Eggshell Membrane Reduces Joint Pain

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ABSTRACT

Can Eggshell Membrane Reduce Joint Pain?

BACKGROUND

While many conventional treatments have been used to remedy chronic joint pain, interest continues to grow in the area of alternative, natural treatments. Eggshell membrane (EM) supplementation is a novel treatment for joint health, and has recently been shown to rapidly and continually improve joint pain in patients with osteoarthritis and joint and connective tissue disorders. The current study aimed to observe the effects of one particular eggshell membrane product (fast joint care+; FJC+) supplementation on chronic joint pain in physically active adults.

METHODS

Sixty adults (40.2 ± 10.2 y; 78.6 ± 10.2 kg) experiencing chronic joint pain supplemented daily with either 500mg FJC+ or placebo, over the course of 4 weeks. Participants also completed a weekly exercise protocol designed to challenge their irritated joint. Participants then rated their joint pain immediately, and one day after, this exercise challenge.

RESULTS

Participants in the FJC+ group reported significantly less joint pain post-exercise following FJC+ supplementation (-16.13 ± 3.60) when compared to those in the placebo group (–4.30 ± 2.84; p=0.00171). In addition, during the 4 week study, both groups experienced decreases in next day joint pain (p=0.0015), although there were no significant differences between the two groups (p>0.05).

CONCLUSIONS

In the current study, daily FJC+ supplementation appeared to decrease post-exercise joint pain vs. placebo, although this effect did not persist 24 hours post-exercise. Because eggshell membrane research is in its infancy, further research may be needed to clarify its utility in managing joint pain.

Why Study Eggshell Membrane?

In the United States, over 20% of adults have reported doctor-diagnosed joint and connective tissue (JCT) disorders; this number has been projected to increase by 40% over the next 25 years [1, 2]. Numerous forms of intervention have been used as treatments to improve joint pain. Conventionally, nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics have been used to address joint pain associated with JCT disorders; however, their long term use has been associated with diverse and severe side effects including cardiac and gastrointestinal complications [3, 4].

Alternative therapies used to treat joint pain include dietary supplements; the most popular of these supplements being glucosamine, chondroitin and methylsulfonylmethane (MSM). While many turn to these complementary treatments to avoid the side effects associated with NSAIDs and analgesics, there is little evidence to support their effectiveness, and the evidence that does exist is equivocal [5]. Several large-scale human clinical trials [6], including the National Institutes of Health-sponsored Glucosamine/Chondroitin Arthritis Intervention Trial, as well as a few additional meta-analyses and reviews [5, 7] have reported limited effectiveness of glucosamine and chondroitin supplementation in reducing joint pain. However, other groups have noted long-term improvements in joint pain from glucosamine supplementation alone [8], and further enhanced effectiveness of combined glucosamine sulfate and chondroitin sulfate, rather than the separate use of either supplement [5, 9]. The question of their effectiveness in JCT populations is subject to ongoing debate.

There has been growing interest in eggshell membrane (EM) supplementation as a treatment for joint pain, as it does not present the side effects of conventional treatments (NSAIDs). Eggshells and their membranes have been extensively analyzed

for their components: the separate layers of the eggshell have been analyzed and found to contain several types of collagen (types X, I, V) [10-12]. Additionally, EM has been found to have notably high concentrations of a number of amino acids [13], collagen-like proteins [14-16], enzymes [17-19] and glycosminoglycans (GAGs).

Glycosaminoglycans are of high interest, as they play key roles in connective tissue [20]. Glucosamine, hyaluronic acid and chondritin sulfate are important GAGs in EM (21, 22). With the high protein and enzyme content, and naturally occurring GAGs in EM, scientists and nutritional supplement companies have speculated that it could present a viable alternative to traditional joint disorder and osteoarthritis treatments. Additionally, while the aforementioned elements of EM have been detected, it should be noted that membrane components have not yet been wholly characterized; there are likely a number of compounds that have yet to be identified in the membrane. Some of these yet undetected elements may contribute to benefits or improvements seen in joint health.

To date, very few studies have investigated the effects of EM supplementation on joint pain and range of motion. In rats, 4 weeks of EM treatment led to significant reductions in many proinflammatory cytokines (measured in plasma), notably including TNF- and IL-1 [23]. Two recent clinical reports [24, 25] investigated the timing and effectiveness of EM supplementation in JCT and osteoarthritis patients experiencing severe pain and limited range of motion. These patients received daily 500mg doses of oral EM for four to eight weeks. Rapid (seven to ten days) and continuous effects were seen in terms of reduced pain and stiffness, as well as improved flexibility. In both investigations, there were no reports of adverse effects with supplementation.

In the present study, we set out to observe the effects of EM (fast joint care+; FJC+) supplementation on joint pain within a physically active adult population experiencing chronic joint pain in one of four joints (ankle, knee, shoulder or elbow). As many adults use exercise to manage joint and connective tissue disorders, this population would likely see great benefit from adjunct therapies designed to reduce pain and increase range of motion.

METHODS

What We Did. And How We Did It.

Prior to commencing the study, all participants gave their informed consent. A total of 60 adults between the ages of 18 and 70 (45 men and 15 women; 40.2 ± 10.2 y; 78.6 ± 10.2 kg; see Table 1) agreed to participate. Each reported chronic pain in one of the following joints: elbow, shoulder, ankle or knee. Participants were recruited online through a popular health and fitness community and data were collected through self reports in a distance-based capacity. Participants were also pre-screened to exclude those who had used any additional medications (methotrexate or immunosuppressants), NSAIDs, analgesics, or joint supplements (MSM, glucosamine or chondroitin) two weeks prior to the start of the study. Those with egg allergies, or who were pregnant or breastfeeding, were also excluded. Participants were asked to refrain from use of pain medications throughout the study period.

TABLE 1. DEMOGRAPHICS OF BOTH SUPPLEMENT AND PLACEBO GROUPS

GROUP	MALES	FEMALES	AGE (YRS)	WEIGHT (KG)	LOCATION OF JOIN PAIN			
					KNEE	SHOULDER	ELBOW	ANKLE
Supplement	23	7	41.0 +/- 10.0	78.6 +/- 10.4	12	10	6	2
Placebo	22	8	39.4 +/- 10.5	78.6 +/- 10.1	13	10	5	2

Sex, age, weight, and reported joint pain area are shown for each group.

In order to participate, individuals had to be exercising regularly, at least three times per week. They were screened for their regular physical activity (reported 4.8 ± 1.1 exercise sessions/wk), and asked to ensure that both their exercise and nutritional regimens remained unchanged over the course of the study.

After matching for age, sex, and affected joint, participants (n=60) were randomly assigned to receive either the EM supplement (fast joint care+; FJC+), or a placebo supplement for 4 weeks. These groups did not differ significantly in terms of age or weight, contained similar numbers of men and women, and contained similar numbers of individuals with shoulder, elbow, knee, and ankle pain (see Table 1). All supplements were provided to subjects in identically marked containers, and all capsules (placebo and FJC+) were identical in appearance (color, flavor, size). All participants were instructed to take their "supplement" once per day, at the same time of day (i.e. first thing in the morning, with breakfast).

Each capsule of the FJC+ supplement contained 500mg of Gallus gallus (chicken) eggshell membrane extract (a commercial preparation sold as fast joint care+ by Genuine Health, Toronto, Ontario); additional non-medical ingredients included rice flour, magnesium stearate, gelatin, and water. The color and flavor matched placebo capsules contained only rice flour, magnesium stearate, gelatin, and water. The individual components of FJC+ were not quantified in the supplement as the product is intended to be used as a complete eggshell membrane extract, without additional ingredients (ie. additional glucosamine, chondroitin, etc.).

In addition to their normal exercise program, participants were asked to complete an additional exercise challenge once per week. This exercise challenge was to be completed on the same day of each week (Monday) and at the same time of day (in the morning, after supplementation and breakfast). The exercise challenge for those with chronic shoulder or elbow pain consisted of pushups. For those with chronic knee or ankle pain, the exercise challenge consisted of jump squats. Each of these sessions involved performing 10 sets of 5 repetitions of the given movement, with 2 minutes of rest between sets.

Immediately after each exercise challenge session, participants rated their specific joint pain on a Visual Analog Scale (VAS) at two time points: within 10 minutes of completing the challenge and 24 hours following the challenge. Compliance to the exercise programming and supplementation schedule was self-reported and logged by participants; those logs were provided to researchers weekly via email. Subjects were also asked to report any side effects during the trial.

Joint pain was assessed using a 100mm visual analog scale (VAS), and participants submitted this information via electronic form. A self-assessment was performed at the two time points (post-exercise, and next day after exercise) for each of the 4 weeks. Each subject was asked to "click on the line below to indicate how severe the pain is on the affected joint with 0 being no pain and 100 being pain as bad as it can be". Responses were submitted electronically on a weekly basis, after each pair of assessments. VAS scores were then measured in millimeters from the left hand end of the scale to the point marked by the subject.

Data were collected across the 4 weeks of supplementation, and analyzed using a two-way ANOVA with repeated measures (i.e. MANOVA). In cases of significant interactions ($p \leq 0.05$) post-hoc analysis was performed using Student's t-test for comparison between groups, and paired t-test for comparison within groups (JMP, SAS Institute Inc., Cary, NC). The VAS ratings were reported on a scale of 0 to 100, with 0 indicating no pain, and 100 representing greatest pain. Where appropriate, change scores were examined after adjusting absolute scores and then comparing between groups with a one-way analysis. All values are reported as mean $\pm$ SEM, and statistical significance was set at $p \leq 0.05$.

To summarize the protocol in brief: During week 1 of the investigation, subjects took their first 500mg dose of FJC+ with breakfast on Monday. After breakfast they immediately performed their first exercise challenge and then rated their joint pain using the VAS described above. In addition, they rated their joint pain on Tuesday, 24h later. During each subsequent week, subjects repeated the same protocol, providing 4 weeks' worth of joint pain data, with week 1 serving as a baseline.

RESULTS

So What Happened?

Following 4 weeks of supplementation, participants in the FJC+ group had a significantly greater decrease in post-exercise joint pain compared to participants in the placebo group (-16.13 ± 3.60 in the FJC+ group and −4.30 ± 2.84 in the placebo group; p=0.0171; see Figure 1). Figure 2 illustrates changes in joint pain between groups across the 4 weeks of supplementation: main effects were found for both time (p=0.0003) and the interaction between group and time (p=0.0354).
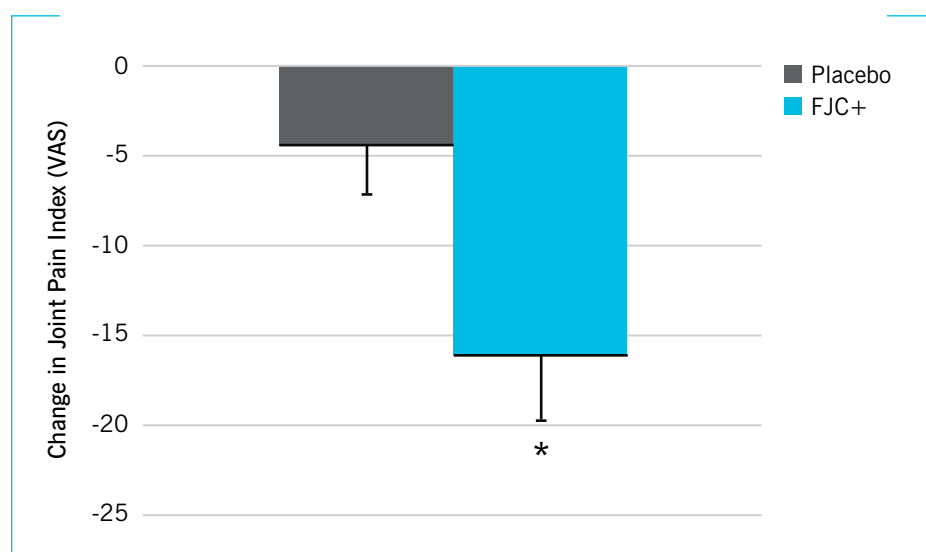
Figure 1. Mean change in joint pain (measured with VAS) following 4 weeks of supplementation. Participants in the FJC+ group experienced significantly larger decreases in post-exercise joint pain compared to participants in placebo group (p=0.0171). Note: absolute scores were adjusted into change scores, which were then compared between groups using a one-way analysis.
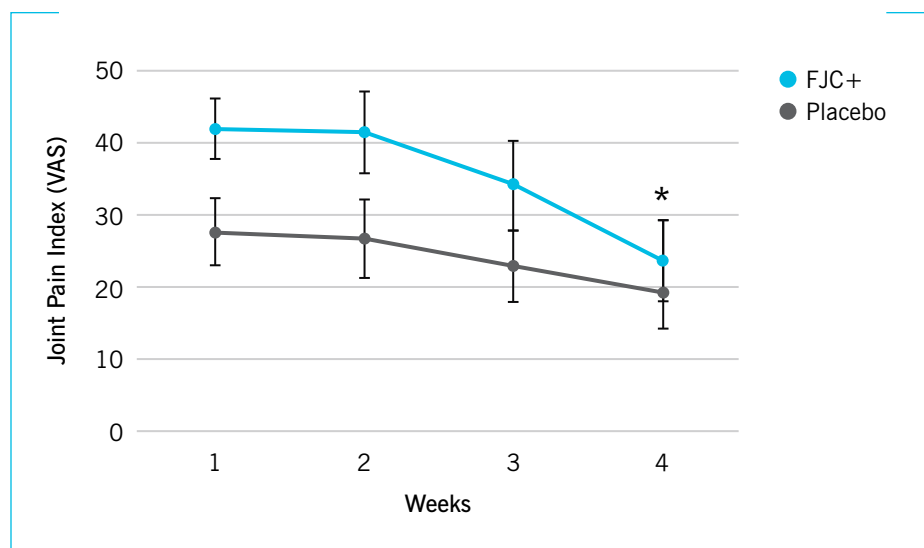
Figure 2. Post-exercise joint pain (measured with VAS) across 4 weeks of supplementation. There was a main effect for time (p=0.0003), and an interaction between time and group (p=0.0354), indicating greater joint pain decreases in the FJC+ group (-43.4%) than the placebo group (-30.6%). Post-hoc analysis showed between group differences from week 1 to week 4 (p=0.0171). Note: higher VAS values indicate more pain.

In accordance with Figure 1, post-exercise joint pain in the FJC+ group decreased by 43.4% while the placebo group experienced a 30.6% decrease in pain over the 4 week period. Post-hoc analysis shows a mean difference between groups when comparing overall change in pain from week 1 to week 4 (p=0.0171).

Next day reports of joint pain also decreased over time (p=0.0015; see Figure 3) with next day joint pain decreasing by 46.7% in the FJC+ group (from 35.34 ± 4.33 during week 1 to 18.82 ± 4.38 during week 4) and by 40.9% in the placebo group (from 26.38 ± 4.58 during week 1 to 15.59 ± 4.01 during week 4). There were no significant differences between the groups' joint pain scores across the 4 weeks of supplementation (p=0.1971 for group and time interaction).
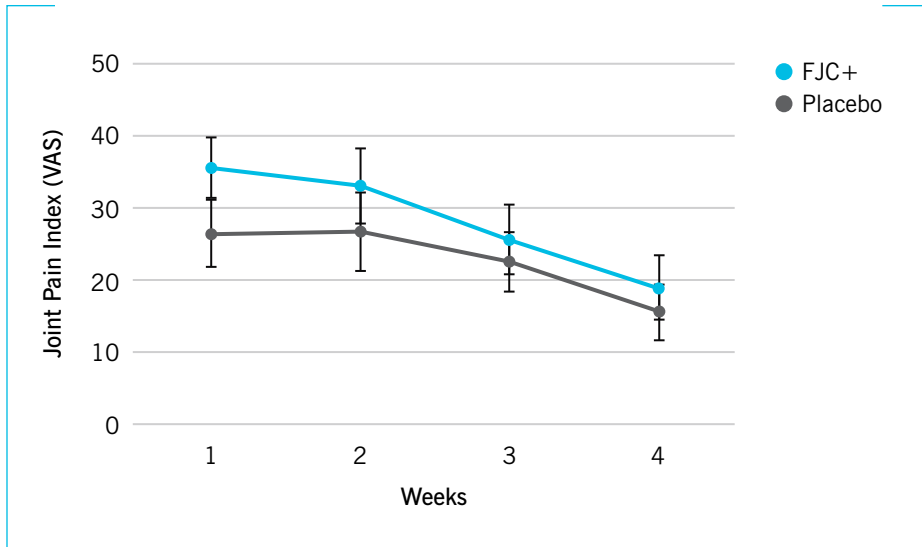
Figure 3. Next day joint pain (measured with VAS) across 4 weeks of supplementation. A main effect was seen for time (p=0.0015). However, there were no significant differences between groups across the 4 weeks (p>0.05), indicating similar joint pain decreases in both the FJC+ group (-46.7%) and the placebo group (-40.9%). Note: higher VAS values indicate more pain.

Participants in both placebo and FJC+ supplementation groups did not report any side effects during the study.

Some Clarifications About Our Work

The results of this investigation suggest that four weeks of supplementation with 500mg FJC+ daily improves post-exercise joint pain vs. supplementation with placebo, specifically in physically active adults experiencing pain in the ankles, knees, shoulders, and elbows.

Other investigations using EM supplementation have observed similar reductions in joint pain, specifically in populations with osteoarthritis and JCT disorders. In one randomized, double-blind, placebo-controlled study, daily oral administration of either 500mg placebo or 500mg EM was given to patients with knee osteoarthritis [24]. After 10 days, rapid improvements in both joint pain and stiffness were seen in the EM group. Improvements in pain and stiffness were sustained (and enhanced) following 60 days of administration. A similar study with JCT patients [25] also observed both rapid (7 days) and sustained (30 days) improvements in pain and flexibility following daily administration of 500mg EM. There were no adverse events reported in either study, and the treatments appeared to be well tolerated by the patients. These statistically and clinically significant outcomes suggest that EM supplementation may be a natural and effective alternative therapy for both clinical populations with limited activity levels as well as physically active populations.

Many of the various components present in EM have been thoroughly analyzed. Eggshells consist of a number of layers: an inner and outer membrane, a mammillary layer (connecting the eggshell and outer membrane), an outer palisade layer, and an outer cuticle covering the eggshell [10]. The inner and outer shell membranes are the first layers of extracellular matrix covering the egg itself [11]; the outer membrane is predominantly made of type I collagen, whereas the inner membrane consists mainly of type V collagen [12]. In addition, type X collagen has been reported to occur in both of these membrane structures [10]. EM amino acid profiles have also shown high concentrations of arginine, glutamic acid, histidine, cystine and proline [13]. Additionally, a number of collagen-like proteins (including hydroxyproline, hydroxylysine, desmosine, and isodesmosine) are primary structural components of the membranes.

Other components have been quantified in EM including: lysyl oxidase (reported to play a role in the development and repair of connective tissue), ovotransferrin, and lysozyme [17-19]. However, the presence of glycosaminoglycans in EM is of particular interest. Glycosaminoglycans (GAGs), such as glucosamine, are composed of repeating hexosamine disasccharides and act as major components of connective tissue [20].

Clearly, there are a number of individual components present in the EM that have known physiological roles in joint and connective tissue; however, EM is novel in that it is a natural extract that provides a combined source of these compounds. The absolute quantity of each component in the EM is not known, and those quantities may likely vary with each extraction in the supplement production process. Additionally, it is plausible that a number of yet unisolated elements, proteins, and enzymes exist in EM, which may also contribute to improved joint and connective tissue health. Therefore, the observed benefits associated with EM supplementation may not be directly attributable to any one specific component of the supplement (ie. glucosamine, chondroitin, etc.); it may be more appropriate to assume that the combined effects of the known—and unknown—components of EM contribute to the observed improvements in joint health.

A number of individual components in EM are known to have important roles in maintaining connective tissue in vivo, though the physiological mechanisms by which those components improve overall joint health through supplementation (flexibility, connective tissue repair and maintenance) have not been measured in humans. One experiment, however, investigated the effects of EM supplementation on systemic pro- and anti-inflammatory markers in rats [23]. In this study, rats were given oral doses of EM for 7 days. Significant decreases were observed in plasma levels of numerous inflammatory antigens following supplementation; thus, it is possible that the anti-inflammatory effects of oral EM supplements may contribute to the improvements in joint pain ratings seen in human trials. More research is warranted to investigate these effects.

Interestingly, the most pronounced effects of FJC+ supplementation in this study were present in post-exercise ratings of joint pain. This may be due to the proposed anti-inflammatory benefits associated with EM. If the exercise challenge used in this investigation led to acute joint inflammation, it stands to reason that the most pronounced impact of EM would be to reduce the pain associated with this post-exercise increase in inflammation. This, however, is highly speculative and more research is needed to confirm both the mechanisms of action of EM as well as the situations in which supplementation would provide the most benefit.

One of the most appealing aspects of EM is that this supplement is a natural therapy, unlike the traditional NSAIDs and analgesics, which have led to documented side effects that include serious cardiovascular and gastrointestinal complications [3, 4]. In comparison, there have been no reports of any adverse effects following EM supplementation in human trials [24, 25], including our own.

CONCLUSIONS

What Did
We Learn?

In conclusion, the three human trials to date (including the present study) have demonstrated statistically significant and clinically relevant improvements in joint pain using 500mg of EM daily. Although more research is needed to further document these effects, as well as to clarify the mechanism of action of EM, the current body of evidence suggests that those who suffer from chronic joint pain may benefit from EM and FJC+ as an alternative therapy for chronic joint pain and perhaps other JCT disorders.

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INTERESTS AND ACKNOWLEDGEMENTS

Who Had A Financial Stake and Who Helped?

COMPETING INTERESTS

Genuine Health Inc (Toronto, Canada) provided the nutritional supplements used in this study. Within the past five years, the author has been an independent consultant for Genuine Health. However, he was not compensated by Genuine Health in any way for the conduct of this study. Nor does he hold stock or shares in the company or receive compensation that is tied directly to product sales. In summary, the author was not paid as a consultant, or in any way in connection with this research. There are no other competing interests to report.