

Effect of a water extract of *Curcuma longa* on emotional states in healthy participants

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Physiological symptoms of mood disturbances, such as fatigue or anxiety, are closely related to inflammation in the central nervous system or the whole body. *Curcuma longa* is widely used as a dietary spice and has been reported to have anti-inflammatory activity. To investigate the effect of a water extract of *C. longa* (WEC) on emotional states, a randomized, double-blind, placebo-controlled, parallel-group study was conducted with healthy participants. Forty-eight participants were randomly assigned to receive five tablets containing 150 mg WEC and 0.40 mg bisacurone (L-WEC group), five tablets containing 900 mg WEC and 2.40 mg bisacurone (H-WEC group), or matching placebo tablets (placebo group) daily for 8 weeks. Participant emotional states were measured every 4 weeks using the Profile of Mood States (POMS). The changes from week 0 to week 8 in the fatigue score of the POMS were significantly lower in the L-WEC group than in the placebo group. This result suggests that daily intake of 150 mg WEC may positively influence emotional fatigue, and further investigation focused on emotional fatigue is needed.

Key words: *Curcuma longa*, emotional states, POMS, total mood disturbance, fatigue

INTRODUCTION

Physiological symptoms of mood disturbance, such as fatigue or anxiety, are both a medical issue associated with chronic disease [1, 2] and a social issue, as healthy people may experience such symptoms as a result of common physical or mental stressors [3–5]. The reported prevalence of fatigue symptoms ranges from 7% to approximately 45% [6].

Recent research indicates that mood disturbances such as fatigue or depression are closely related to inflammation in the central nervous system (CNS) or the whole body [7]. Fatigue symptoms during or after exercise are attributed to an increase in blood inflammatory cytokines and may be a result of CNS inflammatory reactions, or “neuroinflammation” [8]. Both acute psychological stress under laboratory conditions [9] and chronic stress [10] also increase circulating inflammatory cytokines. Fatigue symptoms induced by endotoxin challenges are associated with increases in brain inflammation characterized by microglial activation and in blood inflammatory cytokines [11]. In chronic fatigue syndrome/myalgic encephalomyelitis patients, neuroinflammation is widespread across brain areas and is associated with the severity of neuropsychologic symptoms [12].

Cyclooxygenase-2 inhibitors can decrease fatigue symptoms in patients with multiple sclerosis [13] and improve

symptoms associated with major depression [14]. Inhibition of CNS or whole body inflammation has been put forward as a new antidepressant drug approach [15].

Curcuma longa is a rhizomatous herbaceous perennial plant of the ginger family that is cultured in tropical or subtropical regions worldwide. The deep yellow-orange powder known as turmeric is produced by boiling and drying *C. longa* rhizomes and is commonly used as a spice or traditional drug, especially in Asia [16]. Research shows that a water extract of *C. longa* (WEC) has an anti-inflammatory effect in *in vitro* models [17] and animal models [18, 19]. A WEC also has an anti-stress effect in animal models [20]. Taking into account the relationship between mood disturbances and inflammation [7], a WEC might ameliorate mood disturbances such as fatigue or anxiety through its suppressive effect on CNS or whole body inflammation.

There have been no clinical trials assessing the effects of a WEC on mood states. The aim of this study was to demonstrate the effect of a WEC on mood states in healthy participants. A randomized, double-blind, placebo-controlled clinical trial was designed and conducted to evaluate the effects of an 8-week WEC treatment on mood states measured with the Profile of Mood States (POMS). Additionally, a safety assessment of oral WEC intake was conducted.

MATERIALS AND METHODS

Participants

Healthy participants aged 20–64 years old who regularly drank alcohol were recruited in April 2014 and assessed for eligibility. The inclusion criteria were as follows: aspartate aminotransferase level <40 IU/l, alanine aminotransferase

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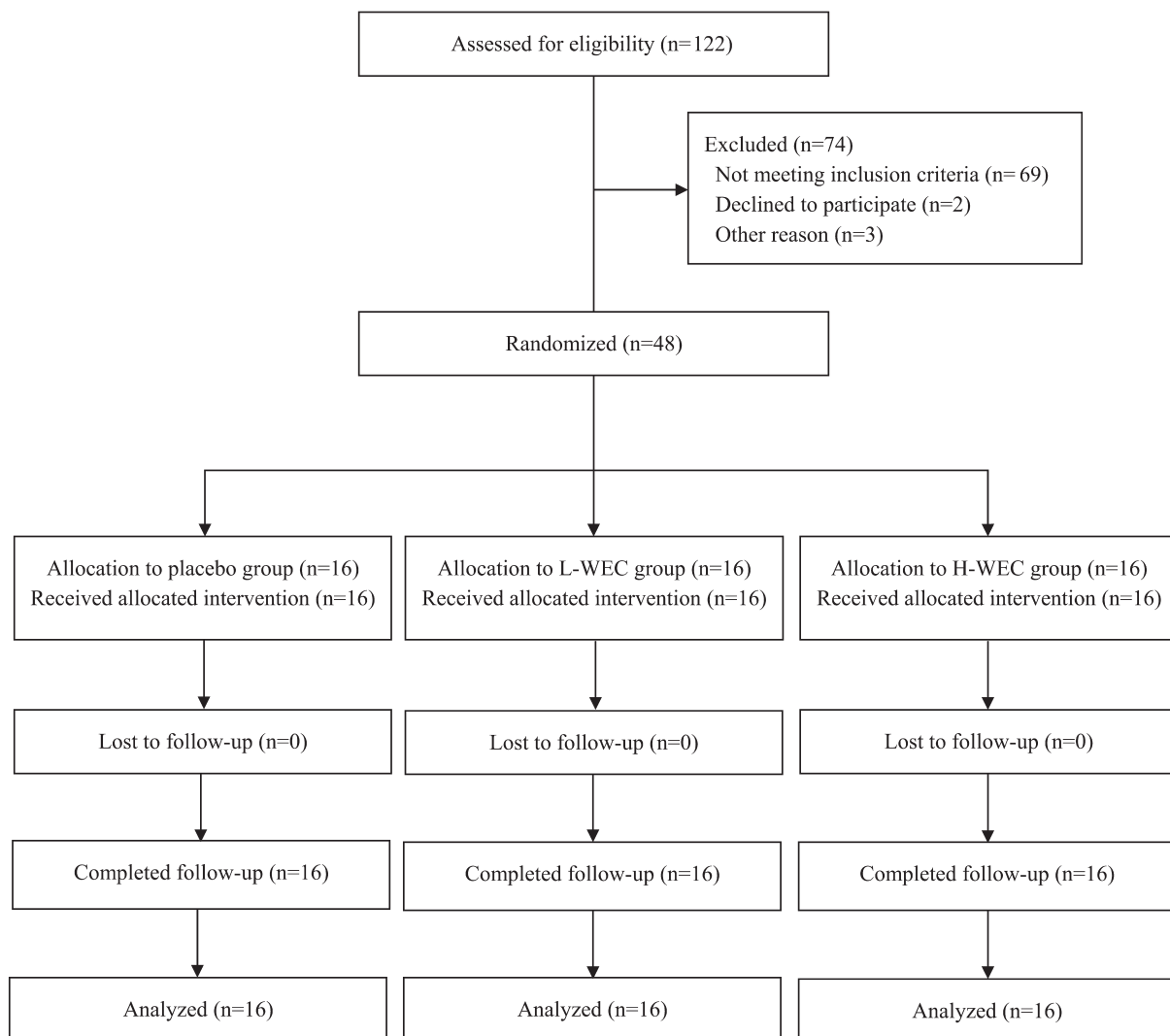


Fig. 1. Flow chart of study participants.

level <45 IU/l, body mass index of 18–30 kg/m², and an alanine aminotransferase level ranking in the highest 48 among the participants. The exclusion criteria were as follows: current history of illness including diabetes, liver, renal, or cardiac disease; a previous history of serious diseases; current treatment with prescription medicine; poor compliance with the clinical trial guidelines; or inappropriate participants as judged by the investigator. Of 122 healthy participants recruited, 48 (27 men and 21 women; mean age 45.4 years) were eligible and randomly assigned to three groups (n=16, respectively). Each group consumed five tablets daily containing 0, 150, or 900 mg WEC for 8 weeks. No participants dropped out during the intervention (Fig. 1). Participants were instructed to continue their habitual diets during the study. Approval of the protocol was obtained from the ethics review board of the medical corporation Kenshokai Fukushima Health Management Center (Osaka, Japan), and

the approval number was 25915. The study was conducted in accordance with the Declaration of Helsinki of 1975 (revised 2013). The procedures were fully explained to the participants, and written informed consent was obtained from each participant before the beginning of the study.

Preparation of the WEC

The water extract of *C. longa* was prepared according to methods described previously [17]. Briefly, *C. longa* rhizomes were incubated with hot water (98°C, 1 hr). The supernatant was concentrated by heating under reduced pressure, mixed with dextrin, and then spray-dried into powder. The powder contained 667 g/kg WEC and 1.78 g/kg bisacurone as the active components.

Experimental design

Forty-eight healthy participants were selected as candidates

Table 1. Baseline characteristics of the enrolled participants

	Placebo	L-WEC	H-WEC
Number of participants	16	16	16
Sex, male:female	9 : 7	9 : 7	9 : 7
Age (yrs)	46.4 ± 9.5	45.0 ± 13.2	44.8 ± 9.4
Weight (kg)	60.4 ± 10.7	60.1 ± 9.0	61.9 ± 10.3
BMI (kg/m ²)	23.1 ± 1.9	22.9 ± 3.1	23.1 ± 2.8
POMS			
Tension–anxiety	43.3 ± 9.5	40.8 ± 7.0	43.4 ± 11.3
Depression–dejection	44.6 ± 8.7	44.7 ± 6.3	45.3 ± 6.6
Anger–hostility	43.3 ± 4.3	46.6 ± 9.1	42.9 ± 6.9
Vigor	45.9 ± 11.4	49.8 ± 8.0	42.8 ± 10.7
Fatigue	44.6 ± 7.5	44.1 ± 7.7	42.8 ± 7.6
Confusion	46.9 ± 10.9	44.6 ± 6.9	47.1 ± 6.7
Total mood disturbance	177 ± 39	171 ± 30	179 ± 34

BMI: body mass index; POMS: Profile of Mood States; WEC: water extract of *Curcuma longa*. Values are numbers or means ± standard deviations.

for enrollment in a randomized, double-blind, placebo-controlled, parallel-group study. Participants were randomly assigned to three groups. Randomization was performed using a sequential series of numbered sealed envelopes that contained computer-randomized allocations to each group. After assignment, the participants consumed either five tablets containing 150 mg WEC and 0.40 mg bisacurone (L-WEC group), five tablets containing 900 mg WEC and 2.40 mg bisacurone (H-WEC group), or five tablets in which the WEC was substituted with dextrin (placebo group) daily for 8 weeks. The participants were instructed not to change their lifestyle, including their dietary habits. Throughout the study, participants recorded their general health, days of medication, and compliance with the dietary regimen daily in a diary. The POMS was performed at weeks 0, 4, and 8 during the intervention and 4 weeks after the end of the intervention. For the safety assessment, anthropometric measurements, biochemical examinations of blood, hematological assessments, and urine tests were performed at weeks 0, 4, and 8 during the intervention and 4 weeks after the end of the intervention. Blood and urine tests were completed by a clinical laboratory testing company, LSI Medience (Osaka, Japan). The study was conducted at the medical corporation Kenshokai Fukushima Health Management Center (Osaka, Japan) from April 2014 to August 2014.

POMS

We analyzed the emotional states of participants using the POMS, which was developed to assess transient distinct mood states [21]. Yokoyama translated the original form into Japanese and developed a brief 30-item version of the POMS to reduce participant burden. The Japanese version of the POMS-Brief has been demonstrated to be reliable and valid for Japanese samples [22]. Each item is self-rated on a scale of 0–4, ranging from “not at all” to “extremely.” Scores for six emotional states are then calculated: tension–anxiety,

depression–dejection, anger–hostility, vigor, fatigue, and confusion. A seventh score of total mood disturbance is also calculated by subtracting the score of the one positively scored subscale, vigor, from the sum of the other five subscales.

Statistical analysis

Comparisons of the baseline values between the placebo group and the treatment groups (L-WEC and H-WEC groups) were performed using Dunnett’s test for multiple comparisons. The same test was used to compare changes from baseline for POMS total scores and the six emotional state scores between the placebo group and the treatment groups (L-WEC and H-WEC groups). All analyses were performed using Statcel4 software (OMS Publishing, Tokorozawa, Japan). A probability value of $p < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline characteristics

All 48 participants completed the study and were included in the statistical analysis. The baseline characteristics are shown in Table 1. There were no significant parameter differences between the placebo group and the treatment groups.

POMS scores

Changes in POMS scores from weeks 0 to 4 and 8 are shown in Table 2. Fatigue scores tended to increase over time in the placebo group, but not in the WEC groups. The changes in fatigue scores from weeks 0 to 8 were significantly lower in the L-WEC group than in the placebo group. None of the other POMS scores showed significant between-group differences at any time point.

Safety assessment

Twelve adverse events (AEs) were recorded during the

Table 2. Changes from baseline scores for emotional states in the Profile of Mood States (POMS)

	Week 4	Week 8	4 weeks after intervention
Tension–anxiety			
Placebo	-0.9 ± 4.2	-1.3 ± 4.9	-0.2 ± 5.9
L-WEC	-1.6 ± 5.1	-1.2 ± 5.1	0.6 ± 7.4
H-WEC	-1.8 ± 8.1	-3.4 ± 9.4	-3.6 ± 9.3
Depression–dejection			
Placebo	0.8 ± 3.8	0.3 ± 2.8	0.6 ± 4.5
L-WEC	-0.9 ± 7.3	-0.1 ± 8.8	0.6 ± 9.3
H-WEC	-2.1 ± 5.5	-1.7 ± 6.3	-1.9 ± 6.3
Anger–hostility			
Placebo	0.8 ± 6.4	-0.5 ± 6.5	0.3 ± 5.1
L-WEC	-3.6 ± 7.5	-3.3 ± 5.8	-2.5 ± 8.1
H-WEC	-2.3 ± 6.8	-1.7 ± 5.5	-0.7 ± 5.1
Vigor			
Placebo	-5.3 ± 8.0	-5.3 ± 7.9	-5.8 ± 8.4
L-WEC	-2.7 ± 6.5	-2.4 ± 7.8	-3.6 ± 7.6
H-WEC	-1.8 ± 7.0	-1.6 ± 5.6	-4.8 ± 5.4
Fatigue			
Placebo	1.6 ± 5.0	3.1 ± 5.3	2.4 ± 5.8
L-WEC	-0.8 ± 5.5	-1.0 ± 5.3*	1.1 ± 6.6
H-WEC	-0.3 ± 2.8	-0.7 ± 4.7	-0.1 ± 5.9
Confusion			
Placebo	2.1 ± 3.7	1.1 ± 5.6	1.6 ± 4.5
L-WEC	-0.7 ± 5.8	0.6 ± 5.5	0.3 ± 6.9
H-WEC	-0.3 ± 5.0	1.6 ± 6.4	0.9 ± 6.5
Total mood disturbance			
Placebo	9.8 ± 15.3	7.9 ± 16.9	10.4 ± 18.7
L-WEC	-4.9 ± 22.2	-2.6 ± 22.0	3.6 ± 30.8
H-WEC	-4.9 ± 25.0	-4.3 ± 27.2	-0.6 ± 27.9

WEC: water extract of *Curcuma longa*. Data are mean values ± standard deviations. *p<0.05 compared with the placebo group at each indicated time point.

study. There were five AEs in the placebo group: common cold symptoms (2), dull feeling in the stomach (1), malaise (1), and abdominal pain and stomach discomfort (1). There were two AEs in the L-WEC group: common cold symptoms (2). There were five AEs in the H-WEC group: diarrhea (1), abdominal pain (1), headache, nausea, and stomach discomfort (1), conjunctivitis (1), and gastrocnemial muscle cramp (1). All AEs were judged by a physician to be mild and unrelated to the dietary intervention. On the basis of the results from the anthropometric measurements, biochemical blood examinations, hematological assessments, and urine tests during the study, a physician also judged that the dietary intervention did not lead to any clinically significant adverse changes.

DISCUSSION

The findings show that fatigue scores tended to increase over time in the placebo group but not in the L-WEC and

H-WEC groups. As a result, the changes in fatigue scores from weeks 0 to 8 were lower in the WEC groups than in the placebo group; in particular, there was a significant difference between the L-WEC group and the placebo group. These results suggest that daily intake of 150 mg WEC may positively influence emotional fatigue.

As previously mentioned, a WEC has an anti-inflammatory effect in *in vitro* models [17] and animal models [18, 19]. Research indicates that mood disturbances such as fatigue or depression are closely related to CNS or whole body inflammation [7], and inhibition of CNS or whole body inflammation has been put forward as a new approach for antidepressant drugs [15]. Therefore, the effect of the WEC on POMS fatigue scores could be attributed to its anti-inflammatory effect. However, to clarify the association between the effect of a WEC on emotional state and inflammation, studies that include measurement of serum inflammatory markers are needed.

To date, at least 235 compounds, primarily phenolic compounds and terpenoids, have been identified from *C. longa* [23]. Curcumin, an important component, has an anti-inflammatory effect [24]. On the other hand, curcumin-free turmeric components such as those in a WEC possess numerous biological activities, including anti-inflammatory activity [25]. Bisacurone has been identified as one of these components [26], and its anti-inflammatory effects have been reported [27]. A water extract of *C. longa* inhibits ethanol-induced liver injury in mice via inhibition of liver inflammation, which is equivalent to the inhibitory effect of bisacurone [19]. If a WEC's action on emotional fatigue is attributed to its anti-inflammatory effect, bisacurone may contribute, at least in part, to this anti-inflammatory effect. However, an examination of the effect of a purified bisacurone compound on POMS fatigue scores is needed.

Further research is needed on the active components of the WEC other than curcumin and bisacurone. It has been suggested that further research on turmeric applications should consider holistic approaches that take into account the chemical complexity of turmeric and its broad foundation as a traditional medicine [28].

In conclusion, our results suggest that daily intake of 150 mg WEC may positively influence emotional fatigue. To clarify the effect of a WEC on emotional states such as fatigue, further investigation is needed.

Conflict of interest

All authors are employees of House Wellness Foods Corporation, and this work was funded by House Wellness Foods Corporation.

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