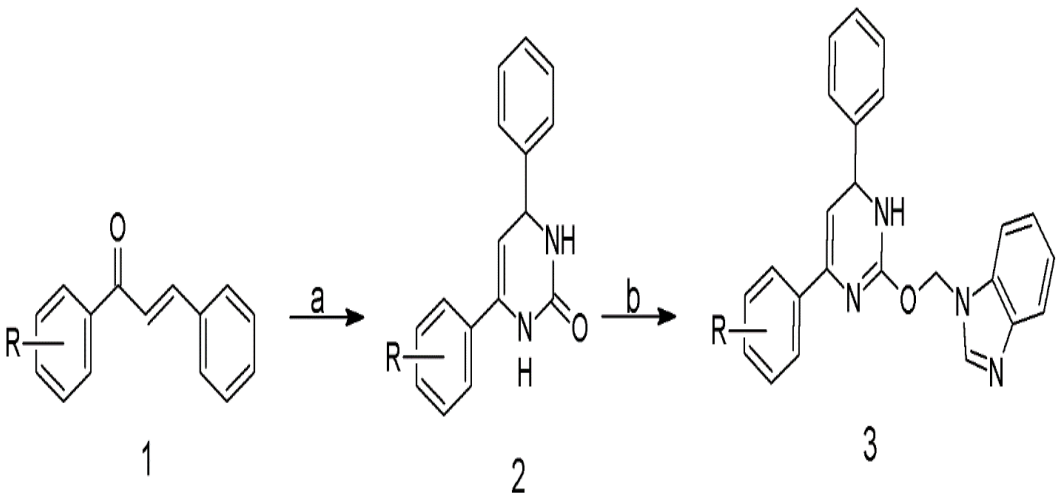
General synthesis of 4,6-dihydropyrimidin-2-one (2a-p):

Appropriate chalcone (**1a-p**) were dissolved in ethanol and added catalytic amount of concentrated sulphuric acid then refluxed for 3–6 h. The reaction was monitored by TLC. After completion of the reaction, the contents were cooled to room temperature and poured into ice-cold water. The solid separated out was filtered, washed, dried and recrystallized from ethanol to afford respective pyrazoline (**2a-p**).

General synthesis of O- Mannich bases of 4,6-dihydro pyrimidine-2-one (3a-p):

Appropriate dihydropyrimidine (**2**, 0.005 M) was dissolved in DMSO(25 ml) in a conical flask, and stirred with 37% HCHO (0.01M), anhydrous potassium carbonate (1.0g) then added benzimidazole(0.005 M) and continued the stirring magnetically for about 2 h. The reaction mixture was then heated under reflux for about 4-5 h. andthen kept in the refrigerator for 48 h, filtered the separated product, washed with small portions of cold water and dried.The crude product was purified by recrystallization from Pet.Ether: Chloroform (1:1 mixture).

Scheme. 1



Reagents and condition: (a). Urea, H_2SO_4, reflux; (b). HCHO, Benzimidazole,K_2CO_3, DMSO, reflux.

1-{[(4,6-Diphenyl-1,6-dihydropyrimidin-2-yl)oxy]methyl}-1H-benzimidazole
MF: $C_{24}H_{20}N_4O$; MW: 380; IR (KBr, cm^{-1}): 3230 (N-H), 3088 (Ar-H), 3056, 2865 (C-H), 1616 (C=N); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.10 (d, 1H, CH), 2.6 (d, 1H, CH), 5.10 (s, 2H, CH_2), 5.46 (s, 1H, NH), 6.78-7.28 (m, 15H, ArH); FAB-MS (m/z): 381 $[M+1]^+$; Elemental analyses Calcd. (Found): C 75.77 (75.49), H 5.30 (5.29), N 14.73 (14.69).

1-({[6-(2-hydroxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole
MF: $C_{24}H_{20}N_4O_2$; MW: 396; IR (KBr, cm^{-1}): 3248 (N-H), 3092 (Ar-H), 3046, 2846 (C-H), 2792 (O-H), 1624 (C=N), 1314 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.22 (d, 1H, CH), 2.56 (d, 1H, CH), 5.28 (s, 2H, CH_2), 5.48 (s, 1H, NH), 6.82-7.46 (m, 14H, ArH), 8.68 (s, 1H, OH); FAB-MS (m/z): 397 $[M+1]^+$; Elemental analyses Calcd. (Found): C 72.71 (72.43), H 5.08 (5.09), N 14.13 (14.08).

1-({[6-(3-hydroxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole
MF: $C_{24}H_{20}N_4O_2$; MW: 396; IR (KBr, cm^{-1}): 3232 (N-H), 3086 (Ar-H), 3048, 2864 (C-H), 2784 (O-H), 1618 (C=N), 1316 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.24 (d, 1H, CH), 2.62 (d, 1H, CH), 5.18 (s, 2H, CH_2), 5.56 (s, 1H, NH), 6.86-7.58 (m, 14H, ArH), 8.70 (s, 1H, OH); FAB-MS (m/z): 397 $[M+1]^+$; Elemental analyses Calcd. (Found): C 72.71 (72.48), H 5.08 (5.09), N 14.13 (14.10)

1-({[6-(4-hydroxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole
MF: $C_{24}H_{20}N_4O_2$; MW: 396; IR (KBr, cm^{-1}): 3236 (N-H), 3074 (Ar-H), 3046, 2828 (C-H), 2782 (O-H), 1622 (C=N), 1323 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.18 (d, 1H, CH), 2.58 (d, 1H, CH), 5.08 (s, 2H, CH_2), 5.42 (s, 1H, NH), 6.78-7.28 (m, 14H, ArH), 8.24 (s, 1H, OH); FAB-MS (m/z): 397 $[M+1]^+$; Elemental analyses Calcd. (Found): C 72.71 (72.52), H 5.08 (5.07), N 14.13 (14.12)

1-({[6-(2-methoxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole
MF: $C_{25}H_{22}N_4O_2$; MW: 410; IR (KBr, cm^{-1}): 3198 (N-H), 3048 (Ar-H), 3026, 2836 (C-H), 1636 (C=N), 1320 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.12 (d, 1H, CH), 2.54 (d, 1H, CH), 3.15 (s, 3H, OCH_3), 5.16 (s, 2H, CH_2), 5.44 (s, 1H, NH), 6.68-7.32 (m, 14H, ArH); FAB-MS (m/z): 411 $[M+1]^+$; Elemental analyses Calcd. (Found): C 73.15 (72.88), H 5.40 (5.39), N 13.65 (13.62)

1-({[6-(3-methoxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole
MF: $C_{25}H_{22}N_4O_2$; MW: 410; IR (KBr, cm^{-1}): 3196 (N-H), 3056 (Ar-H), 3028, 2835 (C-H), 1623 (C=N), 1316 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.12 (d, 1H, CH), 2.64 (d, 1H, CH), 3.24 (s, 3H, OCH_3), 5.16 (s, 2H, CH_2), 5.46 (s, 1H, NH), 6.88-7.48 (m, 14H, ArH); FAB-MS (m/z): 411 $[M+1]^+$; Elemental analyses Calcd. (Found): C 73.15 (72.90), H 5.40 (5.41), 13.65 N(13.64).

1-({[6-(4-methoxyphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)benzimidazole

MF: $C_{25}H_{22}N_4O_2$; MW: 410; IR (KBr, cm^{-1}): 3194 (N-H), 3068 (Ar-H), 3025, 2846 (C-H), 1674 (C=N), 1321 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.14 (d, 1H, CH), 2.64 (d, 1H, CH), 3.18 (s, 3H, OCH_3), 5.16 (s, 2H, CH_2), 5.36 (s, 1H, NH), 6.88-7.38 (m, 14H, ArH); FAB-MS (m/z): 411 $[M+1]^+$; Elemental analyses Calcd. (Found): C 73.15 (73.24), H 5.40 (5.41), N 13.65 (13.67)

1-({[6-(2-methylphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{25}H_{22}N_4O$; MW: 394; IR (KBr, cm^{-1}): 3218 (N-H) 3062 (Ar-H), 3064, 2846 (C-H), 1624 (C=N), 1318 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.06 (d, 1H, CH), 2.22 (s, 3H, CH_3), 2.48 (d, 1H, CH), 5.04 (s, 2H, CH_2), 5.44 (s, 1H, NH), 6.52-7.08 (m, 14H, ArH); FAB-MS (m/z): 395 $[M+1]^+$; Elemental analyses Calcd. (Found): C 76.12 (75.83), H 5.62 (5.61), N 14.20 (14.16).

1-({[6-(3-methylphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{25}H_{22}N_4O$; MW: 394; IR (KBr, cm^{-1}): 3230 (N-H) 3074 (Ar-H), 3052, 2870 (C-H), 1616 (C=N), 1314 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.12 (d, 1H, CH), 2.22 (s, 3H, CH3), 2.58 (d, 1H, CH), 5.18 (s, 2H, CH_2), 5.36 (s, 1H, NH), 6.68-7.18 (m, 14H, ArH); FAB-MS (m/z): 395 $[M+1]^+$; Elemental analyses Calcd. (Found): C 76.12 (75.90), H 5.62 (5.63), N 14.20 (14.19)

1-({[6-(4-methylphenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{25}H_{22}N_4O$; MW: 394; IR (KBr, cm^{-1}): 3226 (N-H) 3082 (Ar-H), 3046, 2836 (C-H), 1618 (C=N), 1323 (C-O); ^1H NMR (300 MHz, $CDCl_3$,δppm): 2.12 (d, 1H, CH), 2.24 (s, 3H, CH3), 2.48 (d, 1H, CH), 5.02 (s, 2H, CH_2), 5.36 (s, 1H, NH), 6.62-7.02 (m, 14H, ArH); FAB-MS (m/z): 395 $[M+1]^+$; Elemental analyses Calcd. (Found): C 76.12 (76.10), H 5.62 (5.63), N 14.20 (14.22).

1-({[6-(2-chlorophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}ClN_4O$; MW: 414; IR (KBr, cm^{-1}): 3236 (N-H) 3086 (Ar-H), 3054, 2868 (C-H), 1620 (C=N),

817 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.14 (d, 1H, CH), 2.68 (d, 1H, CH), 5.22 (s, 2H, CH_2), 5.52 (s, 1H, NH), 6.86-7.84 (m, 14H, ArH); FAB-MS (m/z): 415 $[M+1]^+$; Elemental analyses Calcd. (Found): C 69.48 (69.22), H 4.62 (4.63), N 13.50 (13.46).

1-({[6-(3-chlorophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}ClN_4O$; MW: 414; IR (KBr, cm^{-1}): 3226 (N-H) 3074 (Ar-H), 3022, 2841 (C-H), 1632 (C=N), 818 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.18 (d, 1H, CH), 2.72 (d, 1H, CH), 5.18 (s, 2H, CH_2), 5.62 (s, 1H, NH), 6.88-7.48 (m, 14H, ArH); FAB-MS (m/z): 415 $[M+1]^+$; Elemental analyses Calcd. (Found): C 69.48 (69.25), H 4.62 (4.64), N 13.50 (13.48)

1-({[6-(4-chlorophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}ClN_4O$; MW: 414; IR (KBr, cm^{-1}): 3248 (N-H) 3092 (Ar-H), 3062, 2858 (C-H), 1624 (C=N), 816 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.04 (d, 1H, CH), 2.54 (d, 1H, CH), 5.06 (s, 2H, CH_2), 5.32 (s, 1H, NH), 6.66-7.14 (m, 14H, ArH); FAB-MS (m/z): 415 $[M+1]^+$; Elemental analyses Calcd. (Found): C 69.48 (69.40), H 4.62 (4.63), N 13.50 (13.52)

1-({[6-(2-nitrophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}N_5O_3$;MW: 425; IR (KBr, cm^{-1}): 3242 (N-H) 3074 (Ar-H), 3036, 2842 (C-H), 1622 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.16 (d, 1H, CH), 2.34 (d, 1H, CH), 5.26 (s, 2H, CH_2), 5.58 (s, 1H, NH), 6.82-7.46 (m, 14H, ArH); FAB-MS (m/z): 426 $[M+1]^+$; Elemental analyses Calcd. (Found): C 67.76 (67.50), H 4.50 (4.49), N 16.46 (16.40).

1-({[6-(3-nitrophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}N_5O_3$;MW: 425; IR (KBr, cm^{-1}): 3218 (N-H) 3075 (Ar-H), 3032, 2852 (C-H), 1618 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.20 (d, 1H, CH), 2.82 (d, 1H, CH), 5.38 (s, 2H, CH_2), 5.88 (s, 1H, NH), 6.88-7.68 (m, 14H, ArH); FAB-MS (m/z): 426 $[M+1]^+$; Elemental analyses Calcd. (Found): C 67.76 (67.55), H 4.50 (4.52), N 16.46 (16.52)

1-({[6-(4-nitrophenyl)-4-phenyl-1,6-dihydropyrimidin-2-yl]oxy}methyl)-benzimidazole
MF: $C_{24}H_{19}N_5O_3$;MW: 425; IR (KBr, cm^{-1}): 3220 (N-H) 3078 (Ar-H), 3034, 2855 (C-H), 1617 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$,δppm): 2.18 (d, 1H, CH), 2.68 (d, 1H, CH), 5.24 (s, 2H, CH_2), 5.62 (s, 1H, NH), 6.98-7.86 (m, 14H, ArH); FAB-MS (m/z): 426 $[M+1]^+$; Elemental analyses Calcd. (Found): C 67.76 (68.01), H 4.50 (4.51), N 16.46 (16.48).

Antimicrobial Activity:
Bacillus subtilis (NCIM 2921) and *Staphylococcus aureus* (NCIM 2079) and two gram negative bacteria viz., *Escherichia coli* (NCIM 2068) and *Proteus vulgaris* (NCIM 2027), *Aspergillus niger*and*Cunninghamellaverticulata.*
The compounds tested for their antimicrobial activity using disc diffusion method. Bacterial species were sub-cultured on nutrient agar medium and fungal species on potato dextrose agar medium, which were then incubated at 37 °C for 24 hours and 27 °C for 48 hours respectively. Test substances dilution was made with dimethylformamide itself to obtain a solution of 100 µg/ml concentration were impregnated on sterile discs. Ampicillin and clotrimazole were used as positive controls. The disc impregnated with ethyl acetate was used as negative control. The discs were placed on the surface of the nutrient agar for bacteria and incubated at 37 °C for 24 hours, and on the surface of the potato dextrose agar for fungi and incubated at 27 °C for 48 hours. Inhibition zones were calculated as the difference between disc diameter (6mm) and the diameters of inhibition [19].

RESULTS AND DISCUSSION:

Antibacterial Activity
The compounds **3a-p** and ampicillin were assessed for their *In vitro* antibacterial activity against two gram positive (*B. subtilis* and *S. aureus*) and two gram negative (*E. coli* and *P. vulgaris*). Results of antibacterial activity were summarized in **Table 1**. The data obtained from cup plate method indicated that the compound **3e** and **3o** shows most active antibacterial activity against two gram positive bacteria and one gram negative bacteria (*E. coli)* with a zone of inhibition (mm) 21, 17, 19 and 19, 17, 18 on respective organism.

Antifungal Activity
The antifungal activity of derivatives compared with standard clotrimazole was assessed against two fungal organisms. The synthesized (**3a-p**) derivatives showed variation in the level of activity against the two human pathogenic fungal strains tested [**Table 1**]. The compound **3a** have produced a maximum zone of inhibition and **3d**show minimum zone of inhibition against *A. niger* and *C. vericulata*at 100µg/disc, concentration. The other compounds showed mild to moderate antifungal activity against *A. niger* and *C. vericulata*organisms.
Infectious diseases, also called communicable disease, caused by pathogenic microorganisms like bacteria, viruses and fungi, however the highest

percentage are commonly caused by bacteria.These illnesses were found to be the most significant cause of morbidity and mortality in developing countries, especially in immune compromised patients [20]. Importantly, many of these infectious microorganisms are resistant to many synthetic drugs, in addition to the side effects of synthetic antibiotics reduced by newly synthesized the derivatives. From *in vitro* antibacterial and antifungal data, it is confirmed that that compounds containing methoxyand nitro groups exhibited excellent activity. But overall, all the compounds have displayed significant antibacterial and antifungal activity. The presence of electron withdrawing substituents would be expected to increase the lipophilic character of the molecule, facilitating transport across the microorganism cell membrane and increasing antimicrobial activity [21]. Compound also expected to increase the lipophilic character of the molecule, facilitating transport across the microorganism cell membrane and increasing antimicrobial activity.

Table 1: Antibacterial and Antifungal activities of 3a-p (zone of inhibition in mm) at 100 µg/ml.

Compound	R	*B. subtilis*	*S. aureus*	*E. coli*	*P.vulgaris*	*A.niger*	*C.verticulata*
3a	H	11	--	--	--	12	9
3b	2-OH	13	11	19	13	9	7
3c	3-OH	12	10	--	--	8	6
3d	4-OH	11	9	--	--	6	5
3e	2-OCH_3	21	17	19	--	12	6
3f	3-OCH_3	13	--	--	--	6	--
3g	4-OCH_3	13	11	--	--	7	--
3h	2-CH_3	13	--	--	--	9	6
3i	3-CH_3	15	13	17	--	10	9
3j	4-CH_3	13	11	10	--	8	5
3k	2-Cl	11	--	--	--	9	8
3l	3-Cl	12	11	19	13	9	7
3m	4-Cl	12	10	--	--	7	6
3n	2-NO_2	11	9	--	--	7	5
3o	3-NO_2	19	17	18	--	11	8
3p	4-NO_2	13	--	--	--	6	--
Ampicillin*	--	24	20	23	22	NA	NA
Clotrimazole*	--	NA	NA	NA	NA	16	15

*Ampicillin&Clotrimazole @ 10 µg/ml

CONCLUSION:

The present investigation synthesized 16 molecules (**3a–p**) and characterized based on its physical and spectral data. The synthesized compounds were exhibited potent to moderate anticancer activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Aspergillus niger*and*Cunninghamellaverticulata*. The data obtained that the **3e** and **3o** shows most active antibacterial activity and **3a** have produced a maximum inhibition and **3d**show minimum zone of inhibition against *A. niger* and *C. vericulata*at. Furthermore, our data suggest that generating hybrid compounds containing benzimidazloederivatives are a promising new approach of developing an effective antimicrobial agent.

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