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RESEARCH ARTICLE

Anticonvulsant Effect of *Berberis integerrima* L. Root Extracts in Mice

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Abstract
Berberis integerrima is a member of Berberidaceae family. Berberine is one of the main constituents of this plant, having neuroprotective effect on central nervous system diseases. In this study, the anticonvulsant activity of methanolic extract, and hydromethanolic fraction, and chloroform fraction of *B integerrima* was assessed. The anticonvulsant effect of *B integerrima* was investigated using both pentylenetetrazole (PTZ) and maximal electroshock (MES)-induced seizure models. The LD50 value of the methanolic extract was 302.676 mg/kg. In the PTZ test, methanolic extract (140 and 200 mg/kg, i.p., $p < 0.01$), hydromethanolic fraction (200 mg/kg, $p < 0.01$), and chloroform fraction (200 mg/kg, $p < 0.01$) increased the onset time of hind limb tonic extensions (HLTEs). The protective effect against mortality (convulsion survivors/animals tested) was 2/8 in methanolic extract, and 3/8 in hydromethanolic fraction at a dose of 200 mg/kg and in chloroform fraction at a dose of 140 mg/kg. In the MES test, this plant did not display any significant effect in reducing HLTE duration. According to phytochemical screening, methanolic extract contained alkaloids and tannins. The present study, conducted in mice, indicated that *B integerrima* has anticonvulsant activity in PTZ-induced seizures. It is concluded that *B integerrima* may be useful in petit mal epilepsy.

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1. Introduction

Barberry is an evergreen and self-fertile plant that belongs to Berberidaceae family [1,2]. It is a shrub with yellow-to-brown bark, red-colored fruits, and thick and woody roots covered with a brittle bark [3,4]. This plant propagates through the suckers of root [1]. A variety of *Berberis* sp. are available in Iran, including *Berberis vulgaris* L., *Berberis orthobotrys* Bienert, *Berberis crataegina* D.C., *B integerrima*, and *Berberis khorasanica* Browicz [1,5]. The fruits of barberry are used as food flavor [1]. Many of *Berberis* L. species are used to alleviate insomnia [6], liver disorder, bronchial diseases, and urinary and gastrointestinal discomforts [7], and as an antirheumatic [8], antipyretic, [9], antibacterial [4], and antifungal [7] agent in traditional medicine. Recent pharmacological investigations have shown some pharmacological activities [10], including antimicrobial [11], anti-inflammatory, antinociceptive [12], antihistaminic, anticholinergic [13], potent vasodilatory, and antiarrhythmic activities, as well as increasing the duration of action potential in purkinje fibers and ventricular muscles [14] and decreasing morphine dependence, locomotor activity, and inducing hypnosis [15]. Compounds such as berberine chloride, palmatine chloride, oxyacanthine, berbamine, quaternary protoberberines, and bisbenzylisoquinoline alkaloids are the main constituents of this plant, and berberine alkaloid is mostly found in the roots [2—4,7,8]. Berberine has many pharmacological activities, including its hypotensive, immunostimulating, and sedative properties; it exerts some beneficial effects on central nervous system activities, such as protective effect in Alzheimer's, cerebral ischemia, mental depression, schizophrenia, anxiety, and depression, by increasing the content of norepinephrine, serotonin, or dopamine in the brain [16—18].

Epilepsy is a neurological illness that is characterized by recurrent seizures, and up to 5% of people develop epilepsy in their lifetime [19]. Although several anticonvulsant drugs are used to treat seizure attacks, about 30% of patients are medicated incompletely. Furthermore, current antiepileptic drugs have toxicity and teratogenic effects, which necessitates search for new therapeutic compounds for better management of epileptic disorders [20].

Since there are some reports on the use of constituents of *B integerrima* L. for the treatment of central nervous system diseases and its sedative effect, the anticonvulsant activity of methanolic extract, hydromethanolic fraction, and chloroform fraction of *B integerrima* was evaluated in this study.

2. Materials and methods

2.1. Animals

The study was performed on male albino mice, weighing 25 ± 1 g. Animals were housed in a ventilated room under a 12/12-hour light/dark cycle at 24 ± 2°C and had free access to water and food. All animal experiments were carried out in accordance with Mashhad University of Medical Sciences, Ethical Committee Acts.

2.2. Plant

The root of *B integerrima* was collected from Chenaran (Khorasan Province), Iran, and was identified by Mr Joharchi; voucher samples was preserved for reference in the Herbarium of the Department of Pharmacognosy, School of Pharmacy, Mashhad (Voucher no. 36-0209-1).

2.3. Preparation of extract

B integerrima root was cleaned, dried in shadow, and powdered by a mechanical grinder. For the methanolic extract, the powder (35 g) was macerated in 1000 mL methanol for 7 hours, and the mixture was subsequently filtered and concentrated in vacuum at 40°C. The residue was suspended in normal saline. The concentrated extract was then fractionated with an equal volume of hydromethanolic or chloroform extract three times, to produce two fractions containing nonpolar and polar compounds, respectively.

2.4. Acute toxicity

Different doses of methanolic extracts were injected intraperitoneally into groups of six mice. The number of deaths that occurred after 48 hours of administration was

Table 1 Effect of methanolic extract of *B integerrima* on PTZ-induced seizure in mice.

Treatment	Onset time of HLTE (s)	Mortality protection after 30 min (convulsion survivors/animals tested)	Mortality protection after 24 h (convulsion survivors/animals tested)
Normal saline (10 mL/kg)	163 ± 5.7	0/8	0/8
Diazepam (1 mg/kg)	1234 ± 27.7***	6/8**	6/8**
Methanolic extract (20 mg/kg)	251.1 ± 14.4	0/8	0/8
Methanolic extract (80 mg/kg)	296.4 ± 23.9	0/8	0/8
Methanolic extract (140 mg/kg)	621.1 ± 31.3**	2/8	1/8
Methanolic extract (200 mg/kg)	612.7 ± 19.3**	2/8	2/8

The methanolic extract and diazepam were administered 30 minutes prior to the injection of PTZ. Values are the mean ± SEM for eight mice.
** $p < 0.01$ and *** $p < 0.001$, as compared to control (normal saline), Tukey—Kramer. HLTE = hind limb tonic extension; PTZ = pentylenetetrazole; SEM = standard error of mean.