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REVIEW ARTICLE

Royal Jelly: A Review on Its Composition and Beneficial Effects

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ABSTRACT

Background: The hypopharyngeal and mandibular glands of worker honeybees create a creamy material called royal jelly, which is supplied to the queen and larvae throughout their early stages of development. Due to its numerous health benefits, it has been utilized historically as a vital bee product in traditional medicine from ancient times. It is made up of a combination of proteins, fats, carbohydrates, vitamins, and minerals. Among its advantageous qualities are anti-inflammatory, anti-allergic, antioxidant, hypotensive, and immune-stimulatory actions. It is increasingly fashionable to take it as a dietary supplement to treat a variety of illnesses, including Alzheimer's, diabetes, cancer, and cardiovascular conditions. Royal jelly boosts antioxidant defenses by preventing oxidative stress and lipid peroxidation. **Aim:** The current paper aims to gather information on royal jelly regarding its chemical composition, beneficial properties and ameliorative effects against different toxins. **Conclusions:** In summary, research proved that royal jelly has multiple beneficial properties and that it can ameliorate the toxic effects of different toxins by reducing oxidative stress and apoptosis.

Keywords: Royal jelly; Anti-oxidants;Bee products

INTRODUCTION

The phenolic compounds found in honeybee products have the ability to combat oxidative stress, making them a natural source of antioxidants **[1]**. Workers honeybees' hypopharyngeal glands secrete royal jelly (RJ), which is a mixture of glucose, lipids (fatty acids and sterols), proteins, and minerals. Numerous positive effects include those that are anti-inflammatory, hypotensive, antineoplastic, antioxidant, and immune-regulatory **[2]**.

With so many active ingredients and antioxidants, including polyphenols, royal jelly has remarkable anti-microbial and antioxidant qualities that make it useful for promoting health. It also contains a wide range of vitamins. Additionally, because of its ability to increase fertility, and improve the quality of the sperm, it is employed as a semen diluent **[3].**

Sources: The worker honeybees' hypopharyngeal and mandibular glands secrete royal jelly, which is essential for identifying the caste of the bees. The queen bee feeds on RJ solely during her entire life, which explains why queen bees have longer life span **[4].**

***Physical properties*:** Royal jelly is an acidic, yellowish-white material **[5],** with a gelatinous consistency, a sour and sweet flavor, and a strong smell **[6].**

Chemical Content and Structure: The main ingredients of royal jelly include water (50–60%), proteins (18%), carbs (15%), lipids (3-6%), mineral salts (1.5%), and vitamins **[3]**. It contains the largest amount of water compared to other bee products, and the majority of its lipids are short-chain fatty acids which are accountable for most of its biological effects, especially the lowering of cholesterol and stimulation of glial cells **[7]**. It also contains testosterone, progesterone and estradiol which are key bioactive components **[6]**.

10-hydroxydecanoic acid (10-HDA), which makes up around 80–90% of the fatty substance fraction, is the primary fatty acid in red meat. It is absent from all other natural raw materials and products developed from apiculture **[8]**. This acid is thought

to be one of the main components causing RJ's biological activity **[9]**.

Major royal jelly proteins (MRJPs), which come in nine different types—MRJP1, MRJP2, MRJP3, MRJP4, MRJP5, MRJP6, MRJP7, MRJP8, and MRJP9—make about 80% of soluble RJ proteins. MRJP1 is an important biological activity in numerous ways **[10]**.

The season, temperature, environment, bees' access to honey supplies, pollution, beekeeping practices, and colony genetics are just a few of the variables that can significantly alter the chemical makeup of royal jelly. **[11].**

***Pharmacokinetics*:** Due to various issues that arise, such as the unstandardized production methods in the case of RJ (potential influence of feeding) or the unstandardized processing methods, there is a dearth of information regarding the critical pharmacological processes, such as pharmacokinetics, when it comes to bee products **[12]**.

Diacarboxylic acids are produced from RJ's fatty acids, which are subsequently taken up by the bloodstream and eliminated as urine. Examination of plasma following RJ capsule consumption revealed the presence of dicarboxylic acids but not of hydroxy fatty acids consumed from RJ, such as 3,10-dihydroxydecanoic acid, 10-HDA, and trans-10-hydroxy-2-decenoic acid (10-H2DA). These results indicate that phase I metabolism in the liver oxidizes each fatty acid's terminal hydroxyl group to produce dicarboxylic acids **[13,14].**

BIOLOGICAL ACTIVITIES &USES

Royal jelly has been a common ingredient in cuisine, cosmetics, and traditional medicine. It is heavily studied for the purpose of understanding its beneficial effects which include antioxidant, antimicrobial, and immunomodulatory effects **(Fig. 1) [5]**.

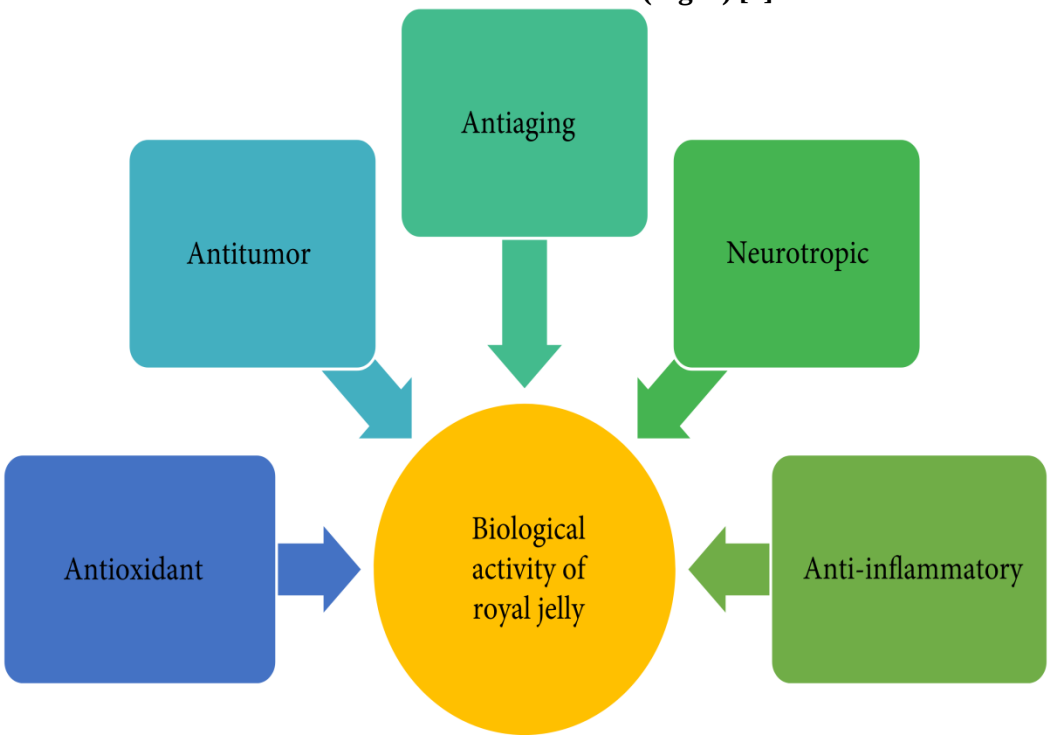

Figure (1): Types of biological activities of royal jelly **[14]**.

Antioxidant effect: Royal jelly has antioxidant and scavenging properties against reactive oxygen species (ROS), these properties include the decrease in oxidative DNA damage and the rise in antioxidant activity **[15]**. By controlling the lipid peroxidation pathway and significantly boosting the body's antioxidant defense system, it can lower oxidative stress and free radicals **[16].**

The oxidative stress brought on by long-term celecoxib therapy was lessened by the oral administration of RJ (300 mg/kg/day) for 30 days **[17].**

***Effects on the reproductive system and fertility*:** Spermatozoa are negatively impacted by excessive ROS production, which negatively affect male fertility. Unsaturated fatty acids are highly concentrated in the plasma membrane of spermatozoa, making it more susceptible to oxidative damage. Numerous studies have shown that RJ has positive effects on male reproductive

organs and fertility in addition to shielding against induced testicular oxidative damage **[2].**

Because royal jelly is useful in treating osteoporosis, perimenopausal symptoms, and restoring hormonal balance by improving the quality of ovules in women and sperm in men, it has been connected to positive benefits on human reproduction. RJ improves male animal reproductive, semen quality, and the outcome of in vitro fertilization when added in moderation **[18].**

When compared to the pregabalin-treated group, the short-term chronic co-administration of royal jelly (1g/kg) increased sperm count and motility. This impact may be attributed to the short-chain fatty acids found in royal jelly, specifically 10-hydroxy-2-decenoic acid, which improves sperm motility, acrosome response, and fertilization **[19].**

***Antibacterial Activity*:** Nowadays, several studies highlight the powerful effect of RJ against bacteria. This effect is attributed to its unique composition, for example its MRJP1 has wound healing and antibacterial properties. MRJP2 also shows antibacterial activity due to its peptide content, which mainly encompasses apidaecin and hymenoptaecin, and its high mannose carbohydrate content. RJ also contains royalisin which is an important type of antimicrobial peptides which destroys bacterial cells **[20]**, additionally, recombinant MRJP4 can kill bacteria by adhering to its cell walls, causing cell wall destruction. RJ's 10-Hydroxy-2-Decenoic Acid was also proved to be able to destroy bacteria **[21]**.

Royal jelly was found to be able to inhibit and eliminate Enterococcus faecalis, Staphylococcus aureus, and Candida albicans making it a potential candidate for endodontic infection control **[22]**.

***Anticancer activity*:** Royal jelly can be combined with anticancer medications due to its beneficial effects and low toxicity. It can be used alone as an antiproliferative substance which helps to suppress further division of cancer cells or with other anticancer drugs for synergistic interaction. interactions between RJ and anticancer drugs can significantly boost the drug's therapeutic efficacy, improve the pharmacodynamic parameters and protect against toxicities brought on by the anticancer drugs. Certain RJ mechanisms of action have been observed with commercially available drugs as it can reduce the genotoxicity and DNA damage when used with cyclophosphamide, or even decrease the cell viability and IC50 with 5-fluorouracil, and it can also improve the entrance of the cells into the apoptotic cycle with Thymoquinone or cisplatin **[23].**

RJ lowered side effects, preserved quality of life during treatment, and enhanced prognosis in cancer patients and animal models. An important factor in RJ's anticancer effects is its 10-HDA, which can inhibit cancer cells proliferation, inflammation and oxidative stress **[24].** RJ's control of cell division markers, can result in the decrease of uncontrollable cell division, lower the rate of carcinogenesis, and the reduction of tumorgenesis **[16].**

***Antiapoptotic effect*:** Oxidative stress is a major cause for apoptosis. RJ's antiapoptotic properties can be due to its ability to inhibit oxidative stress. RJ co-administered with nicotine improved its negative effects regarding oxidative stress and apoptosis **[25]**.

RJ (100 mg/kg) co-administration with moxifloxacin decreased capsase-3 immunohistochemical staining in renal and hepatic rat tissue **[26]**.

***Neurotrophic action*:** RJ is utilized as an adjuvant medication for the treatment of neurodegenerative diseases like Parkinson's disease (PD) and Alzheimer's disease. RJ and its lipids' effects on Parkinson's disease (PD) have been studied both in vivo and in vitro. The findings demonstrate that in animals with Parkinson's disease (PD), they reduce behavioral and histomorphometric dysfunctions and result in structural and clinical improvements. Numerous lines of research show that the flavonoids in RJ lipid derivatives have neuroprotective effects in dopaminergic neurons through the inhibition of oxidative stress **[27]**.

Anti-aging effect: Research indicates that queen bees, who only consume red jalapeño (RJ) throughout their lives, possess learning and memory capacities that are up to five times superior to those of worker bees, who consume honey and pollen **[28].** According to research, RJ can enhance cognitive deficits and increase glial and neuronal cell survival in experimental models of advanced age and Alzheimer's disease. It exhibits neuroprotection through its synaptic signal transduction, antioxidant, anti-inflammatory, and neurotrophin-producing properties, all of which support a healthy neural structure and function.. Moreover, RJ has been shown in animal studies to improve a variety of metabolic and endocrine markers, hence enhancing health and prolonging lifespan. It was also noted that the only RJ compounds investigated in trials on cognitive aging were peptides, 10-HDA, and MRJPs, and that enzyme-treated RJ seemed to be more effective than crude RJ. **[27]**.

Effect on diabetes milletus and insulin resistance: Reducing oxidative stress and inflammation has been shown in studies to mitigate the consequences of diabetes, including insulin resistance, dyslipidemia, hyperglycemia, macrovascular complications (stroke and cardiovascular disease),

and microvascular problems (retinopathy, nephropathy, and neuropathy) **[29].** Oxidative stress is linked to insulin resistance. Consequently, by its antioxidant activity, RJ can reduce insulin resistance **[30].**

RJ lowers blood glucose levels in rats with diabetes. Its 10-hydroxy-2-decenoic acid (10-HDA) is a potentially effective treatment for both people and rat models since it can lower blood glucose and insulin resistance **[31].**

***Effect on blood pressure*:** Impaired vascular endothelium as a result of NO reduction and oxygen free radicals elevation is one of the pathophysiological conditions of hypertension. To prevent hypertension, it's crucial to restore endothelial function or supplement NO. RJ has the ability to lower blood pressure and dilate blood vessels via boosting NO generation. Its 10-H2DA has antihypertensive and vasodilator properties, and its MRJPs have antihypertensive properties **[32]**. Royal jelly might also have antiatherogenic effect due to its ability to improve vascular endothelial function **[33]**.

Anti-inflammatory action and wound healing effect: Royal jelly contains antioxidants that boost the antioxidant system and prevent ROS formation. Therefore, it is believed that RJ exhibits anti-inflammatory benefits. Pro-inflammatory cytokines, including interleukins (IL-1β), IL-18, and tumor necrosis factor-α (TNF-α), are reduced in concentration by it **[34].**

RJ can significantly eradicate Methicillin-resistant Staphylococcus aureus (MRSA) infection, and promote the healing process in the wounds **[35].** When used topically, it has been shown to be effective in healing diabetic foot ulcers and wounds with or without infections. RJ's anti-inflammatory actions on macrophages, which normally infiltrate wound sites 48 hours after injury, may speed up the healing of wounds exposed to it **[36].**

Immunoregulatory effect: Royal jelly shows immunoregulatory activity. Its 10-HDA can have an important effect in T cell proliferation and activation **[37]**.

An immune-mediated disease that is complex is rheumatoid arthritis (RA). Ten-H2DA has demonstrated a positive impact on RA; it first suppresses the expression of connective tissue growth factor, which is followed by the suppression of matrix metalloproteinases (MMPs), important proteases involved in the breakdown of RA tissue **[38].**

***Effect on lipid profile*:** Due to elevated triglycerides and low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C) in the plasma, dyslipidemia is a high-risk factor for cardiovascular illnesses. RJ inhibits the MRJP's ability to absorb cholesterol from the jejunum, resulting in a drop in blood levels of total cholesterol and an increase in HDL-C. Additionally, RJ may increase the activation of hepatic receptors for the manufacture of very low-density lipoproteins, which are precursors of LDL-C, by upregulating cholesterol 7-α-hydroxylase (CYP7A1**) [39].** RJ is an excellent dietary supplement to reduce the risk of cardiovascular diseases because it can lower total cholesterol and raise HDL levels **[40]**.

CONCLUSIONS

In summary, research proved that royal jelly with its unique components have multiple beneficial properties, health promoting effects and the ability to ameliorate the toxic effects of different toxins by reducing oxidative stress and apoptosis.

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