A comparative study on the effects of raisin's extract and fluoxetine on depression symptoms in mice

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Abstract

Depression is the most commonly diagnosed psychiatric disorder that has recently been increased. Patients continuously use antidepressants, especially selective serotonin reuptake inhibitors. The goal of this study was comparing the effects of raisin's extract and fluoxetine on depression symptoms in mice. Sixty female mice in the weight range of 25 to 30 g were divided into six groups of control, depression, fluoxetine (1.2 mg/kg) and 50, 100, and 200 mg/kg of extract. All groups, except for the control group, received intraperitoneal injection of 0.4 mg/kg tetrabenazine to create depression. After last dose, all groups were evaluated using forced swim test and tail suspension test. Immobility time was measured as depression index. Data were analyzed using one-way analysis of variance and Tukey test. Results showed that raisin in 100 and 200 mg/kg doses increased mobility time and movement activity of animal significantly in proportion to control and fluoxetine groups ($p<0.05$) which shows depression reduction. Also, movement activities of these doses were increased significantly in proportion to fluoxetine group. Therefore, raisin's hydro alcoholic extract in 100 and 200 mg/kg doses can be a good replacement for fluoxetine to reduce depression symptoms.

Key words: depression, raisin extract, fluoxetine, mice

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Introduction

People experience a wide range of mood situations, and show also various emotional appearances. One of the common appearances is depression (Kaplan et al. 2014). Researches have shown that depression is related to abnormalities in some neurotransmitters of the brain, including serotonin and norepinephrine. Antidepressants are the most common medications in psychiatry (Berietzke et al. 2012).

Selective serotonin reuptake inhibitors are from items which increase the amount of serotonin in the brain is to maintain a mental balance and are followed with a sense of calm. Serotonin is a neurotransmitter which, upon release, returns to the neuron presynaptic terminals. Fluoxetine (Prozac) is one of the famous serotonin reuptake inhibitors. The mechanism of fluoxetine activity is increase in serotonin level in brain which is done by preventing serotonin reuptake into presynaptic terminals and therefore the amount of serotonin will be increased in brain (Stroud. 2012). Fluoxetine, such as many other drugs has side effects which are Nausea, diarrhea, nervousness, insomnia, and sexual problems such as decreased sexual desire and orgasm. The late concern about using fluoxetine during pregnancy is probable risk of heart abnormalities in the baby (Berietzke et al. 2012).

Nowadays, considering side effects of chemical drugs, the excessive cost of these drugs, reduced acceptability, and also the general eagerness to use herbal medicines, diversity of these drugs and their negligible side effects, researchers tend to study medicinal plants (Abdullahzadeh et al. 2014).

Raisin is a dried fruit which is obtained from drying grape under sunlight. This dried fruit contains high amounts of carbohydrate, polyphenol and essential fatty acids (Samah et al. 2012). Grape contains various chemical

compounds such as catechin, proucianidine, anthocyanin, vidin, epicatechin, and acetylbenic derivatives (Iriti et al. 2006, Mukesh. 2009).

Polyphenol compounds of the grape seed extract stimulate endothelial cells of the blood vessels and improve migraine and prevent heart attacks (Harshal et al. 2011). Considering the prevalence of depression and lack of study about the effects of raisin on reducing depression, this research was carried out to study raisin's effects on reducing depression symptoms.

Materials and method

Sixty female mice in the weight range of 25 to 30g were divided into six groups with 10 mice in each group:

- Control group did not receive any drug
- Depression group received tetrabenazine (0.4 mg/kg) to enforce depression
- Fluoxetine group received 1.2 mg/kg of drug after enforcing depression
- Three experimental groups which received 50, 100, and 200 mg/kg of raisin extract intraperitoneal after enforcing depression.

Animals were kept under similar condition (free access to food and water 12:12 hours photoperiod, 23±2°c temperature and 60% humidity in standard cages made of polycarbonate with a stainless steel lattice ceiling) for two weeks to adapt to environment. Cages floors were covered by sawdust which was changing every two days. All experiments were done from 9 to 17 o'clock. Ethical treatment were observed based on the Brazilian ethics guidelines for animal researches (Animal Science Researches Committee of the Vale do Paraiba University), which was approved by the University's Ethics Committee: code IR.IAU.NAJAFABAD.REC.1396.43. To prepare the hydro alcoholic extract, fruits were dried and then powdered by mill. 200 mg of obtained powder was poured in a sterilized erlen and 40cc of ethylic alcohol was added to it and was kept at room temperature. After 72 hours, erlen contents were filtered using whatman paper and desired doses were prepared.

In this study, fluoxetine (1.2 mg/kg) was prepared from Aria Drug Company and tetrabenazine (0.4 mg/kg) was prepared from Day Darou Salamat Company.

All drugs and extracts were dissolved in normal saline (0.9% physiological serum) and injected intraperitoneally in a given volumes. To evaluate the depression, forced swim test and tail suspension test were used. In suspension test, metal bases with 70cm height plus 50 cm ropes between two bases were used. Mice tails were tied up to this rope and the animal was hanged from tail, then, test was begun with a severe movement of the mouse. The time which animal was motionless, inactive and unresponsive was considered as immobility time. Total suspension time was six minutes which first two minutes was considered for adaption and immobility in next four minutes was measured by chronometer in seconds (Sun. 2004).

In forced swimming test, immobility time was used as depression whereas decrease in it was recorded as anti-depression effect. Mice, after injections, were placed separately in containers (25 × 12 × 8) containing water at a temperature of 25°C. Conventionally, lack of movement of the legs was considered as immobile time. Total test time was six minutes which first two minutes was considered for adaption and swimming and immobility in next four minutes were measured by chronometer in seconds. Swimming was active movements of animal legs and circling around the column. In both tests, all variables were recorded by one person which was not aware of samples groups (Potdar and Kibile. 2011).

Obtained data were analyzed at two descriptive and inferential levels. Average and standard deviation were calculated in descriptive level whereas one way variance analysis plus Tukey test were used for inferential. Data were analyzed using SPSS 22 program.

Results

The effect of hydro alcoholic extract of raisin's extract and fluoxetine on depression symptoms during movement and move less time in the tail suspension test

The results of this study showed that prescription of 100 and 200 mg/kg extracts leads to increase movement and decrease move less time in tail suspension test (Figure 1 and 2).

The effect of hydro alcoholic extract of raisin's extract and fluoxetine on depression symptoms during movement and move less time in the forced swimming test

The results of this study showed that prescription of 100 and 200 mg/kg extracts leads to increase movement time in subjects (Figure 3).

The time of move less shows significant effect of extract on reducing the depression in 100 and 200 mg/kg (Figure 4).

Obtained data were analyzed statistically and results are presented in Table 1.

Raisin extract in 100 and 200 mg/kg doses before suspension test (50 minutes) increased mobility time (in seconds) in proportion to depression and control groups ($p<0.01$). Also, fluoxetine increased mobility time (in seconds) in proportion to depression and control groups ($p<0.01$).

Extract in 100 and 200 mg/kg doses reduced immobility time significantly ($p<0.01$) in proportion to depressed and control groups. Also, fluoxetine reduced immobility time significantly ($p<0.01$) in proportion to depressed and control groups.

Figure 1: Time of movement in the tail suspension test in Control, Depression, Fluoxetine and three experimental groups

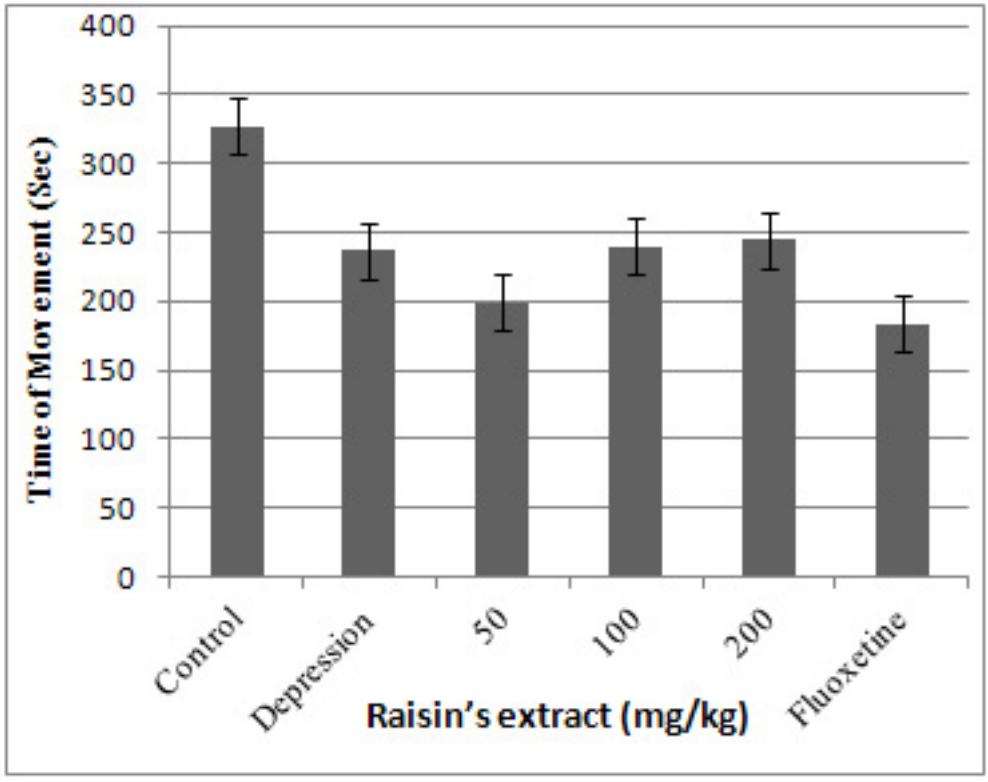

Figure 2: Time of move less in the tail suspension test in Control, Depression, Fluoxetine and three experimental groups

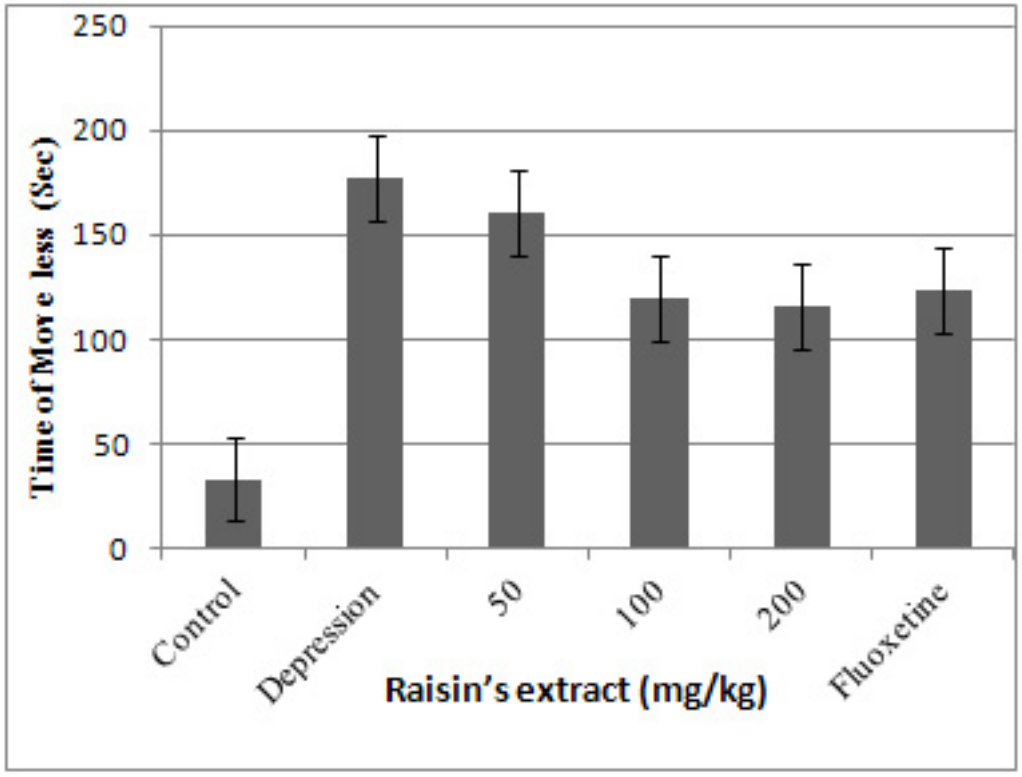

Figure 3: Time of movement in the forced swimming test in Control, Depression, Fluoxetine and three experimental groups

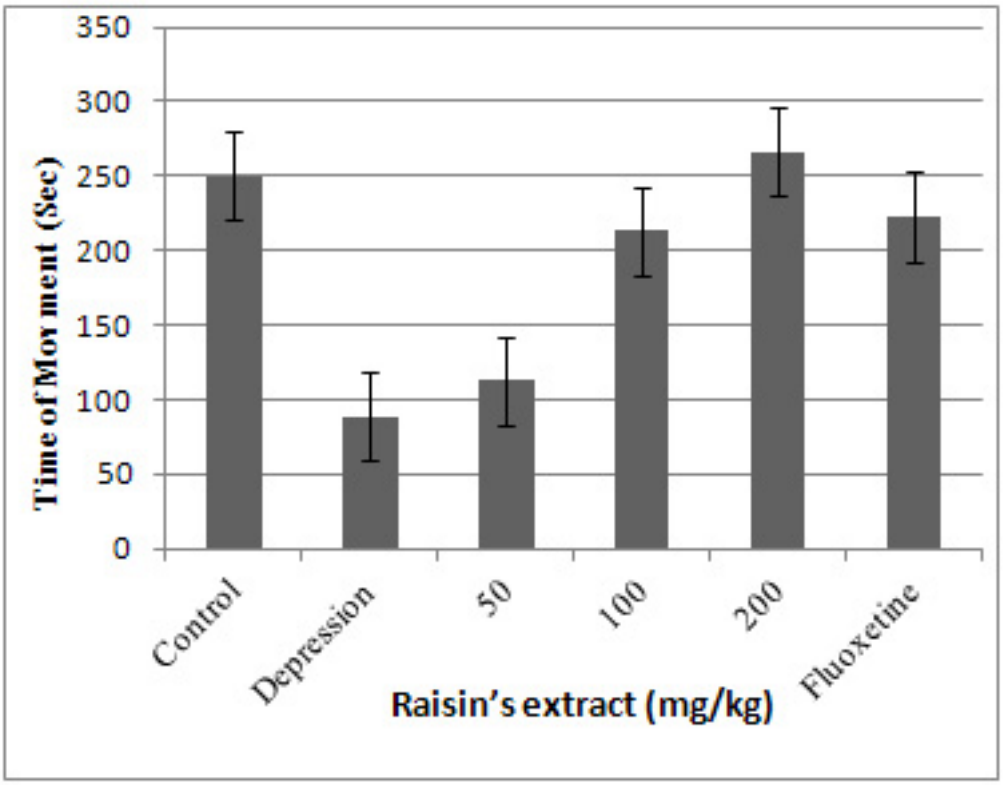

Figure 4: Time of move less in the forced swimming test in Control, Depression, Fluoxetine and three experimental groups

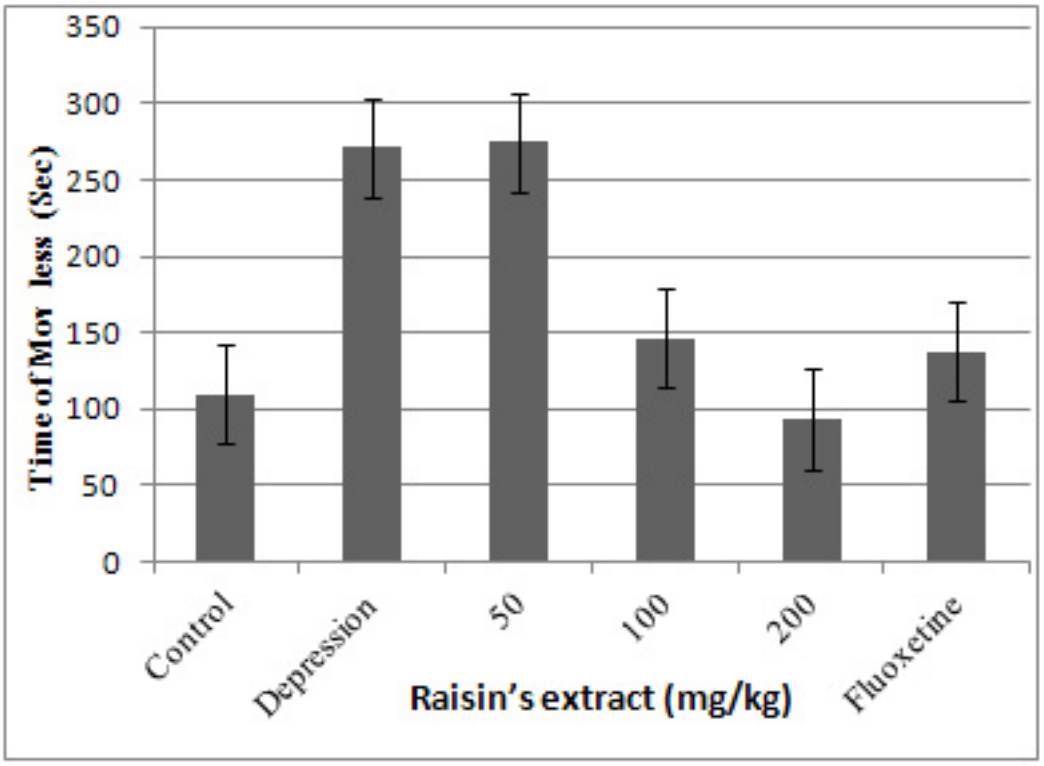

Table 1: Average and standard deviation of variables

	Suspension test (movement)		Suspension test (move less)		swimming test (movement)		swimming test (move less)	
	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation	Average	Standard deviation
Fluoxetine	236.3	18.89	123.7	18.89	222.4	29.69	137.6	29.69
Depressed	183.1	27.83	176.9	27.83	89.1	7.26	270.9	7.26
Control	326.7	27.03	33.3	27.02	250.3	38.67	109.7	38.67
50mg/kg	199.3	28.39	160.7	28.39	112.6	42.47	274.4	42.47
100mg/kg	239.7	30.76	120	30.95	213.3	11.4	146.7	11.4
200mg/kg	244.2	47.41	115.8	47.41	266.7	7.1	93.3	7.1

Discussion

In the current study, the effects of raisin extract and fluoxetine were compared on reducing depression symptoms of animal model by forced swim test and tail suspension test. Results showed that fluoxetine reduced immobility time of mice in tests significantly. Since fluoxetine controls serotonin reduction, it can explain anti depression effect because the mechanism of fluoxetine is increasing serotonin level in brain via preventing reuptake of it to pre-synaptic terminals. With this, fluoxetine can overcome symptoms of depression by correcting serotonin disorder in the brain (Stroud. 2012).

In pathology, decrease in function of some neurotransmitters such as serotonin, epinephrine and dopamine leads to depression and almost all chemical drugs with anti-depression properties increase function of at least one of these chemical messengers (Dalvand et al. 2016). It is important that serotonin reuptake inhibitors, including fluoxetine, are the most widely used antidepressant drug (Berietzke et al. 2012). It should be said that dopamine receptors placed pre-synaptic on the dopamine terminals and inhibition of them leads to releasing dopamine as an effective neurotransmitter that can decrease depression severity (Ebrahimi et al. 2017).

On the whole, results of this study showed that probably raisin's effect on immobility time of mice in suspension and forced swimming tests must be a pre-synapse effect due to a change in serotonin reuptake. Another probability is that raisin can be effective via other anti-depression routes. Since in this test, immobility was reduced and movement was increased, the extract has shown anti-depression effects. By more studies raisin's extract can be proposed in place of fluoxetine to reduce its chemical side effects.

Conclusion

According to results, raisin's extract could reduce depression; but to prove this, more studies are necessary. Therefore, we propose more studies on wider range of doses and also comparing the extract with other anti-depressant drugs.

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