

Clinical Trial Report

June 2025

Evaluating safety and efficacy of a *Curcuma longa*, *Bupleurum falcatum*, *Boswellia serrata* and *Centella asiatica* formulation as an adjunct therapy for mood, sleep and anxiety - A randomized, double-blind, placebo-controlled trial*.

Steels E, Pickering E, Castaneda R, Vigar V 2025

Summary

- This trial enrolled 96 adults (18-75 years) stable on antidepressant medication, experiencing ongoing low mood, anxiety and sleep disturbance. Five people did not complete the trial (n=46 in active group, n=45 in placebo group).
- All participants continued with their prescribed medication and were randomized to an herbal formulation containing *Curcuma longa* (Turmeric) as CurQfenE40®, *Boswellia serrata* (Boswellia) as BosQfen, *Bupleurum falcatum* (Bupleurum), and *Centella asiatica* (Gotu Kola); or to a matching placebo, over an 8 week treatment period in a randomized, double-blind, placebo-controlled trial.
- This study evaluated the efficacy of this phytomedicine formulation, previously shown *in vitro* to exhibit neuroprotective effects, as an adjunct to antidepressant medications, to support low mood, anxiety and disordered sleep. The safety of adding this herbal medicine to existing antidepressants was also assessed.
- The primary outcome was the Montgomery-Åsberg Depression Rating Scale (MADRS). Other outcomes included the Beck Depression Inventory-II (BDI-II), Zung's Self-rating Anxiety Scale (SAS), PROMIS Sleep Disturbance Form (PROMIS), and Patient Global Impression of Change (PGI-C).

Results

- In the active group, 41.7% of participants achieved a 50% or greater reduction in MADRS scale by week 8, compared to only 4.2% in the placebo group.
- Mean MADRS scores decreased by 38% in the active group versus a 9% reduction in the placebo group at week 8 ($p < 0.001$).
- BDI-II mean scores decreased by 48% in the active group versus 35% in the placebo group over the 8 weeks at week 8 ($p = 0.048$).
- Zung anxiety scores decreased by 22% in the active group versus 14% in the placebo group at week 8 ($p = 0.010$).
- PROMIS sleep scores improved by 25% in the active group versus 15% in the placebo group at week 8 ($p = 0.037$).
- PGI-C results show that at week 8 there were 11/47 who felt very much improved in the active group, compared to just 1/47 in the placebo group.
- There were no significant changes in biochemical safety. Treatment was well tolerated and there were no serious adverse events reported. These results indicate that this herbal combination can be taken safely in conjunction with these specific antidepressants, namely selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and tetracyclic antidepressants (TeCAs).

Study Details

Introduction

The complex interactions between the central nervous system (CNS) and inflammation have spurred development of novel treatment strategies, as monotherapies or as add-on treatments for mood-related disorders including depression and anxiety. This research has focused on specific herbal medicines that reduce neuroinflammation and encourage neuroplasticity by supporting brain-derived neurotrophic factor (BDNF). BDNF plays a role in modulating synaptic plasticity, inhibitory and excitatory transmission, and affects the brain's response to stress and mood disorders. It is now recognized that neuroinflammation reduces BDNF levels and contributes to mood disorders such as depression, anxiety and sleep disorders. Research has identified a number of herbal medicines that have the potential to support mental health. *Curcuma longa* (Turmeric), and its active constituent curcumin, has actions including anti-inflammatory, antioxidant, neuroprotective, antidepressant, and cognition-enhancing. Its neuroprotective properties are attributed to its ability to modulate BDNF release in a dose-dependent manner. *Bupleurum falcatum* (Bupleurum) has hepatoprotective, analgesic, anti-inflammatory, antioxidant, antidepressant, and immune-regulatory effects. It may alleviate anxiety and depression by promoting BDNF upregulation and via modulating hypothalamic-pituitary-adrenal reactivity. *Boswellia serrata* (Boswellia), is an anti-inflammatory and antioxidant. Boswellia is reported to facilitate the formation of new nerve networks and inhibit degeneration in the hippocampus. *Centella asiatica* (Gotu Kola) exerts neuroprotective, antioxidant and anti-inflammatory activity. It inhibits neurotoxicity, reduces anxiety, and offers antidepressant-like effects.

Study Overview

This clinical trial was designed to evaluate whether there was any benefit for adjunct supplementation with an herbal combination of Turmeric as CurQfenE40®, Boswellia as BosQfen, Bupleurum and Gotu Kola in adults with mild to moderate depression who have been stable on anti-depressant medication. The trial compared adjunct treatment with this herbal combination to a matching placebo provided in identical doses over an 8-week treatment period in a parallel-arm, randomized, double-blind, placebo-controlled trial. The trial was conducted during 2022-2023 by Evidence Sciences from a single site in Brisbane, Australia. Participants were sourced from around Australia in response to advertising and after screening, eligible participants were equally randomized into one of the two treatment groups (active or

placebo) in a 1:1 ratio. A total of ninety-six people were enrolled (48 on herbal formulation and 48 on placebo) and ninety-one completed the trial (46 on herbal formulation and 45 on placebo).

Participants

All participants were adults (18-75 years), taking prescribed antidepressant medications (drug and dose consistent for minimum four weeks) with ongoing low mood. A depression screening score of ≥ 20 on the Beck Depression Inventory was required at time of study entry (indicating moderate depression or above). Participants were otherwise healthy without diagnosed co-existing mental disorders. Allowable antidepressant types included selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), or tetracyclic antidepressants (TeCAs).

Intervention

Active (an herbal combination of Turmeric as CurQfenE40®, Boswellia as BosQfen, Bupleurum and Gotu Kola) or placebo (microcrystalline cellulose) tablets were provided for eight weeks and were taken orally at a dose of two tablets twice daily, two in the morning and two in the evening. The herbal intervention provided a daily dose of *Curcuma longa* (Turmeric) rhizome extract 468 mg (25.6 g dry rhizome, containing 330 mg curcumin); *Boswellia serrata* (Boswellia) extract 265 mg (6 g dry oleoresin); *Bupleurum falcatum* (Bupleurum) extract 6 mL (3 g dry root); and *Centella asiatica* (Gotu Kola) extract 600 mg (6 g dry leaf). *Curcuma longa* and *Boswellia serrata* ethanolic extracts were each loaded onto a base of galactomannans from Fenugreek seeds and supplied by Akay Natural Ingredients Private Limited (Kerala, India). *Centella asiatica* and *Bupleurum falcatum* were standard ethanolic extracts. Participants were instructed to remain stable on existing antidepressant medication.

Participants and Baseline Characteristics

Ninety-six people were enrolled in total, with forty-eight allocated into each of the treatment arms. Five people did not complete the trial (n=46 in active group, n=45 in placebo group).

The average age of people enrolled in the trial was 50 years and there was a very strong predominance of female participants.

Table 1: Baseline Characteristics by Treatment Group

	Active				Placebo				Comparison Between-group p.
	N	Min	Max	Mean (SD)	N	Min	Max	Mean (SD)	
Female	48			100% female	47			98% female	
Age	48	27	72	49.94 (10.00)	48	31	71	51.02 (9.26)	0.583
MADRS Depression Scale	48	16	43	24.63 (4.91)	48	8	32	23.29 (4.34)	0.162
Beck Depression Index	48	3	49	31.02 (9.52)	46	9	55	32.46 (10.20)	0.483
Zung Anxiety Scale	48	26	66	46.15 (8.47)	47	24	66	45.64 (9.17)	0.780
PROMIS Sleep Scale	48	16	37	29.46 (4.98)	47	16	40	30.19 (5.36)	0.492

Results

MADRS Scores

At baseline, MADRS scores in both groups showed a similar distribution of mild to moderate continued depressive symptoms. After 8 weeks, 20 of 48 participants (41.8%) in the active group had an improvement of ≥50%, compared to 2 of 48 participants in the placebo group. This was a statistically significant difference between groups in favor of the active treatment group (p<0.001).

Change in mean MADRS scores from baseline to week eight was a secondary outcome for the study. MADRS mean scores decreased from 24.63 to 15.19 in the active group (-38%) and from 23.29 to 21.23 (-9%) in the placebo group. The difference between groups was statistically significant (p<0.001), see Table 2 and Figure 2.

Figure 1: Participants per treatment group achieving ≥50% reduction in MADRS scores at week eight

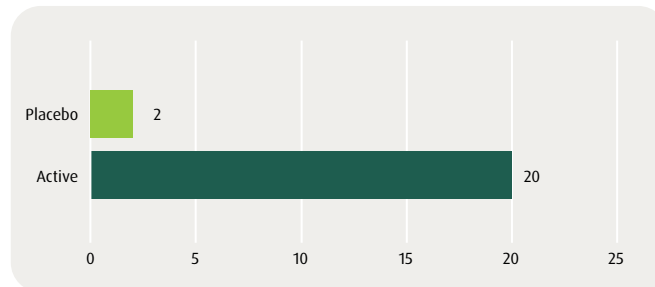


Table 2: MADRS Mean Score Results

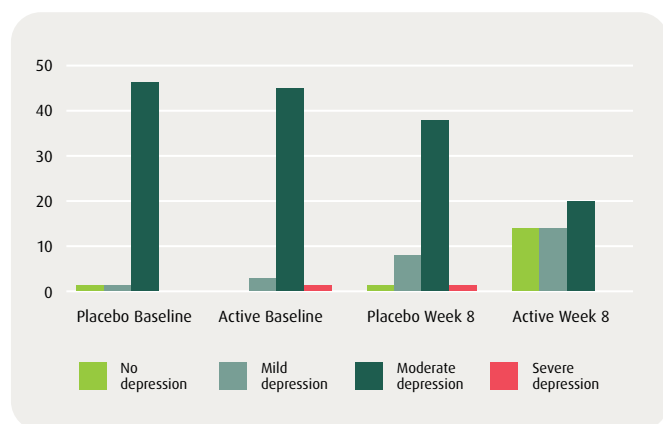
Active (n=48)			Placebo (n=48)			Between Group Difference
Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	P Value
24.63 (4.91)	15.19 (8.06)	-9.44 (-38.3%)	23.29 (4.34)	21.23 (5.59)	-2.06 (-8.9%)	<0.001

Figure 2: Mean MADRS Depression Score – Change Over Time



Using the defined categories of depression severity for the MADRS scores, the active group as a whole moved from a moderate to a mild level of depression. The placebo group as a whole remained in the moderate depression category. Looking at the changes in individuals for each group, the active group had a large number of people moving to no depression (n=14) or mild depression (n=14) by week eight, with no-one showing severe depression on completion of the study, see Figure 3.

Figure 3: Categorical Change in MADRS Depression Rating Per Treatment Group at Baseline and Week 8



Beck Depression Inventory-II

Both active and placebo groups began the study with a high level of severe depression (n=27 and n=26 respectively) and moderate depression (n=19 and n=16 respectively). At the end of the study, the active group showed the majority of participants had moved to either minimal (n=20) or mild (n=11) depression. At the end of the study, the majority of participants in the placebo group stayed in the moderate depression category, with a much smaller number showing minimal (n=9) or mild (n=7) depression, see Figure 4 and 5.

Figure 4: Beck Depression Inventory-II Change Over Time

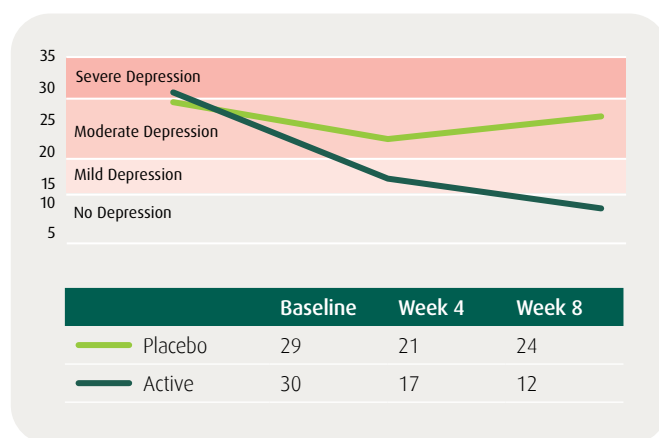
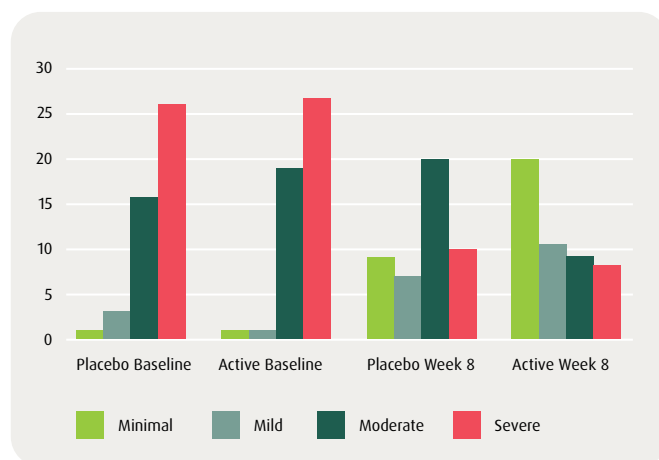


Figure 5: Categorical Change of BDI-II Depression Ratings Per Treatment Group



Zung's Self-rating Anxiety Scale

Zung's SAS mean scores decreased from 46.15 to 35.83 (-22%) in the active group and from 45.64 to 39.19 (-14%) in the placebo group. The difference between groups was statistically significant (p=0.010) when tested with repeated-measures ANOVA. There was also a statistically significant difference in response to the question "I fall asleep easily and get a good night's rest" (p=0.012) and "I feel that everything is all right and nothing bad will happen" (p=0.017).

Figure 6: Change in Zung Mean Total Score for Treatment Groups at Baseline and 8 weeks

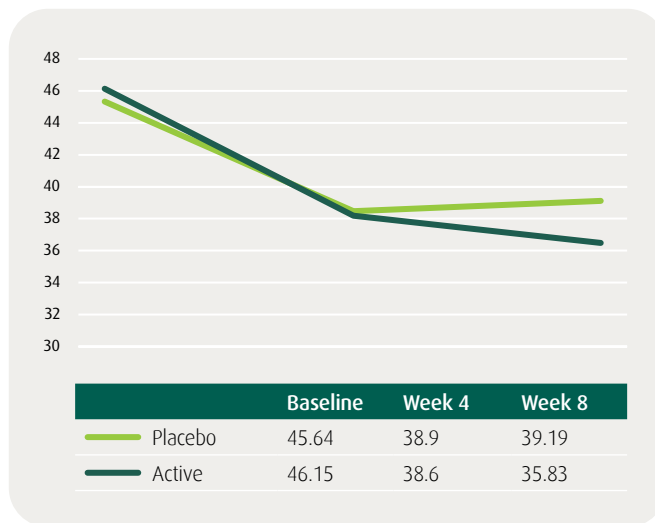


Table 3: Zung's Self-rating Anxiety Scale Results

Active (n=48)			Placebo (n=48)			Between Group Difference
Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	ANOVA P Value
46.15 (8.47)	35.83 (8.64)	-10.31 (-22.4%)	45.64 (9.17)	39.19 (7.28)	-6.45 (-14.1%)	0.01

PROMIS Sleep Scale

PROMIS Sleep Scale mean scores decreased from 29.46 to 21.98 (-25%) in the active group and from 30.19 to 25.66 (-15%) in the placebo group. The difference between groups was statistically significant when tested with t-test for baseline to week 8 (p=0.037).

Figure 7: PROMIS Sleep Disturbance Mean Total Score for Treatment Groups at Baseline and 8 Weeks

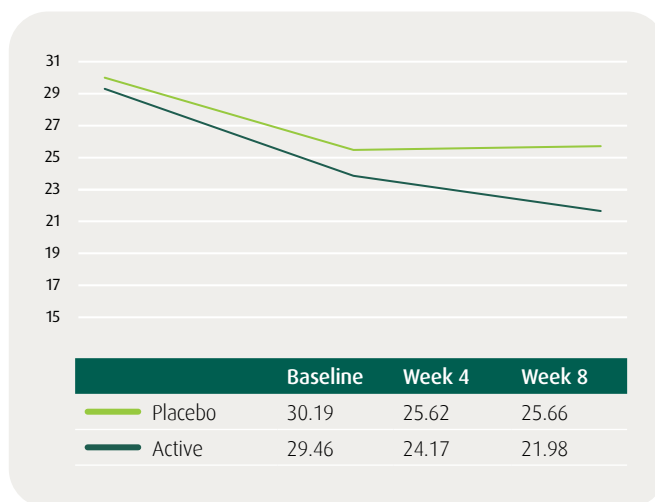


Table 4: PROMIS Sleep Disturbance Scale Results

Active (n=48)			Placebo (n=48)			Between Group Difference
Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	Baseline Mean (SD)	Week 8 Mean (SD)	Baseline to Week 8 Mean Change (%)	T-Test P Value
29.46 (4.98)	21.98 (8.21)	-7.48 (-25.4%)	30.19 (5.36)	25.66 (5.6)	-4.53% (-15%)	0.013

Patient Global Impression of Change

Patient Global Impression of Change (PGI-C) was completed at week 4 and week 8 to obtain information about how each of the participants were feeling their mood and depression symptoms may have changed over the course of the study. Results show that at week 8 there were 11/47 (23.4%) who felt very much improved in the active group, compared to just 1/47 in the placebo group (2.2%), see Table 5 and Figure 8. The mean score was 2.3 at week 8 for the active group and 2.7 at week 8 for the placebo group. Lower scores indicate a greater impression of improvement. This difference was statistically significant (p=0.008).

Figure 8: Patient Global Impression of Change Scores at Week 8

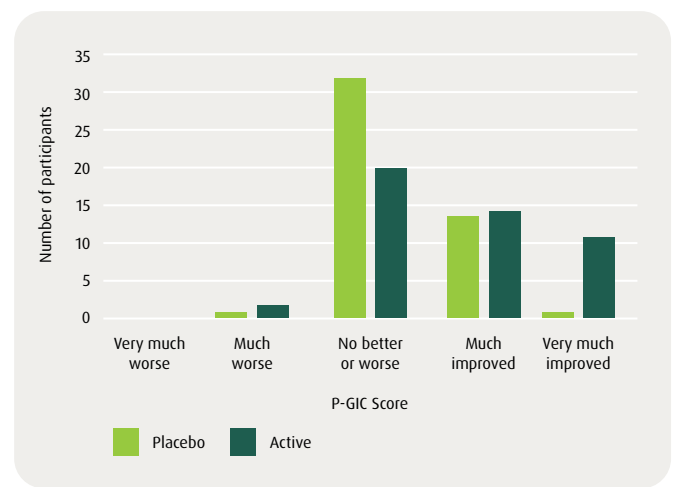


Table 5: Patient Global Impression of Change Results

Level of improvement	Active week 4 (n=43)	Placebo week 4 (n=46)	P value	Active week 8 (n=47)	Placebo week 8 (n=46)	P value
Mean PGI-C score	2.62 (0.64)	2.72 (0.65)	0.459	2.29 (0.87)	2.70 (0.55)	0.008
Very Much Improved	2	1		11	1	
Much Improved	15	15		14	13	
No Better or Worse	24	28		20	32	
Much Worse	2	2		2	1	
Very Much Worse	0	1		0	0	

Safety

There were five withdrawals throughout the study, three in the placebo group and two in the active group. Only one of these was potentially related to an adverse event, with the participant experiencing increased depression, bloating and loose bowels reported at week 8, they were on the placebo arm.

There were sixteen participants reporting minor adverse events (9 on active and 7 on placebo).

Conclusion

This study shows positive effects on mood, anxiety, and depression using a specific herbal formulation containing Curcumin, Boswellia, Gotu Kola and Bupleurum, targeting neuropathways, reinforcing the growing body of evidence that herbal medicines can offer neuroprotective, neuromodulatory, and neuroadaptive benefits. As the first clinical trial of this combination, it builds on existing *in vitro*, animal and limited human studies that suggest these herbs positively impact mental health, and the effects may be linked to changes in BDNF levels and reductions to neuroimmune disruption, oxidative damage, and other inflammatory-driven processes.

This herbal formulation, containing Turmeric as CurQfenE40®, Boswellia as BosQfen, Bupleurum and Gotu Kola, appears to be a safe and effective adjunct treatment in adults on a stable dose of antidepressant medication with persistent low mood.

*Submitted and under review for publication.