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## *Vigna Unguiculata* as an Anxiolytic Agent: Evidence from Animal Model Studies

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**Abstract:** Anxiety has spread worldwide and is only getting worse, posing a serious threat to mental health and general well-being. If anxiety is not managed, it can result in severe depression and other health issues. The current study intends to investigate the pharmacological effects of *Vigna unguiculata*, frequently referred to as white beans, on anxiety models in rodents using albino mice of both genders. The albino mice were administered two doses of white beans over the course of 60 days: 500 mg/kg and 1000 mg/kg. Based on the various doses, the mice were divided into two treatment groups, and a control group was added for comparison. The evaluations, which used a variety of instruments to measure anxiety-like behaviors, were conducted at regular intervals on days 0, 7, 15, 30, 45, and 60. These included the cage-crossing apparatus, head dip apparatus, open field apparatus, elevated plus maze, and light and dark apparatus. These instruments enable the observation and measurement of anxiety-related behaviors displayed by mice under various test situations. According to the research findings, both doses of white beans have a considerable ability to lessen the anxiety-like behaviors of albino mice. However, compared with the 500 mg/kg dose, the larger dose of 1000 mg/kg seemed to possess greater anxiolytic potential. This shows that the anxiolytic effects of white beans are dose-dependent. The potent anxiolytic qualities of white beans are thought to be influenced by substances such as tryptophan, glutamic acid, and methionine. The findings of this experimental study indicate *Vigna unguiculata* (white beans) as a promising natural treatment option for anxiety management. The anxiolytic responses of albino mice provide evidence in favor of researching white beans as a treatment for easing anxiety symptoms in people. The research goal of this study is to evaluate the effect of white beans on anxiety and stress. White beans are a regular diet item that can easily incorporate and produce anxiolytic effects. This research is unique because it addresses a previously unexplored topic, and its primary objective is to raise public knowledge about the health advantages of white beans.

**Keywords:** anxiolytic effect, head dip apparatus, cage crossing, elevated plus maze apparatus, light and dark apparatus, open field apparatus, *Vigna unguiculata*, white beans.

## 豇豆作為抗焦慮劑：來自動物模型研究的證據

**摘要：**焦慮已在世界範圍內蔓延，而且只會變得越來越嚴重，對心理健康和整體福祉構成嚴重威脅。如果不控制焦慮，可能會導致嚴重的抑鬱症和其他健康問題。目前的研究旨在利用白化小鼠和雌雄啮齒類動物，研究野豌豆（通常稱為白豆）對啮齒類動物焦慮模型的藥理作用。在 60 天內，給白化小鼠注射了兩劑白豆：500 毫克/公斤和 1000 毫克/公斤。根據不同劑量，將小鼠分為兩個治療組，並添加對照組進行比較。評估使用各種儀器來測量焦慮樣

行为, 在第 0、7、15、30、45 和 60 天定期进行。这些包括穿越笼子装置、头部浸入装置、开放场地装置、高架十字迷宫、明暗装置。这些仪器能够观察和测量小鼠在各种测试情况下表现出的焦虑相关行为。根据研究结果, 两种剂量的白豆都有相当大的能力减轻白化小鼠的焦虑样行为。然而, 与 500 毫克/公斤剂量相比, 较大剂量 1000 毫克/公斤似乎具有更大的抗焦虑潜力。这表明白豆的抗焦虑作用具有剂量依赖性。白豆的强效抗焦虑特性被认为受到色氨酸、谷氨酸和蛋氨酸等物质的影响。这项实验研究的结果表明, 白豆是一种很有前景的焦虑管理自然治疗选择。白化小鼠的抗焦虑反应为研究白豆作为缓解人类焦虑症状的治疗方法提供了证据。本研究的研究目标是评估白豆对焦虑和压力的影响。白豆是一种常规饮食项目, 可以很容易地融入并产生抗焦虑作用。这项研究是独一无二的, 因为它解决了一个以前从未探索过的话题, 其主要目标是提高公众对白豆健康优势的认识。

**关键词:** 抗焦虑作用, 浸头装置, 笼子穿越, 高架十字迷宫装置, 明暗器具, 旷场仪器, 豇豆, 白豆。

## 1. Introduction

There are two major psychological problems being faced by the world today: anxiety and stress. Anxiety in its advanced form can be very dangerous. This behavioral condition may lead to several other health issues that are hazardous to humans. The world is growing too fast and people are too busy competing with each other, which may lead to feelings of stress, nervousness, or panicking around. Discussions about anxiety have picked up, but this problem remains underexplored. This neurological problem develops into dangerous issues such as panic attacks, agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, and many other phobias [1]. Anxiety in today's world can be due to many motives such as emotional trauma or events, career problems, educational or professional issues, personal life, and environmental conditions [2]. Some drugs may also cause anxiety because their adverse effects are mainly rescindable [3]. Anxiety is also a common symptom of many diseases such as heart disease, asthma, COPD, irritable bowel syndrome, cancer, and hyperthyroidism [4]. There are some neurological states in which anxiety is a major problem, such as attention deficit hyperactivity disorder (ADHD) and autism in children [5]. Anxiety due to autism and ADHD must be treated to improve the mental functioning of children [6]. The main causes of anxiety in autism and ADHD are sleep disturbance, sensory disorders, hyperactivity, and speech and language disorders [7].

Indications of anxiety are very common with low differential ratios, such as high blood pressure, overthinking, increase in heart rate, nervousness, shortness of breath, shivering, sweating, and sometimes diarrhea [8]. The prevalence in the US is about 15.7 million people every year, but the prevalence is difficult to measure because of the small variance ratio in symptoms [9]. The most common psychosocial treatment for stress and anxiety is cognitive behavior therapy in adults [10].

Many benefits of dietary products are being

revealed after studies conducted in the modern era. Researchers are focusing their studies on daily dietary products to cure many neurological diseases and problems [11].

One of the dietary products, *Vigna unguiculata* (white beans), has many beneficial nutritional components. *Vigna unguiculata* is generally known as cowpea or white beans and is an annual herbaceous legume belonging to the genus *Vigna*. Its family is Fabaceae. The subfamily of *Vigna unguiculata* is Papilionoidea. They are rich in proteins, vitamins, and minerals. The main constituents of white beans are amino acids, flavonoid tannins, isoleucine, lysine, and tyrosine phenylalanine, which is in higher concentrations. Therefore, the presence of many beneficial chemical constituents can help in many health problems. Traditionally, it is used for gastrointestinal (GIT) problems such as laxative in constipation, and it also has some antimicrobial activity against both gram-negative and gram-positive bacteria. Some studies have shown that these beans are very useful for antifungal activity [12]. It has some proteins that may help release neurotransmitters, which may help in cognition and brain functions [13]. Essential amino acids such as cysteine, methionine, and tryptophan are in high amounts [14]. Tryptophan helps decrease anxiety and stress issues by increasing the production of serotonin and melatonin [14]. The present study was designed to evaluate the effect of white beans at low and high doses on the anxiety model in rodents.

The criteria for selecting this topic are to evaluate the benefits of white beans on the brain and their effects on anxiety, stress, and panic attacks.

The main application of this study is to include white beans in daily diets to improve against anxiety, stress, and panic attacks.

## 2. Methodology

The anxiety model was prepared on albino mice with a weight range from 20 g to 25 g for both sexes.

Rodents were kept in their normal habitat in cages in the animal house of the Department of Pharmacology at the University of Karachi. Mice were monitored critically to maintain all the environmental factors such as proper care taken for food and water, temperature, and humidity were kept standard that is  $25\pm 2^{\circ}\text{C}$  and 50-60%, respectively.

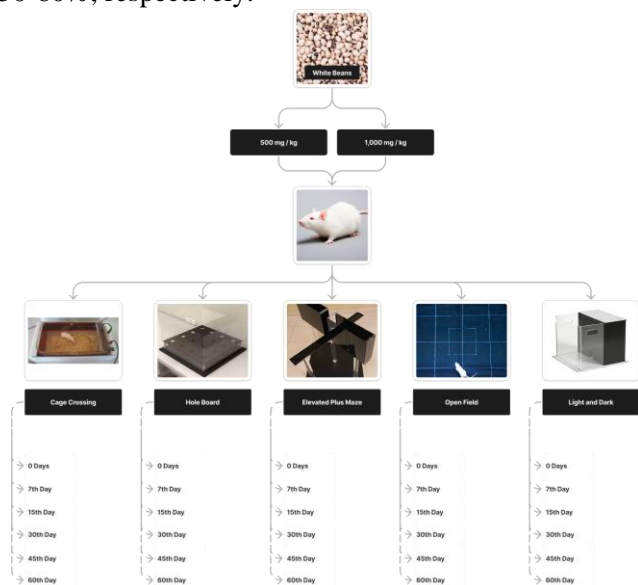


Fig. 1 Research model (Developed by the authors)

Monitoring of 12-hour day and night cycle was also considered.

Animal handling was performed according to the guidelines given by Helsinki Resolution 1964. The study was legally approved and authorized by the Institutional Board of Advanced Studies and Research Videos Resol. No. 10 (P).

## 2.1. Identification and Purchase of *Vigna Unguiculata*

White beans were obtained from the local market and stored in a zip-lock plastic bag at room temperature. Seeds were identified from the Department of Pharmacognosy at the University of Karachi and were given the identification number VUS-02-20.

## 2.2. Preparation of *Vigna Unguiculata* Powder

First, the beans were sorted to remove all the impurities and then washed and rinsed properly with cold water. The beans were then boiled and dried until the water completely vanished. The dried beans were then ground into powder form with the help of an electric grinder. Proper dose pellets were prepared using a few drops of water.

## 2.3. Ethical Approval

All authors declare that the principles of animal laboratory care were followed completely. Animals were kept according to the standard principles of CCAC guidelines in which standard feed and water were given to mice in a clean environment and with a

12-hour day and night cycle.

## 2.4. Model Design and Dose Schedule

For this study, albino mice were taken and divided into 3 groups. All groups comprised six mice. Group I was considered the control group, which received a normal diet. Group II patients were given 500 mg/kg *Vigna unguiculata*. Group III was given 1000 mg/kg *Vigna unguiculata*. The doses prepared as pellets were administered to each mouse of the respective groups daily for 60 days. The readings of all five apparatuses of anxiety were taken at 0, 7<sup>th</sup>, 15<sup>th</sup> day, 30<sup>th</sup> day, 45<sup>th</sup> and 60<sup>th</sup> days on cage crossing, head dip, elevated plus maze, light and dark and open field apparatus.

## 2.5. Cage Crossing

The cage crossing method was used to evaluate anxiety models in rodents according to international standards. The equipment is built of plexiglass, which is square with a size of (26×26×26 cm) and is clear, allowing the rodent's activity to be observed easily. The floor is covered in sawdust. To avoid external disruption, the instrument is placed in a quiet location. The animals were kept in cages because they felt at ease in their surroundings. The readings were recorded for 5 minutes [15].

## 2.6. Head Dip

The head dip test is a useful tool for determining how a medicine affects mouse behavior. The equipment is made of a rectangular hardwood board that measures 35 cm x 45 cm x 45 cm and is enclosed. It has three 2.5 cm-diameter apertures on all sides. The rodent was placed in the apparatus center and given 5 minutes to explore. The poking of the snout was registered [16].

## 2.7. Open Field Test

In anxiety models, the open field test is often used to assess locomotor and behavioral activity. The equipment consists of a square container measuring 76 cm x 76 cm and 42 cm high. There are 25 squares on the floor. Each square is 15 cm in diameter. A central square of 15×15 cm can also be seen in the middle section. For a period of 10 minutes, the mouse was placed separately in the open fields and the number of central and peripheral crossings were noted [17].

## 2.8. Light and Dark Test

The anxiety behavior of rodents was assessed using light and dark. The chamber is 44×21×21 cm in diameter and is made of propylene. It is divided into two halls by a tunnel (7.5 x 7.5 cm) that allows transit from one light compartment to the other dark compartment and vice versa. The translucent sides of the light chamber are exposed, and a lamp is installed to provide illumination. The dark compartment, which is sealed by a black cover, is painted black. The mice

were placed in a light area for ten minutes to study the anxiolytic effect, and the time spent in the light environment was recorded. Rodents, on the other hand, prefer to reside in gloomy areas. The willingness of the mouse to explore the light-unprotected area demonstrates the anxiolytic effect, which is a characteristic that should be studied by researchers [18].

### 2.9. Elevated plus Maze

One of the important tools for assessing anxiety is the elevated plus maze. The apparatus has two open arms (25 x 5 x 0.5 cm) across from each other and perpendicular to two closed arms (25 x 5 x 16 cm) with a center platform that are used for the elevated plus maze test (5 x 5 x 0.5 cm). Closed arms have a high (16 cm) wall to surround the arm, whereas open arms have a negligible (0.5 cm) wall to reduce the number of falls. Plastic materials are used to construct the equipment. The platform is white with clear walls. The elevated plus maze apparatus is available in various materials and colors [19].

### 2.10. Statistical Analysis

SPSS (Statistical Package for Social Sciences) Ver. 26 was used to analyze the data. Two-way ANOVA followed by post hoc Tukey's test was applied for analysis. A p value of less than 0.05 was considered significant.

## 3. Results

### 3.1. Cage Crossing

Figure 1 shows the effect of white beans at doses of

Table 1 Effect of white beans on the head dip model (Developed by the authors)

Groups	0 day	7 <sup>th</sup> day	15 <sup>th</sup> day	30 <sup>th</sup> day	45 <sup>th</sup> day	60 <sup>th</sup> day
Control	47.5±8.19	49.2±5.54	44.8±8.51	45.3±11.74	43.1±9.28	49.6±7.31
White Beans, 500 mg/kg	45.3±7.52	18.5±9.26*	13.1±4.44*	9.8±1.16*	8.8±1.47*	9.5±2.66*
White Beans, 1000mg/kg	49.0±2.68	23.3±8.04*	19.1±3.76*	19.0±3.57*#	18.1±2.13*#	9.5±3.44*

\* For control with other treated groups

### 3.3. Open Field (Centre and Peripheral Squares)

Figures 3 and 4 show the effect of both doses of white beans on the open field central box and the peripheral box, respectively. The control group showed overall significance with the treated groups. In central square crossings on 60<sup>th</sup> day 1000 mg/kg showed better results than 500 mg/kg, whereas the difference between the doses was insignificant when peripheral crossings were compared.

500 mg/kg and 1000 mg/kg on the cage crossing test. The control group showed overall significance with the treated groups. The group taking 500 mg/kg dose showed an anxiolytic effect on 30<sup>th</sup> day while the group taking 1000mg dose showed an anxiolytic effect along with sedation on 60<sup>th</sup> day.

### 3.2. Head Dip

Table 1 indicates the effect of white beans of both doses on the head dip test. The control group showed overall significance with the treated groups. On the 30<sup>th</sup> day, the group taking 500 mg/kg dose showed better anxiolytic effect than the group taking 1000 mg/kg but on the 60<sup>th</sup> day both doses showed the same anxiolytic effect.

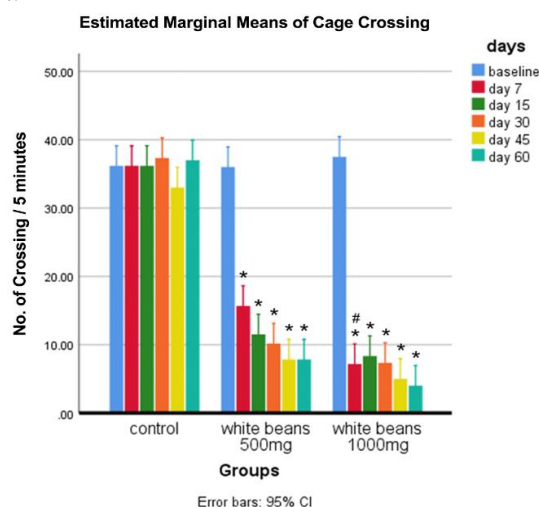


Fig. 2 Effect of white beans on cage crossings (Developed by the authors)

\* For control with other treated groups

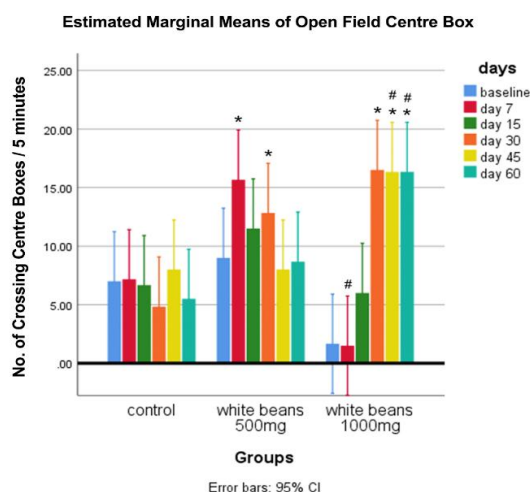


Fig. 3 Effect of white beans on central squares in open field apparatus (Developed by the authors)

\* For control with other treated groups

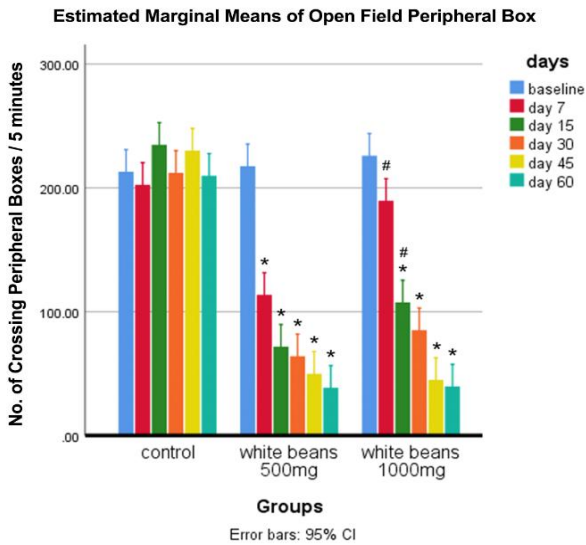


Fig. 4 Effect of white beans on peripheral square crossings in open field apparatus (Developed by the authors)  
\* For control with other treated groups

### 3.4. Light and Dark Test

Figure 5 shows the effect of both doses of white beans on the light and dark apparatus. The control group showed overall significance with the treated groups. The group taking 500 mg/kg dose showed better anxiolytic effect on the 60<sup>th</sup> day than the group taking 1000 mg/kg dose.

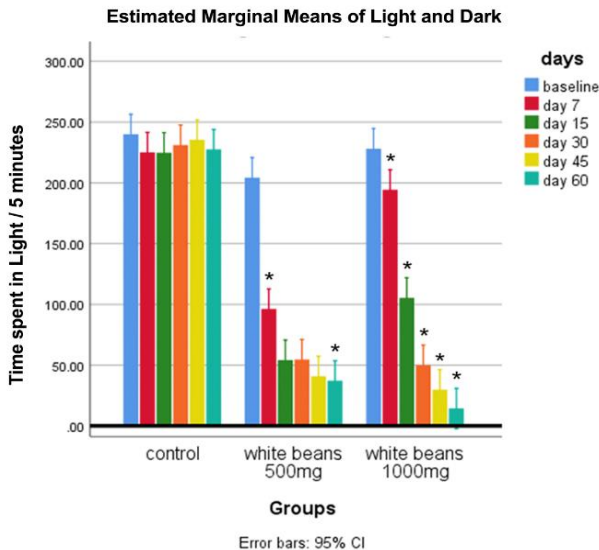


Fig. 5 Effect of white beans on time spent in the light area in the light and dark model (Developed by the authors)  
\* For control with other treated groups

### 3.5. Elevated plus Maze (Open Arm)

Figures 6 and 7 show the effect of white beans at doses of 500 mg/kg and 1000 mg/kg on the time spent in the open arm of the elevated plus maze and the number of transitions in the open arm. The control group showed overall significance with the treated groups. Both groups taking the doses of 500 mg/kg and 1000 mg/kg showed the same anxiolytic effect on the 60<sup>th</sup> day.

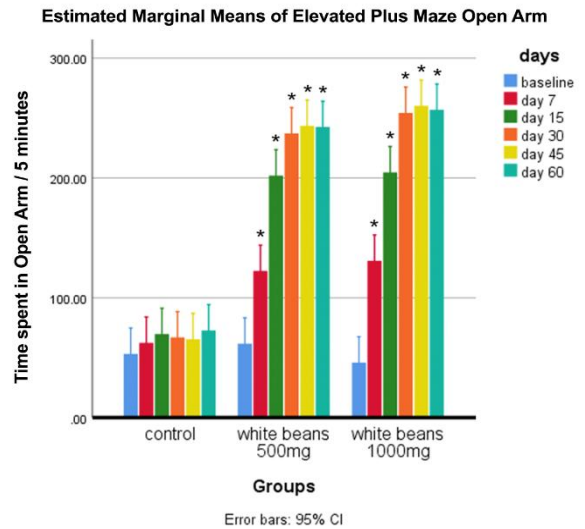


Fig. 6 Effect of white beans on the time spent in open arms in the elevated plus maze model (Developed by the authors)  
\* For control with other treated groups

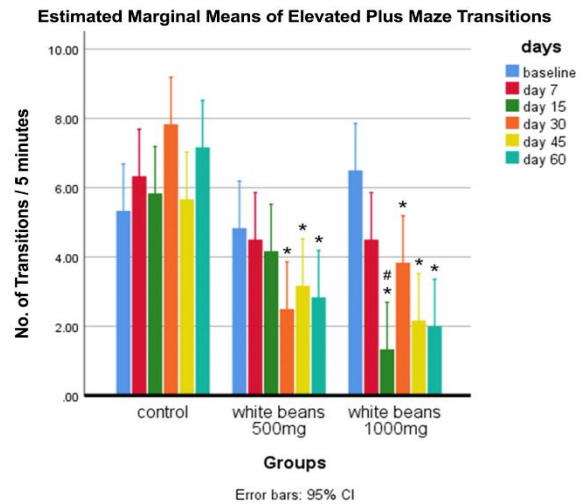


Fig. 7 Effect of white beans on the number of transitions in open arms in the elevated plus maze model (Developed by the authors)  
\* For control with other treated groups

## 4. Discussion

Nature has created dietary products that are all very beneficial for mankind. These food products contain some micro and macronutrients that help the body grow, prevent infections, and treat many diseases [20]. Neurological issues are the most common problems that the world is facing today [21]. These problems can be easily treated with dietary products. White beans have many beneficial constituents that help in brain development, maintaining and improving its function [22].

This study indicated a more significant decrease at 1000 mg/kg doses in cage crossing readings after the 15<sup>th</sup> day. This decrease shows that the animal was in less fear or fearless. This might be because of the presence of glutamic acid, which is approximately 43.6% per 100 g [23]. Glutamic acid reduces anxiety and fear by modulating glutamatergic function via inotropic or metabotropic glutamate receptors [24]. They bind to receptors and increase dopamine neurotransmitters,

which ultimately reduce fear and anxiety [25].

The presence of tryptophan in *Vigna unguiculata* makes 0.5 mg, which is the daily dose required by the human body to perform normal functions [23]. Tryptophan increases serotonin neurotransmitters in the brain, which helps in mood elevation and improves confidence, ultimately reducing stress and anxiety [26]. Higher levels of serotonin in the brain and blood cause a well-being state, which reduces stress [27]. The light and dark experiment is another important test for anxiety. Anxiolytic drugs increase the time that rats spend in light areas, even though rodents are naturally averse to strong light [28]. The results of the light and dark apparatus indicated that rodents treated with *Vigna unguiculata* at both 500 mg/kg and 1000 mg/kg showed a significant increase in time spent in the light compartment. The readings of the 45<sup>th</sup> and 60<sup>th</sup> days show no stress in rodents compared to the control group.

The open-field test is another way to assess anxiety, inquisitiveness, and locomotor in animals [29]. Our findings show a consistent rise in center crossings compared with the control group. We also observed that as the treatment progressed, the number of peripheral crossings decreased. This might be due to the presence of methionine, which is 3.2% in 100 g [23]. Methionine is important for antioxidant mechanisms that are evolved within the cell to defend the cell from damaging radicals, one of which is the methionine sulfoxide reductase system. This system helps in relieving neurological stress by protecting against free radical generation and also enhancing the production of dopamine and serotonin [30].

Hole board apparatus and elevated plus maze are also involved in investigating anxiety and neophilia [31]. Anxiety due to a new environment or any change can be easily assessed using these two apparatuses. The readings for 1000 mg/kg of *Vigna unguiculata* showed a remarkable decrease at days 45 and 60. At high doses, high levels of magnesium contribute to stress relief by decreasing glutamate action and increasing the GABAergic system [32].

The presence of glutamic acid, tryptophan, methionine, and magnesium highlights that incorporating *Vigna unguiculata* into one's daily diet will assist in minimizing stress and anxiety because these components are abundant in white beans.

## 5. Conclusion

The main findings of this investigation unequivocally demonstrate that white beans possess calming properties. Both dosages exhibited anxiolytic effects based on the readings from the model equipment. However, the dose of 1000 mg/kg showed a higher potential for lowering anxiety than the dose of 500 mg/kg. This dietary supplement can rapidly alleviate tension and anxiety; hence, it is advisable to include it in one's diet. Further investigation is required

to explore the potential incorporation of this dietary supplement into pharmaceutical formulations. The scholarly significance of this work is vital for future research endeavors, particularly in integrating the utilization of white beans in pharmaceutical formulations aimed at alleviating tension and anxiety. Herbal or pharmacological remedies may be helpful for anxiety problems. This study introduces a novel approach using various dosages and methodologies to assess the impact on the anxiety model.

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