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EVALUATING THE COGNITIVE AND BIOCHEMICAL IMPACT OF WLTH FOCUS NOW: A RANDOMIZED, PLACEBO-CONTROLLED TRIAL IN GENERALIZED ANXIETY DISORDER

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ABSTRACT

Generalized anxiety disorder (GAD) is associated with cognitive impairments, impacting memory, attention, and executive function. WLTH FOCUS NOW, an herbal nutraceutical containing adaptogenic herbs, has shown potential for cognitive enhancement. This study aimed to evaluate the efficacy of WLTH FOCUS NOW on cognitive performance and acetylcholinesterase (AChE) activity, a biochemical marker associated with cognitive function, in individuals with GAD. A randomized, placebo-controlled, parallel-group trial was conducted with 41 participants aged 18-60 years diagnosed with GAD. Participants were assigned to either the intervention group, receiving a daily dose of WLTH FOCUS NOW (3.5g in 150 ml of water), or a placebo group, administered for 14 days. Primary outcome was AChE activity, measured at baseline, post-intervention, and two-week follow-up. Secondary outcomes included cognitive assessments through the Auditory Verbal Learning Test (RAVLT) and Montreal Cognitive

Assessment (MoCA). The trial group demonstrated significant improvements in RAVLT and MoCA scores compared to the control group, indicating enhanced cognitive performance, particularly in memory and attention domains. AChE levels increased within both groups across time points, with the trial group showing a more pronounced increase post-treatment. However, between-group differences in AChE were not statistically significant. WLTH FOCUS NOW appears to positively impact cognitive function in individuals with GAD, with significant improvements observed in memory and attention. Although AChE levels increased, the lack of significant between-group differences suggests that additional research is needed to establish a direct relationship between AChE activity and cognitive changes. Further studies with larger samples are recommended to validate these findings.

KEYWORDS: Cognitive enhancement, herbal nutraceutical, generalized anxiety disorder, acetylcholinesterase, cognitive function.

INTRODUCTION

Generalized Anxiety Disorder (GAD) is a prevalent and chronic mental health condition characterized by excessive and uncontrollable worry about various aspects of life, persisting for at least six months, as defined by the DSM-5 criteria (Tiirikainen et al., 2019). The lifetime prevalence of GAD is estimated to be approximately 3–8%, indicating its significant impact on the population (Hofmann et al., 2015). Recent studies have highlighted the increased prevalence of GAD among specific populations, particularly during stressful periods, such as the COVID-19 pandemic. A study conducted among medical support staff revealed that 42.1% experienced varying degrees of GAD, which aligns with findings from other regions, but contrasts with lower prevalence rates reported in some studies in China (Ahmed, 2023). The implications of GAD extend beyond individual distress, affecting the overall functioning and quality of life. Individuals with GAD often report difficulties in daily activities, impaired social interactions, and increased healthcare utilization (Wetherell et al., 2010). This disorder is associated with comorbid conditions, including depression and insomnia, which complicate treatment and exacerbate the overall burden of mental health issues (Şahin et al., 2020). The relationship between GAD and cognitive impairment has also been explored, with evidence suggesting that older adults with GAD may experience poorer memory and cognitive function than those without anxiety disorders (Potvin et al., 2010). Generalized anxiety disorder (GAD) affects millions of people globally, impacting their quality of life and often leading them to seek alternative approaches for managing

symptoms. Among these potential avenues are neutraceuticals and food-derived products with purported health benefits, including potential cognitive enhancement. However, robust scientific evidence to support these claims, particularly for specific conditions, such as GAD, remains scarce. This clinical trial aimed to address this knowledge gap by investigating the effects of WLTH FOCUS NOW on auditory verbal learning in individuals with GAD. This specific cognitive domain was chosen because of its relevance to daily activities and sensitivity to changes in cognitive function. Nutraceuticals, such as L-theanine, omega-3 fatty acids, and magnesium, have garnered attention for their potential anxiolytic effects. l-Theanine, an amino acid found in tea, has shown promise in clinical trials, indicating its ability to reduce anxiety symptoms when used as an adjunct to standard treatment for GAD (Sarris et al., 2019). Omega-3 polyunsaturated fatty acids have been associated with improvements in anxiety severity, as evidenced by systematic reviews highlighting their beneficial effects on mood and anxiety disorders (Su et al., 2018). Mg supplementation has also been linked to reduced anxiety levels, with studies demonstrating its efficacy in alleviating symptoms associated with GAD (Tarleton et al., 2017; Oddoux et al., 2022). The role of vitamin D in anxiety management has been increasingly recognized. Research indicates that vitamin D supplementation can ameliorate the severity of GAD, particularly in individuals with vitamin D deficiencies (Eid et al., 2019; Anouti et al., 2022). Interestingly, the present study also assessed acetylcholinesterase (AChE) activity as a potential biomarker of cognitive function. AChE plays a crucial role in the regulation of neurotransmitters, and alterations in its activity have been linked to various cognitive disorders. By measuring AChE levels alongside Auditory Verbal Learning Test (RAVLT) performance and the Montreal Cognitive Assessment (MoCA), this study aimed to gain a deeper understanding of the effects of WLTH FOCUS NOW on cognitive function and its potential mechanisms of action. The study was registered in the Central Clinical Registry (CTRI/2022/08/057635) after obtaining approval from the institutional ethical committee. This study explored the following key questions: Does WLTH FOCUS NOW lead to improved performance on the AVLT compared with placebo in individuals, indicating enhanced learning and memory function? Does WLTH FOCUS NOW lead to improved performance on the Montreal Cognitive Assessment? Are there any specific aspects of AVLT, such as immediate recall, delayed recall, or recognition that show significant benefits following WLTH FOCUS NOW administration? Does WLTH FOCUS NOW influence AChE activity? By delving into both cognitive performance and the potential underlying biological mechanisms, this study offers valuable insights into the potential role

of WLTH FOCUS NOW in supporting cognitive function in individuals with GAD. These findings could contribute to the development of alternative approaches for enhancing learning and memory capacities while managing anxiety symptoms, along with providing preliminary evidence of the possible neural mechanisms involved.

MATERIALS AND METHODS

Trial Design: This study was conducted as an interventional, randomized, parallel-group, placebo-controlled trial to evaluate the effects of Ayurvedic and nutraceutical interventions on learning and cognitive changes in individuals with generalized anxiety disorder (GAD). The trial investigated the efficacy of an herbal nutraceutical, WLTH FOCUS NOW, compared to a placebo.

Participants: Individuals aged 18 to 60 years with learning and cognitive issues related to stress, diagnosed according to specific criteria for cognitive impairment in GAD, were included in the study, regardless of gender. Exclusion criteria were hypertension, cardiac disorders, inflammatory bowel disease (IBD), pregnancy and lactation, sensitivity to herbs, and endocrine disorders.

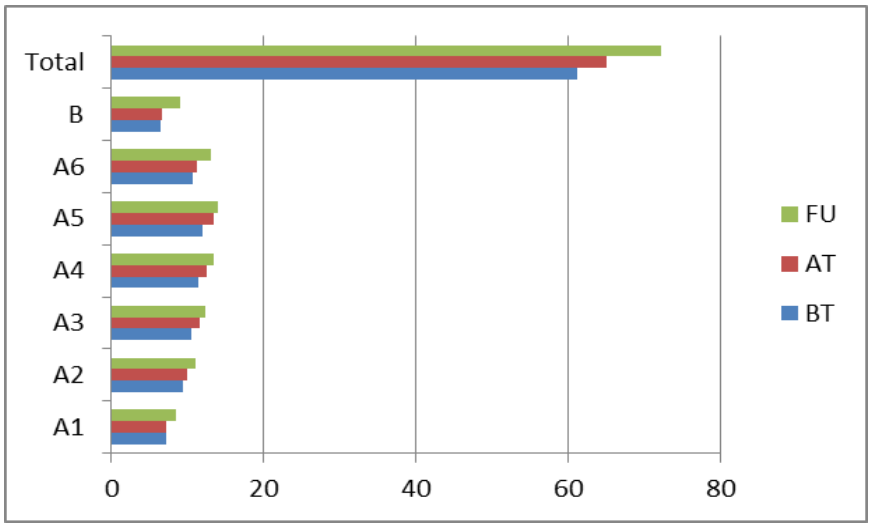
Intervention and Comparator: The intervention group received WLTH FOCUS NOW, an herbal nutraceutical composed of a blend of adaptogenic herbs, provided in a 3.5-gram sachet of powdered formula. The herbal blend was mixed with 150 ml of water and administered once daily for 14 d. Key ingredients in the nutraceutical included Brahmi extract (*Bacopa monnieri*), cinnamon extract (*Cinnamomumzeylanicum*), gotu kola extract (*Centella* asiatica), KSM-66 ashwagandha extract (*Withaniasomnifera*), saffron extract (*Crocussativus* L.), sage extract (*Salviaofficinalis*), and tulsi extract (*Ocimumsanctum*). Additional ingredients included wild-grown Brahmi, cinnamon, and valerian extracts (*Valerianawallichii*). The comparator (placebo) group received a 3.5-gram sachet containing powdered Rawa with added natural flavors mixed with 150 ml of water, administered once daily for 14 days.

Randomization and Blinding: Participants were randomly assigned to either the intervention or placebo group by using a lottery method to generate a random sequence. Blinding was implemented at the participant level, with participants unaware of their group allocation.

Outcomes: The primary outcome was acetylcholinesterase (AChE) activity, assessed at three time points: baseline (before the trial), after the 14-day intervention, and at a follow-up two weeks post-intervention. The secondary outcomes included cognitive function assessments, specifically the Auditory Verbal Learning Test (AVLT) and Montreal Cognitive Assessment (MoCA). These were also measured at baseline, after the 14-day intervention, and at the two-week follow-up. This methodology ensured a controlled and blinded comparison of the effects of the herbal nutraceutical on cognitive and biochemical outcomes in individuals with GAD, thereby facilitating a robust analysis of its efficacy.

RESULTS

A total of 41 individuals participated in this study. The demographic profile was predominantly female (98%), with all participants in the middle socioeconomic class. Participants displayed a variety of dietary habits, both vegetarians and non-vegetarians. The age profile was young, with all participants aged < 30 years old. Participants were randomly assigned to two groups: a trial group and a control group. Owing to participant inconvenience, one data point related to post-trial AChE was missing in the trial group. The following graphs and tables express the details of the Auditory Verbal Learning Test (RAVLT) performance, Montreal Cognitive Assessment (MoCA), and AChE performed for the study.



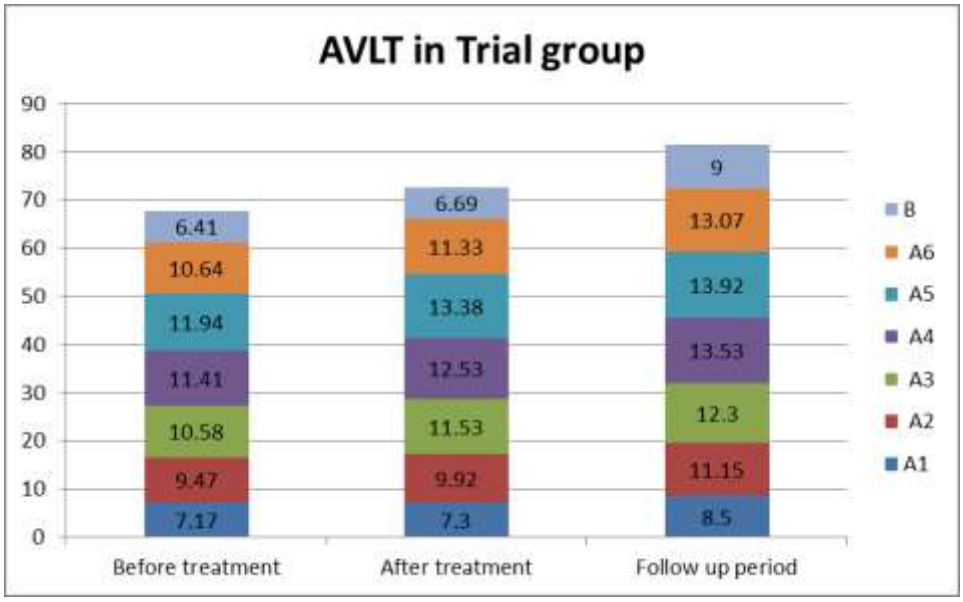
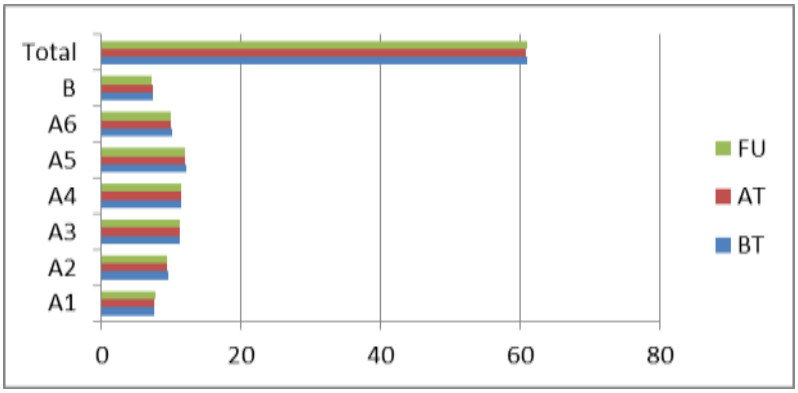


Figure 1 AVLT changes in the trial group: Comparison of RAVLT scores across stages A1 to A6, total post-assessment, and B in the trial group, showing gradual improvement and significant gains post-assessment.

RAVLT performance in the trial group exhibited progressive improvements across sessions A1 to A6, as well as in the total score (total) and post-interference score (B). Notably, the greatest improvement was observed in the total score after the assessments, suggesting an increase in learning ability and memory retention in response to the intervention. This gradual rise from A1 to A6 reflects enhanced cognitive engagement and a possible beneficial effect of trial treatment on memory encoding and recall abilities over time (Figure 1).



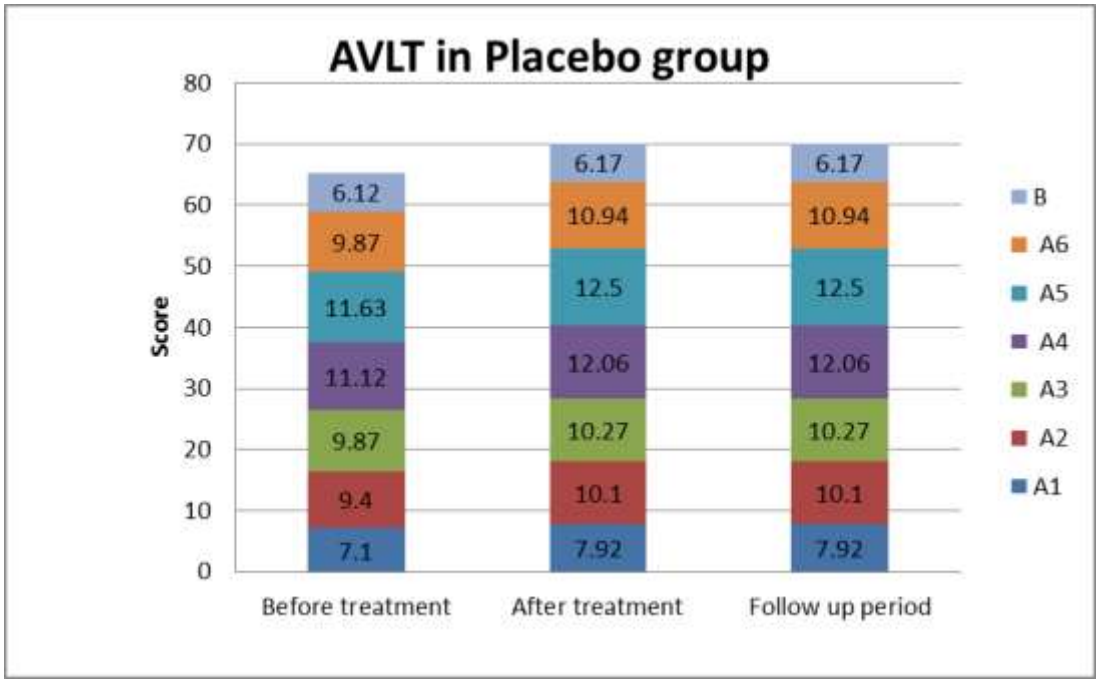
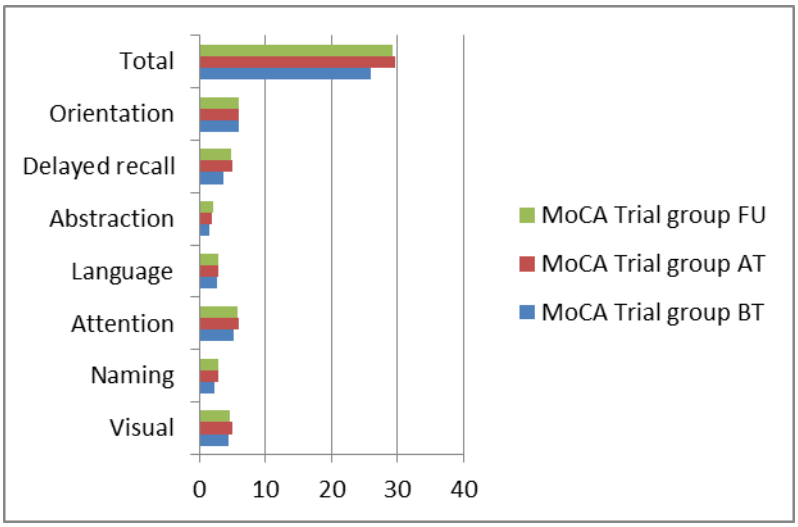


Figure 2: AVLT changes in the control group: RAVLT performance across stages A1 to A6, total post-assessment, and B in the control group, with less pronounced improvement compared to the trial group.

In the control group, RAVLT scores demonstrated incremental progress from A1 to A6. However, compared with the trial group, the improvements in the total scores and post-interference scores were less pronounced. This indicates that while the control group participants experienced a learning curve, the lack of intervention resulted in less substantial cognitive gain. The relatively low total score implies a possible difference in memory performance between the trial and control groups, supporting the potential efficacy of the trial intervention(Figure 2).



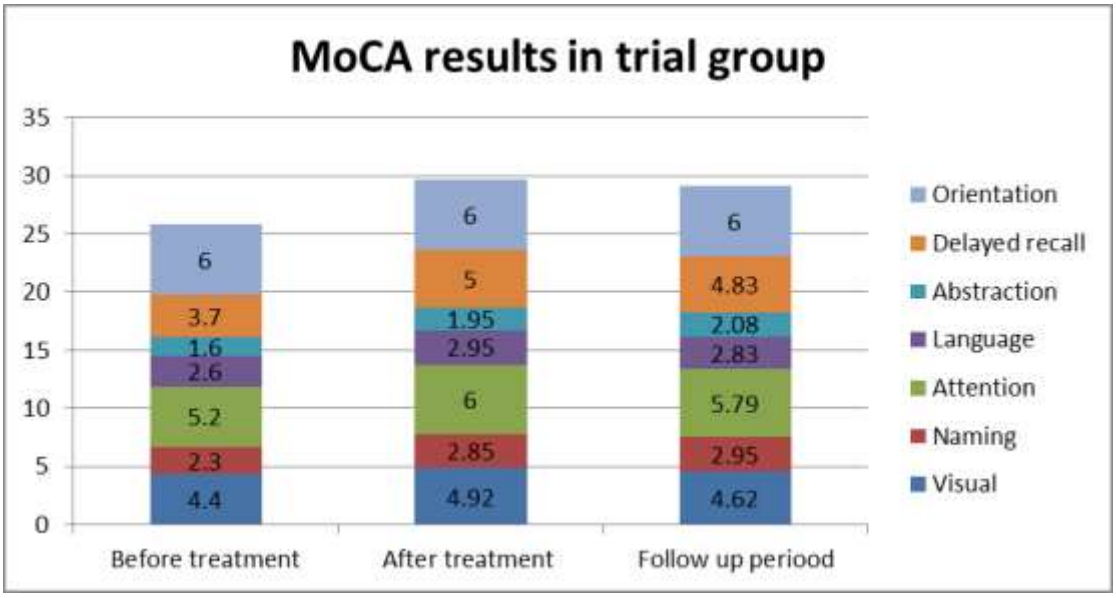
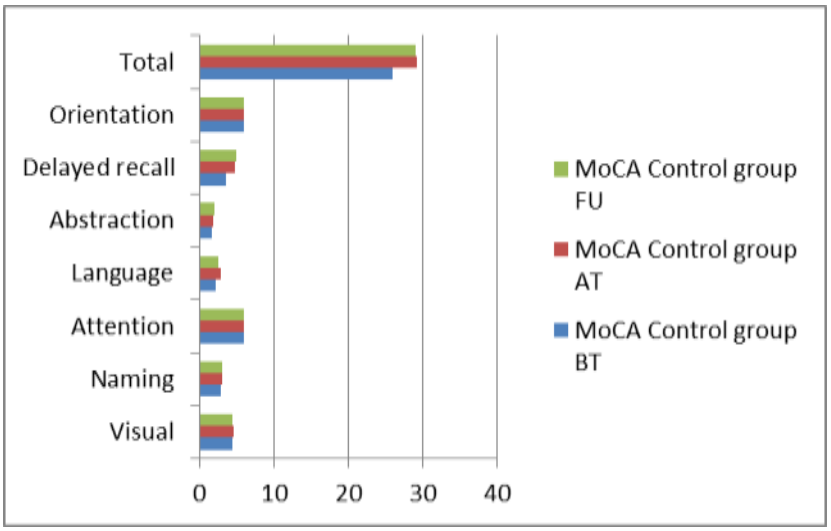


Figure 03: Changes in MoCA in the trial group: MoCA domain scores for the trial group, indicating notable cognitive improvement post-intervention.

MoCA assessments in the trial group revealed notable increases in scores across various cognitive domains including orientation, delayed recall, language, attention, and abstraction. The total MoCA score showed marked improvement following the intervention, indicating an overall enhancement in cognitive function (Figure 3). This outcome highlights the possible effect of trial treatment in augmenting cognitive abilities, especially in the domains associated with memory, attention, and executive function. These results suggest that interventions may contribute to cognitive resilience and functioning.



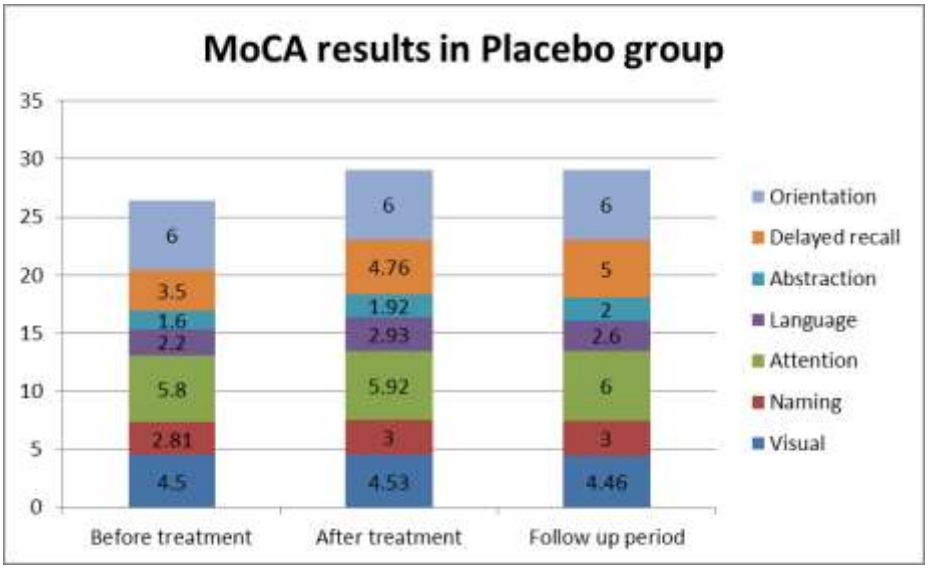


Figure 04: MoCA observations and changes in control group: MoCA scores across cognitive domains in the control group, showing moderate improvement post-intervention.

The MoCA scores in the control group also showed positive changes across similar cognitive domains(Figure 04). However, the improvements were generally smaller than those in the trial group. While the control group exhibited cognitive gains, the less pronounced increase in total MoCA scores suggests limited cognitive benefits in the absence of the intervention. These findings imply that trial treatment may play a role in enhancing specific cognitive functions, with the control group serving as the baseline for natural progression.

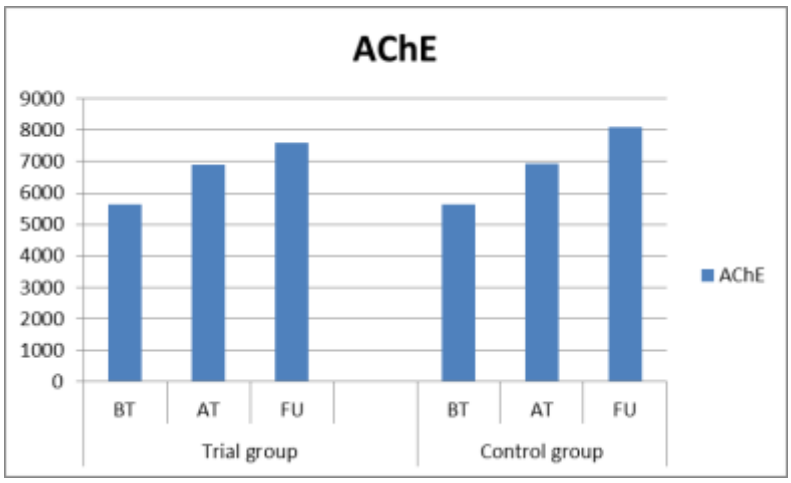


Figure 5: AChE changes in the control and trial groups before treatment, after treatment, and after follow-up: Comparison of AChE levels in the trial and control groups before treatment, after treatment, and after follow-up, highlighting a significant post-treatment increase in the trial group.

AChE levels in both the trial and control groups showed an increasing trend across the three phases: before treatment (BT), after treatment (AT), and follow-up (FU). The trial group exhibited a substantial increase in AChE levels from AT to FU, indicating a sustained physiological response to the intervention. The control group showed a moderate increase, suggesting that while AChE levels naturally increased over time, the trial treatment may have amplified this effect. The differential response between the groups indicates a potential biochemical impact of the intervention on the AChE enzyme, which is often associated with cognitive processes.

Table 1: Paired t-test Results on AChE in Trial and Control Groups.

Parameter	Control Value	Trial Value
P-value	0.0028	0.01585
T	3.5269	2.6045
Sample size (n)	17	24
Average of differences ($\bar{x}_d$)	1297.0588	972.8333
SD of differences (S_d)	1516.3164	1829.8492
Normality p-value	0.0945	0.00003697
A priori power	0.491	0.6504
Post hoc power	0.9113	0.7036
Skewness	0.9041	-2.6592

The paired t-test results (Table 1) revealed significant differences in acetylcholinesterase (AChE) activity between the control and trial groups after the intervention. The p-values for the control group (p = 0.0028) and trial group (p = 0.01585) indicated statistically significant differences, suggesting that the intervention had an impact on AChE levels within each group. The control group had a higher t-value (t = 3.5269) than the trial group (t = 2.6045), which, combined with a larger average difference ($\bar{x}d$ = 1297.0588 vs. 972.8333), suggests a greater effect size in the control group for this measure. Both groups had relatively large standard deviations (SD), with the trial group showing higher variability (Sd = 1829.8492) than the control group (Sd = 1516.3164), indicating individual differences in response to the intervention. Normality testing showed a non-significant result for the control group (p = 0.0945), implying data normality, whereas the trial group showed a significant deviation from normality (p = 0.00003697), suggesting that the distribution of the differences was not normal. This difference in normality could affect the interpretation of the paired t-test, especially in the trial group. The a priori power was higher in the trial group (0.6504) than in the control group (0.491), suggesting a greater ability to detect an effect beforehand in the trial group. However, the post hoc power was higher in the control group (0.9113 vs. 0.7036),

indicating that the actual observed effect size in the control group was sufficiently large to ensure a high power. The paired t-test results (Table 1) indicated significant within-group changes in AChE levels in both the control and trial groups. The larger t-value and average difference in the control group suggest a more pronounced change in AChE levels relative to the trial group, despite both groups achieving statistical significance.

Table 2: Unpaired t-test Results Comparing Trial and Control Groups.

Unpaired t-test	**Trial group**	**Control group**
Mean	1465.1739	1538.3529
Variance	561246.3176	1479799.4048
Stand. Dev.	749.1637	1216.4701
N	23	17
T	**-0.235**	
Degrees of freedom	**38**	
critical value	**2.024**	

Unpaired t-test results (Table 2) were used to compare AChE levels between the trial and control groups after the intervention. The mean AChE level in the trial group (1465.1739) was slightly lower than that in the control group (1538.3529), but the difference was not statistically significant ($t = -0.235$, $p > 0.05$). Both groups showed high variability, with the control group displaying a larger variance (1479799.4048) and standard deviation (1216.4701) than the trial group (variance = 561246.3176, standard deviation = 749.1637). This high variability, particularly in the control group, may have contributed to the lack of significant differences between the groups. The critical value for significance was 2.024, and the calculated t-value of -0.235 fell well below this threshold, suggesting no significant difference in AChE levels between the groups after treatment. The unpaired t-test results (Table 2) highlighted no significant difference in AChE levels between the trial and control groups post-intervention. Although the trial group exhibited slightly lower mean AChE levels, the difference was not statistically significant, suggesting that the intervention did not result in a marked difference between the groups. The high variability, particularly in the control group, may have masked potential differences, which could be due to individual physiological responses or other uncontrolled factors within the population. The high post-hoc power for the paired test in the control group suggests that the significant change observed in that group is robust, while the unpaired test's non-significance suggests that the intervention's effect may not differ substantially between groups.

DISCUSSION

The chief role of AChE is to terminate neuronal transmission and signaling between synapses to prevent ACh dispersal and activation of nearby receptors. Acetylcholinesterase (AChE) plays a pivotal role in neuronal transmission and signaling by regulating the levels of acetylcholine (ACh) at synaptic junctions. ACh is a crucial neurotransmitter involved in various functions, including muscle activation, modulation of neuronal excitability, and synaptic plasticity. AChE is responsible for the rapid hydrolysis of ACh, thereby terminating its action and ensuring precise control over cholinergic signaling (Askar et al., 2011;, Handi, 2024). This enzymatic activity is essential for maintaining the balance between excitatory and inhibitory signals in the nervous system, which is critical for proper neuronal function and communication. The modulation of synaptic transmission by ACh is complex and involves various mechanisms. For instance, ACh can enhance the signal-to-noise ratio of synaptic inputs in sensory cortices, thereby influencing arousal and vigilance (Ramaswamy et al., 2018). Additionally, ACh can shape the signaling of other neurotransmitter systems, such as GABA and glutamate, by altering presynaptic release properties and synaptic plasticity (Saunders et al., 2015). This interaction is particularly evident in the context of cholinergic neurons that co-release ACh and GABA, allowing for nuanced control over excitatory and inhibitory signaling in specific brain regions (Storozhuk et al., 2001; , Granger et al., 2020). Cholinesterase inhibitors are prescribed to treat symptoms related to memory, thinking, language, judgment and other thought processes. Considering these facts, AchE was estimated in the current study. The critical value suggests that there is no significant change between the difference of means between trial and control group on AChE. But it is also interesting to note that in both the groups the AChE values were in the optimal level at the end point. However, the relationship between AChE and cognition is complex, and optimum level of AChE for cognitive function is yet to be established (Marucci et al., 2021). So, the study suggests that the positive changes observed in the subjective criteria may be attributed to some other pathways, or a similar kind of study but in a bigger population is needed to get the concrete conclusion.

The Montreal Cognitive Assessment (MoCA) is a test used to detect mild cognitive decline and early signs of memory loss (Jia et al., 2021). The Montreal Cognitive Assessment (MoCA) is a widely utilized screening tool designed to detect mild cognitive impairment (MCI) and memory loss. It comprises 30 questions that assess various cognitive domains, including attention, memory, executive functions, language, and visuospatial skills. The

MoCA is particularly valued for its brevity, taking less than 15 minutes to administer, and its high sensitivity in identifying cognitive decline compared to other assessments like the Mini-Mental State Examination (MMSE) (Kantithammakorn et al., 2022; Santos, 2023). For instance, the MoCA has demonstrated a sensitivity of 90% for detecting MCI, significantly outperforming the MMSE, which has a sensitivity of only 18% (Kantithammakorn et al., 2022). This makes the MoCA a critical tool in both clinical and research settings for early detection of cognitive decline. The test was done prior and after administering the regime in both the groups. The MoCA test examines seven domains (aspects) of cognitive function with a total of 11 different exercises and tasks. It evaluates visuospatial skills, attention, language, abstract reasoning, delayed recall, executive function, and orientation. The MoCA covers more domains than the MMSE and, as a consequence, has greater sensitivity and specificity; and hence used in this study. The MoCA is useful in determining a patient's level of understanding and ability. Visuospatial skills and executive function are assessed using the modified trail-making test, copy of the cube, clock drawing test, and naming. attention is assessed using the digit span (forward and backward). Nutraceuticals, which include dietary supplements and functional foods, are thought to exert beneficial effects on cognitive health through various mechanisms, such as reducing oxidative stress and inflammation, which are implicated in neurodegenerative diseases like Alzheimer's (Knight et al., 2023). For example, certain compounds like Ginkgo biloba have been shown to improve MoCA scores in patients with vascular MCI, suggesting that these supplements may enhance cognitive function (Li et al., 2019). Furthermore, antioxidants are being investigated for their role in modulating oxidative stress, a key factor in the pathophysiology of Alzheimer's disease (Knight et al., 2023). The integration of MoCA assessments with nutraceutical interventions could provide a comprehensive approach to managing cognitive decline. Concentration and calculation are assessed using the letter A tapping test, and serial 7 subtractions. Language is assessed using sentence repetition and letter F fluency. Abstraction is assessed by asking about similarities and difference between objects where as Memory was assessed by a delayed recall of previous answers. MoCA is scored out of 30. A cut-off score of 26 signifies mild cognitive impairment. MoCA has high test-retest reliability (ICC = 0.92, $p < 0.001$). MoCA has good internal consistency (Cronbach's alpha = 0.82) (Matthews et al., 2019). The positive changes observed in attention, language and delayed recall in our study may be attributed to the ingredients like brahmi, aswaganda, etc. These changes were very negligible in control group. The Rey Auditory Verbal Learning Test (RAVLT) is a neuropsychological assessment designed to test verbal memory in patients. The RAVLT is used to evaluate the

nature and degree of memory dysfunction and to observe changes in memory function over time (Dawidowicz et al., 2021). The procedure is designed as a list-learning paradigm in which the patient hears a list of 15 nouns and is asked to recall as many words from the list as possible. After five repetitions of free-recall, a second "interference" list (List B) is presented in the same manner, and the participant is asked to recall as many words from List B as possible. After the interference trial, the participant is immediately asked to recall the words from List A, which she or he heard five times previously. After a 20 min delay, the participant is asked to again recall the words from List A. In the present study remarkable change was noticed in trial group on total recall points after the second List B evaluation. All theses datas are supportive to narrarte that the current regimen in very effective in learning performance.

The positive changes observed in attention, language and delayed recall in our study may be attributed to the ingredients like brahmi, aswaganda, etc and is a clear indicator for the efficacy of WLTH Focus now in current area of resarch. These changes were very negligible in control group. The WLTH focus now treated individuals have shown amplified delayed recall, as score 5 against 3.7. This reflect the utility of WLTH Focus now in delayed memory recall. The scores of abstraction, language and attention were also improved after the intervention. These scores against placebo group is statistically significant. The trends seen in language and attention shows that WLTH Focus now is a good alternative option for individuals suffering from learning difficulties. This study showed better results in uplifting the cognition, memory and language.

The results and statistical data are in line with the previous study reports. *Centella asiatica*, commonly known as Gotu kola, has been utilized in Ayurveda for over 3000 years, recognized for its diverse therapeutic properties. This herb is particularly noted for its neuroprotective effects, attributed to its active compounds such as asiaticoside and madecassoside, which enhance cognitive function and exhibit antioxidant properties (Singh, 2023; Kumar et al., 2009; Gray et al., 2015). *Centella asiatica* water extract treatment improves cognitive function of aged Alzheimer's disease model Tg2576 and wild-type mice. A research showed a dose-dependent enhancement in memory despite of gender or pathology, devoid of impacting the amyloid plaque burden (Mathews et al., 2021). Treatment-dependent boost in the synaptic markers in the cortex was also evident in that study. Results of an investigation illustrate that treatment during postnatal developmental

stage with *C. asiatica* extract can manipulate the neuronal morphology and promote the higher brain function of juvenile and young adult mice (Mathews et al., 2021). The observations of a clinical trial exposed that, *Centella asiatica*not only significantly ($p<0.01$) attenuated anxiety related disorders but it also significantly ($p<0.01$) reduced stress phenomenon and its correlated depression. *Centella asiatica*further significantly ($p<0.01$) enhanced the willingness for adjustment and cognition. Results indicated that Centella asiatica may be useful in the treatment of Generalized Anxiety Disorder (Gray et al., 2024; Mathews et al., 2021).

Studies showed that administration of *C. sativus* and its constituent principles amplified glutamate and dopamine levels in the brain in a dose-dependent manner (Mathews et al., 2021). Research studies showed that the saffron extract had a moderate (up to 30 %) inhibitory activity on acetyl-cholinesterase (AChE) and it inhibited acetylcholine breakdown which is the key therapeutic approach for AD (Mathews et al., 2021). In a randomized and double-blind clinical trial study, saffron supplementation statistically improved the mood of subjects compared to the placebo group. For six weeks, 30 mg/day of saffron was given and subjects were evaluated based on the Hamilton Depression Rating Scale (HAM-D). The antidepressant effects of aqueous and ethanolic extracts of *Crocus sativus* (saffron) petals and stigmas have been substantiated through various studies. Both extracts exhibit significant antidepressant activity, attributed to their bioactive compounds such as crocin and safranal, which are known to modulate neurotransmitter systems, including serotonin and dopamine pathways (Matraszek-Gawron et al., 2022; Butnariu et al., 2022; Siddiqui et al., 2022). Research indicates that these extracts can enhance mood and reduce depressive symptoms in animal models, demonstrating effects comparable to conventional antidepressants (Kashani et al., 2016; Moshiri et al., 2014). Moreover, the mechanisms underlying these effects include monoamine reuptake inhibition and NMDA receptor antagonism, which contribute to their neuroprotective properties (Matraszek-Gawron et al., 2022; Butnariu et al., 2022). The efficacy of the extracts has been shown to be dose-dependent, with specific concentrations yielding optimal results in reducing immobility in forced swimming tests, a common measure of antidepressant activity (Kashani et al., 2016; Moshiri et al., 2014).

Curcumin, the main principle of C*urcuma longa* is known for its broad spectrum therapeutic and pharmacological actions with well-documented pharmacokinetics, efficacy, and safety. In a study it is found that compared with the placebo group, the curcumin group was associated

with an improvement in working memory (Hedges' g = 0.396, 95% confidence interval (CI) = 0.078 to 0.714, p = 0.015) and a borderline benefit in processing speed (Hedges' g = 0.303, 95% CI = −0.013 to 0.619, p = 0.06) (Tsai et al., 2021). The results suggest a neurogenesis- and cognition-enhancing potential of prolonged curcumin treatment in aged rats, which may be due to its diverse effects on genes related to growth and plasticity. Numerous studies have demonstrated that curcumin can mitigate neurotoxicity and promote neuronal survival in various models of neurodegenerative diseases, including Alzheimer's and Parkinson's disease (Mobinhosseini, 2023; Slowing et al., 2022; Nebrisi et al., 2020; Erfanizadeh et al., 2020; Nguyen et al., 2018). For instance, curcumin has been shown to enhance neurogenesis and cognitive function in aged rats, suggesting its potential in treating age-related cognitive decline (Shen et al., 2012). Additionally, curcumin's ability to modulate inflammatory pathways and reduce oxidative stress contributes to its neuroprotective effects, making it a promising candidate for therapeutic interventions in conditions such as epilepsy and ischemic brain injury (Rusek & Czuczwar, 2021; Drion et al., 2018; Meo et al., 2019).

Reports on *Bacopa monnieri* are also favorable with the current herbal combination. This drug is generally known as *Brahmi* in India has got very significant clinical efficacy in many psychiatric illnesses. As per Ayurveda literature, Brahmi comes under the list of medhyarasayana, a drug used to perk up memory and intellect. The results of a study demonstrated significant consistent improvements in the language behaviour cognitive domain and in a number of the memory sub-domains with the use of this drug. Significant improvements were also seen in hyperactivity and attention-deficit domains. Overall outcome data demonstrated small to medium effect sizes (mean *d* = 0.42). A recent systematic review indicated that of nine clinical double blind placebo controlled *B. monnieri* trials in humans, eight demonstrated improvements in memory, attention, cognition, and mood. The suppression of plasma AChE activity was also observed in an another significant study along with improved working memory. These results suggest that *B. monnieri* can improve attention, cognitive processing, and working memory partly via the suppression of AChE activity (Tatimah et al., 2012). Extract of *Bacopa monnieri* is one of the major constituent of the *WLTH FOCUS NOW*.

Aswagandha (*Withania somnifera*) extract is another main ingredient of the currently studied neutraceutical combination. This has been used in Indian system of medicines for over 3000 years with its neuropharmacological activity, primarily attributed to its bioactive

compounds, particularly withanolides. These compounds have been shown to possess neuroprotective properties, influencing various pathways associated with neurodegenerative diseases such as Alzheimer's disease (Hannan et al., 2020; Ruhela et al., 2016). Research indicates that withanolide A, a major constituent of W. somnifera, demonstrates high plasma protein binding and favorable pharmacokinetics, enhancing its therapeutic potential in central nervous system (CNS) disorders (Singh et al., 2018; LIMA et al., 2018). Furthermore, W. somnifera has been traditionally utilized for its rejuvenating effects, and recent studies corroborate its role in modulating neuroinflammation and oxidative stress, which are critical in neurodegenerative pathologies (Pandey et al., 2018; Yenisetti et al., 2016). The systemic review of human trials shows the strongest evidence for therapeutic efficacy of ashwagandha in alleviation of stress and anxiety symptoms (Lopresti and Smith, 2021). The results of current study is also in line with the previous reports, as this study showed better results in uplifting the cognition, memory and language.

Thus the findings suggest that WLTH FOCUS NOW may be a promising nutraceutical intervention for enhancing cognitive function in individuals with cognitive impairments related to GAD. However, the complex relationship between AChE levels and cognition requires further exploration. Additional studies with larger sample sizes and more controlled variability are needed to confirm the efficacy of this herbal formulation and to better understand its mechanisms in cognitive enhancement.

CONCLUSION

The present work indicate that WLTH FOCUS NOW as a genuine neutraceutical product for learning and cognitive changes and can be recommended for GAD as an adjunct The study demonstrated that the herbal nutraceutical, WLTH FOCUS NOW, containing a blend of adaptogenic herbs, had a positive effect on cognitive performance, memory, and AChE levels in participants with generalized anxiety disorder (GAD). The trial group exhibited significant improvements in cognitive assessments, including the Auditory Verbal Learning Test (RAVLT) and the Montreal Cognitive Assessment (MoCA), compared to the control group, suggesting a beneficial impact of the nutraceutical intervention. Although both groups showed within-group increases in AChE levels over time, the trial group displayed a more substantial post-treatment increase, indicating a potential physiological response associated with the intervention. The paired t-test results revealed statistically significant within-group changes in AChE for both groups, with a larger effect size in the control group. However, the

unpaired t-test indicated no significant difference in AChE levels between the trial and control groups post-intervention, suggesting that while the intervention affected AChE levels within the trial group, it did not result in a marked difference when compared to the control group. The observed variability, particularly in the control group, may have influenced the findings, indicating that individual physiological factors or other uncontrolled variables may play a role in AChE activity. The MoCA and RAVLT results support the hypothesis that WLTH FOCUS NOW can enhance specific cognitive functions, particularly in attention, memory, and executive function. These cognitive improvements may be attributed to the bioactive components in the nutraceutical, including Brahmi, Ashwagandha, and other herbal extracts known for their neuroprotective properties. This aligns with previous literature on the cognitive-enhancing effects of these herbs.

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