

Medicinal Properties of Royal Jelly and its Role in Dentistry – A Review

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ABSTRACT

The common honey bee is a fascinating little insect that offers humans some valuable natural foods with health-promoting benefits. Royal jelly (RJ) is a secretion product of the cephalic glands of nurse bees that have been used for centuries for its extraordinary properties and health effects. This bibliographic study aims to review many of the scientific findings, research, various actions, effects, and some uses of RJ. There are numerous biological properties and effects of RJ: Antioxidant, neurotrophic, hypoglycemic agent, hypocholesterolemic agent and hepatoprotective, hypotensive and blood pressure regulatory, antitumor, antibiotic, anti-inflammatory, immunomodulatory, anti-allergic, general tonic, and anti-aging. This article also implies the role of RJ in dentistry. The antimicrobial activity and the biocompatible nature of RJ can be applicable to many dental procedures. RJ is one of the honey bee product and there still remains much to reveal about its biochemistry and biological activity in future research for our health and life benefit. More research is needed to effectively evaluate its application in dentistry. Data were chosen after the primary survey of all abstracts and selected full articles. A comparison among related data was done by the authors.

KEY WORDS: Antimicrobial property, Dentistry, Health benefits, Honey bees, Royal jelly

INTRODUCTION

Apitherapy^[1] is a branch of alternative medicine that uses honey bee products, including honey, pollen, propolis, royal jelly (RJ), and bee venom. The components of apitherapy aids in many health benefits to the mankind. Honey bees belong to the genus *Apis*, which in Latin means “bee.” This social insect lives in a colony of several thousand bees and is in the order Hymenoptera, family Apidae and subfamily Apinae. The natural honey and other honey bee products as food and medicine have been widely used in current generations. Apitherapists are sure that honey bee products can cure many diseases. Honey bees are golden insects. Apitherapy is about the use of bee products such as honey, pollen, propolis, RJ, bee venom, and to treat ailments such as liver, cardiovascular, and gastrointestinal problems and promotes wound healing. However, they have a minimum application in modern medicine and dentistry due to a lack of scientific evidence.

HISTORY OF APITHERAPY

Since the times of Hippocrates and Galen, apitherapy has been practiced. Ancient Egyptians, Assyrians, Chinese, Greeks, and Romans employed honeybee products for wounds and its use transcends the barriers of culture and diseases of the intestine. However, later it lost its importance due to the evolution of modern medicine. RJ started gaining its value because it was subjected to laboratory and clinical investigations by several research scientists and technologists. Recently, honey bee products are of markable value in traditional medicine as well as modern therapeutics.^[2-4]

HEALTH CLAIMS OF APITHERAPY

Apitherapy is promoted as an alternative medicine for several uses.^[5]

Honey bee products have high nutritional value and immense health benefits.^[6]

- Antiseptic property
- Antioxidant
- Anti-inflammatory

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- Anticoagulant
- Antibacterial
- Wound healing.

Antimicrobial agents are important in reducing the growth and spread of many infectious diseases.^[7] Enzymatic production of hydrogen peroxide brings about the antimicrobial property.^[8] Honey bee product has been found to have an inhibitory effect on around 60 species of bacteria, including aerobes and anaerobes, Gram-positive and Gram-negative. It does not lead to antibiotic resistance in humans and can be used continuously. It possesses both bacteriostatic and bactericidal properties.^[9,10] The antibacterial activity of honey bee product is attributed to one of its main properties in which honey dehydrates the bacteria by taking the moisture out of the environment making the bacteria unable to survive and kills them. The pH of honey is 3.2–4.5 which is acidic and is low enough to inhibit the growth of various microorganisms.^[11]

RISK FACTORS ASSOCIATED WITH APITHERAPY

Bee venom therapy frequently causes adverse reactions.^[12] Venom compounds can act as allergens by causing a spectrum of allergic reactions that usually range from mild, local swelling to severe systemic reactions, anaphylactic shock, or even death in sensitized individuals.^[13]

OTHER PRODUCTS AVAILABLE FROM HONEY BEE

- Bee venom
- RJ
- Propolis
- Pollen.

WHAT IS RJ?

RJ is a honey bee secretion that is used in the nutrition of larvae as well as adult queens.^[14,15] It is a secretion from the glands in the hypopharynx of nurse bees to feed all larvae in the colony. Once all the larvae are fed with RJ, they are destined to become drones (males), workers (sterile females), or queens (fertile females).^[16] When a beehive is in the process of making new queens, the workers construct special queen cells, and the larvae in these cells are fed with copious amounts of RJ. This type of feeding nourishes the queen bee and triggers the development of queen morphology, including the fully developed ovaries needed to lay eggs. After some days, the drone and worker larvae are no longer fed with RJ, but queen larvae are continuously fed with this special substance throughout their development.

COMPOSITION OF RJ^[17]

The color of RJ is white to pale yellow.

- RJ is composed of
- 67% water
- 12.5% protein
- 11% simple sugars (monosaccharides)
- 6% fatty acids and
- 3.5% 10-hydroxy-2-decenoic acid (10-HDA)^[18,19]
- It contains trace minerals, antibacterial and antibiotic components, pantothenic acid (Vitamin B₅),

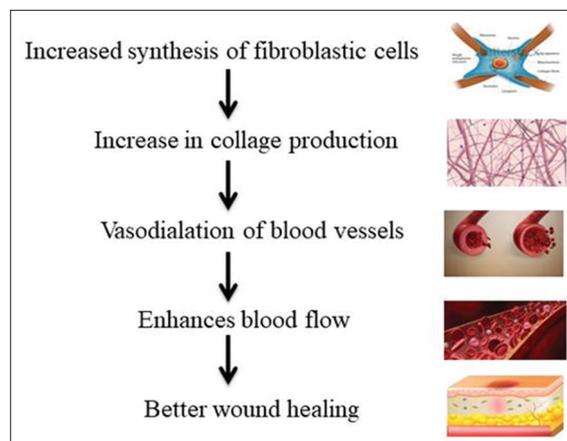


Figure 1: Representing the wound healing activity of royal jelly

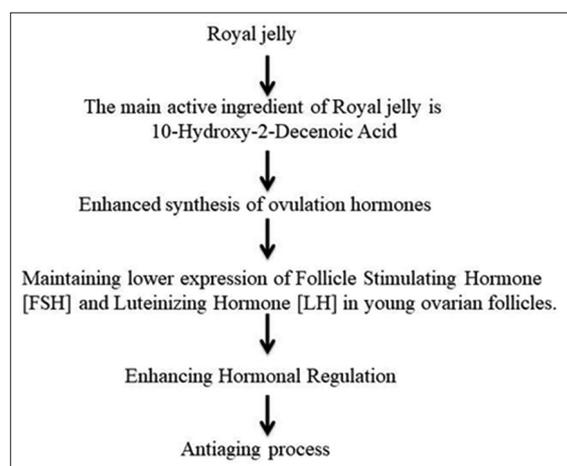


Figure 2: Representing the antiaging property of royal jelly

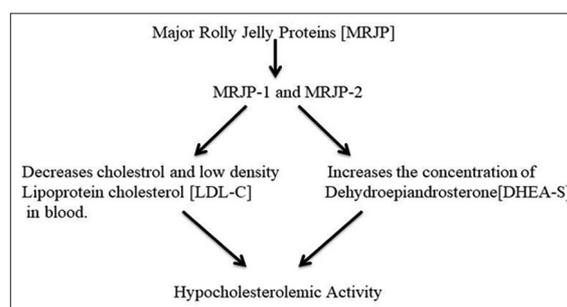


Figure 3: Representing the hypocholesterolemic activity of royal jelly

pyridoxine (Vitamin B₆), and trace amounts of Vitamin C

- Major RJ proteins (MRJPs) are a family of proteins that are secreted by honey bees.^[20] The family consists of nine proteins, of which MRJP1 (also called royalactin), MRJP2, MRJP3, MRJP4, and MRJP5 are present in the RJ secreted by worker bees. MRJP1 is the most abundant and largest in size. The five proteins constitute about 83–90% of the total proteins in RJ.

It contains water, proteins, carbohydrates, and lipids.

- It also contains
- Enzymes
- Vitamins
- Cholinergic factors
- Inositol
- Biopterin
- Neopterin
- Antibiotics.

EPIGENETIC FACTORS^[16,21-23]

The honey bee queens and workers represent one of the most striking examples of environmentally controlled phenotypic polymorphism. A female larva which is destined to become a queen is fed by the enormous amount of RJ and this initiates a cascade of molecular events by co-opting novel genes that arise during evolution, by duplicating existing genes, or by changing the behavior of gene networks using epigenetic regulation, resulting in the development of a queen. The queen–worker developmental process is epigenetically controlled by differential feeding with RJ and this appears to be specifically due to the protein royalactin. DNA methylation in honey bees allows the expression of epigenetic information to be differentially altered by nutritional input. DNA methylation is utilized for storing epigenetic information in the honey bee and that methylation controls heritable states of gene expression underlying larval developmental fate.

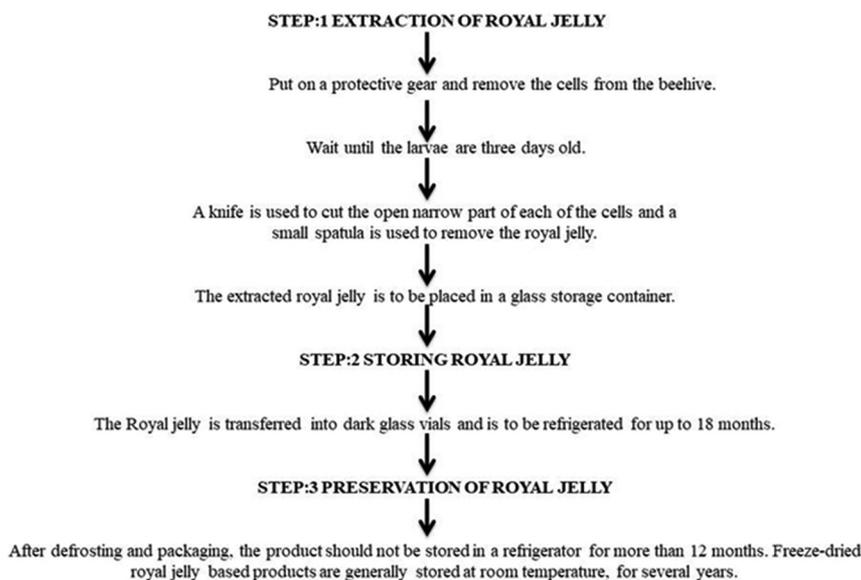
INGREDIENTS IN RJ^[24]

RJ is one of the most valuable products of the beehive.

The most precious ingredient of RJ is 10-hydroxydeconic acids which exert antibacterial and antitumor activities.

RELEVANCE OF RJ TO INTERDISCIPLINARY DENTISTRY^[25-34]

There are studies which aim at introducing a new natural product (RJ) with medicinal value, which can combat periodontal pathogens without causing any side effects to the host body, unlike the synthetic antimicrobials. The so-called MRJPs, MRJP1, MRJP2, MRJP3, MRJP 4, and MRJP5 make up the majority of the proteins in RJ, of which MRJP2, MRJP3, and MRJP5 provide not only nitrogen to the larva but also antimicrobial protection. The mechanisms underlying the antimicrobial activity of MRJP4 were assessed using western blot analysis, immunofluorescence staining, and scanning electron microscopy. Recombinant MRJP4 bound to the cell walls of bacteria, fungi, and yeast and induced structural damage in the microbial cell walls. MRJP4 has an antimicrobial role and exhibits a broad spectrum of antimicrobial activities against bacteria, fungi, and yeast. Minimum inhibitory concentration and minimum bactericidal concentration (MBC) procedures were carried out to assess the antibacterial activity of the jelly. The MBC values were identical and showed a bactericidal effect in the range between 12.5 and 100 µg/ml, suggesting that periodontal



Flow Chart 1: Representing the extraction, storage, and preservation of royal jelly

pathogens tested were susceptible to RJ. Dosage and safety of RJ must be tested before its possible *in vivo* application as a local drug delivery system in the management of endodontic infections. MBC is the lowest concentration of antimicrobial agent and that will prevent the growth of bacteria after subculturing on to antibiotic-free media. The bactericidal property of royal jelly depends upon the minimal inhibitory concentration of the compound. RJ carboxylic acids are known to collectively exert antimicrobial properties against Gram-positive and Gram-negative bacteria and fungi. RJ has two protein components, Royalisin and Jelleins. Jelleins, a peptide of RJ exhibits its antibacterial activity and presents no other similarity with the other antimicrobial peptides from the honeybees. The mechanism of action of Royalisin against Gram-positive bacteria has been demonstrated to induce the disruption and dysfunction of cell walls and membranes. 10-HDA has been identified as a particularly strong antibacterial, especially against dental pathogens *Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus*, and *Escherichia coli*. RJ solution also helps in maintaining the cell viability and proliferative abilities of periodontal ligament fibers in an *in vitro* tooth avulsion condition.

RJ pastes were used as:

- Analgesic
- Anti-inflammatory
- Odontoblasts stimulant
- Regeneration.

USES OF RJ^[35,36]

RJ or gelee royal is a sticky liquid that is produced from queen bees.

It is thick, yet soft, has a characteristic aroma, and slightly spicy acidic-sweet taste.

- It generally enhances immunity^[37]
- Increases metabolism^[38]
- It aids in better wound healing [Figure 1]^[39,40]
- It provides valuable nutrients that are essential to the body. Royalisin found in the RJ of *Apis mellifera* is an antimicrobial peptide. It plays an important role in protecting chemotherapy-induced mucositis in head and neck cancer^[41]
- It reduces the aging process and cures wrinkles and gives healthy skin. RJ and its protein, lipid ingredients have the potential to extend lifespan in various creatures and prevent senescence of human tissues in cell cultures. These findings pave the way to inventing specific RJ anti-aging drugs [Figure 2]^[42-44]
- RJ has also been shown to prevent the cholesterol-elevating effect of nicotine and has lowered serum cholesterol in animal studies. MRJP1 has a high bile acid-binding capacity, which hampers the micelle formation and thereby suppresses the

cholesterol absorption that results in decrease cholesterol [Figure 3]^[45]

- It is found to enhance the neuronal metabolic activities in animal models. There is an occurrence of a neurohormone in RJ which is of considerable interest, as it suggests that acetylcholine – a neurotransmitter might have a different function with nervous transmission^[46,47]
- It cures all the stomach problems by acting like a probiotic. RJ proved to be one of the growth factors for selected probiotic bacteria such as *L. acidophilus* and *Lactobacillus casei*^[48,49]
- RJ is one of the oldest and high potential bee medicines widely used to treat various diseases. Pharmaceutical studies elucidate that RJ has multiple activities that are attributable to their bioactive compounds, including proteins, peptides, lipids, phenolics, and flavonoid compounds. Recently, RJ has shown potential for use against cancer, diabetic, cardiovascular, and Alzheimer's disease in modern pharmaceutical research.^[50]

EXTRACTION OF RJ

Things Generally Needed^[51]

- Beekeepers protective clothing
- Knife
- Tweezers or small forceps
- Spatula
- Collection container
- Dark glass vials
- Freezer or refrigerator.

Steps:

- Put on protective gear
- Removing the cells from the beehive
- Wait until the larvae are 3 days old
- Pull out one of the frames and sweep away the bees
- The frame has to be taken away from the beehive
- A knife is used to cut the open narrow part of each of the cells
- Pull the larvae out of the cells using tweezers or small forceps
- A small spatula is used to remove the remaining RJ
- The extracted RJ is to be placed in a glass storage container.

STORING RJ^[51]

- The RJ is transferred into dark glass vials
- The RJ is to be refrigerated for up to 18 months
- Freeze jelly for up to 24 months.

PRESERVATION OF RJ

After defrosting and packaging, the product should not be stored in a refrigerator for more than 12 months.

Freeze-dried RJ and RJ based products are generally stored at room temperature, for several years [Flow Chart 1]. At present, the various product formulations developed are, however, put in the market without adequate standards for the control of their quality. However, the time of harvest does affect the composition and the major constituents of RJ. Therefore, the existing quality standards of RJ should be revised to include the effect of harvest time on composition and that future international standards take this factor into account.^[52,53]

CONCLUSION

The present review focused on the potential health benefits of RJ. RJ is highly rich in active components which have biological functions in preventing some diseases and promoting good health. RJ has distinct efficacies with significant nutritional properties and functional values. With regards to dentistry, RJ is potential against certain dental pathogens and, therefore, can be used as an obturating material or irrigant for its antibacterial action. The anti-inflammatory property of RJ may be helpful in resolving the inflamed dental pulp. However, it is necessary to conduct further studies to determine the critical mechanisms related to the pharmacological activities of RJ and the appropriate amounts that can be taken to obtain promising health benefits. The requirement for a standardized method for quality evaluation of RJ, that is, qualitative, quantitative, and biological activity, is a necessity.

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