

## Evaluation of Anxiolytic and Antidepressant Activities of aqueous and Methanolic extract of *Hyphaene thebaica* (dour) fruit in Animal Models

Diab Husain Abu baker      Moafa Adel Ahmed      Zwaiti Aya Salem      Abdulkhaleg Sara Ali

Misurata University

Faculty of Medical Technology

Misurata University

Misurata University

Faculty of Pharmacy

Faculty of Pharmacy

Faculty of Pharmacy

### Affiliation

Article information	Abstract
<p>Received 12 08 2025, Accepted 27 08 2025, Available online 28 08 2025</p> <p><b>Key words</b></p> <p>Pain·analgesic·Dour palm·anxiety·depressant Preparation of Dour palm fruit aqueous extract (DPAE). preparation of Dour palm fruit methanolic extract (DPME). Hole cross test (HCT). Open field test (OFT). Light-dark box test (LDBT).</p>	<p>Hyphaene thebaica (HT), also known as the "Dour palm" belonging to family <b>Arecaceae</b>, is a palm tree native to Africa. <b>Aims:</b> The current study sought to evaluate the anxiolytic-like activities, antidepressant, analgesic and properties of (DPME) and (DPAE) in stressed mice. <b>Experimental design:</b> The study was experimental research designed to include four lines: extraction of the plant materials, evaluation of anxiety using three tests: HCT, OFT, and LDBT, while the depressant activity is assessed by TST. The efficacy of the DPME and DPAE-mediated antidepressant and anxiolytic activities was compared with the control groups, diazepam (1 mg/kg, i.p) as an anxiolytic drug, and fluoxetine (20 mg/kg, p.o.) as an antidepressant drug evaluation of peripheral analgesic activities of DPME and DPAE using the chemical method (acetic acid 1%, i.p.). The fourth line was an assessment of the effect of DPME on PILO (280 mg/kg)-induced convulsions. The study was carried out using Albino mice (30±5 g) of either sex, which were divided into several groups with six mice each.</p>

### Introduction

Hyphaene thebaica (HT), also known as the "Dour palm" belonging to family Aceraceae, is a palm tree native to Africa. **Aims:** The current study sought to evaluate the anxiolytic-like activities, antidepressant, analgesic and anti-convulsion properties of (DPME) and (DPAE) in stressed mice. **Experimental design:** The study was experimental research designed to include four lines: extraction of the plant materials, evaluation of anxiety using three tests: HCT, OFT, and LDBT, while the depressant activity is assessed by TST. The efficacy of the DPME and DPAE-mediated antidepressant and anxiolytic activities was compared with the control groups, diazepam (1 mg/kg, i.p) as an anxiolytic drug, and fluoxetine (20 mg/kg, p.o.) as an antidepressant drug

Plants have been used medicinally since ancient civilizations and form the cornerstone of traditional medical systems worldwide. This interaction highlights the importance of understanding the role of plants in drug discovery as well as its relevance in modern health care (1). Plants provide information about many drugs that can be converted into drugs of choice of efficiency and are potential leading indications for current drug regimens (2). Many herbal medicines act on the central nervous system and have therapeutic potential for chronic diseases such as anxiety, depression, migraine, and tumors, which do not respond well to conventional drugs (3). The use of plants in medicine highlights the long-standing relationship between nature and human health, as they provide essential compounds for the treatment of diseases and the maintenance of health (4).

#### Hyphaene thebaica

Hyphaene thebaica, also referred to as the "Doom palm," is a palm tree belonging to the Arecaceae family that bears tasty oval fruit. Many colloquial names for them include doom palm, doom palm, and gingerbread palm (5, 6). It is indigenous to the region of Africa that stretches from Senegal and Mauritania in the west to Egypt, Kenya, and Tanzania in the east. Along the banks of the Nile, it grows in Egypt, Sudan, and the Arabian Peninsula. In woods or scrub, the Doom palm is resistant to fire and drought. It is believed to be drought-tolerant since it grows in wadis and oases (7). Table [1] shows the taxonomical position where the botany department of Science Faculty Misurata University's classified Hyphaene thebaica (8).

Table [1] Hyphaene thebaica's Taxonomical Position

Kingdom	Plantae
Division	Magnoliopsida
Class	Monocotyledones
subclass	Arecidae
order	Arecales
Family	Arecaceae
Subfamily	Coryphoideae
Genus	Hyphaene

#### Pharmacological activities of Hyphaene thebaica fruits:

Numerous health benefits have been discovered for H. thebaica fruits, a safe and natural therapy. As a hematinic agent, they are used to treat bilharzias (9) and hypertension (10). Atherosclerosis and glomerulosclerosis risk can be decreased by the aqueous extract of H. thebaica fruits in nephrotic syndrome patients with hyperlipidemia (11). Flavonoid extracts dramatically boosted adiponectin levels in diabetic rats, boosting insulin's hypoglycemic action without altering blood insulin concentration (12).

Up to a dosage of 5 g/kg b. wt., the decoction of H. thebaica fruits is well tolerated and causes neither death nor morbidity. After one and two months of dosing, the aqueous extracts of H. thebaica fruits considerably reduced the levels of total lipid, cholesterol, triglycerides, and blood glucose (13). A significant correlation exists between triglycerides and coronary heart disease, although the majority of antihypercholesterolemic medications do not lower triglyceride levels (14). The presence of glycosides in the aqueous pulp suspension may contribute to its hypolipidemic characteristics (15).

## **Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of Hyphaene thebaica (doum) fruit in animal model**

---

### **Anxiety**

Anxiety disorders are prevalent mental disorders characterized by the major disruption of mood or emotional tone (16), affecting almost one-fourth of the population at least once in their lifetime (17). Anxiety symptoms include restlessness, heightened alertness, weariness, difficulty concentrating, impatience, muscle tension, sleep disturbance, and irritability (18).

### **Types of anxiety disorders**

Types of anxiety disorders that are excessive and persistent might lead to anxiety disorders. Among these illnesses are generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD).

### **Treatment for Anxiety**

Ethanol being one of the first anxiolytics. Other drugs like barbiturates and carbamates (meprobamate) were used in the first half of the 20th century. Today, serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and GABA receptor modulators (benzodiazepines) that include alprazolam and diazepam are the first-line agents for anxiety treatment (19).

### **Depression**

Depression is a condition marked by a low mood and a loss of interest in daily activities. It frequently includes four additional symptoms: lack of interest, exhaustion, sleeplessness, and changes in weight or appetite (20,21), with symptoms including sorrow, fear, and irritation. They also endure delusions, feelings of excessive guilt, low self-esteem, and suicidal ideation. These symptoms can trigger emotions of hopelessness and suicidal thoughts (22).

Types of depression:

The diagnostic and statistical manual of mental disorders and the international classification of diseases (ICD) classify depression disorder into the various categories. These include major depressive disorder (MDD), persistent depressive disorder (PDD), premenstrual dysphoric disorder (PMDD), and seasonal affective depression (SAD).

Treatment for depression

Antidepressants are classified into several types. These include selective serotonin reuptake inhibitors (SSRIs), with common medications sertraline and fluoxetine. Tricyclic antidepressants (TCAs) such as amitriptyline and imipramine. Monoamine oxidase

### **Materials and Methods**

#### **The following animal models are used to evaluate analgesic medications**

Animal models that are thermal, mechanical, electrical, chemical, and other types are frequently used in the screening process for analgesic medications. Thermal sensations include hot plate, paw withdrawal, and tail flick. Mechanical stimuli include strain gauges and von-Frey filaments. Electrical stimulation of the tail and limb stimulation are examples of mechanical stimuli. Chemical stimulation: the formalin test, the acetic acid-induced writhing test. These methods advance our comprehension of the ways in which analgesics impact various bodily parts (23).

### **Chemicals and drugs**

Chemicals for extraction: methanol (99.98%). The following drugs and chemicals were used in this study: diazepam, fluoxetine, acetic acid, diclofenac sodium (voltaren)<sup>®</sup>, pilocarpine, hyoscine-N-butyl bromide (Buscopan)<sup>®</sup>, and normal saline.

### **Glassware**

Beakers, flasks, measuring cylinders, funnels, gloves, syringes, pipettes, spoons, roll gauze, filter paper, cages.

### **Animals**

Healthy Swiss albino mice (30±5 g) of both sexes were employed to achieve the project's objectives acquired from the animal house (Misurata University's Pharmacy College), housed in room-controlled settings with a temperature of 24 °C± 2 and a 12-hour light/dark cycle, in polypropylene cages with soft wood bedding materials. Every animal had unrestricted access to drinking water and was fed laboratory chow.

### **Collection of plant material**

Dried fruits of *Hyphaene thebaica* were purchased from the Misrata market, Libya. The dried fruits have been cleaned. The Botany Department at the Faculty of Science, Misrata University, classified *Hyphaene thebaica*.

### **Preparation of extraction**

The whole *Hyphaene thebaica* was ground into small-sized bits with a hammer and a home electric blender, then divided into two parts and weighed with a sensitive balance to create an alcoholic (methanolic) and aqueous extract.

### **Preparation of Doum palm fruit aqueous extract (DPAE)**

Two hundred sixty grams of *Hyphaene thebaica* were weighed using the macerated method. It was soaked in a sufficient amount of mineral water (780 ml/1:3 w/v) for 48 hours at room temperature with frequent stirring, then the extract was filtered using clean, sterile gauze first, then using filter paper.

### **preparation of Doum palm fruit methanolic extract (DPME)**

Two hundred sixty grams of the powder were extracted at room temperature, away from light for 48 hours, by the macerated method using (1:3 w/v) 780 ml of 99.8% methanol with frequent stirring. then the extract was filtered using clean, sterile gauze first, then using filter paper.

### **Experimental design**

#### **Assessment of the anti-depressant and anti-anxiety properties of DPAE and DPME**

#### **Hole cross test (HCT)**

A case of 30 x 20 x 14 cm was utilized, with a wooden barrier attached in the center. The cage contained a 3 cm diameter aperture at a height of 7.5 cm in the center. The animals were separated into control, positive control, and two test groups of six animals each. The test groups received DPAE at the dose of 400 mg/kg and DPME at 400 mg/kg body weight intraperitoneally, and the control group received distilled water (0.1 ml/mouse, i.p.). The standard drug diazepam (1 mg/kg, i.p.) was used as a positive control group. Each mouse was individually examined. The mice were passed through the hole from one chamber to another, and the number of passages was counted for 3 minutes at 0, 30, 60, 90, and 120-minute intervals, respectively, after a single treatment administration, using a video camera for observation of the mice (24).

#### **Open field test (OFT)**

The open field test is used to evaluate the locomotion in mice by the number of square crosses. The animals were divided into control, positive control, and two test groups containing six

## **Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of Hyphaene thebaica (doum) fruit in animal model**

---

animals in each. The test groups received DPAE at the dose of 400 mg/kg and DPME at 400 mg/kg body weight intraperitoneally, and the control group received distilled water (0.1 ml/mouse, i.p.). The standard drug diazepam (1 mg/kg, i.p.) was used as a positive control group. Each mouse was individually examined. The open field was divided into a series of squares. Each square is separately colored black and white. The apparatus had a wall of 40 cm height (25). The animals were visited in the squares, and the number of visited squares was counted for 3 min at 0, 30, 60, 90, and 120-min intervals, respectively, after a single treatment administration, using a video camera for observation of the mice.

### **Light-dark box test (LDBT)**

This test involves a specially designed box with one light compartment and another dark compartment, allowing researchers to observe the time spent in each area as an indicator of anxiety levels. The apparatus is a transparent glass box, 40 cm high, 40 cm long, and 42 cm wide, divided into two compartments, each 20 cm wide. The chambers were separated by a partition with a hole in the middle at the bottom. One of the rooms has all the walls painted from the inside with black paint and a movable cover. During the experiments, the apparatus was placed in the laboratory with moderate lighting. The animals were divided into control, positive control, and two test groups containing 6 animals in each. The test groups received DPAE at the dose of 400 mg/kg and DPME at 400 mg/kg body weight intraperitoneally, and the control group received distilled water (0.1 ml/mouse). The standard drug diazepam (1 mg/kg, i.p.) was used as a positive control group. Each mouse was placed individually in the middle of the light compartment, facing the opening of the dark one. The time spent in the light compartment and the number of transitions between the two boxes were recorded for 10 minutes. The LDBT was cleaned with 70% alcohol and allowed to dry between tests (26, 27, 28).

### **In" Anxiolytic activity was evaluated by HCT, OFT, and LDBT, whereas antidepressant-like activity was assessed by the Tail Suspension Test (TST).**

This behavior displayed in rodents subjected to unavoidable and inescapable stresses during the tail suspension test reflects behavioral despair, which reflects depression in humans. Mice were divided into four groups, containing six animals in each. Thirty minutes after giving the extracts, DPAE and DPME (400 mg/kg, i.p.) were used as test groups. The fluoxetine (20 mg/kg, p.o.) was given orally forty-five minutes prior as the standard drug when the control group received distilled water (0.1 ml/mouse, i.p.). Mice were suspended 50 cm above the floor using adhesive tape placed approximately 1 cm from the tip of their tails. The duration of immobility time was recorded for 6 min. after a single treatment administration, using a video camera for observation of the mice. The mice were considered immobile when they passively hung or stayed motionless (29).

## **Results**

### **Assessment of the Antidepressant and Anxiolytic Activities**

#### **Effect of DPME and DPAE in HCT model**

(Table 2) represents the sedative effect of DPME and DPAE by hole cross test in mice. Extracts showed a significantly decreased movement and number of holes crossed at the doses (400 mg/kg) starting as early as 30 min ( $P < 0.0001$ ) by DPME and ( $p < 0.05$ ) by DPAE, with the sedative effect continuing to over time compared to the control. Starting at 30 min, the number of holes crossed from one chamber to another significantly decreased ( $p < 0.0001$ ) by the

standard drug (diazepam, 1 mg/kg). The control group's activity remains constant with little variation in the number of holes traversed, suggesting that there is no discernible behavioral change. Results are illustrated in Figure 3

Table [2] Effect of DPME and DPAE of Hyphaene thebaica and diazepam on hole cross test

Treatments and Doses(mg/kg )	Number of holes crossed (% of inhibition)				
	0 min	30 min	60 min	90 min	120 min
Control 0.1ml/mouse	11.00±0.97	10.00±0.37	10.33±0.76	10.33±0.76	10.00±1.32
Diazepam 1mg/Kg	5.17±2.41*	3.33±0.95** *	4.67±1.41*	5.33±0.84**	4.00±0.68*
DPME 400mg/Kg	1.33±0.42** *	2.50±1.02** *	2.83±1.14* *	1.67±0.76** *	2.67±0.49* *
DPAE 400mg/Kg	2.50±0.85** *	3.67±1.76*	4.00±1.95*	3.67±0.71** *	4.83±1.70*

Values are presented as mean ± SEM (Standard Error Mean); (n = 6). \* p < 0.05, \*\*P< 0.001 and \*\*\* P< 0.0001 significant different from control group.

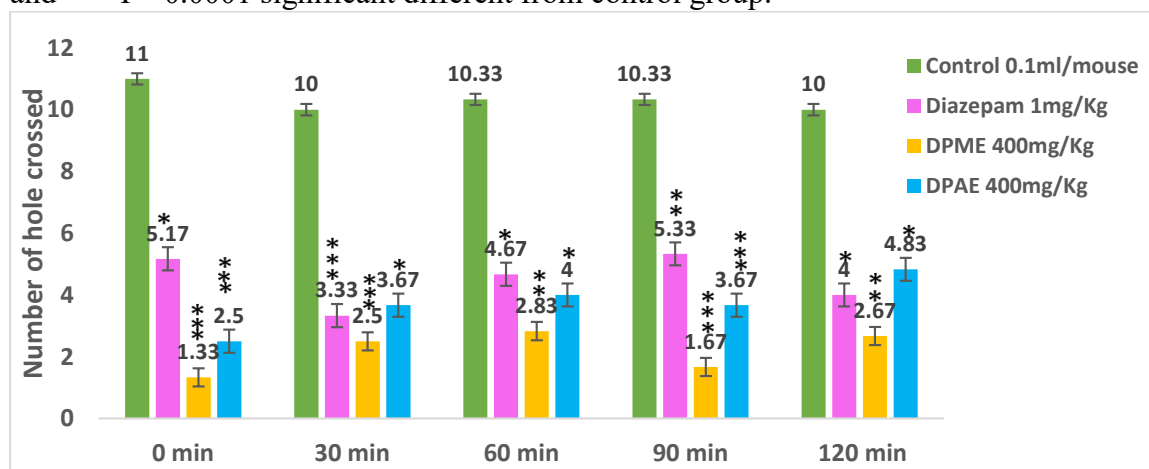


Figure [1] Effect of DPME and DPAE of HT and diazepam on hole cross test. Number of holes crossed.

**Effect of DPME and DPAE in OFT model**

The open field test was performed for 120 min. As shown in Table 3, intraperitoneal administration of DPME and DPAE decreased the locomotor activity in mice at doses of 400 mg/kg. DPME significantly (p <0.05) decreased the number of squares crossed with results similar to diazepam, and DPAE decreased the number of squares crossed (p <0.05) as compared to the control group. Diazepam (1 mg/kg, i.p.) showed a noticeable decrease in locomotion in mice when compared with the control.

Table [3] Effect of DPME and DPAE of Hyphaene thebaica and diazepam on open field test

**Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of Hyphaene thebaica (doum) fruit in animal model**

Treatments and Doses(mg/kg )	Number of squares crossed (% of inhibition)				
	0 min	30 min	60 min	90 min	120 min
Control 0.1ml/mouse	121.67±5.85	71.67±1.87	79.33±3.73	92.67±9.97	91.67±9.90
Diazepam 1mg/Kg	67.33±11.42*	46.33±8.96*	36.5±6.37**	58.67±5.06*	61.83±6.13*
DPME 400mg/Kg	33.5±7.00***	45.33±7.03*	47.67±4.30*	49.33±7.05*	57.33±7.36*
DPAE 400mg/Kg	68.33±5.14**	57±4.49*	55.17±5.02*	71±0.58*	80.17±4.11

Values are presented as mean ± SEM (Standard Error Mean); (n = 6). \* p < 0.05, \*\*P< 0.001, \*\*\*P<0.0001 significant different from control group.

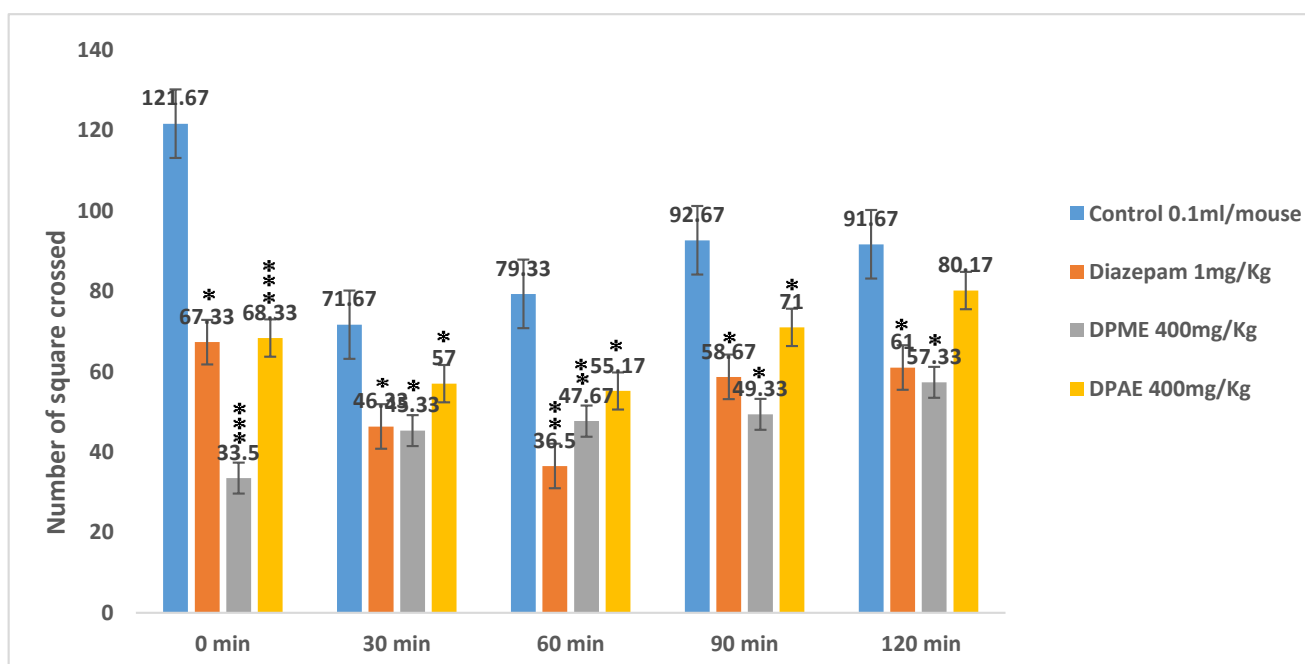


Figure [2] Effect of DPME and DPAE of H.T. on number of squares crossed

**Effect of DPME and DPAE in LDBT model**

Table 5 and Fig. 7, 8 show that administration of DPME at doses of 400 mg/kg exhibited anti-anxiety effects, as determined by a significant increase (P< 0.005) in the time spent in the light chamber (411.40 ± 51.58), and DPAE administration at a dose of 400 mg/kg decreased anxiety-related behavior by a significant increase (p< 0.05) in the time spent in the light chamber (246.67±19.02), compared to the control group (148.17 ± 26.55), and in a similar fashion that was produced by the standard drug diazepam (P< 0.05) (336.33 ± 53.82). As an inevitable result of the length of time the animals spent in the light chamber, the time they spent in the dark chamber was 188.60±51.58, 353.33±19.02 for the two extracts DPME and DPAE, respectively,

and  $263.67 \pm 53.82$  for the diazepam dose ( $P < 0.05$ ), while for the control group it was  $452.83 \pm 26.56$ . Additionally, this extract, DPME, significantly ( $P < 0.05$ ) decreased the number of transitions between light and dark chambers ( $12.33 \pm 2.91$ ); the DPAE number of transitions was  $18.00 \pm 1.67$ , while diazepam (1 mg/kg) decreased significantly the number of transitions compared to the control gro.

Table [4] Effect of DPME and DPAE of Hyphaene thebaica and diazepam on light-dark box test

Treatments and Doses (mg/kg)	Number of transitions	P value vs control	Time in the dark(s)	Time in the light(s)	P value vs control
Control 0.1ml/mouse	$22.50 \pm 2.88$		$452.83 \pm 26.56$	$148.17 \pm 26.55$	
Diazepam 1mg/kg	$13.67 \pm 1.12^*$	0.0171	$263.67 \pm 53.82^*$	$336.33 \pm 53.82^*$	0.0103
DPME 400mg/Kg	$12.33 \pm 2.91^*$	0.0324	$188.60 \pm 51.58^*$	$411.40 \pm 51.58^*$	0.0026
DPAE 400mg/Kg	$18.00 \pm 1.67$	0.2069	$353.33 \pm 19.02^*$	$246.67 \pm 19.02^*$	0.0130

Each value represents the mean  $\pm$  SEM (Standard Error Mean); (n = 6). \*P < 0.05, in comparison with control.

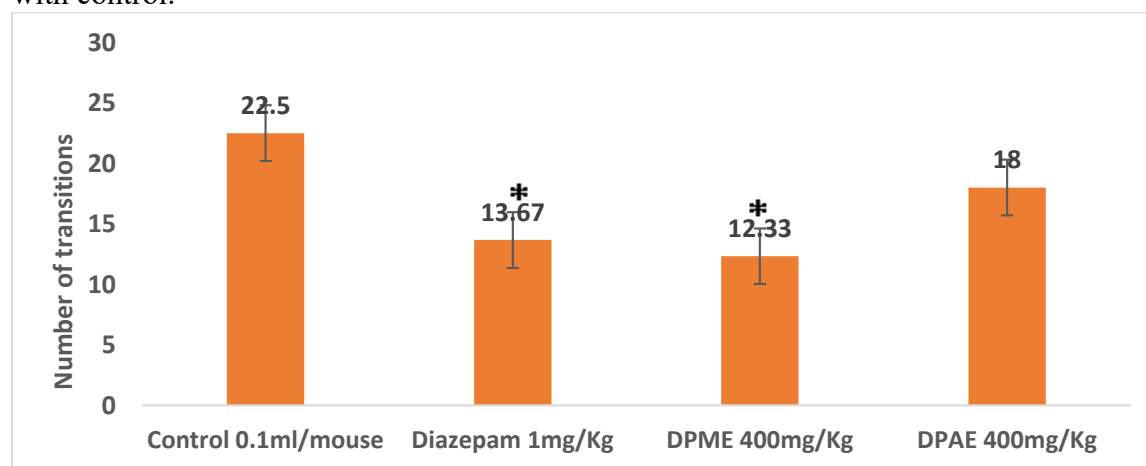


Figure [3] Effect of DPME, DPAE, and diazepam in a light/dark box test in mice; number of transitions between light and dark chambers.

up ( $13.67 \pm 1.12$ ).



**Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of Hyphaene thebaica (doum) fruit in animal model**

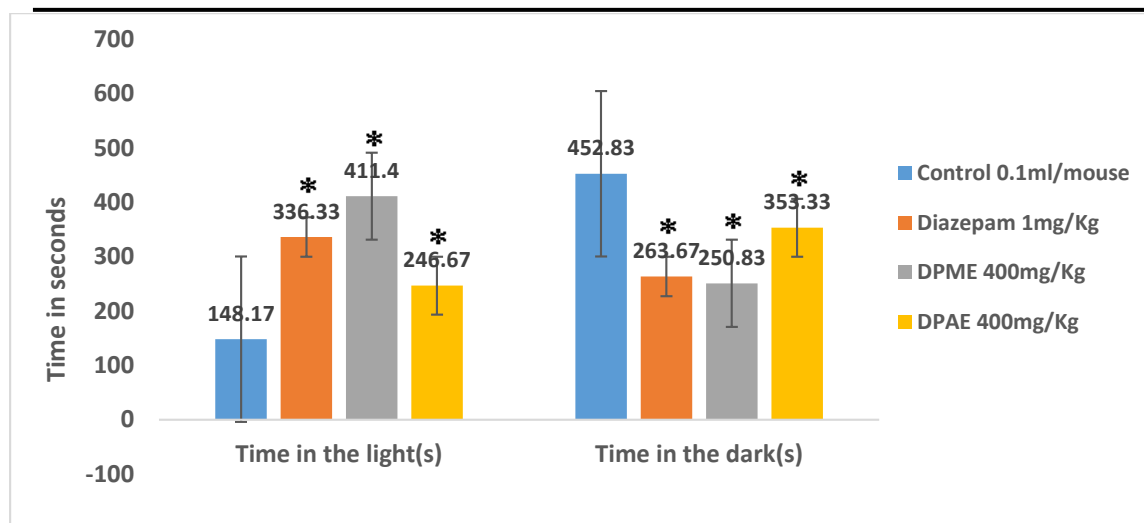


Figure [4] Effect of DPME and DPAE of H.T. on the light/dark box test in mice. Time spent in the light and dark chambers in seconds.

**Effect of DPME and DPAE in TST model**

The results of the tail suspension test (TST), as shown in Table 5, show a significant ( $P < 0.05$ ) decrease in the duration of the immobility time ( $96.33 \pm 15.01$ ) after intraperitoneal administration of the DPME group at doses of 400 mg/kg; the percent decrease in immobility was 26.34%. While in DPAE at a dose of 400 mg/kg, a decrease in duration of immobility time was shown ( $109.50 \pm 12.95$ ), not statistically significant ( $p = 0.1302$ ), and the percent decrease in immobility was 16.83% compared with the control. Oral administration of the standard drug, fluoxetine 20 mg/kg forty-five minutes prior to TST, accomplishes a significant decrease in the duration of the immobility time ( $80.33 \pm 19.22$ ); the percentage decrease in immobility was 38.99%. Compared to the control group (0.1 ml/mouse), it had a duration of immobility time of ( $131.67 \pm 3.60$  seconds), as shown in figures 5 and 6.

Table [5] Effect of DPME and DPAE of Hyphaene thebaica and fluoxetine on tail suspension test

Treatments and Doses(mg/kg)	Immobility time in seconds	P vs control value	% of immobility decrease
Control 0.1ml/mouse	131.67±3.60		
Fluoxetine 20mg/kg	80.33±19.22*	0.0281	38.99%
DPME 400mg/kg	96.33±15.01*	0.0443	26.34%
DPAE 400mg/kg	109.50±12.95	0.1302	16.83%

Each value represents the mean ± SEM (Standard Error Mean); (n = 6). \* $P < 0.05$ , in comparison with control.

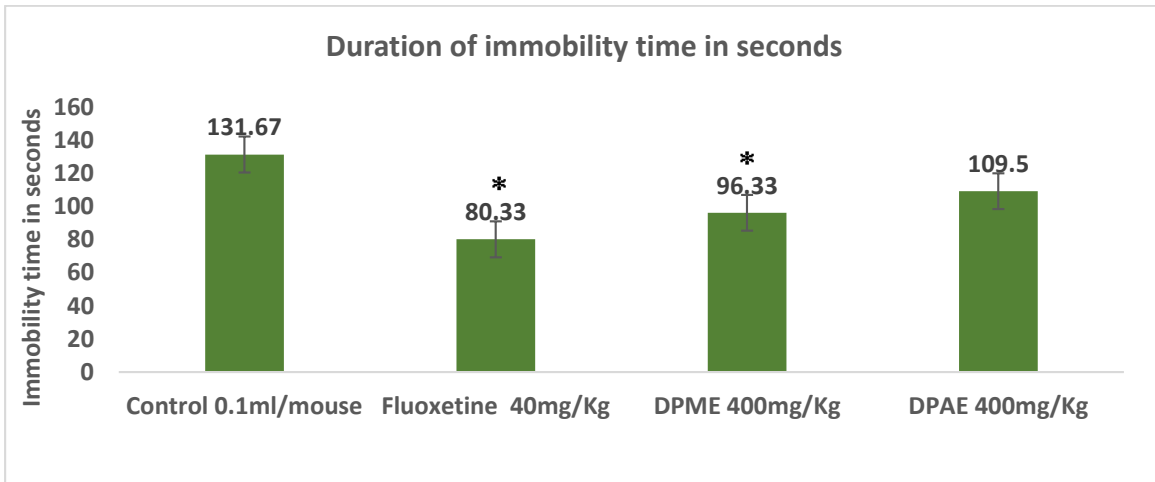


Figure [5] Effects of DPME, DPAE, and fluoxetine on TST. Duration of immobility time in seconds.

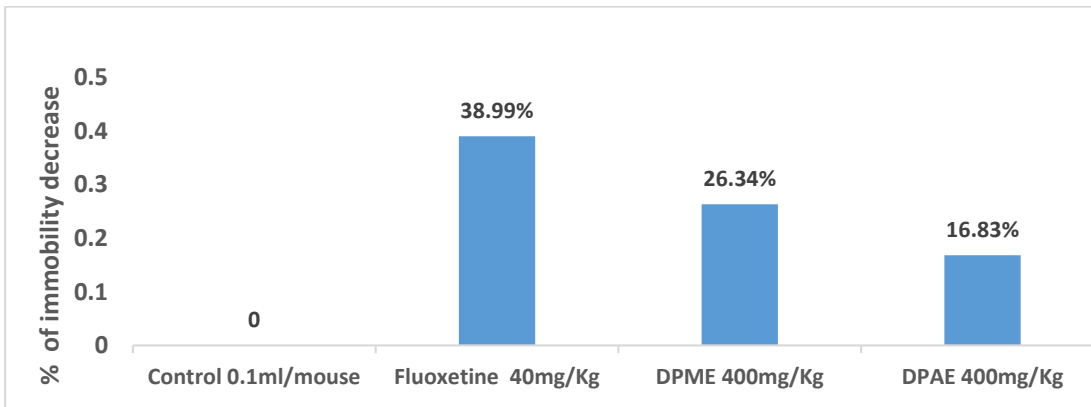


Figure [6] Effect of DPME and DPAE on immobility percentage in TST

### Discussion

The study was conducted for the current graduation project to clarify the anti-depressant, anxiolytic, analgesic, and anti-convulsant activities of the aqueous and methanol extract of *Hyphaene thebaica* fruit in mice. The phytochemical screening of *H. thebaica* refers to the presence of bioactive constituents such as alkaloids, flavonoids, steroids, carbohydrates, saponins, amino acids, terpenoids (30, 31).

Anxiolytic and antidepressant activities of *H. thebaica* fruit aqueous and methanolic extracts were assessed by applying four tests: (HCT), (OFT), (LDB), and (TST). The analgesic activity was also evaluated by widely used models, namely the acetic acid-induced writhing test, and the anticonvulsant activity was evaluated by a pilocarpine-induced test on Swiss albino mice.

Anxiety and depression are linked to oxidative stress and neurotransmitter dysregulation, including GABA, serotonin, and dopamine, with lower antioxidant plasma concentrations potentially contributing to mental diseases (32, 33). Antioxidants, such as superoxide dismutase, catalase, and glutathione peroxidase, help mitigate the harmful effects of oxidative stress. Low-molecular-weight antioxidants like vitamin C and E, flavonoids, and carotenoids are effective in reducing oxidative stress. Flavonoids, with weak pro-oxidation properties, may boost cellular antioxidant systems, acting as preventives for neurological disorders and as antipsychotics (34). The phytochemical analysis of HT fruit revealed the presence of magnesium (35), which is essential for optimal nerve transmission and neuromuscular

## **Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of *Hyphaene thebaica* (doum) fruit in animal model**

---

coordination as well as serving to protect against excitotoxicity (excessive excitation leading to cell death).

We conducted our experiment on the sedative and anxiolytic effects of DPME and DPAE by observing mice spontaneous locomotor activity in both the HCT and OFT. The HCT trial evaluates the sedative properties of two extracts, DPME and DPAE, by measuring the reduction in locomotor activity over time and comparing the results with diazepam, a standard reference drug, and a control group. DPME (400 mg/kg) exhibited a sedative effect similar to that of diazepam, reducing hole-crossing activity. The results of the early onset of activity (30 minutes) and sustained inhibition for 120 minutes suggest that it may act through diazepam-like or additive mechanisms; that is, DPME has potent, long-lasting effects. DPAE (400 mg/kg) also exhibited significant pharmacologic effects but moderately inhibited hole-crossing behavior. As for the OFT, experimental data have shown that the sedative activity of DPME decreased the number of squares crossed, similar to diazepam, while DPAE led to a decrease in the number of squares crossed compared with the control group. These two methods demonstrate the properties of the sedative activity of benzodiazepine (BDZ) compounds.

The anxiolytic effect is demonstrated by the LDBT. This is a scientific approach for assessing anxiety. It was created to predict the potency of therapeutically used compounds. It has been assumed that the time mice spent on the lit side of the box is the most useful and consistent measure of anxiety. In the current investigation, the administration of DPME and DPAE considerably reduced the nervous behavior demonstrated by mice during the LDB test. The mice that were subjected to the LDB test demonstrated a decrease in anxious behavior, as evidenced by a considerable increase in time spent in the light room and transitions between the two boxes. These effects are comparable to those of the anxiolytic medication diazepam.

GABA regulates a variety of central nervous system processes, including motion control, vision, and anxiety. The GABA<sub>A</sub> receptor is the primary mechanism by which benzodiazepines such as diazepam exert their anxiolytic and sedative effects (36). GABA<sub>A</sub> receptors are fast-acting neurotransmitter receptors that have an integrated Cl<sup>-</sup> channel and many allosteric binding sites. Benzodiazepines bind to the alpha (α) subunit of the GABA<sub>A</sub> receptor and prolong chloride channel opening, resulting in sedative or anxiolytic effects (37, 38).

Several experimental studies have demonstrated that the rich plant extracts contain alkaloids and flavonoids that exhibit sedative and anxiolytic properties mediated by their affinity (in vitro) with the benzodiazepine site of the GABAergic complex system and are direct or indirect modulators of this receptor (39). This may apply to HT fruit because it contains flavonoids and alkaloids two compounds known to have biological properties that may include affecting the central nervous system.

The tail suspension test is commonly utilized to evaluate antidepressant-like action in animal models. In this model, shorter immobility times indicate antidepressant action, whereas longer immobility times imply a CNS depression-like effect. However, the experiment was used to monitor the tail suspension test, which allows for rapid and reliable screening of medicines' psychotropic characteristics. Essentially, the measuring method is based on the energy released by mice attempting to escape their suspension (40). During this test, the mice movements were assessed in terms of energy and power development over time. The TST demonstrated that acute treatment of DPME at a dose of 400 mg/kg significantly decreased immobility time ( $p < 0.05$ ) compared to the control group, demonstrating antidepressant effects in mice. Which may be cause for the DPAE to give insignificant ( $p=0.1302$ ) decrease in immobility time. Compliance

results were found after administering the well-known antidepressant fluoxetine, which was utilized as a positive control, resulting in a decrease in immobility time.

The phytochemical analysis revealed the presence of phenylalanine, which was identified from the aqueous extract of HT fruit using HPLC (41), which lowers serotonin concentration in the brain and liver rats, likely due to *in vivo* inhibition of serotonin decarboxylation (42).

Compared to a plant from the same HT family, *Arecaceae*. It was agreed with the study of (Ruckmani, A., Meti, V., & Kavitha) on the evaluation of anti-anxiety and anti-depressant activity, as the first study was on an aqueous and methanolic extract of the *Areca catechu* plant at doses (300 and 250 mg/kg), respectively, which included a set of tests where test results indicated that it had better anti-anxiety activity than diazepam and an antidepressant activity similar to imipramine (43).

### Conclusion

The results obtained from this study indicate that the acute administration of the methanolic extract from the fruits of *Hyphaene thebaica* has potent anxiolytic and antidepressant properties. This effect with methanolic extract was more than the effect of aqueous extract. The activity is represented by a decrease in the number of crossings in HCT, a decrease in the number of squares crossed in OFT, an increase in the time spent by the animal in the light chamber, a decrease in the frequency transitions between the two boxes in the LDBT, and a decrease in immobility time in TST. The psychoactive activity of the extract can be attributed to its phytochemical components, antioxidants, and modulation of neurotransmitters NTs responsible for anxiety and depression disorders. In addition, the extracts were shown to have peripheral analgesic properties (like NSAIDs). This may be attributed to the inhibition of prostaglandin synthesis and the presence of flavonoids, terpenoids, and saponins. In addition to antiepileptic effects against SE induced by pilocarpine, an anticonvulsant study showed the methanolic extract delayed the onset of seizures, and its use over a period of six days reduced the mortality rate caused by the use of pilocarpine.

### References

- (1) Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*, 109(Suppl 1), 69-75.
- (2) Yadav, M., Chatterji, S., Gupta, S. K., & Watal, G. (2014). Preliminary phytochemical screening of six medicinal plants used in traditional medicine. *Journal of Pharmacy and Pharmaceutical Sciences*, 6(5), 540.
- (3) Sarris, J., Panossian, A., Schweitzer, I., Stough, C., & Scholey, A. (2011). Herbal medicine for depression, anxiety, and insomnia: A review of psychopharmacology and clinical evidence. *European Neuropsychopharmacology*, 21(12), 841-860.
- (4) Sofowora, A., Ogunbodede, E., & Onayade, A. (2013). The role and place of medicinal plants in the strategies for disease prevention. *African Journal of Traditional, Complementary, and Alternative Medicines*, 10(5), 210-229.
- (5) Orwa, C., Mutua, A., Kindt, R., Jamnadass, R., & Anthony, S. (2009). *Agro-Forest tree database: A tree reference and selection guide, version 4.0*.
- (6) Auwal, M. S., Shuaibu, A., Lawan, F. A., Sanda, K. A., Njobdi, A. B., Ibrahim, A., et al. (2012). Effect of crude mesocarp extract of *Hyphaene thebaica* (Doum palm) on white blood cells and differential leucocytic count in Wistar albino rats. *Journal of Medical Sciences*, 12, 207-213.

**Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of Hyphaene thebaica (doum) fruit in animal model**

---

- (7) Vandenbeldt, R. J. (1992). Problems with range-wide provenance trials of *Faidherbia albida* on sandy soils in Niger. In R. J. Vandenbeldt (Ed.), *Faidherbia albida* in the West African Semi-Arid Tropics, Proceedings of a Workshop (pp. 83-86). ICRISAT-ICRAF.
- (8) Badr, A. F. B. M. (2006). Classification of flowering plants (1st ed.). Faculty of Science, Tanta University, Dar Al-Andalus for Publishing and Distribution.
- (9) Burkill, H. M. (1997). The useful plants of West Tropical Africa (2nd ed., Vol. 4, pp. 371-373). Kew: Royal Botanical Garden.
- (10) Elmahdy, M. F., & Adris, M. A. (2021). The effect of *Nelumbo nucifera* seeds and *Hyphaene thebaica* on induced animal's hyperlipidemia and hypertension. *Medico-Legal Update*, 21(4), 246-251.
- (11) Habib, D. F., Michael, H. N., Salib, J. Y., Ahmed, N. M., & Agaibyi, M. H. (2014). Hypolipidemic efficacy of *Hyphaene thebaica* (Doum) in experimental nephrotic syndrome. *International Journal of Pharmaceutics*, 4, 28-34.
- (12) Salah, S. H., Abdou, H. S., Abd El Azeem, A. S., & Abdel-Rahim, E. A. (2011). The antioxidative effects of some medicinal plants as hypoglycemic agents on chromosomal aberration and abnormal nucleic acids metabolism produced by diabetes stress in male adult albino rats. *Journal of Diabetes Mellitus*, 1, 6-14.
- (13) Bayad, A. E. (2016). Influences of Doum fruit *Hyphaene thebaica* extract on the reproductive parameters, blood picture, lipid profile, and hepato-renal functions in rats. *MRJMMS*, 4, 384-391.
- (14) El-Hazmi, M. A., & Warsy, A. S. (2001). Evaluation of serum cholesterol and triglyceride levels in 1-6-year-old Saudi children. *Journal of Tropical Pediatrics*, 47, 181-185.
- (15) Modu, S., Kamis, A. B., & Usman, M. J. (2000). In vitro haemolytic activities of *Hyphaene thebaica* L. Mart on human erythrocytes. *Nigerian Journal of Experimental and Applied Biology*, 1, 32-37.
- (16) Greenberg, P. E., Sisitsky, T., Kessler, R. C., Finkelstein, S. N., Berndt, E. R., Davidson, J. R., ... & Fyer, A. J. (1999). The economic burden of anxiety disorders in the 1990s. *The Journal of Clinical Psychiatry*.
- (17) Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, 62(6), 617-627.
- (18) Munir, S., Gondal, A. Z., & Takov, V. (2019). Generalized anxiety disorder. In *StatPearls*.
- (19) Adwas, A. A., Jbireal, J. M., & Azab, A. E. (2019). Anxiety: Insights into signs, symptoms, etiology, pathophysiology, and treatment. *East African Scholars Journal of Medical Sciences*, 2(10), 580-591.
- (20) Frances, A. J., Galanter, M., & Kleber, H. D. (2000). *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR®*. Washington, DC: American Psychiatric Publishing.
- (21) American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*. Washington, DC: American Psychiatric Publishing.
- (22) Alatawi, A., Alghamdi, A., Albalwi, A., Altayar, M., Jalal, M., & Frah, E. (2020). Prevalence of generalized anxiety disorder (GAD) among Saudi medical students and associated risk factors. *International Journal of Research Studies in Medical and Health Sciences*.
- (23) Milind, P., & Monu, Y. (2013). Laboratory models for screening analgesics. *International Research Journal of Pharmacy*, 4(1), 15.

- (24) Takagi, K., Watanabe, M., & Saito, H. (1971). Studies on the spontaneous movement of animals by the hole cross test: Effect of 2-dimethylaminoethane and its acylates on the central nervous system. *Japanese Journal of Pharmacology*, 21, 797-810.
- (25) Gupta, B. D., Dandiya, P. C., & Gupta, M. L. (1971). A psychopharmacological analysis of behavior in rat. *Japan Journal of Pharmacology*, 21, 293-298.
- (26) Crawley, J., & Goodwin, F. K. (1980). Preliminary report of a simple animal behaviour for the anxiolytic effects of benzodiazepines. *Pharmacology, Biochemistry and Behavior*, 13(2), 167-170.
- (27) Michel, B., & Martine, H. (2003). The mouse light/dark box test. *European Journal of Pharmacology*, 463, 55-65.
- (28) Pellow, S., Chopin, P., File, S. E., & Briley, M. (1985). Validation of open closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *Journal of Neuroscience Methods*, 14(3), 149-167.
- (29) Steru, L., Chermat, R., Thierry, B., & Simon, P. (1985). The tail suspension test: A new method for screening antidepressants in mice. *Psychopharmacology*, 85, 367-370.
- (30) Whittle, B. A. (1964). The use of changes in capillary permeability in mice to distinguish between narcotic and non-narcotic analgesics. *British Journal of Pharmacology and Chemotherapy*, 22(2), 246-249.
- (31) Ahmed, F., Selim, M. S. T., Das, A. K., & Choudhuri, M. S. (2004). Anti-inflammatory and antinociceptive activities of *Lippia nodiflora* Linn. *Pharmazie*, 59(4), 329-333.
- (32) Dambisya, Y. M., Lee, S., Sathivulu, V., & Mat Jais, A. (1999). Influence of temperature, pH and naloxone on the anti-nociceptive activity of *Chana striatus* (Hara). *Journal of Ethnopharmacology*, 66(2), 181-186.
- (33) Grases, G., Colom, M., Fernandez, R., Costa-Bauza, A., & Grases, F. (2014). Evidence of higher oxidative status in depression and anxiety. *Oxidative Medicine and Cellular Longevity*, 2014, Article ID 430216, 5 pages.
- (34) Vogelzangs, N., Seldenrijk, A., Beekman, A., Van Hout, H., de Jonge, P., & Penninx, B. (2010). Cardiovascular disease in persons with depressive and anxiety disorders. *Journal of Affective Disorders*, 125(1-3), 241-248.
- (35) Jomova, K., et al. (2023). Reactive oxygen species, toxicity, oxidative stress, and antioxidants: Chronic diseases and aging. *Archives of Toxicology*, 97(10), 2499-2574.
- (36) Inuwa, S. Z., Ndife, J., & Bamalli, Z. (2023). Review on functional values of doum palm fruit. *Dutse Journal of Pure and Applied Sciences*, 9(3a), 29-40.
- (37) Matsumoto, R. R. (1989). GABA receptors: Are cellular differences reflected in function? *Brain Research Reviews*, 14(3), 203-225.
- (38) Barnard, E. A., Skolnick, P., Olsen, R. W., Mohler, H., Sieghart, W., Biggio, G., et al. (1998). International Union of Pharmacology. XV. Subtypes of gamma-aminobutyric acid A receptors: Classification on the basis of subunit structure and receptor function. *Pharmacological Reviews*, 50(2), 291-313.
- (39) Sieghart, W. (1995). Structure and pharmacology of gamma-aminobutyric acid A receptor subtypes. *Pharmacological Reviews*, 47(2), 181.
- (40) Kahnberg, P., Lager, E., & Rosenberg, C. (2002). Refinement and evaluation of a pharmacophore model for flavone derivatives binding to the benzodiazepine site of the GABAA receptor. *Journal of Medicinal Chemistry*.
- (41) Steru, L., Chermat, R., Thierry, B., & Simon, P. (1985). The tail suspension test: A new method for screening antidepressants in mice. *Psychopharmacology*, 85, 367-370.

**Evaluation of Anxiolytic, Antidepressant Activities of aqueous and Methanolic extract of *Hyphaene thebaica* (doum) fruit in animal model**

---

- (42) Amer, R. A. (2016). Characteristics of aqueous doum fruit extract and its utilization in some novel products. *Annals of Agricultural Science*, 61, 25-33.
- (43) Wang, H. L., Harwalkar, V. H., & Waisman, H. A. (1962). Effect of dietary phenylalanine and tryptophan on brain serotonin. *Archives of Biochemistry and Biophysics*, 97(1), 181-184.
- (44) Ruckmani, A., Meti, V., & Kavitha, K. N. (2014). Anxiolytic and anti-depressant activity of *Areca catechu* Linn. in mice. *Journal of Natural Remedies*, 14(2), 1367-1376.

## تقييم المستخلصات المائية والكحولية لثمار نبات الدوما *Hyphaene thebaica* كمضادات للقلق والاكتئاب

### المخلص

استخدمت في هذه الدراسة ثمار نبات الدوما كمضادات للقلق والاكتئاب وذلك باستخدام المستخلص المائي والكحولي وتم الاختبار على فنران التجارب في كلية الصيدلة جامعة مصراتة حيث اسفرت النتائج على ان المستخلصات المذكورة لها خاصية مضادة للاكتئاب والقلق

استلمت الورقة بتاريخ 2025/08/12  
وقبلت بتاريخ 2025/08/27  
ونشرت بتاريخ 2025/08/28

**Pain·analgesic·Doum  
palm·anxiety·depressant**