



جامعة
بنغازي الحديثة



**مجلة جامعة بنغازي الحديثة للعلوم
والدراسات الإنسانية
مجلة علمية إلكترونية محكمة**

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حقوق الطبع محفوظة

شروط كتابة البحث العلمي في مجلة جامعة بنغازي الحديثة للعلوم والدراسات الإنسانية

- 1- الملخص باللغة العربية وباللغة الانجليزية (150 كلمة).
- 2- المقدمة، وتشمل التالي:
 - ❖ نبذة عن موضوع الدراسة (مدخل).
 - ❖ مشكلة الدراسة.
 - ❖ أهمية الدراسة.
 - ❖ أهداف الدراسة.
 - ❖ المنهج العلمي المتبع في الدراسة.
- 3- الخاتمة. (أهم نتائج البحث - التوصيات).
- 4- قائمة المصادر والمراجع.
- 5- عدد صفحات البحث لا تزيد عن (25) صفحة متضمنة الملاحق وقائمة المصادر والمراجع.

القواعد العامة لقبول النشر

1. تقبل المجلة نشر البحوث باللغتين العربية والانجليزية؛ والتي تتوفر فيها الشروط الآتية:
 - أن يكون البحث أصيلاً، وتتوافر فيه شروط البحث العلمي المعتمد على الأصول العلمية والمنهجية المتعارف عليها من حيث الإحاطة والاستقصاء والإضافة المعرفية (النتائج) والمنهجية والتوثيق وسلامة اللغة ودقة التعبير.
 - ألا يكون البحث قد سبق نشره أو قُدم للنشر في أي جهة أخرى أو مستل من رسالة أو اطروحة علمية.
 - أن يكون البحث مراعيًا لقواعد الضبط ودقة الرسوم والأشكال - إن وجدت - ومطبوعاً على ملف وورد، حجم الخط (14) وبخط (Arial 'Body') للغة العربية. وحجم الخط (12) بخط (Times New Roman) للغة الإنجليزية.
 - أن تكون الجداول والأشكال مدرجة في أماكنها الصحيحة، وأن تشمل العناوين والبيانات الإيضاحية.
 - أن يكون البحث ملتزماً بدقة التوثيق حسب دليل جمعية علم النفس الأمريكية (APA) وتثبيت هوامش البحث في نفس الصفحة والمصادر والمراجع في نهاية البحث على النحو الآتي:
 - أن تُثبت المراجع بذكر اسم المؤلف، ثم يوضع تاريخ نشره بين حاصرتين، يلي ذلك عنوان المصدر، متبوعاً باسم المحقق أو المترجم، ودار النشر، ومكان النشر، ورقم الجزء، ورقم الصفحة.
 - عند استخدام الدوريات (المجلات، المؤتمرات العلمية، الندوات) بوصفها مراجع للبحث: يُذكر اسم صاحب المقالة كاملاً، ثم تاريخ النشر بين حاصرتين، ثم عنوان المقالة، ثم ذكر اسم المجلة، ثم رقم المجلد، ثم رقم العدد، ودار النشر، ومكان النشر، ورقم الصفحة.
2. يقدم الباحث ملخص باللغتين العربية والانجليزية في حدود (150 كلمة) بحيث يتضمن مشكلة الدراسة، والهدف الرئيسي للدراسة، ومنهجية الدراسة، ونتائج الدراسة. ووضع الكلمات الرئيسية في نهاية الملخص (خمس كلمات).

3. تحتفظ مجلة جامعة بنغازي الحديثة بحقها في أسلوب إخراج البحث النهائي عند النشر.

إجراءات النشر

ترسل جميع المواد عبر البريد الإلكتروني الخاص بالمجلة جامعة بنغازي الحديثة وهو كالتالي:

- ✓ يرسل البحث إلكترونياً (Word + Pdf) إلى عنوان المجلة info.jmbush@bmu.edu.ly او نسخة على CD بحيث يظهر في البحث اسم الباحث ولقبة العلمي، ومكان عمله، ومجاله.
- ✓ يرفق مع البحث نموذج تقديم ورقة بحثية للنشر (موجود على موقع المجلة) وكذلك ارفاق موجز للسيرة الذاتية للباحث إلكترونياً.
- ✓ لا يقبل استلام الورقة العلمية الا بشروط وفورمات مجلة جامعة بنغازي الحديثة.
- ✓ في حالة قبول البحث مبدئياً يتم عرضة على مُحكمين من ذوي الاختصاص في مجال البحث، ويتم اختيارهم بسرية تامة، ولا يُعرض عليهم اسم الباحث أو بياناته، وذلك لإبداء آرائهم حول مدى أصالة البحث، وقيمتها العلمية، ومدى التزام الباحث بالمنهجية المتعارف عليها، ويطلب من المحكم تحديد مدى صلاحية البحث للنشر في المجلة من عدمها.
- ✓ يُخطر الباحث بقرار صلاحية بحثه للنشر من عدمها خلال شهرين من تاريخ الاستلام للبحث، وبموعد النشر، ورقم العدد الذي سينشر فيه البحث.
- ✓ في حالة ورود ملاحظات من المحكمين، تُرسل تلك الملاحظات إلى الباحث لإجراء التعديلات اللازمة بموجبها، على أن تعاد للمجلة خلال مدة أقصاها عشرة أيام.
- ✓ الأبحاث التي لم تتم الموافقة على نشرها لا تعاد إلى الباحثين.
- ✓ الأفكار الواردة فيما ينشر من دراسات وبحوث وعروض تعبر عن آراء أصحابها.
- ✓ لا يجوز نشر إي من المواد المنشورة في المجلة مرة أخرى.
- ✓ يدفع الراغب في نشر بحثه مبلغ قدره (400 دل) دينار ليبي إذا كان الباحث من داخل ليبيا، و (200 \$) دولار أمريكي إذا كان الباحث من خارج ليبيا. علماً بأن حسابنا القابل للتحويل هو: (بنغازي - ليبيا - مصرف التجارة والتنمية، الفرع الرئيسي - بنغازي، رقم 001-225540-0011. الاسم (صلاح الأمين عبدالله محمد).
- ✓ جميع المواد المنشورة في المجلة تخضع لقانون حقوق الملكية الفكرية للمجلة.

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Anxiolytic effect of acute ginger treatment

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ABSTRACT

One of the most crippling neuropsychiatric disorders of this modern era is anxiety. Therefore, there is an urgent need of a safe and effective treatment, which proves its significance in this disorder. There have been several chemical treatments; however, conventional food would be a better alternative. Therefore, *Zingiber officinale* that used worldwide as a cooking spice and herbal remedy has been used in the present study to investigate its anti-anxiety effect using elevated plus maze (EPM) and light dark model (LDM). Three doses (100, 200 and 400 mg/kg body weight (wt). of 70% ethanol extract) were administered intraperitoneally (i.p.) to mice one hour before starting experiments. Diazepam (1 mg/kg body wt.) was taken as the standard anxiolytic drug. The time elapsed and count of entries in open arms of EPM, enhanced incidence of head dipping in holes and duration of time in lit area of LDM significantly raised in animals administered with extracts at the levels of 200 and 400mg/kg body wt and Diazepam. Our results suggest that the extracts may have a promising anxiolytic activity to regard it as a good treatment of anxiety disorder.

Key words: Anxiety disorder, *Zingiber officinale*, anti-anxiety

التأثير المخدر لعلاج الزنجبيل الحاد

المخلص:

القلق هو أحد أكثر الاضطرابات العصبية والنفسية التي تصيب الإنسان بالشلل في هذا العصر الحديث. لذلك هناك حاجة ماسة إلى علاج آمن وفعال، مما يثبت أهميته في هذا الاضطراب. كان هناك العديد من العلاجات الكيميائية. ومع ذلك، فإن الطعام التقليدي سيكون بديلاً أفضل. لذلك، تم استخدام *Zingiber officinale* الذي يستخدم في جميع أنحاء العالم كتوابل للطبخ وعلاج عشبي في هذه الدراسة للتحقيق في تأثيره المضاد للقلق باستخدام المتاهة المرتفعة (EPM) والنموذج الداكن الفاتح (LDM). تم إعطاء ثلاث جرعات (100 و 200 و 400 ملجم / كجم من وزن الجسم (بالوزن) من مستخلص الإيثانول 70%) داخل الرئة للفئران قبل ساعة واحدة من بدء التجارب. تم أخذ الديازيبام (1 مجم / كجم من وزن الجسم) كدواء قياسي لمزيل القلق. الوقت المنقضي وعدد الإدخالات في الأذرع المفتوحة لـ EPM، زيادة حدوث غمس الرأس في الثقوب ومدة الوقت في المنطقة المضاءة من LDM التي تم رفعها بشكل كبير في الحيوانات التي تدار بمستخلصات بمستويات 200 و 400 مجم / كجم من وزن الجسم والديازيبام. تشير نتائجنا إلى أن المقطعات قد يكون لها نشاط واعد مزيل للقلق لاعتبارها علاجاً جيداً لاضطراب القلق.

INTRODUCTION.

Anxiety and anxiety-spectrum disorders are the most common debilitating neuropsychiatric disorders and becoming increasingly prevalent in modern society (Murphy, 1986). The prevalence is estimated about 10-30%.

One of the most commonly used anti-anxiety drugs is, benzodiazepine. The anti-anxiety effects of benzodiazepine are because of its interaction with gamma-aminobutyric acid (GABA) receptors of brain especially in the midbrain reticular formation. Benzodiazepine has many side effects such as sedation, myorelaxation, ataxia, amnesia and pharmacological dependence. For this reason, new therapeutic approaches and treatments are requiring (Bisson JI, 2007). Since active ingredients of herbal drugs are not accumulated in the body and do not have side effects and as such, they have significant advantages compared to chemical drugs. Many medicinal plants have been used more, including *Zingiber officinale* (Ginger) (Ali BH, 2008, Mosoumen E, 2005).

Ginger belongs to a Zingiberaceae family. It has long been used in traditional medicine of Arab, India, and China for the management of various health problems including gastrointestinal and respiratory disorders as well as in atherosclerosis and reducing pain (Niksokhan M, 2014, Ali BH, 2008). In the recent studies, ginger has been reported as a good source for antioxidant, anti-inflammatory, neuroprotective and anticancer activities (El-Ghorab AH, 2010, Kondeti R S, 2011, Mustafa T, 1990, Shukla Y, 2007). Since the bioactive molecules of ginger are 6-gingerol, flavonoids and phenolic compounds (Connell D, 1969). Recently, researchers have reported that the flavonoids have effect on benzodiazepines receptors (Modaresi M, 2009). Extant flavonoids in medicinal plants cause tranquilizing, anti-anxiety effects by affecting benzodiazepine receptors binding to GABA receptor (Modaresi M, 2009). The current study was conducted to investigate the anti-anxiety properties of the ginger extract in comparable with benzodiazepine in mice.

MATERIALS AND METHODS.

Preparation of *Zingiber officinale* roots extracts.

Fresh ginger was procured from the local market, Benghazi, Libya. The plant was washed and sliced. The active compounds of ginger were extracted by soaking a 100gm of fresh *Zingiber officinale* rhizome in 1 liter of 70% ethanol. The solvent was shaken for 24 hours, filtered, and then evaporated. The extracts of the rhizome of *Zingiber officinale* were suspended in a vehicle comprising 1% (w/v) Tween 20 in distilled water. These extracts were made and used for this study.

Animal experiment.

Animal studies were conducted according to the institute of animal ethical committee regulations approved by the committee for the purpose of the control and supervision of experiments on animals. Swiss albino mice weighing 25 to 30 g were produced from the small animal house in Benghazi University. The animals were housed in an acryl fiber cage in a temperature controlled room (temperature 25 ± 2 o C) and maintained in 12 h light/ dark cycle with free access to food and drinking water ad libitum. All animals were accustomed to laboratory environment for 1 week before starting experiments. Experiments were done at time between 09:00 and 17:00 h.

Experimental design.

Twenty five or thirty mice were divided into five groups with five or six mice in each group: control, diazepam and 100, 200 and 400 mg/kg extract doses. A 0.25 ml of extract suspended in vehicle were administered i.p. to mice one hour before starting the experiment. Diazepam (1 mg/kg) suspended in the vehicle was used as anxiolytic drug. The suspending vehicle (0.25 ml) without any additions was used as control. Mice were then exposed to either elevated plus maze (EPM) or light dark model (LDM) to evaluate the anxiety.

Elevated plus maze (EPM).

As described by Kulkarni *et al.*, The EPM apparatus composed of two opened (30×5 cm) and two closed ($30 \times 5 \times 15$ cm) arms originated from a central platform (5×5 cm) to form a plus sign. The floor of maze and the closed arms were stained with black color. EPM was elevated 50 cm above floor (SK, 2002). Sixty minutes after the administration of different vehicles, the mice were placed individually on the central platform facing the open arm. The numbers when animal entered into opened arm and durations were recorded within a 5 min period; the time of latency to enter opened arm was also calculated within same period. These measures were used as indices of anxiety. Entry into any arm was accounted only when all four paws of the animal came inside the arm. Experiments were done in a quiet room to avoid any change in the animals' behavior.

Light/dark apparatus test.

A box divided by an opaque wall that contains 5×5 hole to connect the two formed chambers. These chambers were equal in size ($20 \times 20 \times 14$ cm, one was dark and other was lit). The dark part was colored with black and closed at the top, while the lit part was stained with a white color and a source of light was placed above it (Belzung C, 1990b). Exposure to intensely illuminated area, causing anxiety-like behavior in animals (M Bourin 2003, D Dhingra, 2012a). The tested mice were placed individually inside the lit compartment when experiment started. Duration of times the animal spent into a lit box and number of head dipping were recorded for 5 min.

Statistical analysis.

Statistical analysis was performed with GraphPad Prism and based on an analysis of variance (ANOVA) followed by Dunnett's test/Tukey's test. Differences of $P < 0.05$ were considered statistically significant.

RESULTS.

Elevated Plus Maze.

The mice in control group spent 2.7 ± 1.3 s in the opened arm (Fig1 A). Compared to a control group, animals treated with diazepam showed a significant increase in the time spent and number of entry into opened arms (Fig1 A and B), Although extracts of *ginger* at concentrations 100, 200, and 400 mg/kg enhanced both number of entrances and time spent in opened arms in dose dependent manner, the lowest dose

did not significantly affect the two measured indices comparable to control group (Fig1 A and B). Different doses of extracts of *ginger* and diazepam treated groups showed a significant reduction in latency to enter these arms (Fig1 C).

Light/dark apparatus

The vehicle treated group spent 54.4 ± 2.01 s in the lit box and showed as 4.6 ± 0.67 as number of head dips, whereas animals treated with extracts of *ginger* (200, and 400 mg/kg) showed a remarkable increase in duration for which animal remained in enlightened compartment and also showed a significant ($P < 0.01$) increase in the number of head dipping (Fig 2 A and B). There was a direct correlation in the dose and both head-dip counts and time spent in lit box, however, these results were less than the effect of Diazepam (DZ) 1 mg/kg on mice (Fig 2 A and B).

DISCUSSION.

Anxiety is considered as one of the most common psychological disorder that hurts human life (Cle'ment Y, 2002, Kjernised KD, 2004). It appears by cognitive, emotional and behavioral components. It can be a natural anxiety which is an emotional response to stressful physiological and social conditions, but there is a pathological anxiety (Afshari TJ, 2010).

Animal behavioral models have become an indispensable tool for studying anxiety disorders and testing anxiety- modulating drugs. The elevated plus maze is based on the premise that exposure to open arm evoked an approach avoidance conflict that was considerably stronger than that evoked by the exposure to an enclosed arm (KC, 1955). Additionally, this test is considered one of the most widely validated tests for assaying new benzodiazepine-like anxiolytic agents (Pellow S, 1985), and diazepam used in this study is one among them. The reduction in entry, time spent, latency to enter opened arm are the indications of high level of fear or anxiety. Anxiolytics drugs increase the proportion of these indices. Imaizumi have shown that diazepam increased the open arm entries and time spent in open arm (Imaizumi M, 1994). Researchers have reported different effects of ginger on EPM (Fatemeh F, 2017, Mohan M, 2006, Harsha S N, 2012), therefore using of EPM in the current study was to support previous pieces of research. In this study, it was observed that ginger extract (GE) 100, 200, and 400 mg/kg) significantly ($P < 0.01$) increased the time spent and number of entrance in opened arms and reduced latency to enter opened arms. This suggests that the GE have an anxiolytics effect.

In the light and dark box model, the very bright environment is a noxious stressor that inhibits the exploratory behavior of rodents. Reduction of number of entries, time spent in the lit chamber are regarded as markers of anxiety (Costall B, 1988). Anxiolytics agents increase light to dark transitions and time spent in lit area (Balaraman R, 2007, Belzung C, 1990a). It is interesting that there are not many studies using the light dark test to evaluate the role of GE on anxiety have been done. Our study showed that GE increased time spent in the lit chamber and number of head dips and therefore the extract reduced the indices of anxiety that developed by using this model.

Despite of extensive research on anxiety, the neurological basis of this disorder is still not clear. It has been shown that interaction of active gradients of

plants including ginger with some of the natural endogenous mediators may explain the anxiolytic mechanism of these plants in the body (Contarino A, 1999, Shih JC, 1999). Experiment of Paladini A has shown that flavonoids and other antioxidant factors were a potent anxiolytic compounds (Paladini A, 1999). Other researchers suggested that some plants have lots of secondary metabolites which directly or indirectly may affect the central nervous system, noradrenalin, GABA neurotransmitter activity (Wood WM, 1991). Many reports states that the active ingredients partially activate serotonin receptor and therefore, involvement the serotonergic system may explain the mechanism of anxiolytic action of ginger rhizome (Andreas N, 2010, Mohan M, 2006), however, the role of other neurotransmitters cannot be ignored. The Mechanism by which the G to play an important role as anxiolytic agent still remains obscured and further studies is needed.

In conclusion, our results showed that higher doses of ginger extract increased time spent and number of entry in the open arms significantly control groups in EPM. In addition the GE treated mice remained longer in lit compartment which indicates anxiety reduction. So, we can conclude that ginger extract can reduce anxiety reactions dose dependently.

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Conflict of interest.

The authors report no declaration of interest.

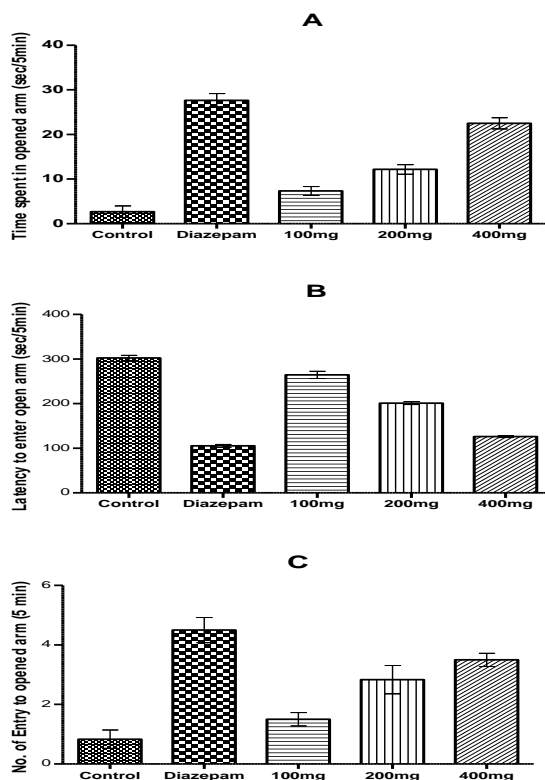


Figure 1: Elevated plus maze test. * indicates significant difference as compared to control group ($p < 0.001$). Values are given as mean \pm SD of six animals

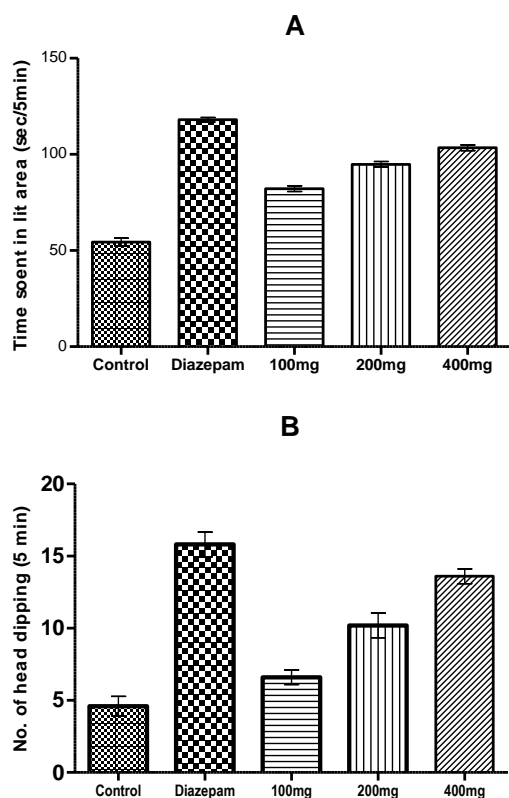


Figure 2: Light/Dark model test. * indicates significant difference as compared to control group ($p < 0.001$). Values are given as mean \pm SD of six animals.

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