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Investigating the Protective Effects of a Tryptophan-Based Diet in Alcoholics: An Experimental Study on Depression and Anxiety

Mayanja Alafat

School of Pharmacy, Kampala International University, Uganda

ABSTRACT

Depression and anxiety are prevalent co-morbidities among individuals with chronic alcohol consumption, posing significant health challenges worldwide. This study aimed to explore the potential protective effects of a tryptophan-based diet against depressive tendencies and anxiety associated with chronic alcohol consumption. Using an experimental design, Wistar rats were subjected to chronic alcohol administration along with varying doses of a tryptophan-based diet over 28 days. Behavioral tests including the Elevated Plus Maze (EPM) and Forced Swim Test (FST) were conducted to evaluate anxiety-like behavior and depressive tendencies, respectively. Results indicated a significant decrease in immobility time in the FST with increasing doses of the tryptophan-based diet, suggesting antidepressant effects. Moreover, the anxiety index decreased while the time spent on open arms increased with higher doses of the diet in the EPM, indicating anxiolytic effects. These findings suggest that a high tryptophan-based diet could serve as a potential intervention for individuals with alcohol-related depression and anxiety.

Keywords: Depression, anxiety, alcohol, tryptophan, diet, alcoholics

INTRODUCTION

Depression is the most disabling disorder worldwide that accounts for the highest proportion of global burden attributable to mental disorders characterized by deep sadness, reduced energy, vegetative nervous system dysregulation, cognitive dysfunction, and even a high suicidal tendency [1] The lifetime prevalence rate for major depression disorder is approximately 16.2% in most developed countries and it's reported to be affecting 350 million people worldwide *in* their lifetimes,[1] and it's estimated that 85 of 100 depressed patients also experience symptoms of anxiety,[2] Depression is highly prevalent and recurrent disorder co-morbid with alcohol related problems [3] and alcoholics are more likely to be diagnosed with an affective disorder with the life time co-prevalence rates ranging from 20-47%, [4] World health organization [5] estimates that 2 billion people consume alcoholic beverages worldwide and Uganda in particular has been reported to have one of the highest levels of alcohol consumption in East Africa [6] Although alcohol consumption is socially acceptable in many societies, chronic use through various mechanism in several studies has shown to disrupt the serotonergic functions an important mediator of mood. Currently with an exception of psychological therapies the rest treatments of depression aim at locking the breakdown or reuptake of serotonin none of them work at increasing serotonin levels but under normal physiological conditions the biosynthesis of serotonin is limited by the availability of the essential amino acid tryptophan [7][8].

Depression is among the major causes of ill mental health in Uganda and the world at large, currently, 1 in 4 suffers from ill mental health and depression [9]. Eight hundred thousand people kill themselves every year due to ill mental health. Chronic alcohol consumption by people has been strongly associated with depression as a result of severe mechanism mainly involving serotonin depletion in the brain. Tryptophan is the amino acid precursor of serotonin, and dietary depletion of tryptophan causes a rapid decrease in the synthesis and release of brain serotonin, as confirmed by brain tissue 1alysis in rats [2][14]. Chronic tryptophan depletions (CTD) have 10wn stronger effects, reducing 5-HT brain levels to 35-40% at 14 days and to 75% at 5-week exposures, [9][15] (alcohol) (ethanol) causes profound changes in the metabolism of the essential amino acid L-trptophan in both man and experimental animals at various stages of alcohol intake, withdrawal, d sobriety [1][16] for instance prenatal exposure alcohol to a rodent decreased serotonin levels and serotonin metabolism [8][11].

Studies have consistently reported that major depressive disorder (MDD) is closely related to suicide, suicidal ideation, suicide planning, and suicide attempts and is a significant risk factor for suicide [10][11] Several antidepressants

currently in use are often associated with anticholinergic or neurological side effects such as dizziness, sedation, sexual dysfunction, insomnia and anxiety. Therefore, much research has focused on identifying natural and alternative therapies for depression with fewer side effects [12][13]. This study was carried out to assess the anxiety response and depression vulnerability following chronic co-administration of alcohol and a high Tryptophan based diet in Wistar rats.

METHODOLOGY

Study Design

This study was experimental; involving alcohol induced depressed wistar rats.

Study Area

Alcohol was bought from one of the laboratory equipment supplier in Ishaka community and the study was carried out in the Pharmacology laboratory of KIUWC, lshaka.

Study Population

The study was conducted in mature experimental wistar albino rats.

Sample Size

A total of 30 wistar albino rats was used.

Inclusion Criteria

Only healthy mature adult male well feeding rats more than 8 weeks old were used for the study.

Exclusion Criteria

Unhealthy and pregnant rats or less than 8 weeks old rats.

Experiment Design

Male Wistar rats, weighing between 100 and 200 grams and approximately 60 days old, were utilized in the study. The rats were housed in rat cages within the animal research facility of the Department of Pharmacology at KIU. Cage maintenance, including cleaning and bedding change, occurred thrice weekly. The rats were subjected to a 12-hour light/dark cycle and provided with standard rodent pellets ad libitum, alongside unrestricted access to water. Following a one-week acclimatization period, the animals were grouped. Computer-generated random numbers were assigned to each group at the commencement of the experimental phase. The rats were then distributed into six groups, each consisting of 5 rats. Treatments were administered intragastrically according to the following protocol:

Group I: received 4g/kg of20% ethanol
Group 2: received 2g/kg ofsoy powder+ 4g/kg of20% ethanol
Group 3: receive 4g/kg ofsoy powder+ 4g/kg of20% ethanol
Group 4: receive 6g/kg of soy powder+ 4g/kg of20% ethanol
Group 5: received 8g/kg ofsoy powder+ 4g/kg of20% ethanol
Group 6: received I0g/kg of soy powder+ 4g/kg of20% ethanol

The rats were weighed twice a week to ensure appropriate dosing based on weight changes. All rats except the control group received single gavage of the test substances twice daily for 28 days

Procedure and Tests

After 28 days the rats were subjected to the following tests, the elevated plus maze (EPM). The test is based on the inborn aversion of rats to open, bright illuminated spaces. The maze consists of two open arms (30 x 5 cm) and two closed arms (30 x 5 cm) enclosed by a sidewall on all edges (height 15 cm). Rat was placed in the center of the maze (central platform) facing the closed arm [8][10]. Total arm entries, percent of entries into the open arm. (open-arm entries/total arm entries) x 100) and time spent in open arms ((open arms/total session duration) xlOO) quantified during 10 min test. Arm entry was only defined when an animal (the mouse mass center) is at least 3 cm on an arm to differentiate entries from stretched attend postures into the arms. It is used to assess the anxiety levels [10][8].

Forced swim test (FST)

The Forced Swim Test is a behavioral test used frequently to evaluate the potential efficacy of prospective antidepressant effect drugs in rats or mice [10][8]. It was conducted by placing experimental animal in an inescapable cylinder (depth 30cm) containing 25degrees Celsius water, for which the experimental animals must swim for 15 minutes. The experimental animals are removed from the water, dried, and placed back in the home cage then allowed to rest for 24 hours, and then repeat the FST after being co-administered with alcohol and a high tryptophan diet, in which the swim session was reduced to 5 minutes. As time progresses during the FST experimental animals became more immobile, having only the ability to keep their heads above the water or by floating. The time of immobility and the latency to the initial immobility period of the swim session are the primary dependent measures of the FST reflecting behavioral despair of the animal models [8],[9] [10] .

Data Analysis

The gathered data underwent organization in Microsoft Excel before being imported into STATAvl4 for analysis. Results were expressed as Mean ± SEM, percentages, and ratios. One-way ANOVA was employed to examine mean disparities among the groups, with Bonferroni correction utilized as the post hoc test to identify sources of statistical variance. A confidence level of 95% was applied, rendering p-values below 0.05 statistically significant.

Ethical Consideration

The experiments was carried out according to the National Institute of Health guide for the care and use of laboratory animals. The guiding principles for more ethical use of animals in

testing was followed.

RESULTS

Elevated Plus Maze

Table 1 Illustrates the number of open arm time, open arm entries, total number of entriesand closed arms entries

Parameter	Mean± SEM						P value
	NC	TGl	TG2	TG3	TG4	TGS	
Open Arm Entries	3.4±0.4	3.8±0.6	4.8±0.4	4.6±0.5	5.8±0.6*	6.6±o.5·	**0.0005**
Closed Arm Entries	5.4±0.7	5.0±0.7	3.6±0.4	3.8±0.4	2.8±0.4•	2.2 ± 0.2·	**0.0011**
Open Arm Time (seconds)	9.6±0.5	16.2±0.9*	20.0±0.7*	25.6± 1.4•	31.8± 1.0•	37.4±1.2•	**<0.0001**
Total Numberof Entries	8.4±1.2	8.8±0.4	8.4±0.5	8.4±0.5	8.6±0.7	8.8±0.6	0.9944

The asterisk (*) indicate a statistically significant difference between the control group and that other test group

CP -Control group TG -Test group 1 to 5 Table!

Significant differences were found between treatments *(P* 0.0001) in the time spent on the open arms. The post hoc test showed that the time spent on the open arms increased with the increasing doses ofthe tryptophan-based diet administered (soy powder).

Table 2: Illustrates the percentage ofentries, time on open arm and anxiety index

Test group	Entries into Open Arm (%)	Time spent on Open Alms (%)	Activity Index
CP	40.5	3.2	0.782
TGl	43.2	5.4	0.757
TG2	57.1	6.7	0.681
TG3	54.8	8.5	0.684
TG4	67.4	10.6	0.610
TG5	75.0	12.5	0.563

In table 2 the percentage of open arm time also increased with the increasing doses of the tryptophan diet but the anxiety index kept on reducing with the higher doses of the diet significantly showing the reducing levels of anxiety with the increasing doses oftryptophan.

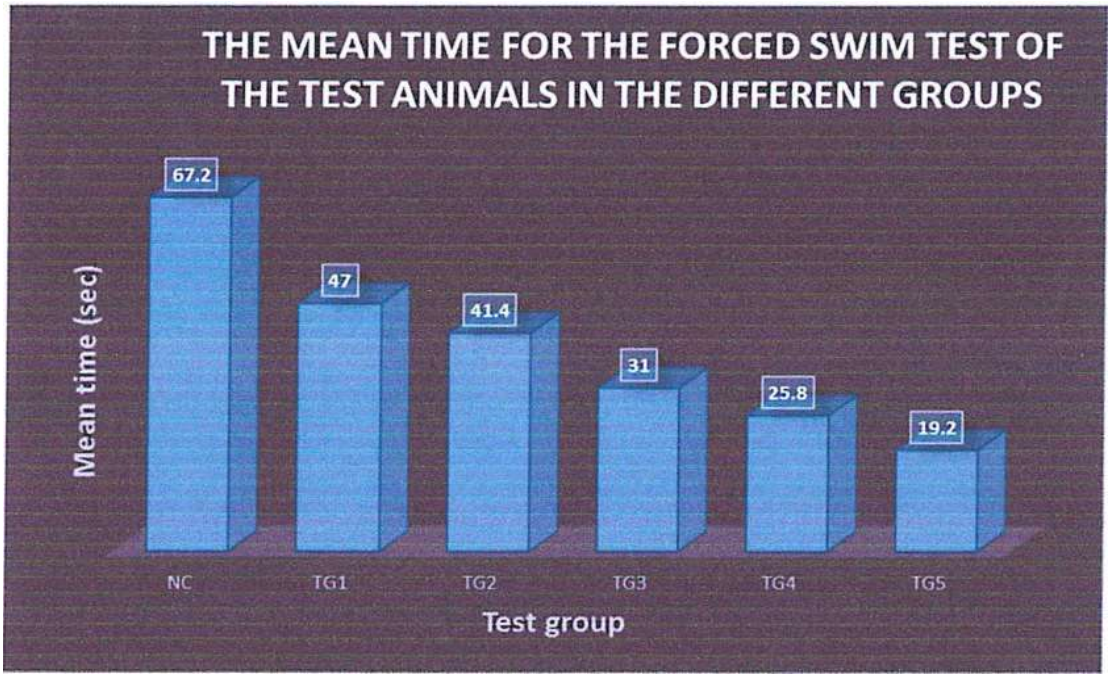

Figure 1: graph showing the anxiety index of the different test groups

Forced Swim Test and FST

Table 3: illustrates the Mean± SEM of immobility time(s) of the groups.

Test group	Time (sec), Mean± SEM	P value
CP	67.2 ± 0.9	**<0.0001**
TG1	47.0± 1.3•	
TG2	41.4± 1.3•	
TG3	31.0± 1.0·	
TG4	25.8± 1.5*	
TG5	19.2± i.2*	

The asterisk (*) indicate a statistically significant difference between the control group and that other test group.

From table 3, there is a significant difference ($p < 0.0001$) in the immobility time. The immobility time significantly decreased with the increasing doses of the diet administered.

DISCUSSION

The present study aimed to investigate the protective effects of a tryptophan-based diet against depression and anxiety associated with chronic alcohol consumption [11], [12]. The findings from behavioral tests, including the Forced Swim Test (FST) and the Elevated Plus Maze (EPM), shed light on the potential therapeutic implications of tryptophan supplementation in mitigating the adverse psychological effects of alcohol [13], [14]. Firstly, the results from the Forced Swim Test revealed a significant decrease in immobility time with increasing doses of the tryptophan-based diet. Immobility in the FST is considered a measure of behavioral despair and is indicative of depressive-like behavior in rodents [15],[16]. The observed reduction in immobility time suggests an antidepressant effect of tryptophan supplementation. This finding aligns with previous research indicating that tryptophan, as a precursor to serotonin, plays a crucial role in regulating mood and emotional states. By replenishing serotonin levels, tryptophan may counteract the serotonin depletion induced by chronic alcohol consumption, thereby exerting antidepressant effects. Secondly, the Elevated Plus Maze test provided insights into the anxiolytic effects of the tryptophan-based diet. The decrease in the anxiety index and the increase in time spent on open arms with higher doses of the diet indicate a reduction in anxiety-like behavior. Anxiety is a common co-morbidity in individuals with depression and chronic alcohol consumption, and its alleviation is crucial for

improving overall mental well-being. The observed anxiolytic effects of tryptophan supplementation suggest its potential utility in managing anxiety disorders, particularly in the context of alcohol-related anxiety. Moreover, the dose-dependent response observed in both the FST and EPM underscores the importance of dosage optimization in maximizing the therapeutic benefits of tryptophan supplementation. Higher doses of the tryptophan-based diet were associated with greater reductions in immobility time and anxiety levels, suggesting a dose-response relationship. However, further research is warranted to determine the optimal dosage and duration of tryptophan supplementation for achieving optimal therapeutic outcomes while minimizing potential adverse effects. Overall, the findings of this study highlight the promising therapeutic potential of tryptophan supplementation in ameliorating the psychological consequences of chronic alcohol consumption. By targeting both depressive and anxiety symptoms, tryptophan-based interventions offer a holistic approach to addressing mental health disorders in individuals with alcohol use disorder. Future studies should aim to elucidate the underlying neurobiological mechanisms mediating the effects of tryptophan supplementation and explore its efficacy in clinical settings. Additionally, long-term studies assessing the safety and sustainability of tryptophan supplementation are essential for informing evidence-based interventions for individuals with alcohol-related mental health disorders.

CONCLUSION

Based on the results of this study, it can be concluded that the high tryptophan-based diet can be a useful food supplement and medical intervention given it has both anxiolytic and antidepressant effects

Recommendations

The toxicity profile of the high tryptophan-based diet should be researched on/ investigated.

REFERENCES

1. Badawy, A. A., Doughrty, D. M., Marsh-richard, D. M., & Steptoe, A. (2009). Pharmacology and Cell Metabolism Activation of Liver Tryptophan Pyrrolase Mediates the Decrease in Tryptophan Availability to the Brain after Acute Alcohol Consumption by Normal Subjects, *44(3)*, 267-271. https://doi.org/10.1093/alcalc/agp00S
2. Crockett, M. J., Clark, L., & Robbins, T. W. (2010). Europe PMC Funders Group Reconcilingthe role of serotonin in behavioral inhibition and aversion: acute tryptophan depletion abolishes punishment- induced inhibition in humans, *29*(38), 11993-11999. https://doi.org/10.l523/JNEUROSCI.2513-09.2009.Reconciling
3. Cross-, S. (2017). HHS Public Access, *21(3)*, 613-633. https://doi.org/10.lll1/adb.12252.HOMER2
4. Hou, Z., Jiang, W., Yin, Y., & Zhang, Z. (2016). The CmTent Situation on Major Depressive Disorder in China: Research on Mechanisms and Clinical Practice. *Neuroscience Bulletin*, *32(4)*, 389 397. https://doi.org/10.1007/sl2264-016-0037-6
5. Ji.irgen, H., Borwin, M., Hans, B., Volz, P., Barnikol, U. B., Seifritz, E., Kasper, S. (2016).
6. The relevance of' mixed anxiety and depression ' as a diagnostic category in clinical practice. *European Archives of Psychiatry and Clinical Neuroscience*, *266(8)*, 725-736. https://doi.org/10.1007/s00406-016-0684-7
7. Kabwama, S. N., Ndyanabangi, S., Mutungi, G., Wesonga, R., Bahendeka, S. K., & Guwatudde,
8. D. (2016). Alcohol use among adults in Uganda: findings from the countrywide non-communicable diseases risk factor cross-sectional survey, *1*, 1-8.
9. Lee, H., Ohno, M., Ohta, S., & Mikami, T. (2013). Regular Moderate or Intense Exercise Prevents Depression-Like Behavior without Change of Hippocampal Tryptophan Content in Chronically Tryptophan-Deficient and Stressed Mice, 8(7), 1-8. https://doi.org/10.1371/journal.pone.0066996
10. Manuscript, A. (2016). NIH Public Access, 87-96. https://doi.org/10.1016/j.pbb.2014.12.007.Gene
11. Merchan, A., Navarro, S. V, Klein, A. B., Aznar, S., Campa, L., & Sufiol, C. (2017). Tryptophan depletion affects compulsive behaviour in rats: strain dependent effects and associated neuromechanisms, 1223-1236. https://doi.org/10.l007/s002l3-017-4561-5
12. Mosienko, V., Beti, B., Beis, D., Matthes, S., Fink, H., Bader, M., & Alenina, N. (2012). Exaggerated aggression and decreased anxiety in mice deficient in brain serotonin. *Translational Psychiatry*, 2(5), el22-9. https://doi.org/10.1038/tp.2012.44
13. Ontario, H. Q. (2013). Screening and Management of Depression for Adults with Chronic Diseases: An Evidence-Based Analysis, 13(8), 1-45.
14. Park, B., Kim, Y. R., Kim, Y. H., Yang, C., Seo, C., Jung, I. C., … Lee, M. Y. (2018). Antidepressant-Like Effects of Gyejibokryeong-hwan in a Mouse Model of Reserpine- Induced Depression, *2018*. https://doi.org/10.1155/2018/5845491

15. Skule, C., Ulleberg, P., Berge, T., Lending, H. D., & Egeland, J. (2017). Interventions for Subjects with Depressive Symptoms with or without Unhealthy Alcohol Use: Are There Different Patterns, 8(May), 1-9. https://doi.org/10.3389/fpsyg.2017.00788
16. Crockett, M. J., Clark, L., & Robbins, T. W. (2010). Europe PMC Funders Group Reconcilingthe role of serotonin in behavioral inhibition and aversion: acute tryptophan depletion abolishes punishment- induced inhibition in humans, 29(38), 11993-11999. https://doi.org/10.1523/JNEUROSCI.2513-09.2009.Reconciling,21

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