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Effect of Royal Jelly on Performance and Inflammatory Response to Muscle Damage: A Systematic Review

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Abstract: Heavy and excessive physical activity can result in injury or muscle damage in ordinary people and athletes, hence diminishing their physical ability during training and competition. It has been established that royal jelly possesses antioxidant and anti-inflammatory effects and enhances athletic performance. This study aims to go through the published research on royal jelly to find evidence that it improves performance and reduces inflammation after muscle injury. The method employed is Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The databases included Pubmed/MEDLINE, Scopus, Web of Science, and Embase. The ten papers' objectives, topic suitability, sample size, research technique, funding, and commentary were assessed. This research review reveals that royal jelly reduces the subjective sense of muscle pain intensity; reduces muscle damage via a decrease in creatine kinase (CK); improves muscle function; modulates pro-inflammatory cytokines such as TNF-a, IL-6, and IL-8; and has an antioxidant impact. Administration of royal jelly at doses ranging from 300 to 3000 mg/day before, during, and 72 hours after exercise enhances performance by lowering EIMD and regulating physical activity-induced inflammation. Conclusion Royal jelly enhances performance and the inflammatory response to muscle injury. Royal Jelly can be used as a dietary supplement by athletes and other physically active people whose activities cause muscle injury and inflammation.

Keywords: royal jelly; performance; muscle damage; exercise; inflammation.

1. Introduction

Excessive and strenuous physical activity can lead to muscular injury or damage in a sedentary individual or athlete (EIMD) [1–4]. Muscle injuries, such as inflammation and DOMS (delayed onset muscle soreness), are characterized by muscular rigidity as well as discomfort [2,5,6]. That often develops 24 hours after high-intensity physical exercise, with the peak of DOMS occurring 24-72 hours later and diminishing after 5-7 days [7,8]. Therefore, athletes or individuals who have DOMS cannot follow exercise routines to the fullest extent, affecting performance in both training and competition sessions and negatively affecting the athlete or individual's psychological state, performance, and training quality [6,9,10].

Numerous health, nutrition, and exercise professionals have conducted comprehensive research on strategies to lower the incidence of EIMD and DOMS, as well as taking non-steroidal anti-inflammatory drugs (NSAIDs) [3,11]. Nevertheless, despite the purported benefits of NSAIDs, clinical evidence suggests that NSAID interventions do not necessarily benefit recovery after EIMD or DOMS [12].

Previous research has demonstrated that nutritional interventions, such as green tea extract, curcumin, and cinnamon, enhance injury recuperation and biomarker changes in individuals and athletes [7,8,13,14]. However, the use of royal jelly to recover individuals and athletes following sports-related injuries is still limited. Royal jelly is known to produce the inflammatory markers CRP and anti-inflammatory adiponectin, decreasing biomarkers associated with EIMD and DOMS [15–17]. However, few studies have looked at the impact of royal jelly on working out, and those have found mixed results, despite periodic investigation. As a result, we assessed the available clinical study data on the effects of royal jelly consumption on EIMD.

2. Materials and Methods

This study follows the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA). This study's analytical structure is compatible with a number of bibliometric studies undertaken on different topics. PICO is the approach used to search for articles. PICO is a library or research data-gathering approach that uses diverse library sources to survey study subjects (books, scientific journals). The population analyzed in academic writing utilizes royal jelly to enhance athletic performance and as a marker for muscle injury.

2.1. Methods for searching and selecting.

Databases are analyzed, including PubMed/MEDLINE, Scopus, Web of Science, and Embase. Journals were included if they addressed royal jelly, exercise, inflammation, performance, or muscular injury. Notes were compiled, titles and abstracts were screened, and full-text articles were verified using reference management software (Mendeley). A total of 40 papers published between 2010 and 2021 were identified.

2.2. Inclusion and exclusion criteria.

Four electronic databases were used in the study's data selection and analysis. Databases, including Pubmed/MEDLINE, Scopus, Web of Science, and Embase, are available. This study's analytic framework is consistent with others utilized to investigate a wide range of issues. Ten papers published between 2010 and 2021 were retrieved. To find all of the articles published about royal jelly between 2010 and 2021, we used a reference manager (Mendeley) to organize our notes, skimmed the titles and abstracts, and then read the full contents of all the papers that piqued our attention. Articles that only appear in abstract form or in publications that are not peer-reviewed are disqualified. Publications that met the inclusion criteria requirements were selected for this systematic review.

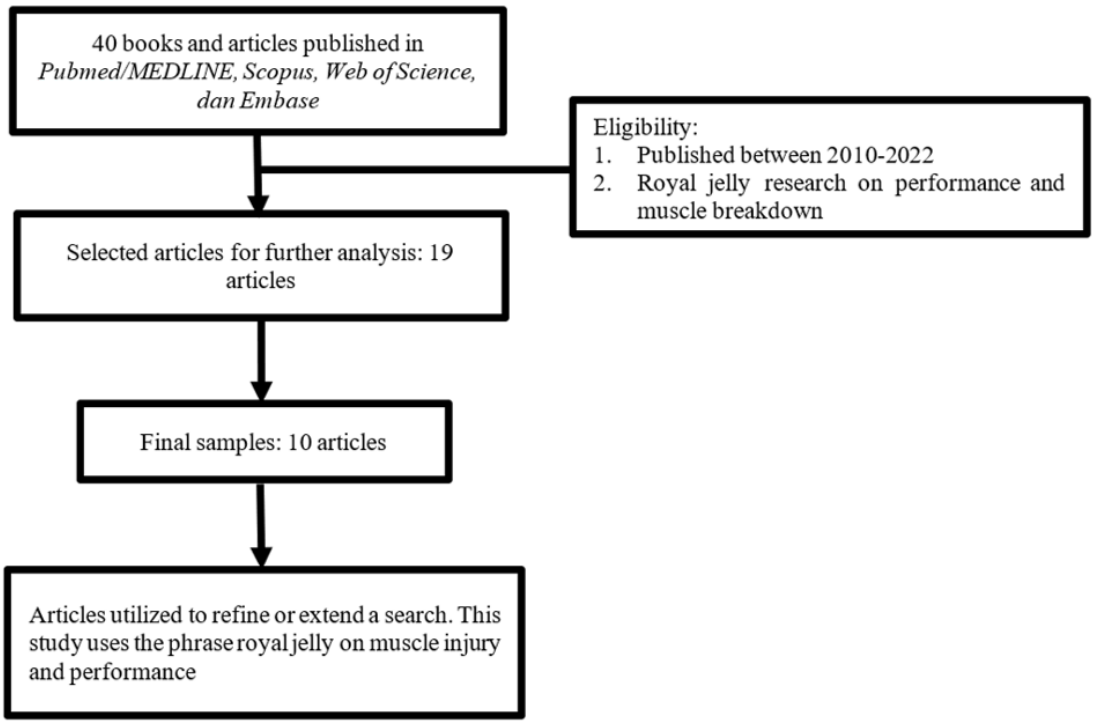

Figure 1. Research design.

3. Results and Discussion

The studies from Tables 1 and 2 are some of the findings from the research included in this literature review.

Table 1. Royal Jelly studies on animal impacts

Author	Sample Characteristics	Study Design	Intervention	Results
(Shirzad M, Yousofi M, Zamanzad B, Sedaghat A, Hosseini M, Shahinfard N, 2014) [18]	Sixty female mice were split into six groups of four, each containing eight-week-old mice. Take Group 1 as a baseline against which the rest of the experiment may be measured. The second group is good control. Subjects in Group 3 received RJ (200 mg/kg) once a day. Patients in Group 4 received RJ (200 mg/kg) twice weekly. RJ (300 mg/kg) was administered once daily to Group 5 and once every two days to Group 6.	Experiment	The sole negative control was a daily application of saline to the wounded area. Positive controls were treated with an ointment containing 2.0% nitrofurazone. The third group received 200 mg/kg of royal jelly daily, whereas the fourth group received the same amount. In the fifth group, 300 mg/kg of royal jelly was administered daily, and in the sixth group, 300 mg/kg of royal jelly was utilized daily. The findings of this study demonstrated that using RJ daily had a greater effect on wound healing than using Nitrofurazone or RJ every two days.	The results of this study reveal that daily consumption of RJ has a greater effect on wound healing than using Nitrofurazone and RJ every two days.
(Aslan & Aksoy, 2015) [19]	Five groups of 35 male Sprague-Dawley white rats weighing 300-380g each were created. Group 1, Control condition Group 2: the EG group. RJ Group is Group 3. Group 4: RJ and EG. Group 5: EG and RJ	Experiment	Group 1 was given a standard meal and drinking water. The second group received normal feed and water containing 1% ethylene glycol. Group 3 was orally gavaged with 100 mg/kg of Royal Jelly. Group 4 was given water containing 1% ethylene	Royal Jelly's antioxidants inhibit ROS generation and assist the antioxidant system. It is believed that Royal Jelly has anti-inflammatory properties through modulating signaling pathways.

Author	Sample Characteristics	Study Design	Intervention	Results
			glycol. In addition, these rats were given 100 mg/kg of Royal Jelly daily by oral gavage. Group 5 was given 1% ethylene glycol-containing water for the first two weeks. During the previous two weeks, mice were given 100 mg/kg of Royal.	
(Takahashi et al., 2018) [20]	The mice with the same mean weight were then divided into four groups: the sedentary control group (Con + Sed) (n = 8), the control training group (Con + Tr) (n = 6), the treated sedentary group RJ (RJ + Sed) group (n = 7), and training treated with RJ (RJ + Tr) group (n = 7).	Experiment	Three weeks of RJ (1 mg/g body weight) or water were given to mice. Resistance training was administered to mice in the training group (20 m/min; 60 minutes; 5 times per week).	These data imply that RJ treatment elicits mitochondrial adaptation in the soleus muscle of ICR through resistance training and AMPK activation. mice

Table 2. Royal Jelly studies human consequences.

Author	Sample Characteristics	Study Design	Intervention	Results
(Morita et al., 2012) [21]	A total of 61 healthy volunteers aged 42-83 years were enrolled and randomly divided into a royal jelly group (n = 31) and a control group (n = 30).	A randomized placebo-controlled, double-blind trial.	3000 mg royal jelly (RJ) or placebo in 100 ml fluid/day taken for 6 months.	The consumption of RJ for six months in humans improved erythropoiesis, glucose tolerance, and mental health.
(Büyükipekçi et al., 2018) [22]	30 healthy 20- to 25-year-old undergraduates were separated into two groups; the control group received corn starch, and the experimental group received honey.	Experiment	The experimental group received 5 grams of royal jelly and 45 grams of honey, for a total of 50 grams, 20 to 30 minutes before breakfast for eight weeks. In the same way, 50 grams of placebo (corn starch) were administered to the control group.	In adolescents who performed maximal strength training, supplementation with royal jelly and honey had no effect on the increase in weight lifted, which was attributed to the weight training but did elicit hormonal alterations.
(Tasdoğan et al., 2020) [23]	20 healthy, sedentary adults aged 21-23 years, divided into two groups; the experimental group and the placebo group.	Placebo-controlled experimental design	For 15 days, the experimental group got 1000 mg/day of Royal Jelly, whereas the placebo group received 1000 mg/day of water. Aerobic and anaerobic power measures were taken in the laboratory one day before and after a 15-day interval in both groups.	It can be said that a royal jelly supplementation taken daily for 15 days at 1000 mg has a positive effect on the aerobic capacity of sedentary men.
(Saritas et al., 2011) [24]	Forty male swimmers, all between the ages of 18 and 25, were scouted. The swimmers were randomly split up into four groups of ten.	Placebo-controlled experimental design	Subjects in groups 1, 2, and 3 received up to 1 g and 500 mg of royal jelly, respectively, while group 4 received a placebo (corn starch). Except for the placebo group, royal jelly capsules were taken 20 to 30 minutes before breakfast once a day for four weeks.	Taking 500 mg, 1 g, or 2 g of royal jelly per day for 30 days did not improve swimming performance. Furthermore, because of its high amino acid content, BUN and creatinine levels tend to rise.
(NAZMI et al., 2014) [25]	Forty male swimmers, all between the ages of 18 and 25, were scouted. The	Placebo-controlled	The first group received 2 g/day, the second group received 1 g/day, the third	Four weeks of royal jelly supplementation in this study had no effect. It is

Author	Sample Characteristics	Study Design	Intervention	Results
	swimmers were randomly split up into four groups of ten.	experimental design	group received 500 mg/day, and the fourth group received a placebo. A total of 20 kilometers of swimming is completed in a four-week training period of two hours per day, five times each week.	suggested to be effective with higher doses and for a longer period of time.
(Pancar, 2021) [26]	Forty male participants were split into four groups before the trial began: a control group of smokers (n = 10), an inspiratory muscle training (BMI) group of 10 people, a group of RJ practitioners (n = 10), and a group of RJ practitioners with BMI practitioners (n = 10).	Randomized experimental study with a control group	The RJ-supplemented group received 1,000 mg/day of RJ in a glass vial between 8.00 and 10.00 am for 4 weeks.	BMI and RJ supplements improved these measures by modifying tobacco users' iron metabolism.
(Meng et al., 2017) [27]	The study's 194 participants were split into three groups: placebo, low-dose pRJ, and high-dose pRJ.	randomized, double-blind, placebo-controlled	The placebo group received no Royal Jelly, whereas the low-dose pRJ group received 1.2 g/day and the high-dose pRJ group received 4.8 g/day.	The intervention had no obvious effect on physical appearance. These data imply that pRJ therapy may not increase muscular strength in the elderly but rather slow its progression.

This literature evaluation set out to determine whether or not royal jelly may mitigate the negative effects of exercise-induced inflammation and enhance performance. Experiments on animals have shown that royal jelly, a honeybee product, has various beneficial pharmacological properties, including anti-tumor, anti-inflammatory, antibacterial, and performance-boosting benefits [20,28–30]. In humans, consuming royal jelly at specific doses can improve performance in athletes and active individuals and mental health and can be used to reduce the effects of inflammation after strenuous physical activity [21–23,27,31,32]. The main results showed that supplementation with a dose of 300 mg/bb royal jelly reduced various inflammatory reactions caused by muscle injury in experimental animals. In contrast, a 3000 mg/bb dose increased physical performance in active individuals and athletes. However, verifying the true effectiveness of royal jelly's antioxidant properties is difficult. In order to provide a clearer analysis, the following results have been categorized based on the varying measurement results from the various investigations [18,21]. The type of exercise, the dosage of each supplement, and the intervention length can all impact the final result. Participants' age, gender, ethnicity, body composition, training level, training variations, diet, and health state may all have a role in the results.

3.1. Anti-inflammatory effects of royal jelly.

In a study conducted on animals, administration of royal jelly at doses of 200 mg/kg and 300 mg/kg for five consecutive days showed a greater effect on wound healing than nitrofurazone [18]. Another study found that a monthly dosage of 100 mg/kg of royal jelly reduced inflammatory indicators such as CRP and IL-6 [19]. Recent research on asymptomatic obese adults has shown anti-inflammatory benefits for patients. The capsule containing 333 mg/bb per day was taken orally to the patients for eight weeks. The treatment of RJ led to a drop in the inflammatory marker CRP, an increase in the anti-inflammatory adiponectin, and a decrease in the cytokine IL-6 [16]. Meanwhile, royal jelly reduces the adhesion of

Pseudomonas aeruginosa bacteria, which causes respiratory tract infections in older individuals. According to cell culture investigations, it protects epithelial cells against excessive inflammatory reactions to P. aeruginosa infection [15].

DNA and tissues can be safeguarded from damage due to royal jelly. These results point to RJ's potential as a natural antioxidant, able to counteract the inflammatory response caused by UVB rays and the resulting oxidative damage. The RJ group showed that the dose of RJ had a direct correlation with its ability to increase NRF2 levels. When a cell needs to defend itself against oxidative stress, it turns to a group of genes coordinated by the transcription factor NRF2. Antioxidant synthesis, mediated by NRF2, increases proportionally to the number of oxidants produced by cells. However, NRF2 expression is downregulated, and antioxidant synthesis is suppressed if cellular oxidant production is excessive and endogenous antioxidants are unable to compensate. Reduced levels of oxidants are one mechanism by which RJ inhibits inflammation; this decreases NF-kB expression and, in turn, TNF-alpha production [33].

3.2. Performance effects of royal jelly.

Results from previous research showed that a daily dosage of 3 grams increased erythropoiesis, glucose tolerance, and mental health in participants aged 48-83 years when supplied for 6 months [21]. A further trial with teenage swimmers found that an intervention of 0.5-2 gam/day of royal jelly had no apparent effect on their performance. Therefore, it was determined in this study that a combination of a larger intervention dose and a longer intervention period was optimal [24,25]. A similar effect was seen in a trial of sedentary people who took royal jelly supplements at a dose of 1 g/bb once a day for 15 days [23]. These improved outcomes indicate that more stimulation by RJ intervention is necessary to produce a rise in maximum mitochondrial enzymatic activity, which would have a significant impact on performance. Several components of RJ, including amino acids/proteins like leucine and 10-hydroxy-2-decenoic acid, which are unique fatty acids present in royal jelly, have been reported to induce the activation of AMPK (50-AMP-activated protein kinase), the main mediator of mitochondrial biogenesis, in skeletal muscle, or myotubes. Meanwhile, royal jelly has a number of ingredients with potential antioxidant effects, including 10-hydroxydecanoic acid, free amino acids including proline, cystine, and cysteine, flavonoids, and phenolic compounds. Studies have revealed that oxidative stress is critical in activating AMPK (50-AMP-activated protein kinase) in skeletal muscle, which can boost performance [20].

In the past, researchers have shown that taking a royal jelly supplement increases lipid peroxidation and prevents its growth. A significant improvement was seen after supplementation by reducing lipid peroxidation. These findings suggest that lipid peroxidation variables may contribute to the rise in aerobic power and can be employed to counteract this trend [23].

The objective of this study was to see how royal jelly affected healthy athletes' performance and how their bodies handled inflammation after muscle damage. Royal jelly reduces inflammation because it blocks the synthesis of inflammatory cytokines, including interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-a). Researchers have shown that taking royal jelly can help with pain relief, reduce inflammation indicators like C-reactive protein and creatine kinase, and improve exercise performance. From one thousand milligrams (mg) to three thousand (mg) per day is optimal. Therefore, this study demonstrates that royal jelly has many advantages, particularly as an anti-inflammatory substance, especially for the recovery process and its influence on performance. There have

been no reports of adverse reactions to consuming royal jelly; instead, the key is to determine the optimal dosage for yourself or your athlete to get the most beneficial effects.

4. Conclusions

There is no definitive proof that ingesting royal jelly can boost performance and reduce the inflammatory response to muscle damage. Those who put their bodies under extreme stress, such as athletes, may find that taking a Royal Jelly supplement helps reduce muscle soreness and inflammation.

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Conflicts of Interest

The authors declare no conflict of interest.

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