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Research Article

THE HEALTH BENEFITS OF ROYAL JELLY

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ABSTRACT

The royal jelly is recognized both traditional and modern medicine as active agents in some biological processes. The royal jelly contains wide variety of nutrients that are essential to proper health and organ function. It can protect liver health, help with fertility issues that are related to hormonal imbalance, diminish the signs of aging, reduce inflammation caused by illness or injury. Their botanical origin has attracted because of the health benefits it can provide when consumed.

INTRODUCTION

Royal Jelly (RJ), or bee's milk, is a creamy product secreted by the glands in the hypopharynx of worker bees for developing and maintaining the queen bee. It is a yellowish-white, acidic secretion, with a slightly acid, pungent odour and a somewhat bitter taste. It is the source food of the queen honeybees, *secreted* from the *hypopharingeal* and *mandibular glands* of worker bees. RJ is a natural *secretion* of *worker bees*, rich in proteins, carbohydrates, vitamins and minerals which is stored in the nest, under field conditions (Bărnuţiu *et al.,* 2011).

RJ appears as a substance with a gelatinous consistency, is partially soluble in water and highly acidic (pH 3.4-4.5) with a density of 1.1 g/mL (Lercker, 2003). It consists of an emulsion of water, proteins, lipids, sugars, vitamins, hormones, enzymes, mineral substances, antibacterial and antibiotic components.

RJ is honey bee secretion. The physiological effects of RJ in humans are still not fully known. However, RJ *is sold* as a dietary supplement and in cosmetics for its alleged tonic and bio-stimulating effects. Although biological activities of RJ are variable**,** it have been correlated to their content of trace elements (Andreas *et al.,* 2005).

Protein and peptides from RJ can attend in defense mechanism of honeybee against microbial pathogens. Protein and peptides showing simple structures, no complex modifying moieties or rare amino acids are expressed and frequently secreted to the hemolymph (Antinelli *et al.,* 2002). The most abundant protein of RJ is albumin1. It represents 50% of protein content of RJ. Peptides from RJ demonstrated total inhibition of bacterial growth for *S. aureus* , *L. Monocytogenes* and *S. typhimurium* only at very high concentrations (≥200 µg/ml) (Bullet *et al.,*1999).The antimicrobial compounds of Royal Jelly have been identified by royalisin, apisimin,jelleines I, II, III,IV,10-HDA, apalbuminaα.

Royalisin

Royalisin found in the royal jelly of the honeybee Apis mellifera is an antimicrobial peptide (Fujiwara *et al.,* 1990). Royalisin peptide consists of 51 amino acid residues, with three intramolecular disulfide linkages, having a calculated molecular mass of 5.52 kDa. Royalisin is an amphipathic protein that shows extensive sequence homology to two other antibacterial proteins, sapecin and phormicins. The peptide was found to have potent antibacterial activity against Gram-positive bacteria, but not against Gram-negative bacteria. Royalisin may be involved in a defense system active against

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bacterially infected bees (Fujiwara *et al.,* 1990). Bilikova *et al.* (2002) explained that royalis in fractions in the concentration 180 µg/ml showed a clearly weaker inhibition against *Bacillus subtilis* as tetracyclin in the concentration 50 µg/mL.

Royalisin inhibits the growth of Gram-positive bacteria, such as Clostridium, Corynebacterium, Leuconostoc, Staphylococcus, and Streptococcus. It also shows the antibacterial activity particularly toward Gram-positive bacteria, such as Bacillus subtilis, Sarcina lutea, American foulbrood caused by a Gram-positive bacterial pathogen, *Paenibacillus larvae larvae* (Bilikova *et al.,* 2001; Bachanova *et al.,* 2002). The royal jelly peptide fraction was found to have antifungal activity inhibiting the model fungus Botrytis cinerea (Bachanova *et al.,* 2002), a plant pathogen, and Alternaria brassica. However, no inhibitory activity against E. coli was observed (Bachanova *et al.,* 2002).

Royalisin is an antibiotic polypeptide because of the prevention of honeybee diseases and royal jelly preservation. Due to its stability at low pH and high temperature, royalisin is a potential antimicrobial peptide for food preservation, therapeutic application and medication.

Apisimin

A peptide named apisimin was found in the royal jelly. The primary structure of apisimin was determined to consist of 54aa, 5540Da which stimulates the proliferation of human monocytes. It is rich in valine, serine. Apisimin doesn't contain Cys, Met, Pro, Arg, His, Tyr, and Trp residues and, while it contains Val, Ser, and Phe (Fontana *et al.,* 2004).

Jelleines

The Jelleines found in the royal jelly of the honeybee Apis mellifera are very short peptides, presenting hydrophobic sequences. Its were purified by reverse-phase high pressure liquid chromatography and sequenced by using MS: (Jelleine-I), (Jelleine-II), (Jelleine-III), and (Jelleine-IV). The peptides were examined with different biological assays such as antimicrobial activity, mast cell degranulating activity and hemolysis. The Jelleines I and III showed exclusively antimicrobial activities against of Gram-positive bacteria and yeast. However, Jelleine-IV was observed no activity in none of the assay. These peptides do not present any similarity with known antimicrobial peptides such as hymenoptaecin, abaecins, apidaecins, and royalisin. The Jelleines are produced constitutively by the workers and secreted into RJ for the protection this bee hive product against microbial infections (Bărnuţiu *et al.,* 2011).

Apalbumina

Apalbumina is the major protein found in the royal jelly having various biological properties (Zhou *et al.,* 2007). It formed α-subunit structure (Šimuth, 2001). Basic subunit consistsapproximately 420 kDa and contains 55 kDa basic monomer. According to the information obtained from microscopic observations, α-apalbumina in aqueous form structures similar to those that occur in royal jelly. It is an auto assembling structure of the protein occurring as the result of oligomerization of these subunits. Although other royal jelly protein oligomerization has ability, it has a high degree of sequence similarity with α-apalbumina. The apalbumina shows the antimicrobial properties particularly toward Gram-positive bacteria such as *Bacillus. subtilis*, *Escherichia. coli*.

10-HAD

Special active substance named 10-Hydroxy-2-Decenoic Acid (10-HDA) was found only in royal jelly in the nature. The content of 10-HDA in RJ is usually around from 1.5%- to 2,0%.It shows antibiotic activity against many bacteria and fungi (*Micrococcus pyogenes, Escherichia coli*, *Neurospora sitophila s.a.*) (Blum *et al*., 1959). *Due* to the anticancer and antibacterial effect of the 10-HDA, it can be added to health food or cosmetics as an active ingredient. The content of 10-HDA is the international standard for the quality of royal jelly and can determine the price of RJ on the international market (Bloodworth *et al.,* 1995). Literature studies showed that 10-HDA promotes the growth of T-lymphocyte subsets and interleukin-2, which might suggest that this fatty acid possesses immunoregulation and anticancer activities (Zhou *et al.,* 2007). Recent studies showed that the 10-hydroxy-2-decenoic acid (10-HDA) found in royal jelly may inhibit the vascularization of tumors (Bullet *et al*., 1999).

The antimicrobial action of 10-HDA against a series of bacterium was studied. It was found that the antimicrobial effect of 10-HDA varied with the pathogenic microbes.10-HDA present the antimicrobial effect against *Escherichia coli, Bacillus subtilis, Staphylococcus aureus* inhibiting the growth of bacterium. It can be determined by HPLC (4, 11, 15, 16); capillary zone electrophoresis(CZE) (15); GC-MS (17);UPLC (11).

MRJPs (Major Royal Jelly Proteins)

Major royal jelly proteins (MRJPs) is the important protein components of RJ. It have been characterized by cDNA cloning and sequencing (Klaudiny *et al.,* 1994; Ohashi *et al.,* 1997; Albert *et al.,* 1996). MRJPs family consists of predominantly 5 proteins (MRJP 1-5) with a molecular mass from 49 to 87 kDa. It have been identified by cDNA cloning, sequencing, SDS-PAGE, two-dimensional gel electrophoresis, and N-terminal sequence analysis (Albert *et al.,* 1996).

The MRJP1, MRJP2, MRJP3 and MRJP5 make up about 82% of total protein content of RJ. They area natural source of essential amino acids and nitrogen for the nutrition of honeybee young female larvae and queen (Santos *et al.,* 2005).

MRJP3 present the potent immunoregulatory effects in vitro, vivo, and potent antiallergic activity. MRJP1 is the protein with molecular mass of 57-kDa. It can significantly stimulate rat hepatocyte DNA synthesis and promote live regeneration. It presents certain structural properties causing its self-oligomerization in RJ and formation of stable complex with apisimin. Thus, It is generally considered that MRJP1 play a role as a potential ingredient of functional foods and its cDNA was transformed into tobacco plant for expression (Bărnuţiu *et al*., 2011).

MRJP3 and MRJP5 are polymorphic proteins with molecular weight owing to extensive repetitive regions in the C-terminal region and various sugar chains attached to the protein. *They* have been considered as a source of essential amino acids and nitrogen in the nutrition of honeybee larvae.

CONCLUSION

RJ is bee products showing antimicrobial activity. The major antibacterial effect of RJ is ascribed to a particular 10-carbon molecule of fatty acid (10-hydroxydecanoic acid). The studies reported that royal jelly against a wide variety of microorganisms all over the world showed strong antimicrobial activity. Antimicrobial peptides are natural. Due to the emergence of resistance of several bacterial strains to antibiotics, the interest toward new antimicrobial agents is rapidly increasing. RJ is a natural product with rich chemical composition and antimicrobial activity against many bacteria, yeast.

They aren't comparable because antimicrobial activity the methods applied of RJ are very different: starting with the raw material preparation, the solvents' choice and the method parameters–strains of bacteria, fungi. There is need of a standardized method for evaluation of qualitative, quantitative and biological activity of royal jelly.

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