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ROYAL JELLY and its efficacy

by Dr Alan Lakin

In addition to possessing antimicrobial activity, Royal Jelly can exert several physiological effects, some of which support its use as a therapeutic agent. Unfortunately, standard experimental protocols are not suited to the circumstances in which Royal Jelly is normally employed, and so the various claims for its efficacy are mostly based on clinical use. It would ***seem,*** *therefore, that the controversy that surrounds Royal Jelly can only be resolved by the documentation and collation of observations by practitioners.*

Royal Jelly must be one of the most controversial therapeutic agents available for use by the Complementary Practitioner. The enthusiastic anecdotal reports of its use by leading personalities in society' contrast with its damnation by antagonists, who cite Royal Jelly as a prime example of the irrationality of the whole basis of alternative medicine[2]. Even so, despite the marketeers' use of evocative terms such as 'Miracle Food', Mystery Food', and so on, genuine sceptics should consider whether there might be some rationale for Royal Jelly being well-established in the traditional medicine of different countries that have been geographically-isolated until recent times (for example, China and Eastern Europe). Furthermore, since Royal Jelly continues to be prescribed by practitioners of Chinese medicine, it is reasonable to assume that their detailed records contain evidence of it having some beneficial effects.

In many respects, the controversy of the use of Royal Jelly as a therapeutic agent, or as a dietary supplement is understandable. Its fervent advocates have created suspicion and doubt in unprejudiced minds by linking its remarkable role in insect physiology with almost miraculous claims for its success in correcting human disorders. On the other hand, equally fervent adversaries have argued that such claims have never been substantiated, and that the high cost of Royal Jelly is a prime example of unscrupulous exploitation of the public.

This review is an attempt to collate and interpret the published information relating to the properties and therapeutic uses of Royal Jelly. Unfortunately, much of the relevant information has been published in relatively obscure journals, and so it has not been possible to provide comprehensive coverage. Even so, some indication of potential applications and of the controversies associated with the use of Royal Jelly should emerge.

While no justification could be found for claims of Royal Jelly being a 'wonder cure', there can be no doubt that it contains biologically-active substances, and that there is experimental evidence to suggest that it can influence the metabolism of isolated tissues and of experimental animals. In addition, even though clinical studies according to recognised, conventional, protocols may not have been undertaken, the published reports of Royal Jelly having been successfully used for the treatment of various human ailments outnumber those that have shown it to have been unsuccessful. As for the high cost of Royal Jelly, this could be a reflection of the incredible amount of effort involved in its collection, coupled with the technical problems associated with storing and transporting the fresh, unprocessed, material.

Nature **of Royal Jelly**

Royal Jelly is not produced by regurgitation. It is secreted by the hypopharyngeal glands **of** 'nurse' worker bees during the sixth and twelfth days of their adult life. Because of its milky-white appearance, it is sometimes called 'bee milk', and its flavour is typically described as being 'quincelike'. (Although this may be masked in commercial preparations because of the addition of honey and other adjuncts.)

Royal Jelly is fed to all bee larvae during the first three days of their development, and then those female larvae destined to become worker bees are changed over to a diet consisting mainly of honey. The female larvae that are to become queen bees continue to receive it throughout their development and throughout their adult life.

TABLE 1. COMPOSITION OF ROYAL JELLY - MAJOR AND MINOR COMPONENTS
(Typical values per bOg fresh material)

Component (units)	Value	(range)	References
Water (g)	66.8	(60.3-69.9)	6,7,8
pH	3.8	*(3.5-4.5)*	9,10
Total Carbohydrates (g)	11.6	(9.0-13.0)	7,8,10
Glucose(g)	4.6		11
Fructose(g)	4.5		11•
Sucrose (g)	1.1		12,13
Trisaccharides	0.3		11
Total Protein (g)	12.3	(11.0-16.7)	7,8,10
Free amino acids (g)	*0.25*		*7*
Lipids(g)	5.1	(3.3-7.6)	*7,14,15*
10-hydroxy-2-decenoic acid (g)	25	(2.0-3.2)	15,16
1 0-hydroxydecanoic (g)	*1.25*		*7*
Ash(g)	1.0		*7*
Potassium (mg)	491	(410-544)	7,17,18
Sodium (mg)	37	*(19-55)*	7,17,18
Magnesium (mg)	30	(15-72)	7,17,18
Calcium (mg)	26	(12-40)	7,17,18
Zinc (mg)	2.7	(2.4-3.0)	17
Minor Components			
Thiamin (mg)	0.4	(0.15-0.74)	19,20
Riboflavin (mg)	1.4	(0.5-2.4)	19,21
Niacin (mg)	4.3	(2.9-14.9)	6,19,20
Pantothenic Acid (mg)	13.2	(65-20.0)	19,20
Pyridoxine (mg)	0.5	(0.2-1.0)	19,20
Mesoinsoitol (mg)	10.0	(7.8-15.0)	20
Biotin (mg)	0.2	(0.02-1.0)	6,20
Folic Acid (mcg)	30	(13-50)	20,21
Acetyl Choline (mg)	10		12
Testosterone (ng)	1		22
Insulin	Trace		23,24

[Note that analytical data tend to vary according to the source of the material analysed and the procedures employed for analysis]

Taking into account the size of worker bees, the amounts that are secreted are considerable, each queen cell containing about 250-300mg Royal Jelly. Even so, since the individual colonies need only produce sufficient for population maintenance, the amounts available for human use are relatively small. In order to raise yields, therefore, apiarists introduce artificial queen cells (containing transplanted larvae) into hives, and these are instinctively supplied with Royal Jelly by the 'nurse' bees.

Both the management of hives and the manual extraction of Royal Jelly from the queen cells are labour-intensive, and so the number of hives and the total effort involved in supplying Japan, say, with its annual consumption of the order of 250 tons almost defeats the imagination!

Much of this is produced in China, where it is estimated that about seven million hives are used for apiculture.

(Comprehensive accounts of the production of Royal Jelly are given in References and 4)•

Chemical Composition

Because of its remarkable effects on the development of bees, the chemical composition of Royal Jelly has intrigued apiculturists and insect physiologists for many years, analytical studies having been published since 1 852~. Despite this interest, it would seem that it is still not possible to prepare a biologically-effective surrogate for Royal Jelly by re-combining those constituents that have been chemically characterised.

As with most biological materials, Royal Jelly has been shown to contain hundreds of components, many of which have been unequivocally identified, even though they are present in trace amounts. Table 1 (previous page) lists only those constituents that are present in significant amounts, or that are considered to be of potential significance. It can be seen that fresh Royal Jelly is made up of about two-thirds water, and that the residual material is comparatively rich in sugars, protein and lipid material. Despite its key role in bee nutrition, it is interesting to note that Royal Jelly is lacking in vitamins A, C and E, and that, apart from zinc, the levels of essential mineral elements are too low to justify their inclusion in the table.

TABLE 2. SPECIFIC BIOLOGICAL EFFECTS OF ROYAL JELLY (Not including effects associated with insect development only)

A.	**Effects ascribed to known components**	**References**
	Antibacterial Activity (iO-hydroxy-2-decenoic acid)	**25,26,27**
	Antibacterial Activity (Protein Fraction - Royalism)	**28**
	Antifungal Activity (1O-hydroxy-2-decenoic acid)	**29**
	Glycaemic Control (Insulin)	**23,24,30,31**
	Male Hormonal Activity (Testosterone)	**22**
	Vasodilator Activity (Acetyl Choline)	**12,32,33**
	Interferon-promoting Activity (Glycoprotein)	**34**
	Reduction of hypertension (Lipid Fraction)	**3 5,36**
B.	**Effects not identified with known components**	
	Anti-tumour effects (Sarcoma-i 80 tuniours)	**37,38**
	Anti-tumour effects (Erlich ascites tumours)	**37,38**
	Inhibition of Erlich tumour cells in vitro	**39**
	Inhibition of pathogenic bacteria	**26,40, 66**

Table 2 gives an overview of the specific biological effects of Royal Jelly or of its known components. (Effects peculiar to insect development have not been included in this table, nor have nutritional properties.) The recent patented claims[34] 36 both Japanese, for fractions prepared from Royal Jelly having interferon-promoting and hypotensive properties are interesting developments, and it is unfortunate that the associated experimental evidence is not available. As analytical and biochemical techniques improve, it is possible that other biologically-active components will be identified and characterised. Furthermore, it could be that the fill biological significance of some of the known constituents remains to be appreciated.

Irrespective of such speculation, it can be seen that Royal Jelly has diverse biological properties, some of which are in keeping with the rationale for its secretion. For example, since Royal Jelly is a complete food for developing bee larvae, and since it is exposed to a relatively warm environment that is laden with spoilage microorganisms, parasites, and so on, it is to be expected that it is nutrient-rich and that it contains anti-microbial agents. Similarly, because of the fundamental importance of Royal Jelly with respect to bee physiology, the presence of various hormonal substances is not surprising.

Scientific interest has been focused on only a few components of Royal Jelly, of which a protein called royalism and an unusual fatty acid, 1O-hydroxy-2-decenoic acid (1O-HDA), deserve special mention. Royalism is unique to Royal Jelly, and it has anti-microbial properties on account of its ability to effect the lysis of bacterial membranes. (Lysozyme, a protein in the white of avian eggs, has similar anti-bacterial properties.) 1O-HDA would also appear to be unique to Royal Jelly, because there seems to be no other natural source (although it can be obtained by chemical synthesis). It, too, has antimicrobial properties, and so some of the observed effects of Royal Jelly might be associated with these components.

It should also be mentioned that Royal Jelly is probably the richest natural source of pantothenic acid, and it could make a significant contribution to the dietary intake of this vitamin when large amounts are consumed.

Physiological and pharmacological effects

Table 3 sumarises most of the published animal studies on Royal Jelly, many having been undertaken to export the rationale of the claims for its beneficial effects.

TABLE 3. REPORTED EFFECTS OF ROYAL JELLY ON EXPERIMENTAL ANIMALS

A.	Studies with mice	References
	Implanted Sarcoma-180 tumour cells retarded	38
	Implanted Sarcoma-180 tumour cells not retarded	41
	Implanted Erlich ascites tumour cells retarded	38
	Implanted Erlich ascites tumour cells not retarded	41
	Implanted solid Sarcoma-180 tumours retarded	41
	Implanted Erlich ascites tumours retarded	41
	Protection given against transplantable leukaemia	42
	No effects on induded leukaemia in mice	38
	Increased phagocytosis of peritoneal macrophages	39
	Hypoglycaemic effect (0/A)	40
	Growth rate retarded by excessive doses	40
B.	Studies with rats	
	Increased oxygen uptake by liver mitochondria (0/A)	43,44
	No hypoglycaemic effect in rats rendered diabetic by injection of streptozotocin	45
	Hypertension reduced by a lipid fraction (0/A)	35,36
	Anti-inflarnmatoiy effects, improved wound healing	45
	Increased body weight of males (0/A)	36
	Increased production of serum luteinizing hormone, testosterone and progesterone in males (0/A)	27
	Increased levels of serum thyroxine, coritsol, glutamic-oxaloaectic transaminase (aspartate aminotransferase) and glutamicpyruvic transaminase (alanine aminotransferase) in males (0/A)	47
	Increased survival following exposure to radiation (A/l)	48

C.	Studies with other animals	
	Rabbits: reduction of blood cholesterol levels induced by cholesterol-rich diets (0/A)	49
	Rabbits: improved reproductive characteristics of females (0/A during rearing)	50
	Hamsters: topical application reduced development of androgen stimulated sebaceous glands	51
	Guinea Pigs: increased growth rate (A/I)	52
	Calves: increased levels of red blood cells and ganima-globulin increased growth rates and resistance to infection	53

Key: 0/A = Oral Administration; A/I = Administration by Injection

While some studies report no effects, there can be little doubt that, if they are taken at face value, the majority strongly suggests that Royal Jelly can influence both the growth and the development of animals. On the other hand, much of the work that has been undertaken is subject to legitimate criticism on the grounds of inadequate experimental design, lack of precision, use of excessive levels of Royal Jelly, and so on. There is also the possibility that some of the observed responses are not pharmacological, but are due to nutritional effects. Even so, there does seem to be a consensus that Royal Jelly cair exert physiological effects and so the temptation to discredit the published work supporting this investigation should be supported.

Disregarding such controversies, of the studies reported in the literature, attention is drawn to those of Ishiguro et al'[3] and Teleb et al~ , who have shown that oral administration of Royal Jelly to rats stimulates mitochondrial activity in liver suspensions. Even though the reasons for this effect were not ascertained, these findings might support the use of Royal Jelly in the treatment of weak and debilitated patients.

Therapeutic uses of Royal Jelly

As is to be expected, published accounts of the effects of Royal Jelly on human subjects are relatively few, and many of these relate to 'one-off' case histories[54] ~ and not to clinical trials. Table 4 is an attempt to collate the ava~i1able information, and it can be seen that certain of the studies (undertaken independently) tend to be mutually supportive. In particular, attention is drawn to the claims that Royal Jelly has been efficacious in the following circumstances: fatigue, debility, anorexia, failure of children to thrive, and geriatric problems.

TABLE 4. EFFECTS OF ROYAL JELLY ON HUMAN SUBJECTS (ORAL ADMINISTRATION)

A.	Claims of Beneficial Effects	References
	Anorexic.	37
	Fatigue'	37,54
	Headaches	37
	Failure of children to thrive	37,56
	Inadequate lactation	56
	Asthmatics	
	Debility (geriatrics)	54,58,59
	Debility (tuberculosis patients)	60
	Debility (infectious hepatitis patients)	61
	Raised levels of blood triglycerides and cholesterol	*55*

B. No ~ No	Observed change in	Effects excretion of gonadotrophins by men	62

Since it would seem that none of the published reports relating to human subjects would stand up to orthodox scrutiny, this is also a contentious area. However, even with conventional clinical trials, unequivocal judgements are difficult when dealing with conditions that cannot be defined objectively, and when the subjective self-assessment of the patient is of paramount importance (in cases of weakness and/or fatigue, for example). As with other unconventional treatments, therefore, it seems that the true situation will only become revealed through meticulous documentation of case histories and by the pooling and collation of such information.

The daily doses employed in reported studies were typically in the range of 200-500mg[54] 57 60 per day, although much larger amounts were used for severely debilitated patients[54] . Also given in the literature are accounts of beneficial effects of treatments involving intramuscular injections of Royal Jelly preparations[48] 63

It is pertinent to note that, apart from isolated reports of skin allergies and dermatitis" 65 usually caused by excessive topical exposure, no reports of adverse effects from the oral administration of Royal Jelly were found in the literature. Similarly, no adverse effects due to the injection of preparations seem to have been reported. (Even so, since administration by this route is potentially hazardous, the appropriate precautions would need to be taken).

Interpretation of observed effects

As explained above, in common with other complete foods, such as the avian egg and mammalian milk, it is not surprising that Royal Jelly would be of high nutritive value to humans, even though it is an insect nutriment. Even so, claims for its efficacy on the basis of its content of essential amino acids, B vitamins, essential fatty acids, trace elements, and so on, would seem to be illogical. The amounts consumed at the levels recommended for its use as a dietary supplement (e.g., [20]0-.500mg daily) would be far too small for it to have any nutritional impact on humans. On the other hand, the reports of the successful treatment of seriously debilitated patients through the use of much larger doses of Royal Jelly might be reasonably explained in terms of nutritional intervention, irrespective of any pharmacological effect.

Likewise, when Royal Jelly has been shown to exert an effect on tissue metabolism or on the physiology of experimental animals, the levels employed are sometimes in excess of the amounts typically recommended for its use as a dietary supplement. It could be argued, therefore, that the prospect of Royal Jelly having a corresponding influence on the human body would be most unlikely apart from the possibility of pharmacological intervention in the case of large doses. While this might be true, caution must be exercised in adopting a too rigorous approach because there are many well-documented examples of profound physiological effects being brought about by repeated doses of minute amounts of biologically-active substances (for example, the beneficial effects of homeopathic preparations, or the detrimental effects of environmental pollutants).

While anti-microbial effects (and possible hormonal effects) can be reasonably assigned to known components of Royal Jelly (see Table 2), so called 'tonic effects' are much more difficult to account for. Although interest tends to be focused on its unique component, l0-HDA[54], it would appear that no definite model of a physiological effect has been proposed. Even so, it is interesting to note that a hypotensive effect is claimed to be caused by a lipid component of Royal Jelly[5].

Conclusions

Royal Jelly is rich in nutrients, it has anti-microbial activity, and it contains a variety of biologically-active constituents. It follows, therefore, that large doses are potentially capable of producing physiological responses, and so it would seem to be irrational to arbitrarily dismiss the claims for beneficial effects arising from such treatments. Obviously, further evidence is needed, and there is strong case for the documentation and collation of relevant case histories.

It seems that the real controversy associated with the use of Royal Jelly is the weight to be given to the published reports and to the many anecdotal claims of it being efficacious when consumed at relatively low levels. Should these be dismissed on the grounds of lack of confirmation by means of conventional trials? Or should credence be given to the argument that the beneficial effects of Royal Jelly are subtle and long-term in their manifestation? This debate mirrors other contentious explanations and discards less acceptable possibilities.

From published information and from numerous anecdotal reports, it would seem that the commonest therapeutic use of Royal Jelly at low levels is to alleviate debility and fatigue (which may, or may not be, associated with a specific illness). Furthermore, it is invariably employed in conjunction with prescribed treatments (so as to provide support and reinforcement), and not as an alternative to them. Because it is exceedingly difficult, or even impossible, to undertake conventional trials in these circumstances, it is again inevitable that a view can only emerge after consideration of the evidence acquired through the accumulation of case histories.

If, therefore, it is decided to evaluate the efficacy of Royal Jelly in the treatment of appropriate cases, the best approach would seem to be to prescribe it as an adjunct to an existing regimen and then to meticulously monitor the subsequent progress of the patient. The Writer would be pleased to receive reports of any such trials, irrespective of their outcome. Such information could form the basis of a subsequent publication.

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