

Original/Alimentos funcionales

Ganoderma lucidum improves physical fitness in women with fibromyalgia

Daniel Collado Mateo¹, Francesco Pazzi¹, Francisco J. Domínguez Muñoz¹, Juan Pedro Martín Martínez¹, Pedro R. Olivares², Narcis Gusi¹ and José C. Adsuar¹

¹Faculty of Sport Science, University of Extremadura, Cáceres, Spain. ²Instituto de Actividad Física y Salud, Universidad Autónoma de Chile, Chile.

Abstract

Introduction: fibromyalgia is a chronic disease characterized by generalized pain, stiffness, poor physical conditioning, non-restorative sleep and poor health-related quality of life. Ganoderma lucidum a type of mushroom that has demonstrated several benefits in different populations. Ceratonia siliqua is a natural therapy rich in antioxidants with potential benefits on health.

Objective: to evaluate the effects of 6-week treatment of *Ganoderma lucidum* and *Ceratonia siliqua* on physical fitness in patients suffering from fibromyalgia.

Methods: sixty-four women with fibromyalgia participated in the study. They took 6 g of *Ganoderma lucidum* or *Ceratonia siliqua* per day for 6 weeks. Different fitness tests were selected in order to evaluate functional capacity.

Results: after the 6-week treatment period, *Ganoder-ma lucidum* significantly improved aerobic endurance, lower body flexibility, and velocity (p < .05). No significant improvement in any physical test was observed in the *Ceratonia siliqua* group.

Discussion and conclusion: Ganoderma lucidum may improve physical fitness in women with fibromyalgia, whereas, *Ceratonia siliqua* seemed to be ineffective at increasing physical fitness. These results may indicate that *Ganoderma lucidum* might be a useful dietary supplement to enhance physical performance of the patients suffering from fibromyalgia.

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Key words: *Chronic pain. Reishi*. Ceratonia siliqua. Ganoderma lucidum. *Nutrition. Endurance. Velocity*.

GANODERMA LUCIDUM MEJORA LA CONDICIÓN FÍSICA EN MUJERES CON FIBROMIALGIA

Resumen

Introducción: la fibromialgia es una enfermedad crónica caracterizada por dolor crónico general, rigidez, condición física pobre, sueño no reparador y mala calidad de vida relacionada con la salud. Ganoderma lucidum es un tipo de hongo que ha demostrado tener diferentes beneficios en diversas poblaciones. La harina de algarrobo (Ceratonia siliqua) es una fuente natural de antioxidantes con potenciales beneficios para la salud.

Objetivo: evaluar los efectos sobre la condición física en mujeres con fibromialgia de un tratamiento de seis semanas con *Ganoderma lucidum* y compararlos con los de un tratamiento con *Ceratonia siliqua*.

Métodos: sesenta y cuatro mujeres con fibromialgia participaron en el estudio. Se hicieron dos grupos, el primer grupo tomó 6 g diarios de *Ganoderma lucidum*, mientras que el segundo tomó 6 g diarios de *Ceratonia siliqua*. Se evaluó la condición física mediante diferentes test físicos validados.

Resultados: después de seis semanas de tratamiento, *Ganoderma lucidum* mejoró significativamente la resistencia aeróbica, la flexibilidad del miembro inferior y la velocidad (p < 0,05). Por otro lado, *Ceratonia siliqua* no mejoró la condición física.

Discusión y conclusiones: Ganoderma lucidum puede mejorar la condición física en mujeres con fibromialgia, mientras que *Ceratonia siliqua* parece no ser efectivo para este propósito. Estos resultados pueden indicar que 6 g diarios de *Ganoderma lucidum* podrían ser un suplemento útil para mejorar la condición física en esta población.

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Palabras clave: *Dolor crónico. Reishi*. Ceratonia siliqua. Ganoderma lucidum. *Nutrición. Resistencia. Velocidad.*

Correspondence: Pedro R. Olivares. Instituto de Actividad Física y Salud, Universidad Autónoma de Chile, Chile. E-mail: olivares.pedro@gmail.com

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Introduction

Fibromyalgia (FM) is a chronic rheumatic disease of unknown etiology. It is characterized by generalized pain, stiffness, and tenderness in at least 11 of 18 specific points¹. In addition, FM is associated with a range of symptoms, such as muscular stiffness, depression, non-refreshing sleep, and cognitive impairments^{2,3}. In European population, the estimated prevalence of FM is around 3% to 5% of the general population⁴.

Differences in physical fitness between FM and healthy women were compared in previous studies. FM patients showed worse results in upper and lower limb strength, balance, flexibility, and aerobic endurance^{5,6}. FM is also associated with high prevalence of overweight and obesity. In this regard, a recent study reported that approximately 72% of women with fibromyalgia are overweight or obese7. This anthropometric difference could be given because FM patients are more prone to physical inactivity than healthy people⁸. This sedentary tendency may be increased by FM symptoms like pain, fatigue, stiffness or depression, while at the same time some of these symptoms could be worsened by physical inactivity, i.e. poor physical conditioning or depression⁹. All of this can lead a reduction in health-related quality of life (HRQoL)¹⁰.

Recommended therapies in FM include pharmacological and non-pharmacological therapies. Among non-pharmacological treatments, physical therapies were reported to be effective at increasing well-being and physical function¹¹. Natural and nutritional therapies are currently being studied in this syndrome because these could be helpful at improving different symptoms¹².

Among those alternative therapies, Ganoderma lucidum (GL), also known as reishi or linghzi, has been widely used and studied in different populations. It is a type of mushroom that has demonstrated his efficacy at increasing vital energy, stimulating the immune system, and promoting health¹³. Previous research investigated its effect as a treatment of different diseases, like cancer¹⁴, diabetes¹⁵, Human Immuno Virus¹⁶, or hepatitis¹⁷. Different properties and effects were also reported, such as anti-inflammatory¹⁸, anti-oxidant¹⁵, antiviral¹⁹, neuroprotective²⁰, and hypotensive²¹. Effects of GL on physical conditioning still remain unknown in humans. To our knowledge, only one investigation²² assessed the effects of GL on physical fitness, and they concluded that the antioxidant effect of GL could protect endurance athletes from overtraining. Effectiveness in increasing antioxidant enzymes activities was also investigated in mice²³. This study shown the evidence that GL possessed protective effects against a strenuous exercise that could induce oxidative stress. Furthermore, relevant effects on physical condition and fatigue were reported in breast cancer patients²⁴. However, the mechanism under these improvements remains unknown.

Ceratonia siliqua (CS) is a natural therapy that has been consumed in many Mediterranean countries in culinary preparations of beverages and confectionery. It is also called carob tree and it is obtained from the fruit of the CS tree. CS flour is rich in polyphenols and it acts as an antioxidant in the body^{25,26}. Given its low prize, CS can be considered a "low cost" source of antioxidants. In mice, antidepressant effects were also reported in previous studies²⁷. However, to our knowledge, those results have not been studied in human samples.

Recent studies hypothesized that oxidative stress may have a relevant role in the pathophysiology of FM²⁸. This, along with the effects of oxidative stress in physical condition²², suggests that antioxidant sources could improve physical fitness in FM patients.

Given the potential effects of GL and CS, not only as antioxidant sources (especially the GL, which may have other benefits cited above), the aim of the present study was to evaluate the effects of GL and CS on physical fitness in patients suffering from FM. A secondary objective was to evaluate the safety of GL and CS treatments.

Methods

Participants

All participants were recruited from three FM associations. The following inclusion criteria were set: 1) be diagnosed with FM by a rheumatologist; 2) be able to communicate effectively with study staff; 3) be older than 18 years old; 4) Give written-informed consent. On the other hand, exclusion criteria were the following: 1) be pregnant; 2) change their daily activity during the 6 weeks of treatment; 3) be taking immunosuppressive; 4) be suffering from diabetes; 5) be participating in other investigations; 6) be taking C vitamin supplementation; 7) be taking anticoagulants, and 8) have taken GL and/or CS as a treatment before. Additionally, an algometer (PainTest[™] FPX 25 Algometer. Wagner Instruments, Greenwich, USA) was used in order to check FM diagnosis. Participants without acute painful response in at least 11 of 18 specified tender points stimulated with a pressure of 4 kg/ cm² were excluded.

Figure 1 shows the flow diagram of participants. A total of 70 subjects were initially recruited. Sixty-seven of them were women and 3 were men. Five participants were excluded because they did not meet the inclusion criteria and 1 declined to participate. A total of 64 women took part in the study. All of them signed the informed consent in accordance with the updated Declaration of Helsinki.

This study was approved by the Biomedical Ethics Committee of the University. The trial was registered in the Australian New Zealand Clinical Trials, register number: ACTRN12614001201662.

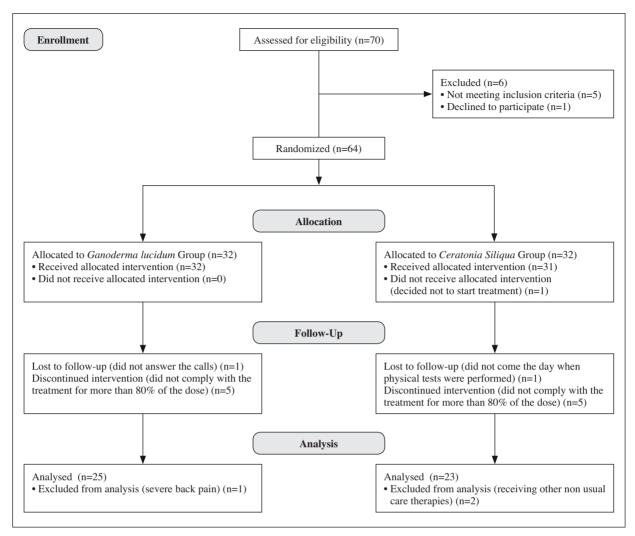


Fig. 1.-Flow Diagram of participants.

Procedures

The current study is a randomized, double blind, clinical trial. Participants were randomly assigned to one of the following two groups: GL group (GLG) or CS group (CSG). Subjects were informed about the existence of both group, but they did not know which group they were in. Randomization and allocation processes were conducted by one of the researchers using random code numbers. This researcher was not involved in data acquisition or statistical analysis. Thus, the following people were blinded: a) people receiving the treatment; b) people administering the treatment; c) people assessing the outcomes; and finally, d) people analyzing the results.

After initial measurement, participants took GL or CS during a period of 6 weeks. GLG ingested 3g of GL dissolved in warm water twice a day (6g per day). The first intake was at breakfast; whereas the second one was at dinner. CSG took 6 daily grams of CS with the same administration indications. The company "MundoReishi" provided the substances, and the Chair of Mycology of the University of Valladolid (Spain) was responsible to analyze GL.

Data collection

In order to evaluate functional capacity and physical fitness, the following well-known tests were selected:

 Upper Body Muscular Strength: It was assessed using two tests: the handgrip test and the arm curl test. The handgrip strength was measured using a hand dynamometer (Takei TKK 5401 Digital Handgrip Dynamometer, Tokyo Japan). Patients had to squeeze the dynamometer with an optimal grip-span²⁹. The better of two attempts for each hand was used in the analyses. The second tool was the "Arm curl test"³⁰. It quantifies the number of repetitions that the patient is able to lift a hand weight (2.3 kg) in 30 seconds. One trial with each hand was performed by the patients.

- Lower body muscular strength. The 30s-Chair stand test was used. Participants started this test seated on a chair with their hands over their shoulders. They should stand-up and sit-down as fast as possible within 30 seconds³¹. The number of times they stand-up were recorded.
- Upper Body Flexibility was assessed using the back scratch test³². In this test, the distance between fingers behind the back is measured and the overlap is scored positively.
- Lower Body Flexibility: it was measured using the chair-sit-and-reach test³⁰. In this test, participants were seated on a chair and they had to extend their legs: first, the right leg, and second, the other one. Then, they were instructed to reach the extended leg with the middle finger of the corresponding hand and hold this position. Best score was registered.
- Balance and agility: the 3 meters version of the Timed-Up-and-Go Test (TUG)³³ was used to assess agility and dynamic balance. Participants were asked to sit on a chair, placing their back against the backrest of the chair. At the signal, they should walk to a line 3 meters away, turn around, walk back to the chair and sit-down. Best score of two trials was used in the analyses.
- Aerobic Endurance was measured using the 6-min walking test³⁰. This test aims to determine the maximum distance that participants were able to walk in 6 minutes. It was performed around a square measuring 20 meters each side.
- Velocity: Participants were asked to walk 20 meters as fast as possible. Mean velocity was calculated dividing the 20 meters by the time taken to complete this 20 meters³⁴.
- Balance: it was measured using Biodex Balance System (Shirley, NY, USA). This device objectively measures the ability of a subject to stabilize himself. It also quantifies the tilt about each axis during static and dynamic conditions. Clinical Test of Sensory Integration of Balance (CTSIB) protocol was used. This test was performed with different devices by previous studies³⁵. However, it is the first time, to our knowledge, that this protocol is carried out with Biodex Balance System. In all tests, patients maintained their feet on the platform during 30 seconds with a rest of 10 seconds between each test. The following tests were performed to quantify postural sway under four different sensory conditions according to the CT-SIB:
 - Eyes open on firm surface to measure somatosensory, visual and vestibular sensory inputs.
 - Eyes closed on firm surface to estimate somatosensory and vestibular inputs, since visual input is not available.

- Eyes open on unstable surface. In this test somatosensory capacity is compromised, thus visual and vestibular inputs are measured.
- Eyes closed on unstable surface. Only vestibular information was estimated by compromising somatosensory information and visual feedback.
- Trunk Endurance was evaluated by using the Ito, Shirado method³⁶. Flexor endurance was assessed at first. Patients started the test in supine position and they should raise their lower extremities with 90° flexion of the hip and knees joints. For extensor muscles, participants should be in prone position while holding their sternum off the floor. Subjects must maintain these positions as long as possible in both tests.

Statistical analysis

Values of descriptive variables were calculated in order to characterize the two groups. Student's *t* test for independent samples was used to compare the characteristics of GLG and CSG at baseline. Distribution of data was checked using the Kolmogorov-Smirnov test with Lilliefors significance.

The analysis of variance (ANOVA) for repeated measures was used to calculate the effects of the treatment on the physical fitness outcomes. Paired t test was calculated in order to estimate the changes of both groups comparing from baseline.

In addition to the efficacy analysis, which comprises the participants who took at least 80% of the doses and completed the task, an intent-to-treat analysis was performed. It comprises the 64 initial participants. Data of all participants that came to the post-treatment measures were utilized, including data coming from the people who did not take at least 80% of the doses (n=10). Post-treatment data of the remainder of the sample (n=6) was imputed according to the mean change of their group. The level of significance was set at p<.05. Analyses were performed using SPSS software (version 21).

Results

Characteristics of participants at baseline are shown in table I. No statistically significant difference was observed between GLG and CSG at baseline.

Initially, 64 women were randomly allocated in 2 equal groups. However, final sample comprised 48 women: 25 belonging to GLG and 23 belonging to CSG. Starting from these 64 patients, a total of 5 participants of each group did not took at least 80% of the dose and were excluded; 1 subject decided not to start the treatment after the randomization was performed; another woman did not answer the calls and

Characteris	Table I tics at baseline of the two gives	roups	
	<i>GLG</i> (<i>n</i> =25)	<i>CSG</i> (<i>n</i> =23)	р
Age (years)	56.25 (8.05)	53.62 (11.75)	.367
Height (cm)	157.16 (4.63)	156.13 (6.16)	.514
Weight (kg)	64.21 (9.87)	61.50 (13.50)	.429
Muscular mass (%)	62.00 (7.31)	64.76 (8.77)	.245
Fat mass (%)	34.80 (7.67)	32.33 (7.92)	.285
BMI	26.00 (3.82)	25.20 (4.83)	.522
Date when fibromyalgia symptoms started	1993 (12.09)	1992 (12.76)	.652

*Values expressed as mean (SD). BMI: Body Mass Index. GLG: Ganoderma lucidum group. CSG: Ceratonia siliqua group.

was lost; 2 women considerably changed their usual therapies and were excluded too; 1 woman was not able to complete physical fitness tests because she had an acute musculoskeletal injury; 1 woman did not show up when measurements was performed (Fig. 1). Finally, 48 women were included in the efficacy analysis (GLG=25; CSG=23), whereas 64 (GLG=32; CSG=32) were taken in consideration of intent to treat analysis.

Effects of GLG and CSG on physical fitness are represented in table II. After the 6-week treatment period, a statistically significant difference in aerobic endurance was observed between both groups (p<.05). Furthermore, GLG obtained significant improvements (p<.05) in lower body flexibility and velocity in efficacy analysis compared with CSG. However, only the improvement in lower body flexibility was significant in the intent to treat analysis (Table III).

Discussion

The main finding of the current paper was that 6g/ day of GL for 6 weeks improved the physical fitness of women suffering from FM. Specifically, we observed improvements on aerobic endurance, walking velocity, and lower limb flexibility. On the other hand, CS seemed to be rather ineffective in improving physical fitness in FM patients. To our knowledge, this is the first study that assesses the effects of CS and/or GL on physical condition in FM patients.

Given the lack of studies about the potential mechanism of GL and CS in physical fitness, it is difficult to explain how GL may improve aerobic endurance, velocity, or flexibility. The best explanation based on previous studies is the antioxidant effect^{37,38}. In addition, the oxidative/antioxidative status was suggested to be a critical factor in physical and mental health of FM patients^{28,39}. However, both GL and CS are antioxidant sources. Therefore, based on our results, there can be no assurance that the reported improvements are caused by an antioxidant effect. In this context, further researches on the physiological effects of GL in the physical condition are needed.

Although the current study is not able to precisely explain how physical condition is improved, the relevance of our findings is very large. To our knowledge, this is the first study that investigates the effects of GL and/or CS on the physical fitness of a population with a specific disease. Therefore, this study lays the foundation for future research focused on the GL effects on physical fitness in pathologies characterized by poor physical conditioning. At the same time, findings from the previous study in cyclists are confirmed²². In this way, the current study is also an important entry point for future studies on the effects of GL in sport performance.

The relevance of the physical condition in women suffering from FM is widely known. In fact, it is closely related with the satisfaction with life and wellbeing⁴⁰, because it is obviously related with the ability of perform activities of daily living. Furthermore, aerobic endurance and flexibility are extremely related with HRQoL. The reported treatment effect in velocity is higher than the minimal real change, which was calculated in patients with chronic pain (osteoarthritis) and it was 0.07 m/s³⁴.

Safety of both GL and CS were also demonstrated in the current paper. A total of 10 participants did not complete the minimum 80% of the treatment. Of these, 5 belonged to the GLG and other 5 to the CSG, which means a 15.63% of the total sample. The most common complaint in those 10 participants were mild nausea, diarrhea, discomfort, and nervousness. Some participants opined that the reason of those reactions were the bad taste. In all cases the reactions were mild or moderate and the participants were asked to reduce the dose to 3 grams per day. However, no one of the patients that reduced the dose were able to continue the treatment and all of them ceased it. This could suggest that the daily amount of GL and CS is not the cause of those complaints.

The current study has several limitations. The most important limitation is the lack of previous studies that

		Effect	ts of 6 weeks	of GL	Table II vs CS treatme	Table II Effects of 6 weeks of GL vs CS treatment on physical conditioning	ıl conditionin	00					
			BTG				CSG						
Outcome measure	Test	Mean (SD) at baseline	Mean (SD) after treatment	P^{a}	Intra-Group Effect Size	Mean (SD) at baseline	Mean (SD) after treatment	P^a	Intra-Group Effect Size	F	þ	Treatment effect Mean (95% CI)	Global Effect Size
	Right Handgrip (kg) GLG (n=25) CSG (n=23)	19.58 (4.98)	19.92 (4.33)	.601	-0.072	20.36 (4.09)	20.28 (5.68)	.910	0.016	0.201	.656	-0.42 (-1.47 to 2.32)	0.132
Upper Body Stren-	Left Handgrip (kg) GLG (n=24) CSG (n=23)	18.33 (4.92)	18.91 (3.85)	.482	-0.131	18.73 (3.99)	19.39 (5.11)	.420	-0.143	0.005	.946	0.07 (-2.37 to 2.21)	0.021
gth	Arm Curl Right (reps) GLG (n=25) CSG (n=23)	10.20 (3.55)	13.36 (4.04)	<.001	-0.830	10.09 (2.99)	12.91 (3.42)	.001	-0.877	0.145	.705	-0.34 (-1.43 to 2.09)	0.112
	Arm Curl Left (reps) GLG (n=24) CSG (n=23)	10.48 (4.11)	13.81 (4.40)	<.001	-0.782	10.41 (3.64)	12.67 (2.96)	.001	0.681	1.784	.188	-1.07 (-0.54 to 2.68)	0.398
Upper Body Flexibility	Back Scratch (cm) GLG (n=25) CSG (n=22)	-4.12 (10.99)	-3.80 (10.63)	.761	-0.029	-5.36 (8.71)	-5.86 (8.35)	.754	0.058	0.197	.659	-0.82 (-2.90 to 4.54)	0.133
Lower body flexibility	Chair Sit and Reach (cm) GLG (n=25) CSG (n=23)	-0.20 (8.69)	4.00 (9.85)	<.001	-0.452	-0.35 (9.39)	22 (8.98)	.893	-0.014	9.060	.004	-4.06 (1.38 to 6.75)	0.887
Balance and agility	Timed-Up-Go (s) GLG (n=25) CSG (n=22)	7.29 (1.29)	6.85 (1.02)	.007	0.378	7.31 (1.10)	7.00 (1.30)	.329	0.257	0.144	.706	0.13 (-0.80 to 0.54)	0.113
Aerobic endurance	6 m Walking (m) GLG (n=25) CSG (n=22)	507.00 (73.88)	528.97 (72.08)	.006	-0.301	477.73 (79.69)	469.49 (120.45)	.643	0.080	4.260	.045	-30.19 (-6.33 to 66.75)	0.497
Lower body strength	Chair stand Test (reps) GLG (n=25) CSG (n=22)	10.26 (1.71)	11.14 (2.08)	.005	-0.462	10.22 (2.03)	10.86 (2.52)	.051	-0.279	0.343	.561	-0.25 (-0.59 to 1.08)	0.175
Velocity	20-m walk test (m/s) GLG (n=25) CSG (n=23)	3.35 (0.52)	3.54 (0.54)	.002	0.254	3.26 (0.42)	3.24 (0.52)	.883	-0.059	4.491	.040	0.30 (-0.72 to .11)	0.625

		Effec	ts of 6 weeks	of GL	Table II (cont.) vs CS treatment	Table II (cont.) Effects of 6 weeks of GL vs CS treatment on physical conditioning	al conditionin	8					
			GLG				CSG						
Outcome measure	Test	Mean (SD) at baseline	Mean (SD) after treatment	P^a	Intra-Group Effect Size	Mean (SD) at baseline	Mean (SD) after treatment	P^a	Intra-Group Effect Size	F	P^b	Treatment effect Mean (95% CI)	Global Effect Size
Balance. Eyes Open Firm Surface GLG (n=25)	Stability Index (°)	4.63 (1.68)	4.77 (1.42)	.478	060'0-	4.72 (1.62)	4.32 (2.26)	.238	0.203	2.066	.157	-0.54 (-0.21 to 1.30)	0.424
CSG (n=23)	Swing Index (°)	0.78 (0.59)	0.51 (0.24)	.021	0.599	0.73 (0.44)	0.62 (0.45)	.255	0.247	1.239	.271	0.16 (-0.43 to 0.12)	0.329
Balance Eyes Closed Firm Surface GLG (n=25)	Stability Index (°)	4.83 (1.50)	4.70 (1.61)	.591	0.083	4.66 (1.66)	4.20 (2.06)	.205	0.245	0.657	.422	-0.33 (-0.49 to 1.15)	0.239
CSG (n=23)	Swing Index (°)	1.19 (0.62)	0.99 (0.50)	.080	0.355	1.01 (0.56)	0.90 (0.45)	.136	0.216	0.348	.558	0.08 (-0.34 to 0.18)	0.174
Balance Eyes Open Unstable Surface GLG (n=25)	Stability Index (°)	4.02 (1.65)	4.14 (1.41)	.635	-0.078	3.97 (1.52)	4.38 (1.83)	.210	-0.243	0.483	.490	0.28 (-1.09 to 0.53)	0.205
CSG (n=23)	Swing Index (°)	1.42 (0.63)	1.26 (0.65)	.218	0.249	1.22 (0.44)	1.05 (0.37)	.001	0.418	0.008	.931	-0.01 (-0.26 to 0.29)	0.026
Eyes Closed on Unstable Surface GLG (n=25)	Stability Index (°)	4.90 (1.37)	4.92 (1.50)	.933	-0.013	4.57 (1.85)	4.89 (2.45)	.279	-0.147	0.469	.497	0.29 (-1.14 to 0.56)	0.202
CSG (n=23)	Swing Index (°)	3.22 (0.97)	3.22 (1.24)	766.	0.000	2.93 (1.07)	2.82 (.99)	.562	0.106	0.157	.693	-0.10 (-0.43 to 0.65)	0.117
Trunk Endurance	Abdominal (s)	46.18 (39.47)	54.55 (39.80)	.321	-0.211	39.45 (34.69)	41.49 (37.74)	.817	-0.056	0.272	.605	-6.33 (-18.19 to 30.87)	0.242
CSG (n=19)	Lumbar (s)	54.01 (40.84)	59.36 (45.81)	.666	-0.123	49.73 (41.22)	46.41 (40.75)	LTT.	0.081	0.261	.612	-8.66 (-25.58 to 42.92)	0.168
GLG: ganoderma lucidun interval.	GLG: ganoderma lucidum group; CSG: ceratonia siliqua group; ^a p interval.		f t-test; ^b p -value	ss of an	alysis of varian	ice for repeated	measures to co	mpare d	ifferences betw	sen grou	ips afte	of t-test; ^b <i>p</i> -values of analysis of variance for repeated measures to compare differences between groups after treatment; CI: confidence	nfidence

Table III

	Effe	Effects of 6 weeks of GL or CS treatments on physical conditioning. Intent-to-treat analysis	of GL or CS	treatm	table III tents on physi	cal condition	ing. Intent-to-	-treat a	ınalysis				
			GLG (n=32)	32)			CSG (n=32)	(2)					
Outcome measure	Test	Mean (SD) at base line	Mean (SD) after treatment	P^a	Intra-Group Effect Size	Mean (SD) at base line	Mean (SD) after treatment	b^a	Intra-Group Effect Size	F	P^b	Treatment effect Mean (95% CI)	Global Effect Size
	Right Handgrip (kg)	19.81 (4.87)	18.17 (4.82)	.885	0.338	19.98 (4.33)	18.51 (4.16)	.571	0.346	0.042	.838	0.28 (-1.92 to 1.37)	0.052
Upper Body	Left Handgrip (kg)	18.17 (4.82)	18.56 (4.37)	.535	-0.084	18.51 (4.16)	19.47 (4.72)	.147	-0.215	0.399	.530	0.56 (-2.35 to 1.22)	0.160
Strength	Right arm curl (reps)	9.76 (3.44)	12.82 (3.95)	000.	-0.826	9.06 (3.34)	12.45 (4.08)	000.	-0.909	0.182	.672	0.32 (-1.83 to 1.19)	0.108
	Left arm curl (reps)	10.36 (3.87)	13.65 (4.23)	000.	-0.811	9.92 (3.83)	12.65 (3.89)	000	-0.707	0.674	.415	-0.56 (-0.80 to 1.93)	0.209
Upper Body Flexibility	Back Scratch (cm)	-4.00 (11.02)	-3.50 (10.87)	.560	-0.045	-5.00 (10.39)	-6.25 (10.55)	.282	0.119	1.514	.223	-1.74 (-1.09 to 4.58)	0.313
Lower body flexibility	Chair Sit and Reach (cm)	-0.28 (8.38)	3.02 (9.20)	000.	-0.375	-0.34 (11.62)	0.43 (10.16)	397	-0.070	4.312	.044	-2.53 (0.06 to 4.99)	0.527
Balance and agility	Timed-Up-Go (s)	7.25 (1.18)	6.89 (1.05)	.010	0.322	7.43 (1.49)	7.18 (1.62)	.288	0.160	0.163	.688	0.09 (-0.64 to 0.42)	0.103
Aerobic endurance	Six minutes walking test (m)	505.59 (71.40)	524.76 (70.89)	.008	-0.269	484.46 (80.52)	474.79 (117.4)	.478	0.096	3.661	.060	-28.84 (-1.29 to 58.99)	0.486
Lower Body strength	n Chair stand test (reps)	10.29 (1.72)	11.04 (2.03)	.007	-0.398	10.03 (2.40)	10.75 (2.81)	.003	-0.275	0.006	.940	-0.02 (-0.65 to 0.70)	0.020
Velocity	20-m walk test (m/s)	3.36 (0.50)	3.51 (0.56)	.006	-0.282	3.27 (0.47)	3.25 (0.58)	808.	0.037	3.581	.063	-0.15 (-0.01 to 0.33)	0.481
Balance Eyes Open	Stability Index(°)	4.60 (1.78)	4.82 (1.51)	.318	-0.133	4.60 (1.56)	4.49 (2.32)	.726	0.055	0.740	.393	-0.33 (-0.43 to 1.09)	0.218
	Swing Index(°)	0.79 (0.62)	0.53 (0.30)	.005	0.533	0.80 (0.51)	0.68 (0.58)	.087	0.219	1.628	.207	0.14 (-0.35 to 0.07)	0.324
Balance Eyes Closed	Stability Index(°)	4.93 (1.65)	4.84 (1.77)	.660	0.052	4.64 (1.65)	4.37 (1.94)	.330	0.149	0.268	.607	-0.17 (-0.50 to 0.86)	0.131
	Swing Index(°)	1.19 (0.68)	0.96 (0.49)	.037	0.388	1.08 (0.60)	0.93 (0.59)	.029	0.252	0.306	.582	0.07 (-0.31 to 0.17)	0.141
Balance Eyes Open IInstable Surface	Stability Index(°)	4.18 (1.59)	4.41 (1.50)	.311	-0.148	3.93 (1.42)	4.35 (1.74)	.117	-0.264	0.279	.599	0.18 (-0.88 to 0.51)	0.134
UIISIAUIC JULIAVO	; , , , ,	1.42	1.25			1.30	1.16					0.03	

0.078

0.078 .781 0.03 (-0.27 to 0.20)

0.231

.029

1.16 (0.67)

1.30(0.53)

0.285

.105

1.25(0.60)

1.42 (0.59)

Swing Index(°)

	E_{j}	Table III (cont.) Effects of 6 weeks of GL or CS treatments on physical conditioning. Intent-to-treat analysis	t of GL or CS	treatm	Table III (cont.) tents on physical	nt.) ical condition	ing. Intent-to	-treat c	ınalysis				
			GLG (n=32)	2)			CSG (n=32)	32)					
Outcome measure	Test	Mean (SD) at base line	Mean (SD) after treatment	P^a	Intra-Group Effect Size	P^a Intra-Group Mean (SD) Effect Size at base line	Mean (SD) after treatment	p^a	Intra-Group Effect Size	F	P^b	Treatment effect Mean (95% CI)	Global Effect Size
Eyes Closed on	Stability Index(°)	4.97 (1.48)	5.02 (1.54)	.845	-0.033	4.60 (1.68)	4.93 (2.18)	.171	-0.169	0.681 .413	.413	0.28 (-0.96 to 0.40)	0.210
	Swing Index(°)	3.32 (1.02)	3.32 (1.24)	.995	0.000	2.98 (1.00)	2.95 (1.13)	.870	0.028	0.013 .910	.910	-0.02 (-0.42 to 0.48)	0.029
с	Abdominal(s)	45.55 (36.52)	53.90 (36.98)	.209	-0.227	36.36 (34.10)	40.62 (37.16)	.434	-0.119	0.235 .630	.630	-4.09 (-12.78 to 20.96)	0.123
Trunk Endurance	Lumbar(s)	53.82 (38.69)	58.86 (44.09)	.598	-0.121	47.66 (39.08)	49.17 (41.05)	.858	-0.037	0.079 .780	.780	-3.54 (-21.71 to 28.80)	0.071
GLG: ganoderma lucidu interval.	GLG: ganoderma lucidum group; CSG: ceratonia siliqua group; ^a p interval.	siliqua group; ^a p o	f t-test; ^b p-value	s of ane	alysis of varian	ice for repeated	measures to co	mpare d	lifferences betw	een grot	ups afte	of t-test; "p-values of analysis of variance for repeated measures to compare differences between groups after treatment; CI: confidence	onfidenc

could explain the mechanisms under the differences observed. In addition, given that the two treatments were antioxidant sources, it is impossible to conclude whether the changes are based on the antioxidant effects or not. The second is the lack of knowledge about the most adequate dose of both GL and CS in adult women. Furthermore, the dose and indications of both treatments had to be the same in order to keep the double-blind. Third, duration of the treatment could be insufficient to increase some physical fitness variables. Finally, although no statistically significant differences in many physical tests were observed, treatment effects could not be discarded due to the small sample size.

Despite all these limitations, it can be concluded that GL may be effective in improving endurance, lower body flexibility, and velocity. On the other hand, CS seemed to be ineffective in improving physical fitness in women suffering from FM. However, more studies with longer intervention periods and different doses of GL and CS are required. Similarly, further studies focused on the mechanisms under the reported improvements are needed.

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Conflict of Interest

The authors declare there are not competing financial interests existing.

References

- Wolfe F, Smythe HA, Yunus MB, *et al.* The american-college-of-rheumatology 1990 criteria for the classification of fibromyalgia - report of the multicenter criteria committee. *Arthritis and rheumatism* 1990; 33(2): 160-72.
- Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2,596 people with fibromyalgia. *Bmc Mus*culoskeletal Disorders 2007; 8.
- Wilson HD, Robinson JP, Turk DC. Toward the Identification of Symptom Patterns in People With Fibromyalgia. Arthritis & Rheumatism-Arthritis Care & Research 2009; 61(4): 527-34.
- Branco JC, Bannwarth B, Failde I, et al. Prevalence of Fibromyalgia: A Survey in Five European Countries. Seminars in arthritis and rheumatism 2010; 39(6): 448-53.
- Aparicio VA, Segura-Jimenez V, Alvarez-Gallardo IC, et al. Fitness Testing in the Fibromyalgia Diagnosis: The al-Andalus Project. *Medicine and science in sports and exercise* 2015; 47(3): 451-9.

- Aparicio VA, Carbonell-Baeza A, Ruiz JR, et al. Fitness testing as a discriminative tool for the diagnosis and monitoring of fibromyalgia. Scandinavian journal of medicine & science in sports 2013; 23(4): 415-23.
- Segura-Jimenez V, Aparicio VA, Alvarez-Gallardo IC, Carbonell-Baeza A, Tornero-Quinones I, Delgado-Fernandez M. Does body composition differ between fibromyalgia patients and controls? The al-Andalus project. *Clinical and experimental rheumatology* 2015; 33(1 Suppl 88): 25-32.
- Rusu C, Gee ME, Lagace C, Parlor M. Chronic fatigue syndrome and fibromyalgia in Canada: prevalence and associations with six health status indicators. *Health promotion and chronic disease prevention in Canada* 2015; 35(1): 3-11.
- Everson-Hock ES, Green MA, Goyder EC, et al. Reducing the impact of physical inactivity: evidence to support the case for targeting people with chronic mental and physical conditions. *Journal of public health* 2015.
- Gusi N, Tomas-Carus P, Hakkinen A, Hakkinen K, Ortega-Alons A. Exercise in waist-high warm water decreases pain and improves health-related quality of life and strength in the lower extremities in women with fibromyalgia. *Arthritis & Rheumatism-Arthritis Care & Research* 2006; 55(1): 66-73.
- 11. Busch AJ, Schachter CL, Overend TJ, Peloso PM, Barber KAR. Exercise for fibromyalgia: A systematic review. *Journal of Rheumatology* 2008; 35(6): 1130-44.
- Shaver JL, Wilbur J, Lee H, Robinson FP, Wang E. Self-Reported Medication and Herb/Supplement Use by Women with and without Fibromyalgia. *Journal of Womens Health* 2009; 18(5): 709-16.
- Batra P, Sharma AK, Khajuria R. Probing Lingzhi or Reishi Medicinal Mushroom Ganoderma lucidum (Higher Basidiomycetes): A Bitter Mushroom with Amazing Health Benefits. *International journal of medicinal mushrooms* 2013; 15(2): 127-43.
- Liang Z, Yi Y, Guo Y, Wang R, Hu Q, Xiong X. Chemical characterization and antitumor activities of polysaccharide extracted from Ganoderma lucidum. *International journal of molecular sciences* 2014; 15(5): 9103-16.
- Pan D, Zhang D, Wu J, *et al.* Antidiabetic, antihyperlipidemic and antioxidant activities of a novel proteoglycan from ganoderma lucidum fruiting bodies on db/db mice and the possible mechanism. *PloS one* 2013; 8(7): e68332.
- Akbar R, Yam WK. Interaction of ganoderic acid on HIV related target: molecular docking studies. *Bioinformation* 2011; 7(8): 413-7.
- 17. Li Y, Yang Y, Fang L, Zhang Z, Jin J, Zhang K. Anti-hepatitis activities in the broth of Ganoderma lucidum supplemented with a Chinese herbal medicine. *The American journal of Chinese medicine* 2006; 34(2): 341-9.
- Yoon HM, Jang KJ, Han MS, *et al.* Ganoderma lucidum ethanol extract inhibits the inflammatory response by suppressing the NF-kappaB and toll-like receptor pathways in lipopolysac-charide-stimulated BV2 microglial cells. *Experimental and therapeutic medicine* 2013; 5(3): 957-63.
- Zhang W, Tao J, Yang X, *et al.* Antiviral effects of two Ganoderma lucidum triterpenoids against enterovirus 71 infection. *Biochemical and biophysical research communications* 2014; 449(3): 307-12.
- Zhang W, Zhang Q, Deng W, *et al.* Neuroprotective effect of pretreatment with ganoderma lucidum in cerebral ischemia/ reperfusion injury in rat hippocampus. *Neural regeneration research* 2014; 9(15): 1446-52.
- Tran HB, Yamamoto A, Matsumoto S, *et al.* Hypotensive effects and angiotensin-converting enzyme inhibitory peptides of reishi (Ganoderma lingzhi) auto-digested extract. *Molecules* 2014; 19(9): 13473-85.

- Rossi P, Buonocore D, Altobelli E, et al. Improving Training Condition Assessment in Endurance Cyclists: Effects of Ganoderma lucidum and Ophiocordyceps sinensis Dietary Supplementation. Evidence-based complementary and alternative medicine : eCAM 2014; 2014: 979613.
- Zhonghui Z, Xiaowei Z, Fang F. Ganoderma lucidum polysaccharides supplementation attenuates exercise-induced oxidative stress in skeletal muscle of mice. *Saudi journal of biological sciences* 2014; 21(2): 119-23.
- 24. Zhao H, Zhang Q, Zhao L, Huang X, Wang J, Kang X. Spore Powder of Ganoderma lucidum Improves Cancer-Related Fatigue in Breast Cancer Patients Undergoing Endocrine Therapy: A Pilot Clinical Trial. *Evidence-based complementary and alternative medicine : eCAM* 2012; 2012: 809614.
- 25. El Hajaji H, Lachkar N, Alaoui K, *et al.* Antioxidant activity, phytochemical screening, and total phenolic content of extracts from three genders of carob tree barks growing in Morocco. *Arabian Journal of Chemistry* 2011; 4(3): 321-4.
- Yousif AK, Alghzawi HM. Processing and characterization of carob powder. *Food chemistry* 2000; 69(3): 283-7.
- 27. Agrawal A, Mohan M, Kasture S, *et al.* Antidepressant activity of Ceratonia siliqua L. fruit extract, a source of polyphenols. *Natural product research* 2011; 25(4): 450-6.
- Rossi A, Di Lollo AC, Guzzo MP, *et al.* Fibromyalgia and nutrition: what news? *Clinical and experimental rheumatology* 2015; 33(1 Suppl 88): S117-25.
- Ruiz-Ruiz J, Mesa JLM, Gutierrez A, Castillo MJ. Hand size influences optimal grip span in women but not in men. *Journal* of Hand Surgery-American Volume 2002; 27A(5): 897-901.
- Rikli RE, Jones CJ. Development and validation of a functional fitness test for community-residing older adults. *Journal of Aging and Physical Activity* 1999; 7(2): 129-61.
- Park DC, Glass JM, Minear M, Crofford LJ. Cognitive function in fibromyalgia patients. *Arthritis and rheumatism* 2001; 44(9): 2125-33.
- Rikli RE, Jones CJ. Senior fitness test manual: Human Kinetics; 2013.
- Podsiadlo D, Richardson S. The timed up and go a test of basic functional mobility for frail elderly persons. *Journal of the American Geriatrics Society* 1991; 39(2): 142-8.
- Motyl JM, Driban JB, McAdams E, Price LL, McAlindon TE. Test-retest reliability and sensitivity of the 20-meter walk test among patients with knee osteoarthritis. *BMC musculoskeletal disorders* 2013; 14: 166.
- Alias HA, Justine M. The impact of a submaximal level of exercise on balance performance in older persons. *TheScientificWorldJournal* 2014; 2014: 986252-.
- 36. Ito T, Shirado O, Suzuki H, Takahashi M, Kaneda K, Strax TE. Lumbar trunk muscle endurance testing: An inexpensive alternative to a machine for evaluation. *Archives of Physical Medicine and Rehabilitation* 1996; 77(1): 75-9.
- Lamprecht M, Hofmann P, Greilberger JF, Schwaberger G. Increased lipid peroxidation in trained men after 2 weeks of antioxidant supplementation. *International journal of sport nutrition and exercise metabolism* 2009; 19(4): 385-99.
- Gomez-Cabrera MC, Borras C, Pallardo FV, Sastre J, Ji LL, Vina J. Decreasing xanthine oxidase-mediated oxidative stress prevents useful cellular adaptations to exercise in rats. *The Journal of physiology* 2005; 567(Pt 1): 113-20.
- La Rubia M, Rus A, Molina F, Del Moral ML. Is fibromyalgia-related oxidative stress implicated in the decline of physical and mental health status? *Clinical and experimental rheumatology* 2013; 31(6 Suppl 79): S121-7.
- Juuso P, Skar L, Olsson M, Soderberg S. Meanings of feeling well for women with fibromyalgia. *Health care for women international* 2013; 34(8): 694-706.