



Royal Jelly

Updated: May 1, 2022.

OVERVIEW

Introduction

Royal jelly is a milk-like secretion of honey bees that is used to feed larvae for 3 days for the worker bees and drones and until full development for the queen. Royal jelly has been used widely as a dietary supplement for its purported health prompting properties. Royal jelly is generally well tolerated and has not been linked to serum aminotransferase elevations during therapy or to instances of clinically apparent liver injury.

Background

Royal jelly is a milk-like secretion of honey bees (*Apis mellifera*) that is used to feed larvae in the honeycomb. Larvae that are to develop into drones (males) or worker bees (infertile females) are fed directly and for 3 days only. Larvae that are to become queens (fertile females) are fed the royal jelly secretions in large amounts and until they are fully developed. Royal jelly is harvested from the individual queen bee cells in honey bee hives and used as an emollient in topical creams as well as a dietary supplement for purported medicinal properties. Royal jelly consists of water, proteins, amino acids, fatty acids, simple carbohydrates, vitamins and minerals. The active component that stimulates and modulates larval development is believed to be a series of “major royal jelly proteins” (MRJP). These MRJP alter DNA methylation resulting in an epigenic, nutritionally-driven change in expression of genes responsible for larva development. Royal jelly is used topically in creams and orally in dietary supplements purported to be beneficial for general health and well being. The bases of these claims have not been substantiated, but in vitro and animal studies suggest that components of royal jelly have antiinflammatory and antioxidant properties. Royal jelly is generally well tolerated without adverse events except for rare allergic reactions particularly in patients with a history of asthma or atopic disease. The hypersensitivity reactions can include urticaria, pruritus, erythema, laryngeal edema, wheezing, chest tightness, hypotension, cardiovascular collapse, and in rare instances death. The reactions arise within minutes of ingestion are most likely due to allergy to one of the major royal jelly proteins.

Other names: Jalea Real, Bee Saliva, Honey Bee Milk

Hepatotoxicity

Liver injury attributable to royal jelly has not been reported. In clinical trials of royal jelly as therapy of various conditions, side effects were rarely mentioned and ALT elevations and hepatotoxicity were not reported. Despite availability and widespread use as an alternative therapy, there have been no published reports of royal jelly induced liver injury.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

Royal jelly has many components, but none of them has been shown to be particularly hepatotoxic.

Outcome and Management

Hepatotoxicity from royal jelly has not been reported.

Drug Class: Herbal and Dietary Supplements, Bee Products

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Royal Jelly – Generic

DRUG CLASS

Herbal and Dietary Supplements

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Royal Jelly	8031-67-2	Apitherapy	Not Applicable

ANNOTATED BIBLIOGRAPHY

References updated: May 1, 2022

Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 731-4.

(Expert review of hepatotoxicity published in 1999; several herbal medications are discussed, but not royal jelly).

Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 733-54.

(Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of royal jelly).

Leung R, Thien FC, Baldo B, Czarny D. Royal jelly-induced asthma and anaphylaxis: clinical characteristics and immunologic correlations. J Allergy Clin Immunol. 1995;96(6 Pt 1):1004–7. PubMed PMID: 8543734.

(Among 7 patients [6 women, 1 man, ages 19 to 66 years] with hypersensitivity reactions to oral royal jelly [in liquid and capsule forms] usually with acute severe attacks of asthma or anaphylaxis within minutes of ingestion, all had positive skin prick tests as well as IgE antibody that reacted with royal jelly protein extracts).

Schiano TD. Hepatotoxicity and complementary and alternative medicines. Clin Liver Dis. 2003;7:453–73. PubMed PMID: 12879994.

(Comprehensive review of herbal associated hepatotoxicity, including common patterns of presentation; no mention of royal jelly).

Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. Aliment Pharmacol Ther. 2003;18:451–71. PubMed PMID: 12950418.

- (Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series, most common agents being celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma huang [3], pennyroyal [1], skullcap [2], Chinese herbs [9], valerian [1]; royal jelly is not mentioned).*
- Testi S, Cecchi L, Severino M, Manfredi M, Ermini G, Macchia D, Capretti S, et al. Severe anaphylaxis to royal jelly attributed to cefonicid. *J Investig Allergol Clin Immunol.* 2007;17(4):281. PubMed PMID: 17694707.
- (28 year old man with long-standing asthma developed dyspnea, wheezing, cough and chest tightness shortly after ingesting royal jelly on two occasions was found to have a positive skin test to royal jelly).*
- Katayama M, Aoki M, Kawana S. Case of anaphylaxis caused by ingestion of royal jelly. *J Dermatol.* 2008;35:222–4. PubMed PMID: 18419679.
- (26 year old Japanese woman with a history of asthma, atopic dermatitis and food allergies developed anaphylaxis, generalized erythema and swelling of lips 5 minutes after ingesting a beverage of crude royal jelly with progressive respiratory distress requiring temporary intubation).*
- García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. *Rev Esp Enferm Dig.* 2008;100:688–95. [Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry]. Spanish. PubMed PMID: 19159172.
- (Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, none due to royal jelly).*
- Münstedt K, Bargello M, Hauenschild A. Royal jelly reduces the serum glucose levels in healthy subjects. *J Med Food.* 2009;12:1170–2. PubMed PMID: 19857086.
- (In 20 healthy volunteers undergoing 2 glucose tolerance tests one week apart, the second after a single 20 gm dose of royal jelly, glucose levels were slightly lower after the royal jelly but insulin and C-peptide levels were similar).*
- Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. *Pharmacoepidemiol Drug Saf.* 2009;18:1039–47. PubMed PMID: 19650152.
- (Review of 778 spontaneous reports of adverse reactions to herbals to Swedish Registry found none attributed to royal jelly).*
- Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. *Hepatology.* 2010;52:2065–76. PubMed PMID: 20949552.
- (Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury of which 12 [9%] were due to herbals, including several herbal mixtures, usnic acid, Ma Huang, black cohosh, and Hydroxycut, but not royal jelly).*
- Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. *Liver Int.* 2012;32:1543–56. PubMed PMID: 22928722.
- (A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements does not include any attributed to royal jelly).*
- Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther.* 2013;37:3–17. PubMed PMID: 23121117.
- (Systematic review of literature on HDS associated liver injury does no mention royal jelly).*
- Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. *Hepatology.* 2014;60:1399–408. PubMed PMID: 25043597.

- (Among 839 cases of liver injury from drugs collected in the US between 2004 and 2013, 130 were due to HDS products, including 45 from body building agents [probably anabolic steroids] and 85 from diverse HDS products, but none were attributed to royal jelly).*
- Paola F, Pantalea DD, Gianfranco C, Antonio F, Angelo V, Eustachio N, Elisabetta DL. Oral allergy syndrome in a child provoked by royal jelly. *Case Rep Med.* 2014;2014:941248. PubMed PMID: 24799914.
- (A 7 year old healthy child developed oral allergy symptoms on 2 occasions 10 minutes after ingestion of royal jelly with lip and tongue edema and palate itching).*
- Taavoni S, Barkhordari F, Goushegir A, Haghani H. Effect of Royal Jelly on premenstrual syndrome among Iranian medical sciences students: a randomized, triple-blind, placebo-controlled study. *Complement Ther Med.* 2014;22:601–6. PubMed PMID: 25146061.
- (Among 110 female medical studies students with premenstrual syndrome treated with royal jelly capsules [1000 mg] or placebo once daily] for two menstrual cycles, symptoms decreased with royal jelly but not placebo; no mention of adverse events).*
- Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. *Gastroenterology.* 2015;148:517–532.e3. PubMed PMID: 25500423.
- (Extensive review of herbal associated liver injury does not discuss royal jelly specifically).*
- Lambrinouadaki I, Augoulea A, Rizos D, Politi M, Tsoltos N, Moros M, Chinou I, et al. Greek-origin royal jelly improves the lipid profile of postmenopausal women. *Gynecol Endocrinol.* 2016;32:835–839. PubMed PMID: 27227757.
- (Among 36 postmenopausal women treated with oral royal jelly [150 mg] daily for 3 months, serum HDL cholesterol levels increased [60 to 65 mg/dL] while LDL cholesterol decreased slightly [144 to 136 mg/dL]; no mention of adverse events or changes in serum ALT levels).*
- Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, et al; Spanish DILI Registry. Herbal and dietary supplement-induced liver injuries in the Spanish DILI Registry. *Clin Gastroenterol Hepatol.* 2018;16:1495–1502. PubMed PMID: 29307848.
- (Among 856 cases of hepatotoxicity enrolled in the Spanish DILI Registry between 1994 and 2016, 32 were attributed to herbal products, the most frequent cause being green tea [n=8] and Herbalife products [n=6], while none were attributed to royal jelly).*
- Sharif SN, Darsareh F. Effect of royal jelly on menopausal symptoms: A randomized placebo-controlled clinical trial. *Complement Ther Clin Pract.* 2019;37:47–50. PubMed PMID: 31470366.
- (Among 200 postmenopausal woman treated with royal jelly [1000 mg] or placebo once daily for 8 weeks, menopausal symptoms improved with royal jelly therapy but not placebo; no mention of adverse events).*
- Lima WG, Brito JCM, da Cruz Nizer WS. Bee products as a source of promising therapeutic and chemoprophylaxis strategies against COVID-19 (SARS-CoV-2). *Phytother Res.* 2021;35:743–750. PubMed PMID: 32945590.
- (Review of the preclinical and clinical evidence for the activity of bee products [including royal jelly, beeswax, bee pollen, bee venom and propolis] against SARS-CoV-2; no mention of adverse events).*
- Matsushita H, Shimizu S, Morita N, Watanabe K, Wakatsuki A. Effects of royal jelly on bone metabolism in postmenopausal women: a randomized, controlled study. *Climacteric.* 2021;24:164–170. PubMed PMID: 32880201.
- (Among 72 postmenopausal women treated with royal jelly [3000 mg daily] or placebo for 6 months, bone mineral density did not change in those receiving royal jelly but decreased to some extent in those on placebo; no mention of adverse events).*

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J. Herb-induced liver injury: Systematic review and meta-analysis. *World J Clin Cases*. 2021;9:5490–5513. PubMed PMID: 34307603.

(Systematic review of the literature on herb-induced liver injury identified 446 references describing 936 cases due to 79 different herbal products, the most common being He Hou Wu [91], green tea [90], Herbalife products [64], kava kava [62], greater celandine [48], and aloe vera [22], but royal jelly was not mentioned).

Li JD, Cui L, Xu YY, Guan K. A case of anaphylaxis caused by major royal jelly protein 3 of royal jelly and its cross-reactivity with honeycomb. *J Asthma Allergy*. 2021;14:1555–1557. PubMed PMID: 35221696.

(56 year old Chinese woman developed two episodes of anaphylaxis with urticaria, pruritus, laryngeal edema, hypotension and collapse within 1 hour of consuming royal jelly and was found to have a positive skin prick test to crude extracts of royal jelly; immunoblotting with her serum identified evidence of antibodies to purified royal jelly protein 3).

Bessone F, García-Cortés M, Medina-Caliz I, Hernandez N, Parana R, Mendizabal M, Schinoni MI, et al. Herbal and dietary supplements-induced liver injury in Latin America: experience from the LATINDILI Network. *Clin Gastroenterol Hepatol*. 2022;20:e548–e563. PubMed PMID: 33434654.

(Among 367 cases of hepatotoxicity enrolled in the Latin American DILI Network between 2011 and 2019, 29 [8%] were attributed to herbal products, the most frequent being green tea [n=7], Herbalife products [n=5] and garcinia [n=3] while none were attributed to royal jelly).

El-Seedi HR, Eid N, Abd El-Wahed AA, Rateb ME, Afifi HS, Algethami AF, Zhao C, et al. Honey bee products: preclinical and clinical studies of their anti-inflammatory and immunomodulatory properties. *Front Nutr*. 2022;8:761267. PubMed PMID: 35047540.

(Extensive review of the preclinical and clinical studies of honey bee products including royal jelly, beeswax and bee pollen; no mention of adverse event rates or hepatotoxicity).