Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Ethnopharmacology 102 (2005) 46–52
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

A pharmacological study on *Berberis vulgaris* fruit extract

Mohammad Fatehi [a,b,*], Tarek M. Saleh [b], Zahra Fatehi-Hassanabad [a,b], Khadige Farrokhfal [a], Mostafa Jafarzadeh [a], Samaneh Davodi [a]

[a] *Department of Physiology and Pharmacology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[b] *Department of Biomedical Sciences, AVC, University of Prince Edward Island, 550 University Avenue, Charlottetown, PEI, Canada C1A 4P3*

Received 8 November 2004; received in revised form 15 May 2005; accepted 15 May 2005
Available online 1 July 2005

Abstract

Berberis vulgaris fruit (barberry) is known for its antiarrhythmic and sedative effects in Iranian traditional medicine. The effects of crude aqueous extract of barberry on rat arterial blood pressure and the contractile responses of isolated rat aortic rings and mesenteric bed to phenylephrine were investigated. We also examined effect of the extract on potassium currents recorded from cells in parabrachial nucleus and cerebellum rejoins of rat brain. Administration of the extract (0.05–1 mg/100 g body weight of rat) significantly reduced the mean arterial blood pressure and heart rate in anaesthetized normotensive and desoxycorticosteron acetate-induced hypertensive rats in a dose-dependent manner. Concentration–response curves for phenylephrine effects on isolated rat aortic rings and the isolated mesenteric beds in the presence of the extract were significantly shifted to the right. Application of the extract (1–50 μg/ml) shifted the activation threshold voltage to more negative potentials, leading to an enhancement in magnitude of the outward potassium current recorded from cells present in rat brain slices of parabrachial nucleus and cerebellum. This effect on potassium current may explain the sedative and neuroprotective effects of barberry. The present data support the hypothesis that the aqueous extract of barberry has beneficial effects on both cardiovascular and neural system suggesting a potential use for treatment of hypertension, tachycardia and some neuronal disorders, such as epilepsy and convulsion.

Keywords: Berberidaceae; *Berberis vulgaris* fruit; Rat; Hypertension; Tachycardia; Vascular contractility; Potassium currents

1. Introduction

Berberis vulgaris L. var. *asperma* Don (Berberidaceae) is a bush with yellow to brown coloured bark. The plant has obovate leaves, bearing pendulous yellow flowers in spring succeeded by oblong red coloured fruits (barberry). Various parts of this plant including its root, bark, leaf and fruit have been used as folk medicine for long in Iran. In Iranian traditional medicine several properties, such as antibacterial, antipyretic, antipruritic and antiarrhythmic activities for different parts of *Berberis vulgaris* have been reported with unknown mechanisms of actions (Zargari, 1983; Aynehchi, 1986; Nafissi, 1990). As it is increasingly believed now that traditional medicines become more popular worldwide, there is accumulating evidence suggesting medicinal plants are unlimited reservoirs of drugs. The amazing structural diversity among their active components makes them a useful source of novel therapeutic compounds. Researchers with interest in natural products have intensified their efforts towards scientific evaluation of traditional medicines. Previous pharmacological studies on berberine, an isoquinoline alkaloid found in root and bark of *Berberis vulgaris*, demonstrated that it possessed potent vasodilatory and antiarrhythmic activity, and prolonged the action potential duration in Purkinje fibres and ventricular muscles (Chiou et al., 1991; Ricciopo, 1993; Kathleen, 2000). There is some evidence for antiinflammatory and antinociceptive effects of isoquinoline alkaloids found in *Berberis vulgaris* (Kupeli et al., 2002).

* Corresponding author. Tel.: +1 902 566 0936; fax: +1 902 566 0832.
E-mail address: mohfatehi@yahoo.com (M. Fatehi).

0378-8741/$ – see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2005.05.019

Barberry is extensively used as food additive and its juice is recommended to cure cholecytitis (Zargari, 1983). Nevertheless, little pharmacological analysis has been performed on barberry. It has been shown that the crude extract of barberry has antihistaminic and anticholinergic activities (Shamsa et al., 1999). There are no reports based on scientific observation in the literature on the hypotensive activity of *Berberis vulgaris* fruit. Therefore, in the present study, the effects of *Berberis vulgaris* fruit extract on rat heart rate, rat blood pressure, contractility of rat aortic ring and perfusion pressure in rat isolated mesenteric bed were studied. Cardiovascular studies were performed on both normotensive and hypertensive rats to verify whether the extract had the ability to modify cardiovascular functions under pathological conditions. Also, since it has recently been reported that berberine blocked potassium currents in acutely isolated CA1 pyramidal neurons of rat hippocampus (Wang et al., 2004), it became of our interest to examine possible effect of the extract on potassium currents recorded from cells in parabrachial nucleus (PBN) and cerebellum regions of rat brain in vitro. To determine if barberry affects the heart via the CNS, brain slices including the PBN were used. We chose the PBN because it is a key interface between the brainstem and forebrain structures involved in autonomic regulation (Saleh and Connell, 1997, 2003). Cerebellum has its importance due to controlling motion and motor activity. The main objective for this study was to elucidate whether experimental observations in animal models and isolated tissues could support the positive health claims regarding barberry's therapeutic properties.

2. Materials and methods

2.1. Preparation of the extract

Berberis vulgaris fruit was collected from farms in the Birjand area of Khorasan, Iran and authenticated at the Herbarium of Mashhad School of Pharmacy (voucher no. 2003B15). Some 10 g dried barberry was extracted in boiling water (100 ml, for 5 min). The filtered aqueous extract was concentrated in a rotary vacuum evaporator and dried by exposure to hot air to yield 522 mg solid material. The stock solution of the extract (10 mg/ml) was prepared from this solid material on the day of experiment.

2.2. Induction of experimental hypertension

The experiments were performed in accordance with Animal (scientific procedures) Act of 1986 (Britain). For cardiovascular experiments, male Sprague–Dawley rats (purchased from Razi Institute, Mashhad, Iran) weighing between 200 and 250 g were used. Animals were housed in temperature- and humidity-controlled, light-cycled quarters and randomly divided into two groups. One group received saline injection (0.5 ml/kg, twice weekly, for 5 weeks, s.c., $n = 25$) whereas the other group were injected with desoxycorticosteron acetate (DOCA)-salt (20 mg/kg, twice weekly, for 5 weeks, s.c., $n = 25$) and NaCl (1%) was added to their drinking water. Using this protocol, hypertension was induced in the second group of rats. This model of hypertension (DOCA-salt-induced hypertension) has been used by several investigators (e.g. Somers et al., 2000; Fareh et al., 2000; Fatehi-Hassanabad et al., 2004).

2.3. Measurement of blood pressure and heart rate

Five weeks after the first saline or DOCA injection, rats were anaesthetised with sodium thiopental (30 mg/kg, i.p.) The right common carotid artery was catheterized for the measurement of blood pressure and heart rate, right and left jugular veins were cannulated for the administration of drugs and the extract, respectively. The trachea was cannulated and the animals were allowed to breathe spontaneously. Body temperature was recorded using a rectal thermistor probe and was maintained at $37 \pm 1\,^{\circ}C$ using an incandescent lamp placed over the abdomen. After 20 min stabilization period, arterial blood pressure (systolic, diastolic and mean pressure) and heart rate were measured.

2.4. Isolated aortic rings

The descending thorasic aorta was excised and trimmed free of adhering fat and connective tissues (Cordellini, 1999). The aorta was cut into rings (2 mm width) and vertically mounted in a 10 ml tissue bath containing Krebs solution of the following composition (in mM): 118.4 NaCl, 4.7 KCl, 1.2 $MgSO_4$, 1.2 KH_2PO_4, 25 $NaHCO_3$, 2.5 $CaCl_2$ and 11.1 glucose which was maintained at about 37 °C and bubbled with a mixture of 95% O_2 and 5% CO_2. The preparations were allowed to equilibrate for at least 1 h under a resting tension of 1 g. Changes in tension were recorded with an isometric transducer and displayed on a Washington recorder. Cumulative concentration–response curves for phenylephrine (0.001–1 μM) were constructed using tissues removed from normotensive and hypertensive rats in the absence and presence of the extract.

2.5. Isolated and perfused mesenteric beds

The abdominal cavity was opened by a mid-line incision through the linea alba and the mesenteric bed was excised using the procedure described previously (Fatehi-Hassanabad et al., 1995). The isolated mesenteric beds were placed on a Petri dish mounted in a heated water-bath (about 37 °C) and perfused at a constant rate (5 ml/min; Gilson Minipuls 2) with Krebs solution bubbled with a mixture of 95% O_2 and 5% CO_2. The preparations were allowed to equilibrate for 30 min before recording the perfusion pressure. The cumulative concentration–response