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NOTES

Anticonvulsant Activity of Some Metal Chelates Derived from 5,5-Diphenyl-2,4-Imidazolidinedione

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Metal chelates of 5,5-diphenyl-2,4-imidazolidinedione with Cu(II), Co(II) and Ni(II) of the type $ML_2 \cdot (H_2O)_2$ (where M = Cu(II), Co(II) and Ni(II), L = 5,5 diphenyl-2,4 imidazolidinedione) have been prepared and characterised on the basis of various physico-chemical data. They have been screened for anticonvulsant activity. Some of them have significant activity.

5,5-Diphenyl-2,4-imidazolidinedione compound is of great medicinal importance[1]; it has an effect in the treatment of grand mal epilepsy and psychomotor epilepsy. It has also a membrane stabilizing effect and is useful in the treatment of cardiac arrhythmia[2, 3]. A variety of recent observations indicate that the metal complexes are more potent and less toxic in many cases as compared to the parent drug[4–6]. We therefore have undertaken the investigation of the interaction of Cu(II), Co(II) and Ni(II) metal ions with 5,5-diphenyl-2,4-imidazolidinedione, and to see the change in activity of drug due to complex formation.

Metal chlorides used were of AnalaR/BDH grade; ligand 5,5-diphenyl-2,4 imidazolidinedione was obtained by courtesy of Parke Davis India Ltd., Bombay.

Synthesis of bis-5,5-diphenyl-2,4-imidazolidinedionatodiaquo copper(II) (B_1)

To a hot aqueous solution of copper(II) chloride, a solution of the ligand in the same solvent was added in 1 : 2 stoichiometric ratio. After refluxing over water bath for 1 h a solid of brown crystals was precipitated. The resulting solid was dried over anhydrous $CaCl_2$ and then at 110°C for 1 h; m.p. 208° (Found: C, 60.18,; H, 4.45; N, 9.48. $Cu(C_{15}H_{11}N_2O_2)_2(H_2O)_2$ requires C, 59.98; H, 4.30; N, 9.23%).

Synthesis of bis-5,5-diphenyl-2,4-imidazolidinedionatodiaquo cobalt(II) (B_2)

To an aqueous solution of cobalt(II) chloride, a solution of the ligand in the same solvent was added in 1 : 2 stoichiometric ratio. After refluxing over water bath for 1 h a solid of bluish grey colour was precipitated. The resulting solid

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was recrystallised and dried over anhydrous $CaCl_2$ and then at 110° for an hour; m.p. 161° (Found: C, 60.93; H, 4.78; N, 9.48; $Co(C_{15}H_{11}N_2O_2)_2(H_2O)_2$ required C, 60.31; H, 4.45; N, 9.37%).

Synthesis of bis-5,5 diphenyl-2,4 imidazolidinedionatodiaquo nickel(II) (B_3)

To an aqueous solution of nickel(II) chloride, an aqueous solution of ligand was added in 1:2 stoichiometric ratio. After refluxing over water bath for 1 h a solid of light green colour was precipitated. The resulting solid was dried over anhydrous $CaCl_2$ and then at 110°C for 1 h; m.p. 290°C (Found: C, 59.88; H, 4.59; N, 9.29; $Ni(C_{15}H_{11}N_2O_2)_2(H_2O)_2$ required C, 60.33; H, 4.37; N, 9.38%).

The compounds and three metal complexes, *i.e.*, B_1, B_2 and B_3 have been studied for anticonvulsant activity in mice against supramaximal electroshock (48 mA, 0.2 sec induced convulsions at 20 mg/kg i.p. 1 h prior to electroshock test (mice).

Supramaximal electroshock seizure test (mice)

A modification of the method of Swinyard *et al.*[7] was used. The compounds were administered as aqueous suspension in gum acacia in groups of 5 mice each at 20 mg/kg i.p. A current stimulus of 48 mA for 0.2 seconds delivered through ear electrodes produced tonic extension of hind limbs in control mice. Abolution of this response by a compound 1 h after drug pretreatment was taken as the criterion of its anticonvulsant activity.

Compound B (phentytoin) at 20 mg/kg i.p. afforded protection in 70% mice. At this dose B_1 (copper phenytoin) produced protection in 40% mice, B_2 (cobalt phenytoin) in none and B_3 (nickel phenytoin) in 20% mice only.

Among the metal chelates of phenytoin studied copper phenytoin exhibited maximum anticonvulsant activity. In cobalt and nickel phenytoin there was significant reduction or loss of activity. Compared to phenytoin, however, the activity was reduced after metal chelation at 20 mg/kg i.p. in mice.

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