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Royal jelly is an effective and relatively safe alternative approach to blood lipid modulation: A meta-analysis

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ABSTRACT

Royal jelly is a functional food with several health promoting properties. The aim of present meta-analysis was to examine the role of royal jelly in blood lipid profiles. We systemically searched PUBMED, the Cochrane Library, Scopus, Web of Science and Google Scholar to identify eligible studies up to July 2017. Clinical trials which investigated the efficacy of royal jelly on adult blood lipid parameters were included. A random effects model was used for quantitative data synthesis. The pooled analysis of six trials suggested that royal jelly reduces total cholesterol blood levels. No significant change was observed in triglycerides, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol blood concentrations. Subgroup analysis revealed a greater impact of RJ on the decrease of Total cholesterol and the increase of high-density lipoprotein cholesterol levels in studies with a long-term follow-up (≥ 90). This meta-analysis suggested that Royal jelly consumption might effective on improvement of lipid parameters.

1. Introduction

Dyslipidemia is a leading risk factor for the development of CVD, characterized by elevated levels of low-density lipoprotein cholesterol (LDL-C) and/or triacylglycerol (TG), and/or reduced levels of high-density lipoprotein cholesterol (HDL-C) (Sahebkar, 2017). Poor control of dyslipidemia is related to a set of problems that reduces quality of life, increases mortality and imposes huge costs on social healthcare systems (Yusuf, Reddy, Ounpuu, & Anand, 2001). There is well-established evidence for the efficacy of common drugs to treat dyslipidemia, even though most of them possess considerable adverse effects (Sahebkar, 2017; Yan et al., 2006). Over recent decades, evidence shows a growing interest in finding natural alternatives to lipid-modifying therapy (Parikh, Parikh, & Kothari, 2014). The lack of sufficient information in understanding the effects of medicinal plants on the disease and its possible side-effects is an important problem faced by doctors (Bahmani et al., 2015).

Royal jelly (RJ) is a milky viscous substance and one of the most interesting functional foods (Nagai & Inoue, 2004; Pourmoradian, Mahdavi, Mobasseri, Faramarzi, & Mobasseri, 2014). RJ is produced primarily from the hypopharyngeal and mandibular secretory glands of young worker bees (*Apis mellifera*) (Buttstedt, Moritz, & Erler, 2014), and is composed of water, carbohydrates, proteins, free amino acids, lipids, vitamins (mainly thiamine, niacin, riboflavin), minerals (mainly iron and calcium) and significant amounts of bioactive substances (Bincoletto, Eberlin, Figueiredo, Luengo, & Queiroz, 2005). Today, RJ is widely utilized in many countries as a commercial product, especially in food supplements and cosmetics (Ramadan & Al-Ghamdi, 2012). RJ has been used as a human medicine and shown to possess several pharmacological effects, including immunomodulatory (Okamoto et al., 2003), antioxidant (Nakajima, Tsuruma, Shimazawa, Mishima, & Hara, 2009) antitumor (Townsend, Brown, Felauer, & Hazlett, 1961; Townsend et al., 1960), neurogenesis-promoting (Hattori, Nomoto, Fukumitsu, Mishima, & Furukawa, 2007) and vasoactive properties (Matsui et al., 2002). Evidence from animal studies has documented the potential benefits of RJ consumption on lipid metabolism (Nakajin, Okiyama, Yamashita, Akiyama, & Shinoda, 1982; Vittek, 1995). Also, the lipid-lowering characteristics of RJ have been addressed in some human studies (Chiu et al., 2017; Lambrinoudaki et al., 2016), whereas others have not suggested any improvement (Morita et al., 2012).

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Because of these inconclusive results, this meta-analysis was conducted to determine whether RJ supplementation can positively modulate blood lipid parameters.

2. Material and methods

This meta-analysis was designed in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009), and its protocol was registered on PROSPERO international prospective register of systematic reviews (registration number: CRD42017069198(.

2.1. Search strategy

Electronic databases, including: PubMed (MEDLINE) (http://www.ncbi.nlm.nih.gov/pubmed), Cochrane Library (http://www.cochranelibrary.com/), Scopus (http://www.scopus.com/), the Web of Science (http://www.thewebofknowledge.com/) and Google Scholar (https://scholar.google.com/) were systematically searched to identify relevant publications up to July 2017. One-handed search method was applied to optimize search strategy for each database without any restrictions by “Royal Jelly” terms in combination with the wild-card ‘*’ and Medical Subject Heading (MeSH) terms. References of all retrieved articles were hand-searched to find eligible trials that might have been missed.

2.2. Study selection

Two researchers independently performed the screening process, involving a title/abstract review, and full paper text search, to determine whether the studies were eligible for inclusion in the systematic review and meta-analysis. Any inconsistencies in study selection were resolved by a third author.

All trials were included if they investigated the efficacy of RJ on each of the following lipid parameters: total cholesterol (TC), TG, LDL-C and HDL-C. Publications were discarded under the following conditions: RJ supplementation was combined in a mixture with other substances; duplicated data; and not meeting the initial objective.

2.3. Data extraction and quality assessment

A quality assessment of the studies involved with a control group was conducted by using a jaded scale (Jadad et al., 1996). This scale is based on three broad perspectives: randomization concealment (2 points), blinding (2 points), and dropout rate (1 point). The overall quality score of each publication varies from 0 to 5. We considered ≤ 2 score as low, 3 score as moderate and ≥ 4 score as high quality. In addition, the National Institutes of Health quality assessment tools were used for before–after (pre–post) studies with no control group (NHLBI & International, 2014). These tools include 12 questions to assess selection bias, information bias, measurement bias, and confounding factors. The overall score of each study, if it was ≤ 3, between 4 and 6, and ≥ 7, were considered as low, moderate and high quality, respectively.

Two of the authors independently reviewed eligible studies that passed the initial assessment, and the following information was abstracted: characteristics of study (first author’s last name and publication year), characteristics of participants (number of participants, mean age, BMI and condition of subjects), study description (setting, duration and intervention dosage), and outcomes.

2.4. Statistical analysis

Meta-analysis was conducted using STATA software (version 11.0; Stata Corporation). To calculate the effect size, lipid parameter concentrations (TC, LDL-C, HDL-C and TG) were collated in mg/dl. In any reported case, SEM (standard error of the mean), and Standard deviation (SD) was calculated using the following formula (Higgins & Green): SD = SEM × sqrt (n), (n: number of subjects).

In studies where net changes were not directly reported in the intervention and control groups, the effect size was computed by subtracting the values at the endpoint of the intervention from those at the baseline. The standard deviations of mean differences were calculated by using [SD = square root [(SD pre-treatment)^2 + (SD post-treatment)^2 − (2R × SD pre-treatment × SD post treatment)], with the correlation coefficient (R) assumed to be 0.5 (Higgins & Green, 2011). The random-effects model was used for pooling analysis due to compensate for the heterogeneity of studies (Dersimonian & Laird, 1986; Higgins & Green, 2011). Inter-trial heterogeneity was assessed by I-square (I^2) (Higgins & Green, 2011) test and H^2 (Sterne, Gavaghan, & Egger, 2000) among studies included. A subgroup analysis was performed to determine potential sources of inter-study heterogeneity. Additionally, inter-subgroup heterogeneity was evaluated through a fixed-effect model. The effect size was expressed as weighed mean difference (WMD) and at 95% confidence interval (CI). Sensitivity analyses was applied to determine the influence of individual studies on the overall effect size. Publication bias was assessed by Egger’s regression asymmetry test and Begg's rank-correlation methods (Egger, Smith, Schneider, & Minder, 1997; Sterne, Bradburn, & Egger, 2008). P-Values < .05 were considered statistically significant.

3. Result

A summary of the study screening and selection process is presented in Fig. 1. Initial systematic search yielded 1286 unique citations after the removal of duplicates. Articles were reviewed and 1275 publications were excluded whose title/abstract did not meet the inclusion criteria. From the remaining studies, five articles were discarded for the following reasons: conducted on animals (n = 3); were review studies (n = 2). Ultimately, six articles were eligible and included in the meta-analysis.

3.1. Study characteristics

The primary characteristics of the trials included are shown in Table 1. Six trials (Chiu et al., 2017; Guo et al., 2007; Lambrinoudaki et al., 2016; Mobasseri, Pourmoradian, Mahdavi, & Faramarzi, 2014; Morita et al., 2012; Munstedt, Henschel, Hauenschild, & von Georgi, 2009) comprising 237 participants, with a mean age of nearly 50, provided data on the effects of RJ consumption on blood lipid levels. Of these included studies, 4 studies (Chiu et al., 2017; Guo et al., 2007; Mobasseri et al., 2014; Morita et al., 2012) were controlled parallel trials, whereas the remaining studies (Lambrinoudaki et al., 2016; Munstedt et al., 2009) had a single-arm design. The studies were conducted in Japan (Guo et al., 2007; Morita et al., 2012), Taiwan (Chiu et al., 2017), Germany (Munstedt et al., 2009), Greece (Lambrinoudaki et al., 2016) and Iran (Mobasseri et al., 2014). Of six studies, two included female participants with Type 2 diabetes (Mobasseri et al., 2014), two had participants with hypercholesterolemia (Chiu et al., 2017; Munstedt et al., 2009), two included healthy volunteers (Guo et al., 2007; Morita et al., 2012) and one trial involved healthy postmenopausal women (Lambrinoudaki et al., 2016). Two trials included female participants exclusively (Lambrinoudaki et al., 2016; Mobasseri et al., 2014), while the remaining 4 studies recruited both sexes (Chiu et al., 2017; Guo et al., 2007; Morita et al., 2012; Munstedt et al., 2009). TG, TC, LDL-C and HDL-C blood concentrations were the most commonly reported outcomes among the included articles. The daily dose of RJ consumption varied from 0.35 to 10 g, and the duration of treatment ranged from 30 to 180 days. Most studies had zero dropout participants during the follow-up period, and no outcome data was missing. Almost all of the studies reported good compliance with no adverse effect of consuming RJ. These articles were published from 2009 to 2016.