ORIGINAL ARTICLE

The Effects of Two-week Fungal-based Essence in Healthy Malaysian Adults: A Pilot Randomized Controlled Trial

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ABSTRACT

Introduction: Despite many edible fungi being claimed to be potential sources of functional food, clinical trials on the effect of fungal-based essence on cognitive function are generally lacking. This study aimed to determine the effect of a commercialised fungal-based essence on general health, perceived stress, and fatigue levels, derived from their questionnaire-based perceptions after the consumption of fungi extract. **Materials and methods:** A randomised, double-blind, placebo-controlled clinical trial was conducted among the healthy Malaysian adult volunteers using the hot water extraction of five edible fungi species, i.e., *Boletus edulis, Cordyceps militaris, Ganoderma lucidum, Hericium erinaceus,* and *Lentinula edodes*. Forty participants were allocated a 3:1 ratio to receive fungal-based essence and chicken essence. The questionnaire was carried out at baseline and on day 14, with data from 40 participants being analysed, while the 10-person control group was given chicken essence. **Results:** The T-test analysis showed that the ingestion of fungal-based essence improved general health, lowered perceived stress, and reduced fatigue levels significantly in both the test and control groups. **Conclusion:** Our findings support the consistent uptake of fungal-based essence, which could be effective for the improvement of general health and overcoming stress, as well as a promising candidate for use as an anti-fatigue food.
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INTRODUCTION

Fatigue and perceived stress have become common health issues among adults. While stress arises from the physiological and psychological reactions to challenges or threats, previous perceived stress can trigger fatigue (1), which is defined as the loss of strength due to mental or physical exertion, increasing the risk of various diseases (2). Fatigue is generally classified as physical fatigue and psychological fatigue (3). Physical fatigue happens when the body's muscles are engaged in physical movements for an extended period of time. It is considered physical tiredness or weakness due to physical exertion or prolonged periods of activity. Psychological fatigue, on the other hand, refers to a state of exhaustion or weariness that may affect the mind and cognitive processes rather than the body. It is usually caused by prolonged or intense mental activities or emotional factors.

In recent years, there has been a growing interest in natural nutrients and supplements as potential solutions to improve health levels, i.e., the development of immunity to sickness and the enhancement of cognitive functions. Eventually, researchers have generated observational and efficacy data to support the role of a quality diet in reducing depression risk and managing its symptoms (4). With studies that could provide evidence that certain foods, diets, and their components have a potential impact on human health, the consumer's perception of food has changed extensively over the years. Foods that may improve the overall state of the body while assisting in disease treatment are known as functional foods (5).

In the Asian region, the product of the water extraction process using either the whole plant or livestock, i.e., ginseng and chicken, is considered a functional food that is popular among the locals (6). The common practice involves dissolving the raw ingredients of these functional foods in water for several hours at a high temperature. This process removes fat and cholesterol and forms liquid nutrients known as the essence, which the locals then consume for health preservation purposes. Based on the literature, the chicken essence has the potential to metabolise stress-related substances in the blood, promote recovery from mental fatigue, increase exercise performance, and reduce physical fatigue (7). The plant-based essence, such as the ginseng essence, contains at least four different herbs, including ginseng (*Panax ginseng*), American ginseng (*P. quinquefolius*), lotus seed (*Nelumbo nucifera*), and the lily bulb (*Lilium longiflorum*). The pharmacological properties and nutritional effects of these herb combinations have proven to be powerful in hepatoprotection (8).

Despite the popularity of functional food consumption, there has been a lack of scientific study on fungal-based essence. The majority of studies have focused on the nutrient richness of edible fungi for a healthy diet and weight management (9), as well as the balanced amino acid profile of edible fungi as a potential source for protein uptake (10). Other studies highlighted the domestication and harvesting of edible fungi as a primary product for food (11) as mushrooms and mycelia provide dietary protein, lipids and fatty acids, vitamins, fibre, and flavour (12). Therefore, in addition to their use in culinary applications, fungi with significant nutritional values also serve as tools for preventing, healing, or treating various health conditions and diseases. Therefore, it is believed that medicinal fungi engage more than hundreds of therapeutic functions, such as antitumor, immunomodulating, antioxidant, and antidiabetic, among others (13).

In the present study, we examine the effect of a commercialised fungal-based essence on general health, perceived stress, and fatigue levels among healthy adults in Malaysia. The fungal-based essence contains five different edible fungi species, including *Boletus edulis, Cordyceps militaris, Ganoderma lucidum, Hericium erinaceus,* and *Lentinula edodes*. These fungi species contribute to various health developments, such as improving sleep quality, neuroprotective, antidepressant effects, cell-mediated immunity, promoting cellular energy production, reducing non-alcoholic fatty liver disease, cardiovascular and metabolic disease, relieving fibromyalgia, anticancer, anti-ageing, etc. (14, 15, 16, 17). Under the hypothesis that the fungal-based essence would perform similarly to the chicken essence in general, its consumption over a certain time period should be able to improve the general health while also reducing the perceived stress and fatigue of its consumers. The findings of this study would outline a foundation for consumers, nutritionists, and food-related industries to identify the potential of fungal-based essence to improve general health and reduce stress and fatigue.

MATERIALS AND METHODS

Participants

Recruitment for the study involved face-to-face enquiries about interest in participating. Individuals who are interested in participating were required to meet the specific inclusion and exclusion criteria. A total of 40 healthy adult participants, between the ages of 18 and 59, who were willing to consume the fungal-based essence drink through convenience sampling, were enrolled. The sample size was calculated based on the equation below, while the recruitment of participants was based on a stratified randomisation of the gender group. The group randomly assigned the participants to either the treatment or the control group. All of whom were provided with written informed consent prior to participation (Supplemental Data 1).

$$n = \left\{ \frac{z_{\alpha/2} + z_{\beta} \bullet SD}{d} \right\}^2$$

(1) in which,

n = the required samples size
$Z_{\alpha/2}$ = Z-value corresponding to the desired significance level
Z_{β} = Z-value corresponding to the desired power (1-β)
SD = standard deviation
d = allowable difference (effect size)

Experimental design

Participants used a simple random sampling method to assign a 3:1 ratio of the test group to the control group under a double-blinded design. We use a 3:1 ratio to achieve an optimal balance between gathering sufficient information about the test's effects. A larger test group size relative to the control group can enhance the statistical power of the study to detect differences in outcomes. As a result, having more data points in the test group can aid in better estimating the effect size (18). Because both of the essence drinks for the test and control groups have an identical colour appearance, they were number-labelled for identification and tracking purposes. The blinding code is kept strictly confidential by the principal investigators until the study is completed. For the test group, 30 participants would receive the fungal-based essence drink, while 10 participants from the control group would receive the chicken essence drink. Every participant received a total of 14 bottles, each containing 75 mL of fungal-based essence, to consume daily over 14 To enhance the consumption experience, the participants were advised to warm the essence drink in hot water before consuming it after breakfast. fast. This study used a commercially produced fungal-based essence. Both fungal-based essence and chicken products were provided by Happy Health (M) Sdn Bhd (138919-K). Only the blind code will reveal any serious adverse effects related to consumption. Participants could, however, request that their assigned groups be revealed on the 30th day after project completion.

Inclusion criteria
All participants must be verified as Malaysian citizens, aged between 18 and 59, who have not consistently consumed any form of essence drink for the past three months. The body mass index of each participant should be in the normal range. Participation should be voluntary, and participants should agree to comply with the relevant ethically informed consent.

Exclusion criteria
Volunteers suffering from psychiatric or neurological conditions, as well as chronic or malignant diseases such as cancer, heart conditions, liver problems, renal disorders, or other metabolic diseases, were ineligible to participate in the study. Pregnant and lactating women were not included, and individuals who had participated in investigational drug trials within the four weeks prior to the screening were also excluded. This was done to avoid potential confounding variables. Additionally, volunteers who had consumed food supplements in the two weeks preceding the study were not considered, while professional athletes were excluded to maintain a consistent sample group. Individuals who had undergone significant lifestyle changes in the four weeks prior to screening were also ineligible. To prevent adverse reactions during the study, volunteers with a history of allergies to mushrooms and chicken were also excluded.

Questionnaire observation indices
The primary outcome measures for this study were based on the perceived health and well-being, energy levels, and stress levels of the participants in the test group. These were measured using three types of validated questionnaires, i.e., the General Health Questionnaire (GHQ), Perceived Stress Scale (PSS), and Chalder Fatigue Scale (CFS). The participants were required to complete these questionnaires before starting the intervention (days 0 and 5) in the presence of an invigilator from the project team.

The 30-item GHQ serves as a screening tool for mental disturbances, aiding in the identification of states of depression, anxiety, or psychiatric morbidity in the respondents (Supplemental Data 2) (19). For studies carried out in Malaysia, the GHQ-30 has demonstrated reliability and stability, with a Cronbach's α coefficient of 0.93, indicating a satisfactory level of internal consistency among the scale items.

The PSS is a tool for assessing stress levels (20). The PSS consists of 10 items, of which items 4, 5, 7, and 8 receive reverse scoring. Each item is rated on a 4-point scale, resulting in a total possible score of 40 (Supplemental Data 3). The PSS used in this study has a coefficient of 0.78, according to the Cronbach’s α.

The CFQ, on the other hand, is a questionnaire that assesses the level of fatigue associated with exhausting illnesses. The 11-item CFQ is often divided into two parts (Supplemental Data 4). The first part measures physical fatigue (questions 1–7), and the second part measures mental fatigue (questions 8–11). This study modifies the CFQ from the FS-14 fatigue questionnaire (21). The overall Cronbach’s α coefficient for the CFQ used in this study is 0.88, indicating a high level of internal consistency among the 11 evaluated items. The scale uses a 3-point Likert scoring system, where 0, 1, 2, and 3 represent experience levels of “less than usual”, “no more than usual”, “more than usual”, and “much more than usual”, respectively.

Statistical analysis
Data analyses were conducted using the IBM Statistical Package for the Social Sciences (SPSS) Statistics 22.0. The data are presented in the form of averages and standard deviations, as well as medians and ranges, and should meet the criteria for a normal distribution. Paired t-tests are used to compare within the test and control groups, and independent t-tests are applied for the between-group comparisons. In cases where the data do not conform to a normal distribution, the Wilcoxon signed-rank test is used to compare within-group comparisons, while the Mann-Whitney U test is applied for between-group comparisons.

Ethical Clearance
This study was approved by the Research Ethics Committee, Faculty of Health and Life Sciences, INTI International University, No. INTI-IU/FHLS-RC/BPHTI/JAN2023/005.

RESULTS

A total of 40 participants were recruited for this study, and their ages ranged from 19 to 52 years (mean = 34). The sampled population was gender-balanced, with 22 females and 18 males. Among them, six females and four males were randomly placed in the control group, and no dropout was recorded. The respondents reported no adverse effects throughout the study period.

Changes in health
For the GHQ, the average health condition prior to intervention of study, for both the test group (n=30) and control group (n=10) were 37 (±15.05) and 42.1(±5.21), respectively (Table I). There was no significant difference between the two groups before the intervention of the study (0.355, $p > 0.05$), as well as after the 14-day test period (0.484, $p > 0.05$). After two weeks of taking the essences every day, the GHQ score went down for both the test group and the control group (test: 12.83±7.12, control: 11.1±5.21). There was a significant difference in the change in score between “before ingestion” and “after ingestion” (0.000, $p < 0.05$).

Table I: Results of score for the GHQ before and after ingestion

Test (n=30)			Control (n=10)			Significance	
Before	After	Before-After	Before	After	Before-After	Before-Before	After-After
37.0±15.05	12.83±7.12	0.000*	42.1±14.53	11.1±5.21	0.000*	0.355	0.484

Note: The finding is significant when *P<0.05.

Perceived stress

For the perceived stress level (Table II), both the test group and control group had similar median scores, which were 22 and 22.5, respectively. The reduction in perceived stress among participants in both groups after ingestion was significant, in which the median score after ingestion was 15.0 and 17.5, respectively, and the p-value for both groups was 0. The study detected no significant difference between the test group and control group before the intervention (0.355, p > 0.05) or after the 14-day test period (0.484, p > 0.05).

Table II: Results of score for the PSS before and after ingestion

Test (n=30)			Control (n=10)			Significance	
Before	After	Before-After	Before	After	Before-After	Before-Before	After-After
22.0 (8.00)	15.0 (6.50)	0.000*	22.5 (2.5)	17.5 (2.50)*	0.007*	0.423	0.627

Note: The finding is significant when *P<0.05.

Fatigue sensation

Analysis of the CFS in both physical and psychological forms revealed significant differences for both the test group and the control group (Table III). Between days 0 and 15, the p-value for both groups was less than 0, with p = 0.000 for the test group and p = 0.007 for the control group. Additionally, the CFS for both groups is similar in both the physical and psychological forms, with the median score before the intervention of the study being 12.0 and 4.5, as well as 11.0 and 5.5 for the test group and control group, respectively. Prior to the study intervention, the median for the total CFS was the same for both groups, which was 17.0, while the total median of the CFS was 5.5 and 6.0 for the test group and control group, respectively. No significant difference was observed between the two groups, either before or after the intervention of the study.

Table III: Results of score for the CFS before and after ingestion

	Vegan (n=30)			Control (n=10)			Significance	
	Before	**After**	**Before-After**	**Before**	**After**	**Before-After**	**Before-Before**	**After-After**
Physical fatigue	12.0 (3.00)	3.0 (4.50)	0.000*	11.0 (5.50)	3.5 (5.00)	0.007*	0.321	0.617
Psychological fatigue	4.5 (2.25)	2.0 (3.00)	0.000*	5.5 (4.25)	3.0 (2.25)	0.007*	0.44	0.962
Total	17.0 (7.25)	5.5 (6.75)	0.000*	17.0 (9.75)	6.0 (6.75)*	0.007*	0.802	0.605

Note: The finding is significant when *P<0.05.

DISCUSSION

The study was conducted on 40 participants, of whom 30 were allocated to the test group. The number of test subjects (excluding the control group) is somewhat less than those reported in similar studies in Malaysia that analysed the effect of chicken essence consumption, i.e., 38 (22) and 56 (23). Nevertheless, the sampling size is sufficient to provide reliable findings, as the suggested sample size per group for a pilot study with no prior information would require a minimum of 12 per group (24). Between the test group and control group of this study, it is anticipated that the participants consuming either the fungal-based or the chicken-based essence experienced the same outcome in terms of general health, perceived stress, and fatigue levels. The participants from both groups showed a positive change in their general health level after 14 days. Despite earlier findings revealing that the ingestion of chicken essence could provide beneficial effects to the consumer (25), for the first time, we identified that the ingestion of fungal-based essence over a period could also perform the same. Based on the individual health benefits that the fungal species used in the preparation of the fungal-based essence could deliver, it is expected that the effective absorption of the nutrients from the fungus would somewhat improve the quality of life of the volunteers (26).

The quality of diet could plausibly manipulate mental health (27), and at the same time, healthy eating seems to be one of the useful habits that is protective against experiencing depression and anxiety (28). At least eight pathways, including inflammation, oxidative stress, mitochondrial dysfunction, gut microbiota, tryptophan-kynurenine metabolism, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, epigenetic change, and neurogenensis, may be susceptible to dietary manipulation (27). This study selects fungi species for the preparation of the essence, which contains bioactive compounds proven to affect most depression-causing mechanisms. The biological effects of *Boletus edulis* are associated with mechanisms such as anti-inflammatory (29), anti-oxidative (30), gut microbiota (31), and epigenetic change (32). Meanwhile, *C. militaris* enhances mechanisms such as anti-inflammatory (33), antioxidative (34), HPA axis (33), and neurogenensis (33). *Ganoderma lucidum* also contributes to mechanisms such as anti-inflammatory (35), HPA axis (36), and neurogenensis (37). In the case of *H. erinaceus*, it improves processes like neurogenensis (38) and prevents inflammation (39). It also improves the gut microbiota (40) and works with the HPA axis (39). *Lentinula edodes* also helps with things like reducing inflammation (41), protecting mitochondria (42), taking care of the gut microbiota (43), and changing epigenetics (41). Given the scientific evidence on these biological properties that could contribute to the positive effect of depression-related mechanisms, the positive change in the perceived stress level among the participants that consumed the fungal-based essence is much anticipated.

Polysaccharides also exhibit anti-fatigue activities, and we can evaluate the anti-fatigue effect of the peptides in vivo. For instance, researchers commonly use the force-swimming test to assess mice's swimming endurance following nutrient administration (44). In this study, the fatigue level of the participants in the test group showed a positive improvement, indicating that the fungi used in the preparation of the essence contain anti-fatigue functions. Evidently, this study has determined that three out of five fungi used in the fungal-based essence, namely *C. militaris* (45), *G. lucidum* (46), and *H. erinaceus* (47), possess anti-fatigue properties. However, we do not rule out the possibility that B. edulis and L. edodes do not exhibit such effects, given that traditional Chinese medicine often uses L. edodes as a tonic to counter fatigue associated with ageing (48).

CONCLUSION

This study provides important insights into the effectiveness of fungal-based essence in improving general health, perceived stress, and fatigue levels. Future research on the development of fungal-based essences for physical and mental health can benefit from the findings. It also contributes to the development of evidence-based dietary recommendations. For future similar studies, we suggest including a large sample size of participants and measuring a range of outcomes that are beyond the primary outcomes, such as nutrient uptake, physical activity levels, and health biomarkers. Furthermore, it may be beneficial to conduct a long-term follow-up study to assess the sustainability of the effects of a fungal-based health supplemental diet and investigate any potential adverse effects on the participants. Investigating the effectiveness of a fungal-based diet in combination with other lifestyle interventions, such as exercise, meditation, or stress management techniques, could provide a more comprehensive understanding of the potential benefits of a holistic approach to both physical and mental health.

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