RESEARCH ARTICLE

Synthesis, Characterization, and Evaluation of Cancer Prevention Activity of Novel Modified Heterocyclic Compounds

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Abstract

Anticancer approaches may employ change of molecular structure to enhance preventive influence of chemical agents. The present examination concerned the potential anticancer impact of modified heterocyclic compounds. A strategy was developed to combine tetrazole moieties from different diamines with 2-aminobenzoic and substituted benzoyl chloride compounds with attention to synthesis, characterization and assessment of cancer preventive activity, applying IR, 1HNMR, 13CNMR and Mass spectra.

Keywords: Cytotoxicity- heterocycles- multicomponent reactions and sodium azide

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Introduction

A significant number of heterocyclic compounds demonstrate the organic or pharmacological activities. Henceforth every one of the subordinates of heterocyclic compounds is utilized for the pharmaceutical applications. From these compounds, benzimidazole subsidiaries are generally utilized as a part of the pharmaceutical territories. The heterocyclic compounds have been entrancing in the gathering of concentrates expanded (Barker et al., 1995; Sushil et al., 2008; Gravatt et al., 1994). The union of a couple of new benzimidazole subsidiaries and examine for their substance and antimicrobial deeds have picked up and given more significance to present day traverse for natural and therapeutic reasons. Benzimidazole focus has been ahead of time of prestigious because of the way that its subordinates have been started to get a wide scope of pharmacological properties. Benzimidazole derivatives are useful heterocycles, having convincing pharmacological exercises, for example, anthelminthic (Karen et al., 2006), anti-inflammatory (Vinodkumar et al., 2008), anticancer (Popp et al., 1911; Kruse et al., 1989; Islam et al., 1991; Ramla et al., 2007; Denny et al., 1990), antimicrobial (Divaeva et al., 2006; Davoodnia et al., 2007; Kus et al., 2004; Abdel-Rahman et al., 1983; Soliman et al., 1984), cell reinforcement (Fukuda et al., 1984; Nakano et al., 1999; Can-Eke et al., 1998), anticoagulant (Mertens et al., 1987). Benzimidazole is having different heterocycles which have a wide scope of pharmacological properties. Benzimidazole derivatives are basic classes of heterocyclic mixes and are presented to have central nerves systems (CNS) exercises, for example, anticonvulsant and CNS depressant, antihistaminic action (Khairnar et al., 1981), and other biological significance, so it is mysterious to generation various benzimidazole subsidiaries and tried their successful anticancer activities.

Materials and Methods

Chemistry

This present work has been done to prepare benzimidazole subsidiaries all through a many advance process. For this reason, the required 4-(1-Methyl-1H-benzo[d]imidazol-2-yl) aniline (1) was prepared according to the literature procedure (Bhushan et al., 2009; Rahul et al., 2006; Ramanatham et al., 2008; Zhan-Hui et al., 2007; Jadhav et al., 2009; CananKus et al., 2003; Mahajan et al., 2006;), the buildup response between the compound (1) and p-phenylenediamine with acidic acid. Gotten the yield was affirmed by a stretching frequency band at 1,605 cm^{-1} with a top at carbonyl 1,687 cm^{-1} in the Infrared range. Compound (1) was changed over to 4-(1-Methyl-1H-benzo[d]imidazol-2-yl)aniline (1) was treated with p-phenylenediamine, Formation of close stretching frequency peak of 3,432.37 cm^{-1} (NH_2) and another stretching frequency of 3345.20 cm^{-1} (N-H) likewise utilized for anticipating the structure of (1). It took after nucleophilic response when (1) has been responded with benzoyl chloride (Varma et al., 2010) within the sight of pyridine as a base. The p-phenylenediamine and benzimidazole compound were responded to create another compound (2). The new IR recurrence district at 3074.93 cm-1. 1HNMR singlet at δ 4.0 (CH_3) for methylene protons and a singlet at 10.2 (s, 1H, NH), 8.0-8.1 (1H, Ar-He/Hc) proton was in the presence of the benzimidazole ring structure. It's stretched

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out to consolidate with substituted aromatic acidchloride derivatives (3-6). An intermediate product has formed when the compound (2) responded with phosphorous pentachloride and took after treated with sodium azide, a last compound tetrazole moiety (Rastgar Mirzaei et al., 2008; Bhaskar et al., 2010; Todd Eary et al., 2007) was framed (7-11). The tetrazole development of IR recurrence is 1602cm-1 and 1244 cm-1. 1HNMR at δ protons, 4.0 (CH3) for methylene, 7.2 – 7.8 (m, 2H, Ar-Hb/Ha/Hc/Hd/Hg/Ho) and 8.2 (d, 1H, Ar-Hm) separately guaranteed the yield of conclusive mixes (7-11).

Results

Experimental

Reagents and Solutions

Melting points focuses were recorded on a REMI Series Instrument. Thin Layer Chromatography was identified on silica gel covered plates and plates were examined under iodine jostle. Infra-Red spectra were recorded in KBr pellets on Schimadzu FT-IR Spectrophotometer. 1H and 13C-NMR spectra were measured on Bruker (AC 400MHz). Elements investigation information was finished by Perkin-Elmer arrangement – II Analyzer 2400. All the compound reagents and solvents were utilized as a part of systematic review.

4-(1-Methyl-1H-benzo[d]imidazol-2-yl)aniline (PB1)

p-Phenylenediamine (0.1 moles) and anthranilic acid (0.1 moles) were warmed in a water bath for 1hr 20 min, It's taken after to cool and included 10% NaOH blending until base nature. The yield was separated, cleaned with super cold water, decolorize and wiped proceed and dried out. The yield was recrystallized from ethanol. To a blend of compound (1) (2 m moles) in dimethylformamide (10 mL) was sodium hydride (55%, 2 mmol) was included at 0°C. After the culmination of this procedure warm for 2hrs 45min, the response stay cooled to 0°C and the alkyl halide (2.4 mmol) was included at 0°C. The response blend was then permitted to warm to room temperature and mixed for 3hrs. After the culmination of the response, water (50 mL) was gradually added to response blend and extricated with ethyl acetic acid derivation (50 mL). The organic layer was washed with water (50 mL), Brine and dried over anhydrous magnesium sulfate and thought under vacuum to yield the relating N-substituted different derivative vice. The yield was recrystallized from hot aq. ethanol to get unadulterated yield. m.p. 122 °C. The Yield was 73%.

Infrared Spectral Data (KBr), value in cm-1 3395.22 (s, NH_2), 3,286.28 (s, N-H, 2oamine), 3,039.41 (Ar- CH), 1,639.53 (s, C=N), 1,451.53 (CH3), 1,333.76 (s, C-N); 1H NMR Spectral Data (DMSO/TMS), δ values in ppm

Table 1. In Vitro Cytotoxic Activity [Median (Range) values] and Selectivity Index (SI) of the Crude Compared with 5-FU

Cell line	Ethanol with compounds	5-FU
CL-6;		
Calcein-AM: IC_{50} (µg/ml)	10.95 (10.87-11.12)	89.87 (89.57-90.84)
SI	18.09	3.19
Hoechst33342: IC_{50} (µg/ml)	53.13 (48.25-55.13)	95.29 (92.84-98.24)
SI	4.63	3.12
HepG2;		
Calcein-AM: IC_{50} (µg/ml)	71.89 (69.88-73.14)	74.86 (73.42-77.96)
SI	2.76	3.83
Hoechst33342: IC_{50} (µg/ml)	92.88 (87.15-94.26)	118.60 (115.67-120.19)
SI	2.68	2.51
HRE;		
Calcein-AM: IC_{50} (µg/ml)	198.15 (196.99-205.67)	286.74 (275.78-286.74)
SI	1	1
Hoechst IC_{50} (µg/ml)	245.91 (234.87-250.17)	297.39 (289.57-311.87)
SI	1	1

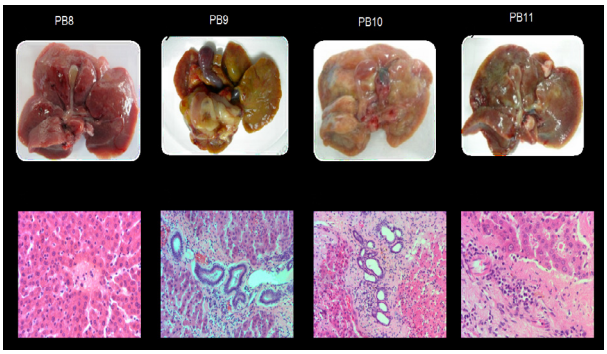

Figure 1. Pictorial Representation of Anticancer Activity

Table 2. Survival Time [Median (Range) Values] of 5-FU Treated

Control Swiss mice		Treated Swiss mice					
		Daily regimen			Every alternate regimen		
5-FU Treated[a] Std	Untreated control[b] Std	High Dose	Medium Dose	Low Dose	High Dose	Medium Dose	Low Dose
PB7 (22-28)	PB7 (16-20)	50.1 (52-57)	48.5 (49-53)	43.3 (44-49)	52 (53-58)	51.2 (50-55)	43.9 (44-49)
PB8 (22-28)	PB8 (16-20)	53.4 (52-57)	49.5 (49-53)	45.6 (44-49)	54.8 (53-58)	51.9 (50-55)	45.7 (44-49)
PB9 (22-28)	PB9 (16-20)	51 (52-57)	50.1 (49-53)	42.9 (44-49)	52.7 (53-58)	49.9 (50-55)	42.8 (44-49)
PB10 (22-28)	PB10 (16-20)	49.9 (52-57)	49.1 (49-53)	46.2 (44-49)	55.6 (53-58)	52.9 (50-55)	46 (44-49)
PB11 (22-28)	PB11 (16-20)	56.3 (52-57)	52.5 (49-53)	46.7 (44-49)	55.2 (53-58)	53.2 (50-55)	47.1 (44-49)

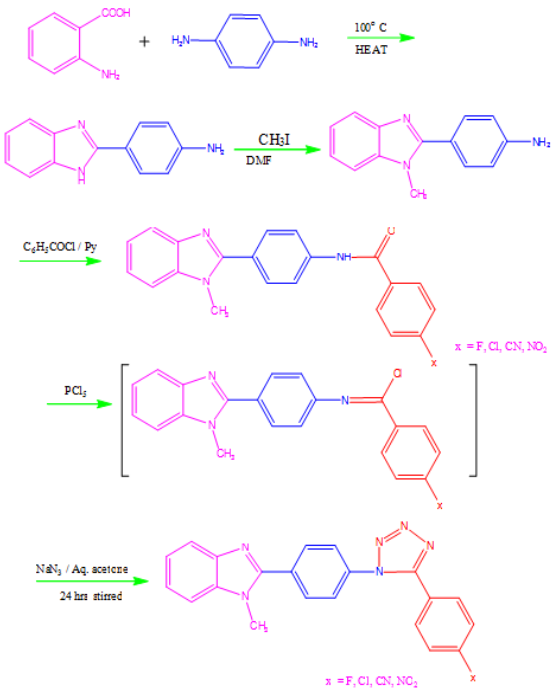

Figure 2. Reaction Scheme

7.5 (m), 7.2 (m), 7.9 (d), 6.5, 5.3 (s), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 153, 146, 143, 136, 128, 123, 12.7, 119, 115, 110, 32.

N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl) benzamide (PB2)

It was set up by utilizing PB2 (1; 0.01 mole) of and benzoyl chloride (0.1 moles) was refluxed with pyridine (40 mL) for 15hrs. That yield was undisturbed and included with icy ice, neutralized with the assistance of conc. HCl which created yield. The yield was separated by filtration and cleaned with frosty ice water. The yield was recrystallized from ethanol and separated by column chromatography. m.p. 162°C. The Yield was 70%.

Infrared Spectral Data (KBr), value in cm-1 3432.37, 3345.20, 3074.93, 1687.42, 1653.31, 1569.83, 1268.21, 1158.37; 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 10.2 (s, 1H), 8.0 (d), 7.6 (m), 7.7 (m), 7.8 (d), 8.1, 7.5, 7.2 (m), 4.0 (s). 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 153.0, 143, 138,136,134,132, 129, 127, 126, 123, 119, 110, 32.

4-Chloro-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl) phenyl)benzamide (PB3)

The title compound 3 was formed with the reaction between PB2 (1; 0.01 mole) and 4-chloro aromatic acid (0.1 moles) of the former course. The yield was filtered and cleaned with chilly ice water. The yield was recrystallized from ethanol and cleaned by column chromatography, m.p.184 °C. The Yield was 65%.

Infrared Spectral Data (KBr), value in cm-1 3,481.10, 3,289.02, 3,095.89, 1,664.50, 1,576.79, 1,512.67, 1,293.15, 1,162.02 (s, C-N), 760.93; 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 10.2 (s), 8.0 (d), 7.7 (m), 7.9 (m), 8.1 (d), 7.5 (d), 7.2, 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 165.0, 153.0, 143.0, 138, 134,123, 120 (C-4a), 110, 32 (CH_3).

4-Fluoro-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl) phenyl)benzamide (PB4)

The title compound 4 was framed with the response between PB2 (1; 0.01 mole) and 4-fluoro aromatic acid (0.1 moles) of the former course. The yield was filtrated and cleaned with cool ice water. The yield was recrystallized from ethanol and cleaned by column chromatography, m.p. 173°C. The Yield was 60%.

Infrared Spectral Data (KBr), value in cm-1 3,467.33 (s), 3,289.52 (s), 3,089.52, 1,680.10, 1,600.92, 1,522.81, 1,299.85, 1,181.03, 1,102.48 (C-F); 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 10.2 (s, NH), 8.1 (m, Ar-H), 7.4 (m, Ar-H), 7.8 (d, 1H, Ar-H), 8.1 (m), 7.6 (m), 7.2 (m, 2H), 4.0 (s, CH3); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 166.1 (=C(F), 164.4, 153.0, 143, 138-136, 130.2, 129, 127, 123, 119.8, 110, 32.

4-Cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl) phenyl)benzamide (PB5)

The title compound 5 was framed with the response between PB2 (1; 0.01 moles) and 4-cyano aromatic acid (0.1 moles) of the former course. The yield was filtrated and cleaned with icy ice water. The yield was recrystallized from ethanol and cleaned by column chromatography, m.p. 203°C.The yield was 68%.

Infrared Spectral Data (KBr), value in cm-1 3,506.66 (s, N-H 1°amine), 3,315.07 (s, N-H), 3,080.41 (s, Ar-C-H), 2,281.48 (C≡N), 1,683.34 (s, C=O), 1,599.48 (s, C=N), 1,566.88 (C=C aromatic amine), 1,293.16 (s, C-N), 1,178.44 (s, C-N); 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 10.2 (s), 8.2 (d), 8.1 (m), 7.8 (d), 8.1 (m), 7.6 (m), 7.2 (m), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 164.8, 153, 143, 138, 136, 132, 129, 128, 127.2, 126, 123, 120, 118.2, 110.1, 32.

N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl)-4-nitrobenzamide (PB6)

The title compound 6 was formed with the response between PB2 (1; 0.01 mole) and 4-nitro aromatic acid (0.1 moles) of the first course. The yield was filtrated and cleaned with super cold water. The yield was recrystallized from ethanol. It was cleaned by column chromatography. m.p. 211°C. 71% of yields were acquired.

Infrared Spectral Data (KBr), value in cm-1 3490.830, 3,321.21, 3,092.40, 1,692.78, 1,608.00, 1,520.70, 1,360.35, 1,307.60, 1,189.24; 1H NMR Spectral Data (DMSO/TMS), δ values in ppm δ 10.2 (s), 8.1 (m), 8.4 (d), 7.8 (d), 8.1 (m), 7.6 (m), 7.2 (m), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm δ 165, 153-151, 143, 138, 136, 130, 128.1, 127.0, 124-123, 110, 32.

1-Methyl-2-(4-(5-phenyl-1H-tetrazol-1-yl)phenyl)-1H-benzo[d]imidazole (PB7)

Compound (2) (0.01mole) treated alongside the measure of PCl5 (0.01mole) at 100° C until the point that the assessment of HCl exhaust wrapped up. That mixture

has some free $POCl_3$. By refining of that none responded $POCl_3$ were expelled with low weight. At that point it was permitted to respond with a super cold arrangement of NaN_3 (0.02 moles), 40 mL of CH_3)2CO and added sodium acetic acid derivation to continue permitting to reflux overnight. The untreated arrangement was partitioned and dissipates to acquire the yield. The yield separated and cleaned with super cold water. The yield was recrystallized from the mixture of benzene and pet-ether, m.p. 209°C. The Yield was half.

Elemental analysis for $C_{21}H_{16}N_6$: C, 72.01; H, 5.06; N, 24.00; Found: C, 72.10; H, 5.00; N, 24.15; Infrared Spectral Data (KBr), value in cm^{-1} 3,294.23 (s, N-H), 3,077.38 (s, Ar-C-H), 1,667.16 (s, C=N), 1,605.65 (C=N, tetrazole), 1,246.96 (tetrazole, N-N=N); 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 8.2 (d), 7.9 (m), 7.6 (m), 7.3 (m), 7.0 (m), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 153, 143-137, 132,128, 127,123, 120, 32; Mass Spectra Data Values, m/z (%) 353.1524 (0.30), 352 (0.02), 339.1422 (0.18), 337 (0.02), 277.1216 (0.17), 275 (0.01), 251.0917 (0.21), 223 (0.01), 221.1175 (0.10), 209.1145 (0.18), 207 (0.02), 145.0620 (0.40), 131.0725 (1.00), 103.0676 (0.77), 77.0456 (0.62)

2-(4-(5-(4-Fluorophenyl)-1H-tetrazol-1-yl)phenyl)-1-methyl-1H-benzo[d]imidazole (PB8)

The title compound was prepared by the regular procedure. The yield was recrystallized from the blend of benzene – petroleum ether. It was cleaned by column chromatography and m.p. 241° C. The Yield was 52%.

Elemental analysis for C21H15FN6: C, 68.10; H, 4.08; N, 22.69; Found: C, 68.15; H, 4.03; N, 22.85; Infrared Spectral Data (KBr), value in cm^{-1} 3,306.45, 3,084.66 (aromaticC-H stretching), 1,675.80 (C=N stretching), 1,610.08 (C=N, tetrazole), 1,260.00 (tetrazole, N-N=N), 1,116.08 (C-F); 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 7.8 (m), 7.3 (m), 7.7 (m), 7.8 (m), 7.6 (m), 7.2 (m), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm163, 153, 143-137, 131,126-123, 122-120 (C-4a), 116, 110, 32; Mass Spectra Data Values, m/z (%) 371.1259 (0.38), 373 (0.01), 357.1323 (0.36), 355 (0.02), 353 (0.01), 351.1524 (0.20), 295.1123 (0.21), 293 (0.02), 277.1216 (0.17), 257.0532 (0.08), 255 (0.01), 251.0917 (0.22), 249 (0.02), 241 (0.01), 239.0810 (0.30), 209.1145 (0.19), 207 (0.02), 131.0725 (1.00), 121.0424 (0.50), 95.0471 (0.58), 77.0456 (0.64).

4-(1-(4-(1-Methyl-1H-benzo[d]imidazol-2-yl)phenyl)-1H-tetrazol-5-yl)benzonitrile (PB9)

The title compound was prepared by the regular procedure, the yield was recrystallized from the blend of benzene – petroleum ether and cleaned by column chromatography and m.p. 264° C. The Yield was 55%.

Elemental analysis for $C_{22}H_{15}N_7$: C, 69.90; H, 3.90; N, 26.12; Found: C, 69.97; H, 3.92; N, 26.04; Infrared Spectral Data (KBr), value in cm-1 3302.05 (s, N-H), 3,093.97 (s), 1,699.27, 1,617.31, 1,499.10, 1,309.60, 1,290.70, 1,194.89; 1H NMR Spectral Data (DMSO/TMS), δ values in ppm 8.0 (m), 7.8 (m), 7.6 (m), 7.5 (m), 7.2 (m), 4.0 (s); 13C NMR Spectral Data (DMSO/TMS), δ values in ppm 153, 143, 136-131, 130, 128.2, 127-123, 120, 119, 112-110, 32; Mass Spectra Data Values, m/z (%) 379.1659 (0.22), 375 (0.2), 365(0.01), 363.1392 (0.17), 353.1524 (0.30), 351 (0.02), 303.1223 (0.18), 301 (0.01), 277.1216 (0.18), 225 (0.02), 251.0917 (0.30), 209.1145 (0.19), 207 (0.01), 173 (0.02), 171.0251 (0.33), 139.0021 (0.40), 137 (0.01), 131.0725 (1.00), 77.0456 (0.64).

2-(4-(5-(4-Chlorophenyl)-1H-tetrazol-1-yl)phenyl)-1-methyl-1H-benzo[d]imidazole (PB10)

The title compound was prepared by the regular procedure, the yield was recrystallized from the mixture of benzene – petroleum ether and cleaned by column chromatography and m.p. 252° C. The Yield was 50%.

Elemental analysis for $C_{21}H_{15}C_1N_6$: C, 64.98; H, 4.02; N, 22.04; Found: C, 64.89; H, 4.10; N, 22.09; Infrared Spectral Data (KBr), value in cm-1 3280.88 (N-H streching), 3,076.24, 1,675.08, 1,604.46, 1,230.00, 786.00; 1HNMR Spectral Data (DMSO/TMS), δ values in ppm 8.1 (m), 7.9 (m), 7.6 (m), 7.4 (m), 7.1 (m), 6.9 (m), 4.0 (s); 13CNMR Spectral Data (DMSO/TMS), δ values in ppm 153, 143, 136-134, 132-130.3, 129.1, 128.3, 125, 121, 110, 32; Mass Spectra Data Values, m/z (%) 389.1375 (0.40), 387 (0.01), 373.1059 (0.20), 371(0.02), 353.1524 (0.24), 351 (0.01), 313.0823 (0.50), 311 (0.01), 277.1216 (0.18), 275 (0.02), 257.0532 (0.08), 255 (0.02), 251.0917 (0.20), 249 (0.02), 209.1145 (0.18), 207 (0.01), 181.0251 (0.35), 179 (0.02), 139.0021 (0.40), 137 (0.01), 131.0725 (1.00), 113.3541 (0.37), 111 (0.02), 77.0456 (0.63).

1-Methyl-2-(4-(5-(4-nitrophenyl)-1H-tetrazol-1-yl) phenyl)-1H-benzo[d]imidazole (PB11)

The title compound was prepared by the regular procedure, the yield was recrystallized from the blend of benzene – petroleum ether and cleaned by column chromatography and m.p. 301° C. The Yield was 60%.

Elemental analysis for $C_{21}H_{15}N_7O_2$: C, 63.47; H, 3.80; N, 24.67; O, 8.05; Found: C, 63.43; H, 3.84; N, 25.65; Infrared Spectral Data (KBr), value in cm^{-1} 3,303.66 (s, N-H), 3,050.79 (s, C-H), 1,704.33 (s, C=O), 1,614.42 (C=N, tetrazole), 1,528.64 (C=C aromatic amine), 1,361.60 (Ar-NO_2), 1,317.02 (s, C-N 1°aromatic amine), 1,170.30 (s, C-N); 1HNMR Spectral Data (DMSO/TMS), δ values in ppm 8.5 (m), 8.1 (m), 7.9 (m), 7.6, 7.4, 7.0, 4.0 (s); 13CNMR Spectral Data (DMSO/TMS), δ values in ppm 153, 148-143, 136.8, 131- 130, 129-127, 125, 123, 120, 32; Mass Spectra Data Values, m/z (%) 399.1410 (0.34), 397 (0.02), 383.1059 (0.17), 381 (0.01), 353.1524 (0.30), 351 (0.02), 323.0923 (0.20), 321 (0.01), 277.1216 (0.18), 275 (0.01), 267.0711 (0.04), 257.0532 (0.08), 255 (0.02), 251.0917 (0.24), 249 (0.01), 209.1145 (0.19), 207 (0.01), 191.0251 (0.75), 189 (0.02), 149.0477 (0.73), 131.0725 (1.00), 123.0341 (0.38), 77.0456 (0.67)

Discussion

The anticancer activity

Anticancer activity of in vivo

Animals

The age of 6-8 week and weight 105-120 g of Swiss mice were utilized and nourished with a store eating

regimen and water. The endorsement technique was acquired from the Ethics Committee for Research in Animals.

The toxicity study of acute and subacute

Intense and subacute lethality tests were performed by the OECD rule for chemicals. Swiss mice (5 males and 5 females for each gathering) were nourished (by means of gastric gavage) with three measurements levels of ethanol with compound (resuspended in a blend of refined water and Tween-80, 4:1, v:v), i.e., 1,000, 3,000, and 5,000 mg/kg body weight. The control Swiss mice were sustained with the blend of refined water and Tween-80.

Autopsy and histopathology

For both toxicity and anticancer action assessment, all organs were expelled at autopsy and watched perceptibly. Tests were settled in 10% formalin solution. Specimens were washed in phosphate buffer three times, at that point got dried out in a rising arrangement of ethanol for 15 min each and installed in paraffin, trailed by segmenting and staining with hematoxylin and eosin.

Statistical analysis

Data are expressed as median (range) values. A significant difference between quantitative data of more than two data sets was performed by Kruskal-Wallis test. A significant difference between two quantitative data sets was performed by Mann-Whitney test. The statistical significance level was set at α=0.05 for all tests.

Results for anticancer activity

In vivo model for evaluation of toxicity and anticancer activity

Toxicity test

For the acute and subacute toxicity studies, single oral doses of rough ethanol with compounds at all of the three levels (1,000, 3,000, and 5,000 mg/kg body weight) did not cause mortality in any animal (0% mortality) amid the examination time frame. Just stomach disturbance was seen in all animals quickly subsequent to encouraging them with the concentrate. The animals, however, recouped from the side effect inside one hour of dosing. The normal everyday admission of water and sustenance, including the normal body weight of animals, were practically identical in all gatherings. No anomalous histopathology was seen in any imperative organ at examination.

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