

RESEARCH ARTICLE



Antidepressant Effects of White Ginger (*Mondia whitei*) and Turmeric (*Curcuma longa*) Composite Tea in Wistar Rat Model of Chronic Unpredictable Mild Stress

Gbolagade-Akanbi Abiola Monsurat^{1*}, Oyewole Olu Isreal¹, Salawu Sule Ola² Adedeji Victor Adedapo² and Gbolagade Omolola Hubeidah³

¹Department of Biochemistry, Osun State University, Osogbo, Nigeria; ²Department of Biochemistry, Federal University of Technology, Akure, Nigeria; ³Department of Biotechnology & Food Technology, Durban University of Technology, South Africa

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Abstract: Monoaminergic dysfunction, cellular oxidative damage, hyperkinesis of hypothalamic–pituitary–adrenal (HPA) axis as well as neuroinflammation are relevant to chronic unpredictable mild stress model (CUMS)-induced depression. This study evaluates the possible depression-reducing effects, mechanistic pathways, sedative interaction and sensory acceptability of *Mondia whitei*–*Curcuma longa* composite tea in Chronic Unpredictable Mild Stress (CUMS)-exposed rats. Male Wistar rats were placed under chronic unpredictable mild stress conditions for a period of 3 weeks, followed by oral administration of functional tea blends (100:0, 75:25, 50:50, 25:75, 0:100; w/w) for 21 days. Forced swim, Tail suspension, and open field tests were used as behavioral analysis. Sedative modulation was assessed by measuring the diazepam-induced sleeping time. The neurochemicals (dopamine, monoamine oxidase, acetylcholinesterase), oxidative stress (GSH, GST, GPx, SOD, CAT), corticosterone and inflammatory cytokines (TNF- α , IL-6, IL-4 and IL-10) were assessed. CUMS Group showed increased immobility time, MAO and AChE activities, corticosterone and pro-inflammatory cytokines ($p < 0.05$), and decreasing dopamine & antioxidant enzyme activities. *Mondia whitei*–*Curcuma longa* treatment significantly inhibited depressive-like behaviors and corrected biochemical changes, with the 50:50 mixture showing the greatest antidepressant-like effect. Composite formulations also prolong the duration of diazepam-induced sleep and exhibit suitable sensory acceptability. The findings provide preliminary preclinical evidence supporting further investigation of the composite tea in experimental models of stress-related depressive-like behaviors.

Keywords: Depression, chronic stress, turmeric, white ginger; oxidative stress.

1. INTRODUCTION

Depression is a complex neurological condition characterized by constant sadness, anhedonia, cognitive impairment, and altered neurotransmission. According to a world health report, about 450 million individuals worldwide suffer from a mental or behavioral disease. Around the world, depression affects around 300 million people of all ages, and it frequently results in disability and suicide (Leis *et al.*, 2019). By 2020, depression is predicted to be the next principal source of disease burden worldwide, behind heart disease.

*Correspondence should be addressed to Gbolagade-Akanbi Abiola Monsurat, Department of Biochemistry, Osun State University, Osogbo, Nigeria; Tel: +2347065611246; E-mail: abiola.akanbi@uniosun.edu.ng

Despite neuropsychiatric advances, the precise pathogenesis remains elusive (Milic *et al.*, 2025). Recent study implicates monoaminergic dysfunction (Hamon *et al.*, 2013), HPA axis impairment (Correia *et al.*, 2024), reduced brain-derived neurotrophic factor (BDNF) (Thornton, 2023), altered neuroplasticity (Fuchs *et al.*, 2004), increased pro-inflammation (Maeng & Hong, 2019), oxidative stress (Bhatt *et al.*, 2020), and gut microbiome imbalance (Peirce & Alviñ, 2019) in neuronal dysfunction and behavioral abnormalities associated with depression. While antidepressants have been clinically available for several decades, their efficacy remains suboptimal (Blackburn, 2019). Only about 33% of patients respond to the first antidepressant prescribed, which has significant side effects such as sexual dysfunction, agitation, or insomnia, among other side effects. Because HPA-axis dysregulation, oxidative stress, and neurological inflammation contribute to the pathogenesis of depression, alternative therapy targeting this specific pathway are required (Ruberto *et al.*, 2020; Elias *et al.*, 2022).

There is mounting evidence that food choices and dietary patterns may influence the prevention and treatment of depression (Ortega *et al.*, 2022). Consequently, foods with strong antidepressant effects are being investigated as potential supplements or alternatives to antidepressants. *Mondia whitei* (Hook.f.) Skeels belong to the subfamily Periplocoideae of the Apocynaceae (formerly the family Asclepiadaceae). An endemic species found in Africa, *M. whitei* has been beneficial to the people since ancient times. It has several significant applications, including nutritional, cultural, and medical. It is used in traditional medicines to treat diverse illnesses, according to Aremu *et al.*, (2011) ethanolic extract of *Mondia whitei* displayed substantial anti-inflammatory, antiepileptic, anticonvulsant and antidepressant-like effects both *in vivo* and *in vitro*, and moderate inhibitory effect on neuronal uptake of serotonin (Aremu *et al.*, 2011).

Similarly, *Curcuma longa* L, also called turmeric, is a perennial herb belonging to the Zingiberaceae (ginger) family and is widely grown throughout Asia, India, China, and other tropical nations. Curcumin's therapeutic qualities have attracted a lot of research interest (Lopresti, 2022). Due to its potent antioxidant and anti-inflammatory qualities, curcumin which is the major active ingredient in *Curcuma longa* has been demonstrated to enhance a number of medical conditions, such as cancer, nervous system disorders, metabolic syndrome, oral diseases, and others. Curcumin's neuroprotective properties are demonstrated by experimental studies via a variety of routes. By regulating JNK/NF- κ B/Akt signaling, Khan *et al.* demonstrated that dietary curcumin protects Lipopolysaccharide-induced neuronal inflammation and cognitive decline in rats (Khan *et al.*, 2019). In both Alzheimer's disease and depression models, treatment with curcumin supplementation has been demonstrated to restore levels of brain-derived neurotrophic factor (BDNF), regulate monoaminergic neurotransmission, and mitigate various pathological processes such as oxidative stress and neuroinflammation (Alam *et al.*, 2024). Furthermore, curcumin's strong antioxidant qualities regulate stress reactions, reducing anxiety-like behaviors while maintaining the benefits of acute stress on cognition (Haider *et al.*, 2015). This dual modulation implies that when taken as a dietary supplement, curcumin may maximize physiological stress responses.

Although both *Mondia whitei* and *Curcuma longa* individually possess neuroprotective, antioxidant, anti-inflammatory, and antidepressant-like activities, no previous study has explored the combined formulation as functional tea. Therefore, the current research explored the combined effect of this combination in a Chronic Unpredictable Mild Stress (CUMS)-induced depression rat model through modulation of oxidative stress, neuroinflammation and neurotransmitter disturbances.

2. METHODOLOGY

2.1. Sample Collection and Preparation

White ginger and turmeric rhizome were purchased at the Ibadan, Oyo State, Nigeria, local market. The Department of Plant Science and Biotechnology at the Federal University of Technology in Akure, Ondo State (FUTA), Nigeria, verified the authenticity of the plant samples (voucher number FUTA/0467 for *Curcuma longa* and FUTA/0468 for *Mondia whitei*). After washing and thinly slicing the plants, each sample was dried at room temperature until a constant weight was obtained and ground into a fine powder using a laboratory grinder. The resulting powder was weighed and blended or formulated in the weight to weight ratio (w/w): 100% *Mondia whitei*, 75% *Mondia whitei*:25% *Curcuma longa*, 50% *Mondia*

whitei:50% *Curcuma longa*, 25% *Mondia whitei*:75% *Curcuma longa*, and 100% *Curcuma longa*. and packaged in a tea bag (containing one gram of the mixture of samples). For tea preparation, one tea bag containing 1 g of the composite tea was infused in 20 mL of freshly boiled distilled water for 10 min and allowed to cool to room temperature. The resulting infusion had a concentration of 50 mg/mL. Fresh tea was prepared daily and administered orally by gavage at a dose of 50 mg/kg body weight once daily for 21 consecutive days. The volume administered to each animal was calculated according to its body weight to achieve the required dose. The dose was selected based on the human-equivalent dose calculated using the body surface area conversion factor of 6.2, as described by Reagan-Shaw *et al.* (2008).

2.2. Handling of Experimental Animals and Design

Adult male Wistar rats (180–220g), were obtained from the Animal Breeding Unit, Federal University of Technology Akure, Nigeria. The rats were kept in standard cages in a regulated environment (12-hour light/dark cycle, $22 \pm 2^\circ\text{C}$ temperature, $55 \pm 10\%$ humidity), were given normal rat feed and had free access to water *ad libitum* and were allowed to acclimatize for 7days prior to experimentation. All procedures complied with the ARRIVE guidelines and the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

2.3. CUMS Procedure

Depressive-like phenotypes were induced in the rats ($n = 6$, each group) by chronic unpredictable mild stress daily for 21 days (Dai *et al.*,2010). Stressors were administered daily with variable inter-stressor intervals ranging from 3 to 8 hours. To prevent habituation and stressor adaptation, two distinct stressors were randomly selected and paired each day, ensuring that no individual stressor was repeated on 2–3 consecutive days. The animals utilized as controls were those that were allowed to roam freely in their cages without any stressors. The rats received treatment for 21 days. The stressor used are shown in the Table 1 below.

Table 1. Chronic Unpredictable Mild Stress (CUMS) protocol and stressors applied during the experimental period.

Stressors	Duration	Days
Cold water immersion	1 minutes	1, 4, 7, 10, 13, 16, 19
Deprivation of Food and Water	12 hours intervals	2, 4, 8, 10, 14, 16, 19
Cage Tilting	12 hours intervals	3, 5, 9, 12, 15, 18, 21
Tail pinch	1 minutes	1, 6, 8, 11, 15, 18, 21
Cage Shaking	10 minutes	2, 5, 7, 11, 13, 17, 20
Physical restraint	1 hour	3, 6, 9, 12, 14, 17, 20

2.3.1. Experimental Design

After acclimatization, the animals were randomly allocated to groups by an independent colleague using body-weight-stratified block randomization to minimize baseline weight differences. Daily treatments and CUMS stressors were administered by the primary investigator. A total of 48 rats were randomly assigned to eight groups, with six rats in each group, as shown below:

Group I: (Normal Control): Received 1 mL of distilled water.

Group II: (Stressed group): Received 1 mL of distilled water.

Group III: Stressed +Standard Drug (10 mg/kg fluoxetine)

Group IV: Stressed + *Mondia whitei* tea (100: 0)

Group V: Stressed + *Mondia whitei* and *Curcuma longa* tea (ratio 75:25)

Group VI: Stressed + *Mondia whitei* and *Curcuma longa* tea (ratio 50:50)

Group VII: Stressed + *Mondia whitei* and *Curcuma longa* tea (ratio 25:75)

Group VIII: Stressed + *Curcuma longa* tea ratio (0:100)

At the end of the treatment all of the animals were sacrificed by cervical dislocation after being subjected to anesthetics and their brains removed rapidly washed in ice cold 1.15% (v/v) potassium chloride solution, weighed after being blotted with filter paper and homogenized using a Teflon homogenizer in 10% (w/v) phosphate-buffered saline PBS (pH 7.4), the resulting homogenate was centrifuged at 10,000 x g for 25 minutes at 4°C, and the supernatant was utilized for biochemical studies. Before the brain was removed, blood was obtained via cardiac puncture into the tube for further biochemical analysis. The research involving the use of animal (Wistar rats) were conducted according to the approved ethical standard and guidelines approved by Osun State Health Research Ethics Committee (OSHREC), Ministry of Health, Osogbo, Osun State, Nigeria (Approval No.: OSHREC/PRS/2024/842/01/244; Date of approval: 31 January 2024) (Figure 1).

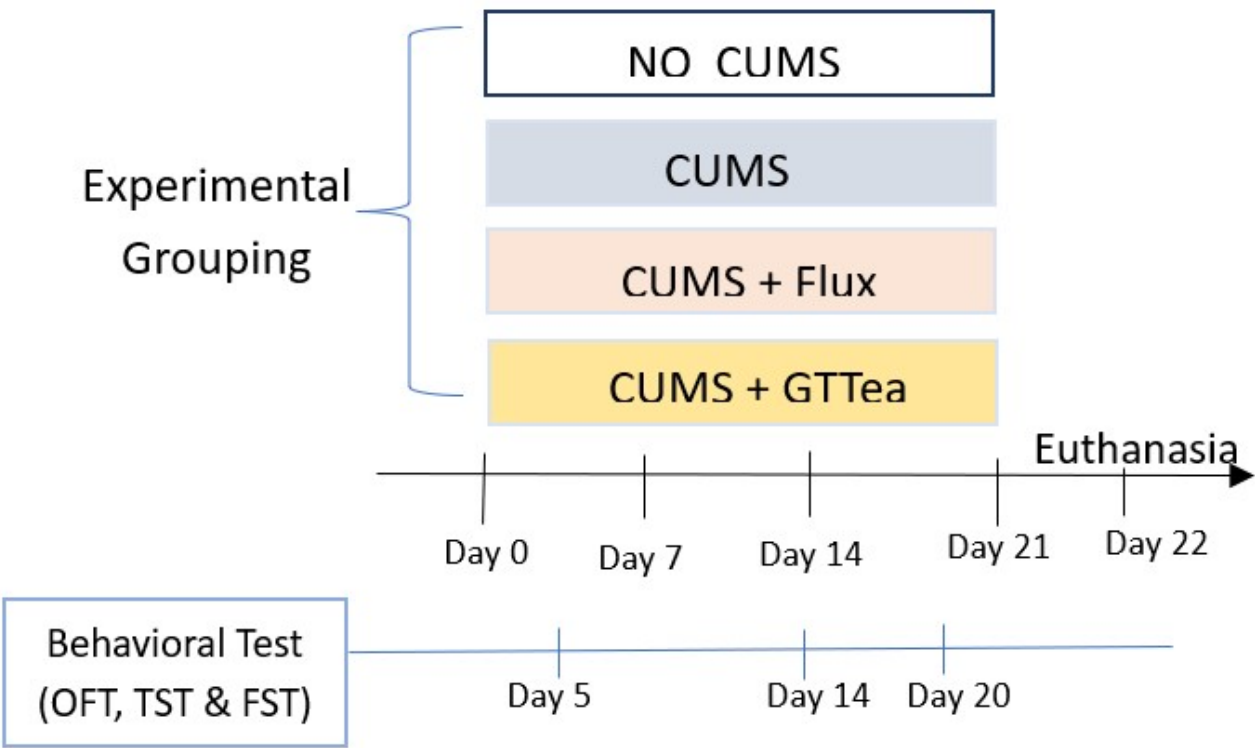


Figure 1: Experimental procedure for CUMS induction, treatments and behavioral tests.

Abbreviations: CUMS: chronic unpredictable mold stress; GTTea: White Ginger-turmeric tea; OFT-Open field test; TST: Tail suspension test; FST: Forced swim test; Flux: Fluoxetine.

2.4. Preliminary Evidence of an Effect on Diazepam-induced Sleeping Time

Two sets of three animals each were used for each sample in the diazepam-induced sleeping time test, with a third group serving as a control. While the other group received the proper tea, the control group was administered diazepam. The tea was given orally at the appropriate dosages (50mg/ml/kg). Both groups received an intraperitoneal dose of diazepam (1.5 mg/kg body weight) 30 min after receiving corresponding extract. They were monitored for the loss of their righting reflex, or normal posture, which was thought to be an indication that sleep had begun. The test samples' hypnotic activity was measured using the duration between the loss and the subsequent regaining of the righting reflex (Akingbesote & Salawu, 2023).

2.4.1. Experimental Design

Group	Drug/Tea	Purpose
NC	Diazepam	Control
SC	SC + Diazepam	-ve control
SC + Fluoxetine	SC + Diazepam + Fluoxetine	+ve control
100G	Diazepam + SC + 100T	Test sample
75G:25T	Diazepam + SC + 75G:25T	Test sample
50G:50T	Diazepam + 50G:50T	Test sample
25G:75T	Diazepam + 25G:75T	Test sample
100T	Diazepam + 100T	Test sample

2.5. Measurement of Antistress, Anxiolytic and Antidepressant Effect of the Tea

This study used the Open Field Test (OFT) to evaluate anxiety and the Forced Swim Test (FST) and Tail Suspension Test (TST) to study depression. These models have been used extensively in evaluating anxiety reducing and depression alleviating properties of the tea.

2.5.1. Behavioural Tests

Behavioral testing was conducted on Day 5, 14, 20 early in the morning. To eliminate test-induced stress carryover and fatigue, assays were performed in sequence from least to most inherently stressful (OFT, TST and FST)

2.5.2. Forced Swim Test

Rat behavior was noted and examined. OFT for neurobehavioral assessments. For this evaluation, a modified version of Porsolt methodology (Porsolt *et al.*, 1997) was used.

2.5.3. Tail Suspension Test

For this TST evaluation, a modified Steru (Steru *et al.*, 1985) approach was used.

2.5.4. Open-Field Test

Abdelsalam and Safar's modified method was used for this test (Abdelsalam & Safar, 2015).

2.5.5. Sensory Evaluation of the Functional Tea

Thirty judges, both male and female, from the Biochemistry Department at FUTA, Ondo State, comprised the semi-trained panel. The panelists were given tea cups and hot water to infuse the medicinal tea samples that were wrapped in their own tea bags. The panelists were instructed to use a 9-point Hedonic scale, with nine representing extreme like and 1 representing extreme dislike, to assess several samples for appearance, taste, aroma, aftertaste, and overall acceptability after learning the descriptive terms of the sensory scales. Drinkable water was offered for mouthwash in between each evaluation, and coded samples were presented at random (Umeh *et al.*, 2025).

2.6. Biochemical Analysis

According to Perry *et al.* (2000) (Perry *et al.*, 2000), the substrate acetylthiocholine iodide was used to measure AChE activity in brain tissue. Using adrenaline (0.06 mg/ml) as a substrate, the activity of superoxide dismutase (SOD) of brain tissue was measured using the method outlined by Alia *et al.* (2003) (Alia *et al.* 2003). According to Sinha (1972) (Sinha 1972), catalase activity was also examined in the experimental rats' brains. A Coomassie blue-based method was used to determine the protein content (Bradford, 1976). While glutathione peroxidase (GSH-Px) activity in brain tissue was measured using the procedure

outlined by Paglia and Valentine (1967) (Paglia & Valentez, 1967), glutathione-S-transferase (GST) activity and reduced glutathione (GSH) levels in brain tissue were measured using the technique employed by Akinyemi et al. (2014) (Akinyemi *et al.* 2014). The EIA kit (Cayman Chemical Company, US) was used to estimate the serum corticosterone level. A previously described approach was used to measure the tea's impact on MAO (EC 1.4.3.4) activity in rats' brains (Turski *et al.*, 1972).

2.7. Inflammatory Cytokine

Serum Tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), interleukin-4 (IL-4), and interleukin-10 (IL-10) levels were evaluated by means of ELISA with Quantikine Immunoassay kits (R&D Systems, Minneapolis, MN), following the manufacturer's protocol and the method described by Paim et al. (2011) (Paim *et al.*, 2011).

2.8. Statistical Analysis

Data were analyzed using the GraphPad Prism 8.02 (GraphPad Software Inc., CA, USA). The data are shown as the mean $\pm$ standard error of the mean (mean $\pm$ SEM). Analysis for significance level was done by calculating the Mean values using one-way ANOVA. The significance was accepted at $p < .05$ after Tukey's post hoc test. The estimated number of animals required is based on a power analysis program from InStat. The experiment required 6 animals by power analysis based on the following: variance of up to 25% (standard deviation), significance at a minimum difference between means of 50%, 95% power, and 5% type-I error rate

3. RESULTS

Table 2 displays the 30 panelists' sensory evaluations of the various tea blends. Some samples showed no notable difference ($p > 0.05$) in appearance, whereas others showed a significant difference ($p < 0.05$). The control sample had the highest sensory appearance, whereas sample 100T (100% turmeric) had the lowest, with the appearance result ranging from 6.32 to 8.96 with 75G:25T showing the highest appearance when compared to the other *Mondia whitei*–*Curcuma longa* composite tea samples. Significant differences in taste were noted. Panelists gave samples 75G:25T (75% white ginger:25% turmeric) the lowest taste rating (6.33), while the COM received the highest grade (8.96). Although the panelists found all of the samples to have acceptable tastes, there were significant differences ($p < 0.05$) in each sample. The panelists' perceptions of the tea based on Aroma also showed significant variations ($p < 0.05$). Aroma received a mean score between 5.59 and 8.33. The results indicated that sample 100G (100% white ginger) had the lowest aroma score, whereas the control sample (commercial tea) had the greatest aroma score. It was found that the aroma improved with the amount of ginger. The respondents preferred the control sample's scent above the others. There was a significant difference ($p < 0.05$) in aftertaste between the composite tea and the commercial tea. With the commercial tea showing the highest after taste followed by 75G:25T and 50G:50T (50% white ginger: 50% turmeric), with 25G:75T (25% white ginger:75% turmeric) and 100T (100% turmeric) showing the least after taste. All of the teas were found to be generally acceptable, with no discernible differences, according to the overall acceptability. With the greatest overall acceptability scores—the others ranged from 7.75 to 6.97—the commercial (COM) tea samples were, nevertheless, the most favored. The preference for these samples may have resulted from the higher ginger content, which was deemed acceptable by the majority of panelists. Additionally, in terms of general acceptability, 100T was the least favored product.

Preliminary evidence of the effect of the composite tea on diazepam-induced sleeping time was assessed. Administration of diazepam produced marked differences in sleep parameters across the experimental groups (Table 3). The stress-control group showed a longer latency (10.55 min) to loss of the righting reflex and a shorter sleep duration (30.83 min) than the normal control group, which showed a latency of 6.20 min and a sleep duration of 70.03 min. Treatment with Fluoxetine and the composite tea restored more balanced sleep patterns, increasing duration while maintaining moderate latency. Interestingly, there was an increase in sleep duration and decrease in sleep latency with increased turmeric.

The forced swim test in Figure 2a demonstrated the behavioral impact of ginger and turmeric tea; there was a significant difference in immobility time ($p < 0.0001$) among the stressed, NC group, and the treated groups. However, the SC groups showed highest immobility time indicating depression based on the length of time spent immobile in the water. Interestingly, these were reduced or reversed in groups treated with fluoxetine and the composite tea. However, the composite 50G:50T tea exhibits the shortest immobility time, indicating reverse in depression or behavioral despair upon addition of turmeric and white ginger tea treatment.

Additionally, the tail suspension test was displayed in Figure 2b. The results indicate a substantial change ($p < 0.0001$) in the stressed group when compared to the normal control group signifying depression, this was reversed with the administration of fluoxetine and composite tea. 50G:50T tea composite exhibited the shortest immobility period when compared to other treated groups.

Rats' depression-like activity during the OFT was evaluated by counting the number of entrances into the middle zone (Figure 2c) and the amount of time they spent there (Figure 2d). The number of entries in the center zone and the amount of time spent there indicated a higher level of despair in the second control group (stress only). For the treated groups, there was a considerable increase in both the quantity of entries and the amount of time spent ($p < 0.0001$) in the central zone.

Table 2. Sensory Analysis of the Different Tea Blend

Sample	Appearance	Taste	Aroma	After taste	Overall Acceptability
100G	6.44 ^c ± 1.25	5.85 ^d ± 1.32	7.20 ^b ± 1.21	7.00 ^a ± 1.60	7.75 ^b ± 1.25
75G:25T	7.46 ^b ± 1.63	6.33 ^c ± 2.10	7.00 ^b ± 1.88	7.20 ^a ± 1.88	7.84 ^b ± 1.43
50G:50T	7.25 ^b ± 1.84	6.43 ^c ± 1.63	6.67 ^c ± 1.19	7.10 ^a ± 1.98	7.55 ^b ± 1.71
25G:75T	7.15 ^b ± 1.46	7.59 ^b ± 1.76	6.35 ^c ± 0.59	6.88 ^b ± 1.7	7.01 ^b ± 1.71
100T	6.32 ^c ± 1.16	7.69 ^b ± 1.80	5.59 ^d ± 0.89	6.30 ^b ± 0.94	6.97 ^c ± 1.25
Com	8.96 ^a ± 1.24	8.63 ^a ± 1.25	8.33 ^a ± 1.03	7.90 ^a ± 0.99	8.45 ^a ± 1.54

Note: Results are expressed as mean ± standard deviations (SD) of three determinations. Averages followed by different letters differ significantly ($p < 0.05$). Means sharing the same superscript letter are not significantly different ($p \geq 0.05$).

Table 3. Sedative effect of the composite tea

GROUP	DOSE OF DIAZEPAM (mg/kg)	SLEEP LATENCY (MIN)	SLEEP DURATION (MIN)
NC	1.5	6.20 ^b ± 0.33	70.03 ^c ± 0.21
SC	1.5	10.55 ^a ± 0.25	30.83 ^c ± 0.95
SC + Fluoxetine	1.5	7.71 ^b ± 1.08	62.27 ^d ± 0.71
100G	1.5	7.92 ^b ± 1.01	71.73 ^c ± 0.34
75G:25T	1.5	6.83 ^c ± 1.11	77.33 ^c ± 1.04
50G:50T	1.5	6.06 ^d ± 0.47	83.54 ^b ± 1.34
25G:75T	1.5	5.74 ^c ± 0.88	88.47 ^b ± 0.12
100T	1.5	5.31 ^f ± 0.74	93.24 ^a ± 0.16

Note: Results are expressed as mean ± standard deviations (SD) of three determinations. Averages followed by different letters differ significantly ($p < 0.05$). Means sharing the same superscript letter are not significantly different ($p \geq 0.05$).

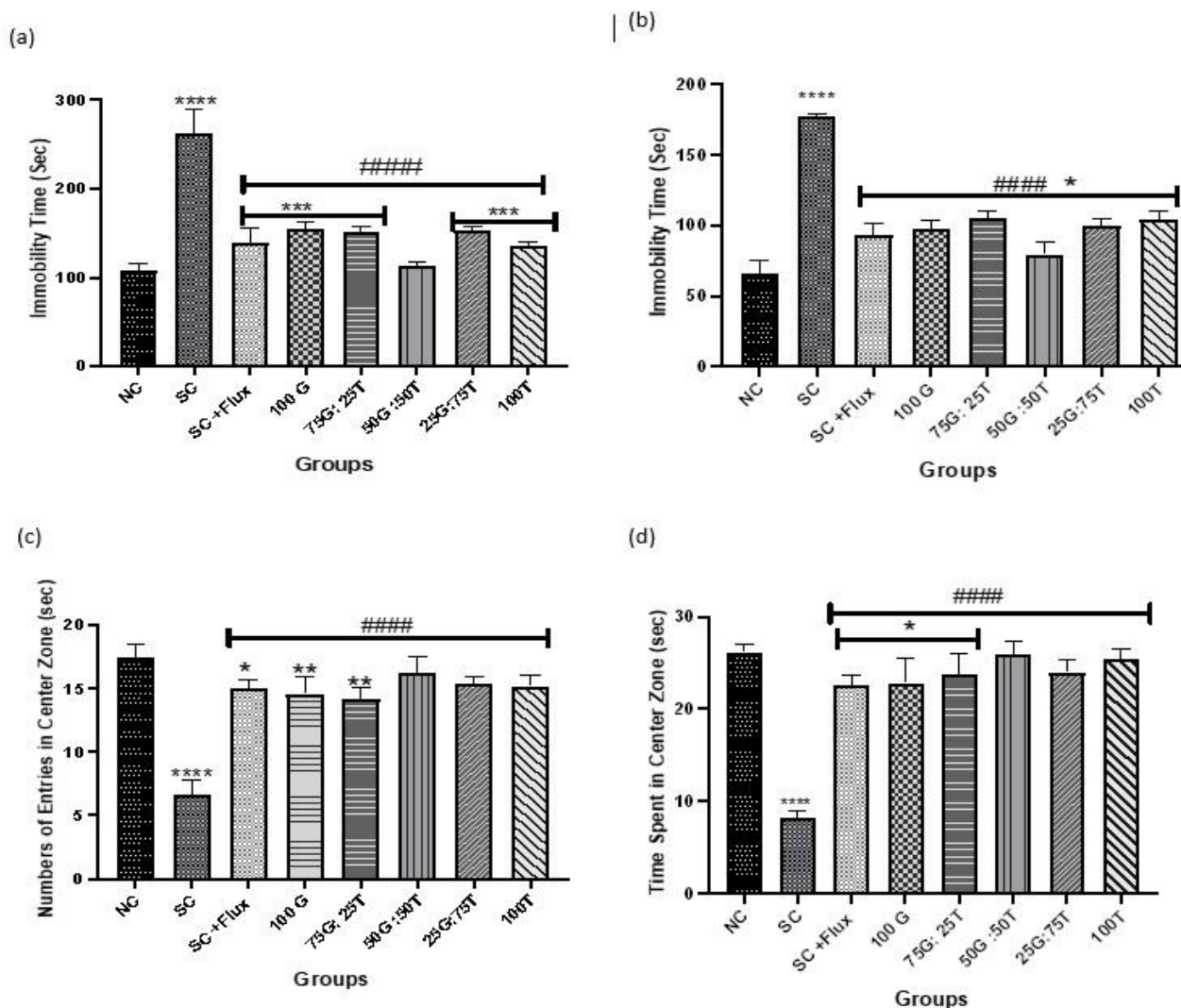


Figure 2: Effects of CUMS, fluoxetine and white ginger-turmeric tea administration on behavioral patterns. (a)FST (b)TST (c)OFT (No. of times) (d) OFT (No. of entries). Bars represent mean $\pm$ SEM (n = 6). Values are statistically different at * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p < .0001$ Vs NC, # $p < .05$; ## $p < .01$; ### $p < .001$; #### $p < .0001$ Vs. SC.

Abbreviations: NC: normal control; Sc: stressed; SC + FLUX: stress + fluoxetine; G: white ginger; T: turmeric

Figure 3a displays the effect of fluoxetine and the composite tea treatment on dopamine levels of the rats. The results show that Dopamine levels significantly differed among experimental groups ($p < 0.0001$), a notable distinction between the stressed rats and the normal control was noted, indicating a condition of illness or depression. However, upon treatment with fluoxetine.

Furthermore, a significant difference was noted between the NC, the stressed group and treated groups ($p < 0.0001$). The activity of MAO was increased in the SC group compared to NC indicating a depressed state (Figure 3b). Low MAO activity was observed in the treated group compared to SC untreated group. 50G:50T, on the other hand, had the least activity of MAO.

The AChE was accurately depicted in Figure 3c. High levels of AChE activity, a sign of depression, were seen in the SC group. Comparing the SC group to NC rats revealed a substantial difference in AChE activity ($p < 0.0001$). Upon treatment with composite tea and fluoxetine, the activity was reduced. When all the treated groups were compared, 50G:50T showed the least amount of activity; there was no discernible difference between the NC group and the treated rat.

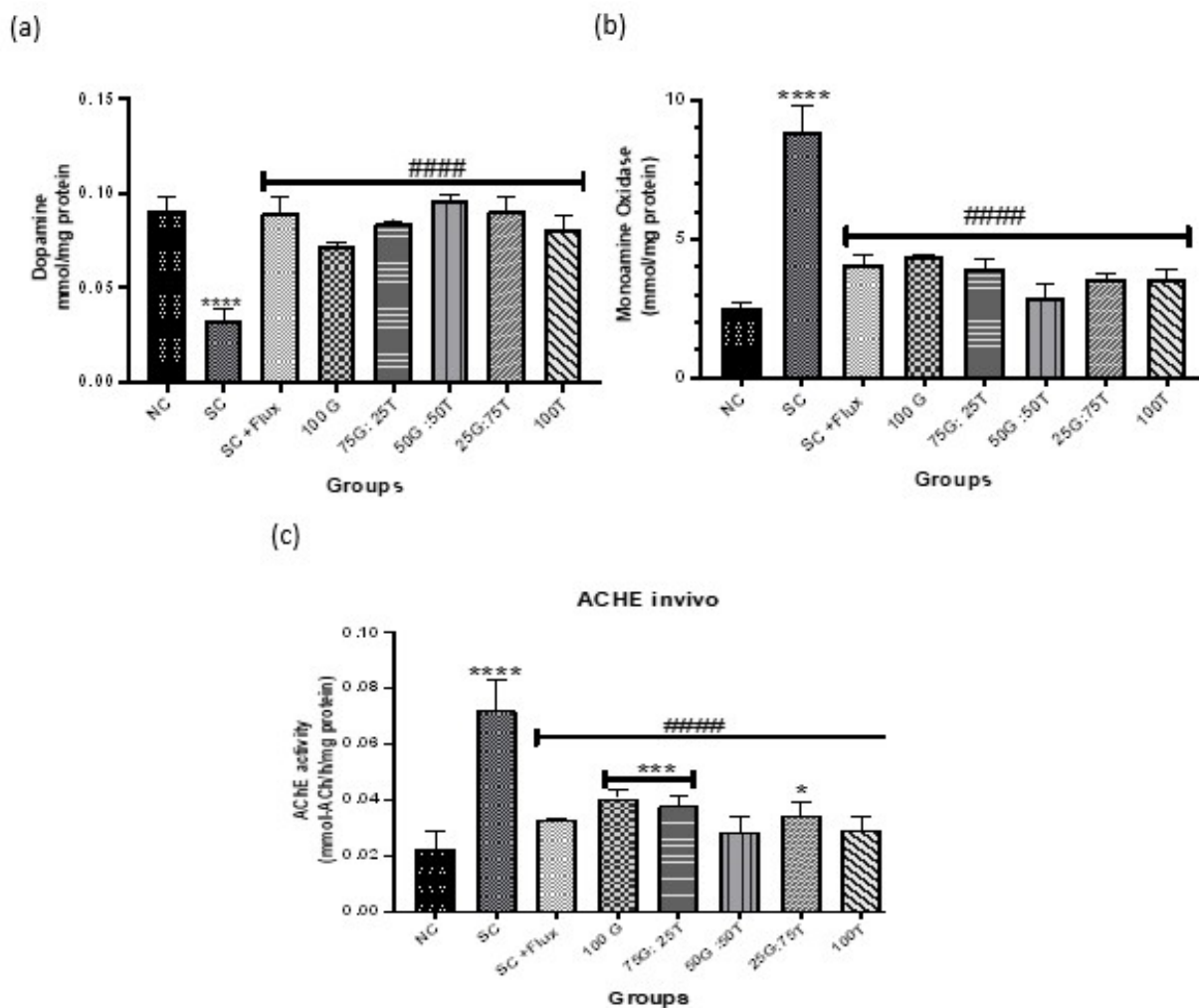


Figure 3: Effects of CUMS, fluoxetine and white ginger-turmeric tea administration on Dopamine, Monoamine Oxidase and AChE. (a) Dopamine (b) Monoamine Oxidase (c) AChE. Bars represent mean $\pm$ SEM ($n = 6$). Values are statistically different at * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p < .0001$ Vs NC, # $p < .05$; ## $p < .01$; ### $p < .001$; #### $p < .0001$ Vs SC.

Abbreviations: NC: normal control; Sc: stressed; SC + FLUX: stress + fluoxetine; G: white ginger; T: turmeric

Figures 4a (GSH), 4b (GST), and 4c (GPX) display the antioxidant parameters in the brains of the rats. While the untreated group exhibited a substantial decrease ($p < 0.0001$) in the activity of reduced glutathione, white ginger and turmeric composite tea demonstrated an increase in antioxidant capacity of stress-induced depression in rats when compared to the rats that were not treated, indicating an improvement in GSH (Figure 4a). The SC group's glutathione-S-transferase activity was shown to be significantly decreased ($p < 0.0001$) (Figure 4b). This was reversed, by administering a white ginger and turmeric tea blend. Additionally, 50G:50T showed the highest levels of GSH and GST, while the other treatment groups' levels were similar to the normal control level.

Glutathione peroxidase activity significantly differed among treatment groups ($p < 0.0001$). Untreated depressed rats (SC) had a much-reduced level of GPx, as shown in Figure 4c. However, after receiving the tea, the activity of GPx increased to a level that was both greater and equivalent to the normal control. The greatest GPx activity was shown by 50G:50T and 75G:25T revealing the antioxidant potential of the tea mix.

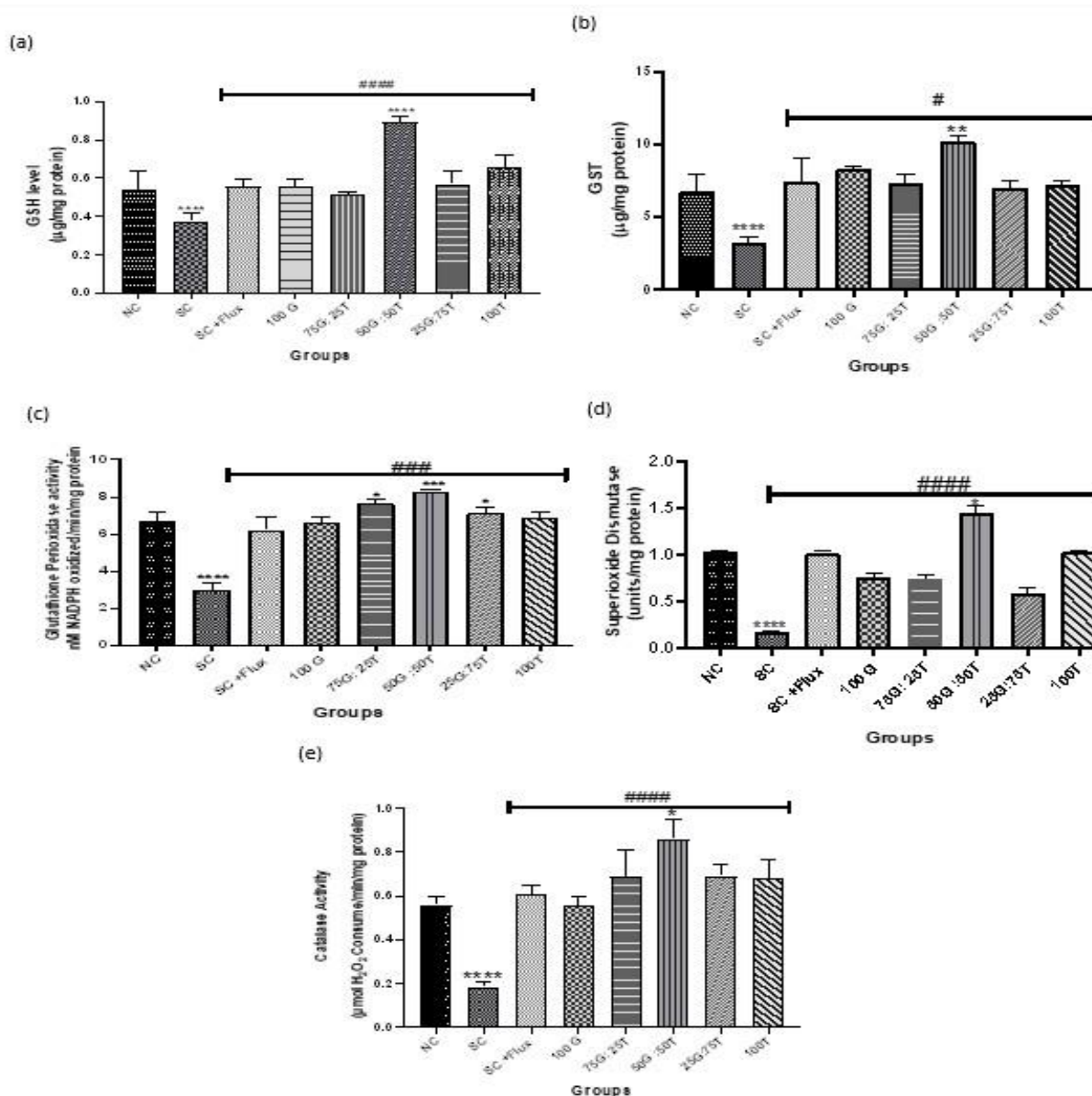


Figure 4: Effects of CUMS, fluoxetine and white ginger-turmeric tea administration on antioxidant status. (a): GSH, (b): GST, (c): GPx, (d): SOD (e): CAT. Bars represent mean $\pm$ SEM (n = 6). Values are statistically different at * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p < .0001$ Vs NC, # $p < .05$; ## $p < .01$; ### $p < .001$; #### $p < .0001$ Vs. SC.

Abbreviations NC: normal control; Sc: stressed; SC + FLUX: stress + fluoxetine; G: ginger; T: turmeric

When the SC group of SOD and CAT activity were compared to the NC group, significant differences were observed ($p < 0.0001$) as seen in Figures 4d and 4e, respectively. Nevertheless, the enzyme activities were increased by treatments using the fluoxetine and the tea blend. Amazingly, among the rats that received treatment, the group that received 50G:50T exhibited the highest levels of SOD and CAT activity in both normal and depressed rats.

The rats' corticosterone levels are shown in Figure 5. The findings demonstrated that, in comparison to the NC group, stress significantly raises ($p < 0.001$) corticosterone in the SC group. Stress-induced corticosterone increase is attenuated ($p < 0.0001$) even near the normal control level in the SC + FLUX group treated with fluoxetine and the tea blend. When compared to the SC + FLUX group and normal control, the 50G:50T and 25G:75T tea formulations exhibited the lowest level showing that they have the highest effect on corticosterone.

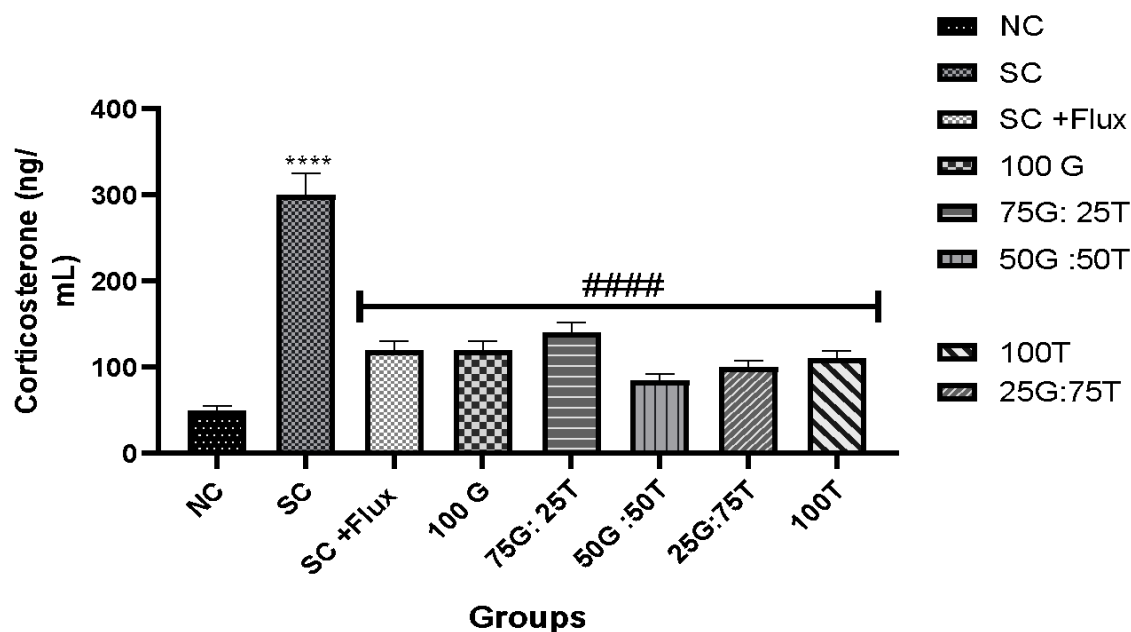


Figure 5: Effects of CUMS, fluoxetine and white ginger-turmeric tea administration on serum corticosterone. Bars represent mean $\pm$ SEM (n = 6). Values are statistically different at * $p < .05$ Vs NC, # $p < .05$ Vs. SC. Values are statistically different at * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p < .0001$ Vs NC, # $p < .05$; ## $p < .01$; ### $p < .001$; #### $p < .0001$ Vs. SC.

Abbreviations NC: normal control; Sc: stressed; SC + FLUX: stress + fluoxetine; G: white ginger; T: turmeric

The effects of different tea compositions on pro-inflammatory cytokines (TNF- α and IL-6) were shown in Figures 6a and 6b significantly differed ($p < 0.0001$). Stress-induced untreated rats showed a considerable rise in these cytokines. When the rats were given tea samples, a reduction in these cytokines was observed. The 50G:50T group had the lowest levels of pro-inflammatory cytokines among the treatment groups. Similarly, the tea blend's anti-inflammatory (IL-4 and IL-10) effect was evaluated as seen in Figure 6c and 6d, in which a significant difference ($p < 0.0001$) in IL-4 and IL-10 was observed. There was a significant decrease in the stressed untreated group (SC) but a significant rise after treatment with the composite tea and the commercial drug.

4. DISCUSSION

Chronic low mood, disinterest, and reduced activity are hallmarks of depression, a prevalent mental illness that can result into suicidal thoughts and actions. Because the CUMS model can mimic the pathophysiological changes observed in human depression, it is therefore often used in depression studies (Zheng *et al.*, 2010). Dietary strategies have been encouraged in health care for the treatment and management of depression. Appropriate application or incorporation of functional food can help reduce the risk of developing depression or mitigating the severity (Ortega *et al.*, 2022). However, functional food showed no or low advised side effects when compared to the conventional drugs and these foods are generally accepted making it a good approach. Previous research findings revealed that both *Mondia whitei* and *Curcuma longa* are rich in diverse phytochemicals. Both plants are rich sources of flavonoids, phenolics, alkaloids, terpenoids, saponins and other secondary metabolites (Ikuomola *et al.*, 2024). Flavonoids and polyphenols have been reported to have antidepressant-like effects by modulating monoaminergic neurotransmitters, reduction of oxidative stress, and neuroinflammation (Figueiredo *et al.*, 2025). Studies reveal that Curcuma regulates serotonin, dopamine and norepinephrine neurotransmission while suppressing inflammatory pathways in depression (Ramaholimihaso *et al.*, 2020). Alkaloids in *Mondia* have been reported to have modulated monoaminergic systems (Edah *et al.*, 2020). In addition, the antioxidant and anti-inflammatory properties of these phytochemicals help in protecting the neurons, reducing stress-induced behavioral changes caused by oxidative stress and improving synaptic transmission (Tkaczenko *et*

al., 2025). Therefore, the combined effect of the phytochemicals present in both *Mondia whitei* and *Curcuma longa* contributes to the antidepressant-like effect observed in this study.

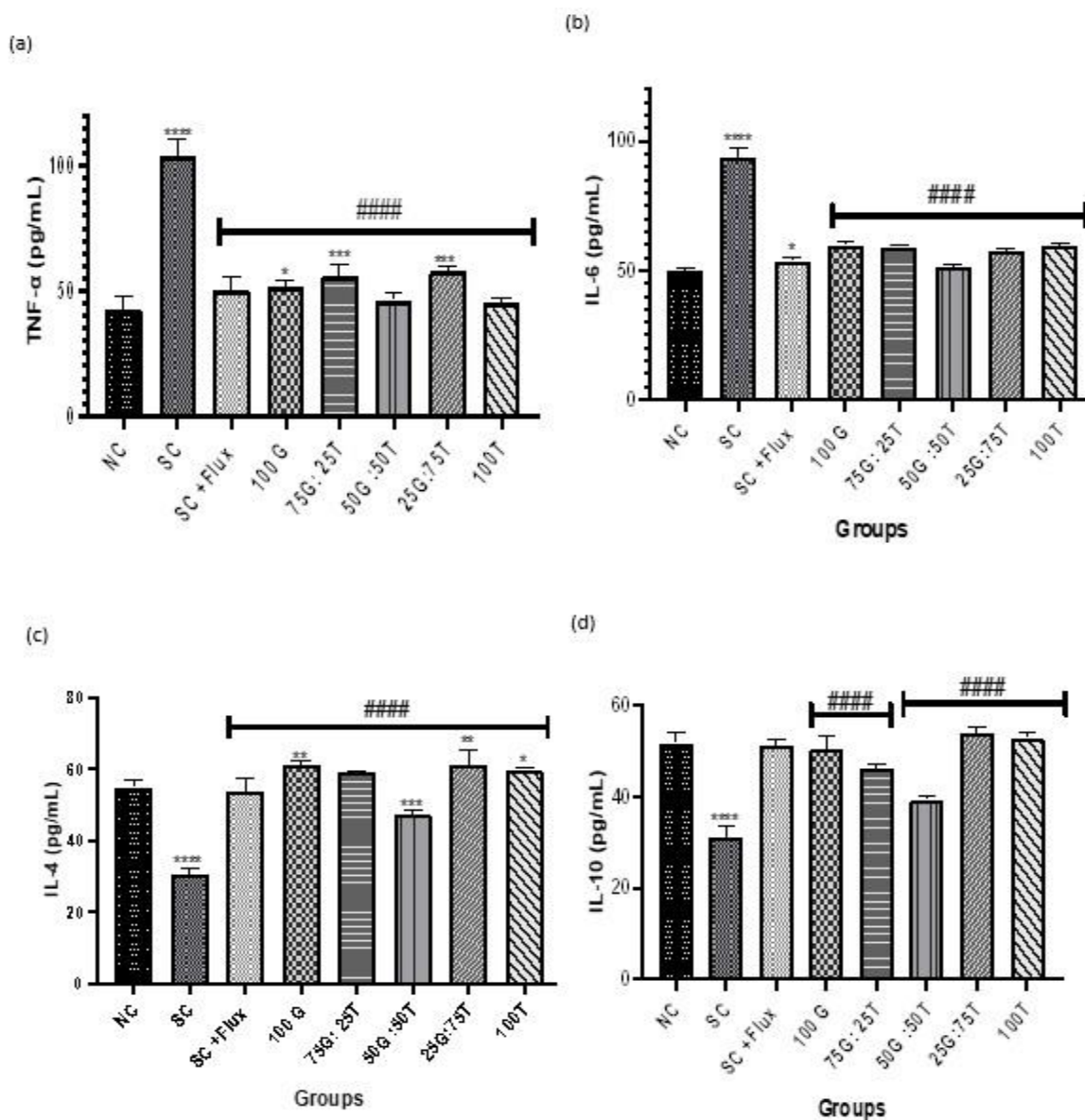


Figure 6: Effects of CUMS fluoxetine and white ginger-turmeric tea administration on inflammatory markers. (a): TNF- α , (b):IL-6, (c): IL-4, (d): IL-10. Bars represent mean $\pm$ SEM (n = 6). Values are statistically different at * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p < .0001$ Vs NC, # $p < .05$; ## $p < .01$; ### $p < .001$; #### $p < .0001$ Vs. SC.

Abbreviations: NC: normal control; Sc: stressed; SC + FLUX: stress + fluoxetine; G: white ginger; T: turmeric

As seen in Figure 2 composite tea treatment showed antidepressant-like effect on the CUMS rats in the OFT, FST and TST models. Treatment with the fluoxetine and the composite tea showed increase in both the number of center zone admissions and the duration of time spent in the center zone. This improvement suggests a reduction in stress-induced depressive-like behavior and a return to regular exploratory activity in OFT. Two verified models for evaluating potential antidepressant drugs and depressive-like in rodents are the TST and FST. The immobility time depicts the anti-depressant-like activity. In this research a decrease in immobility time was observed in both FST and TST as compared to the untreated group showing the anti-depressant-like effect of the tea blend.

The sensory profile of the formulations reveals that the amounts of turmeric (T) and white ginger (G) significantly affected consumer perception as compared to the commercial sample. Moderate blending of white ginger and turmeric (50G:50T) appeared to enhance overall sensory balance, suggesting that their flavor and bioactive ingredients complement one another. In food manufacturing, appearance is crucial since it greatly influences whether or not food products are accepted by consumers (Meijer *et al.*, 2021). Given that visual attributes significantly influence consumer acceptability and expectations, 100T (100% turmeric) had the lowest appearances which may be due to the more intense yellow coloration of turmeric. However, color blending likely improved appearance with 75G:25T showing the highest score (Lawless & Heymann, 2010). In sensory evaluation, taste is also seen to be quite significant. One crucial characteristic of a food product is taste, which is the flavor sensation that is experienced in the mouth and throat when coming into contact with a material. In this study, 75G:25T had the lowest taste rating which may be due to the higher percentage of white ginger present. However, the unique warm, slightly spicy flavor of white ginger balanced the sharpness of white ginger, resulting in improved taste as more turmeric was added. Given that flavor is a major factor in food selection (Drewnowski, 1999), this probably helped to make foods more palatable at moderate substitution levels. However, higher turmeric concentrations reduced the aroma's acceptability, perhaps as a result of the dominant volatile chemicals masking the white ginger's crisper notes (Chen *et al.*, 2020). In organoleptic estimation, overall acceptability is a significant metric since it affects panelists' acceptance and selection of the various samples and is essential to decision-making. Because higher concentrations of turmeric contain more polyphenolic chemicals, which can contribute astringency or bitterness, they may be associated with poorer aftertaste ratings (Singh *et al.*, 2025). Intermediate white ginger-turmeric blends often performed better in terms of sensory equilibrium than single-component formulations (Al-Khazaleh, 2021). This is in line with the concepts of product development optimization.

Insomnia or sleep disorder are closely linked with depression, although the underlying biological mechanism is not fully understood. Persistent lack of sleep or insomnia has been independently a risk factor for the development and progression of depression and is associated with poorer clinical outcome and reduced sensitivity to antidepressant medications. Studies have shown that both sleep latency and duration can be used to predict the severity of depression. Evidence also suggests that treatment of insomnia alongside antidepressant drugs can have an immense effect on insomnia and depression. The present research demonstrated that white ginger–turmeric tea improves therapeutic effectiveness by extending sleep duration while maintaining latency within a physiologically acceptable range. This effect may be associated with the bioactive constituent presence in white ginger and turmeric, particularly gingerol and curcuminoids which have been reported to influence GABAergic and serotonergic pathways implicated in sleep regulation, depression, and stress-related disorders (Sochacka & Lachowicz, 2025; Mohammadzadeh *et al.*, 2024). The study reveals that ginger-turmeric tea blend can alter the sleep-inducing effects of diazepam in a manner similar to that of antidepressants. The best outcomes were obtained with moderate turmeric-rich blends (specifically, 25G:75T) which prolonged sleep duration while maintaining regulated onset. However, the specific mechanisms underlying these effects were not directly investigated in the present study. Therefore, the potential of these formulations as complementary interventions for stress-related depressive conditions warrants further investigation.

The cholinergic system is made up of acetylcholine which is a neurotransmitter released from cholinergic neurons, as well as cholinesterase enzymes that control their function (Kokaz *et al.*, 2020). The cholinergic scheme in the central nervous system (CNS) is essential for memory functions and depressive-like behaviors in experimental animal models (Pannu, 2025). Acetylcholine facilitates nerve impulse transmission between neurons by acting within the synaptic cleft. Following synaptic transmission, the enzyme acetylcholinesterase (AChE) rapidly hydrolyzes acetylcholine into choline and acetate. Choline can be recycled back into the presynaptic neuron for acetylcholine resynthesis since this enzymatic breakdown stops the neurotransmitter signal. Memory problems and emotional disorders including depression and depressive-like behaviors can arise from any imbalance in the activity of these neurotransmitters, which can lead to poor or nonexistent signal transmission from the brain to peripheral organs (Pannu, 2025; Halász *et al.*, 1975). Therefore, substances that inhibit the acetylcholine esterases can help alleviate depres-

sive-like effects through modulation of cholinergic neurotransmission. AChE activity was considerably higher in the untreated rats in this study, which suggests that it may be one of the main causes of depression-like effect observed in stressed untreated rats. However, AChE activity was shown to have decreased following treatment with the composite tea under study, as illustrated in Figure 3. This result is aligned with other published research showing that plant extracts and phytochemicals, particularly phenolic compounds, are strong AChE inhibitors and that ingesting them may help treat neurological conditions (Akomolafe *et al.*, 2019; Oboh *et al.*, 2022).

A class of enzymes known as monoamine oxidases (MAO) uses oxygen to cleave the amine group from monoamines during the process of oxidative deamination. In addition to inactivating monoamine neurotransmitters, MAOs show a vital role in the breakdown of monoamines consumed through diet (Hou *et al.*, 2026, Xiao *et al.*, 2024). Since MAOs are essential for the inactivation of neurotransmitters, a variety of neurological and psychiatric conditions are believed to be influenced by MAO dysfunction, or excessive or insufficient MAO activity including Schizophrenia (Ding & Bao, 2026; Xu & Yang, 2022), depression (Kim *et al.*, 2022), attention deficit disorder (Nikolaus *et al.*, 2022), substance misuse (Edinoff *et al.*, 2022), and migraines (García-Azorín *et al.*, 2020). One of the main pharmacological types recommended to treat depression is monoamine oxidase inhibitors. According to some studies, MAO inhibitors (MAOIs) are more effective than other classes of antidepressants in treating specific phenotypes of depression. When treatment-resistant depression does not improve with tricyclic antidepressants, MAOIs may be useful (Shaldam *et al.*, 2026; Hoffman *et al.*, 2023). Dopamine, a type of Monoamine neurotransmitter that controls mood, motivation, reward, and emotional reactions is dopamine. The mesolimbic pathway, often known as the reward pathway, is one of the main dopaminergic circuits linked to depression. The nucleus accumbens, a part of the brain closely linked to pleasure and reward processing, is connected to the ventral tegmental area (VTA) by this pathway (Ranaldi, 2023). When this route malfunctions, it can lead to anhedonia, a primary sign of depression marked by a diminished capacity for pleasure, which is commonly seen in distressed albino rats. In this study, The SC-untreated rats showed a markedly elevated MAO activity and reduced dopamine level (Figure 3) which may indicate alterations in monoaminergic neurotransmission associated with depressive-like and anhedonia-related behaviors.

Interestingly, a significant reduction in MAO activity and an increase in dopamine was observed upon treatment with white ginger and turmeric tea formulations resulting in improved mood and activity with 50G:50T tea blend showing highest ameliorative effect. The potential inhibitory effect of this tea blend may be associated to the phytochemicals present and it supports previous findings that phytochemicals such as flavonoids and polyphenols have powerful neuroprotective effects.

It has been established that behavioral depression in male Wistar rats is caused by antioxidant depletion, a reduction in the amount of glutathione peroxidase (GSH-Px), and a rise in lipid peroxidation and nitric oxide (NO) in the brain's cortex and medulla (Atagün & Canbek, 2022). Superoxide dismutase (SOD) levels and depression severity were discovered to be significantly correlated, indicating that antioxidant enzymes may be state markers of depression (Mucci, 2024).

An enzyme called superoxide dismutase catalyzes the dismutation (or partitioning) of the superoxide O_2^- into H_2O_2 and regular molecular oxygen (O_2) alternatively. Superoxide, a byproduct of oxygen metabolism, can harm cells in multiple ways if it is not properly regulated. (Fujii *et al.*, 2022). Glutathione-S-transferase helps to conjugate harmful electrophilic chemicals with GSH, which improves cellular detoxification, while catalase and glutathione peroxidase further detoxify hydrogen peroxide. Stressed untreated rats in this study had low levels of GST, GSH, GPx, SOD, and catalase (Figure 4), indicating an altered antioxidant status that may be associated with oxidative stress in the stressed animals. Upon administration of the tea blend, the activities of these antioxidant enzymes were restored, suggesting that the tea may have the potential to attenuate oxidative stress. The seen antioxidant effect correlates with previous findings that phytochemicals found in common herbs, spices, fruits, vegetables, and medicinal plants like flavonoids and phenolics can prevent oxidative stress or damage as observed in the *Mondia whitei*–*Curcuma longa* composite tea (Hossain *et al.*, 2025).

Corticosterone, the main glucocorticoid hormone in rodents, is a crucial marker of stress and hypothalamic-pituitary-adrenal (HPA) axis activity (Knezevic *et al.*, 2023), the secretion is strictly controlled to help the body cope with stress by releasing stored energy and modifying neurological and immunological functions (Sitorus & Silitonga, 2025). However, in animal models, the development of depressive-like behaviors has been closely associated with prolonged increase of corticosterone levels brought on by excessive or chronic activation of the HPA axis (Nandam *et al.*, 2020). Neurogenesis, synaptic plasticity, and neurotransmitter balance are negatively impacted by prolonged high corticosterone exposure in brain regions linked to mood regulation, particularly the prefrontal cortex and hippocampus. In depression experimental models, stress-induced corticosterone hypersecretion is commonly utilized as an indicator of HPA axis dysfunction. Elevated corticosterone levels have been linked to depressive symptoms such as anhedonia, anxiety, behavioral despair, and cognitive impairment (Wu *et al.*, 2025). Therefore, it is proposed that interventions capable of normalizing corticosterone levels may have antidepressant and stress-relieving properties. Figure 5 shows that CUMS exposure significantly increased serum corticosterone levels in the stress control (SC) group compared with the normal control (NC) group (**** $p < 0.001$), indicating an altered stress response in the CUMS-exposed animals. This finding is consistent with previous research demonstrating that prolonged stress can increase corticosterone release and is associated with behavioral and physiological changes resembling depression. The observed reduction in corticosterone levels following tea treatment suggests that the formulations may help attenuate the stress response and may be associated with modulation of HPA-axis activity. Plant-derived compounds such as flavonoids, polyphenols, and saponins have been investigated for their potential to modulate corticosterone responses (Balogun *et al.*, 2025). This reduction in corticosterone may contribute to the behavioral improvements observed in the treated rats, potentially through effects on stress-related neuronal and neurotransmitter processes. Overall, these findings suggest that the antidepressant-like effects of the tea formulations may be partly associated with their phytochemical constituents and their potential to attenuate stress-related increases in circulating corticosterone. However, because other components of HPA-axis activity were not directly assessed, the involvement of HPA-axis modulation remains a proposed mechanism rather than a mechanism directly demonstrated in the present study.

In this study, TNF- α and IL-6, which are pro-inflammatory cytokines, were detected in the rats' blood. Results indicated that untreated rats (stressed group) had significantly greater levels of these cytokines than the control group ($p < 0.001$) (Figure 6). Fluoxetine and tea treatment significantly ($p < 0.001$) decreased TNF- α levels in the serum compared with the stress group. Nevertheless, the 50G:50T treatment exhibited the lowest TNF- α level, suggesting a greater decrease in inflammatory response among the tea formulations. Increased interleukin (IL)-6 has been recognized as a potential marker associated with depression (Yamasaki *et al.*, 2020). Reduced IL-10 and IL-4 expression may influence HPA-axis activity and glucocorticoid responsiveness observed in depressive conditions, and IL-10 has been reported to suppress adrenocorticotrophic hormone-induced steroid production, which may contribute to the regulation of hypothalamic-pituitary-adrenal (HPA) axis homeostasis (Drela, 2025). Furthermore, previous studies have reported concurrent increases in IL-6 and decreases in IL-10/IL-4 in experimental models associated with depressive-like behaviors. Thus, altered levels of these cytokines may be associated with the severity of depressive-like symptoms seen in the stressed rats.

Additionally, compared with controls, the stressed rats in the present study showed significantly greater TNF- α levels, and IL-6 and significantly higher IL-4/IL-10 ratios (Figure 6). When compared with the stressed group, the tea blend treatment groups had much lower IL-6 and TNF- α levels, while their IL-10/IL-4 levels were higher. In contrast, the fluoxetine group showed noticeably greater levels of IL-10/IL-4 and much lower IL-6 and TNF- α . These findings suggest that the antidepressant-like effects observed following white ginger–turmeric tea and fluoxetine treatment may be associated with modulation of the inflammatory response, characterized by reduced pro-inflammatory cytokines such as IL-6 and TNF- α . However, the present study did not directly establish a causal relationship between cytokine modulation and the observed behavioral effects; therefore, inflammatory pathways may represent one of the mechanisms contributing to the effects of the tea formulations.

CONCLUSION

The present research revealed that *Mondia whitei*–*Curcuma longa* composite tea displays significant antidepressant-like effects in CUMS-induced rats. The observed effect mechanism may be through modulation of monoaminergic neurotransmission, attenuation of oxidative stress, suppression of neuroinflammation and changes in corticosterone levels. Among the tested formulations 50:50 blend demonstrated the most pronounced effect *in vivo*. The findings provide preliminary evidence that the composite tea may modulate behavioral and biochemical alterations associated with CUMS in rats. Further studies, including mechanistic, dose-response, safety, and clinical investigations, are required before any conclusions regarding human therapeutic efficacy can be drawn

AUTHORS' CONTRIBUTION

The authors confirm their contributions to the paper as follows: study conception and design, methodology: Gbolagade-Akanbi A.M, Oyewole O.I., Salawu S.O. data collection: Gbolagade-Akanbi A.M, Adedeji V. A, Gbolagade O.H; analysis and interpretation of results, draft manuscript preparation, writing – review and editing:, Gbolagade-Akanbi A.M, Oyewole O.I., Salawu S.O, Adedeji V. A , Gbolagade O.H. All authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The author confirms that this article's content has no conflict of interest.

DATA AVAILABILITY STATEMENT

Data can be obtained upon request

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Declared none.

STATEMENT OF ETHICS

This Study protocol was reviewed and approved by the Osun State health Research Ethic committee (OSHREC), Ministry of Health, Osogbo, Osun state, Nigeria, approval number Approval No.: OSHREC/PRS/2024/842/01/244; Date of approval: 31 January 2024.

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