Pharmacological Reports
2009, 61, 245–251
ISSN 1734-1140

Characterization of the anticonvulsant activity of doxepin in various experimental seizure models in mice

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Abstract:
In this paper, the anticonvulsant characteristics of doxepin were evaluated in numerous experimental seizure models, including maximal electroshock (MES)-, pentylenetetrazole (PTZ)-, isoniazid (ISO)-, 3-mercaptopropionic acid (3-MP)-, bicuculline (BIC)-, thiosemicarbazide (THIO)-, and strychnine (STR)-induced seizures. In addition, the acute adverse-effect profile of doxepin with respect to impairment of motor coordination was assessed with a mouse rotarod test. The evaluation of the time-course and dose-response relationships for doxepin provided evidence that the peak maximum anticonvulsant activity and acute adverse effects occurred 5 min after intraperitoneal (*ip*) administration. The results also revealed that doxepin had excellent anticonvulsant activity against maximal electroshock-induced seizures in mice with a median effect value (ED_{50}) of 6.6 mg/kg. The assessment of acute adverse effects in the rotarod test revealed that doxepin induced acute neurotoxicity, and its median toxic dose (TD_{50}) was 26.4 mg/kg. Additionally, doxepin showed anticonvulsant activity in several chemically-induced seizure models, including ISO, 3-MP, BIC, and THI. Based on this study, we can conclude that the antidepressant drug doxepin may be useful for treatment of depression in patients with epilepsy due to its short time to peak maximum anticonvulsant activity after *ip* administration (5 min) and remarkable anticonvulsant activity (6.6 mg/kg).

Key words:
doxepin, maximal electroshock, rotarod test, pentylenetetrazole, 3-mercaptopropionic acid, bicuculline, thiosemicarbazide, strychnine