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Chemical and Biological Studies of 2-(2'- pyridyl) Benzimidazole and Its Synthesized Derivatives

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ABSTRACT

A series of 2-(2'-Pyridyl) benzimidazole (Ia) compound was synthesized and derivative compounds **1-11** were characterized through physical and spectral data was carried out by UV, IR, Mass and nuclear magnetic resonance spectroscopy (^{1}H NMR). All these synthesized compounds were screened *in vitro* at different doses for their phytotoxicity and nematicidal activity against Rootknot nematode *Meloidogyne incognita*. The activities obtained were compared with the reference drugs as, Paraquat for phytotoxic and Furadan for anthelmintic activity.

Keywords: *Benzimidazole, Phytotoxicity, Nematicidal activity, Meloidogyne incognita*

Introduction

Benzimidazole is an important pharmacophore and a heterocyclic aromatic organic compound with privileged structure in medicinal chemistry. This compound is the fusion of benzene and imidazole having bicyclic in nature. It is an important moiety of choice which possesses many biological and pharmacological properties. The most prominent benzimidazole compound in nature is N-ribosyl-dimethylbenzimidazole, which serves as an axial ligand for cobalt in vitaminB_{12} [1].

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Benzimidazoles are involved in a great variety of biological processes. Some of their polyfunctional derivatives have been proved as bacteriostats or bactericides, as well as fungicides [2]. This ring system was proved to be very important as it is involved in numerous antiparasitic, antitumoral and antiviral drugs [3,4]. It is also well known that these molecules are present in a variety of antioxidant and antiallergic agents [5-7]. Many derivatives of benzimidazole show antiparasitic [15] and antiprotozoal [8] activities. In recent years, benzimidazole derivatives have attracted particular interest due to their anticancer activity or as potential *in vitro* anti-HIV agents [9, 10].

In view of the biological significance of benzimidazoles it was of immense interest to synthesize and biologically evaluate their derivatives. The synthesized compounds were subjected to evaluate nematicidal and phytotoxic activities of new derivatives of benzimidazoles.

Materials and Methods

Reagents were purchased from Aldrich Chemical Company. The solvents were of analytical grade from E. Merck, Germany and were purified by a standard method i.e. distilled three times prior to use. TLC was examined by using pre-coated silica gel, GF-254. Spots were visualized under ultraviolet light at (254 nm and 366 nm) using HP-UV/Visible lamp (Dessaga Heidelberg), as well as in iodine vapors were also employed for the detection of spots. On GallenKamp melting point apparatus all melting points were determined and are uncorrected structure elucidation of derivative of benzimidazole were performed by using various spectroscopic techniques. Electronic absorption spectra were recorded in methanol on shimadzu uv/visible 1601 spectrophotometer. Infrared (IR) spectra were carried out on Avatar 330 FTIR Thermo Nicolet Spectrometer. Mass spectra were determined under electron impact (EI) condition using varian Massen spectrometer MAT 312, MAT 113D MASPEC system. The ^{1}H-NMR measurements were performed on a Bruker AM spectrometer operating at 400 MHz. The chemical shift values are reported in ppm (δ), relative to tetramethyl silane as an internal standard and the coupling constant (J) are in Hz.

Synthesis of 2-(2'- Pyridyl) Benzimidazole derivatives

2-(2'-Pyridyl) benzimidazole **(Ia)** and the corresponding substituted phenacyl halide in equimolar quantities (0.01 mole) were dissolved separately in acetone (15-20 ml) and mixed together in a round bottom flask (Scheme 1). Reaction mixtures were refluxed on a water bath for about 5-6 h. The progress of the reaction was monitored through thin layer chromatography using the solvent system, $CHCl_3$-MeOH (in varying proportions). The precipitates were filtered off, and washed with warm acetone to remove the un-reacted starting material. The products thus obtained were re-crystallized from organic solvents. The pure compounds were dried in vacuum over anhydrous calcium sulphate.

Nematicidal Activity

At the Laboratory of National Nematological Research Centre (NNRC), University of Karachi, Pakistan the experimental study was investigated. From the different sources (which were susceptible / specific host plants), maintained under net house conditions at NNRC, stock culture of Rootknot nematode *Meloidogyne incognita* was obtained.

Egg masses of M. *incognita* picked by hand with a fine forceps from an infected egg plant root whose surface was sterilized in distilled water and was then transferred to a small coarse sieve or nylon net lined with tissue paper to cover the bottom of the sieve or net that was placed on a plastic tray or plate containing sufficient amount of water. The tray was incubated at room temperature (27 5°C) for 48 hours in order to get regular supply of the inoculum for the experiment.

Stock solutions (1mg/ml) of pure compounds were prepared in 5% DMSO (Merck, Germany). To find the nematicidal activity of synthesized compounds of class benzimidazole, 100 freshly hatched 2nd stage Juveniles were picked-up from tray and were introduced separately in different stock solutions of pure compounds. The movements of the nematodes were checked by touching them with the hair needles after 24, 48 and 72 hours, the juveniles were observed for mortality under stereoscopic microscope. After 72 hours of exposure period, nematodes showing mortality were transferred to other cavity block containing distilled water and after 24 hours, their mortality was confirmed by touching the nematodes [11,12]. The standard deviation and % age mortality was calculated and the treatment was replicated thrice for the determination of average percentage of mortality. Commercially available nematicide, furadan showed 100% mortality at the same concentration used in the present study as a standard drug for comparison. In control treatment (5% DMSO), mortality was not observed after 24 hours; however the mortality of root knot juveniles were negligible after 72 hours [13].

Phytotoxicity Bioassay

This assay can quickly determine the phytotoxic bioassay of the synthesized compounds against *Lemna minor*. It is a floating aquatic plant, used as a tool to monitor the effects of different chemical constituents as inhibitors or stimulators. The selected method consisted mainly of *Lemna minor* and E-medium (mixture of various constituents in distilled water). *Lemna minor* Linn. breed and collected from the esteemed premises of University of Karachi by standard protocol. The Lemna bioassay was carried out by the modified protocol by Mclaughlin [14].The fronds were first washed with water and then inorganic sterilized E-Medium having pH 5.5 to 6.0 adjusted by adding KOH pellets proceeding to use. The synthesized compounds doses of 10, 100 and 1000µg/ml have been inoculated in three flasks, overnight allowing the solvent to evaporate. On the next day 20 fronds in each flask along with 20 ml of E. medium had been kept in Fisons Fi-Totron 600 H growth cabinet, 9000 lux intensity, 56±10 relative humidity and 12 h day length for 7 days at 27-29°C while examination had conducted daily during incubation. On 7th day to determine growth inhibition or proliferation of fronds in the flasks numbers of fronds per doses were counted. Standard herbicide 'Paraquat' was used in this study, which have the level of toxicity (0.015µg/ml) against duckweed [13].

Results

Synthesis of 2-(2'- Pyridyl) Benzimidazole derivatives

The synthesized compounds **1-11** were characterized through physical and spectral data.

1-[2-(3'-Nitrophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (1)

Light Cream powder; Yield 52 %; mp 250 °C; **UV** $\lambda_{max}^{(MeOH)}$ nm (log ε): 219 (4.02); **IR** (KBr)ν_{max} cm^{-1}: 3018, 1715, 1612, 1576,

1539, 1339; **EIMS** *m/z*: 358 (11), 194 (100), 164 (6), 122 (12), 118 (22); **^{1}H-NMR** (300 MHz, DMSO-d^6); **δ**: 9.01 (1H, d, *J* = 8.0 Hz, H-15), 8.77 (1H, d, *J* = 8.0 Hz, H-12), 8.76 (1H, m, H-2'), 8.62 (1H, m, H-4'), 8.47 (1H, m, H-14), 8.00 (1H, m, H-6'), 7.97 (1H, m, H-5'), 7.94 (1H, dd, *J* = 7.8, 1.4 Hz, H-9),7.71 (1H, m, H-7), 7.38 (1H, m, H-8), 7.32 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 6.98 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 54.06; H, 3.30; N, 12.95. Calcd for $C_{20}H_{14}N_4O_3$ (358): C, 54.08; H, 3.31; N, 12.93 %

1-[2-(3',4'-Dihydroxyphenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium chloride (2)

Grey powder; Yield 30 %; mp 296 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 231 (4.00); **IR** (KBr)ν_{max} cm^{-1}: 3617, 3029, 1716, 1597, 1558, 1339; **EIMS** *m/z*: 346 (10), 194 (100), 151 (22), 133 (18), 109 (10), 91 (25), 77 (14); **^{1}H-NMR** (300 MHz, DMSO-d^6); **δ**: 9.27 (1H, d, *J* = 7.9 Hz, H-12), 8.99 (1H, d, *J* = 8.1 Hz, H-15), 8.44 (1H, m, H-14), 7.70 (1H, m, H-7), 7.50 (1H, dd, *J* = 8.0, 1.5 Hz, H-9), 7.47 (1H, dd, *J* = 8.3, 1.8 Hz, H-6), 7.44 (1H, d, *J* = 1.5 Hz, H-2'), 7.33 (1H, m, H-8), 7.33 (1H, d, *J* = 8.1 Hz, H-5'), 6.98 (1H, dd, *J* = 7.8, 1.5 Hz, H-6'), 6.95 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 58.18; H, 4.23; N, 10.23. Calcd for $C_{20}H_{15}N_3O_3$ (346): C, 58.20; H, 4.25; N, 10.24 %

1-[2-(4'-Chlorophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (3)

Brown crystal; Yield 52 %; mp 278 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 259 (4.11); **IR** (KBr)ν_{max} cm^{-1}: 3040, 1716, 1625, 1554, 1338, 746; **EIMS** *m/z*: 348 (8), 194 (100), 153 (12), 119 (18), 111 (20); **^{1}H-NMR** (400 MHz, DMSO-d^6); **δ**: 9.25 (1H, d, *J* = 7.9 Hz, H-12), 8.98 (1H, d, *J* = 8.1 Hz, H-15), 8.43 (1H, m, H-14), 7.76 (2H, d, *J* = 7.5 Hz, H-3', H-5'), 7.70 (2H, d, *J* = 7.5 Hz, H-2', H-6'), 7.70 (1H, m, H-7), 7.50 (1H, dd, *J* = 8.0, 1.5 Hz, H-9), 7.47 (1H, dd, *J* = 8.0, 1.7 Hz, H-6), 7.32 (1H, m, H-8), 6.95 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 54.96; H, 3.28; N, 9.51. Calcd for $C_{20}H_{14}N_3OCl$ (348): C, 54.98; H, 3.30; N, 9.52 %

1-[2-(2'-Nitrophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (4)

Off white powder; Yield 54 %; mp 210 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 243 (3.98); **IR** (KBr)ν_{max} cm^{-1}: 3029, 1720, 1629, 1580, 1528, 1346; **EIMS** *m/z*: 358 (15), 194 (100), 164 (10), 122 (15), 118 (20); **^{1}H-NMR** (400 MHz, DMSO-d^6); **δ**: 9.00 (1H, d, *J* = 7.9 Hz, H-12), 8.98 (1H, d, *J* = 8.1 Hz, H-15), 8.48 (1H, m, H-14), 7.92 (1H, m, H-5'), 7.79 (1H, m, H-3'), 7.77 (1H, m, H-7), 7.68 (1H, dd, *J* = 8.0, 1.5 Hz, H-9), 7.68 (1H, dd, *J* = 7.0, 1.4 Hz, H-6'), 7.38 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 7.31 (1H, m, H-8), 7.29 (1H, m, H-4'), 6.44 (1H, m, H-13), 5.02 (2H, s, H-7'); Anal. found C, 49.48; H, 3.29; N, 11.54. Calcd for $C_{20}H_{14}N_4O_3$ (358): C, 49.49; H, 3.30; N, 11.52 %

1-[2-(4'-Nitrophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (5)

Golden yellow powder; Yield 50 %; mp 247 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 218 (2.99); **IR** (KBr)ν_{max} cm^{-1}: 3025, 1706, 1631, 1570, 1520, 1344; **EIMS** *m/z*: 358 (11), 194 (100), 164 (12), 122 (18), 118 (22); **^{1}H-NMR** (300 MHz, DMSO-d^6); **δ**: 9.00 (1H, d, *J* = 7.9 Hz, H-12), 8.98 (1H, d, *J* = 8.0 Hz, H-15), 8.47 (1H, m, H-14), 8.40 (2H, d, *J* = 7.9 Hz, H-2', H-6'), 8.35 (2H, d, *J* = 7.9 Hz, H-3', H-5'), 7.77 (1H, m, H-7), 7.65 (1H, dd, *J* = 8.0, 1.5 Hz, H-9), 7.33 (1H, m, H-8), 7.32 (1H, dd, *J* = 8.1, 1.5 Hz, H-6), 6.44 (1H, m, H-13), 5.01 (2H, s, H-7'); Anal. found C, 54.00; H, 3.21; N, 12.53. Calcd for $C_{20}H_{14}N_4O_3$ (358): C, 54.01; H, 3.23; N, 12.54 %

1-[2-(4'-Fluorophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (6)

Off white shiny crystal; Yield 62 %; mp 225 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 248 (4.00); **IR** (KBr)ν_{max} cm^{-1}: 3030, 1698, 1635, 1589, 1337; **EIMS** *m/z*: 331 (9), 194 (100), 137 (17), 119 (11), 95 (15); **^{1}H-NMR** (300 MHz,CD_3OD); **δ**: 9.01 (1H, d, *J* = 7.8 Hz, H-12), 8.96 (1H, d, *J* = 8.0 Hz, H-15), 8.39 (1H, m, H-14), 8.19 (2H, d, *J* = 7.7 Hz, H-2', H-6'), 7.72 (1H, m, H-7), 7.68 (1H, dd, *J* = 8.0, 1.7 Hz, H-9), 7.36 (1H, m, H-8), 7.34 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 7.19 (2H, d, *J* = 7.7 Hz, H-3', H-5'), 6.44 (1H, m, H-13), 5.01 (2H, s, H-7'); Anal. found C, 57.98; H, 3.47; N, 10.04. Calcd for $C_{20}H_{14}N_3OF$ (331): C, 57.99; H, 3.45; N, 10.06 %

1-[2-(2',4'-Difluorophenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (7)

Brown shiny crystal; Yield 30 %; mp 234 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 252 (4.14); **IR** (KBr)ν_{max} cm^{-1}: 3028, 1710, 1639, 1600, 1340, 910; **EIMS** *m/z*: 349 (15), 194 (100), 155 (22), 136 (11), 113 (20), 95 (16); **^{1}H-NMR** (300 MHz, DMSO-d^6); **δ**: 9.00 (1H, d, *J* = 7.8 Hz, H-12), 8.64 (1H, d, *J* = 8.0 Hz, H-15), 8.40 (1H, m, H-14), 7.68 (1H, dd, *J* = 8.0, 1.7 Hz, H-9), 7.65 (1H, m, H-7), 7.64 (1H, d, *J* = 7.3 Hz, H-6'), 7.36 (1H, m, H-8), 7.33 (1H, dd, *J* = 7.9, 1.5 Hz, H-6), 7.25 (2H, dd, *J* = 7.3, 1.4 Hz, H-5'), 7.23 (1H, d, *J* = 1.4 Hz, H-3'), 7.21 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 57.98; H, 3.47; N, 10.04. Calcd for $C_{20}H_{13}N_3OF_2$ (349): C, 57.99; H, 3.45; N, 10.06 %

1-(2-Oxo-2-phenylethyl)-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (8)

Light off white powder; Yield 17 %; mp 206 °C;

UV λ_{max} $^{(MeOH)}$ nm (log **ε**): 312 (4.12); **IR** (KBr)ν_{max} cm^{-1}: 3030, 1730, 1601, 1520, 1339; **EIMS** *m/z*: 313 (9), 194 (100), 119 (18), 77 (11); **^{1}H-NMR** (400 MHz, DMSO-d^6); **δ**: 9.02 (1H, d, *J* = 7.8 Hz, H-12), 8.53 (1H, d, *J* = 8.0 Hz, H-15), 8.50 (1H, m, H-14), 7.68 (1H, dd, *J* = 8.0, 1.7 Hz, H-9),7.64-7.70 (5H, m, H-2'-H-6'), 7.64 (1H, m, H-7), 7.33 (1H, m, H-8), 7.31 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 7.21 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 58.03; H, 3.86; N, 16.83. Calcd for $C_{20}H_{15}N_3O$ (313): C, 58.05; H, 3.88; N, 16.85 %

1-(2-[1',1''-Biphenyl]-4-yl-2-oxoethyl)-2-(2-pyridinyl)-1*H*-

benzimidazol-1-ium bromide (9)
Dark off white powder; Yield 50 %; mp 240 °C;

UV $\lambda_{max}^{(MeOH)}$ nm (log ε): 215 (4.12); **IR** (KBr)ν_{max} cm^{-1}: 3015, 1690, 1610, 1539, 1337; **EIMS** *m/z*: 389 (8), 195 (22), 194 (100), 153 (15), 118 (28); **^{1}H-NMR** (300 MHz, CD_3OD); δ: 9.00 (1H, d, *J* = 7.8 Hz, H-12), 8.50 (1H, m, H-14), 8.40 (1H, d, *J* = 8.0 Hz, H-15), 7.93 (2H, d, *J* = 7.4, H-2', H-6'), 7.76 (2H, d, *J* = 7.4 Hz, H-3', H-5'), 7.67 (1H, m, H-7), 7.67 (1H, dd, *J* = 8.0, 1.7 Hz, H-9), 7.36-7.67 (5H, m, H-2"-H-6"), 7.36 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 7.33 (1H, m, H-8), 7.21 (1H, m, H-13), 5.00 (2H, s, H-7'); Anal. found C, 64.89; H, 3.98; N, 8.68. Calcd for $C_{26}H_{19}N_3O$ (389): C, 64.90; H, 3.99; N, 8.65 %

1-[2-(4'-Methoxyphenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (10)
Light grey powder; Yield 56 %; mp 230 °C;

UV $\lambda_{max}^{(MeOH)}$ nm (log ε): 293 (3.12); **IR** (KBr)$\nu_{max}cm^{-1}$: 3008, 1620, 1571, 1340, 1108; **EIMS** *m/z*: 343 (11), 194 (100), 149 (22), 118 (19), 107 (11), 77 (17); **^{1}H-NMR** (300 MHz, CD_3OD); δ: 9.00 (1H, d, *J* = 7.8 Hz, H-12), 8.50 (1H, m, H-14), 8.34 (1H, d, *J* = 7.9 Hz, H-15), 7.85 (2H, d, *J* = 7.1, H-2', H-6'), 7.69 (1H, m, H-7), 7.67 (1H, dd, *J* = 8.0, 1.5 Hz, H-9),7.36 (1H, dd, *J* = 7.9, 1.5 Hz, H-6), 7.33 (1H, m, H-8), 7.15 (1H, m, H-13), 6.50 (2H, d, *J* = 7.1 Hz, H-3', H-5'), 5.01 (2H, s, H-7'), 3.60 (3H, s, OMe-4'); Anal. found C, 57.23; H, 4.35; N, 10.24. Calcd for $C_{21}H_{17}N_3O_2$ (343): C, 57.26; H, 4.38; N, 10.26 %

1-[2-(2',5'-Dimethoxyphenyl)-2-oxoethyl]-2-(2-pyridinyl)-1*H*-benzimidazol-1-ium bromide (11)
Off white powder; Yield 22 %; mp 204 °C;

UV $\lambda_{max}^{(MeOH)}$ nm (log ε): 330 (4.00); **IR** (KBr)ν_{max} cm^{-1}: 3010, 1683, 1625, 1338, 1110; **EIMS** *m/z*: 373 (8), 194 (100), 179 (18), 148 (20), 137 (21), 117 (12), 106 (18); **^{1}H-NMR** (400 MHz, DMSO-d^6); δ: 9.02 (1H, d, *J* = 7.7 Hz, H-12), 8.43 (1H, m, H-14), 8.39 (1H, d, *J* = 7.9 Hz, H-15), 7.71 (1H, d, *J* = 7.0 Hz, H-3'), 7.70 (1H, dd, *J* = 7.0, 1.4 Hz, H-4'), 7.69 (1H, m, H-7), 7.30 (1H, m, H-8), 7.67 (1H, dd, *J* = 7.9, 1.6 Hz, H-9), 7.37 (1H, dd, *J* = 8.0, 1.5 Hz, H-6), 7.31 (1H, s, H-6'), 7.15 (1H, m, H-13), 5.01 (2H, s, H-7'), 4.00 (3H, s, OMe-2'), 3.75 (3H, s, OMe-5'); Anal. found C, 56.12; H, 4.28; N, 9.41. Calcd for $C_{22}H_{22}N_3O_3$ (373): C, 56.14; H, 4.29; N, 9.39 %.

Discussion

Nematicidal Activity
Root-knot nematodes (*Meloidogyne incognita*) are the important plant pests which causes millions of damage each year to vegetables, turf grasses, ornamental plants, and food crops [11]. Efforts to eliminate or minimize the loss caused by nematodes in agricultural settings have typically involved the use of soil fumigation with standard materials such as furadan, chloropicrin, methyl bromide and dazomet which volatilize to spread the active ingredient throughout the soil. Such fumigation materials can be toxic and may create an environmental hazard. Various non fumigant chemicals have also been used, but these too create serious environmental problems and can be highly toxic to humans [12].

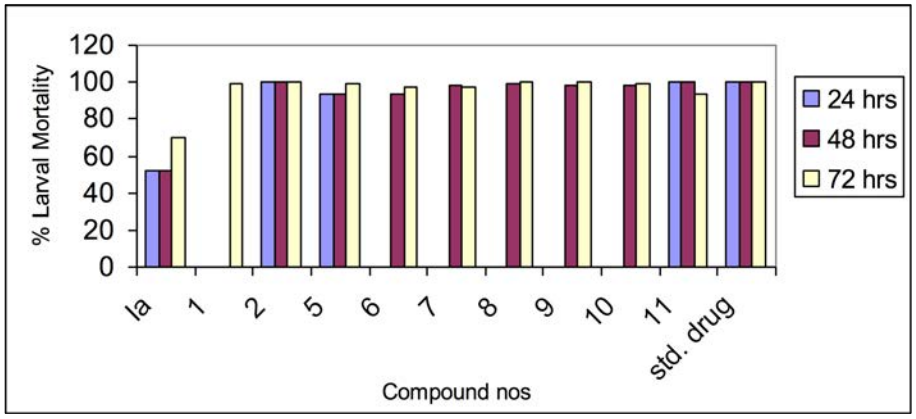
The effect of parent molecule 2-(2´-pyridyl) benzimidazole and its eleven novel derivatives on larval mortality of root knot nematode *Meloidogyne Incognita* was determined after 24 hours, 48 hours and 72 hours at 1 mg/ml concentration. The results of the *in vitro*-experiments were shown in **Table 1 and Graph 1**.

Parent molecule 2-(2´-pyridiyl) benzimidazole showed 50% mortality after 24 hours and 70% mortality after 48 hours and 72 hours, while the derivatives, **2**, **5** and **11** showed highest 100% mortality in the compound at the concentration of 1mg/ml. These compounds showed highest toxicity against *M. incognita* whereas in compounds **3** and **4** juveniles were alive up to 72 hours hence showed non-significant activity. It was interesting to note that the compounds, **6**, **7**, **8**, **9** and **10** showed no activity after 24 hours while the same compounds exhibited 99-100% mortality after 48 hours and 72 hours. It was found that the compound **5** showed 93.3% mortality after 24

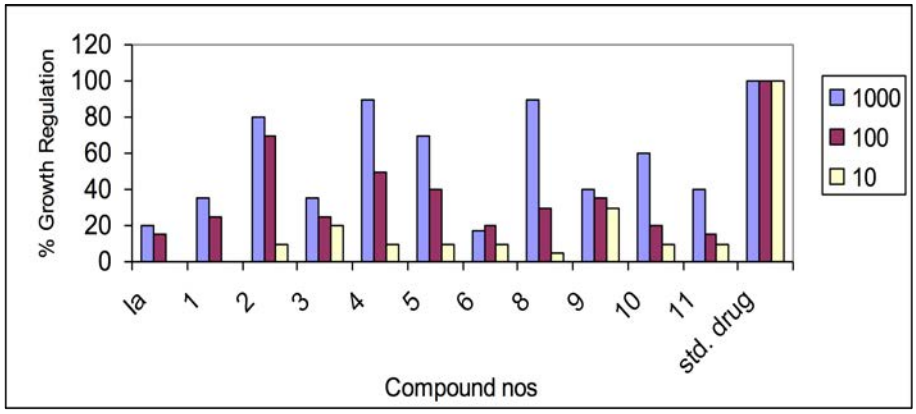
Table 1: Larval mortality of parent molecules 2-(2´-pyridyl) benzimidazole (Ia) and its derivatives (1–11) against *M. incognita*

Compound No	Nematicidal activity (1mg/ml)		
	24 hours	48 hours	72 hours
Ia	51.6±2.88	51.6±2.88	70±0
1	0	0	99±0
2	100±0	100±0	100±0
3	0.0	0	0
4	0.0	0	0
5	93.3±4.1	94±3.62	99.6±0.57
6	0.0	94±3.66	97.6±2.51
7	0.0	98.3±2.82	100±0
8	0.0	99±1	100±0
9	0.0	98.3±2	99±1
10	0.0	98.3±2.88	99.3±1.1
11	100±0	100±0	100±0
Furadan	100±0.41	100±0.41	100±0.9

Graph 1: Larval mortality of parent molecule 2-(2´-pyridyl) benzimidazole (Ia) and its derivatives (1 - 11)



Graph 2: Phytotoxic Activity of 2-(2´-pyridyl) benzimidazole (Ia) and its derivatives (1-11) by Lemna Bioassay



hours, 94% mortality after 48 hours and 99.6% mortality after 72 hours. This research finding showed that the metabolites might be responsible to produce that response. The reason was unknown and needed further investigation.

Phytotoxic Activity

Phytotoxic activities of all newly synthesized derivatives of compound 2-(2´-Pyridyl) benzimidazole were carried out by using the modified method given by McLaughlin et al 1991. The parent molecule and its derivatives showed phytotoxic activity against *Lemna* plant. The screening was performed at three levels of concentrations i.e. 10, 100, 1000µg/ml. This activity was found more significant at high concentration. The results of phytotoxic bioassay are mentioned in **Graph 2.**

The parent compound **Ia** showed no significant activities at all concentration levels, however the derivatives, **1** and **3** showed low to moderate activity 35% and 25% at the concentrations of 1000 and 100 µg/ml concentration respectively while compounds **2,4,5 and 8** showed 80, 90, 70 and 90% growth regulation at 1000 µg/ml level respectively and all these compounds exhibited low activity at 10 µg/ml.

Compound **2,** having two hydroxyl groups at *meta* and *para* positions in the phenyl nucleus showed 80% growth regulation whereas compound **4** having a nitro group at *ortho* position exhibited 90% growth regulation. Therefore, it can be predicted that the nitro group might be more responsible for phytotoxic activity as compared to the hydroxyl group. Similarly, the compound **8,** which contained unsubstituted phenyl moiety, also expressed significant result which was comparable to that of the nitro group containing compound. The enhanced activity of this compound might be due to the additional aromatic ring in its parent structure.

Among the methoxy derivatives compound **10,** containing one methoxy group and compound **11** containing two methoxy groups expressed different responses. Compound **10,** 1-[2-(4´-methoxyphenyl)-2-oxo-ethyl]-2-(2´-pyridinyl)-1*H*-benzimidazol-1-ium bromide with one methoxy group was more active 60% than that of the compound **11,** 1-[2-(2´, 5´dimethoxyphenyl)-2-oxo-ethyl]-2-(2´-pyridinyl)-1*H*-benzimidazole- 1- ium bromide 40% at the same concentration 1000 µg/ml. It meant introduction of one more methyl group in compound **11,** attenuated its activity.

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