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SYNTHESIS OF BENZIMIDAZOLES AS ANTIMICROBIAL AGENTS

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Suitably substituted *o*-phenylenediamines on treatment with S-methyl isothiourea and methyl chloroformate gave different benzimidazole carbamates (**14-19**).

Benzimidazole derivatives possess antifungal[1], antitubercular[2], antihistaminic[3], antiviral[4], anticancer[5] and anti HIV[6], activities.

In the present study, a series of benzimidazole carbamates with different substituents at 5 and 6 positions were synthesized and investigated for antimicrobial activity.

Antimicrobial activity

The antimicrobial activity was tested by agar cup-plate method[7] (IP). The test organisms used were *B. subtilis* (MTCC 441), *S. aureus* (MTCC 1430), *P. aeruginosa* (MTCC 424), *E. coli* (MTCC 1573), *C. albicans* (MTCC 183) and *R. stolonifer* (MTCC 162) which were procured from IMTECH, Chandigarh. The conc used were 4 mg/ml, 2mg/ml, 1mg/ml and 0.5 mg/ml in 5% v/v dimethyl sulfoxide (DMSO). The standard used was 1% w/v Fluconazole for fungi and 1% w/v Doxycycline for bacteria. 5% v/v DMSO was used as control. Compounds **14,15** and **18** showed marked antifungal activity whereas compounds **16, 17** and **19** were only marginally active. Compounds **15** and **18** showed good activity against Gram positive bacteria. The activity of the compounds was conc dependent, wherein an increase in the conc resulted in increased activity.

Experimental

Melting points were determined in open capillary tubes and are uncorrected. Purity of the compounds was checked by TLC using Silica gel G (0.2 mm plates). The compounds were characterized by their IR (using Shimadzu FTIR spectrophotometer) and NMR spectral data. 3-Chloro-4-fluoro aniline (**1**) used in this study was procured from Hi-Media Chemicals, Bangalore.

Substituted orthophenylenediamines (**8-13**) were obtained as per literature procedures[8].

Synthesis of benzimidazole carbamates (14-19)

An aq solution of sodium hydroxide (25%) was added to a well stirred ice cold mixture of methyl chloroformate (0.02 mol) and S-methyl isothiourea (0.01 mol) in water (5 ml) until pH 8.0, keeping the temp below 12°. The pH of the reaction mixture was adjusted to 5.0 with gl acetic acid. To the suspension so obtained, various substituted 1,2-diaminobenzenes (0.01 mol) were added followed by addition of water (40 ml). The resulting mixture was stirred at 95° for 2 hr. The product so obtained was filtered at pump and air dried. The dried powder was resuspended in methanol (100 ml) and refluxed for 30 min to yield

Table-1
Characterization data of the synthesized compounds

Compd	M.P. (°C)	^{1}H NMR (δ ppm)
14	330-332	1.1 (3H, CCH_3), 1.3-3.2 (9H, piperidine CH_2), 3.7 (3H, OCH_3), 7.1-7.2 (2H), 11.7, 12.6 (2H,NH)
15	198-200	-
16	260-263	1.5-3.2 (10H piperidine CH_2), 3.7 (3H OCH_3), 7.1-7.2 (2H), 11.5, 12.1 (2H, NH)
17	350-352	-
18	275-277	-
19	347-350	0.9 (6H, CH_3), 1.9-3.1 (4H, CH_2) 3.7 (3H, OCH_3), 7.1-7.2 (2H), 1.6-12.6 (2H, NH)