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Original Article

Involvement of altered serotonergic responses in fennel oil induced antidepressant, anxiolytic and antinociceptive effects in rats

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ABSTRACT

The usage of herbs as a nat ural drug has mount up all over the world. Fennel (*Foeniculum Vulgare* Mill) it is a common herb. Traditionally it is used as a carminative agent, antioxidant, diuretic, anti-inflammatory, anti-hirsutism and many more. Present study is designed to evaluate the behavioral effects of fennel oil in rats. In the present study antidepressant, anxiolytic and analgesic effects of repeated administration of fennel oil has been monitored in rats. Forced swim test and elevated plus maze test has been used to monitor the antidepressant and anxiolytic effect respectively. However analgesic effect of fennel oil has been monitored by hot plate test. Rats treated with fennel oil showed significant increase in struggling time in Forced Swim Test (FST). Increased locomotor activity in novel environment and a significant increase in the time spent in open arm in elevated plus maze (EPM) was exhibited by fennel oil treated rats. Analgesic activity monitored by hot plate test showed significant increase in latency time in test compared to control rats. Results of present study show that fennel oil has potential antidepressant, anxiolytic and analgesic activity.

Key Words: Antidepressant, Anxiolytic, Analgesic, Fennel Oil

INTRODUCTION

Foeniculum vulgare Mill commonly known as fennel is a widely distributed plant on most tropical and subtropical regions and has been long used for the culinary and medicinal purposes. The chemical composition of fennel includes anethole, fenchone, methyl chavicol [1] essential oils, fatty acids, phenylpropanoids, monoterpenids, cormarins. It also contains titerpenoids, tannins, flavonoids, cardiac glycosides, saponins and other types of compounds [2]. Aqueous extract of fennel has antioxidant activity higher than some famous antioxidant such as ascorbic acid [3]. In vitro studies have shown potential antioxidant activity of phenolic extract and aqueous extract of fennel [4].
Fennel may be considered as a best natural antioxidant which may contribute to the daily antioxidant diet [5]. Data exists which shows its central analgesic effects [6]. Apart from many beneficial effects on body, large number of investigations has been done to diagnose neurobiological changes in behavior and biochemical changes following repeated administration of fennel oil. Over the past few years great advances have been made in the understanding of central nervous system and in the pathophysiology of the major psychiatric disorders. The goal of this study is to analyze the antidepressant, anti-anxiety and analgesic effects of natural substance fennel from its oil and to focus on the probability of emerging new approach to treat mental ailments in more natural way.

MATERIAL AND METHODS

Animals: Experiment were carried out on locally bread male rats (Sprague Dawley) purchased from Agha Khan University Hospital weighing 150-200gm. Animals were kept individually with free access to standard rodent diet and water at normal

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room temperature for at least 3-4 days before the start of experiment for adaptation.

Experimental Protocol: Rats were divided randomly into 2 groups control group and test group. Fennel oil was purchased from the local market and the dose of 0.5ml was selected for the treatment. The oil was given orally to the test animals for 3 weeks where as the control group was given water for 3 weeks at dose of 0.5ml/day

Behavioral Analysis:

Open Field Testing*:* The locomotor activity of control and fennel oil (*Foeniculum vulgare* oil) treated rats were monitored in novel environment in an open field apparatus which consisted of square area 76x76 cm with opaque walls of 42 cm high. The floor was divided by lines into 25 equal squares. The test was performed in a quiet room under white light to avoid any noise effect as described by [7]. Animals were placed in the center square of the open field (one at a time). Activity in open field was determined by monitoring latency to move and number of squares crossed for five minutes [8]. Activities of control rats and drug treated rats were monitored in a balance design to avoid order effect.

Elevated Plus Maze Test*:* Novel test for the selective identification of anxiolytic and anxiogenic drug effects, in the rat, is the elevated plus maze. Plus maze apparatus consist of 4 equal size arms. The two opposite arms are open while other opposite two are closed [9, 10]. The length of each arm was 50 cm and width 10 cm. Arms were joined by the central area of 5 cm. The length of the wall of the closed arm was 40 cm. The maze was elevated from floor at 60 cm. To determine activity a rat was placed in the center of the plus maze and the time spent in the open arm and number of entries in open arm was monitored for 5 minutes.

Forced Swim Test (FST)*:* Assessment of depressive symptoms was monitored by FST following 3 weeks of oral administration of Fennel oil. FST was performed to monitor the antidepressant activity [11]. It was performed as described earlier [12]. To monitor the antidepressant activity rats are placed individually in tank (53, 19, 28 cm) .The water is filled up to 18cm. The height of the water is such in which animal is supposed to swim. Animal is subjected in the swim tank for 5 minutes and behavioral scoring was performed by noting struggling time. After each test, rats were dried with a towel and placed in home cage.

Hot Plate Test*:* The hot plate test was used to estimate the latency of responses of thermal stimuli according to the method described by [13]. The apparatus consists of metal plate surrounded by a transparent cylinder. The metal plate is keep at constant temperature which can be varied from 50 to 55 ^{0}C. It seems to produce reliable and fairly stable pain threshold to measure analgesic activity. The rats were placed on the heated surface maintained at 50 ^{O}C. The time between placement on hot plate and occurrence of licking fore paw was recorded as the response of latency. A maximal cut off time of 30s was used to prevent the tissue damage [14].

Statistical Analysis: Results are represented as mean $\pm$ SD. Data was analyzed by student *t*-test. $p<0.05$ was considered to be significant.

RESULTS

Effect of Repeated Administration of Fennel Oil in Open Field Activity: Fig 1 shows the effect of repeated administration of fennel oil on exploratory activity in open field in rats. Data analyzed by student's *t*-test showed significant increased number of square crossed in open field in ***Fennel Oil*** treated rats ($p<0.01$) as compared to control rats.

Effect of Repeated Administration of Fennel Oil in Elevated Plus Maze: Fig 2 shows the effect of repeated administration of fennel oil on elevate plus maze activity in rats. Data analyzed by student's *t*-test showed significant increase in the time spent in open arm in ***Fennel Oil*** treated rats ($p<0.01$) as compared to the control rats.

Effect of Repeated Administration of Fennel Oil in Forced Swim Test: Fig 3 shows the effect of repeated administration of fennel oil on struggling time in FST in rats. Data analyzed by student's *t*-test showed a significant increase in the struggling time in the ***Fennel Oil*** treated rats ($p<0.01$) as compared to the control rats.

Effect of Repeated Administration of Fennel Oil in Hot Plate Test: Fig 4 shows the effect of repeated administration of fennel oil on analgesic activity in hot plate test in rats. Data analyzed by student's *t*-test showed a significant increase in the latency to lick in the ***Fennel Oil*** treated rats ($p<0.01$) as compared to the control rats.

DISCUSSION

Currently there is global interest in finding new and safe compounds from natural sources to treat different ailments. Nature has always proved to be the most beneficial source for medicinal treatments, having a wide variety of herbs which have strong

potential therapeutic uses and could be used in the form of extract, suspensions, oils and sprays or ingested directly to treat different ailments. In the present study, effect of fennel oil was studied on several animal behaviors such as open field, elevated plus maze (EPM), forced swim test(FST) and hot plate. These tests are classic measures for screening nervous system action providing information about psychomotor performance, anxiety and depression, fennel oil was used to assess anti-anxiety and antidepressant and analgesic activity in rats.

Fennel and its herbal drug preparation are used for dyspeptic complaints. It has potent hepatoprotective action against CCL_4 induced acute injury and anti-inflammatory effect in rats [15, 16]. Analgesic activity in rats is assessed by hot plate test in which rats are placed on hot metal plate and the temperature is kept constant and latency to lick is observed in order to determine the pain relieving activity of a conventional or novel drug or compound. In present study latency to lick is significantly increased in oil treated rats as compared to their respective control rats. The analgesic activity of fennel oil has been reported previously [17-19]. Increased latency to lick in hot plate test following the administration of fennel oil observed in present study shows the analgesic potential of oil.

Open field is a classical standard test to check the exploratory, locomotor and anti-anxiety effects of drugs in rodents [20]. In the present study animals treated with fennel oil showed increased locomotor activity in open field. The number of squares crossed by the oil treated rats was significantly greater than their respective controls. Anxiety is a fear response for which there is no reason. Elevated plus maze test has been used to assess the anxiety levels in rats [10]. Since rats have innate fear of open and brightly illuminated areas, they enter less in open arms and they stay for a shorter period of time in an open arm. Anxiolytic compounds reduce animal aversion in open arm [21]. Increase in number of entries in open arms as well as time spent in open arm in response to typical anxiolytics such as benzodiazepine has been reported [9]. It is observed in the present study that rats treated with the fennel oil spent more time in open arm as compared to their respective controls. This gives the evidence of anti-anxiety potential of fennel oil.

Forced swim test (FST) is a measure of antidepressant activity in rats [22]. Increased struggling time and decrease immobility time is taken as a measure of antid.epressant effect of any drug. It is observed in the present study that struggling time was significantly increased in rats treated with fennel oil as compared to their respective control rats. These results show the antidepressant effect of fennel oil. Antidepressants produce this effect by increasing the availability of 5-HT to its receptors [23]. Inhibition of 5-HT reuptake increases the availability of 5-HT to its receptors that are involve in depression [24]. Inhibition of 5-HT reuptake by antioxidants has also been reported [25]. Antioxidant activity of fennel oil has been reported [3]. Anethole an antioxidant is important component of fennel oil [1]. Inhibition of monoamine oxidase (MAO) by anethole has been reported [26]. Results of present study suggest that antioxidant activity of fennel oil and its component [1, 3] as well as inhibition of monoamine oxidase by its component anethole [26] may play important role in antidepressant like effect of fennel oil**.** Inhibition of 5-HT reuptake by antioxidants [25] and inhibition of MAO by anethole [26] could increase the availability of 5-HT in synapse and this increased 5-HT may desensitize 5-HT receptors involved in anxiety. This effect may be attributed to the anxiolytic activity of fennel oil observed in the present study however, more studies are warranted regarding these findings.

CONCLUSION

Finding of present study shows that repeated administration of Fennel oil attenuates the depressive and anxiogenic behavior, so it has anti-depressant and anxiolytic activity. Moreover, Fennel oil also increases the analgesic effect in rats by decreasing the pain sensation.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

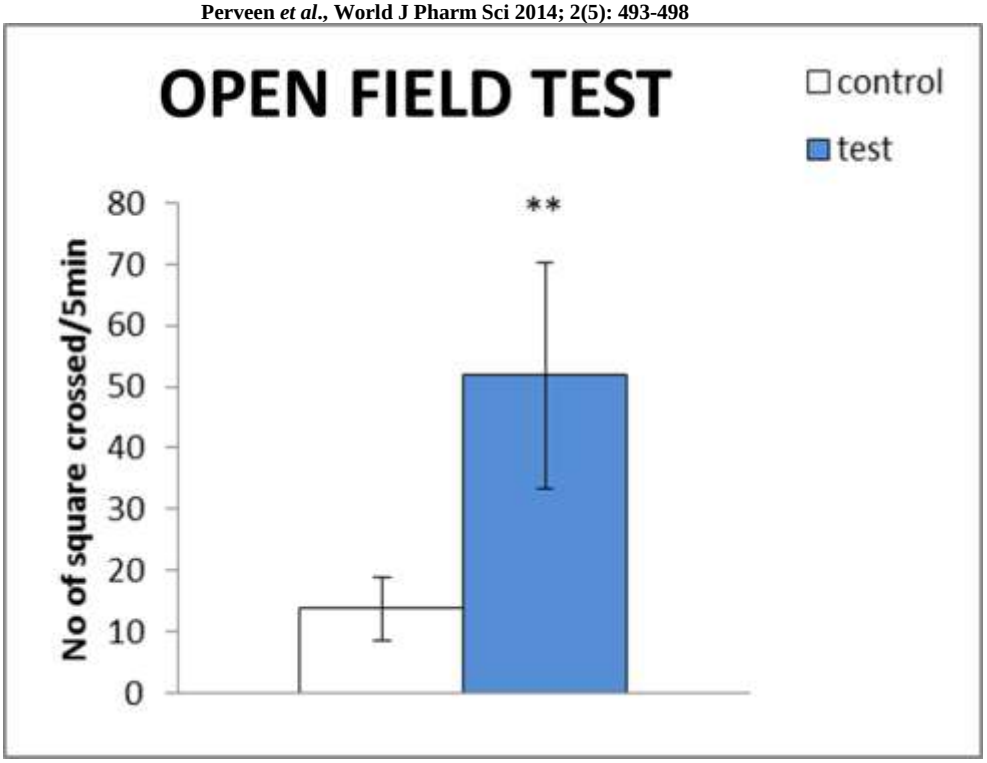

Figure 1: Effect of repeated administration of *Foeniculum vulgare* mill oil (0.5ml/day) for three weeks on rats in open field test. Values are mean ± SD (n=8). Significant differences by Student's *t*-test; ** ($p<0.01$) from controls

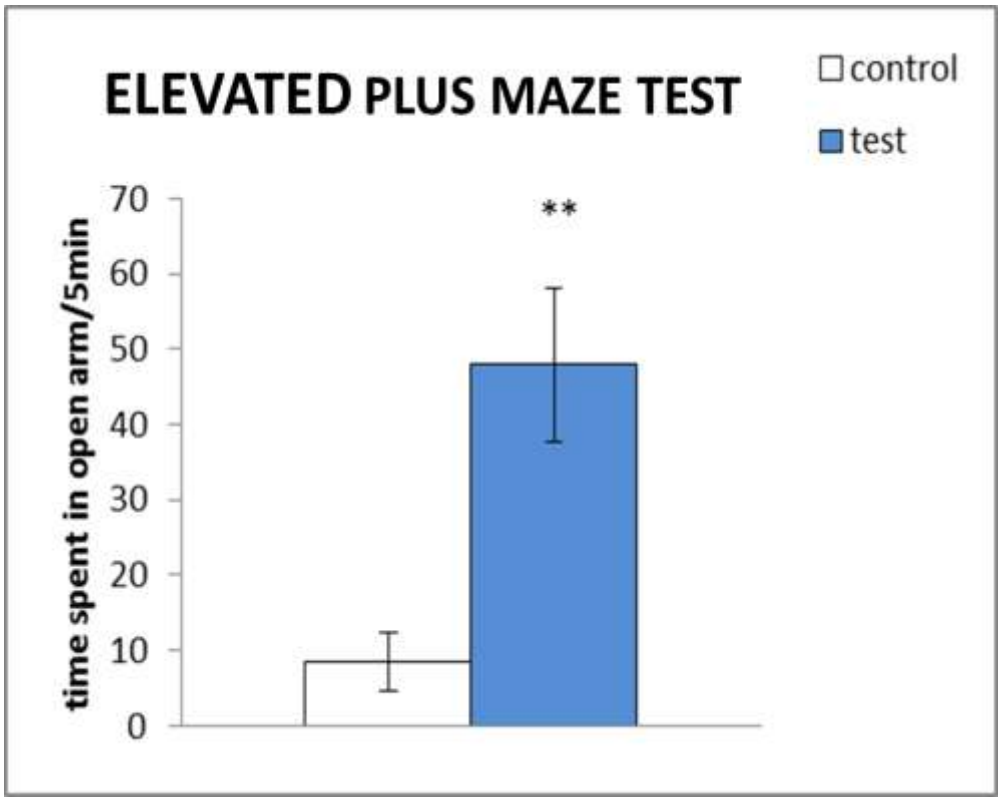

Figure 2: Effect of repeated administration of *Foeniculum vulgare* mill oil (0.5ml/day) for three weeks on rats in elevated plus maze test. Values are mean ± SD (n=8). Significant differences by Student's *t*-test; ** ($p<0.01$) from controls

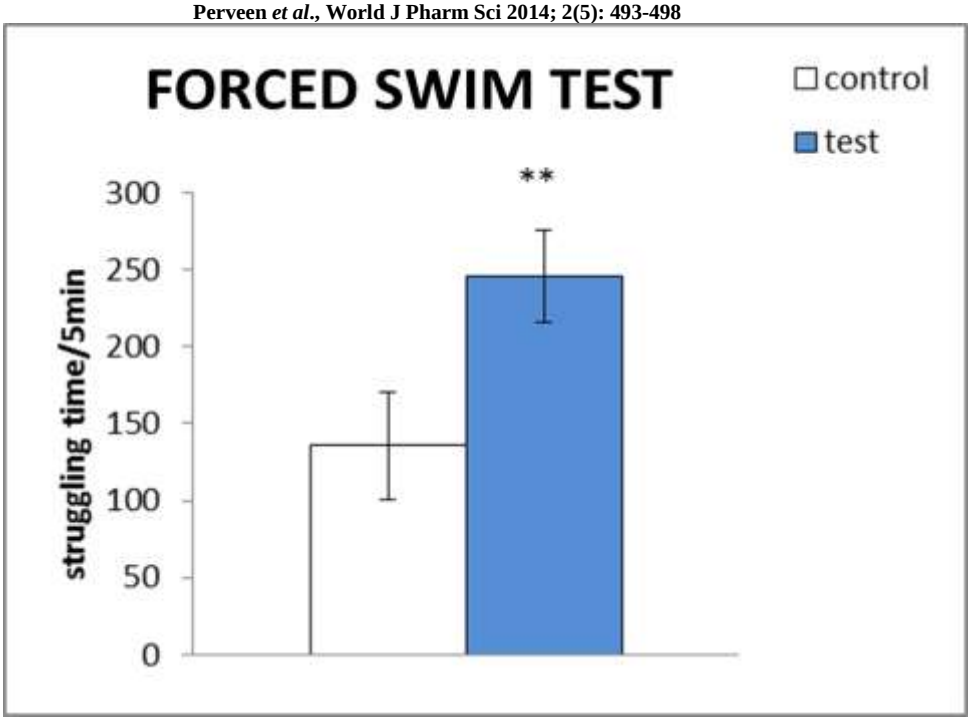

Figure 3: Effect of repeated administration of *Foeniculum vulgare* mill oil (0.5ml/day) for three weeks on rats in forced swim test. Values are mean ± SD (n=8). Significant differences by Student's *t*-test; ** ($p<0.01$) from controls

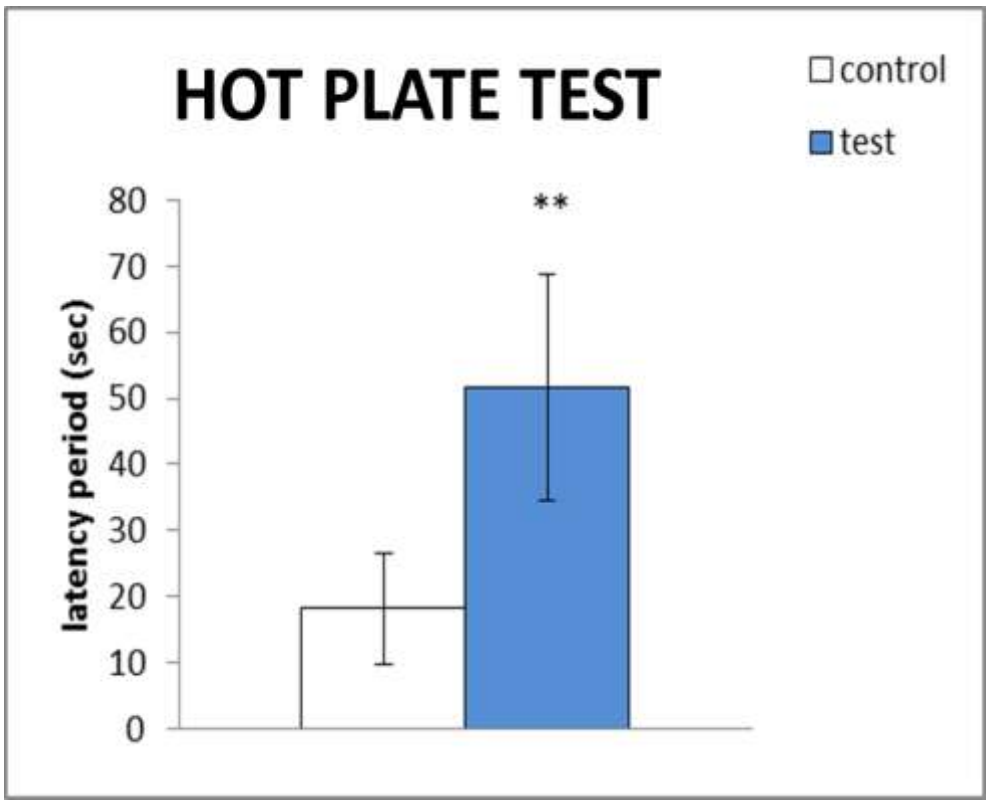

Fig 4: Effect of repeated administration of *Foeniculum vulgare* mill oil (0.5ml/day) for three weeks on rats in hot plate test. Values are mean ± SD (n=8). Significant differences by Student's *t*-test; ** ($p<0.01$) from controls

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