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Original Article

Study on Ginger as a Treatment for Stress and Anxiety Comparing With Diazepam

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Abstract

Background: The psychological anxiety is considered one of the most significant animals of the modern era. The most common causes natural indictors that lead to tension, severe stress and un-desirable mental problems or disease are stress Anxiety problems or disease that considered as most frequently appearing as disorders. Anxiety disease is diagnosing as condition that showed or indicate to serious and severe or pathological case as the essential disturbance emotional tone. **Aim:** In this study, ginger was tested in both diluted and concentrated forms suspension to evaluate its potential to alleviate psychological anxiety. it was compared against a positive control (diazepam) and negative control (water). To determine the anti-anxiety action of plant Ginger syrup extract. Diazepam is golden standard act as blocking or antagonized of stress and anxiety.**Methodology:** Experimental study was conducted in 2026. using animals albino mice and elevated plus-maze model (EPM) as a good standard technique for determined anti-anxiety behavior and stress inhibited. It is a validated and reliable measure of psychological anxiety, an animal's movement and crossing in an open area of elevated plus-maze indicates the absence of psychological anxiety, whereas its movement in an enclosed area indicates the presence of psychological anxiety.**Results:** This study, which relied on the use of ginger extract to reduce symptoms of anxiety like behavior and stress, because when treated animals with ginger lead to increased time spent and number of crossing and number of entries to open arms of elevated plus-maze instrument. clearly indicate or showed me that this extract is good and beneficial in stress management and reducing anxiety, especially after comparing it to golden standard Diazepam, the leading drug in this field. This clear results to important natural products as ginger extraction replace chemical substances.**Conclusion:** This experimental study using male albino mice as animals, was it is been done to appear possibility effects of plant Ginger extraction to inhibit stress and anxiety behavior by using elevated plus-maze technique. This experimental study, was indicate or observed clear antagonized or blocking action to stress and anxiety induced-like behavior by used plant ginger extract or suspension in safe compatible suitable concentration. These good results to important ginger natural substances replace chemical compounds.

Keywords : Ginger, Behavior, Stress, Anxiety, Diazepam.

Introduction

The more common un-desirable mental problems or disease are stress [1] Anxiety disease that considered as most frequently appearing as disorders [2]. Anxiety disease is diagnosing as condition that showed or indicate to severe or pathological case as the essential disturbance emotional tone. Anxiety, which may be not showed to pathological condition of normal stress or fear, is diagnostic by mood disturbances like of thinking, physiological action and behavior [3]. The condition of anxiety contains panic disorder and phobic disorder, as anxiety general disorder, social phobia related to family as genetic problem, specific phobia, compulsive disorder, acute anxiety disorder, and post-traumatic anxiety disorder [4.] Also, there are adjustment disorders with anxiety properties or features [5]. And general medical conditions disorder and products induce stimulate anxiety disorders. [6]

Signs And Symptoms

The majority of people suffer from mental health disorder may appear agoraphobia especially after the beginning or appearance of panic problems or disorder. [7]. The frequently or repeated panic disorder may lead to Agoraphobia phenomenon as behavioral outcome of repeated panic disease. [8]. Generalized anxiety disorder (GAD) appear without clear psychiatric problem or disorder, [9]. Especially with the experiencing patients consistent worry over multiple areas of her or his life at least for (6 months) phobia within social area describes stress, fear and anxiety in social Cases problems indicate to disappear of wellbeing and social interaction. [10]. The fear of some animals (especially cats, snakes, big rodents, and street dogs); indicate to specific phobia is showed similar signs, symptoms and behavior, but is stimulated by a fear of other animals as insects (especially spiders and bees or hornets); water, automobile driving; storms; and injections. [11]. compulsive-obsessive disorder (COD) is

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showed the repeated behaviors (compulsions), [12]. which lead to diminish anxiety related to unwanted, intrusive thoughts or (Obsessions). Also mainly seen behaviors are washing or cleaning in sensitive to concerns about dirty or contamination, or frequently checking to see if a stove is turned off in sensitive to concerns over a starting of fire. [13]. The main common people sensitive or response to repeatedly check work because, to obsessive self-doubt. [14]. Patients rarely present with poor physical health complaints as their firstly concern. This describe underlying symptoms of anxiety disorder. [15]. This is particularly more occurred in panic disorder, which is indicate to a less time of intense fear and a sense of impending., doom, with physical symptoms, [16]. Such as heart pain, nausea, dizziness and difficult of breath. Oftenly, these patients suffer from anxiety will first present to an emergency department When diagnostic by phenomenon of agoraphobia, the people fears have a panic disorder in a place that difficult to escape. [17]. This verification observation in the anxious patient showed avoiding such situations, with subsequent mental disorder or mental disturbances in normal life functioning. [18].

Etiology and Psychological Basis of Anxiety

The most anxiety diseases etiology, was not clear verify or understood, but it is important to study and research it. In general, the probability of occurring anxiety disorder includes a group of life style, psychological behaviors, and genetic causes. **[19].** The most common disorder of anxiety is so heterogeneous but appear in different factors. **[**20**]** Other disorders of anxiety are more related with stress life experience. disorders of anxiety and stress often are considered as an abnormal version of arousal.**[**21**].** Panic disease or disorder, characterized by a stronger genetic factor than others. commonly is known the arousal because of deals of study in humans and animals named "fight-or-flight action or response," this is indicated to the acute stress action or response. **[**22**]** Cannot understanding the acute stress action or response because, showed critical to the social normal response to stressors. but it's constricted for anxiety understanding have come to the forefront in recently **[**23**].** Most recent theories of behavior indicate to importance of two types of learning: observational learning and classical conditioning. **[**24**].** Both of theories have some evidence to be sure them. **[**25**]** In classical conditioning theory, need to a neutral stimulus to support the ability to appear a fear action or response after many times of pairings with a frightening (unconditioned) indicator. **[**26**]**. But in observational learning theory, behavior of fear it happens by registered others' actions to fear-such as stimuli. about general disorder of anxiety, not suggested the negative and positive reactions is seen as leading to anxiety,a knowledge factors, such as education, understanding and training also about stress behavior, important play a clear role in the anxiety etiology **[**27**].** A serious clear factor is the individual's sensation, which can intensify the response. sense of uncontrollability is considered as one of the most salient cognitions negative in anxiety. **[**28**].** Cognitions especially Negative are repeated occurring in people with anxiety. **[**29**] .** Most recent models of psychology of anxiety interference with role of patient's vulnerability, which involves both acquired and genetic predispositions **[**30**].** Other theories called psychological anxiety theories: such as behavioral theories, psychoanalytic, psychodynamic theory, and cognitive theories. **[**31**].** The Psychodynamic theories have concentrated on good study of common appear signs and symptoms of anxiety disorders. **[**32**].** Hence, there are no important researches to verify or support this theory (psychodynamic theories), they are accepting or suitable to scientific clarified experimental study.

Phathophysiology

There is concentrated between neurotransmitters that changes in certain one neurotransmitter system sure to changes in another, involving widely feedback techniques or mechanisms. [33]. The most important inhibitory neurotransmitters are GABA and Serotonin that reduce and calm the stress action or response [34]. The main galls for therapeutic products are these neurotransmitters and very important, while pathophysiological definition techniques have not yet been detected, defect modulation within the central nervous system led to stress and anxiety behavior or symptoms.[35]. The outcome of heightened sympathetic arousal of comparable levels leads toemotional, Physical features. [36]. most common researches showed that a genetic ability to resulting stress and an anxiety disease or disorder. [37]. Therefore, stressors related to environment sure play a role, in comparable levels. [38]. Most systems of neurotransmitter have been connected to have a clear important role in one or more of the modulatory steps included. [39]. The main commonly related systems are the noradrenergic and serotonergic neurotransmitter systems. [40]. In general consideration, it is thought that an under control or activation of the serotonergic system and an over control or activation of the noradrenergic system are included. Both systems modified regulate and are regulated by other mechanisms or pathways in the central nervous system, most new researches there has been some concentration in the function of corticosteroid action and

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its relationship to signs and symptoms of stress and anxiety [41].

Treatment of Anxiety

The list of important current medicines or drugs that are used as anti-anxiety as: Neurokinin receptor antagonists, (Cholecystokinin) CCKB antagonists, Corticotropin-releasing factor (CRF) modulators, $GABA_A$ receptor modulator (benzodiazepines and related drugs),Serotonin receptor modulators. Medicines or Drugs that used to to inhibit or decrease stress and anxiety have been used by people for hundreds of years. Ethanol was used as first anti-anxiety treatment and continues to be consumed by humans. Other medicines or drugs involved Carbamates (Meprobamate) and the barbiturates and they were consumed in the first half of the 20th century and verify observed the part of these drugs continue to be used or consumed today.

Aim of work

This experimental study was designed to estimate probable anti-anxiety action of plant Ginger syrup extract (test) , as blocking for anxiety, using model is elevated plus-maze (EPM) as a good standard technique for determined behavioral conditions for experimental animals and demonstrate the anti-anxiety action of compounds or drugs. hence, the actions of plant Ginger syrup extract were compared with standard diazepam (positive control) and with water (Negative control) to appear whether the characteristics of behavior of plant ginger syrup extract differs from this verify standard anti-anxiety medicine or drug.

Material and Method

In this experiment was used animals as male mice of albino type weighing (26 ± 1 gm), were breeding inside animal house of Pharmacology Department in Faculty of Pharmacy - University of Tripoli-Libya. This breeding of animals were housed in suitable place at temperature (21 ± 2°), was constant in suitable room on a 12/12h cycle of light- dark. Good pure water and Food were given for animals ad libitum.

Chemicals and Drugs

In this experimental study was used plant of Ginger (test) as fresh from Tripoli-Libya and golden standard diazepam, (Positive control) was bringer from company of Sigma Aldrich Germany. And also used water as (negative control).

Drugs Administration

Plant ginger syrup extract was administered by orally route. Ginger syrup extract (test) was prepared through take a suitable dose of dried ginger powder and mix it with an appropriate suitable amount of pure distilled water in bases of (approximately 5 gm/1-liter or50 mg/100 ml) to form a suspension and calculate the suitable dosage based on the weight of each animal (100 mg / kg) and administered it through using feeding tube at a known concentration to stable or ensure the good correct dose. Control given at volume of (5 ml/ kg) mice body weight. Golden Standard Diazepam (positive control) was dissolved in suitable volume of normal saline including Tween 80 (2%) as a vehicle or solvent. Standard Diazepam was taken through intraperitoneally (I.P.) route, according to safe dose base of (1mg / kg).

Instrument

Elevated plus-maze. (EPM)

This equipment was made of material named Plexiglas and including of two open arms in opposite sides (6 x 25 cm) crossed with two enclosed arms in opposite sides of the dimension with (20 cm) height. Arms of (EPM) were established with a central square (6x 6 cm) to create plus sign shape of instrument. [42]. The maze was kept elevated about (40 cm) in a dimly lit room above the floor. (See figure: 2.1.4.A.)

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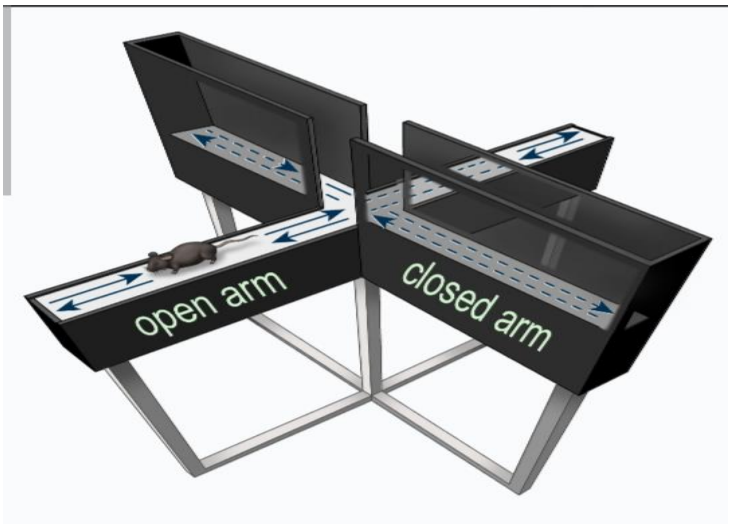

Figure: 1 ELEVATED PLUS - MAZE.

Elevated Plus-Maze Test (EPM).

This experimental technique or test called elevated plus-maze test was accomplishing inside a closed calm room with slow illumination. [43]. The animals were placed individually on the central area of square of the plus maze to side an enclosed arm. The entries number and time spent made by the mice, in next during (5 min) on closed and open arm was registered. determined the arm entry when all the four limbs of animals were on the arm. [44]. The instrument was care necessary cleaned after each trial or experiment. If was observed open arm entries increase and also increase in time spent to open arms is showed that character of anxiety or anxiolytic actions, as mice naturally he heads to the closed arms. [45]. (EPM) is fast, selective and suitable technique to determined anxiogenic and anxiolytic medicine actions bellow identical condition [46].

Effect of acute dose of plant ginger syrup extract and standard diazepam, on parameters of anxiety using elevated plus-maze. (EPM). The experimental animals (Mice) were grouped randomly to (3) groups (N = 12, each group). This trial was prepared to evaluate the anti-anxiety action of plant ginger syrup extract (100mg / kg), [47]. and standard anti-anxiety medicine diazepam (1 mg/kg) on parameters of anxiety estimated in animal's albino mice using technique of elevated plus-maze test as showed before (2.2.1). [48]. Plant Ginger suspension was taken orally but standard diazepam was taken (I.P.) to albino mice. Group was considered as Control administered or received an equivalent volume of water(orally.) half hour after exposure to stimulus cat urine smell. [49]. Directly then were examined on the instrument elevated plus-maze for (5 min.) [50].

The experiment was performed to investigate the effect of acute administration of ginger and diazepam in mice. using elevated plus-maze. The animals were divided into water (negative control) and different treated groups (n= 12, each group. Group (1) = received water and Group (2) = received diazepam 1mg/kg and Group (3) = received diluted ginger suspension 10mg/kg and Group (4) = received concentrated ginger suspension 10mg/kg. The treated groups received ginger suspension orally and diazepam (10mg/kg) intraperitoneally acute administration. Then, the animals were tested in elevated plus- maze to evaluate their effects on anxiety parameters. (Time spent in open arms, number of line cross in open arms and number of entries in open arms). All animals were tested in elevated plus-maze.

Statistical analysis

A descriptive statistical analysis was performed on the parameters of samples within each experiment. To find out whether the observed samples were normally distributed, the non-parametric Kolmogorove – Smirnov maximum deviation test for goodness of fit was used. If the parameters were normally distributed, the treatments were compared by applying one –way ANOVA. For multiple comparison Post Hoc tests, additional least significant difference (LSD) tests were performed, when appropriate,

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to detect any significant differences between the treated groups and the control group, and between the combined drugs and drug itself. The differences were considered to be significant at (P<0.05). All analyses were conducted using the SPSS (software packing version 13) for IBM compatible computer.

Result.

Acute administration of ginger and diazepam reduced anxiety using elevated plus- maze.

Effects on time spent in open arms.

The mean duration of time spent in open arms of water treated group (negative control) using elevated plus- maze test (n=12, each group) was (56.7 ± 6.5 seconds) which was very highly significantly different from diazepam treated group (179.7 ± 2.8 sec.), (P<0.001). Similarly the mean duration of time spent in open arms of mice treated with diluted ginger (101 ± 5.2 sec.) and concentrated ginger (164 ± 5.7 sec.) was also very highly significantly different from water treated group (p < 0.001).

Diazepam produced the highest anxiolytic effect compared with ginger treated groups. (see figure 3.1.1).

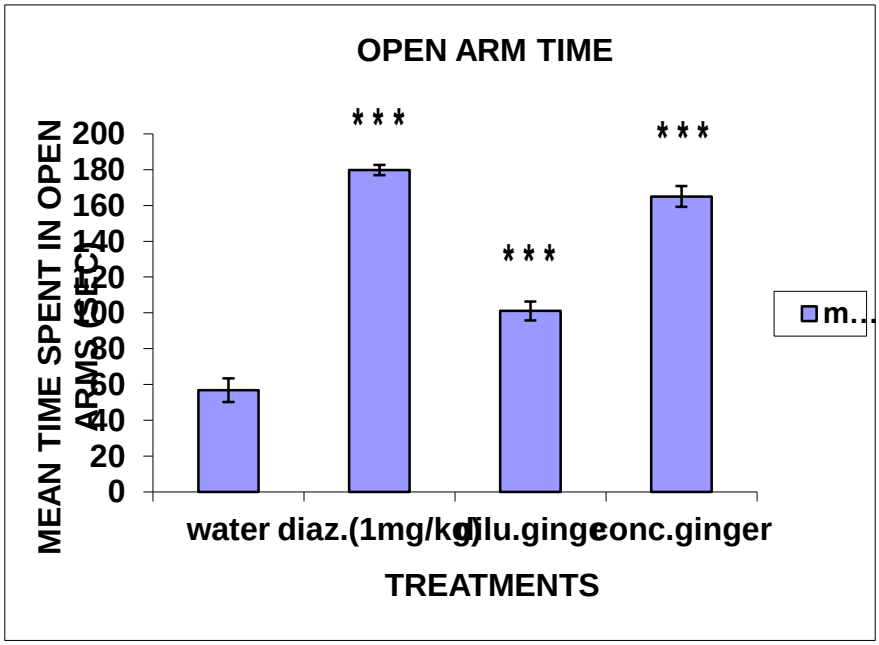

Figure :2 Effects of ginger and diazepam on the time spent (seconds) in open arms of elevated plus- maze (n=12 , each group).

*** *** p < 0.001 = very highly significantly different.

Doses 100mg/kg (Ginger), 1mg / kg (diazepam) and water 1ml/kg (control).

All data are mean values with (±S.E.M) and compared with control.

dilu. = diluted and conc. = concentrated.

Effects on number of line crossing into open arms.

The mean number of line cross into open arms of mice received water (control group) (8.7 ± 1) was very highly significantly different from diazepam treated group (29 ± 2.6), (P<0.001). The number of line cross into open arms by animals treated with diluted ginger (19.7 ± 0.7) was also very highly significantly different and was just highly significantly different (p<0.01) by animals treated with concentrated ginger (17.7 ± 2.7) compared with control (see figure, 3.1.2.).

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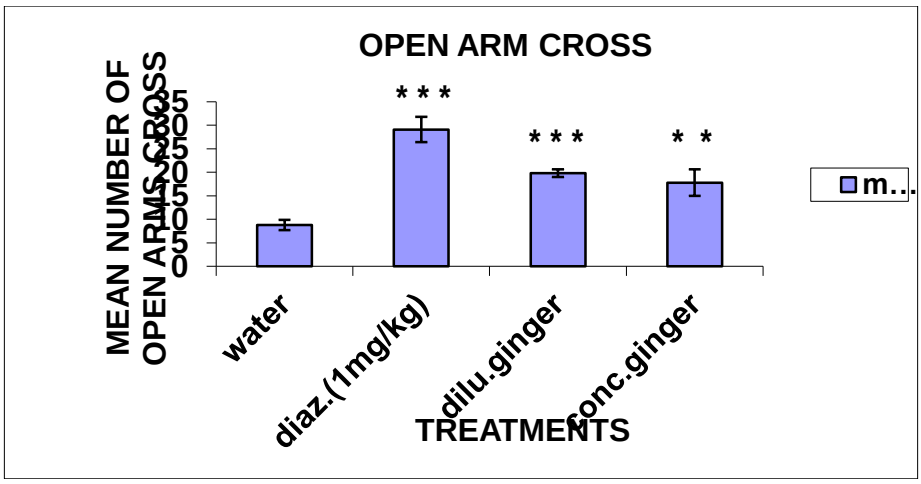

Figure :3 Effects of ginger and diazepam on the number of line cross into open arms of elevated plus- maze (n=12 , each group)**.**

***** p<0.01= highly significantly different.
*** *** P < 0.001 **=** very highly significantly different**.**
Doses 100mg/kg (ginger), 1mg / kg (diazepam) and water 1ml/kg (control**).**
All data are mean values with (±S.E.M) and compared with control.
dilu. = diluted and conc. = concentrated.

Effects on number of entries into open arms.
The number of entries into open arms of group treated with water (control group) (6.6 ± 0.4) which was not significantly different from diazepam treated group (5.6 ± 0.1). However, the number of entries into open arms of groups treated with diluted ginger (10 ± 0.4) and concentrated ginger (9.5 ± 1.3). ginger was highly significantly (P<0.01) and only significantly different (P<0.05) from water treated groups respectively. (see figure, 3.1.3).

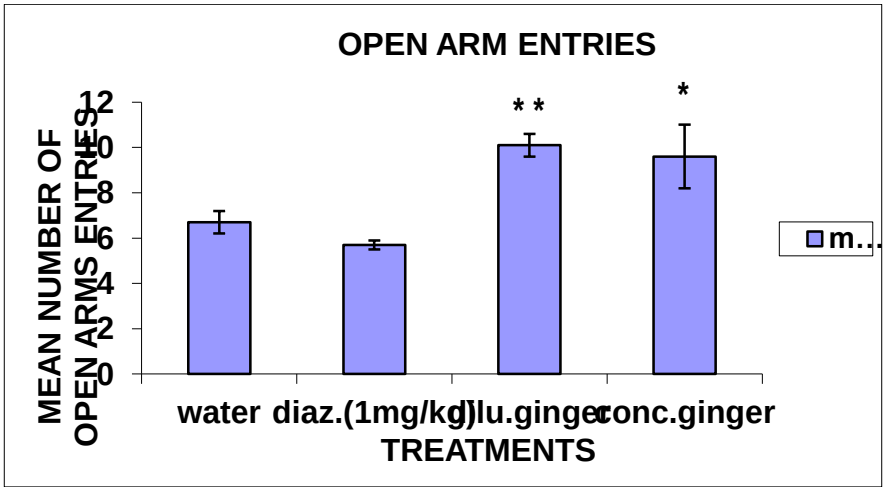

Figure :4 Effects of ginger and diazepam on the number of entries into open arms of elevated plus- maze (n=12, each group).
p<0.05= significantly different.
****** P<0.01= highly significantly different.
Doses 100mg/kg (ginger), 1mg / kg (diazepam) and water 1ml/kg (control).
All data are mean values with (±S.E.M) and compared with control.

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dilu. = diluted and conc. = concentrated.

Table: 3.1. Actions of standard diazepam (DZP) and plant ginger suspension on parameters of anxiety using elevated plus-maze (EPM).

Action on number of entries, number of crossing and time spent in open arms of Elevated plus-maze instrument. (EPM).

Table: 1. Effects of Ginger and diazepam on different anxiety parameters using elevated plus- maze.

Treatments	Time spent in open arms (seconds)	Number of line cross in open arms	Number of entries in open arms
Negative control (water)	**56.7 ±6.5**	**8.7±1**	**6.6±0.4**
Diluted ginger (10mg/kg)	**101 ± 5.2*** **	**19.7±0.7*** **	**10±0.4** **
Concentrated ginger (10mg/kg)	**164 ± 5.7*** **	**17.7±2.7** **	**9.5±1.3***
Diazepam (1mg/kg)	**179.7 ±2.8*** **	**29 ±2.6*** **	**5.6±0.1**

Statistical significance: *p < 0.05 , **p < 0.01 and ***p < 0.001 respectively.
Test. =Ginger, control = water.
All data are mean values with (±S.E.M) and compared with control.
N = number of mice in each group.
All data are compared with (control).

Discussion

From this experiment was observed the elevated plus-maze (EPM) Technique or tests it's very important to estimate anxiety behavior by clear manner and also were used as model of validated animal of stress or anxiety that are predictive of medicine sensitive or responses in humans. [51]. This technique, which are related to natural aversion of mice to side of open arms or spaces, are response to the actions of both anxiogenic and anxiolytic products in mice. [52]. The technique of elevated plus-maze was conducted for use in some rodents by After or following the trials of [53]. And was used procedure to modified for consumed this instrument in the all rodents established by [54]. These many modifications of the essential technique or method have since been used to determine the anxiolytic effects of many medicine or drugs such as group of benzodiazepines. When using technique of (EPM) , the number of entries onto the open arms and number of line coss in open arms and the time spent in the open arms of the maze are taken as parameters for anxiety behavior. Therefore, these parameters if increased indicate to decrease anxiety and stress of animals. Anti-anxiety medicines or compounds stimulate All of these indicators. The standard anti-anxiety drug diazepam resulted a clear significant stimulate in the time spent amount on the open arms of the maze (179.7 ±2.8 Seconds). during (5 minutes) and and the number of line cross in open arms (29 ±2.6) and the entries number in the open arms of maze (5.6 ± 0.) Times). during (5 minutes). Also when taken of plant diluted ginger suspension was registered a significant increase in the time spent amount on the open arms of the plus- maze (101± 5.2 Seconds). And the number of line cross in open arms (19.7 ±0.7) and observed the entries number onto the open arms of maze (10 ± 0.4 Times). Also when taken of plant concentrated ginger suspension was registered a significant increase in the time spent amount on the open arms of the plus- maze (164± 5.7 Seconds). And the number of line cross in open arms (17.7 ±2.7) and observed the entries number onto the open arms (9.5±1.3). All above results were Compared with suitable control but less than standard diazepam. These characteristics are inhibited by classical types of anti-anxiety drug as diazepam and plant ginger suspension as natural products and blocked by anxiogenic products as stimulus smell of urine cats:

1- Gingerol-enriched ginger extract effects on anxiety -like behavior in a neuropathic pain model via colonic microbiome-neuroimmune modulation. [55].

2- Gingerols and shogaols of zingiber officinale var. sunti valeton as potential allosteric agonists of human GABAA receptors by in silico pharmacology approach. [56].

3- Network pharmacology -guided evaluation of Ginger and cornelian cherry extracts against depression and

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metabolic dysfunction in estrogen-deficient chronic stressed rats. [57].

4- High -hydrostatic pressure extract of Ginger extracts anti-stress effects in immobilization- stressed rats. [58].

5- 6- Gingerol extracts anti-depressant effect through regulating the PPARy signaling pathway. [59].

All these studies indicate the validity of my finding, which are that ginger extract is important in treating anxiety and reducing stress, and there is no difference in the results. Regarding the main or essential contributions to this experimental work, a researcher or specialist in the field of medicinal drugs or Phytochemistry helped me to extract active ingredients of Ginger plant using a special device or technique apart from that, there was no any governmental or private funding for the completion of this experimental study. It must be clarified and showed that the geographical boundaries of my study are the Tripoli-City.

Recommendation

I recommend further in -depth good scientific research focused on extracting safe pharmacological dosage of ginger extract and using it in various medical and nutritional applications, such as in control of anxiety and treatments of stress, and other ailments. It is also important to promote the use of safe, natural alternatives to both patients and researchers, encouraging them to avoid products and chemical substances or synthetic drugs.

Conclusion

This experimental trial or study using animals of male albino mice was it is being done to verification possibility role of plant Ginger suspension to inhibit stress and anxiety behavior.

The essential verify instrument was used is elevated plus-maze model.

The golden standard anxiolytic medicine or drug-diazepam (DZP) and plant Ginger syrup extract were used to reduce and modify stress and anxiety like behavior.

From this experimental study, I was observed obvious antagonized action to anxiety induced-like behavior by used plant ginger suspension in compatible suitable concentration.

The probable mechanisms to reduce or diminish anxiety by plant ginger syrup extracts may related to Rennin angiotensine system (RAS) interference with GABA neurons or Noradrenalin (NA), release of hormones, stimulation of (AT_2) receptors or other mechanism, therefore, we need many researches and studies to determine and founded these mechanisms and Further experimental studies to verify into the probable relation or involvement of above mechanisms are envisaged.

Ethical statment

. This study was reviewed and approved by the Scientific Research and Ethics Committee at the University of Tripoli, Libya, under ethical approval reference number SREC/010/353.

Author contributions

In this study, I tried hard to do the work on many months, and since I am a pharmacist and a specialist in pharmacology, I reared the experimental animals, which mice, and conducted the study in a specialized pharmacology laboratory, recording the experiments and the results of the work.

Conflict of interest

we were clearly declaring no conflict of interest related to the publication of this work or experimental study.

Acknowledgment

Many thanks to those who provided me with some logistical support for this study, such as pregnant female animals or white laboratory mice, and also to those who advised on the ideal way to prepare ginger.

Summary

- Elevated plus- maze model (EPM) was used to evaluate the anxiolytic effect of ginger and the ginger effect was compare with the standard drug diazepam.
- Ginger at both forms, diluted and concentrated (10mg/kg) produces anxiolytic action in albino mice.
- This study may indicate a possible involvement of GABAA, α2- adrenergic and androgens receptors in the mediation of anxiolytic action of Ginger.
- Further studies are required to confirm these results by using other models of anxiety and to probe the other possible mechanisms involved in the anxiolytic action of Ginger.

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