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Anthocyanins modify diazepam dependence in rats

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Background

Chronic use of high doses of benzodiazepines may lead to development of tolerance and dependence. Long-term administration of diazepam causes CNS changes: significantly increased amount of GABA required for neuronal activity inhibition; reduced efficacy of diazepam on GABA-evoked Cl- currents [1]; functional changes in the chloride channel related to withdrawal signs [2]; changes in glutamate receptors [3]. Our previous data showed that anthocyanins diminished diazepam toxicity and significantly enhanced the survival of mice, treated with lethal doses of diazepam. Anthocyanins are naturally occurring flavonoids with various pharmacological activities. Literature data determine flavonoids as benzodiazepine receptor ligands [4]. We estimated withdrawal signs in the experimental rats in order to evaluate the effects of anthocyanins on diazepam dependence.

Materials and methods

Wistar rats were divided into three groups: I - diazepam; II - diazepam + anthocyanins 100 mg/kg; III - diazepam + anthocyanins 200 mg/kg. Rats were treated for 60 days. We evaluated fast breathing, hypermotility, seizures, tremor and piloerection as withdrawal signs after discontinuation of diazepam.

Results

Our results showed that the administration of anthocyanins significantly decreased abstinent signs of diazepam dependent rats. The most prominent effects were observed in the "diazepam + anthocyanins 200 mg/kg" group.

Conclusions

Anthocyanins administered together with diazepam are able to diminish diazepam dependence and can be used preventively in cases that require chronic therapy with benzodiazepines.

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