Journal of Ethnopharmacology 225 (2018) 336–341

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Neuroprotective effect of *Asparagus racemosus* root extract via the enhancement of brain-derived neurotrophic factor and estrogen receptor in ovariectomized rats

Laddawan Lalert[a], Hathairat Kruevaisayawan[b], Patcharada Amatyakul[c], Kornkanok Ingkaninan[d], Onrawee Khongsombat[a,e,*]

[a] Department of Physiology, Faculty of Medical Science, Naresuan University, Phitsanulok 65000, Thailand
[b] Department of Anatomy, Faculty of Medical Science, Naresuan University, Phitsanulok 65000, Thailand
[c] Department of Obstetrics and Gynecology, Faculty of Medicine, Naresuan University, Phitsanulok 65000, Thailand
[d] Pharmaceutical Chemistry and Pharmacognosy, Faculty of Pharmaceutical Sciences and Center of Excellence for Innovation in Chemistry, Naresuan University, Phitsanulok 65000, Thailand
[e] Center of Excellence in Medical Biotechnology, Naresuan University, Phitsanulok, Thailand

ARTICLE INFO

Keywords:
Asparagus racemosus
Estrogen receptor
Brain-derived neurotrophic factor
Ovariectomy

ABSTRACT

Ethnopharmacological relevance: *Asparagus racemosus* (AR) is well known as an Ayurvedic rasayana which used traditionally by Ayurvedic practitioners for nervous disorders and prevent aging. In our previous study it was found that ethanol AR root extract can improve learning and memory impairment, induced by an ovariectomy, but the extract's mechanisms as a neuroprotective property are still unknown.

Aim of the study: This study aimed to examine the effects and mechanisms of ethanol AR root extract on the alteration of brain-derived neurotrophic factor (BDNF) and estrogen receptor (ER) subtypes in ovariectomized (OVX) rats.

Materials and methods: Adult female Wistar rats were divided into five groups, 4 groups underwent ovariectomy, and one group was designed to be the sham control group. Two groups were gavaged with propylene glycol for sham, and a second group similarly prepared for OVX. Two further groups of OVX rats were gavaged once daily, one group with 100 mg/kg b.w. of ethanol AR root extract and the second group with 1000 mg/kg b.w. of ethanol AR root extract. The fifth group was gavaged once daily with 0.1 mg/kg b.w. of 17α-ethynylestradiol (EE). BDNF, ERα and ERβ expression were evaluated by western blot analysis.

Results: The western blot analysis revealed that the OVX rats showed a significant decrease in BDNF and a down-regulation of ERα and ERβ in the frontal cortex and hippocampus. It was also demonstrated that EE and AR root extract increased BDNF, ERα and ERβ in the frontal cortex and hippocampus of ovariectomized rats.

Conclusions: Based on these results, the enhancement of BDNF and ERs up-regulation may be involved in the neuroprotective effects of ethanol AR root extract in ovariectomized rat.

1. Introduction

Asparagus racemosus (AR), also known as shatavari (family Asparagaceae), is an important medicinal plant endemic to tropical India and Thailand. It is well known drug in Ayurvedic rasayana that prevent aging, increase longevity and improve mental function. In addition, it is recommended in Ayurvedic texts for the prevention and treatment of gastric ulcers, dyspepsia and as a galactagogue (Alok et al., 2013). The major active compounds in the root of AR are steroidal saponins such as asparacoside, shatavarin IV, V and XI (Onlom et al., 2017a, 2017b, 2017c) and other constituents such as racemosol and asparagamine (Bopana and Saxena, 2007). The phytoestrogenic properties of AR are widely known and used as a hormonal modulator in a stimulant health tonic for women (Joseph, 1998), which has effects similar to endogenous estrogen (Saxena et al., 2010). The neuroprotective properties of AR have also been documented. The oral administration with AR root methanolic extract (50, 100 and 200 mg/kg b.w.) for 7 days could enhance the memory and protect against scopolamine-induced amnesia in rodents (Ojha et al., 2010). It has also previously been reported that the mice pre-treated with AR root acetone extract at

* Corresponding author at: Department of Physiology, Faculty of Medical Science, Naresuan University, Phitsanulok 65000, Thailand.
E-mail address: onraweek@nu.ac.th (O. Khongsombat).

https://doi.org/10.1016/j.jep.2018.07.014
Received 8 December 2016; Received in revised form 1 June 2018; Accepted 11 July 2018
Available online 31 July 2018
0378-8741/ © 2018 Elsevier B.V. All rights reserved.

the dose of 18 mg/kg b.w mixed with diet daily for 2 weeks could prevent the neuronal damage induced by kainic acid (Parihar and Hemnani, 2004). In addition, Saxena and co-workers demonstrated that *Asparagus racemosus* root extract (100 mg/kg b.w.) for 30 days could increase the percentage of normal cell in stress group stress in experimental animals as well as show a significant increase in test score of extract treated patients as compared to stress group patients (Saxena et al., 2007). Furthermore, AR root extract has been demonstrated for its adaptogenic activity against different kinds of stressors in animals (Rege et al., 1999).

Menopause is defined as the cessation of the menstrual cycle in women along with a decrease in ovarian steroidal hormones such as estrogen and progesterone. The deprivation of estrogen in menopausal women is considered not only to disturb reproductive functions but also produces many psychological symptoms such as anxiety, difficulty concentrating, depression and forgetfulness (Miquel et al., 2006). Clinical study has suggested that ovarian hormone withdrawal after menopause could increase the risk of Alzheimer's disease (AD), a neurodegenerative disorder (Gao et al., 1998). Several lines of evidence have suggested that estrogen may exert its neuroprotective effect by maintaining brain homeostasis through regulation of neuroinflammation, oxidative stress, cerebral blood flow, extracellular glutamate levels and neuroprotective signaling (Acaz-Fonseca et al., 2014; Arevalo et al., 2015a). Moreover, some mechanisms of estrogen are involved in the regulation of plasticity of synaptic circuits in key cognitive brain regions, such as the somatosensory cortex, the prefrontal cortex and the hippocampus (Arevalo et al., 2015b). Decrement of brain-derived neurotrophic factor (BDNF) levels is associated with neurodegenerative disorder relating to learning and memory impairment (Lindsay et al., 1991; Sohrabji and Lewis, 2006). Many studies indicated that estrogen modulates BDNF expression in the hippocampus and cerebral cortex (Spencer et al., 2008; Luine and Frankfurt, 2013). Estrogen exerts its effects by binding to classical ER subtypes, ERα and ERβ. These receptors distribute in several brain areas including the frontal cortex and hippocampus where specifically associated with recognition memory. Previous studies have shown that following long-term ovariectomized (OVX) in rats, the expression of ERα showed the down-regulation in the telencephalon and hippocampus (Navarro et al., 2013) while shot-term OVX in rats found the up-regulation of ERα in the hippocampus (Cardoso et al., 2010). However, these effects of OVX were reversed by exogenous estradiol administration. Furthermore, the expression of ERβ was found to be decreased in the rat brain of three-month OVX (Rose'Meyer et al., 2003). The estrogen replacement therapy (ERT) relieves menopausal symptoms as well as prevents cardiovascular disease and osteoporosis including decrease the risk for neurodegenerative disorder. However, there are several concerns over the ERT because it produces serious side-effects such increased risk for endometrial cancer, breast cancer and venous thromboembolic events (Barrett-Connor and Grady, 1998).

The results obtained from our previous study have revealed that the administration of AR root extract for three months could reverse the learning and memory impairment induced by ovariectomy, relating to diminished neuronal damage in medial prefrontal cortex and hippocampus without effect on circulating estradiol concentration (Lalert et al., 2013). These suggested that AR root extract might bind directly to the estrogen receptors without enhancing the endogenous estrogen levels to improve memory dysfunction induced by OVX. Although AR is well known for its phytoestrogenic and neuroprotective properties, the beneficial effects and mechanisms of AR on learning and memory impairment induced by OVX rat are not clearly understood. Based on our previous results, the present study aims to investigate the effects of the chronic administration of AR root extract on the alterations of BDNF and ER subtypes on the brain regions associated with learning and memory process, the frontal cortex and hippocampus, in an animal model of estrogen deficit, OVX rats.

2. Materials and methods

2.1. Plant material and preparation of crude extract

The AR roots were collected from Ampur Muang, Rayong, Thailand. The voucher specimen of the plant was kept at the Pharmaceutical Botany Mahidol (PBM) herbarium, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand (Collection no. RKT 0005). The main chemical components of this plant sample have been reported previously as saponin glycosides (Onlom et al., 2017a, 2017b, 2017c). The roots of AR were dried by hot air oven at 45 °C for 24 h before milled into coarse powder. After that the dried powdered roots of AR (5 kg) was macerated at room temperature with hexane for 3 days. Then residue was macerated with 95% ethanol for 3 days, and was filtered and extracted again to provide the crude AR ethanolic extract with 10.94% yield. The extract contained 7.4% of saponin glycosides equivalent to shatavarin IV determined by ELISA using monocolonal antibody against shatavarin IV (Onlom et al., 2017b). Moreover, HPLC-Q-TOF-MS/MS analysis as described in the previous study (Onlom et al., 2017a) indicated that the major saponins in the extract was shatavarin IX (5.94 ± 0.03 mg/g) (Supplementary data). The extract was mixed with 20% propylene glycol to stock suspension in a dose of 100 and 1000 mg/kg b.w. Doses were chosen on the basis of prior studies demonstrating pro-cognitive effects and absence of toxicity (Lalert et al., 2013; Kumar et al., 2010). The suspension was administered by gavage once daily.

2.2. Animals

Eight-weeks-old (260–310 g) female Wister rats were obtained from the National Laboratory Animal Center Mahidol University, Nakhon Pathom, Thailand. The rats were acclimatized for at least one week before starting the experiment. They were housed two-three per cage under a standard 12 h dark/light at constant temperature of 24 ± 1 °C. The animals were allowed free access to food (C.P.082, S.W.T. Co. Ltd, Thailand) and tab water ad libitum. The experiments were comply with standard of animal care and use established under the ethical guidelines and policies of Naresuan University, and all protocols were approved by the Ethical committee for the Use of Animal, Naresuan University, Thailand (No.56040051).

2.3. Surgery and treatments

Before the experiments begun, all animals were examined for estrous cycles by using vaginal cornification assay for three consecutive cycles to select the rats with normal estrus cycle (Everett, 1948). Bilaterally ovariectomy or sham-operating was performed under the anesthetized by an intraperitoneal injection of sodium pentobarbital 50 mg/kg b.w. during a diestrus phase. The ovariectomy was performed by making a small 1 cm dorsolateral incision. The ovaries surrounded by fat were exposed and the vessels supplying to the ovaries were ligated and ovaries were removed. Sham surgery was performed in the same manner without removing the ovaries. (Sayed et al., 2013). After the operation, all animals were leaved in home cage for 15 days to recover from the surgery. During the recovery period, vaginal smear were taken once daily to confirm that all animal were an anestrus. After that the animals were randomly divided into following five groups (n = 6 in each group) that included group 1 (sham); sham-operated rats with vehicle administration (propylene glycol; PG), group 2 (OVX); OVX rats with vehicle administration, group 3 (OVX + AR100); OVX rats with 100 mg/kg b.w. of AR root extract administration, group 4 (OVX +;AR1000); OVX rats with 1000 mg/kg b.w. of AR root extract administration and group 5 (OVX + EE); OVX rats with 0.1 mg/kg b.w. of 17α-ethynylestradiol administration (EE) as a positive control. All experimental groups were administrated by gavage once daily for 90 days. At the end of the experimental periods, all rats were euthanized

Download English Version:

https://daneshyari.com/en/article/8532079

Download Persian Version:

https://daneshyari.com/article/8532079

Daneshyari.com