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Synthesis, Spectral Studies and Biological Evaluation of Some Benzimidazole Derivatives containing Sulfonamide

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ABSTRACT

In the present study, we have reported the synthesis, spectral studies and biological evaluation of some benzimidazole derivatives containing sulfonamide. Benzimidazoles and sulfonamides play an important role in medical field with so many pharmacological activities such as antimicrobial, antiviral, antidiabetic and anticancer activity. The potency of these clinically useful drugs in treatment of microbial infections and other activities encouraged the development of some more potent and significant compounds. The structures of the compounds (C1-C6 & D) were elucidated by spectral studies and screened for antibacterial activity against various strains of Escherichia coli and Staphylococcus aureus and antifungal activity against Candida albicans. The derivatives have shown moderate to good activity when compared with standard antibiotic Ampicillin and Amphotericin B. And the compound D was screened for anti-cancer activity to National Cancer Institute, USA.

Key words: Substituted Sulfonamides, Benzimidazoles, Anti-microbial activities and anticancer activity.

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INTRODUCTION

Antimicrobial agents are the drugs, chemicals, or other substances that kill or slow the growth of microbes. They include antibacterial drugs, antiviral agents, antifungal agents, antiparasitic drug [1]. For the past 60 years, antimicrobial chemotherapy has been the mainstay of medical intervention against infectious diseases caused by various pathogens. Since then, numerous classes of antimicrobial agents have been discovered, and literally hundreds of drugs are available for use today. Antimicrobials are among the most commonly used of all drugs [2]. Since the introduction of penicillin in the 1940s, antimicrobials have a history of success in controlling morbidity due to infectious diseases [3]. The regular use of antimicrobial agents causes various problems such as toxicity, hypersensitivity reactions, drug resistance, super infection (suprainfection), nutritional deficiencies and masking of an infection [4]. The incidence of invasive microbial infections caused by opportunistic pathogens, often characterized by high mortality rates, has been increasing past two decades. Patients who become severely immunocompromised because of underlying diseases such as leukemia or recently acquired immunodeficiency syndrome or patients who undergo cancer chemotherapy or organ transplantation are particularly susceptible to opportunistic microbial infection. Almost all major classes of antibiotics have encountered resistance in clinical applications. The emergence of bacterial resistance to β-lactam antibiotics, macrolides, quinolones and vancomycin is becoming a major world-wide health problem. Despite of the availability of a number of antimicrobial agents the main matter of concern in the treatment of microbial infections is the limited number of efficacious antimicrobial drugs [5].

Infectious microbial diseases remain pressing problems world-wide, because resistance to a number of antimicrobial agents among variety of clinically significant species of microorganisms has become an important global health problem. One way to battle with this challenge is the conscious usage of the currently marketed antibiotics; the other is the development of novel antimicrobial agents. Hence, there will always be a vital need to discover new chemotherapeutic agents to avert the emergence of resistance and ideally shorten the duration of therapy [6]. The outcome of numerous attempts to new structural prototype in the search for effective antimicrobials indicates that the benimidazoles still remain as one of the most versatile class of compounds against microbes [7].

Anticancer drugs either kill cancer cells or modify their growth. Cancer or neoplastic disease, may be regarded as a family of related disorders. A common feature in different forms of cancer is an abnormal and uncontrolled cell division, frequently at a rate greater than that of most normal body cells. The neoplasm may be benign or malignant. Bening tumours do not metastasise, malignant tumours do. Metastasis is due to ability of neoplastic diseases to invade other tissues if a malignant cell floats away in the body fluids and locates in a distant place of the organism. So there occurs a secondary growth originating from the primary tumour[8]. The benzimidazole ring system is an important pharmacophore in medicinal chemistry and modern drug discovery. 2-Substituted benzimidazoles have been known to act as potential anticancer [9-12]. Due to great potential of the moiety, synthesis of sulfonamide bearing benzimidazole

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derivatives was carried out to evaluate their antimicrobial & anticancer potential. The synthesized compound D was submitted to National Cancer Institute (NCI) for anticancer activity.

We reported here a study on synthesis of some novel benzimidazole derivatives containing sulfonamide. These derivatives were screened for antibacterial activity against various strains of Staphylococcus aureus, and Escherichia coli antifungal activity against Candida albicans and were screened for anticancer activity.

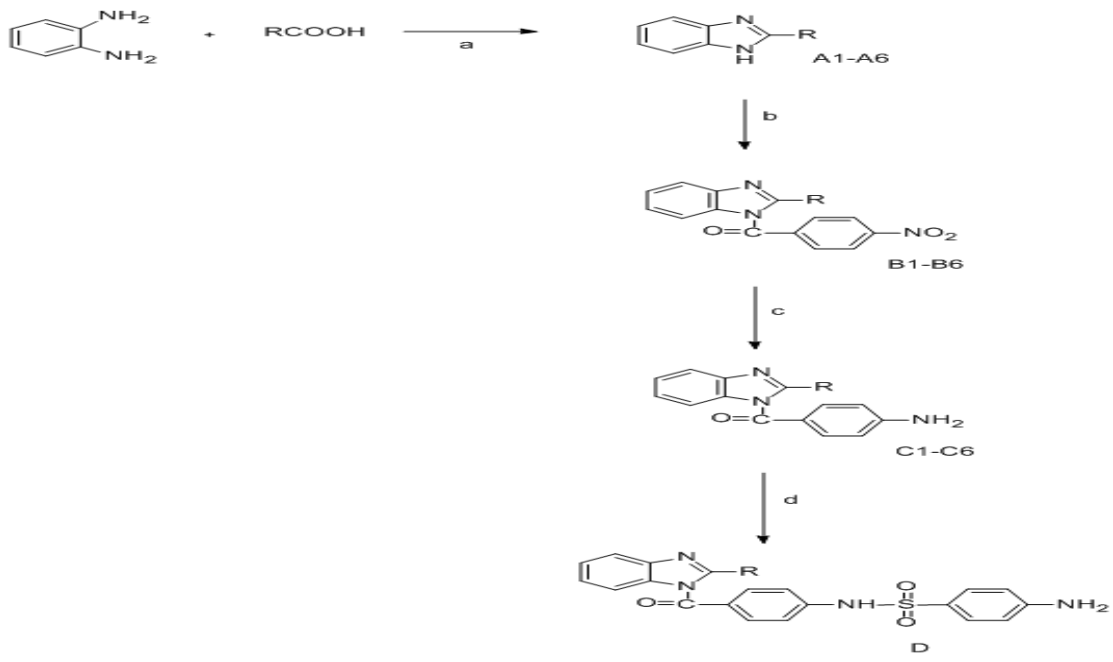
MATERIALS AND METHODS

Chemistry

All solvents were distilled and dried where necessary before use. All the reactions were monitored with the help of thin-layer chromatography using pre-coated aluminium sheets with 60F254 silica gel, 0.2 mm layer thickness (E. Merck). Various solvent systems used for developing the chromatograms were (a) chloroform: methanol (9:1), (b) ethyl acetate: hexane (7:3). Melting points of the synthesized compounds were recorded on the Perfitt melting point apparatus. IR was acquired on a shimadzuinfra red spectrometer. ^{1}H NMR and ^{13}C-NMR spectra of the synthesized compounds were scanned in DMSO with a Bruker Advance II 400 NMR Spectrometer operating at 400 MHz in SAIF, Panjab University (Chandigarh). Mass spectra (low resolution) of the synthesized compounds were recorded at MAT 120 in SAIF, Panjab University, Chandigarh.

Synthesis of the compounds: Various **benzimidazole** derivatives were synthesized using reaction **scheme**

Reaction scheme



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Reaction for synthesis of benzimidazoles derivatives

Reactant (a)NH_4OH, H_2O, C_2H_5OH **(b)** 4-nitrobenzoyl chloride, NaOH, Acetone, THF **(c)-** $SnCl_2$,NH_4OH CH_3COOH **(d)** $ClSO_3H$, CH_2Cl_2, NaOH

Synthesis of 1H-benzo[d]imidazole (A1): o-phenylenediamine (5.4 g, 0.25 mole) and Formic acid 90% (3.2 g, 0.34 mole) was heated on water bath for 2 hrs at 100°C. Then slowly cooled and resultant mixture was basified with aqueous sodium hydroxide solution. The solid obtained was filtered and recrystallized with boiling water[13].

Synthesis of 2-methylbenzimidazole (A2): Mixture of (5.43g, 0.03 mole) o-phenylenediaminedihydrochloride, 20ml of water and (5.4g, 0.09) of acetic acid was heated under reflux for 45 min. Reaction was cooled and basified with conc. Ammonia solution, the precipitated product was filtered and recrystallized in 10% aqueous ethanol[13].

Synthesis of 2-benzylbenzimidazole (A3): Used (5.43g, 0.03 mole) of o-phenylenediaminedihydrochloride, 20ml of H_2O, Phenylacetic acid (12.3g, 0.09mole) and refluxed for 45 min. The reaction mixture was cooled and basified with conc. ammonia solution. Precipitated solid was filtered and recrystallized from 40% aqueous ethanol solution[13].

Synthesis of 2-phenyl-1H-benzo[d]imidazole (A4): A mixture of 6g o-phenylenediamine, 6g of benzoic acid and 25ml of 4N dilute HCl was refluxed for 2 hrs at 180-185 °C. The reaction mixture was cooled and poured on to the crushed ice. Then the product was recrystallised in boiled water using charcoal [14].

Synthesis of 4-(1H-benzo[d]imidazol-2-yl)phenol (A5): A mixture of salicylic acid (5g) and o-phenylenediamine 3.9g was stirred in conc. Polyphosphoric acid (29.3 ml) at 220°C for 6 hrs. The hot mixture was poured into vigoursly cold water (300 ml). A greenish precipitate was obtained after neutralization with aqueous ammonia. Then filtered and dissolved in ethanol[15].

Synthesis of 2-(2,3-dinitrophenyl)benzimidazoles (A6): A mixture of dinitrobenzoic acid (5g) and o-phenylenediamine 3.9g was stirred in conc . Polyphosphoric acid (29.3 ml) at 220°C for 6 hrs. The hot mixture was poured into vigoursly cold water (300 ml). Precipitate was obtained after neutralization with aqueous ammonia. Then filtered and dissolved in ethanol[15].

Synthesis of Benzoylation of 2-substituted benzimidazole (B1-B6) General procedure: 4-nitrobenzoyl chloride (2g) was dissolved in acetone (2.5 ml). This mixture was then added drop wise to the solution containing benzimidazoles (0.54 g) and NaOH 1g in (22.73 ml) of H_2O for 30-60 min at 40 °C. It was allowed to stir for 10-12 hrs and after completion was diluted with H_2O. Filtered, dried and recrystallized in THF[16].

Synthesis of Reduction of 2-substituted-1H-benzoyl[d]imidazol-1-yl)(4-nitrophenyl) methanone (C1-C6) General procedure: The above mentioned products B1-B6 (2g, 0.09 moles)

and Tin (5 g, 0.295 moles) with conc. HCl (11ml) was refluxed on flame for 30-45 min. The reaction mixture was then cooled and decanted with water. Conc. Ammonia solution (d 0.88) was added to basify the mixture. Heated on water bath for 20 min the filtered and wash with hot water. The washings were combined and solid was removed. The liquid was acidified with glacial acetic acid and evaporated on water bath till crystals were formed. Then filtered and dried[17].

Synthesis of 2-substituted-1H-benzo[d]imidazole-1-carbonyl)phenyl) sulfamoyl)phenyl) acetamide(D) General procedure: 20 g (0.148 mol) of dry acetanilide and 50 ml (0.77 mol) of chlorosulfonic acid was drop wise added with continuous shaking. The reaction mixture was then heated on a water bath for an hour. The reaction mixture formed was poured on 500 g of ice carefully. Filtered with washing with cold water and the sulfonyl chloride formed was dried. (NaOH, water, CH_2Cl_2, 25˚C) A mixture of 20 ml of 1M aqueous NaOH, 5 ml of methylene chloride, 0.5 g of the (4-aminophenyl)(2-substituted-1H-inden-3-yl)methanone and 0.5 g of sulfonyl chloride was shaken or stirred for 20 min vigorously and was allowed to stand. The organic and aqueous layer were separated and aqueous layer was carefully acidified with 6M HCl. Precipitates formed were separated[18].

(4-aminophenyl)(1H-benzo[d]imidazol-1-yl)methanone (C1): Yield 71%, M.P. (280-282)˚ C. ^{1}H NMR (DMSO): 6.79-7.98 (m, 9H, Ar-H), 4.36 (br S, 2H, NH_2). ^{13}C NMR (ppm): 166.68, 154.65, 140.99, 137.52, 131.98, 123.52, 122.28, 115.20. IR (υ cm^{-1}): CH- 2946.05, NH_2- 3299.01, 3202.97, C=O- 1629.64, NH bend- 1603.46.

(4-aminophenyl)(2-methyl-1H-benzo[d]imidazol-1-yl)methanone (C2): Yield 68%, M.P. (285-286)˚ C. ^{1}H NMR (DMSO): 6.60-8.10 (m, 8H, Ar-H), 5.33 (br S, 2H, NH_2), 2.11 (S, 3H, CH_3). ^{13}C NMR (ppm): 166.30, 155.65, 140.22, 134.61, 132.28, 126.89, 118.93, 114.61, 16.89. IR (υ cm^{-1}): CH- 2935.57, NH_2- 3059.74, 3124.59, C=O- 1678.08, NH bend- 11557.86, CH- 3338.01.

(4-aminophenyl)(2-benzyl-1H-benzo[d]imidazol-1-yl)methanone (C3): Yield 72%, M.P. (299-302) ˚ C. ^{1}H NMR (DMSO): 7.11-8.12 (m, 14H, Ar-H), 5.10 (br S, 2H, NH_2), 3.41 (S, 2H, CH_2). ^{13}C NMR (ppm): 167.60, 155.81, 140.45, 138.52, 137.65, 129.44, 128.11, 126.74, 122.16, 115.13, 112.18. IR (υ cm^{-1}): CH-2958.41, NH_2- 3065.33, 3131.98,C=O- 1671, NH bend- 1602.79, CH_2 (aliphatic)- 3171.26.Mass : 251.11 [m+], 252.14 [m+1].

(4-aminophenyl)(2-phenyl-1H-benzo[d]imidazol-1-yl)methanone (C4): Yield 60%, M.P. (286-288)˚ C. ^{1}H NMR (DMSO): 7.23-8.24 (m, 11H, Ar-H), 4.89 (br S, 2H, NH_2). ^{13}C NMR (ppm): 166.78, 158.89, 140.93, 138.81, 132.19, 128.89, 127.42, 122.86, 122.86, 118.37, 112.37. IR (υ cm^{-1}): CH-3062.81, NH_2- 3267.37, 3346.05, C=O- 1672.95, NH bend- 1595.74.

(4-aminophenyl)(2-2-hydroxyphenyl)-1H-benzo[d]imidazol-1-yl)methanone (C5): Yield 72%, M.P. (304-308)˚ C. ^{1}H NMR (DMSO): 6.87-8.01 (m, 12H, Ar-H), 4.93 (br S, 2H, NH_2), 12.15 (br S, 1H, OH). ^{13}C NMR (ppm): 166.93, 158.19, 140.78, 138.89, 132.81, 130.06, 122.64, 120.38,

118.37, 115.75, 112.37. IR (υ cm^{-1}): CH- 2946.05, NH_2- 3202.97, 3309.69, C=O- 1661.96, NH bend- 1612.96, OH- 3415.38.

(4-aminophenyl)(2-2,3-dinitrophenyl)-1H-benzo[d]imidazol-1-yl)methanone (C6): Yield 75%, M.P. (300-303°) C. ^{1}H NMR (DMSO): 7.02-8.09 (m, 11H, Ar-H), 4.59 (br S, 2H, NH_2). ^{13}C NMR (ppm): 164.46, 159.20, 153.97, 146.52, 138.42, 134.85, 134.58, 131.34, 129.23, 123.93, 121.46, 118.43, 112.42. IR (υ cm^{-1}): CH- 2958.13, NH_2- 3172.41, 3132.33, C=O- 1673.01, NH bend- 1602.76.

N-(4-(N-(4-2-methyl-1H-benzo[d]imidazol-1-carbonyl)phenyl)sulfomyl) phenyl)acetamide(D): Yield 31%, M.P. (318-320°) C. ^{1}H NMR (DMSO): 7.39-8.23 (m, 12H, complex of Ar-H & NH), 4.37 (br S, 2H, NH_2), 2.59 (S, 3H, CH_3), 2.13 (S, 3H, CH_3). ^{13}C NMR (ppm): 168.75, 161.48, 157.24, 154.87, 148.19, 141.05, 133.74, 133.70, 130.59, 128.08, 122.84, 122.64, 118.89, 117.83, 114.64, 24.75. IR (υ cm^{-1}): CH-2925.30, NH_2-3349.97, 3415.36, C=O- 1681.80, 1609.14, NH bend- 1570.86, CH_3- 3061.96, 3338.01.

Antimicrobial susceptibility test

The newly synthesized compounds were screened for their antibacterial and antifungal screening using filter paper disc method.

The antibacterial activity of test compounds were evaluated against Gram-positive bacteria, Staphylococcus aureus and Gram-negative bacteria, Escherichia coli.

Antifungal activity was screened against fungal strain, Candida albicans.

The antimicrobial activity was performed by filter paper disc method at concentration 100 µg/ml. Mueller hinton agar (MHA) & Potato dextrose agar (PDA) were employed as culture medium and DMSO was used as solvent control for antimicrobial activity. Ampicillin and Amphotericin B were used as standard for antibacterial and antifungal activities respectively.

The potato dextrose agar (PDA) media was taken in a 1000 ml beaker and made up the volume to 1000 ml with water then the media was sterilized by autoclaving at 121°C for 15 min at 15-16 psi pressure. The media removed and cooled at 40-45°C. Whatmann filter paper-1 discs (6mm) was sterilized by dry heat were saturated with test solution and placed on (PDA) media in petridishes in triplicate. The petridishes were covered and set aside for an hour , and then incubated at 37°C for 48 hrs. The zones of inhibition were measured and the average of three readings was calculated[19].

In vitro cancer screen at NCI-USA

The screening is a two-stage process, beginning with the evaluation of all compounds against the 60 cell lines at a single dose of 10 µM. The output from the single dose screen is

reported as a mean graph and is available for analysis by the COMPARE program. Compounds which exhibit significant growth inhibition are evaluated against the 60 cell panel at five concentration levels. The human tumor cell lines of the cancer screening panel are grown in RPMI 1640 medium containing 5% fetal bovine serum and 2 mM L-1 glutamine. For a typical screening experiment, cells are inoculated into 96 well microtiter plates in 100 µL at plating densities ranging from 5,000 to 40,000 cells/well depending on the doubling time of individual cell lines. After cell inoculation, the microtiter plates are incubated at 37 °C, 5 % CO2, 95 % air and 100 % relative humidity for 24 h prior to addition of experimental drugs.

After 24 h, two plates of each cell line are fixed in situ with TCA, to represent a measurement of the cell population for each cell line at the time of drug addition (Tz). Experimental drugs are solubilized in dimethyl sulfoxide at 400-fold the desired final maximum test concentration and stored frozen prior to use. At the time of drug addition, an aliquot of frozen concentrate is thawed and diluted to twice the desired final maximum test concentration with complete medium containing 50 µg/ml gentamicin. Additional four, 10-fold or ½ log serial dilutions are made to provide a total of five drug concentrations plus control. Aliquots of 100 µl of these different drug dilutions are added to the appropriate microtiter wells already containing 100 µl of medium, resulting in the required final drug concentrations.

Following drug addition, the plates are incubated for an additional 48 h at 37 °C, 5 % CO2, 95 % air, and 100 % relative humidity. For adherent cells, the assay is terminated by the addition of cold TCA. Cells are fixed in situ by the gentle addition of 50 µl of cold 50 % (w/v) TCA (final concentration, 10 % TCA) and incubated for 60 minutes at 4°C. The supernatant is discarded, and the plates are washed five times with tap water and air dried. Sulforhodamine B (SRB) solution (100 µl) at 0.4 % (w/v) in 1 % acetic acid is added to each well, and plates are incubated for 10 minutes at room temperature. After staining, unbound dye is removed by washing five times with 1 % acetic acid and the plates are air dried. Bound stain is subsequently solubilized with 10 µM trizma base, and the absorbance is read on an automated plate reader at a wavelength of 515 nm. For suspension cells, the methodology is the same except that the assay is terminated by fixing settled cells at the bottom of the wells by gently adding 50 µl of 80 % TCA (final concentration, 16 % TCA). Using the seven absorbance measurements [time zero, (Tz), control growth, (C), and test growth in the presence of drug at the five concentration levels (Ti)], the percentage growth is calculated at each of the drug concentrations levels. Percentage growth inhibition is calculated as:

$$[(Ti-Tz)/(C-Tz)] \times 100 \text{ for concentrations for which } Ti \geq Tz$$
$$[(Ti-Tz)/Tz] \times 100 \text{ for concentrations for which } Ti < Tz.$$

Three dose response parameters are calculated for each experimental agent. Growth inhibition of 50% (GI_{50}) concentration from $[(Ti-Tz)/(C-Tz)] \times 100 = 50$, which is the drug concentration resulting in a 50% reduction in the net protein increase (as measured by SRB staining) in control cells during the drug incubation. The drug concentration resulting in total growth inhibition (TGI) is calculated from Ti = Tz. The LC_{50} (concentration of drug resulting in a

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50% reduction in the measured protein at the end of the drug treatment as compared to that at the beginning) indicating a net loss of cells following treatment is calculated from [(Ti-Tz)/Tz] x 100 = -50. Values are calculated for each of these three parameters if the level of activity is reached; however, if the effect is not reached or is exceeded, the value for that parameter is expressed as greater or less than the maximum or minimum concentration tested[20-22].

RESULTS AND DISCUSSION

To materialize the proposed scheme we synthesized2-substituted 1-[H]-benzimidazole and derivatives (A1-A6) by using o-phenylenediaminedihydrochloride with different acids such as formic acid, acetic acid , phenylacetic acid, benzoic acid, salicylic acid and dinitrophenyl acid. THF were suitable solvents used for recrystallizing to yield pure product. Benzoylation of the 2-substituted benzimidazoles were carried out in presence of p-nitrobenzoyl chloride dissolved in acetone and benzimidazoles in sodium hydroxide solution. The product formed is coded as B1-B6. Reduction of the 2-substituted-1H-benzomidazol-1-yl(4-nitrophenyl)methanones(B1-B6) was done with tin and HCl reflux. Basification of the reaction further gave the reduced product (C1-C6). The physical data and the yield of the synthesized compounds are given in Table-1.

Table 1: Physical data of compounds (A-D)

Compounds	Yield (%)	m.p. (ºC)	Molecular Formula
A1	60	171-173	$C_7H_6N_2$
A2	50	177-180	$C_8H_8N_2$
A3	48	235-236	$C_{14}H_{12}N_2$
A4	33	238-239	$C_{13}H_{10}N_2$
A5	76	237-239	$C_{13}H_{10}N_2O$
A6	55	293-295	$C_{13}H_8N_4O_4$
B1	61	278-279	$C_{14}H_9N_3O_3$
B2	58	281-282	$C_{15}H_{11}N_3O_3$
B3	47	298-299	$C_{21}H_{15}N_3O_3$
B4	55	285-287	$C_{20}H_{13}N_3O_3$
B5	50	300-301	$C_{20}H_{13}N_3O_4$
B6	65	293-295	$C_{20}H_{11}N_5O_7$
C1	71	280-282	$C_{16}H_{13}NO$
C2	68	285-286	$C_{17}H_{15}NO$
C3	72	299-302	$C_{23}H_{19}NO$
C4	60	286-288	$C_{22}H_{17}NO$
C5	72	304-308	$C_{22}H_{17}NO_2$
C6	75	300-303	$C_{22}H_{15}N_3O_5$
D	31	318-320	$C_{23}H_{20}N_4O_4S$

All the compounds were confirmed by its IR spectrum, which showed the presence of particular functional groups. The absorption at 3128-3029 are characteristic of v(C-H) and v(C=C) respectively. The appearance of imidazole proton (C_5-H) around δ 8 and the aromatic proton signals showed δ (7.1-8.2) in the ^{1}H NMR spectra. The ^{13}C-NMR and Mass spectral data on synthesized compounds are also in accordance with the proposed structures.

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The synthesized compounds C1-C6 and D were screened for their in vitro antibacterial activity against Staphylococcus aureus and Escherichia coli and antifungal activity against Candida albicans by measuring the zone of inhibition in mm (Table-2) in comparison with those of the standard drugs ampicillin and amphotericin B. The antibacterial activity data reveals that the compounds (C1-C6) and D exhibited good antibacterial activity against various strains of bacteria as compared to standard Ampicillin.

Table 2: Antibacterial and antifungal activities of compounds (C1-C6 & D)

Cpd. no.*	Diameter of zone of inhibition (mm)		
	Gram-positive bacteria	Gram negative bacteria	Fungi tested
	S.aureus	E.coli	C.albicans
C1	12.4 ± 0.4	11.9 ± 0.4	NA
C2	12.9 ± 0.5	11.8 ± 0.3	NA
C3	13.8 ± 0.3	12.4 ± 0.6	NA
C4	13.2 ± 0.2	12.8 ± 0.3	NA
C5	13.3 ± 0.6	12.9 ± 0.1	NA
C6	11.3 ± 0.5	10.9 ± 0.4	NA
D	13.6 ± 0.2	13.3 ± 0.2	NA
Ampicillin	16.0 ± 0.2	15.9 ± 0.3	_
Amphotericin B	_	_	14.0 ± 0.1

(-) activity not evaluated, (NA) no activity observed * compound number, Control: DMSO
± SD (n=3) of inhibition zone was taken as mean.

The antifungal screening results showed no activity against Candida albicans strain as compared to standard Amphotericin B.

The tumor growth inhibition properties of the compound **D** with the **NCI code ID-105360** selected by the National Cancer Institute (NCI), USA, were screened on 56 and 57 human tumor cell lines at the NIH, Bethesda, Maryland, USA, under the drug discovery program of the NCI in a primary one dose anti cancer assay.

Primary in vitro one dose anticancer assay was performed in full NCI 60 cell panel representing leukemia, melanoma and cancers of lung, colon, brain, breast, ovary, kidney and prostrate in accordance with the protocol of the NCI, USA. The compounds were added at a single concentration (10^5 M) and the culture was incubated for 48 h. End point determinations were made with a protein binding dye, Sulforhodamine B. The compound D showed moderate anticancer activity in table-3.

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Table 3: NCI in vitro testing result of compound D at single dose level in µM

Panel	Cell Line	GI_{50}(Concentration per cell line)
Non-Small Cell Lung Cancer	A549/ATCC	70.77
	EKVX HOP-62	42.59
	NCI-H226	95.37
	NCI-H23	72.86
	NCI-H322M	88.80
	NCI-H460	64.95
	NCI-H522	86.10
		31.86
Colon Cancer	COLO 205	99.07
	HCC-2998	92.21
	HCT-116	70.32
	HCT-15	73.45
	HT29	73.65
	KM12	84.83
	SW-620	91.10
CNS Cancer	SF-268	89.76
	SF-295	71.40
	SF-539	96.24
	SNB-19	87.66
	SNB-75	90.45
	U251	75.18
Melanoma	LOX IMVI	88.64
	M14	91.65
	MDA-MB-435	71.82
	SK-MEL-2	71.17
	SK-MEL-28	99.19
	SK-MEL-5	90.22
	UACC-257	94.20
	UACC-62	52.73
Ovarian Cancer	IGROV1	82.56
	OVCAR-3	91.95
	OVCAR-4	74.24
	OVCAR-5	92.39
	OVCAR-8	76.30
	NCI/ADR-RES	78.51
	SK-OV-3	104.90
Renal Cancer	786-0	66.97
	A498	81.01
	ACHN	86.09
	CAKI-1	61.83
	SN12C	70.21
	TK-10	73.71
	UO-31	61.14
Prostate Cancer	PC-3	60.39
	DU-145	75.70
Breast Cancer	MCF7	81.55
	MDA-MB-231/ATCC	73.37
	HS 578T	90.97
	BT-549	65.28
	T-47D	67.95
	MDA-MB-468	66.99

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CONCLUSION

All the newly synthesized benzimidazole derivatives containing sulfonamide were analysed with different spectral techniques and screened in vitro for their antibacterial activity against both Gram-positive and Gram-negative strains of bacteria and also subjected for the antifungal activity. The results of antimicrobial screening reveals all compounds exhibited good activity against all strains and no activity against Candida albicans. The newly synthesized compounds of series were also screened for anticancer activity to National Cancer Institute, USA.

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REFERENCES

[1] Black JG. Microbiology, Principles and applications. 3rded, Prentice Hall Publishers. 1996; 356-387.
[2] Bruinsma NS, Verloo D, Tiemersma E, Monen J, Goossens H, Ferech M. Emerg Infect Dis 2008; 14: 1722-1730.
[3] Verma AK, Chandra R, Tiwari RK, Singh D, Singh J. Bioorg Med Chem Lett 2006; 16:413-416.
[4] Tripathi KD. Esssentials of Medical Pharmacology, Jaypee Brothers Medical Publishers (P) Ltd. 2008; 668-673.
[5] Ansari KF, Lal C. Eur J Med Chem 2009; 44: 2294-2298.
[6] Ozkay Y, Tunali Y, Karaca H, Srikdag I. Eur J Med Chem 2010; 45: 3293-3298.
[7] Narasimhan B, Sharma D, Kumar P, Judge V, Narang R. Eur J Med Chem 2008; doi:10.1016/j.ejmech.2008.08.010.
[8] Kapoor VK. Medicinal and Pharmaceutical Chemistry. Vallabh Prakashan Delh. 2005; 2nd: 591.
[9] Prudhomme M. Recent Pat Anti-Canc Drug Discovery 2006; 1: 55-68.
[10] Kumar D, Jacob MR, Reynolds MB, Kerwin SM. Bioorg Med Chem 2002; 10: 3997-4004.
[11] Hranjec M, Kralj M, Piantanida I, Sedic M, Suman L, Pavelic K, Karminski Zamola G. J Med Chem 2007; 50: 5696-5711.
[12] Piskin AK, Ates-Alagoz Z, Atac FB, Musdal, E Buyukbingol. Turk J Biochem 2009; 34:39-43.
[13] Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR. Vogel textbook of practical organic chemistry, Longman-ELBS. 2007; 5: 1162-1163.
[14] Sreena K, Ratheesh R, Rachana M, Poornima M. HYGEIA 2009; 1: 21-22.
[15] Buendia XQ, Ruiz AE, Huero AP. Inorg Chimica Acta 2008; 361: 2759-2767.
[16] Gupta SK, Pancholi SS, Agarwal D, Khinchi MP. J Pharm Sci res 2010; 4: 228-231.
[17] Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR. Vogel textbook of practical organic chemistry,Longman-ELBS. 2007; 5: 896.
[18] Goker H, Ozden S, Yildiz S, Boykin DW. Eur J Med Chem 2005; 40:1062-1069.

[19] Alcamo EI. Fundamentals of microbiology, Jones and Bartlett Publishers 1994; 11-115.
[20] Alley MC, Scudiero DA, Monks PA, Hursey ML, Czerwinski MJ, Fine DL, Abbott BJ, Mayo JG, Shoemaker RH, Boyd MR. Cancer Res 1988; 48: 589-601.
[21] Grever MR, Schepartz SA, Chabner BA. Semin Oncol 1992; 19: 622-638.
[22] Boyd MR, Paull KD. Drug Dev Res 1995; 19: 91-109.