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MICROWAVE ASSISTED IMPROVED METHOD FOR THE SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SUBSTITUTED BENZIMIDAZOLE CARBOXAMIDE DERIVATIVES.

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ABSTRACT:
Substituted Benzimidazole derivatives containing carboxamide linkages are known to exhibit diverse biological activities. Therefore, in present work, we have designed a series of Benzimidazole derivatives containing substituted carboxamide linkage (5a-j) as a new class of antimicrobial agents. Synthesis of titled compounds was carried out by two different methods viz.conventional method and Microwave method. All the synthesized compounds were evaluated for *in vitro* antibacterial and antifungal activities. In general, compounds with electron donating groups showed good antibacterial and antifungal activities. Among the tested compounds, compound 5i exhibited highest antimicrobial activity against the tested microorganisms.

KEYWORDS: Microwave assisted synthesis, Benzimidazole derivative, benzoyl chloride, antimicrobial activity.

INTRODUCTION

Substituted Benzimidazole derivatives and their analogs have been used as precursors for synthesis of various biologically active molecules. Benzimidazoles, which are part of the many drugs structure, are known to exhibit interesting biological activities. A large number of Benzimidazole derivatives possess powerful antibacterial, antifungal[v], anti-inflammatory activity[vi]. Benzimidazole derivatives find applications as anthelmintic[vii-ix], vasodilator, antipsychotic, narcotic analgesic[x] , cardiotonic[xi], antiulcerative, Immunopotentiator[xii].
Benzimidazoles have also attracted attention as a new class of orally active synthetic antibiotics with a unique mechanism of inhibition of synthesis of bacterial protein. Literature survey reveals that less attention has been given to the synthesis of amino imidazole linked Benzimidazoles.
Therefore, in the present investigation, along with the conventional method, we decided to develop microwave assisted method for the synthesis of substituted Benzimidazole carboxamide derivatives, as the imidazole rings with amide linkage at second position has been found to possess good anti-bacterial, antifungal, anti-inflammatory activity.
Synthesis of substituted amino Benzimidazole derivatives has been attempted by different methods[xiii-xxi], where different supported catalysts have been used, and the reaction is amine and halogenated nitro benzene dependent reaction. It has been observed that the substituents have great influence on the formation of substituted Benzimidazole derivatives and also the reaction time and percent yield varies with the type of substituent.

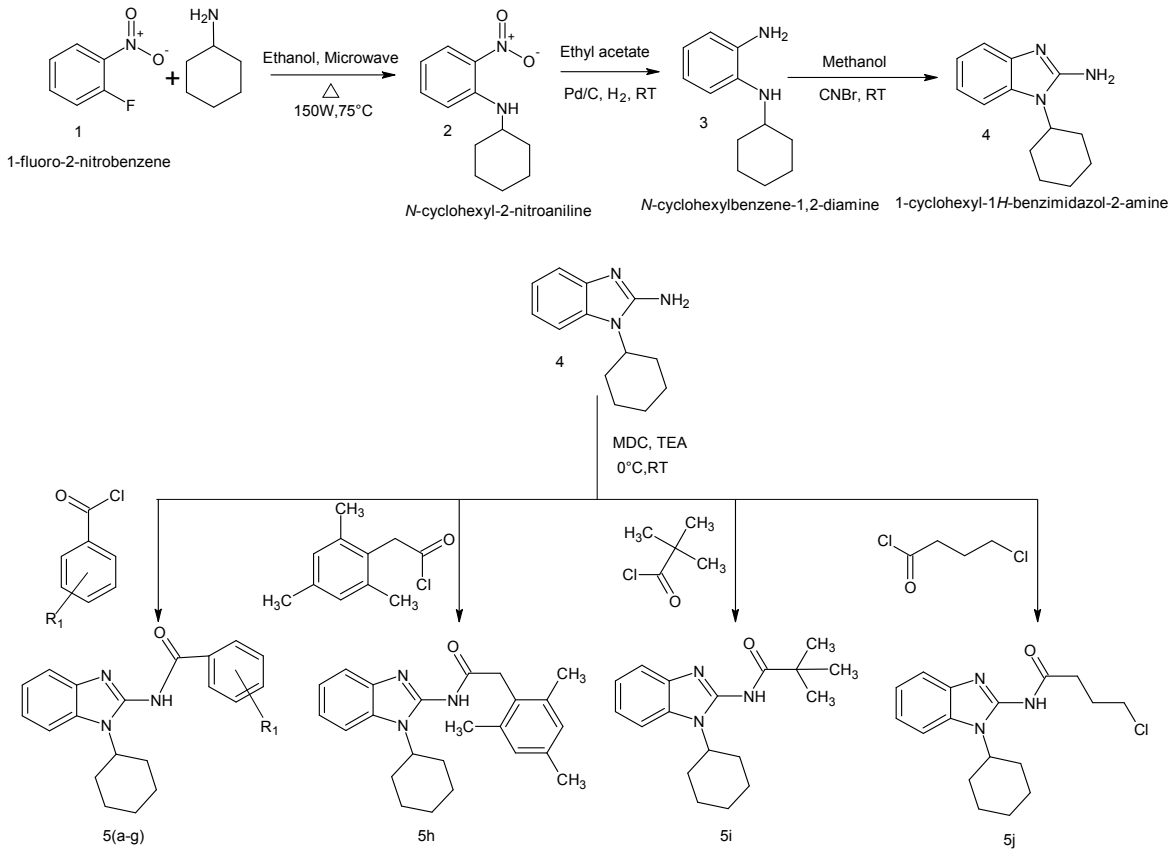
Hence, with a view to further assess the pharmacological profile of this class of compounds, it was thought worthwhile to synthesize some novel substituted Benzimidazole carboxamide derivatives by convert the substituted 2-amino Benzimidazole and substituted acyl chloride moieties in a single carboxamide molecular framework. The present work deals with the synthesis and antimicrobial screening of ten novel derivatives incorporating substituted Benzimidazole ring and carboxamide linkage.

MATERIAL AND METHODS

Measurements

Starting materials were obtained from s.d.fine, spectrochem and Lancaster. All the solvents and reagents were of laboratory reagent grade and were dried in advance and re-distilled before use. Column chromatography with silica gel was used to purify the crude products. The reactions were monitored by thin layer chromatography (TLC) which was performed on 200 μm thick aluminum sheets having silica gel 60, F254 as adsorbent. The solvent system used for developing the TLC plate was hexane and ethyl acetate (1:1). Spots were visualized under UV-light. Melting points were determined in open capillary tubes and are uncorrected. IR spectra have been recorded on Shimadzu FTIR spectrophotometer model IR Prestige-21 (cm^{-1}, in KBr). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-400 (400 MHz FT-NMR) in DMSO-d6 and TMS was used as internal standard. Peak values are shown in ppm, in the δ scale. Mass spectra were recorded on a Waters micromass ZQ. Elemental analyses were carried out on EAW 1108, Eager 200 strip chart CHN analyzer.

REACTION SCHEME



Where R1 = a) hydrogen, b) 4-fluro, c) 4-chloro, d) 2-chloro, e) 2-fluro, f) 2, 6-difluro, g) 4-nitro.

SYNTHESES OF N-CYCLOHEXYL-2-NITRO ANILINE (2)

Method A: Conventional Method

A mixture of 1-Fluro-2-nitro benzene (7.09 mMol) and Cyclohexylamine (10.63 mMol) in 15-20 ml ethanol was heated on oil bath at 75-80°C for 15-20 hr with constant stirring. The progress of reaction was monitored on TLC, after completion of reaction; reaction mixture was cooled to room temperature. Then further cooled and maintained at 0-5°C for 30 min. During this time product separated as deep orange crystals, was filtered and washed with 2×25 ml ice-cold water, followed by 2×25 ml ethanol. The wet product was dried under vacuum for 30 min. and then dried at 40°C for 2 hr under vacuum, to obtain the *N*-cyclohexyl-2-nitro aniline (2) with 50 to 60% yield.

Method B: Microwave Assisted Syntheses

A mixture of 1-Fluro-2-nitro benzene (7.09 mMol) and cyclohexylamine (9.21 mMol) in 10-12 ml ethanol was placed in the CEM Discover microwave and was irradiated at 150 W and 75°C for 40 to 50 minutes with constant stirring. The progress of the reaction was monitored on TLC. Upon completion of reaction, reaction mixture was cooled to room temperature and then maintained at 0-5°C for 30 min. During this time product separated as deep orange crystals, was filtered and washed with 2×25 ml ice-cold water, followed by 2×25 ml ethanol. The wet product was dried under vacuum for 30 min. and then dried at 40°C for 2 hr under vacuum, to obtain the compounds (2) with 80 to 85% yield.

SYNTHESES OF *N*-CYCLOHEXYL-1,2-DIAMINES (3)

A mixture of *N*-cyclohexyl-2-nitro aniline (2) (5.68 mMol), 10 % Pd/C (125 mg, 0.1w/w) and 50-60 ml ethyl acetate was stirred under H_2 gas pressure 2.0 kg/cm^2 in an autoclave at room temperature for 45-60 min with constant stirring. Progress of the reaction was monitored by TLC, after completion of reaction, the catalyst was separated by vacuum filtration through celite bed (25 g) and washing with 2×25 ml ethyl acetate. Filtrate was concentrated under vacuum below 50°C on rotary evaporator and then the product was dried at 45°C for 2 hr under vacuum to obtain the compounds (3) as brown to red colored semi solids with 90 to 95% yield.

SYNTHESES OF 1-CYCLOHEXYL-1*H*-BENZIMIDAZOL-2-AMINE (4)

A mixture of *N*-cyclohexyl-1,2-diamines (3) (5.17 mMol) and cyanogen bromide (5.17 mMol) in 15-20 ml methanol was stirred on magnetic stirrer at room temperature for 3-4 hr. Upon completion of reaction, methanol was distilled out under vacuum below 50°C on rotary evaporator. Then 50 ml ice-cold water was added to reaction mixture and the mixture was stirred at room temperature for 30 min. During this time solid product separated was filtered and washed with 2×25 ml ice-cold water, followed by 2×25 ml ethyl acetate. The wet product was dried under vacuum for 30 min and then dried at 40°C for 2 hr under vacuum to obtain the compounds (4) with 60 to 75% yield.

SYNTHESES OF SUBSTITUTED *N*-(1-CYCLOHEXYL-1*H*-BENZIMIDAZOL-2-YL) BENZAMIDE DERIVATIVES 5(a-g)

A mixture of *N*-cyclohexyl-1*H*-benzimidazol-2-amine (4) (0.93 mMol) and (1.32 mMol) of substituted Benzoyl chloride and (2.32 mMol) triethyl amine as base in 10-20 ml dichloromethane (5-10 vol.) as solvent was stir on magnetic stirrer at 0-15°C for 2-4 hr with constant stirring. Monitor progress of reaction on TLC, after completion of reaction, added 20-30 ml ice cooled water to reaction mixture and stirred reaction mixture at room temperature for 10 min. Stop stirring and allow reaction mixture to settle, separate product enriched dichloromethane layer. Dry the dichloromethane layer over 15-20 gm sodium sulphate and distilled out dichloromethane under vacuum below 40°C. Crude sticky solid obtained, which is

purified by column chromatography by using silica gel as stationary phase and ethyl acetate and hexane as eluent to obtained pure product (5a-g) in 60-75 % yield.

5a: N-(1-cyclohexyl-1H-benzimidazol-2-yl)benzamide 5a.
White crystalline solid, yield 75%, MP 145-147^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.28 – 1.60 (m , 3H) , 1.70 – 1.95 (m , 5H) , 2.35 – 2.40 (d , 2H) , 4.85 – 4.95 (t , 1H) , 7.05 – 7.15 (m , 2H) , 7.40 – 7.75 (m , 5H) , 8.20 – 8.30 (d , 2H) , 12.82 (bs , 1H). LC-MS m/z $[M+H]^+$ 320.00. Elemental Anal: Calcd for $C_{20}H_{21}N_3O$: C(75.21%) , H(6.63%) , N(13.16%). Found C(75.18%) , H(6.60%) , N (13.18%).

5b: N-(1-cyclohexyl-1H-benzimidazol-2-yl)-4-fluorobenzamide 5b.
White solid, yield 65%, MP 137-139^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.35 – 1.65 (m , 3H) , 1.70 – 1.95 (m , 5H) , 2.35 – 2.40 (t , 2H) , 4.80 – 4.85 (t , 1H) , 7.15 – 7.30 (m , 4H) , 7.45 – 7.80 (m , 3H) , 8.05 – 8.15(t , 1H) , 12.90 (bs , 1H). LC-MS m/z $[M+H]^+$ 338. Elemental analysis: Calcd for $C_{20}H_{20}N_3OF$: C(71.20%) , H(5.97%) , N(12.45%). Found C (71.18%) , H (6.00%) , N (12.4%).

5c: 4-chloro-N-(1-cyclohexyl-1H-benzimidazol-2-yl)benzamide 5c.
White crystalline solid, yield 72%, MP 140-142^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.30 – 1.60 (m , 3H) , 1.65 – 1.95 (m , 5H) , 2.30 – 2.40 (t , 2H) , 4.85 – 4.90 (t , 1H) , 7.10 – 7.30 (m , 2H) , 7.50 – 7.60 (m , 3H) , 7.65 – 7.70 (d , 1H) , 8.20 – 8.30 (d , 2H) , 12.80 (bs , 1H). LC-MS m/z $[M+H]^+$ 354. Elemental analysis: Calcd for $C_{20}H_{20}N_3OCl$: C(67.89%) , H(5.70%) , N(11.88%). Found C(67.85%) , H(5.72%) , N(11.85%).

5d: 2-chloro-N-(1-cyclohexyl-1H-benzimidazol-2-yl)benzamide 5d.
White solid, yield 70%, MP 137 – 139^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 11.35 – 1.60 (m , 3H) , 1.65 – 1.90 (m , 5H) , 2.35 – 2.45 (t , 2H) , 4.90 – 4.95 (t , 1H) , 7.15 – 7.30 (m , 2H) , 7.50 – 7.65 (m , 3H) , 7.70 – 7.75 (d , 1H) , 8.25 – 8.30 (d , 2H) , 12.85 (bs , 1H). LC-MS m/z $[M+H]^+$ 354. Elemental analysis: Calcd for $C_{20}H_{20}N_3OCl$: C(67.89%) , H(5.70%) , N(11.88%). Found C(67.87%) , H(5.68%) , N(11.84%).

5e: N-(1-cyclohexyl-1H-benzimidazol-2-yl)-2-fluorobenzamide 5e.
White solid, yield 66%, MP 139 – 141^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.31 – 1.62 (m , 3H) , 1.65 – 1.98 (m , 5H) , 2.40 – 2.45 (t , 2H) , 4.90 – 4.95 (t , 1H) , 7.10 – 7.30 (m , 4H) , 7.40 – 7.80 (m , 3H), 8.05 – 8.10 (t , 1H) , 12.85 (bs , 1H). LC-MS m/z $[M+H]^+$ 338. Elemental analysis: Calcd for $C_{20}H_{20}N_3OF$: C(71.20%) , H(5.97%) , N(12.45%). Found C(71.16%) , H(5.95%) , N(12.43%).

5f: N-(1-cyclohexyl-1H-benzimidazol-2-yl)-2,6-difluorobenzamide 5f.
White solid, yield 68%, MP 134 – 136^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.20 – 1.55 (m , 3H) , 1.60 – 1.90 (m , 5H) , 2.45 – 2.55 (t , 2H) , 4.95 – 5.00 (t , 1H) , 7.20 – 7.40 (m , 4H) , 7.45 – 7.75 (m , 2H), 8.15 – 8.20 (t , 1H) , 12.90 (bs , 1H). LC-MS m/z $[M+H]^+$ 356. Elemental analysis: Calcd for $C_{20}H_{19}N_3OF_2$: C(67.59%) , H(5.39%) , N(11.82%). Found C(67.60%) , H(5.37%) , N(11.80%).

5g: N-(1-cyclohexyl-1H-benzimidazol-2-yl)-4-nitrobenzamide 5g.
Yellow crystalline solid, yield 75%, MP 146 – 148^{o}C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.40 – 1.65 (m , 3H) , 1.70 – 2.05 (m , 5H) , 2.35 – 2.45 (t , 2H) , 4.95 – 5.00 (t , 1H) , 7.20 – 7.30 (m , 2H) , 7.60 – 7.65 (d , 1H) , 7.75 – 7.80 (d , 1H) , 8.30 – 8.40 (d , 2H) , 8.45 – 8.50 (d ,

2H) , 13.00 (bs , 1H). LC-MS m/z $[M+H]^+$ 365. Elemental analysis: Calcd for $C_{20}H_{20}N_4O_3$: C(65.92%) , H(5.65%) , N(15.38%). Found C(65.90%) , H(5.50%) , N(15.35%).

SYNTHESIS OF *N*-(1-CYCLOHEXYL-1*H*-BENZIMIDAZOL-2-YL)-2,4,6-TRIMETHYL-2-PHENYLACETAMIDE (5h)

A mixture of compounds 1-cyclohexyl-1*H*-benzimidazol-2-amine (4) (0.93 mMol), (1.32 mMol) of 2,4,6-trimethyl-2-phenylacetyl chloride and (2.32 mMol) triethyl amine as base in 30 ml dichloromethane (15 vol.) as solvent was stir on magnetic stirrer at 0-15°C for 4-5 hr with constant stirring. Monitor progress of reaction on TLC, after completion of reaction, added 30 ml ice cooled water to reaction mixture and stirred reaction mixture at room temperature for 10 min. Stop stirring and allow reaction mixture to settle, separate product enriched lower dichloromethane layer. Dry the dichloromethane layer over 15 gm sodium sulphate and distilled out dichloromethane under vacuum below 40°C. Crude sticky solid obtained, which was purified by column chromatography by using silica gel as stationary phase and ethyl acetate and hexane as eluent to obtained pure product *N*-(1-cyclohexyl-1*H*benzimidazol- 2-yl)-2,4,6-trimethyl-2-phenylacetamide (5h).

White solid, yield 65%, MP 136 – 138°C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.30 – 1.55 (m , 3H) , 1.65 – 2.00 (m , 5H) , 2.30 (s , 9H) , 2.35 – 2.45 (t , 2H) , 4.85 – 4.90 (s , 2H) , 4.95 – 5.00 (t , 1H) , 7.20 – 7.30 (m , 2H) , 7.50 – 7.55 (d , 1H) , 7.75 – 7.80 (d , 1H) , 8.30 – 8.40 (d , 2H) , 12.80 (bs , 1H). LC-MS m/z $[M+H]^+$ 376. Elemental analysis: Calcd for $C_{24}H_{29}N_3O$: C(76.76%) , H(7.78%) , N(11.19%) . Found C(76.74%) , H(7.75%) , N(11.20%).

SYNTHESIS OF *N*-(1-CYCLOHEXYL-1*H*-BENZIMIDAZOL-2-YL)-2,2-DIMETHYL PROPANAMIDE (5i)

A mixture of compounds 1-cyclohexyl-1*H*-benzimidazol-2-amine (4) (0.93 mMol), (1.32 mMol) of trimethyl acetyl chloride (Pivaloyl chloride) and (2.32 mMol) triethyl amine as base in 25 ml dichloromethane (12.5 vol.) as solvent was stir on magnetic stirrer at 0-20°C for 3-5 hr with constant stirring. Monitor progress of reaction on TLC, after completion of reaction, added 25 ml ice cooled water to reaction mixture and stirred reaction mixture at room temperature for 10 min. Stop stirring and allow reaction mixture to settle, separate product enriched lower dichloromethane layer. Dry the dichloromethane layer over 15 gm sodium sulphate and distilled out dichloromethane under vacuum below 40°C. Crude sticky solid obtained, which was purified by column chromatography by using silica gel as stationary phase and ethyl acetate and hexane as eluent to obtained pure product *N*-(1-cyclohexyl-1*H*-benzimidazol-2-yl)-2,2-dimethylpropanamide (5i).

White solid, yield 75%, MP 134 – 136°C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.35 – 1.55 (m , 3H) , 1.60 – 1.95 (m , 5H) , 2.30 – 2.40 (t , 2H) , 2.90 (s , 9H) , 4.95 – 5.00 (t , 1H) , 7.20 – 7.30 (m , 2H) , 7.50 – 7.55 (m , 2H), 12.85 (bs , 1H). LC-MS m/z $[M+H]^+$ 300. Elemental analysis: Calcd for $C_{18}H_{25}N_3O$: C(72.21%) , H(8.42%) , N(14.03%) . Found C(72.20%) , H(8.40%) , N(14.01%).

SYNTHESIS OF 4-CHLORO-*N*-(1-CYCLOHEXYL-1*H*-BENZIMIDAZOL-2-YL) BUTANAMIDE (5j)

A mixture of compounds 1-cyclohexyl-1*H*-benzimidazol-2-amine (4) (0.93 mMol), (1.32 mMol) of 4- chloro butyryl chloride and (2.32 mMol) triethyl amine as base in 30 ml dichloromethane (15 vol.) as solvent was stir on magnetic stirrer at 0-25°C for 3-4 hr with constant stirring. Monitor progress of reaction on TLC, after completion of reaction, added 30 ml ice cooled water to reaction mixture and stirred reaction mixture at room temperature for 10 min. Stop stirring and allow reaction mixture to settle, separate product enriched lower dichloromethane layer. Dry the dichloromethane layer over 15 gm sodium sulphate and distilled out dichloromethane under

vacuum below 40°C. Crude sticky solid obtained, which was purified by column chromatography by using silica gel as stationary phase and ethyl acetate and hexane as eluent to obtained pure product 4-chloro-*N*-(1-cyclohexyl-1*H*-benzimidazol-2-yl)butanamide (5j).
White solid, yield 60%, MP 131 - 133°C (dec), ^{1}H NMR (400 MHz, DMSO-d_6): 1.35 – 1.65 (m , 3H) , 1.70 – 1.95 (m , 5H) , 2.30 – 2.40 (t , 2H) , 3.90 – 4.00 (m , 2H) , 4.30 – 4.40 (t , 2H) , 4.50 – 4.60 (t , 2H) , 4.85 – 4.90 (t , 1H) , 7.20 – 7.30 (m , 2H) , 7.40 – 7.45 (d , 2H) , 12.90 (bs , 1H). LC-MS m/z $[M+H]^+$ 320. Elemental analysis: Calcd for $C_{17}H_{22}N_3OCl$: C(63.84%) , H(6.93%) , N(13.14%) . Found C(63.82%) , H(6.90%) , N(13.10%).

RESULTS AND DISCUSSION:

The synthetic strategies adopted for the synthesis of the target compounds are depicted in above Scheme. After investigating published methods [I-IV and XIII-XXI], we found that microwave assisted method of synthesis for N-cyclohexyl-2-nitro aniline **(2)**, compared to the conventional method, demonstrated several advantages, in terms of reaction time and overall yield. Intermediate *N*-cyclohexyl-1,2-diamines **(3)** is prepared in a straight-forward manner by the reduction of N-cyclohexyl-2-nitro aniline **(2)** with hydrogen gas in the presence of 5% palladium on carbon in ethyl acetate solvent. Intermediate *N*-cyclohexyl-1*h*benzimidazol-2-amine **(4)** is prepared by cyclization of intermediate **(3)** with cyanogen bromide in methanol solvent. The compound *N*-cyclohexyl-1h-benzimidazol-2-amine **(4)** on reaction with appropriate benzoyl chloride under basic conditions to give corresponding desired compounds **5(a-j)**. The structures of all the newly synthesized compounds were elucidated on the basis of their spectral (IR, NMR and mass) and elemental analyses data. The synthesized compounds **5(a-j)** were also assayed for their antimicrobial activity.

ANTIMICROBIAL ACTIVITY:

All petri dishes (diameter 86 mm) and graduated measuring pipettes were dry heat sterilized in a canister at 420°C for 4 hours. Media were steam sterilized at 121°C (15 psi) for twenty minutes in an autoclave. Bacterial and fungal cultures were grown at 37°C and 28°C, respectively on sterile nutrient agar (NA) and potato dextrose agar (PDA)[xxii-xxiii]. The cultures were preserved at 4°C, and maintained by repetitive sub-culturing after every 3 months. All the compounds were dissolved in DMSO of stock 20 mg ml-1 and tested against the microbial strains *Escherichia coli*, *Staphylococcus aureus, Aspergillus niger* . Standard solutions of antimicrobial agent (Ofloxacin, 20 mg ml^{-1}) and (fluconazole, 20 mg ml^{-1}) were taken as positive control and DMSO as negative control. 1 ml of each bacterial test culture in saline (107 CFU ml^{-1}) was inoculated in to a sterile Nutrient Agar plate. Similarly, 1 ml each of the fungal spore suspension in, Tween 80 solution (107 spores ml^{-1}) were inoculated into a sterile Potato Dextrose Agar plate and 3 wells were made on the surface of the agar plates using a sterile borer. 40 µl of compound solutions, 40 µl positive and negative control solutions were added in each well. The plates were incubated at 37°C and 28°C respectively for 24 hrs and zones of inhibition were measured [xxiv].

Table: Antimicrobial activity of compounds 5(a-j)

Compound	*Escherichia coli*	*Staphylococcus aureus*	*Aspergillus niger*
5.a	09	12	03
5.b	00	00	06
5.c	11	13	10
5.d	10	11	05
5.e	00	00	00
5.f	12	14	11
5.g	00	00	00
5.h	00	00	00
5.i	16	14	12
5.j	11	10	00
Ofloxacin	41	44	-
Fluconazole	-	-	22
DMSO	00	00	00

*Zone of inhibition in mm

The organism selection was from different classes of microbes, with diverse habitat. The strain utilized showed the susceptibility toward the antibiotics used, where *Escherichia coli*, *Staphylococcus aureus* and *Aspergillus niger* at 40 µg concentration of Ofloxacin and Fluconazole showed 41, 44 and 22 mm zone of inhibition. Out of all the compounds antimicrobial activity was represented by 5a, 5c, 5d, 5f, 5i and 5j at 40 µg in the range 3-16 mm. *E.coli* a representative of enteric Gram-Ve bacteria at 40 µg exhibited 12 and 16 mm zone of inhibition for compounds 5f and 5i respectively. 5i, 5f, 5c and 5a exhibited 14, 14, 13 and12 mm zone of inhibition against *Staphylococcus aureus*. Compound 5c, 5f and 5i exhibited 10, 11 and 12 mm zone of inhibition, for *Aspergillus niger* respectively at 40 µg concentration. The compounds have shown mild to moderate antimicrobial activity. Among the compounds tested, compound 5i i.e. *N*-(1-cyclohexyl-1*H*-benzimidazol-2-yl)-2,2-dimethylpropanamide showed highest activity.

CONCLUSIONS:

In conclusion we synthesized a new series of amide derivatives of benzimodazole from 1-fluoro-2-nitrobenzene by two methods viz. conventional and microwave assisted method. All the synthesized compounds have been characterized by elemental analysis, ^{1}H NMR spectroscopy and mass spectrometry and screened for antimicrobial activity against *Escherichia coli, Staphylococcus aureus* and *Aspergillus niger*. Some compounds showed good activity.

Structure Activity Relationship:

The results of present investigation reveal that benzimidazole amide derivative show remarkable

antimicrobial activity at 40 mg/ml concentrations. Based on the activity data values the following order of increasing activity could be established. Benzimidazole amide derivative 4-chloro benzamide (5c) > 2,6- difluorobenzamide (5f) > 2,2-dimethylpropanamide (5i) > 2-chloro benzamide (5d) > benzamide (5a).On the basis of the calculated activity data against control compound Ofloxacin and Fluconazole following structure relationship could be established.

1. Among the amide compounds, 4-chloro benzene substituents exhibited more activity than 2-chloro, 2-6 difluro substituents.
2. In amide derivatives, substitution at 2 and 4 position conferred better activity than 3-position.
3. Chloro derivatives showed the highest activity amongst respective series.
4. In Chloro derivatives substitution at 2-position conferred better activity than 4-position.

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