

SYNTHESIS OF ALKYL CATECHOLS AND EVALUATION OF THEIR ANTIBACTERIAL AND CYTOTOXIC ACTIVITY

**BINA S. SIDDIQUI*, QAYYUM ADIL, SABIRA BEGUM
AND SALIMUZZAMAN SIDDIQUI**

H.E.J. Research Institute of Chemistry, University of Karachi,
Karachi-75270, Pakistan.

**KHURSHED ALI KHAN, SHAKEEL AHMED KHAN
AND SYED MOHAMMAD KHALID**

Department of Microbiology, University of Karachi,
Karachi-75270, Pakistan.

ABSTRACT

A series of potential biologically active mono-, di- and tetra- alkyl catechols were prepared through Friedel- Crafts alkylation of catechol, and evaluated for their antibacterial and cytotoxic activity. The mono-substituted alkyl derivatives showed maximum antibacterial activity in vitro which increased with the increasing length of the alkyl chains. Primary screening results indicated that all the monoalkyl derivatives except 4- (2-octyl) catechol inhibited the growth of *B. bronchoseptica* and maximum zones of inhibition were observed in case of monohexyl catechols (both n- and 2-hexyl) and monobenzyl derivative. In case of Gram-negative organisms growth of *pneumoniae* and *A. cakoaceticus* was inhibited by several derivatives. Mono-3-octyl-, monononyl- and monobenzyl catechols markedly inhibited the growth of *Kl. pneumoniae*. Mono-2-heptyl catechol inhibited the growth of six Gram-negative bacteria. Minimum inhibitory concentration of six most active compounds of the series was determined against Gram-positive and Gram-negative organisms; it ranged from >100 µg/ml to 10 µg/ml. The antibacterial activity of catechol was not significant.

Cytotoxicity test done by brine shrimp assays showed that the order of cytotoxicity decreases in going from mono- to tetra- alkyl catechols, and among the mono- alkyl products, a decrease in order of cytotoxicity was noted in going from mono-methyl catechol (LD₅₀=59) to monopentyl catechol (LD₅₀=173) after which the order of cytotoxicity gradually increased upto the largest alkyl substituent tested i.e. monononyl catechol (LD₅₀=114). Methyl and ethyl catechol, which were almost inactive in respect of their antibacterial activity possessed pronounced cytotoxicity as compared to higher homologues. Catechol itself did not show significant cytotoxicity (LD₅₀=393.27).

Introduction

Catechol (pyrocatechol) and its derivatives possess diverse biological activity such as hyperglycemic (Cavalca *et al*, 1955), thiamine decomposing (Hasegawa *et al*, 1956, Horman *et al*, 1982), antigonadotropic (Gumbinger *et al*, 1981, Winterhoff *et al*., 1988), antimutagenic (Pashin *et al*, 1986) and allelopathic (Moroz *et al*., 1983) activity and are known to act as antisclerotic agents (Tarasova *et al*, 1966), convulsants (De Ropp *et al*, 1969) and antibiotics (Malama *et al*., 1974). Catechol also finds its use in the preparations for the treatment of skin wounds, such as burn wounds and herpes. It has further been shown that in Phenolic compounds the order of biological property is dependent on the number of hydroxyl groups and nature of other substituents. Thus, for example, in the series of 4-n-alkyl resorcinols the germicidal activity becomes greater as the alkyl group lengthens from ethyl to propyl to butyl and so on. A similar increase appears in other phenolic compounds (Miller *et al*, 1938). Similarly, when the antimutagenic activity of various di hydroxy aromatic antioxidant compounds, pyrocatechol, hydroquinone and 2, 6-di-tertbutylhydroquinone was studied, it was observed that the most potent antimutagen was 3,5-di-tertbutyl pyrocatechol and that the antimutagenic effects of pyrocatechol and hydroquinones depended upon the position of OH and tertbutyl group (Meyer *et al*, 1982).

Taking into account this back ground, a series of alkyl catechols has been prepared and their cytotoxic and antibacterial activity studied. Friedel-Crafts alkylation of pyrocatechol with alkyl halides ranging from methyl to nonyl and benzyl) using BF₃- etherate as a catalyst resulted in a series of alkyl catechols. The reaction product after separation through flash column chromatography furnished three derivatives in each case, namely, mono-, di- and tetra- substituted catechols. The least polar compounds obtained from flash column were tetra-substituted products, the mono-substituted being the most polar compounds. The mono-alkyl derivatives (n-butyl to noctyl) of catechol have been communicated earlier (Miller *et al*, 1938), whereas di-and tetra-substituted derivatives as well as benzyl and nonyl derivatives (mono-, di-and tetra- substituted) are being reported for the first time.

Materials and Methods

IR and UV spectra were measured on JASCO IRA-1 and Rye- Unicam sp. 800 spectrometers respectively. Mass Spectra were recorded on Finnigan Mat-112. The ¹H NMR spectra were recorded in CDCl₃ on a Bruker AM-300 spectrometer operating at 300 MHz. The chemical shifts are reported in δ (ppm) and coupling constants in Hz. Rash column (model Eyela) chromatography (Still *et al*, 1978) was used with silica-gel (E.Merck, 9385) as adsorbent and chloroform and chloroform-methanol (gradually increasing the ratio of methanol) as eluents. Purity of the products was checked on TLC plates coated with silica gel PF₂₅₄ (E.Merck).

General Procedure for Alkylation of Pyrocatechol

Pyrocatechol (0.1 g) was taken in a 100 ml two-necked flask fitted with a magnetic stirrer. The flask was cooled in an ice bath and alkyl halide (0.001 mole) and BF₃-etherate (0.001 mole) were added. The reaction mixture was stirred (0-4°C) for 20 minutes with good cooling. Stirring was continued further for 24 hours at room temperature. Dry ether was added to the reaction mixture which was successively washed with 4% NaHCO₃ solution, water and finally with brine solution. The ethereal layer was dried over anhydrous sodium sulphate and freed off the solvent under reduced pressure. The reaction mixture was separated through flash column chromatography with the solvent system chloroform-methanol (9.5:0.5) ultimately furnishing three products tetra-alkyl, di-alkyl and mono-alkyl derivatives of pyrocatechol in the order of polarity.

4-Benzyl catechol [2]: Brown rods: mp 98°C; IR 3400, 1590, 1240, 1020 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.84 (s, 2H, H-1'), 6.62 (dd, 1H, *J* = 8.0, 2.01 Hz, H-5), 6.65 (d, 1H, *J* = 2.01 Hz, H-3), 6.75 (d, 1H, *J* = 8.0 Hz, H-6), 7.15 (d, 2H, *J* = 7.50 Hz, H-3', H-7'), 7.17 (dd, 1H, *J* = 7.40, 7.25 Hz, H-5'), 7.26 (dd, 2H, *J* = 7.50, 7.40 Hz, H-4', H-6'); HRMS *m/z* 200.0837 (M⁺) C₁₃H₁₂O₂ requires 200.0842.

4,5-Dihenzyl catechol [3]: Brown rods: mp 88°C; IR 3410, 1590, 1120, 1015 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.81 (s, 4H, 2xCH₂), 6.59 (s, 2H, H-3, H-6), 7.04 (d, 2H, *J* = 8.10 Hz, H-3', H-7'/H-3'', H-7''), 7.05 (d, 2H, *J* = 8.10 Hz, H-3', H-7'/H-3'', H-7''), 7.14 (dd, 1H, *J* = 7.30, 7.25 Hz, H-5'/H-5''), 7.15 (dd, 1H, *J* = 7.30, 7.25 Hz, H-5'/H-5''), 7.24 (dd, 2H, *J* = 8.10, 7.25 Hz, H-4', H-6'/H-4'', H-6''), 7.25 (dd, 2H, *J* = 8.10, 6.90 Hz, H-4', H-6'/H-4'', H-6''); HRMS *m/z* 290.1306 (M⁺) C₂₀H₁₈O₂ requires 290.1315.

3,4,5,6-Tetrabenzyl catechol [4]: Brown rods: mp 71°C; IR 3390, 1595, 1100, 1010 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.90-3.95 (s, 8H, 4xCH₂), 6.95-7.28 (m, 20H, aromatic); HRMS *m/z* 470.2245 (M⁺) C₃₄H₃₀O₂ requires 470.2276.

4-Nonyl catechol [5]: Yellow needles: mp 92°C; IR 3400, 2950-2850, 1590, 1270 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.17 (t, 3H, *J* = 7.65 Hz, CH₃), 1.59-1.62 (m, 14H, 7xCH₂), 2.51 (t, 2H, *J* = 7.56 Hz, Ar-CH₂), 6.63 (dd, 1H, *J* = 8.04, 2.02 Hz, H-5), 6.71 (d, 1H, *J* = 2.02 Hz, H-3), 6.76 (d, 1H, *J* = 8.04 Hz, H-6); HRMS *m/z* 236.1801 (M⁺) C₁₅H₂₄O₂ requires 236.1762.

4,5-Dinonyl catechol [6]: Yellow needles: mp 84°C; IR 3500, 2900-2850, 1590, 1280 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.06 (t, 3H, *J* = 7.56 Hz, CH₃), 1.17 (t, 3H, *J* = 7.56 Hz, CH₃), 1.58-1.63 (m, 28H, 14xCH₂), 2.65 (t, 2H, *J* = 7.39 Hz, Ar-CH₂), 2.67 (t, 2H, *J* = 7.70 Hz, Ar-CH₂), 6.72 (s, 2H, H-3, H-6); HRMS *m/z* 362.3184 (M⁺) C₂₄H₄₂O₂ requires 362.3219.

3,4,5,6-Tetranonyl catechol [7]: Yellow needles: mp 76°C; IR 3450, 2900-

2825, 1595, 1275 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.15-1.18 (m, 12H, 4xCH₃), 1.60-1.62 (m, 56H, 28xCH₂), 2.49-2.68 (m, 8H, 4xAr-CH₂); HRMS m/z 614.2284 (M^+) $\text{C}_{42}\text{H}_{78}\text{O}_2$ requires 614.2373.

4-(2-Octyl) catechol [8]: Brown rods: mp 72°C; IR 3400, 2900- 2800, 1595, 1265 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.73 (t, 3H, $J = 7.36$ Hz, CH₃), 0.90 (d, 3H, $J = 7.33$ Hz, CH₃), 1.45-1.60 (m, 10H, 5xCH₂), 3.62 (m, 1H, CH), 6.55 (dd, 1H, $J = 8.05$, 1.98 Hz, H-5), 6.65 (d, 1H, $J = 1.98$ Hz, H-3), 6.76 (d, 1H, $J = 8.05$ Hz, H-6); HRMS m/z 222.1619 (M^+) $\text{C}_{14}\text{H}_{22}\text{O}_2$ requires 222.1615.

4,5-Di-(2-octyl) catechol [9]: Brown rods: mp 65°C; IR 3440, 2900-2850, 1590, 1275 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.75 (t, 6H, $J = 7.10$ Hz, 2xCH₃), 0.92 (d, 6H, $J = 6.95$ Hz, 2xCH₃), 1.49-1.61 (m, 20H, 10xCH₂), 2.97 (m, 2H, 2xCH), 6.72 (s, 2H, H-3, H-6); HRMS m/z 334.2877 (M^+) $\text{C}_{22}\text{H}_{38}\text{O}_2$ requires 334.2873.

3,4,5,6-Tetra-(2-octyl) catechol [10]: Brown rods: mp 62°C; IR 3450, 2900-2850, 1595, 1270 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.79-0.88 (m, 24H, 8xCH₃), 1.45-1.59 (m, 40H, 20xCH₂), 2.95 (m, 4H, 4xCH); HRMS m/z 559.3127 ($\text{M}^+ + 1$) $\text{C}_{38}\text{H}_{71}\text{O}_2$ requires 559.3118.

4-(3-Octyl) catechol [11]: Brown rods: mp 102°C; IR 3400, 2910-2800, 1590, 1270 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.60, 0.77 (each t, 3H, $J = 7.03$ and 7.34 Hz, 2xCH₃), 1.46-1.58 (m, 10H, 5xCH₂), 2.96 (m, 1H, CH), 6.64 (dd, 1H, $J = 8.21, 1.89$ Hz, H-5), 6.67 (d, 1H, $J = 1.89$ Hz, H-3), 6.75 (d, 1H, $J = 8.21$ Hz, H-6); HRMS m/z 222.1617 (M^+) $\text{C}_{14}\text{H}_{22}\text{O}_2$ requires 222.1624.

4,S-Di-(3-octyl) catechol [12]: Brown rods: mp 97°C; IR 3400, 2910- 2800, 1590, 1270 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.80-0.85 (m, 12H, 4xCH₃), 1.47-1.59 (m, 20H, 10xCH₂), 2.90-3.00 (m, 2H, 2xCH), 6.69 (s, 2H, H-3, H-6); HRMS, m/z 334.2871 (M^+) $\text{C}_{22}\text{H}_{38}\text{O}_2$ requires 334.2793.

3,4,5,6-Tetra-(3-octyl) catechol [13]: Yellow rods: mp 95°C; IR 3450, 2900-2800, 1595, 1280 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.71-0.85 (m, 24H, 8xCH₃), 1.50-1.62 (m, 40H, 20xCH₂), 2.76-3.01 (m, 4H, 4xCH); HRMS m/z 558.1241 (M^+) $\text{C}_{38}\text{H}_{70}\text{O}_2$ requires 558.1230.

4-Heptyl catechol [14]: Yellow needles: mp 87°C; IR 3400, 2910-2800, 1595, 1270, 1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.18 (t, 3H, $J = 7.62$ Hz, CH₃), 1.57-

1.62 (m, 10H, 5xCH₂), 2.53 (t, 2H, $J = 7.50$ Hz, Ar-CH₂), 6.62 (dd, 1H, $J = 8.05$, 1.89 Hz, H-5), 6.71 (d, 1H, $J = 1.89$ Hz, H-3), 6.76 (d, 1H, $J = 8.05$ Hz, H-6); HRMS m/z 208.1463 (M⁺) C₁₃H₂₀O₂ requires 208.1504.

4,5-Diheptyl catechol [15]: Yellow needles: mp 92°C; IR 3350, 2900-2850, 1598, 1280, 1165 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.24 (t, 6H, $J = 7.53$ Hz, 2xCH₃), 1.49-1.55 (m, 20H, 10xCH₂), 2.64 (t, 4H, $J = 7.51$ Hz, 2xAr-CH₂), 6.72 (s, 2H, H-3, H-6); HRMS m/z 306.2558 (M⁺) C₂₀H₃₄O₂ requires 306.3041.

3,4,5,6-Tetraheptyl catechol [16]: Yellow needles: mp 88°C; IR 3350, 2900-2850, 1590, 1300, 1165 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.741.85 (m, 12 H, 4xCH₃), 1.58-1.62 (m, 40 H, 20xCH₂), 2.54-2.57 (m, 8H, 4xAr-CH₂); HRMS m/z 502.1449 (M⁺) C₃₄H₆₂O₂ requires 502.1503.

4-(2-Heptyl) catechol [17]: Brown rods: mp 78°C; IR 3500, 2900- 2850, 1595, 1260, 1020 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.73 (t, 3H, $J = 7.38$ Hz, CH₃), 0.83 (d, 1 H, $J = 7.08$ Hz, CH₃), 1.51-1.64 (m, 8H, 4xCH₂), 2.25 (m, 1H, CH), 6.65 (dd, 1H, $J = 8.06$, 1.98 Hz, H-5), 6.65 (d, 1H, $J = 1.98$ Hz, H-3), 6.76 (d, 1H, $J = 8.06$ Hz, H-6); HRMS m/z 208.1509 (M⁺) C₁₃H₂₀O₂ requires 208.1512.

4,5-Di-(2-heptyl) catechol [18]: Brown rods: mp 87°C; IR 3510, 2900-2850, 1590, 1275, 1040 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.79 (t, 3H, $J = 7.25$ Hz, CH₃), 0.81 (t, 3H, $J = 8.02$ Hz, CH₃), 0.82 (d, 3H, $J = 7.12$ Hz, CH₃), 0.84 (d, 3H, $J = 7.07$ Hz, CH₃), 1.58-1.67 (m, 16 H, 8xCH₂), 2.23 (m, 1H, CH), 2.25 (m, 1H, CH), 6.47 (s, 2H, H-3, H-6); HRMS m/z 306.2017 (M⁺) C₂₀H₃₄O₂ requires 306.2563.

3,4,5,6-Tetra-(2-heptyl) catechol [19]: Brown rods: mp 94°C; IR 3525, 2910-2850, 1598, 1250, 1025 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.75-0.84 (m, 24H, 8xCH₃), 1.57-1.63 (m, 32 H, 16xCH₂), 2.74-2.98 (m, 4H, 4xCH); HRMS m/z 502.4513 (M⁺) C₃₄H₆₂O₂ requires 502.4624.

4-Hexyl catechol [20]: Yellow plates: mp 61°C; IR 3450, 2950-2850, 1595, 1200, 990 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.16 (t, 3H, $J = 7.60$ Hz, CH₃), 1.53-1.70 (m, 8H, 4xCH₂), 2.53 (t, 2H, $J = 7.75$ Hz, Ar-CH₂), 6.63 (dd, 1H, $J = 8.04$, 2.01 Hz, H-5), 6.71 (d, 1H, $J = 2.01$ Hz, H-3), 6.76 (d, 1H, $J = 8.04$ Hz, H-6); HRMS m/z 194.1297 (M⁺) C₁₂H₁₈O₂ requires 194.1309.

4,5-Dihexyl catechol [21]: Yellow plates: mp 56°C; IR 3450, 2950- 2800, 1590, 1230, 1060 cm⁻¹; ¹H-NMR (CDCl₃) δ 0.78 (t, 3H, $J = 7.45$ Hz, CH₃), 0.85 (t, 3H, $J = 7.08$ Hz, CH₃), 1.54-1.71 (m, 16H, 8xCH₂), 2.52-2.54 (m, 4H, 2xAr-CH₂), 6.72 (s, 2H, H-3, H-6); HRMS m/z 278.2245 (M⁺) C₁₈H₃₀O₂ requires 278.2216.

3,4,5,6-Tetrahexyl catechol [22]: Yellow plates: mp 68°C; IR 3450, 2950-2850, 1595, 1230, 1070 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.82-0.85 (m, 12H, 4xCH₃), 1.55-1.72 (m, 32H, 16xCH₂), 2.52-2.53 (m, 8H, 4xAr-CH₂); HRMS m/z 446.4123 (M^+) $\text{C}_{30}\text{H}_{54}\text{O}_2$ requires 446.4119.

4-(2-Hexyl) catechol [23]: Colour-less needles: mp 84°C; IR 3450, 2950-2850, 1590, 1200, 995 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.173 (t, 3H, $J = 7.37$ Hz, CH₃), 1.17 (d, 3H, $J = 6.92$ Hz, CH₃), 1.50-1.62 (m, 6H, 3xCH₂), 2.53 (m, 1H, CH), 6.59 (dd, 1H, $J = 8.01, 2.04$ Hz, H-5), 6.64 (d, 1H, $J = 2.04$ Hz, H-3), 6.75 (d, 1H, $J = 8.01$ Hz, H-6); HRMS m/z 194.1306 (M^+) $\text{C}_{12}\text{H}_{18}\text{O}_2$ requires 194.1299.

4,5-Di-(2-hexyl) catechol [24]: Colour-less needles: mp 79°C; IR 3500, 2900-2850, 1595, 1210, 995 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.81-0.87 (m, 6H, 2xCH₃), 1.21-1.22 (m, 6H, 2xCH₃), 1.50-1.65 (m, 12H, 6xCH₂), 2.81-2.84 (m, 2H, 2xCH), 6.69 (s, 2H, H-3, H-6); HRMS m/z 278.2245 (M^+) $\text{C}_{18}\text{H}_{30}\text{O}_2$ requires 278.2267.

3,4,5,6-Tetra-(2-hexyl) catechol [25]: Colour-less needles: mp 77°C; IR 3440, 2900-2800, 1590, 1220, 1000 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.78-0.89 (m, 12H, 4xCH₃), 1.20-1.22 (m, 12H, 4xCH₃), 1.56-1.65 (m, 24H, 12xCH₂), 2.80-2.84 (m, 4H, 4xCH); HRMS m/z 446.4123 (M^+) $\text{C}_{30}\text{H}_{54}\text{O}_2$ requires 446.4319.

4-(3-Hexyl) catechol [26]: Brown plates: mp 67°C; IR 3500, 2950-2850, 1595, 1265, 1100 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.72 (t, 3H, $J = 7.35$ Hz, CH₃), 0.83 (t, 3H, $J = 7.05$ Hz, CH₃), 2.54 (m, 1H, CH), 6.59 (dd, 1H, $J = 8.01, 2.00$ Hz, H-5), 6.68 (d, 1H, $J = 2.00$ Hz, H-3), 6.75 (d, 1H, $J = 8.10$ Hz, H-6); HRMS m/z 194.1306 (M^+) $\text{C}_{12}\text{H}_{18}\text{O}_2$ requires 194.1309.

4,5-Di-(3-hexyl) catechol [27]: Brown plates: mp 63°C; IR 3550, 2950-2870, 1590, 1270, 1010 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.70-0.83 (m, 12H, 4xCH₃), 1.57-1.62 (m, 12H, 6xCH₂), 2.49 (m, 1H, CH), 2.52 (m, 1H, CH), 6.67 (s, 2H, H-3, H-6); HRMS m/z 278.2245 (M^+) $\text{C}_{18}\text{H}_{30}\text{O}_2$ requires 278.2268.

3,4,5,6-Tetra-(3-hexyl) catechol [28]: Brown plates: mp 55°C; IR 3510, 2950-2800, 1590, 1270, 1010 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.69-0.83 (m, 24H, 8xCH₃), 1.54-1.62 (m, 24H, 12xCH₂), 2.24-2.94 (m, 4H, 4xCH); HRMS m/z 446.4123 (M^+) $\text{C}_{30}\text{H}_{54}\text{O}_2$ requires 446.4119.

4-Pentyl catechol [29]: Yellow plates: mp 88°C; IR 3510, 2900-2850, 1590, 1300-1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.17 (t, 3H, $J = 7.60$ Hz, CH₃), 1.57-1.64 (m, 6H, 3xCH₂), 2.53 (t, 2H, $J = 7.58$ Hz, Ar-CH₂), 6.62 (dd, 1H, $J = 8.05, 2.01$ Hz, H-5), 6.71 (d, 1H, $J = 2.01$ Hz, H-3), 6.76 (d, 1H, $J = 8.05$ Hz, H-6); HRMS m/z 180.1150 (M^+) $\text{C}_{11}\text{H}_{16}\text{O}_2$ requires 180.1091.

4,5-Dipentyl catechol [30]: Yellow plates: mp 86°C; IR 3450, 2910-2850,

1595, 1295-1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.22 (t, 6H, $J = 7.57$ Hz, $2\times\text{CH}_3$), 1.56-1.60 (m, 12H, $6\times\text{CH}_2$), 2.63 (t, 4H, 7.59 Hz, $2\times\text{Ar-CH}_2$), 6.72 (s, 2H, H-3, HL); HRMS m/z 250.1932 (M^+) $\text{C}_{16}\text{H}_{26}\text{O}_2$ requires 250.2001.

3,4,5,6-Tetrapeotyl catechol [31]: Yellow plates: mp 91°C ; IR 3400, 2900-2825, 1590, 1280-1165 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.17 (t, 6H, $J = 7.87$ Hz, $2\times\text{CH}_3$), 1.21 (t, 6H, $J = 7.55$ Hz, $2\times\text{CH}_3$), 1.56-1.67 (m, 24H, $12\times\text{CH}_2$), 2.33-2.57 (m, 8H, $4\times\text{Ar-CH}_2$); HRMS m/z 390.3097 (M^+) $\text{C}_{26}\text{H}_{46}\text{O}_2$ requires 390.2998.

4-Butyl catechol [32]: Yellow needles: mp 57°C ; IR 3500, 2900-2800, 1595, 1265, 1020 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.17 (t, 3H, $J = 7.60$ Hz, CH_3), 1.54-1.60 (m, 4H, $2\times\text{CH}_2$), 2.51 (t, 2H, $J = 7.36$ Hz, Ar-CH_2), 6.62 (dd, 1H, $J = 8.05, 2.00$ Hz, H-5), 6.71 (d, 1H, $J = 2.00$ Hz, H-3), 6.76 (d, 1H, $J = 8.05$ Hz, H-6); HRMS m/z 166.0993 (M^+) $\text{C}_{10}\text{H}_{14}\text{O}_2$ requires 166.0983.

4,5-Dibutyl catechol [33]: Yellow needles: mp 87°C ; IR 3450, 2900-2800, 1595, 1280, 1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.22 (t, 3H, $J = 7.58$ Hz, CH_3), 1.24 (t, 3H, $J = 7.52$ Hz, CH_3), 1.55-1.60 (m, 8H, $4\times\text{CH}_2$), 2.50 (m, 4H, $2\times\text{Ar-CH}_2$), 6.72 (s, 2H, H-3, H-6); HRMS m/z 223.1697 ($\text{M}^+ + 1$) $\text{C}_{14}\text{H}_{23}\text{O}_2$ requires 223.1701.

3,4,5,6-Tetrabutyl catechol [34]: Yellow needles: mp 94°C ; IR 3450, 2900-2800, 1595, 1280, 1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 0.79-0.86 (m, 12H, $4\times\text{CH}_3$), 1.55-1.63 (m, 16H, $8\times\text{CH}_2$), 2.29-2.50 (m, 8H, $4\times\text{Ar-CH}_2$); HRMS m/z 334.2871 (M^+) $\text{C}_{22}\text{H}_{38}\text{O}_2$ requires 334.2872.

4-Propyl catechol [35]: Brown plates: mp 74°C ; IR 3450, 2900-2850, 1590, 1265-1160 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.16 (t, 3H, $J = 7.63$ Hz, CH_3), 1.62-1.64 (m, 2H, CH_2), 2.49 (t, 2H, $J = 7.60$ Hz, Ar-CH_2), 6.62 (dd, 1H, $J = 8.04, 1.99$ Hz, H-5), 6.71 (d, 1H, $J = 1.99$ Hz, H-3), 6.76 (d, 1H, $J = 8.04$ Hz, H-6); HRMS m/z 152.0893 (M^+) $\text{C}_9\text{H}_{12}\text{O}_2$ requires 152.0901.

4,5-Dipropyl catechol [36]: Brown plates: mp 79°C ; IR 3425, 2925-2850, 1595, 1280-1165 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.17 (t, 3H, $J = 6.21$ Hz, CH_3), 1.19 (t, 3H, $J = 7.31$ Hz, CH_3), 1.57-1.62 (m, 4H, $2\times\text{CH}_2$), 2.46 (t, 2H, $J = 7.18$ Hz, Ar-CH_2), 2.61 (t, 2H, $J = 7.62$ Hz, Ar-CH_2), 6.73 (s, 2H, H-3, H-6); HRMS m/z 194.1401 (M^+) $\text{C}_{12}\text{H}_{18}\text{O}_2$ requires 194.1356.

3,4,5,6-Tetrapropyl catechol [37]: Brown plates: mp 60°C ; IR 3400, 2900-2850, 1595, 1295-1165 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.10 (t, 6H, $J = 7.29$ Hz, $2\times\text{CH}_3$), 1.18 (t, 6H, $J = 7.36$ Hz, $2\times\text{CH}_3$), 1.58-1.63 (m, 8H, $4\times\text{CH}_2$), 2.44-2.55 (m, 8H, $4\times\text{Ar-CH}_2$); HRMS m/z 278.2290 (M^+) $\text{C}_{18}\text{H}_{30}\text{O}_2$ requires 278.2215.

4-Ethyl catechol [38]: Brown rods: mp 58°C ; IR 3550, 2950-2800, 1595, 1280-1140, 990 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 1.21 (t, 3H, $J = 7.37$

Hz, CH₃), 2.53 (q, 2H, $J = 7.52$ Hz, Ar-CH₂], 6.62 (dd, 1H, $J = 8.05, 1.89$ Hz, H-5), 6.71 (d, 1H, $J = 1.89$ Hz, H-3), 6.77 (d, 1H, $J = 8.05$ Hz, H-6); HRMS m/z 138.0680 (M^e) C₈H₁₀O₂ requires 138.0745.

4-Methyl catechol [39]: Brown rods: mp 66°C; IR 3500, 2900-2850, 1595, 1240, 1020 cm⁻¹; ¹H-NMR (CDCl₃) δ 2.51 (s, 3H, CH₃), 6.61 (dd, 1H, $J = 8.04, 2.05$ Hz, H-5), 6.71 (d, 1H, $J = 2.05$ Hz, H-3), 6.77 (d, 1H, $J = 8.04$ Hz, H-6); HRMS m/z 124.0499 (M⁺) C₇H₈O₂ requires 124.0531.

Biological Results and Discussion

Antibacterial Activity

Compounds [1-39] were evaluated for their antibacterial activity against 12 Gram-positive and 16 Gram-negative bacteria and on the basis of the primary screening results, their activity in relation to structure was established. It was found that the substitution of hydrogen in catechol with alkyl groups generally increased the activity and the order of increase depended on the length of the alkyl substituents. With the Gram-positive bacteria an increase in activity was noted with increasing length of the alkyl chain. Among the straight chain monoalkyl derivatives, monononyl catechol inhibited the growth of a maximum number of bacteria whereas in case of Gram-negative organisms mono-2-heptyl catechol was found to be the most active. On the other hand, substitution of one benzyl group showed a pronounced activity against Gram-positive bacteria, specially *C. diptleriae* Cxerosis, *St. pyngenes* S. curette *S. eider*-midis and *B. bronchoseptica*. The same derivative inhibited the growth of only two Gram-negative bacteria *Kl. pneumoni* and *Sh. flexneri*. The data further show that introduction of one benzyl group reduced the activity against Gram-negative bacteria while the same moiety enhanced the activity against Gram-positive bacteria. The second benzyl group reduces the activity against both Gram-positive and Gram-negative bacteria (Table I).

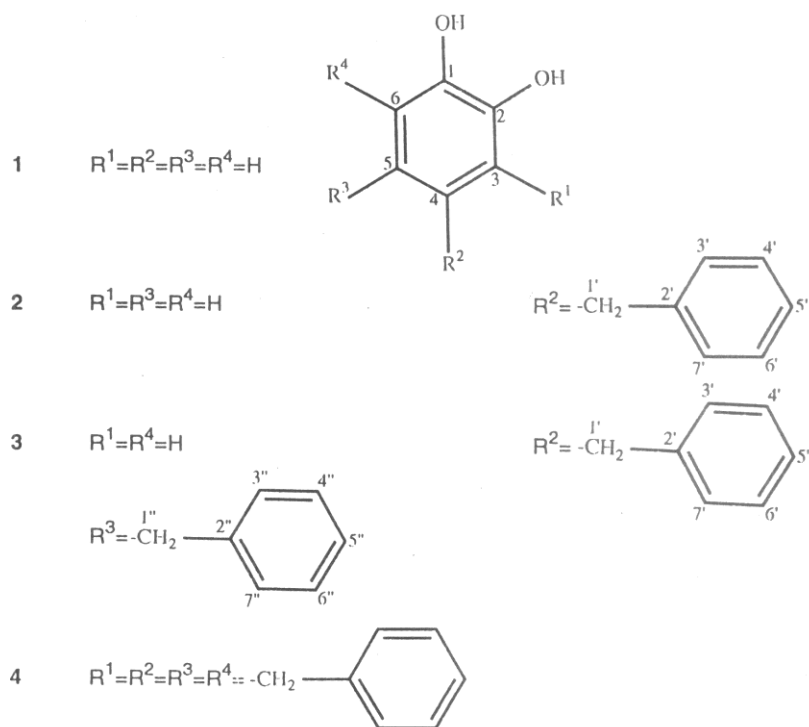
Minimum inhibitory concentration of six compounds was determined against 10 Gram-positive and 8 Gram-negative bacteria. 4,5-di-(2-heptyl)-catechol was found most effective against a number of Gram-positive organisms and its MIC ranged from >100 $\mu\text{g/ml}$ to 10 $\mu\text{g/ml}$, while the MIC of other compounds was found >103 $\mu\text{g/ml}$, (Table II).

Cytotoxicity Test

The cytotoxicity test for compounds [1-39] was performed by brine shrimp assays (Meyer *et al*, 1982). Generally the monoalkyl derivatives of pyrocatechol possess maximum toxicity as compared to di- and tetra-substituted derivatives. Among the mono-substituted compounds activity decreased with increasing length of the alkyl side chain upto the pentyl derivatives, after which

the order of cytotoxicity gradually increased upto the largest alkyl substituent tested i.e. monononyl catechol. As compared to other straight chain derivatives, monobenryl catechol and mono-(2-octyl)catechol showed highest LD₅₀ values i.e. 62.27 and 54.92 µg/ml respectively. Thus mono-(2-octyl)catechol was found to possess maximum cytotoxicity as compared to other monoalkyl catechols. In the case of dialkyl catechols the activity observed was less than that of monoalkyl catechols. However, among these, maximum cytotoxicity was exhibited by di-(2-octyl)catechol with LD₅₀=56.66 µg/ml. Dibutyl catechol with LD₅₀= 667.76 µg/ml was found to be least active among the dialkylcatechols.

In most of the tetraalkyl catechols the activity was not remarkable. The complete results are reported in Table III.



5	$R^1=R^3=R^4=H$	$R^2=-CH_2-(CH_2)_7-CH_3$
6	$R^1=R^4=H$	$R^2=R^3=-CH_2-(CH_2)_7-CH_3$
7	$R^1=R^2=R^3=R^4=-CH_2-(CH_2)_7-CH_3$	
8	$R^1=R^3=R^4=H$	$R^2=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_5-CH_3$
9	$R^1=R^4=H$	$R^2=R^3=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_5-CH_3$
10	$R^1=R^2=R^3=R^4=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_5-CH_3$	
11	$R^1=R^3=R^4=H$	$R^2=-\overset{\text{CH}_2-CH_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$
12	$R^1=R^4=H$	$R^2=R^3=-\overset{\text{CH}_2-CH_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$
13	$R^1=R^2=R^3=R^4=-\overset{\text{CH}_2-CH_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$	
14	$R^1=R^3=R^4=H$	$R^2=-CH_2-(CH_2)_5-CH_3$
15	$R^1=R^4=H$	$R^2=R^3=-CH_2-(CH_2)_5-CH_3$
16	$R^1=R^2=R^3=R^4=-CH_2-(CH_2)_5-CH_3$	
17	$R^1=R^3=R^4=H$	$R^2=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$
18	$R^1=R^4=H$	$R^2=R^3=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$
19	$R^1=R^2=R^3=R^4=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_4-CH_3$	
20	$R^1=R^3=R^4=H$	$R^2=-CH_2-(CH_2)_4-CH_3$
21	$R^1=R^4=H$	$R^2=R^3=-CH_2-(CH_2)_4-CH_3$
22	$R^1=R^2=R^3=R^4=-CH_2-(CH_2)_4-CH_3$	
23	$R^1=R^3=R^4=H$	$R^2=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(CH_2)_3-CH_3$

24	$R^1=R^4=H$	$R^2=R^3=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(\text{CH}_2)_3-\text{CH}_3$
25	$R^1=R^2=R^3=R^4=-\overset{\text{CH}_3}{\underset{ }{\text{CH}}}-(\text{CH}_2)_3-\text{CH}_3$	
26	$R^1=R^3=R^4=H$	$R^2=-\overset{\text{CH}_2\text{-CH}_3}{\underset{ }{\text{CH}}}-(\text{CH}_2)_2-\text{CH}_3$
27	$R^1=R^4=H$	$R^2=R^3=-\overset{\text{CH}_2\text{-CH}_3}{\underset{ }{\text{CH}}}-(\text{CH}_2)_2-\text{CH}_3$
28	$R^1=R^2=R^3=R^4=-\overset{\text{CH}_2\text{-CH}_3}{\underset{ }{\text{CH}}}-(\text{CH}_2)_2-\text{CH}_3$	
29	$R^1=R^3=R^4=H$	$R^2=-\text{CH}_2-(\text{CH}_2)_3-\text{CH}_3$
30	$R^1=R^4=H$	$R^2=R^3=-\text{CH}_2-(\text{CH}_2)_3-\text{CH}_3$
31	$R^1=R^2=R^3=R^4=-\text{CH}_2-(\text{CH}_2)_3-\text{CH}_3$	
32	$R^1=R^3=R^4=H$	$R^2=-\text{CH}_2-(\text{CH}_2)_2-\text{CH}_3$
33	$R^1=R^4=H$	$R^2=R^3=-\text{CH}_2-(\text{CH}_2)_2-\text{CH}_3$
34	$R^1=R^2=R^3=R^4=-\text{CH}_2-(\text{CH}_2)_2-\text{CH}_3$	
35	$R^1=R^3=R^4=H$	$R^2=-\text{CH}_2-\text{CH}_2-\text{CH}_3$
36	$R^1=R^4=H$	$R^2=R^3=-\text{CH}_2-\text{CH}_2-\text{CH}_3$
37	$R^1=R^2=R^3=R^4=-\text{CH}_2-\text{CH}_2-\text{CH}_3$	
38	$R^1=R^3=R^4=H$	$R^2=-\text{CH}_2-\text{CH}_3$
39	$R^1=R^3=R^4=H$	$R^2=-\text{CH}_3$

Table-1. Screening of Catechol and its Derivatives for Anti-Bacterial Activity *in vitro* (Zones of inhibitions in millimeters of compounds) (1-13).

Compound Number	1	2	3	4	5	6	7	8	9	10	11	12	13
GRAM NEGATIVE													
<i>Salmonella typhi</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella typhi Para A</i>	0	10	0	10	14	10	10	0	0	0	0	10	0
<i>Salmonella typhi Para B</i>	0	-	-	-	-	-	-	-	-	-	-	-	-
<i>Salmonella typhimurium</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella gallinarum</i>	0	10	0	0	10	0	0	0	0	0	0	0	0
<i>Salmonella pullorum</i>	10	10	0	0	0	0	0	0	0	0	0	0	0
<i>Shigella dysenteriae</i>	12	0	0	0	0	0	0	0	0	0	0	0	0
<i>Shigella flexneri</i>	16	22	0	18	22	14	10	0	0	22	0	0	0
<i>Shigella sonnei</i>	6	-	-	-	-	-	-	-	-	-	-	-	-
<i>Shigella boydii</i>	8	-	-	-	-	-	-	-	-	-	-	-	-
<i>Entamoeba coli</i>	0	-	-	-	-	-	-	-	-	-	-	-	-
<i>Enterobacter aerogenes</i>	11	0	0	0	0	0	0	0	0	0	0	0	0
<i>Enterobacter cloacae</i>	12	-	-	-	-	-	-	-	-	-	-	-	-
<i>Klebsiella pneumoniae</i>	16	42	20	20	30	30	24	0	18	0	28	18	10
<i>Klebsiella ozaenae</i>	18	10	10	15	16	12	12	-	0	0	0	28	19
<i>Pseudomonas aeruginosa</i>	8	-	-	-	-	-	-	-	-	-	-	-	-
<i>Vibrio cholerae</i>	10	-	-	-	-	-	-	-	-	-	-	-	-
<i>Vibrio parahaemolyticus</i>	11	-	-	-	-	-	-	-	-	-	-	-	-
<i>Proteus vulgaris</i>	16	-	-	-	-	-	-	-	-	-	-	-	-
<i>Proteus mirabilis</i>	12	-	-	-	-	-	-	-	-	-	-	-	-
<i>Serratia marescens</i>	18	0	0	0	0	0	0	0	0	0	0	0	0
<i>Aeromonas hydrophila</i>	8	0	0	0	0	0	20	10	0	0	0	0	0
<i>Acinetobacter calcoaceticus</i>	18	0	0	0	0	0	0	0	0	0	0	0	0
<i>Citrobacter freundii</i>	8	0	0	0	0	0	0	0	0	0	0	0	0
GRAM POSITIVE													
<i>Corynebacterium diphtheriae</i>	11	32	12	28	36	20	12	0	11	0	14	0	0
<i>Corynebacterium hoffmanii</i>	12	21	13	14	20	16	15	0	0	0	10	0	0
<i>Corynebacterium xerosis</i>	9	28	0	26	16	12	16	0	10	0	0	10	9
<i>Streptococcus pyogenes</i>	12	32	14	30	28	20	16	0	13	20	21	6	0
<i>Streptococcus faecalis</i>	15	25	10	12	16	13	10	0	16	20	20	0	0
<i>Staphylococcus aureus</i>	16	30	14	22	22	18	20	0	0	0	14	0	6
<i>Staphylococcus epidermidis</i>	18	34	14	25	28	16	18	0	0	0	18	0	0
<i>Bacillus subtilis</i>	12	22	14	14	22	16	15	0	0	0	12	10	0
<i>Bacillus anthracis</i>	14	-	-	-	-	-	-	-	-	-	-	-	-
<i>Bordetella bronchoseptica</i>	12	31	14	20	22	15	14	0	0	0	22	0	0

- Activity not studied

Table 1. Screening of Catechol and its Derivatives for Anti-Bacterial Activity *in vitro* (Zones of inhibitions in millimeters of compounds) (14-26).

Compound Number	14	15	16	17	18	19	20	21	22	23	24	25	26
GRAM NEGATIVE													
<i>Salmonella typhi</i> Para A	18	0	0	18	14	14	14	0	10	0	0	0	18
<i>Salmonella typhi</i> Para B	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella typhimurium</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella pullorum</i>	0	0	0	14	16	0	0	0	0	0	0	0	0
<i>Shigella sonnei</i>	-	-	-	-	-	-	-	-	-	-	0	0	0
<i>Entamoeba coli</i>	0	0	0	0	16	0	0	0	0	0	0	0	0
<i>Enterobacter cloacae</i>	18	12	0	20	36	12	0	0	0	0	12	0	0
<i>Klebsiella ozaenae</i>	12	12	12	24	22	14	10	0	18	14	14	0	0
<i>Pseudomonas aeruginosa</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Proteus vulgaris</i>	18	12	0	20	36	12	11	0	0	14	24	0	18
<i>Serratia marescens</i>	14	0	0	24	20	0	-	0	0	0	0	0	18
<i>Aeromonas hydrophila</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Acinetobacter calcoaceticus</i>	20	18	18	18	20	20	20	0	10	0	20	0	18
GRAM POSITIVE													
<i>Corynebacterium diphtheriae</i>	16	18	10	30	20	12	0	0	0	14	12	0	0
<i>Corynebacterium hoffmanii</i>	10	0	0	14	20	0	0	0	0	0	0	0	0
<i>Corynebacterium xerosis</i>	20	20	12	20	20	18	18	16	0	20	20	0	16
<i>Streptococcus pyogenes</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Streptococcus faecalis</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Staphylococcus aureus</i>	14	12	10	20	0	0	14	0	0	16	20	0	14
<i>Staphylococcus epidermidis</i>	22	12	0	22	20	12	20	12	0	24	20	0	18
<i>Bacillus subtilis</i>	18	13	13	18	18	0	12	0	0	15	13	0	0
<i>Bacillus anthracis</i>	20	0	0	28	20	0	18	0	0	17	17	0	15
<i>Bordetella bronchiseptica</i>	20	20	24	24	24	30	30	0	16	18	20	0	28
<i>Listeria monocytogenes</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Listeria ivanovii</i>	0	0	0	0	0	0	0	0	0	0	0	0	0

- Activity not studied

Table 1. Screening of Catechol and its Derivatives for Anti-Bacterial Activity *in vitro* (Zones of inhibitions in millimeters of compounds) (27-39)

Compound Number	27	28	29	30	31	32	33	34	35	36	37	38	39
GRAM NEGATIVE													
<i>Salmonella typhi</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella typhi</i> Para A	12	10	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella typhi</i> Para B	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella typhimurium</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella gallinarum</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Salmonella pullorum</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Shigella dysenteriae</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Shigella flexneri</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Shigella sonnei</i>	0	0	20	16	13	17	14	10	19	14	13	11	16
<i>Shigella boydii</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Entamoeba coli</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Enterobacter aerogenes</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Enterobacter cloacae</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Klebsiella pneumoniae</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Klebsiella ozaenae</i>	0	0	15	16	10	16	14	12	16	11	14	12	12
<i>Pseudomonas aeruginosa</i>	0	-	0	0	0	0	0	0	0	0	0	0	0
<i>Vibrio cholerae</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Vibrio parahaemolyticus</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Proteus vulgaris</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Proteus mirabilis</i>	-	-	0	0	0	0	0	0	0	0	0	0	0
<i>Serratia marescens</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Aeromonas hydrophila</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Acinetobacter calcoaceticus</i>	10	24	16	18	11	17	17	16	18	13	15	14	15
<i>Citrobacter freundii</i>	-	-	15	16	12	15	16	15	18	15	14	14	12
GRAM POSITIVE													
<i>Corynebacterium diphtheriae</i>	0	12	11	13	10	9	12	10	10	10	11	10	11
<i>Corynebacterium hoffmanii</i>	0	0	12	15	10	12	12	12	14	12	11	11	11
<i>Corynebacterium xerosis</i>	0	10	9	12	9	12	13	10	12	10	9	9	10
<i>Streptococcus pyogenes</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Streptococcus faecalis</i>	0	0	11	13	9	12	11	10	10	10	1	11	10
<i>Staphylococcus aureus</i>	0	0	13	12	10	12	12	13	12	12	16	12	10
<i>Staphylococcus epidermidis</i>	16	0	18	21	10	17	22	16	21	17	16	14	15
<i>Bacillus subtilis</i>	0	0	16	16	11	15	15	14	18	12	16	12	14
<i>Bacillus ntracis</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Bordetella bronchoseptica</i>	0	20	19	17	14	18	18	15	17	16	18	15	16
<i>Listeria monocytogenes</i>	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>Listeria ivanovii</i>	0	0	0	0	0	0	0	0	0	0	0	0	0

-Activity not studied

Table 2. Minimum Inhibitory Concentration of Catechol and its Derivatives ($\mu\text{g/ml}$) of compounds (1,2,5,17,18,20).

Compound Number	1	2	5	17	18	20
GRAM NEGATIVE						
<i>Salmonella typhi</i> Para A	>100	-	-	>100	-	-
<i>Shigella flexneri</i>	>100	>100	>100	-	-	-
<i>Enterobacter cloacae</i>	>100	-	-	>100	>100	-
<i>Klebsiella pneumoniae</i>	>100	>100	>100	-	-	-
<i>Klebsiella ozaenae</i>	>100	-	-	100	25	-
<i>Proteus vulgaris</i>	>100	-	-	>100	>100	-
<i>Serratia marescens</i>	>100	-	-	>100	>100	-
<i>Acinetobacter calcoaceticus</i>	>100	-	-	25	10	>100
GRAM POSITIVE						
<i>Corynebacterium diphtheriae</i>	>100	>100	>100	100	10	-
<i>Corynebacterium hoffmanii</i>	>100	>100	100	>100	25	-
<i>Corynebacterium xerosis</i>	>100	>100	-	>100	10	>100
<i>Streptococcus pyogenes</i>	>100	>100	100	25	10	-
<i>Streptococcus faecalis</i>	>100	>100	-	>100	10	-
<i>Staphylococcus aureus</i>	>100	>100	>100	>100	100	-
<i>Staphylococcus epidermidis</i>	>100	-	100	-	-	>100
<i>Bacillus subtilis</i>	>100	>100	50	50	10	-
<i>Bacillus anthracis</i>	>100	-	-	10	10	100
<i>Bordetella bronchoseptica</i>	>100	>100	100	25	10	-

- Activity not studied

Compound No.	Compound Name	LD ₅₀ g/ml
14	4-Heptyl catechol	151.59
15	4,5-Diheptyl catechol	149.12
16	3,4,5,6-Tetraheptyl catechol	> 1000
17	4-(2-Heptyl) catechol	122.19
18	4,5-Di-(2-heptyl) catechol	> 1000
19	3,4,5,6-Tetra-(2-heptyl) catechol	> 1000
20	4-Hexyl catechol	113.91
21	4,5-Dihexyl catechol	203.29
22	3,4,5,6-Tetrahexyl catechol	> 1000
23	4-(2-Hexyl) catechol	115.31
24	4,5-Di-(2-hexyl) catechol	415.50
25	3,4,5,6-Tetra-(2-hexyl) catechol	> 1000
26	4-(3-Hexyl) catechol	446.37
27	4,5-Di-(3-hexyl) catechol	> 1000
28	3,4,5,6-Tetra-(3-hexyl) catechol	> 1000
29	4-Pentyl catechol	173.00
30	4,5-Dipentyl catechol	464.33
31	3,4,5,6-Tetrapentyl catechol	> 1000
32	4-Butyl catechol	122.61
33	4,5-Dibutyl catechol	667.76
34	3,4,5,6-Tetrabutyl catechol	> 1000
35	4-Propyl catechol	117.72
36	4,5-Dipropyl catechol	264.30
37	3,4,5,6-Tetrapropyl catechol	> 1000
38	4-Ethyl catechol	88.56
39	4-Methyl catechol	59.94

References

- Cavalca, L., Gilardi, F. (1955). Molecular structure and hyperglycemic effect of catecholamines. *Attisoc. lombardo Sci. med boil*, **10**: 154-158.
- De Rapp, R. S., Kastl, L., Furst, A. (1969). Biochemical and behavioral effect of some substituted catechol. *Arch. Jut. Pharmacodyn. Ther.*, **181**: 127-132.
- Gumbinger H. G., Winterhoff, H., Sourgens, H., Kemper, F. It, Wylde R. (1981). Formation of compounds with antigonadotropic activity from inactive phenolic precursors. *Contraception*. **23** :661-666.
- Hasegawa, E, Sakamoto, S., Nagayama K., Fujita, A. (1956). Thiamine-decomposing activity of Bavonoids and phenols. *J. Vitiatio.*, **2** : 31-38.
- Horman, I., Brambilla, E. (1982). The alleged antithiamine activity of o-diphenols: an artefact of oxygen in the thiochrome method. *Int. J. Victim. Nutr Res.*, **52** : 133-141.
- Malama, A. A., Slavinskaya, N. P., Cherenkevich, A. N. (1974). Antibiotic properties of melanin pigments. *Antibiotic*. **19**: 324-327.
- Meyer, B. N, Ferrigni, N. R., Putnam, J. E, Jacobsen, L. B., Nichols, D. E.; McLaughlin, J. L. (1982). Brine shrimp: A convenient general bioassay for active plant constituents. *Planta Medico*. **45**: 31-34.
- Miller, E., Hartung, W. H., Rock, H. J., Crossley, F. S. (1938). Antiseptics: Alkyl catechol. *J. Am. Chem. Soc.*, **60** : 740.
- Moroz, P. A., Komissarenko, N. F. (1983). Allelopathic activity of several phenolic compounds. *Rol. Toksinov Rastik, Mikrob. Proiskhozhd. Allelopatii*. 118-122.
- Pashin, Yu. V., Bentkhen, T. I, Bakhitova L. M. (1986). Comparative study of the antimutagenic activity of diphenols. *Genetika*. **22**: 709-711.
- Still, W. C., Kahn, M., Mitra A. (1978). Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.*, **43** : 2923-2925.
- Tarasova, L. S. (1966). Poly phenols as potential antisclerotic agents. *Fenol'nye Soedin. Ikh Biol. Funkts, Mater. Vies. Slink, 1st* . 377-383.
- Winterhoff, H, Gumbinger, H. G., Sourgens, H. (1988). On the antigonadotropic activity of *Lithospermum* and *Lycopus* species and some of their phenolic constituents. *Planta Medico*. **54**: 101-106.