

Anxiolytic Effect of Ethanolic Extract of Medjool Dates of *Phoenix Dactylifera* in Mice

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ABSTRACT

Background: Anxiety is one of the most frequent psychiatric disorders, affecting 33.7% of the general population. However, the consumption of healthy diets has been found to help, at least in part, in the prevention and treatment of anxiety-like disorders.

Methods: In this study, the anxiety behaviors of mice subjected to chronic intake of low-and high doses of ethanolic extract of Medjool dates (*Phoenix Dactylifera*) were evaluated in comparison to the counterparts of control mice. The elevated zero maze (EZM) test and marbles burying test were used as models of choice for evaluating anxiety behaviors in these mice. In addition, phytochemical analysis of major secondary metabolite groups was done.

Results: The findings of this study revealed that the ethanolic extract of dates is rich in flavonoids and steroids with known activity as anxiolytics, such as kaempferol. Mice received a low dose (300 mg/kg) of the extract exhibited lower anxiety in the EZM than the untreated mice (negative control), which was determined by a significant increase in the latency to the closed area, a significant decrease in the time spent in the closed area and a significant increase in the number of the entries to the open quadrants. The anxiolytic effect of low dose extract was comparable to that produced in positive control mice treated with diazepam (1.5 mg/kg, i.p) in all tested parameters. Data obtained from the marble burying test also showed a significant anxiolytic effect by low dose (300 mg/kg) of the extract as compared to untreated mice, which was manifested by significant decrease in the total number of buried marbles. The anxiolytic effect of low dose extract in the marbles burying test was comparable to that produced in counterparts of positive control mice treated with fluoxetine (5mg/kg, i.p). On the other hand, chronic intake of high doses (2583 mg/kg) of the extract did not cause any significant anxiolytic effect in the EZM and marbles burying tests.

Conclusions: Overall, these results indicate that regular intake of low dose of ethanolic extract of Medjool dates may help to prevent and manage anxiety disorders. However, further studies are recommended to elucidate the putative mechanism underlying the anxiolytic effect of these dates.

Keywords: Anxiety, elevated zero mazes, *Phoenix dactylifera*, marbles burying, Medjool dates.

INTRODUCTION

Anxiety is a normal body emotion that aids humans in responding effectively to potentially dangerous or unpleasant

situations.¹ However, people with anxiety disorders experience overwhelming and persistent fears that affect their everyday activities and disturb their social interactions.² Anxiety is a crucial component in the developing of cardiovascular diseases and has been frequently associated with other risk factors, such as depression, substance abuse, obesity and sleep disorders.³⁻⁶ Despite the fact that the

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etiology of anxiety disorders remains unclear, it is thought to be linked to a variety of genetic, neurochemical, and metabolic factors.⁷ According to data acquired from large population-based surveys, anxiety illness affects up to 33.7% of the population at some point in their lives.⁸ Anxiety and Depression Association of America has envisaged that anxiety disorders are the most common mental illness in the United States, impacting 18.1 % of the population each year.⁸ Examples of anxiety disorders include generalized anxiety disorder, social anxiety disorder (social phobia), specific phobias, separation anxiety disorder and obsessive-compulsive disorders.⁹ The symptoms of anxiety might start as early as childhood or adolescence and last into adulthood.¹⁰ When the symptoms become overwhelming or counseling becomes ineffective, pharmacotherapy may be considered to assist patients in coping with their anxiety. During the last decades, treatment options for anxiety disorders have expanded to include both prescription drugs and natural remedies.⁸ Given that anxiety disorders are associated with a subset of underlying metabolic disturbances, that are influenced by lifestyle factors, complementary nutritional interventions for anxiety appear to be effective.¹¹ Several studies demonstrated that dietary phytochemicals such as phenolics, carotenoids, and dietary fibers posse strong antioxidant and anti-inflammatory properties and maintain metabolic hemostasis.¹² In addition, the use of medicinal plants is believed to enhance brain function owing to modulatory effects on the gut-brain axis and neurochemical transmission.¹³ Accumulating research have suggested that herbal supplements and fruits may be beneficial as alternative safe options for the management of anxiety and other psychiatric illness.¹⁴

Traditional Mediterranean fruits are an excellent source of therapeutic agents for a wide range of disorders, including psychiatric illnesses.¹⁵ Dates, which are fruits of the date palm tree (*Phoenix dactylifera*), are a staple food in many Middle Eastern countries that are oval-shaped fruits, yellow in color, some of which tend to be red, with sweet taste.¹⁶ Dates are among the fruits that Arabs and Muslims hold in high regard

and consume on regular basis, particularly during the fasting month of Ramadan.¹⁷ Dates have been reported to have various health benefits including anti-tumor, antioxidant and anti-inflammatory properties.¹⁷ In addition, dates have been traditionally claimed for their ability to strengthen nerves and improve cognition and memory, resulting in the person becoming calm, clear-minded and alert.¹⁸

There are several types of dates, among which Medjool dates are traditionally known as "king of dates" owing to their rich texture, large size and wonderful taste, which combines the flavor of caramel, wild honey and some cinnamon. Medjool dates are originally from Morocco, but they have since moved to the United States, Iraq, Iran, South Asia, Jordan, and Palestine. Jordanian Medjool dates, which constitute 14% of global production, appear to achieve the rigorous standards for Medjool date farming. The Jordan Valley, which is the lowest area in the world above sea level, is considered one of the most suitable regions in the world for the production of Medjool dates due to its distinctive weather and fertile soil.¹⁹ Though there have been many traditional claims on the therapeutic properties of Medjool dates, little is known about their neurobehavioral effects when consumed on a daily basis. According to previous studies, Medjool dates contain phytoactive compounds like flavonoids, phenolics and sterols which have been shown to affect brain functions.²⁰ In this regard, the current research was carried out to see if an ethanol extract of Medjool dates could have therapeutic benefits on the central nervous system. The present work aimed to investigate the possible anxiolytic-like effects of the ethanolic extract of Medjool dates in mice using the elevated zero-maze and marbles burying tests as animal models of anxiety. We hypothesized that supplementation with Medjool dates extract could reduce anxiety-like behaviors in mice.

MATERIALS AND METHODS

Chemicals

Ethanol (96%) was obtained from EMSURE (Darmstadt, Germany). Diazepam and Fluoxetine were

obtained from Sigma Aldrich (Massachusetts, USA).

Dates fruit extraction

One kilogram of fully ripe Tamr stage date palms (Medjool variety) was obtained from Haroun Al-bader Al-Odwan farm, in West Shona-Jordan. The harvest was of October 2020. Medjool dates (*Phoenix dactylifera* L. cv. *Medjool*) identified by Professor Nihad AlSmairat from the University of Jordan referred to The Illustrated Guide to the Cultivation of Date Palms and Dates book.²¹

Phoenix dactylifera Ethanolic Extract Preparation

First, seeds were removed from the *Phoenix dactylifera* fruits. The flesh was cut into very small pieces and separated into many trays. As *Phoenix dactylifera* is very wet, the small pieces were covered using soft fabric, then dried under the sun for a week. After that, the fruits were dried using Gallenkamp oven (CAMBRIDGE, UK) for about three weeks at 50°C until they were completely dry. The dried pieces were pulverized into fine particles using MEGA coffee grinder (China), mortar, and pestle, then sieved until we obtained a sugar-like texture. Finally, the powder was stored in a dry glass container.

Dry *Phoenix dactylifera* powder was macerated in

absolute ethanol, using the method of El Abed H *et al.* with minor modification.²² Briefly, 15g of powder were macerated in 100ml absolute ethanol, and stirred for 24 hours at room temperature, using a hot plate (Thermo SCIENTIFIC CIMAREC) with magnetic stirrer (STUART SCIENTIFIC-UK). The extract was filtered using *Xinxing* Qualitative filter paper 125mm. Ethanol was evaporated and disposed using Rotavapor device associated with a heating bath R-300 (BUCHI Labortechnik, Switzerland) and vacuum pump V-700 (BUCHI Labortechnik, Switzerland). The extract became viscous and had acaramel-like texture and was kept in the round bottom flask for few hours for air drying, then it was stored in a dry glass container and was ready to be used. Each amount of the extract was dissolved in distilled water before use.

Phytochemical Screening of *Phoenix dactylifera* Ethanolic Extract

Phytochemical screening tests were used to detect the secondary plant metabolite groups including alkaloids, flavanoids, steroids, saponins, and tannins present in the ethanolic extract, using standard procedures with some modifications (Table 1).^{23, 24}

Table 1. Phytochemical Screening Tests

Test	Procedure	Observation in case of positive result	Indication
Ferric Chloride test	Crude extract was mixed with 2ml of a 2% FeCl ₃ solution	Blue-green or blue-black color	Polyphenols and Tannins
Frothing test	Crude extract was mixed with 5ml distilled water and vigorously shaken for 30 seconds.	Formation of stable and high froth, more than 1cm	Saponins
Cyanidine test	Two milliliter of concentrated hydrochloric acid was added to a half gram (0.5g) of crude extract dissolved in methanol. Effervescence was observed by adding a spatula full of magnesium turnings to the mixture.	Presence of brick reddish color.	Flavonoids
Dragandroff's test	In a test tube, the extract was mixed with 1ml of dragandroff's test.	Orange to reddish brown precipitate.	Alkaloids

Test	Procedure	Observation in case of positive result	Indication
Lieberman-Burchard test	About 0.5g of the crude extract was dissolved in 0.5ml dichloromethane to give a dilute solution and then 0.5 ml of acetic anhydride added, followed by three drops of concentrated sulphuric acid.	A blue-green coloration	Steroids

The exact phytochemicals compounds in the extract were detected by Liquid Chromatography with tandem mass spectrometry LC-MS/MS (SHIMADZU, **Japan**).

Husbandry of experimental animals

Balb-c mice (weighing 20–25 g) were obtained from animal house of Al-Zaytoonah University of Jordan (Amman, Jordan). All mice were housed under regulated conditions (22-25°C, a 12 h light-dark cycle) in polyacrylic cages. The mice were cared in accordance with the guide of the Canadian Council on Animal Care,²⁵ and the study protocol was approved by the ethical committee at Al-Zaytoonah University of Jordan (2017–2016/22/40).

Animal groups and treatments

The mice were divided into four groups (six animals per cage), acclimatized to laboratory conditions for 7 days, and then treated as follows:

Negative control: mice of this group were given free access to drinking water without receiving any drugs or plant materials.

Positive control: mice of this group were treated with diazepam (1.5 mg/kg) or fluoxetine (5 mg/kg) at 30 minutes prior to behavioral experimentations. The duration of treatment was based on standardized protocol in the previous studies.²⁶⁻²⁸

Dates (low dose) group: mice were treated by 300mg/kg of *Phoenix dactylifera* extract dissolved in distilled water for 30 days prior to behavioral testing.

Dates (high dose) group: mice were treated by 2583mg/kg of *Phoenix dactylifera* extract dissolved in distilled water for 30 days prior to behavioral testing.

The low dose (300mg/kg) of *Phoenix dactylifera*

extract was chosen because it has previously been found to be a functional and effective dose in a mouse study.²⁶ The high dose of *Phoenix dactylifera* extract (2583mg/kg) is similar to one piece of *Phoenix dactylifera* fruit consumed in one day by a human. One date weighs about 15g, and the equivalent dose was converted from human to mouse dose in mg/kg by multiplying the human dose by 12.3, the constant used to calculate the mouse dose based on the surface area difference between human and mouse.²⁹

The observers of the behavioral tests were blinded to the treatments in all experimental sessions.

Behavioral tests

Elevated zero maze test

Anxiety behaviors were assessed using the elevated zero maze (EZM) apparatus. The anxiety behaviors were evaluated using a method described previously in the literature.^{30, 31} The EZM is made up of four quadrants (two closed quadrants enclosed by 30 cm high walls, and the other two open quadrants left uncovered), that have a 5cm wide circular corridor, and are placed so that the two quadrants of each kind are opposite each other. The maze has a diameter of 60cm and stands 50cm off the ground. The test began with each mouse being placed in an open quadrant, with its head facing one of the closed arms. The latency to the closed arms, time spent in the closed arms, and the total number of enters to open quadrants were measured as indices for anxiety.

Marbles burying test

This experiment was conducted in a polypropylene mouse cage (42x24x12cm) with a metal grid top as described previously.³² The floor of the cage was coated with a 5 cm

thick layer of bedding material, with 20 clean glass marbles (diameter 1.5 cm) were evenly arranged on top in a parallel pattern. The experiment was conducted by placing each mouse individually in the cage for 30 minutes. At the end of the experimental session, the mouse was removed, and the number of marbles buried to at least two-thirds was counted and used as an index of anxiety. Fluoxetine was used as a reference drug to assess the burying activity. Fluoxetine, the drug of choice for treatment of obsessive-compulsive disorder (OCD), has been frequently used as a reference in the marbles burying test.^{27,33}

Statistical Analysis

Results obtained from animal experimentation were presented as mean \pm SD. Graph pad prism

(www.graphpad.com) was used to conduct comparative measurement using One-way ANOVA with Tukey's post-test. A probability level (p-value) of 0.05 or less was considered significant.

RESULTS

Phytochemical Screening of *Phoenix dactylifera* ethanolic Extract

Phytochemical screening confirmed the presence of various phytochemical components, including polyphenols, tannins, flavonoids and steroids. A positive sign (+) indicates the presence of the compound while negative sign (-) indicates the absence of that compound (Table 2).

Table 2. Qualitative phytochemical screening of *Phoenix dactylifera* extract

Compound	Result
Polyphenols and Tannins	+
Saponins	-
Flavonoids	+
Alkaloids	-
Steroids	+

The following bioactive phytochemical compounds were identified using LC-MS/MS: kaempferol, campesterol, lutein, apigenin, genistein, isoquercetin, isofucosterol, neoxanthin, stigmasterol, β -carotene, glycitein, violaxanthin, antheraxanthin, formononetin, caffeine, β -sitosterol, quercetin, diadzein, rutin, secoisolariciresinol, ferulic acid, pelargonin, coumestrol, syringic acid, sinapic acid, luteolin, pinoresinol, chlorogenic acid, lariciresinol, o-cinnamic acid, caffeic acid, catechin, p-hydroxybenzoic acid, protocatechuic acid, vanillic acid, matairesinol, gallic acid, and resveratrol.

Effect on anxiety behaviors in EZM test

Data obtained from the EZM test are shown in Fig.1-3. The results showed that chronic intake of extract at low concentration produced considerable anxiolytic effects, determined by a significant increase in the latency to the closed area, a significant decrease in time spent in the closed area and a significant increase in the total number of entries to the open areas as compared to the effect of the negative control group. These effects were comparable to those produced by diazepam. On the other hand, chronic intake of high concentration did not reduce anxiety-like behaviors at all tested parameters.

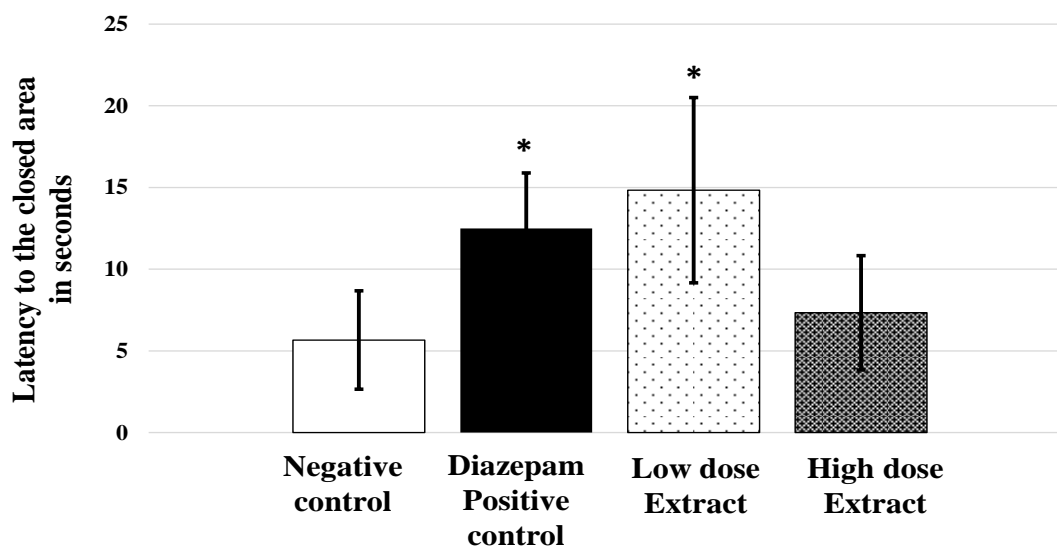


Figure 1: Latency to the closed arms. (*) indicates significant difference from negative control group. One-way ANOVA results (df=3, F=6.8, p value= 0.002). Post-hoc Tukey HSD test results showed significant difference between group received diazepam and negative control (p value=0.0037) and significant difference between group received low dose of extract and negative control (p value=0.004).

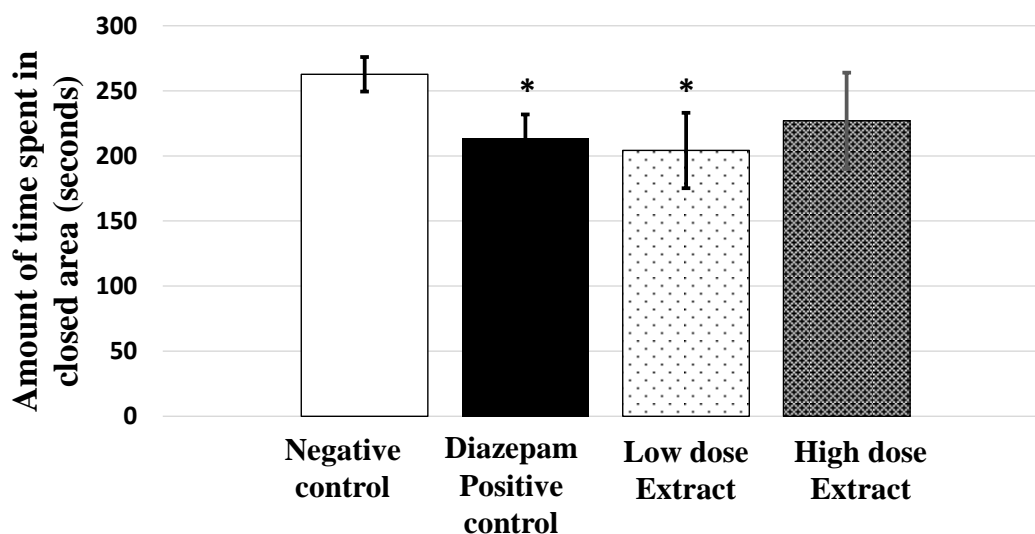


Figure 2: Amount of time spent in the closed arms.

(*) indicates significant difference from negative control group. One-way ANOVA results (df=3, F=5.8, p value= 0.005). Post-hoc Tukey HSD test results showed significant difference between group received diazepam and negative control (p value=0.02) and significant difference between group received low dose of extract and negative control (p value=0.004).

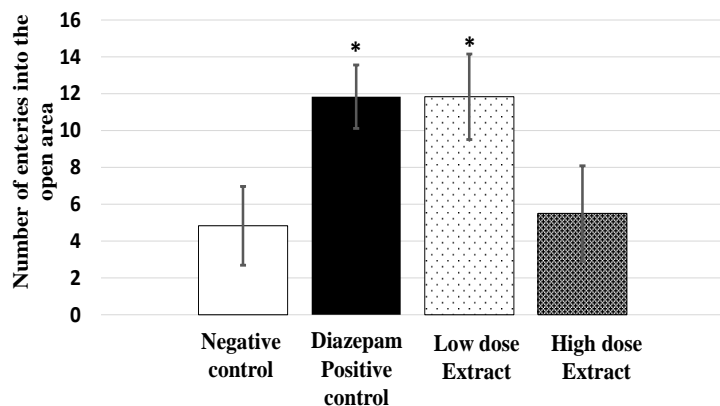


Figure 3: Number of entries into open area.

(* indicates significant difference from negative control group. One-way ANOVA results (df=3, F=18.2, p value= 6.1e-06). Post-hoc Tukey HSD test results showed significant difference between group received diazepam and negative control (p value=0.001) and significant difference between group received low dose of extract and negative control (p value=0.001).

4.2. Effect on marbles burying behavior

The findings of the marbles burying test are presented in Fig.4. The results showed that mice subjected to chronic intake of low concentration of the extract showed significant decrease in marbles burying behavior as compared to the counterparts of the negative control. The reduced burying

behavior by these mice was comparable to that observed in the fluoxetine treating group. In contrast, mice exposed to the high concentration of the extract did not show any significant decrease in the marbles burying behavior as compared to mice of negative control.

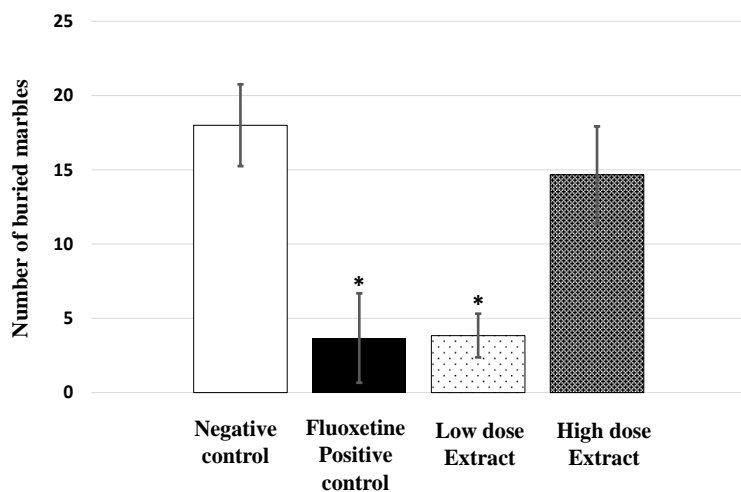


Figure 4: Number of marbles buried during marbles burying test.

(* indicates significant difference (p<0.05) from negative control group. One-way ANOVA results (df=3, F=44.5, p value= 4.9e-09). Post-hoc Tukey HSD Test results showed significant difference between group received fluoxetine and negative control (p value=0.001) and significant difference between group received low dose of extract and negative control (p value=0.001).

DISCUSSION

The cultivation of the Medjool date palm in Jordan is a relatively recent story that has achieved widespread economic success in recent decades.¹⁹ The Jordan Valley, the lowest region in the world above sea level, is known for its great agricultural potential, which is characterized by exceptional climatic conditions including hot summer and moderate winter, as well as the abundance of water supply and fertile soil.³⁴ Accordingly, there is a strong popular belief that Medjool dates grown in the Jordan Valley may exert a great beneficial effect for the maintenance of body homeostasis that has not yet been verified. In this regard, the present work was conducted to prepare an ethanolic extract of Medjool dates from Jordan Valley and evaluate its behavioral effects in mice. The chemical analysis revealed that the whole ethanolic extract of Medjool dates contains phytochemical secondary metabolite groups, such as phytosteroids and flavonoids, that had been previously identified to be effective as anxiolytic agents in prior studies (Table 2). These chemicals are supposed to work as a combination therapy for the management of anxiety by acting on several molecular targets (Table 3). In many cases, the use of whole plant extracts provides more pharmacological benefits than using single separated components.³⁵ Aside from their potential to concentrate the bioactive chemicals, the co-existence of phytochemicals in the whole extracts may exert an interplay effect in terms of enhancing the overall pharmacokinetic and pharmacodynamic effects.³⁶ In various toxicological research in animals, the use of the whole date extracts from different solvents was shown to exhibit a neuroprotective effect against oxidative damage, neuronal damage, spatial learning and memory impairment.^{37, 38} However, this study was conducted to support the conventional claim that regular consumption of dates improves brain function and maintains nervous system homeostasis, including the potential to induce fearlessness trait. In behavioral research, the use of laboratory models with a specific design, known as

"mazes", is a typical method.^{14, 31} The term "maze" is used in behavioral studies to express a complex design of interlocking passages that is shaped in a way that stimulates distinctive behavioral responses.³⁹ Within maze apparatus, laboratory animals display a set of well-recognized behaviors that can be quantitatively analyzed to assess the emotional and cognitive functions.⁴⁰ The zero-maze apparatus is one of the most sensitive and reliable paradigms for evaluating anxiety-like behavioral in mice.^{41, 42} From an experimental point of view, the EZM test provides relatively stable results for multiple trials throughout several days and weeks.⁴² The functional principle of the EZM test is based on the fact that mice display natural aversion toward the open area while preferring to hide themselves in a closed area from potential threats. In particular, the anxiety behaviors in the EZM test were found to be highly sensitive to the drugs that act selectively on the GABAergic nervous system such as diazepam.⁴¹ In this study, data obtained from the EZM test showed that supplementation with low concentration of the date extract caused a significant anxiolytic effect that was comparable to the diazepam effects. Collectively, these results suggest that Medjool Dates will be helpful for the prevention and management of anxiety disorders, which may be attributed in part to a modulatory effect on the GABAergic system. The GABAergic effect could be partially related to the presence of some GABA modulators in the extract such as kaempferol and stigmaterol.⁴³

The anxiolytic effect of the ethanolic extract was also evidenced in the marbles burying test. Marble burying behavior has been examined frequently in research to assess anxiety-related compulsive behavior.⁴⁴ In Psychiatry Diagnostic & Statistical Manual of Mental Disorders (3rd Edition, 3rd Edition Revised, 4th and 5th editions), obsessive-compulsive disorder (OCD) was classified as an anxiety disorder.⁴⁵ It has been well recognized that anxiety behavior in the marbles burying test has a compulsive component, indicating that mice fail

to habituate to anxiety even after several trials of the experiment.³² As a result, this test is commonly regarded as a reliable paradigm for studying obsessive-compulsive disorders.⁴⁶ The principle of this experiment is based on the frequent tendency of mice to bury marbles as frightening objects.⁴⁴ It is thought that burying behavior is controlled by the serotonergic system.⁴⁴ Fluoxetine, a serotonin reuptake inhibitor, has been frequently used as a reference in the marbles burying test. Accordingly, the reduced burying behavior by ethanolic extract of the dates may partially indicate the involvement of the serotonergic system in the mechanism of action. Moreover, the presence of various neuromodulators that act on the serotonergic nervous system, such as genistein

and ferulic acid, may contribute to the serotonergic effect.^{47, 48}

In both the EZM and marbles burying tests, high dose consumption of the extract was ineffective in reducing the anxiety behaviors in mice. This could be due to saturated pharmacokinetics, suggesting significant interaction between various components present in the extract.^{49, 50} In addition, the concentrated ethanolic extract may contain a sufficient amount of anxiogenic chemicals that may counteract the anxiolytic effect of other components present in the extract. For example, caffeine, which was found in trace amounts in Medjool dates, may present at a relatively high dose in the concentrated extract causing a paradoxical anxiogenic effect in mice.^{51, 52}

Table 3. Examples of anxiolytic chemicals available in the Medjool date extract

Chemicals	Examples	Effect on animal model (s)	References
Phytoestrogens	Genistein	Relieving anxiety-like behaviours in ovariectomized rats and in post-traumatic stress disorder models	35
		Regulating symptoms of obsessive-compulsive disorders in streptozotocin-induced diabetic mice	40
Phytosterols	Stigmasterol	Exerting anxiolytic and anticonvulsant effects in pentylenetetrazol-treated mice	43
	B-sitosterol	Alleviating anxiety and exerting a synergetic anxiolytic effect with established anxiolytic drug in mice	53
Flavonoids/ isoflavones	Kaempferol	Exerting anxiolytic activities in the elevated plus maze test in mice	54
	Formononetin	Protecting neurons from N-Methyl-D-aspartate-evoked excitotoxic injury and exerting anxiolytic effect in an inflammatory pain mouse model	55
	Quercetin	Mitigating anxiety-like behavior and normalizing hypothalamus-pituitary -adrenal axis hypersensitivity in a mouse model of mild traumatic brain injury	56
	Rutin	Reducing anxiety-like behaviors in pentylenetetrazol-treated mice	57
Xanthians	Caffeine	Producing anxiogenic and anxiolytic effects at dose dependent manner	52
Phenolic acids/ benzoic acid	Ferulic acid	Alleviating anxiety and other abnormal behaviours in isolation-reared mice and promoting anxiolytic effect in the light-dark test in zebrafish	48

Chemicals	Examples	Effect on animal model (s)	References
	Caffeic acid	Producing anxiolytic effect in elevated plus maze test in mice	58
	Vanillic acid	Reducing anxiety like behavior and impulsivity following global cerebral ischemia in rodents	59
	Gallic acid	Inducing anxiolytic effect in streptozotocin-induced diabetic mice	60

Table 4. underlying mechanism of anxiolytic effects of various chemicals in the ethanolic extract

Chemicals	Mechanism of action	References
Genistein	Enhancing serotonergic transmission in the amygdala	40
Stigmasterol	Exerting a modulatory effect on Gamma-aminobutyric acid system, particularly by enhancing GABA-induced currents at GABA _A receptors	43
Quercetin	Normalizing hypothalamus-pituitary -adrenal axis hypersensitivity	56
Ferulic acid	5-HTA receptor partial agonist activity	48
Caffeic acid	N-methyl-D-aspartate receptor antagonist activity	61, 62, 63

CONCLUSION

Results from the current work suggest that ethanolic extract of Medjool dates may contain bioactive compounds that are capable of reducing anxiety and compulsive behaviours. The underlying mechanism of anxiolytic effect may involve several molecular targets including, at least in part, a modulatory effect on the GABAergic and serotonergic nervous systems. Overall, this study demonstrated that ethanolic extract of Medjool dates could be explored as a valuable source of phytoactive compounds that may provide safe and effective treatment options for a variety of anxiety disorders. However, more researches are needed to map out the total anxiolytic effects of these dates using extract from other solvents.

One limitation of the present study is that only two doses were used, with a considerable gap between them, making it difficult to determine whether the anxiolytic effect of dates extract was dose-dependent. In addition, further investigations are needed to confirm the anxiolytic effect of Medjool dates using additional behavioral models such as the open field, light dark box, and acute restraint tests.

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Declaration of Interest

The authors report that they have no conflicts of interest.

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التأثير المزيل للقلق للمستخلص الكحولي الإثنانولي لتمر المجهول على الفئران المخبرية

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ملخص

الخلفية: القلق هو أحد الاضطرابات النفسية الأكثر شيوعاً، حيث يصيب 33.7% من عامة السكان. ومع ذلك، فقد وجد أن استهلاك الأنظمة الغذائية الصحية يساعد، على الأقل جزئياً، في الوقاية من الاضطرابات الشبيهة بالقلق وعلاجها. **الطرق البحثية:** في هذه الدراسة، تم تقييم سلوكيات القلق لدى الفئران التي تعرضت للتناول المزمن لجرعات منخفضة وعالية من المستخلص الكحولي لتمور المجهول (*Phoenix Dactylifera*) مقارنة بنظيراتها من الفئران الضابطة التي لم تتناول التمر. تم استخدام اختبار ارتفاع متاهة الصفر واختبار دفن كرات الرخام كنماذج مفضلة لتقييم سلوكيات القلق لدى هذه الفئران. بالإضافة إلى ذلك، تم إجراء تحليل كيميائي نباتي لمجموعات الأيض الثانوية الرئيسية لمستخلص تمر المجهول.

النتائج: بينت نتائج هذه الدراسة أن مستخلص تمر المجهول غني بالفلافونويد والستيرويدات مع نشاط معروف باسم مزيلات القلق مثل الكايمفيرول. أظهرت الفئران التي تلقت جرعة منخفضة (300 مجم / كجم) من المستخلص قلقاً أقل من خلال استخدام اختبار ارتفاع متاهة الصفر من الفئران التي لم تتناول مستخلص التمر، والذي تم تحديده من خلال زيادة كبيرة في زمن الوصول إلى المنطقة المغلقة وانخفاض كبير في الوقت الذي يقضيه في المنطقة المغلقة و أيضاً زيادة كبيرة في عدد الإدخالات إلى الأرباع المفتوحة. كان تأثير مزيل القلق لمستخلص التمر من الجرعة المنخفضة مشابهاً للتأثير الناتج في الفئران التي عولجت بالديازيبام (1.5 مجم / كجم) في جميع المتغيرات المختبرة الدالة على مستوى القلق. بالإضافة إلى ما سبق، أظهرت نتائج اختبار دفن كرات الرخام فرقا احصائياً في إزالة القلق بجرعة منخفضة (300 مجم / كجم) من مستخلص التمر مقارنة بالفئران التي لم تتناول مستخلص التمر، والذي تبين من خلال انخفاض في العدد الإجمالي لكرات الرخام المدفون. إضافة إلى ذلك، كان التأثير المزيل للقلق لمستخلص التمر من الجرعة المنخفضة في اختبار دفن كرات الرخام مشابهاً للتأثير الناتج في الفئران التي عولجت بفلوكستين (5 مجم / كجم). من ناحية أخرى، فإن تناول جرعات عالية من مستخلص التمر (2583 مجم / كجم) لم يسبب أي تأثير مزيل للقلق في متاهة الصفر المرتفعة واختبارات دفن كرات الرخام.

الاستنتاجات: بشكل عام، تشيرالنتائج هذه الدراسة إلى أن تناول جرعة منخفضة بانتظام من المستخلص الكحولي من التمر المجهول قد يساعد في منع وإدارة اضطرابات القلق. ومع ذلك، يوصى بإجراء مزيد من الدراسات لتوضيح الآلية المفترضة الكامنة وراء التأثير المزيل للقلق لدى تمر المجهول.

الكلمات الدالة: القلق، متاهة الصفر المرتفعة، فينيكس داكلتيليفيرا، دفن كرات الرخام، تمر المجهول.

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