A NOTE ON ROYAL JELLY

A Critical Evaluation

By A. D. Dayan

From the Department of Pharmacology, London Hospital Medical College

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Royal jelly is a secretion of the honey bee which is essential for the development of queen bees. Its composition is not yet completely known. It contains proteins, lipids, carbohydrates, fatty acids (one of which is unique) and vitamins. The biological effects of the jelly are disputed. It has antibiotic power; it affects the adrenal cortex and can cause hyperglycaemia; and it has an antitumorigenic effect in mice. There is no good evidence that it has oestrogenic activity, or that it affects the growth, longevity or fertility of animals. Clinically it has been used as a general tonic, to ward off the effects of old age and to ease sufferers from chronic degenerative diseases. It seems likely that the novelty of the treatment and not the substance itself has been responsible for whatever successes it has had in these conditions.

Royal jelly is a milky white highly viscous secretion from the paired salivary glands of the worker (western) honey bee (*Apis mellifera* L.)[1–3]. For the first 3 days of life it is the sole food of all bee larvae. After 3 days, future worker bees are weaned onto honey and nectar, while the future queens continue to be fed on royal jelly, which is in some way responsible for their development into mature female insects. Royal jelly has been known and studied for many years, but its effects on bees, other animals and man have been studied only recently. It contains a number of unique compounds, some with unusual biological properties, and it has been used clinically to relieve the effects of old age and various degenerative diseases. Several new discoveries have been made since the subject was last critically reviewed[1].

Collection, Stability and Composition of Royal Jelly

Repeated attempts have been made to analyse royal jelly since von Planta's original work in 1888, but owing to the small quantities available and to its instability, some of the compounds responsible for its biological activities have yet to be identified. Methods of collection are often not stated. Weaver and Kuiken[4] placed young female larvae in cups in a queenless colony. After 2 to 3 days the cups were removed, the larvae separated and the jelly scraped out. Townsend and Lucas[5] and Goillot[6] removed queen cells from ordinary colonies and squeezed out the jelly.

Microscopic examination shows only a few pollen grains and apparently no other solid contaminants in royal jelly. This is important because even quite small amounts of pollen could greatly alter the composition of the jelly. For instance the vitamin content of honey is attributed to such contamination[7].

If royal jelly is stored at room temperature it changes slowly from a milk white jelly to a slightly yellow gum, and finally, after some weeks,

to a brittle amber solid. The taste is altered from that of a "seasoned ragout" to "rather acid"[1]. In the laboratory, queen bees can be reared from larvae only if they are fed on jelly which is not more than 2 hours old[8]. Goillot[6] has shown that there are complex changes in its conductivity shortly after secretion and Chauvin and Lavie[9] have pointed out that the antibiotic and hyperglycaemic effects are not demonstrable until the jelly has been stored for some hours. The experiments and therapeutic trials with royal jelly have been done on specimens stored for at least several weeks, and the results may well be due to substances developing during the ageing of the jelly. The instability of the jelly makes comparison between fresh jelly from the hive and the usual laboratory material difficult, and probably explains some of the contradictory experimental findings.

Published analyses of royal jelly have been in quite good agreement although done on composite specimens. The samples have been stored after drying, *in vacuo* over P_2O_5 or by lyophilisation, and have been kept at various temperatures for periods up to several months. The composition of several commercial preparations has been described and criticised as weak and impure[10].

The main classes of compounds found in royal jelly are shown in Table I, where it may be seen that the fresh material has a high moisture content and the solids are largely proteins and carbohydrates.

TABLE I

OVERALL COMPOSITION OF ROYAL JELLY[1,5,11,12]

Constituent	Per cent weight of fresh specimen (pH = 5)
Moisture	65–70
Protein	15–20
Carbohydrate	10–15
Lipid	1·7–6
Pollen	Trace
Ash:	0·7–2·0
P	up to 0·5
S	up to 0·6
Na, K, Fe, Cu, Mg, Mn, Ca	Trace
Undetermined	up to 3

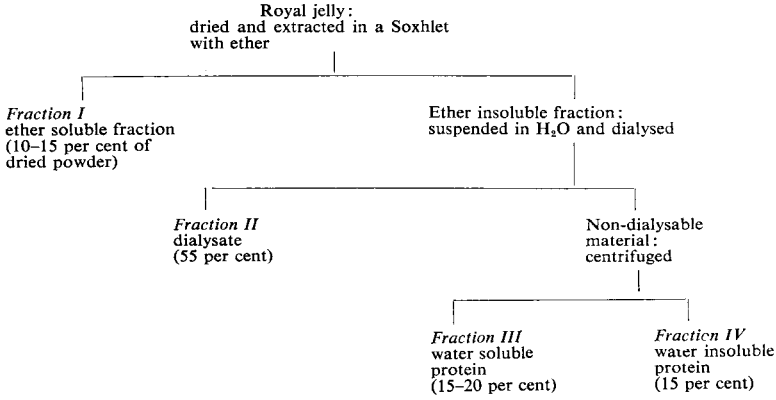
Fractionation of royal jelly, following the scheme of Townsend and Lucas[5], has involved the separation of ether-soluble, water-soluble and dialysable constituents (Table II). Fraction I (Table III) is a pale yellow semi-crystalline solid, which contains phenols, beeswax, sterols and fatty acids. The chief fatty acid has the formula $C_{10}H_{18}O_3$. It was isolated by Abbot and French[13] and later shown to be 10-hydroxy-Δ^2-decenoic acid[14,15]. As it is not found in either pollen or nectar it is presumably synthesised by the bee. Its purpose is unknown.

Fraction II, the water soluble and dialysable constituents, contains 20 per cent of uronic acids, some unidentified nitrogenous compounds, and 50 per cent of various reducing sugars. These are mainly glucose, fructose, ribose and saccharose[5,16]. Fraction III consists of water soluble proteins in the proportion of two-thirds of albumin to one-third of

globulin, and it is only feebly antigenic[13,17–19]. The content of free and combined amino acids is shown in Table IV. The presence of hydroxyproline, histidine and tryptophan is disputed[4,5,20]. Taurine is found in fairly large amounts as is common in invertebrate tissues. de Groot[21]

TABLE II

FRACTIONATION OF ROYAL JELLY BY THE SCHEME OF TOWNSEND AND LUCAS[5]



has shown that the amino acid content of this mixture of proteins is sufficient to fulfil the requirements of honey bees and also that it is readily digested and metabolised by rats. The water insoluble protein of fraction IV dissolves only in alkalis and gives positive colour reactions for tryptophane, tyrosine and arginine.

TABLE III

COMPOSITION OF FRACTION I[5]

Constituent	Per cent weight of fraction
Acids	80
Phenols	4–10
Waxes	5–6
Sterols	3–4
Phospholipids	0·4–0·8

Royal jelly contains a number of vitamins[1,7] of which pantothenic acid is present in a higher concentration than in any pollen, honey or other natural source (Table V). The low content of vitamin C is almost certainly due to vitamin C oxidase activity[22].

Several other compounds have been isolated from the jelly, viz: a unique pteridine of unknown function, 2-amino-4-hydroxy-6(1,2-dihydroxypropyl) pteridine[23]: acetylcholine, 800 μg./g. of fresh material[24]: a non-specific cholinesterase and an acid phosphatase[16].

Biological Effects of Royal Jelly

Almost the only undisputed biological action of royal jelly is in producing the differentiation of queen bees from workers. The responsible substances are unknown, but there has been speculation about the

importance of the high concentration of pantothenic acid. There is independent evidence of the importance of minute amounts of hormones in the structure and activities of bee colonies, so it is possible that the differentiating substance will be found in such minute quantities as to make analysis difficult[3]. Apart from this physiological activity on bees, royal jelly has been reported to have divers effects on living organisms.

TABLE IV

FREE AND COMBINED AMINO ACIDS OF ROYAL JELLY[4,18]

Amino acid	As free compound	As protein constituent
Alanine	+	+
Arginine	+	+
Aspartic acid	+	+
Cystine	−	+
Glutamic acid	+	+
Glycine	+	+
Histidine	−	?
Hydroxyproline	−	?
Isoleucine and/or leucine	+	+
Lysine	+	+
Methionine	−	+
Phenylalanine	−	+
Proline	+	+
Serine	+	+
Threonine	−	+
Tyrosine	+	+
Tryptophan	−	?
Valine	+	+
B-Alanine	+	
Glutamine	+	
Taurine	+	

TABLE V

VITAMIN CONTENT OF ROYAL JELLY[1,1]

Vitamin	Concentration μg./g. of fresh material
A	nil
B	
Thiamine	2
Riboflavine	10
Pyridoxine	2
Nicotinic acid	75
Biotin	2
Folic acid	0·3
Inositol	100
Pantothenic acid	250
C	3–5
D	trace
E	trace

Oestrogenic and gonadotropic activity. This was first suggested by Heyl[25] because royal jelly was known to stimulate the ovaries of bees. He found that the injection of aqueous or pyridine extracts into immature female rats caused premature formation of graafian follicles. This was not confirmed by Melampey and Stanley[26], Townsend and Lucas[27] or Hinglais and others[28]. Abbot and French[13] observed no effect when the ether-soluble fraction (fraction I) of royal jelly was injected into spayed rats. In normal rats injections interrupted the oestrus cycle. Chauvin and Herbert[29] noted great stimulation of the seminal vesicles of rats in one series of injections of royal jelly, but this has not been confirmed by them

or by other workers. There is therefore no evidence of any oestrogenic or gonadotropic activity of royal jelly in rats or mice, and presumably there is no such action in other mammals.

Fertility. More rapid maturation and a 60 per cent increase in the rate of egg laying was noticed when an ether extract of royal jelly was fed to a colony of Drosophila[27]. This was only a preliminary report, and no further evidence has been obtained. Earlier suggestions of a high vitamin E content have been disproved[30].

Longevity. Queen bees live considerably longer than workers and attempts have therefore been made to isolate "longevity factors" from royal jelly. It was shown that Drosophila flies fed on a diet with added royal jelly lived longer (17 days) than those receiving "normal" diet (13 days). However, if extra pantothenic acid was added to the "normal" diet the difference disappeared, suggesting that the "normal" diet was deficient in this substance[31]. The greater life span of the queen is possibly due to her lower energy expenditure[1].

Adrenal cortical actions. It was noticed[26] that a series of injections of royal jelly in rats caused involution of the thymus and lymphoid tissues. These findings have been confirmed[29] in mice receiving a larger dose (about 5 mg./mouse). Other changes, which were similar to the effects of corticosteroid injections, have been shown in the adrenal cortical enzymes and the hepatic glycogen content. Similar experiments in guinea pigs[19] produced haemorrhage and congestion of the adrenal glands 24 hours after injection of royal jelly, but there was no change in their ascorbic acid content. There was a slight neutropenia and reticulocytosis. This was explained as an anti-ACTH effect to which the animal had responded by a so-called "reaction of alarm". Aged solutions of royal jelly (stored for a week at 1°) produced hyperglycaemia when injected into mice[32]. The blood sugar one hour after injection was double the control blood sugar level. 6 mg. of jelly counteracted the effects of 5 units of insulin. There is evidence that royal jelly has effects on the adrenal glands, on blood sugar concentration and on lymphoid tissue of various animals, but it is not yet possible to say how they are caused. The only reported human trial in which urinary 17-ketosteroid excretion was measured was inconclusive.

Antibacterial activity. Royal jelly does not show any bacterial or fungal growth when kept at room temperature in non-sterile containers[33,34]. There is now evidence of antibiotic powers against a range of organisms including *Micrococcus pyogenes*, *E. coli* and *M. tuberculosis*[28,35–38,39]. The antituberculosis fraction was found to be soluble in water and ethanol[28]. 10-hydroxydecenoic acid has been investigated as the compound responsible for the antibacterial and antifungal activity of royal jelly[15], but it is probably too weak, having only one-quarter of the activity of penicillin against *M. pyogenes*, and less than one-fifth of that of chloramphenicol against *E. coli*[40]. The antibiotic activity is found only after the jelly has been stored for some time[9].

Antitumorigenic action. Very recently it has been found that mice injected with a mixture of viable leukemia cells, lymphosarcoma cells and

royal jelly developed no tumours[41]. This effect appears to be due to 10-hydroxydecenoic acid, but the mechanism of its action is unknown.

Miscellaneous effects. Royal jelly was found to have no significant effect on the rate of growth of young rats nor on their resistance to fatigue[37]. When tested on homogenates of rat diaphragm, constituents of royal jelly were found to increase oxygen uptake. This is suggested to be due to an effect on oxidative phosphorylation[42].

Clinical and Therapeutic Uses of Royal Jelly.

Royal jelly has been used mainly on the continent of Europe as a non-specific tonic for people who do not feel quite fit, or who have some mild chronic discomfort. It has been given to sufferers from rheumatism[43] because it "lessened their discomfort and produced a definite sense of well-being so that the patient was better able to live with his disease and his fellow men". It is claimed that it can relieve such effects of senility as apathy, loss of intelligence and personality degeneration. It is also claimed to help those patients who complain of inability to concentrate, neurasthenia and easy fatigue due to over-work and strain[44]. Some other effects of ageing are said to be prevented and even reversed[19,45–49]: "the cells are rejuvenated and the glands restored to a balanced state"[48], and arthritis, neuralgia and vascular insufficiency are greatly relieved[50]. There have been several claims that royal jelly can accelerate the growth of premature infants[51–55], but the reports are of very few cases and the increases in weight so small that it is impossible to show any definite effect. It has even been said[48] that royal jelly "helps the body to combat cancer by aiding reactive connective tissue formation", but no evidence is given to support this statement.

In all these reported treatments very small quantities of royal jelly have been used, and doses given were about the same as those employed in mice by Ardry[19] and Chauvin[29]. It is usually administered as some form of lyophilised preparation orally, sub-lingually or parenterally. Ardry[19] states that oral administration has no effect but others[44,48] have claimed good results by this route. Royal jelly has also been given by iontophoresis for certain joint conditions and has been used topically as a hair lotion for scurf[50]. The commercial preparations of royal jelly have been described as weak and impure mixtures[10].

One case of "poisoning" has been reported[56] in which a man swallowed about 5 g. of royal jelly. For the next few days he felt full of vitality and energy and was unable to sleep. He felt warm although his temperature was not raised. After a few days he made a complete recovery and did not show any ill effects during the next 4 years.

Apart from the confusion about how to give royal jelly and how much to use, it must be pointed out that the reports of its effectiveness are based on small numbers of short-term case histories of patients with just those symptoms which are relieved by any new therapy. From the information given it is impossible to decide whether royal jelly has had any effect, and it seems likely that its value was psychological and due only to the novelty and glamour of the treatment.

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