Effects of Honeybee on Mammals

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Honeybee products have positive effects on the reproductive performance of mammals. Many honeybee product constituents are biologically active, with antioxidant, antimicrobial, antiviral, anti-inflammatory, immunomodulatory, antifungal, wound-healing, and cardio-protective properties.

Keywords: reproduction ; mammals ; honeybee products ; active compounds

1. Introduction

Procreation is a pivotal innate physiological event for all creatures. For humankind, reproductive health and fertility are of particular importance for maintaining social, mental, and physical health status. Supporting adequate reproductive performance in food-producing animals is also important to humans, enabling mass production to maintain food security. However, reproductive events and fertility of individuals/organisms are greatly impacted by modern lifestyle circumstances such as increased exposure to environmental and behavioral stresses. According to a World Health Organization report, 60–80 million couples, representing 8–12% of couples worldwide, are currently experiencing infertility [1][2][3]. Similarly, poor reproductive efficiency is evoked in production animals owing to management practices for producing animal products in massive quantities [4]. Therefore, research endeavors to improve and maintain adequate reproductive health are essential for humankind and animals.

The use of natural products as alternatives to synthetic prophylactic and therapeutic drugs is increasingly recommended to improve many aspects of human and animal health [5]. Honeybee products, including honey, propolis, royal jelly, bee pollen, beeswax, drone brood, bee venom, and bee bread, contain several natural bioactive components with various pharmaceutical and nutritional properties. Given the chemical constitutes of these products, honeybee products may have beneficial prophylactic and therapeutic effects on reproductive health in mammals. For example, honey is an energy-rich product that contains substantial concentrations of polyphenolic compounds with antioxidant activity [6][7][8][9], which can improve reproductive events by improving energy status [10][11] and/or redox status [12]. Additionally, propolis has many pharmaceutical properties thanks to its enrichment with flavonoids, which are polyphenolic compounds required for maintaining reproductive health, particularly under stressful conditions such as heat stress [13][14]. Furthermore, products such as royal jelly and drone brood contain sex hormones, and thus can be used to modulate endocrine system functions [15].

2. Honeybee Products and Reproductive Health

2.1. Biological Effects of Honeybee Products on Reproduction

Owing to the diversity of chemical constituents in honeybee products, a wide range of biological effects on reproductive functions could be achieved via several biological mechanisms/pathways. For example, most honeybee products contain phenolic compounds, widely known to affect reproduction in mammals. Phenolic compounds can regulate gonadal steroidogenesis and the functionality and metabolism of sex steroid hormones [16][17]. In addition, phenolic compounds can affect the expression of genes and activity of enzymes (aromatase, topoisomerases I and II, and extracellular signal-regulated kinases) involved in the regulation of reproductive events. Phenolic compounds can also contribute to cellular apoptotic/proliferation, epigenetic, antioxidant, and inflammatory pathways [18]. Metabolic status may also be affected by phenols owing to their ability to regulate metabolic hormone signals such as growth hormone, insulin-like growth factors, and triiodothyronine, as well as lipid, protein, and carbohydrate metabolism. Furthermore, sex hormones have been detected in some bee products, such as royal jelly and drone brood, which can thus modulate endocrine system functions [15]. Drone brood is rich in male sex hormones, especially testosterone, producing an androgenic effect that enhances male sex features. Drone brood can also be classified as a natural anabolic agent that can increase body muscle weight in male individuals [19][20]. Additionally, nutrients, vitamins, and minerals can directly affect reproductive tissues, reinforcing their functions and improving gametogenesis and/or the quality of gametes [21]. Therefore, honeybee products can provide

effective tools for improving reproductive functions in vivo and assisted reproductive technique (ART) outputs in vitro. The potential effects of honeybee products on mammalian reproductive functions and ARTs are shown in **Figure 1**.

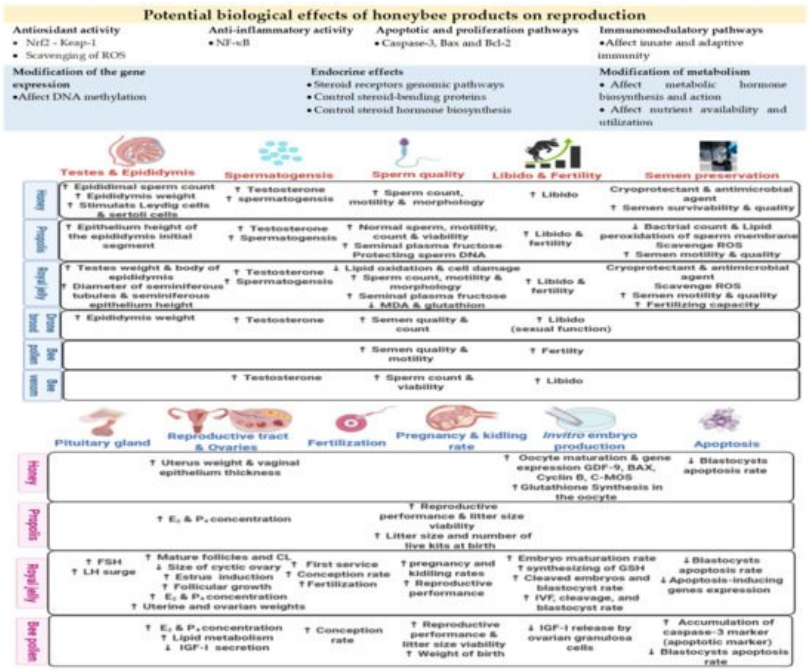

Figure 1. Potential effects of honeybee products on reproductive functions and assisted reproductive techniques (ARTs) in mammals. BAX: bcl-2-like protein 4, Bcl-2: B-cell lymphoma 2, C-MOS: complementary metal–oxide–semiconductor, E_2: estradiol-17β, FSH: follicle stimulating hormone, GDF-9: growth differentiation factor 9, IGF-I: insulin-like growth factor I, LH: luteinizing hormone, Nrf2-Keap-1: nuclear factor erythroid 2-related factor 2-Keap-1, NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells, P_4: progesterone, ROS: reactive oxygen species.

2.2. Applications for Improving Male Fertility

Recent studies on the effects of honeybee products on male reproductive performance in mammalian species are shown in **Table 1**. Several studies have supported the traditional use of honey as a natural product to enhance reproductive efficiency and fertility in males [22][23][24]. Honey has been demonstrated to improve libido, erectile function, spermatogenesis, epididymal sperm count, and normal sperm percentage, and reduce the percentage of sperm head and tail abnormalities and chromatin damage in mammalian species, including humans [25][26] and rats [22][23][24]. The positive effects of honey on male reproductive performance are attributed to several different mechanisms. Honey can increase the activity of enzymes that affect sperm quality, such as sorbitol dehydrogenase [22], which converts sorbitol into fructose, an important nutrient for sperm metabolism and motility. Additionally, honey administration improves spermatogenesis by enhancing male sex hormones, specifically testosterone. This enhancement was mediated by luteinizing hormone synthesis, Leydig cell viability, upregulation of steroidogenic acute regulatory protein expression, and aromatase activity in the testes [27]. In addition, bioactive compounds with antioxidant activity (e.g., antioxidant polyphenols such as flavonoids and phenolic acids) can provide reproductive organs with a robust defense system against oxidative stress induced by elevated levels of reactive oxygen species (ROS) [24]. Furthermore, honey can treat dysfunctional erection or impotence by modulating the biosynthesis of nitric oxide, a chemical substance involved in vasodilatation that affects erectile function [25][26].

Table 3. Summary of some recent studies on the effects of different honeybee products on reproductive performance of males in different mammalian species.

Animal Species	Treatment/Honeybee Product	Result	Suggested Mode of Action
Rats [25]	**1 mL/100 g BW of honey for 65 days**	• Improved semen quality (sperm count, sperm motility, and sperm morphology)	• Improving spermatogenesis and steroidogenesis
Rats [22]	**Drinking 5% solution of Palestinian honey for 20 days**	• Increased relative weight of epididymis and epididymal sperm count • Increased SDH and reduced LDH activities	• Providing energy source for sperm cells by increasing sorbitol dehydrogenase activity • Protecting germ cells against oxidative stress due to antioxidant activity of pinocembrin, pinostrobin, vitamins, and glucose oxidase
Rats [23]	**0, 0.2, 1.2, and 2.4 g/kg BW/day of Malaysian honey for 4 weeks**	• At 1.2 g/kg BW/day, increased epididymal sperm count	
Rats [24]	**1.0 mL/100 g BW/day of Gelam honey for 60 days**	• Improved spermatogenic cells and sperm count and percentage of normal sperm and decreased abnormal sperm	• Improving spermatogenic cells proliferation
Rats [28]	**2.5%, 5%, 7.5%, 10%, and 12.5% of propolis extract for 18 days**	• At 10%, increased T level, spermatogenesis, and sperm motility	• Antiestrogen effect due to flavonoids (kaempferol, quercetin, and isorhamnetin) content
Rabbits [29]	**0, 0.25, 0.50, 0.75, 1.0, and 1.25 g/kg diet of propolis for 94 days**	• At 1.25 g/kg diet, improved semen quality	• Antioxidant properties of the flavonoids
Rabbits [30]	**0.5 and 1 g/animal/day of Egyptian propolis for 6 weeks during summer months**	• At 0.5 g/animal/day, improved T level, semen volume, sperm motility, morphology, and viability traits, as well as seminal plasma fructose levels	• Antioxidant and anti-inflammatory effects
Rabbits [14]	**150 mg/kg diet of vitamin E or propolis for 10 consecutive weeks during summer months**	• Both treatments improved libido, sperm count and viability, seminal plasma fructose and total protein level, and improved plasma antioxidant activity (TAC and MDA) and T level	• Antioxidant agent providing protection against lipid peroxidation
Pre-pubertal rabbits [31]	**15 mg/kg BW of propolis with/without 200 mg royal jelly + 0.25 mL bee honey**	• Both treatments accelerated age of puberty and improved libido, ejaculate volume, sperm concentration, sperm motility and morphology, seminal plasma fructose levels, blood plasma T levels, and fertility	• Antioxidant agent

Animal Species	Treatment/Honeybee Product	Result	Suggested Mode of Action
Rats [32]	**3, 6, and 10 mg/kg BW/day of Brazilian green propolis extract for 56 days**	• At 6 mg/kg/day, increased sperm production and greater epithelium height of the epididymis initial segment	• Protecting sperm DNA fragmentation from thiobarbituric acid-reactive substances
Rats [33]	**1 g/kg BW of royal jelly with or without hydrogen peroxide (0.5%) in drinking water for one month**	• Royal jelly with or without hydrogen peroxide increased testicular weight and the body of epididymis, sperm count, T and glutathione levels, and decreased sperm deformity percentage	• Stimulating gonadotropins secretion owing to acetylcholine stimulation • Improving spermatogenesis by zinc • L-arginine and carnitine amino acid • Antioxidant activity of vitamin C, vitamin E, and arginine
Pups [34]	**125, 250, and 500 mg/day/kg diet of royal jelly proteins**	• At 125 and 250 mg/day/kg diet, improved development of testis at neonate period until pubescent, testis weight, diameter of seminiferous tubule, and height of seminiferous epithelium	• Antioxidant, antibacterial, anti-inflammatory activities of amino acids and 10- hydroxy -2- decanoic fatty acid • Spermatogenesis stimulating effects of l-arginine and carnitine amino acids
Rabbits [35]	**0, 50, 100, and 150 mg/kg BW of Chinese royal jelly**	• All doses increased total sperm output	• Decreasing cellular damage, lipids peroxidation, and DNA fragmentation due to antioxidant activity
Pre-pubertal rabbits [36]	**0.25 mL honey, 200 mg royal jelly, and 200 mg royal jelly + 0.25 mL honey**	• All treatments accelerated puberty, improved ejaculate volume and sperm quality, seminal plasma fructose concentration, T and cholesterol levels, conception rate, and litter size	• Antioxidant agent

Animal Species	Treatment/Honeybee Product	Result	Suggested Mode of Action
Sheep [37]	**10, 15, and 20 mg/kg diet of apistimul preparation (drone brood) for 95 days**	• Improved the qualitative and quantitative characteristics of the ejaculate • Increased the amount of hemoglobin and erythrocytes in the blood • Increasing the weight of the seminal glands and epididymis	• Positive effects of sex hormones and sulfhydryl groups in the drone brood on semen quality variables
Pigs (junior boars) [38]	**Parenteral injection with alcohol extracts of the drone brood**	• After injection of the drone brood homogenate extract, 33.3% of boars recovered their sexual function in 30 days, while 83.3% of breeders recovered in 2 months	
Rabbits [39]	**Injection of 0.1, 0.2, and 0.3 mg/rabbit of bee venom twice weekly for 20 weeks**	• At all levels, improved libido, sperm concentration, viability T level, and blood biochemical (total protein, albumin, and glucose), as well as antioxidant markers (TAC, GST, and GSH)	• Growth promoter • Anti-inflammatory, anti-microbial, and antioxidant activity
Rabbits [40]	**0, 100, 200, and 300 mg of bee pollen/kg BW**	• At 200 mg/kg BW, improved semen quality, fertility rate, and blood biochemicals profile	• Antioxidant activity

BW: body weight, DNA: deoxyribonucleic acid, GSH: glutathione, GST: glutathione-S-transferase, g: gram, kDa: kilo dalton, kg: kilogram, LDH: lactate dehydrogenase, MDA: malondialdehyde, mg: milligram, ml: milli, SDH: sorbitol dehydrogenase, SOD: superoxide dismutase, T: testosterone, and TAC: total antioxidant capacity.

Propolis is another honeybee product shown to improve the reproductive performance of mammalian males. Several studies confirmed that administration of propolis improved sperm count and testis, seminal vesicle, and epididymis weights, and reduced the percentage of sperm head and tail abnormalities [14][28][29][30][31][32]. Moreover, the administration of propolis extract increased serum testosterone levels, coupled with increased activity and expression of testicular steroidogenesis enzymes including 3β-hydroxysteroid dehydrogenase (3β-HSD) and 17β-hydroxysteroid dehydrogenase (17β-HSD) [41], improving testosterone levels [42]. Propolis also shows strong antioxidant and modulatory activity on cellular mitochondrial energy production [28].

Royal jelly also produced many beneficial effects on male reproductive performance in mammals. As indicated by studies conducted on adult male rats [32][43][33][34] and rabbits [31][35][36], royal jelly enhanced spermatogenesis, steroidogenesis, sperm quality traits, and libido of treated males. Interestingly, royal jelly contains acetylcholine (1 mg/g dry weight), a peripheral and central neurotransmitter. Acetylcholine can stimulate gonadotropin secretion at both hypothalamic and hypophyseal levels, consequently increasing plasma testosterone levels. Most studies have focused on the major products of honeybees (honey, propolis, and royal jelly); however, beneficial effects of other honeybee products, such as drone brood [38][37], bee venom [39], and bee pollen [40], on male reproductive health have also been reported. These products contain active constituents that can affect reproductive functions, such as apistimul in drone brood [38].

2.3. Applications for Improving Female Fertility

Table 2 summarizes recent studies on the effects of honeybee products on female reproductive performance in mammalian species. Honey [44], royal jelly [45][46][47][48][49][50], propolis [51][52], and bee pollen [51][52][53][54] were demonstrated to improve female reproductive performance in several mammals. Treatment with royal jelly improved estrus response and pregnancy rate in ewes by enhancing ovarian follicle growth and development and estradiol

secretion [49]. Interestingly, Gimenez-Diaz [47] and Kridli [55] reported that royal jelly can mimic the actions of gonadotropins to improve estrus response and conception rate in ewes, providing a promising natural alternative to equine chorionic gonadotropin (eCG). The positive effects of royal jelly on reproductive performance may be partially ascribed to its estrogenic effects [50].

Table 2. Effect of bee products on reproductive performance of females of different mammalian species.

Animal Species	Treatment/Honeybee Product	Result	Suggested Mode of Action
Ovariectomized rats a model for menopausal symptoms in women [44]	**0.2, 1.0, and 2.0 g/kg/day of Tualang honey for 2 weeks**	• At all levels, increased uterus weight and vaginal epithelium thickness, restored the morphology of the tibia bones, and decreased P_4 and E_2 levels	• Estrogenic activity of flavonoids (kaempferol and quercetin) • Antioxidant activity
Rabbits and offspring [51]	**150 and 300 mg/kg diet/day of bee pollen and/or propolis (Bp + Pro) three times a week along eight parities**	• At 150 or 300 mg of Bp + Pro alone or together, improved reproductive performance, milk production, litter size viability and weights, and immune status of does	• Antibacterial, antiviral, antiparasitic, anti-inflammatory, immunomodulatory, and antioxidant properties. • Improving gastrointestinal microflora homeostasis • High nutritional value (polyunsaturated fatty acids, mineral, vitamins, and amino acids)
Rabbits [52]	**0.2 g/kg BW of bee pollen and/or propolis compared with 35 mg/kg BW prebiotic (inulin and/or MOS)**	• MOS and bee pollen with or without propolis treatments increased P_4 and E_2 levels and fertility • Bp with propolis increased litter size and number of live kits at birth	• Antioxidant activity of flavonoids and carotenoids • Improving nutritional status • Presence of natural growth promoters • Improving lipid metabolism owing to the action of linolenic fatty acid in bee pollen • Improving sex steroidogenesis
Rats [53]	**3 and 5 g/kg feed mixture of rape seed bee pollen**	• At 5 k/kg, decreased IGF-I release by rat ovarian fragments, and increased P_4 and E_2 secretion	• Regulating ovarian steroidogenesis • Regulating antiapoptotic and pro-proliferating pathways

Animal Species	Treatment/Honeybee Product	Result	Suggested Mode of Action
Rabbits and offspring [54]	**100, 200, and 300 mg/kg BW of bee pollen extract for 1 week before and after mating**	• At 200 mg/kg BW, increased E_2, conception rate, litter size and survival at birth, and milk yield and body weight of kits	• Improving nutritional status • Antioxidant activity of flavonoids, carotenoids, and phenolic constituents • Improving lipid metabolism
Polycystic ovarian syndrome animal model using female rats [45]	**200 and 400 mg/kg/day of royal jelly for 4 weeks**	• Increased FSH and TAC levels and decreased LH, E_2, T and MDA levels, and the size of cystic follicles	• Antioxidant properties of caffeic acid and anti-inflammatory properties of sebacic acid • Anti-androgenic effect • Modulating estrogenic activity by 10-HDA and HDAA
Sheep [49]	**250 mg/ewe of royal jelly during 12 days of estrous synchronization**	• Induced estrus and increased first service conception rate	• Gonadotropin hormones-like action
Sheep [46]	**400 mg/ewe of royal jelly during the period of CIDR-treatment**	• Improved pregnancy and lambing rates	• Gonadotropin hormones-like action
Rats [50]	**Intraperitoneal treatment with 100, 200, and 400 mg/kg BW/day royal jelly for 14 days**	• At all levels, increased uterine and ovarian weights and the serum levels of P_4 and E_2, and number of mature follicles and corpora lutea	• Royalactinn, a 57 kDa protein, acts as a growth promoter • Amino acid roles in tissue synthesis and body growth • Steriodogenesis stimulating effects, particularly progesterone • Antioxidant activity

W: body weight, Bp: bee pollen, CIDR: progesterone (P_4)-releasing devices, eCG: equine chorionic gonadotropin, E_2: estradiol, FSH: follicle stimulating hormone g: gram, HDAA: hydroxy-decenoic acid, 10-HAD: 10-hydroxy-2-decenoic acid, kDa: kilo Dalton, kg: kilogram, LH: luteinizing hormone, MDA: malondialdehyde, MOS: mannan-oligosaccharides, mg: milligram, ml: milli, P_4: progesterone, Pro: propolis, T: testosterone, TAC: total antioxidant capacity.

The positive effects of bee pollen on female reproductive performance are well-documented. Bee pollen can improve rabbit doe reproductive performance and milk production and enhance the immune status and growth performance of their offspring [53][54][55]. These results were attributed to the high micronutrient content (e.g., polyunsaturated fatty acids, minerals, vitamins, amino acids) and biological actions of flavonoids, carotenoids, and phenolic compounds in bee pollen [50]. Furthermore, bee pollen can regulate sex steroidogenesis, specifically progesterone and estradiol [56][57]. Hormonal balance is important for adjusting the mechanisms underlying the fate of ovarian follicles, involving cross-dialog between pro-apoptotic (caspase-3, Bax) and pro-survival anti-apoptotic (Bcl-2) molecules [56][57]. The dose and time of administration of bee pollen can both affect these pathways; positive and negative effects on ovarian follicle development and growth could be obtained using different administration methods [56].

In models designed to study menopausal symptoms, Zaid et al. [44] noticed that daily consumption of Tualang honey for two weeks by ovariectomized female rats suppressed menopause-related reproductive disorders, including uterine atrophy, vaginal epithelium atrophy, and osteoporosis. The positive effects of Tualang honey are likely due to flavonoids, particularly kaempferol and quercetin, which have weak estrogenic activity. Further, flavonoids are strong free radical scavengers, protecting organisms from the destructive actions of ROS [18][44]. Interestingly, local vaginal application of honey and royal jelly before sexual intercourse improved fertility in couples having trouble conceiving [57].

References

1. Pasupuleti, V.R.; Sammugam, L.; Ramesh, N.; Gan, S.H. Honey, Propolis, and Royal Jelly: A Comprehensive Review of Their Biological Actions and Health Benefits. Oxid. Med. Cell. Longev. 2017, 2017.
2. Zulkhairi Amin, F.A.; Sabri, S.; Mohammad, S.M.; Ismail, M.; Chan, K.W.; Ismail, N.; Norhaizan, M.E.; Zawawi, N. Therapeutic properties of stingless bee honey in comparison with european bee honey. Adv. Pharmacol. Sci. 2018, 2018.
3. Kumar, N.; Singh, A.K. Trends of male factor infertility, an important cause of infertility: A review of literature. J. Hum. Reprod. Sci. 2015, 8, 191.
4. Mizrahi, A.; Lensky, Y. Bee Products: Properties, Applications, and Apitherapy; Springer: Berlin/Heidelberg, Germany, 2013; ISBN 1475793715.
5. El-Desoky, N.I.; Hashem, N.M.; Elkomy, A.; Abo-Elezz, Z.R. Physiological response and semen quality of rabbit bucks supplemented with Moringa leaves ethanolic extract during summer season. Animal 2017, 11.
6. Viuda-Martos, M.; Ruiz-Navajas, Y.; Fernández-López, J.; Pérez-Álvarez, J.A. Functional properties of honey, propolis, and royal jelly. J. Food Sci. 2008, 73, 117–124.
7. Cornara, L.; Biagi, M.; Xiao, J.; Burlando, B. Therapeutic properties of bioactive compounds from different honeybee products. Front. Pharmacol. 2017, 8, 1–20.
8. Miguel, M.G.; Antunes, M.D.; Faleiro, M.L. Honey as a complementary medicine. Integr. Med. Insights 2017, 12, 1–15.
9. Szczêsna, T. Protein content and amino acid composition of bee-collected pollen from selected botanical origins. J. Apic. Sci. 2006, 50, 81–90.
10. Silici, S. Bal Arısı Ürünleri ve Apiterapi. Turk. J. Agric. Food Sci. Technol. 2019, 7, 1249.
11. Hashem, N.M.; Abd El-Hady, A.M.; Hassan, O.A. Inclusion of phytogenic feed additives comparable to vitamin E in diet of growing rabbits: Effects on metabolism and growth. Ann. Agric. Sci. 2017, 62.
12. Wehbe, R.; Frangieh, J.; Rima, M.; El Obeid, D.; Sabatier, J.M.; Fajloun, Z. Bee venom: Overview of main compounds and bioactivities for therapeutic interests. Molecules 2019, 24, 2997.
13. Alvarez-Suarez, J.M. Bee Products—Chemical and Biological Properties; Springer: Berlin/Heidelberg, Germany, 2017; ISBN 9783319596891.
14. Hashem, N.M.; El-Hady, A.A.; Hassan, O. Effect of vitamin E or propolis supplementation on semen quality, oxidative status and hemato-biochemical changes of rabbit bucks during hot season. Livest. Sci. 2013, 157, 520–526.
15. Maghsoudlou, A.; Sadeghi Mahoonak, A.; Mohebodini, H.; Toldra, F. Royal jelly: Chemistry, storage and bioactivities. J. Apic. Sci. 2019, 63, 17–40.
16. Hashem, N.; Gonzalez-Bulnes, A.; Simal-Gandara, J. Polyphenols in Farm Animals: Source of Reproductive Gain or Waste? Antioxidants 2020.
17. Hashem, N.M.; El-Azrak, K.M.; Nour El-Din, A.N.M.; Sallam, S.M.; Taha, T.A.; Salem, M.H. Effects of Trifolium alexandrinum phytoestrogens on oestrous behaviour, ovarian activity and reproductive performance of ewes during the non-breeding season. Anim. Reprod. Sci. 2018.
18. Hashem, N.M.; El-Azrak, K.M.; Sallam, S.M.A. Hormonal concentrations and reproductive performance of Holstein heifers fed Trifolium alexandrinum as a phytoestrogenic roughage. Anim. Reprod. Sci. 2016, 170.
19. Sawczuk, R.; Karpinska, J.; Miltyk, W. What do we need to know about drone brood homogenate and what is known. J. Ethnopharmacol. 2019, 245.
20. Silici, S. Chemical Content and Bioactive Properties of Drone Larvae (Apilarnil). Mellifera 2019, 19, 14–22.
21. Hosny, N.S.; Hashem, N.M.; Morsy, A.S.; Abo-Elezz, Z.R. Effects of organic selenium on the physiological response, blood metabolites, redox status, semen quality, and fertility of rabbit bucks kept under natural heat stress conditions. Front. Vet. Sci. 2020, 7, 290.

22. Abdul-Ghani, A.S.; Dabdoub, N.; Muhammad, R.; Abdul-Ghani, R.; Qazzaz, M. Effect of Palestinian honey on spermatogenesis in rats. J. Med. Food 2008, 11, 799–802.
23. Mohamed, M.; Sulaiman, S.A.; Jaafar, H.; Sirajudeen, K.N.S. Effect of different doses of Malaysian honey on reproductive parameters in adult male rats. Andrologia 2012, 44, 182–186.
24. Syazana, N.S.; Hashida, N.H.; Majid, A.M.; Durriyyah Sharifah, H.A.; Kamaruddin, M.Y. Effects of Gelam honey on sperm quality and testis of rat. Sains Malaysiana 2011, 40, 1243–1246.
25. Igbokwe, V.U.; Samuel, O. Pure Honey Potent Fertility Booster: Activities of Honey on Sperm. IOSR J. Dent. Med. Sci. 2013, 9, 43–47.
26. Meo, S.A.; Al-Asiri, S.A.; Mahesar, A.L.; Ansari, M.J. Role of honey in modern medicine. Saudi J. Biol. Sci. 2017, 24, 975–978.
27. Banihani, S.A. Mechanisms of honey on testosterone levels. Heliyon 2019, 5, e02029.
28. Handayani, N.; Gofur, A. Does propolis extract alleviate male reproductive performance through gonadotropic hormone levels and sperm quality? IOP Conf. Ser. Earth Environ. Sci. 2019, 276.
29. De Moraes, G.V.; Mataveli, M.; de Moura, L.P.P.; Scapinello, C.; Mora, F.; Osmari, M.P. Inclusion of propolis in rabbit diets and semen characteristics. Arq. Ciências Veterinárias Zool. UNIPAR 2015, 17, 227–231.
30. Gabr, S. Effect of oral administration of rabbit bucks with egyptian propolis during summer, in Egypt. Egypt. J. Rabbit Sci. 2013, 23, 161–178.
31. El-Sherbiny, A. Effect of some bee products on reproductive phenomena of male New Zealand white rabbits. Egypt. J. Rabbit Sci. 2015, 25, 119–136.
32. Capucho, C.; Sette, R.; de Souza Predes, F.; de Castro Monteiro, J.; Pigoso, A.A.; Barbieri, R.; Dolder, M.A.H.; Severi-Aguiar, G.D.C. Green Brazilian propolis effects on sperm count and epididymis morphology and oxidative stress. Food Chem. Toxicol. 2012, 50, 3956–3962.
33. Hassan, A.A. Effect of royal jelly on sexual efficiency in adult male rats. Iraqi J. Vet. Sci. 2009, 23, 155–160.
34. Shi, Z.; Enayatullah, H.; Lv, Z.; Dai, H.; Wei, Q.; Shen, L.; Karwand, B.; Shi, F. Freeze-dried royal jelly proteins enhanced the testicular development and spermatogenesis in pubescent male mice. Animals 2019, 9.
35. El-Hanoun, A.M.; Elkomy, A.E.; Fares, W.A.; Shahien, E.H. Impact of royal jelly to improve reproductive performance of male rabits under hot sumer conditions. World Rabbit Sci. 2014, 22, 241–248.
36. Khadr, A.; Abdou, A.; El-Sherbiny, A. Age of puberty and fertility of male new zealand white rabbits orally administered with royal jelly or/ and bee honey. J. Anim. Poult. Prod. 2015, 6, 201–217.
37. Shoinbayeva, K.B.; Omirzak, T.; Bigara, T.; Abubakirova, A.; Dauylbay, A. Biologically active preparation and reproductive function of stud rams. Asian J. Pharm. 2017, 11, 184–191.
38. Bolatovna, K.S.; Rustenov, A.; Eleuqalieva, N.; Omirzak, T.; Akhanov, U.K. Improving reproductive qualities of pigs using the drone brood homogenate. Biol. Med. 2015, 7, 2.
39. El-Hanoun, A.; El-Komy, A.; El-Sabrout, K.; Abdella, M. Effect of bee venom on reproductive performance and immune response of male rabbits. Physiol. Behav. 2020, 223, 112987.
40. Attia, Y.A.; Al-Hanoun, A.; Bovera, F. Effect of different levels of bee pollen on performance and blood profile of New Zealand White bucks and growth performance of their offspring during summer and winter months. J. Anim. Physiol. Anim. Nutr. 2011, 95, 17–26.
41. Rizk, S.M.; Zaki, H.F.; Mina, M.A.M. Propolis attenuates doxorubicin-induced testicular toxicity in rats. Food Chem. Toxicol. 2014, 67, 176–186.
42. Yousef, M.I.; Kamel, K.I.; Hassan, M.S.; El-Morsy, A.M.A. Protective role of propolis against reproductive toxicity of triphenyltin in male rabbits. Food Chem. Toxicol. 2010, 48, 1846–1852.
43. Guo, H.; Ekusa, A.; Iwai, K.; Yonekura, M.; Takahata, Y.; Morimatsu, F. Royal jelly peptides inhibit lipid peroxidation in vitro and in vivo. J. Nutr. Sci. Vitaminol. (Tokyo) 2008, 54, 191–195.
44. Zaid, S.S.M.; Sulaiman, S.A.; Sirajudeen, K.N.M.; Othman, N.H. The effects of tualang honey on female reproductive organs, tibia bone and hormonal profile in ovariectomised rats—Animal model for menopause. BMC Complement. Altern. Med. 2010, 10, 82.
45. Hamid, N.A.; Bakar, A.B.A.; Zain, A.A.M.; Hussain, N.H.N.; Othman, Z.A.; Zakaria, Z.; Mohamed, M. Composition of Royal Jelly (RJ) and its anti-androgenic effect on reproductive parameters in a polycystic ovarian syndrome (PCOS) animal model. Antioxidants 2020, 9, 499.

46. Husein, M.Q.; Haddad, S.G. A new approach to enhance reproductive performance in sheep using royal jelly in comparison with equine chorionic gonadotropin. Anim. Reprod. Sci. 2006, 93, 24–33.
47. Gimenez-Diaz, C. Improved reproductive response of sheep in intrauterine insemination program with the use of royal jelly. Afr. J. Biotechnol. 2012, 11, 12518–12521.
48. Husein, M.Q.; Kridli, R.T. Reproductive responses following royal jelly treatment administered orally or intramuscularly into progesterone-treated Awassi ewes. Anim. Reprod. Sci. 2002, 74, 45–53.
49. Kridli, R.T.; Husein, M.Q.; Humphrey, W.D. Effect of royal jelly and GnRH on the estrus synchronization and pregnancy rate in ewes using intravaginal sponges. Small Rumin. Res. 2003, 49, 25–30.
50. Ghanbari, E.; Khazaei, M.R.; Khazaei, M.; Nejati, V. Royal jelly promotes ovarian follicles growth and increases steroid hormones in immature rats. Int. J. Fertil. Steril. 2018, 11, 263–269.
51. Attia, Y.A.; Bovera, F.; Abd Elhamid, A.E.H.; Nagadi, S.A.; Mandour, M.A.; Hassan, S.S. Bee pollen and propolis as dietary supplements for rabbit: Effect on reproductive performance of does and on immunological response of does and their offspring. J. Anim. Physiol. Anim. Nutr. 2019, 103, 959–968.
52. Attia, Y.; Bovera, F.; El-Tahawy, W.; El-Hanoun, A.; Al-Harthi, M.; Habiba, H.I. Productive and reproductive performance of rabbits does as affected by bee pollen and/or propolis, inulin and/or mannan-oligosaccharides. World Rabbit Sci. 2015, 23, 273–282.
53. Kolesarova, A.; Bakova, Z.; Capcarova, M.; Galik, B.; Juracek, M.; Simko, M.; Toman, R.; Sirotkin, A.V. Consumption of bee pollen affects rat ovarian functions. J. Anim. Physiol. Anim. Nutr. 2013, 97, 1059–1065.
54. Attia, Y.A.; Al-Hanoun, A.; Tag El-Din, A.E.; Bovera, F.; Shewika, Y.E. Effect of bee pollen levels on productive, reproductive and blood traits of NZW rabbits. J. Anim. Physiol. Anim. Nutr. 2011, 95, 294–303.
55. Kridli, R.T.; Al-Khetib, S.S. Reproductive responses in ewes treated with eCG or increasing doses of royal jelly. Anim. Reprod. Sci. 2006, 92, 75–85.
56. Adriana, K.; Capcarova, M.; Bakova, Z.; Branislav, G.; Miroslav, J.; Milan, S.; Sirotkin, A.V. The effect of bee pollen on secretion activity, markers of proliferation and apoptosis of porcine ovarian granulosa cells in vitro. J. Environ. Sci. Heal. Part B Pestic. Food Contam. Agric. Wastes 2011, 46, 207–212.
57. Abdelhafiz, A.T.; Muhamad, J.A. Midcycle pericoital intravaginal bee honey and royal jelly for male factor infertility. Int. J. Gynecol. Obstet. 2008, 101, 146–149.
