ANTIDEPRESSANT EFFECT OF KAEMPFEROL, A CONSTITUENT OF SAFFRON (*CROCUS SATIVUS*) PETAL, IN MICE AND RATS

Hossein Hosseinzadeh*, Vahidehsadat Motamedshariaty and Farzin Hadizadeh*****

*Correspondence author: Pharmaceutical Research Center, Department of Pharmacodynamy and Toxicology, Faculty of Pharmacy, Mashhad University of Medical Sciences, P.O.Box 91775-1365, Mashhad. I.R.Iran. Email: hosseinzadehh@mums.ac.ir, Fax: 98 511 8823251

** Pharmaceutical Research Center, Department of Pharmacodynamy, Mashhad University of Medical Sciences, IR. Iran.

***Biotechnology and Pharmaceutical Research Center, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Running title: Antidepressant effect of kaempferol

ABSTRACT

The antidepressant activity of kaempferol, a *Crocus sativus* petal constituent, was evaluated using forced swimming test in mice and rat. Fluoxetine (20 mg/kg), as a positive control, and kaempferol (100 and 200 mg/kg in mice and 50 mg/kg in rats) intraperitoneally reduced immobility in mice. This study confirmed the antidepressant effect of kaempferol in mice and rats.

Keywords: Kaempferol; *Crocus sativus*; Saffron, Antidepressant activity, Forced swimming test

INTRODUCTION

Saffron (*Crocus sativus*) is a bulbous perennial of the iris family (Iridaceae) treasured for its golden-colored, pungent stigmas, which are dried and used to flavor and color foods as well as a dye. One of its principal coloring pigments is crocin, which is easily soluble in water. The principal element giving saffron its special ‘‘bitter’’ flavor is the glycoside picrocrocin. The main aroma factor in saffron is safranal, which comprises of about 60% of the volatile components of saffron [1]. Saffron extract or its active constituents have shown different activities on the central nervous system such as antidepressant [2-3], anticonvulsant [4], memory enhancer [5] and sedative [6].

Our previous study showed that the aqueous and ethanolic extracts of stigma (0.2-0.8 g/kg) decreased immobility time in comparison with normal saline in the forced swimming test (FST). Safranal (0.15-0.5 ml kg) and crocin (50-600 mg/kg) also reduced immobility time. This study demonstrated antidepressant activity of saffron and its constituents in mice [2]. Recently, the antidepressant effect of saffron stigma [3, 7-8] and petal [9-10] extracts was demonstrated in clinical trial study. As petal extract showed antidepressant activity in animal [11] and human [9-10], in this study the antidepressant

activity of one constituent of this extract, kaempferol [12], was evaluated in mice and rats.

MATHERIAL AND METHODS

Animals

Male albino mice 20-25 g and Wistar rats 200-220 g were obtained from a random bred colony in the animal house of Mashhad University of Medical Sciences. Animals were housed in colony room 12/12 hr light/dark cycle at 21 ± 2°C and had free access to water and food.

Forced swimming test

The forced swim test was used for the evaluation of antidepressant activity in mice and rats. Mice and rats were placed individually in Pyrex cylinders (10 × 45 cm) which were filled with water at 24-25 °C to a 30-cm depth. They were removed 15 min later, dried and placed in their home cage. Twenty-four hours after their first exposure, the animals were replaced in the swim apparatus for 6 min and behaviors were monitored. Kaempferol (from Sigma) and normal saline were administered intraperitoneally 60 min prior to the test session. After two min swimming, behavioral activities were evaluated during four min. Immobility was assigned when no additional activity was observed other than that required to keep the animal's head above the water. A time sampling technique was employed, whereby, the predominate behavior in each 5 sec period of 4 min test was recorded [13].

Statistical analysis

The data were expressed as mean ± SEM and tested with analysis of variance followed by the multiple comparison test of Tukey-Kramer.

Results and conclusion

Fluoxetine (20 mg/kg) significantly reduced immobility behaviors in the mice and rats forced swimming test (FST). Kaempferol also reduced immobility behaviors in mice (100 and 200 mg/kg) and rats (50 mg/kg) (Figures 1 and 2).

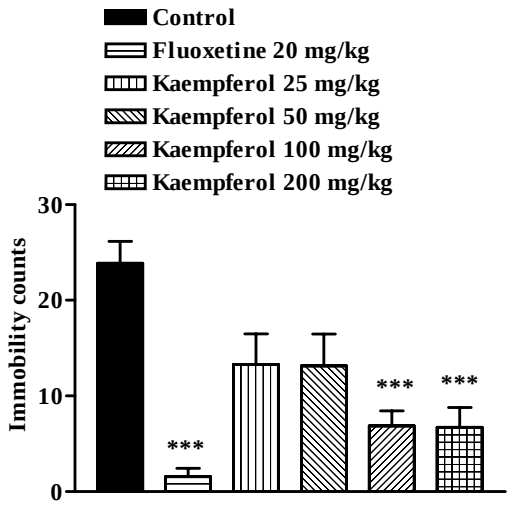

Figure 1. The effect of kaempferol on immobility behavior in mice. Agents were administered to rats intraperitoneally 60 min prior to the test. Values are the mean ± S.E.M. for 8 mice; ***p<0.001, as compared to saline, Tukey-Kramer test.

Agents which decrease the immobility time in FST have antidepressant effects [14]. The selective serotonin reuptake inhibitors such as fluoxetine [13, 15] decrease

immobility times. As kaempferol reduced immobility behaviors, thus this agent has antidepressant activity.

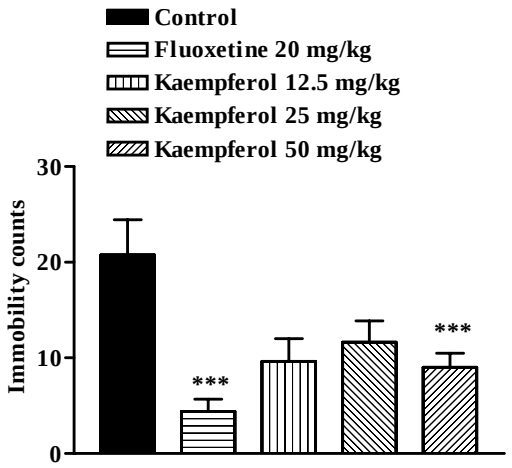

Figure 2. The effect of kaempferol on immobility behavior in rats. Agents were administered to rats intraperitoneally 60 min prior to the test. Values are the mean ± S.E.M. for 8 rats; ***p<0.001, as compared to saline, Tukey-Kramer test.

A number of recent preclinical [2, 11] and clinical studies [3, 7-10] indicate that stigma and petal of *C. sativus* have antidepressant effect. The antidepressant effect of *C. sativus* petal as well as stigma aqueous and ethanolic extracts has been shown in mice [11]. It was reported that two constituents of saffron, safranal and crocin, also have antidepressant activity in mice [2]. Recently, in small preliminary double-blind and randomized comparison of saffron and imipramine in the treatment of mild to moderate depression was demonstrated [3]**.** In two other studies, the efficacy of petal of *C. sativus* in the treatment of mild-to-moderate depression was confirmed [9-10].

The results of this study indicate that the saffron petal component, kaempferol, may be of valuable agent in the treatment of depression.

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