Bee-Products in Male Reproductive Impairment

Subjects: Chemistry, Medicinal

Contributor: Joseph Suleiman

Bee products are sources of functional food that have been used in complementary medicine to treat a variety of acute and chronic illnesses in many parts of the world. The products vary from location to location as well as country to country.

Keywords: bee products ; preventive ; therapeutic ; male reproductive impairment

1. Introduction

Honeybees produce various products containing many biochemical components such as minerals, vitamins, and polyphenols, which are biologically active [1]. These compounds have served as preventive and therapeutic agents in the last four decades and have been used in apitherapy [2]. Bee products are used for the treatment of some conditions such as multiple sclerosis, arthritis, wounds, pain, gout, shingles, burns, tendonitis, and infections [3]. Therefore, apitherapy being a simple, convenient, and available method is practiced in traditional self-heath care and also holds promise for the treatment of periodontal diseases, mouth ulcers, and other diseases of the oral cavity as well [4]. The bee products include bee venom, honey, pollen, royal jelly, propolis, bee bread, bee brood, and beeswax, which are produced by four types of insects: honeybees (Apis), stingless bees, honey wasps, and honey ants [5]. Usually, honey bees are of four species, namely *A. mellifera*, *A. cerana*, *A. dorsata*, and *A. florea*.

Honey is a light or dark amber liquid formed by bees from the nectar of flowers [6], while propolis is a sticky, greenish–brown product used as a coating to build their hives. The royal jelly is a milky substance that contains water, proteins, sugar, fats, vitamins, salts, and amino acids. Similarly, bee pollen is a pellet from flower pollen gathered by worker honeybees and used as the nutritional sources for the beehive. Additionally, bee venom is an acidic colorless liquid made up of enzymes, sugars, minerals, and amino acid, beeswax is a mixture of pollen oils and wax to form a yellow or brown color, while bee bread is a mixture of pollen and nectar or honey [7][8][9][10][11].

Meanwhile, nowadays, there are many studies investigating the potential protective and therapeutic roles of these bee products in health, including male infertility [12][13][14][15]. The World Health Organization guidelines revealed that 15–25% of couples struggle to conceive, and approximately half of these cases are caused by infertility in males due to alteration in sperm concentration, motility, and/or morphology, which is present in samples collected [16]. Several mechanisms have also been identified as possible cause(s) of infertility, which include defects in the steroidogenic pathway, the imbalance in the pro and antioxidant activity, the irregularities in the apoptotic pathway, the imbalance of the pro and anti-inflammatory markers, and the generation of the reactive oxygen species.

2. Role of Bee Products in Male Reproductive Impairment

There are a lot of studies of bee products used in ameliorating male reproductive impairment. Table 1, Table 2, Table 3, Table 4, Table 5 and Table 6 show the summary of various effects of bee products on the male reproductive system in various animal models and human.

2.1. Effects of Bee Pollen on Male Reproductive Parameters

The administration of 100 mg/kg bw/day of bee pollen on streptozotocin (STZ)-induced diabetic rats for 4 weeks caused significant increases in testis weight, testosterone, LH, and FSH as well as sperm count, motility, and viability, which is suggested partly by scavenging toxic and mutagenic electrophiles and free radicals/modification of antioxidant pathways due to the presence of flavonoids [12]. Algerian bee pollen (100 mg/kg bw) administered for 15 days showed an increase in spermatogenesis and a decline in Sertoli cells destruction by lowering lipids, and it also showed anti-inflammatory and protective effects against testis cell injury due to the potentiated synthesis of proteins. Similarly, 60 mg/animal/day of Turkish bee pollen over a 30-day period showed increases in testosterone level and sperm counts in a rats model via its antioxidant activity [17].

Furthermore, the Indian bee pollen of 100 mg/kg/bw caused a decrease in MDA levels, while there were increases in SOD, GR, GPx, GST, CAT, and GSH in rifampicin and isoniazid-induced toxicity in rats through its antioxidant activity. In addition, lead-induced rats treated with 100 mg/kg bw of Algerian bee pollen showed an increase in spermatogenesis and a decline in the destruction of Sertoli cells (Table 1).

Table 1. Effects of bee products on male reproductive parameters.

s/n	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Bee pollen (Egypt)	100 mg/kg bw/day for 4 weeks	Streptozotocin (STZ)-injection (single dose)	Rats	i.p	-	↑ Testis weight, testosterone, LH, FSH, sperm count, motility and viability, ↓ MDA, ↑ (SOD, GR, GPx, GST, CAT, and GSH)	Act by scavenging toxic and mutagenic electrophiles and free radicals/modification of antioxidant pathways due to presence of flavonoids	[12]
2.	Bee pollen (India)	100 mg/kg bw	Rifampicin 100 mg/kg bw/day and isoniazid 50 mg/kg bw/day	Rats	Oral	-	↓ MDA, ↑ (SOD, GR, GPx, GST, CAT, and GSH)	Presence of bioactive elements (caffeic acid phenethyl ester, myricetin, kaempherol, isoquercetin, and flavonoids) convert the reactive free radicals to inactive products	[18]
3.	Bee pollen (Algeria)	100 mg/kg bw for 15 days	30 mg mg/kg bw of lead acetate	Rats	Oral	-	↑ Spermatogenesis and ↓ Sertoli cells destruction	Acts by lowering lipid, anti-inflammatory, and protective effect against testis cell injury due to potentiated synthesis of proteins	[19]
4.	Bee pollen (Turkey)	60 mg/per animal (30-day)		Rats	Oral		↑ Testosterone level and sperm counts	Beneficial effects	[17]

2.2. Effects of Bee Venom on Male Reproductive Parameters

Few studies have been reported on the effects of bee venom on the testicular damage; Egyptian bee venom at doses of 0.1, 0.2, and 0.3 mg/rabbit twice weekly administered over 20 weeks showed increases in TAC, GST, GSH, testosterone spermatogenesis, and fertility. These may be due to the stimulation of the pituitary gland to release the adrenocorticotropic hormone, which causes release of the sex hormones such as testosterone in blood circulation, which have significant effects on spermatogenesis and fertility [20]. In a related study carried out in mice treated with Iraqi bee sting, it provided protection and the maintenance of some sexual efficiency parameters via its ability to release cortisol that inhibits Sertoli cells from releasing activin-B, which normally stimulates spermatogonia to induce mitosis to form spermatocytes [10] (Table 2).

Table 2. Effects of bee venom and bee wax on male reproductive parameters.

/n	Bee Products	Dose/Duration of Treatment	Substance used to Induce Stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Bee Venom (Egypt)	0.1 (G1), 0.2 (G2) and 0.3 (G3) mg/rabbit twice weekly over 20 wks	High temperature	Rabbits	Intravenous injection	-	↑ TAC, GST, GSH, IgA, IgM, Testosterone, spermatogenesis and fertility	These effects could be attributed to pituitary gland stimulation to release the adrenocorticotropic hormone, which causes release of the sex hormones such as testosterone in blood circulation, which has significant effects on spermatogenesis and fertility	[20]
2.	Bee Venom (Iraq)	155 stings	hydrogen peroxide	Mice	Stings	-	Protection and maintenance of some sexual efficiency parameters	Cortisol inhibits Sertoli cells from releasing activin-B, which normally stimulates spermatogonia to induce mitosis to form spermatocytes	[10]
3.	Bee venom (Romania)	700 µg BV/kg		Rats	Injection	-	↓ Testicular weight and Sertoli cells, ↑diameter in seminiferous tubules	Mellitin interacts with the proteins in tight junctions between the adjacent Sertoli cells	[13]
4.	Bee wax (USA)	15 mg bees wax pellet containing 3.0 mg		Mice	Injection	-	Differential testicular response to photoperiod	Post-pineal mechanism	[21]

2.3. Effects of Honey on Male Reproductive Parameters

Studies carried out in Nigeria revealed that 100, 200, and 400 mg/kg of honey administered on rats and 2.5, 5, and 7.5 mg/kg of testosterone i.p. showed increases in sperm count; this might be due to the fact that chrysin (5,7-dihydroxyflavone) blocked the conversion of androgens into estrogens with a consequent increase in testosterone [22]. On the other hand, 70 g of Iranian honey supplementation administered on humans for 8 weeks showed significantly less elevation in seminal IL-1β, IL-6, IL-8, TNF-α, ROS, and MDA levels and increases in seminal SOD, catalase, and TAC concentrations through its antioxidant, anti-inflammatory, and anti-apoptotic properties due to the presence of phenols and flavanoids [23]. Similarly, 1.0 mL/100 g body weight of honey administered in nicotine-induced old rats showed increases in the fertility of juvenile male rats by increasing sperm motility and the number of morphologically normal sperm; however, the exact mechanisms require further study [24].

In addition, 0.05 mL of honey administered for 4 weeks showed diminished degenerative changes of seminiferous tubules and increased plasma levels of testosterone significantly in CCL-induced rats via reduction of the elevated levels of free radicals and an increased antioxidant defense system [25]. Furthermore, rats treated with 1.0 mL/100 g of Egyptian honey for 60 days showed significant increases in sperm count and the number of sperm with normal morphology, the honey acted as a physiologic modulator of spermatogenic cells proliferation, which influence the cell cycle of the seminiferous epithelium; thereby, it increases spermatogenesis [14]. Similarly, studies carried out in Iran by Hadi and Mohammed [26][27] revealed that 10% of honey (1 mL of honey and 9 mL of IVF culture medium) with doses of 1.2 and 1.8 g/kg bw enhances sperm motility, increases testosterone, FSH, and LH hormones as well as diameters of seminiferous tubules; this might be a result of the antioxidant properties of honey.

Conversely, 1.2 g/kg of Malaysian honey showed increases in the percentages of rats achieving intromission, ejaculation, mating, and fertility indexes as well as increases in testis, epididymis weights, percentages of abnormal spermatozoa, and sperm motility; in this case, the mechanism through which honey acts is by its counteraction on oxidative stress within penile tissues via its antioxidant property due to the possession of phenols [28][29].

Likewise, 0.2, 1.2, and 2.4 g/kg^{-1} of Malaysian honey administered for 4 weeks in rats revealed increases in epididymal sperm count without affecting spermatid count and reproductive hormones [30][31]. Furthermore, 1, 2, and 2.5 mL of

Nigerian honey administered to rats for 21 days improved the sperm quality and spermatogenesis rate, and there was no sign of degeneration or cellular loss in the testicular histoarchitecture. It is imperative to note that the presence of zinc in honey and its accumulation in the testis during early spermatogenesis may be important in DNA synthesis and regulate spematogonial proliferation [32]. In other similar studies, 1 mL/100 g of bw of Nigerian honey administered for 65 days increases the sperm count and sperm motility, and it also improves the sperm morphology through the reduction of lipid peroxidation and oxidative stress on the sperm cells by reactive oxygen species such as superoxide and hydrogen peroxide. The authors of [33][34][35] revealed that rats treated with 100 mg/kg bw of Nigerian honey for 35 days had improvements in sperm motility, viability, morphology, counts, FSH, LH, and testosterone. The rats treated with 5% Palestinian honey for 20 days induced spermatogenesis in rats by increasing epididymal sperm count, relative weight of the epididymis, SDH activity, and reducing LDH activity; however, the mechanisms require further study [36].

Saudi Arabian honey (20 mg/kg bw/day) ameliorates octylphenol toxic effects and reduces the histopathological stress toxicity on the testis in rats; also, the combined administration of honey and royal jelly reduces sperm abnormality and chromosomal aberrations as well as ameliorates GSH and MDA in cyclophosphamide toxicity in mice; therefore, the presence of CAPE served as a protective agent against chemotherapy-induced oxidative stress [9][37]. The honey drone milk is a product that is secreted by honey bees through their hypopharyngeal and mandibular glands; thus, the Hungarian honey drone milk (110 mg/kg/day) increases the relative weights of the androgen-dependent organs and the plasma testosterone level in castrated rats and then increases the tissue mRNA and protein level of SLAP (Spot14-like androgen-inducible protein). This was done through the scavenging of free radicals by polyphenols before they can interact with DNA [38], while 70 g of honey supplement administered to humans for 8 weeks in Iran increases seminal IL-1b, IL-6, IL-8, TNF-α, ROS, and MDA levels and significantly decreases the levels of seminal SOD, catalase. Kelulut honey 2.0 g/kg weight administered 28 days to diabetic rats revealed significant increases in SOD activity and GSH level as well as significant decreases in protein carbonyl and MDA levels in sperm and testis, whereas the histology of the epididymis showed a decrease in spermatozoa and spermatogenic cells density in the testis of the diabetic group [11] (Table 3).

Table 3. Effects of honey on male reproductive parameters.

s/*n*	Bee Products	Dose/Duration of Treatment	Substance used to Induce stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Honey (Nigeria)	100, 200, and 400 mg/kg	-	Rat	Oral	2.5, 5, and 7.5 mg/kg of testosterone i.p	↑ Sperm count	Chrysin (5,7-dihydroxyflavone) blocked the conversion of androgens into oestrogens with a consequent increase in testosterone	[22]
2.	Honey (Egypt)	0.05 mL (4 weeks)	5 mL/kg of 0.3% CCL 4 daily subcutaneously (4 Weeks)	Mice	Oral	-	↓ Degenerative changes of seminiferous tubules and ↑ plasma levels of testosterone significantly	Via reduction of the elevated levels of free radicals and increase in the antioxidant defense system	[25]
3.	Honey (Malaysia gelam honey)	1.0 mL/100 g (60 days)	-	Rats	Oral	-	↑ Sperm count and number of sperm with normal morphology	Acts as a physiologic modulator of spermatogenic cells proliferation, which influence the cell cycle of the seminiferous epithelium thus, ↑ spermatogenesis	[14]

s/n	Bee Products	Dose/Duration of Treatment	Substance used to Induce stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
4.	Honey (Malaysia)	1.2 g/kg bw/daily	Cigarette 8 min 3 times/day	Rats	Oral	-	↑ Intromission and ejaculation, mating, and fertility indexes	Acts as a physiologic modulator of spermatogenic cells proliferation, which influence the cell cycle of the seminiferous epithelium and thus increase spermatogenesis	[29]
5.	Honey (Malaysia)	1.2 g kg^{-1} bw daily (21 days)	Prenatal restraint stress (three times per day) from day 11 of pregnancy until delivery	Rats	Oral	-	↑ Testis and epididymis weights as well as improved the percentages of abnormal spermatozoa and sperm motility	Acts partly by its counteraction on oxidative stress within penile tissues via its antioxidant property	[28]
6.	Honey (Malaysian honey)	0.2, 1.2, and 2.4 g kg^{-1} (4 weeks)	-	Rats	Oral	-	↑ Epididymal sperm count without affecting spermatid count and reproductive hormones	Due to its one or more constituents that could protect germ cells against oxidative stress. This might have further enhanced spermiogenesis	[30]
7.	Honey (Nigeria)	1, 2, and 2.5 mL of honey daily for 21 days	-	Rats	Oral	0.3 mL FSH drug for 6 days	Improves the sperm quality and spermatogenesis rate and no sign of degeneration or cellular loss in the testicular histoarchitecture	Suggestive of zinc accumulating in the testis during early spermatogenesis, and important in DNA synthesis and the regulation of spematogonial proliferation	[32]
8.	Honey (Nigeria)	1 mL of honey per 100 g of bw (65 days)	-	Rat	Oral	Manix capsules (6220 mg/100 mL of drug solution)	↑ Sperm count, sperm motility, and improves sperm morphology	↓ Lipid peroxidation and oxidative stress on the sperm cells by reactive oxygen species such as super oxide, hydrogen peroxide	[34]
9.	Honey (Nigeria)	(100 mg/kg bw) (35 days)	Nicotine (1.0 mg/kg bwt)	Rats	Oral	-	↑ Sperm motility, viability, morphology, counts, FSH, LH, and testosterone	Mediated by its counteraction on oxidative stress	[35]
10.	Honey supplements (Iran)	70 g (8 weeks)	8 weeks of intensive cycling training	Humans	Oral	-	↓ Seminal interleukin (IL)- 1 b, IL-6, IL-8, tumor necrosis factor (TNF)-α, ROS, MDA, ↑ Levels of seminal SOD and catalase	↓ Seminal plasma cytokines and oxidative stress biomarkers as well as increasing seminal antioxidant levels	[23]

s/n	Bee Products	Dose/Duration of Treatment	Substance used to Induce stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
11.	Honey (Palestinian Honey)	5% honey for 20 days	-	Rats	Oral	-	Induces spermatogenesis in rats by ↑ epididymal sperm count, relative weight of the epididymis, SDH activity, and ↓ LDH activity	Needs further experiments to establish mechanism	[36]
12.	Honey (Saudi Arabia)	20 mg/kg body weight/day) orally daily for 4 weeks	Octylphenol (0.1 and 1.0 mg kg−1 bw)	Rats	Oral	-	Ameliorates toxic effects and ↓ histopathological stress toxicity	Further studies required	[9]
13.	Honey (Taulang) (Malaysia)	0.4 mL/100 g/kg/day of honey for 28 days	-	Rats	Oral	-	↑ Sperm counts significantly	Further studies required	[31]
14.	Honey bee and pollen grains (Saudi Arabia)	(1 g/kg) 2 weeks	Cyclophosphamide (10 mg/kg) i.p	Mice	Oral	-	Sperm abnormality, chromosomal aberrations, ameliorates GSH activity	Presence of CAPE as protective agent against chemotherapy-induced oxidative stress	[37]
15.	Honeybee Drone milk (Bulgaria)	110 mg/kg/day	-	Castrated Rats	Oral	-	↑ Relative weights of the androgen-dependent organs and the plasma testosterone level in castrated rats and tissue mRNA and protein level to SLAP	Scavenging of free radicals by polyphenols before free radicals can interact with DNA	[38]
16.	Honey (Iran)	10% of honey	-	Mice	IVF	-	Enhances sperm motility and pregnancy rate of female mice	Antioxidant activity	[26]
17.	Honey (Gelam) (Malaysia)	2.0 mL/100 g bw	Nicotine (N) group were intraperitoneally (i.p.) injected with 5.0 mg/kg	Rats (4–5 weeks old)	Intra peritoneal	-	↑ Fertility of female mice rats by increasing sperm motility and number of morphologically normal sperm	Further study required	[24]

2.4. Effects of Propolis on Male Reproductive Parameters

Iraqi propolis of 200 mg/kg bw decreases the sperm concentration, sperm motility, rate of viability, and normal sperms as well as decreases the weights of testes, epididymis, prostate gland, seminal vesicles, serum testosterone, FSH, and LH levels with a significant increase in sperm abnormalities in acrylamide-induced toxicity in rats through the antioxidative effectiveness of propolis mainly by its flavonoids and phenolic content [39]. Egyptian propolis extract (50 mg/kg bw) decreases LPO levels, normalizes CAT, SOD, GPx, and GST activities, while GSH content was increased in testicular tissue in chlorpyrifos-induced toxicity in rats. The protective effect can be due to scavenging MDA molecules by propolis active ingredients or inhibition of mitochondrial and cytosolic lipoperoxidation chain reactions [40]. Egyptian propolis of 200 mg/kg b.w. for 3 weeks decreases testicular oxidative stress, inflammatory, and apoptotic markers in doxorubicin-induced toxicity in rats due to its possession of phenolic compounds [15]. Egyptian propolis (50 mg/kg bw/day extract decreases dead and abnormal sperm and TBARS, and it increases testosterone, GSH, 17-ketosteroid reductase, CAT, and GST in aluminum chloride-induced toxicity in rats through its antioxidant properties [41].

Turkish propolis (100 mg/kg/day) prevented the rise in malondialdehyde, xanthine oxidase levels, and HSP-70 expression and improved testicular morphology and JTBS in methotrexate-induced toxicity in rats through scavenging free radicals and thereby protected against lipid peroxidation [42]. Similarly, the combination of Turkish propolis (200 mg/kg/days, gavage) and pollen (100 mg/kg/days, by gavage) decreases levels of TOS, NF-κB, and MDA using L-NAME (40 mg/kg, i.p.) for induction of hypertension in rats; this was done by inhibiting the functioning of inflammatory pathways [43]. The in vitro study carried out by [44] shows that Chilean propolis protects sperm membrane from the deleterious action of oxidative attack, reducing TBARS formation and LDH release by exhibiting a strong antioxidant activity of propolis. Similarly, 1 uL of Czech Republican propolis maintains sperm motility and improves the total mitochondrial respiratory efficiency in human spermatozoa through its antioxidant properties [45]. Egyptian propolis (50 mg/kg bw/day) improves the structure of seminiferous tubules, and their lumens were full of bundles of sperms. In addition, all the parameters of seminiferous tubules and total numbers of Sertoli cells, round spermatids, daily sperm production, and Leydig cells were ameliorated through decreases in the levels of free radicals and lactate dehydrogenase as a result of the presence of flavonoids [46]. Egyptian propolis administered to rabbits at 100, 200, and 300 mg/kg bw/day, respectively for two weeks (one week before and after mating) for five consecutive times shows that the bunnies belong to rabbits treated with bee propolis which shows the best improvement for all the studied traits due its antioxidant nutrients, including vitamins, minerals, phenolic constituents, and enzymes [47].

Egyptian propolis (50 mg/kg bw) revealed significant decreases in CAT, SOD, GPx, and GST in chlorpyrifos-induced toxicity [40]. Rats treated with 3, 6, and 10 mg/kg/day of green Brazallian propolis show higher sperm production and greater epithelium height of the epididymis initial segment and no induction of oxidative stress, and the exact mechanism is still under investigation [48]. The co-administration of Turkish propolis (200 mg/kg/days, gavage) and pollen (100 mg/kg/days, by gavage) that lasted 14 of 28 days showed decreases in TOS, NF-κB, MDA, TAS levels, PON1, and CAT activities in testis tissue; it acted through its protective effect of antioxidant mechanisms [43]. Furthermore, Malaysian propolis (300 mg/kg bw) administered on streptozotocin-induced rats caused increases in testosterone level, steroidogenic, and sperm parameters by increasing penile cGMP and serum testosterone levels due to the presence of phenols [49] (Table 4).

Table 4. Effects of propolis on male reproductive parameters.

s/n	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Propolis (Iraq)	200 mg/kg bw (4 weeks)	Acrylamide (150 mg/kg BW)	Rats	Oral	-	↓ Sperm concentration, sperm motility, rate of viability, normal sperms, weights of testes, epididymis, prostate gland, seminal vesicles, serum testosterone, FSH, LH levels with significant ↑ sperm abnormalities	Anti-oxidative effectiveness of propolis mainly via its flavonoids and phenolic content	[39]
2.	Propolis (Egypt)	50 mg/kg bw extract (70 days)	Chlorpyrifos (9 mg/kg) (insecticide)		Oral	-	↓ LPO level, normalized CAT, SOD, GPx, and GST activities, ↑ GSH content in testicular tissue	Protective effect can be due to scavenging MDA molecules by propolis active ingredients or inhibition of mitochondrial and cytosolic lipoperoxidation chain reactions	[40]
3.	Propolis (Egypt)	Propolis extract (200 mg kg 1; p.o.) for 3 weeks	Doxorubicin 18 mg kg 1 total cumulative dose of Dox i.p.	Rats	Intraperitoneal	-	↓ Testicular oxidative stress, inflammatory and apoptotic markers	Tumor necrosis factor-related apoptosis inducing ligand via phenolic compounds	[15]
4.	Propolis (Egypt)	50 mg propolis/kg bw/day	Aluminium chloride 34 mg $AlCl_3$/kg bw (70 days)	Rats	Oral	-	↓ Dead and abnormal sperm and TBARS, and ↑ testosterone, GSH, 17-ketosteroid reductase, CAT, and GST	Antioxidant property of propolis	[41]
5.	Propolis (Turkey)	100 mg/kg/day (oral gavage) (15 days)	Methotrexate (20 mg/kg)	Rats	Oral	-	↓ Malondialdehyde, xanthine oxidase levels, and HSP-70 expression and improves testicular morphology and JTBS	Scavenging free radicals and thereby protection against lipid peroxidation	[42]
6.	Propolis (Balikesir, Turkey)	Propolis (200 mg/kg/days, gavage) and pollen (100 mg/kg/days	L-NAME (40 mg/kg, i.p.) for induction of hypertension	Rats	Oral	-	↓ Levels of TOS, NF-κB, and MDA	Inhibiting the functioning of inflammatory pathways	[43]
7.	Propolis (Chilean propolis)	-	benzo[a]pyrene, hydrogen peroxide (H_2O_2) and hydrogen peroxide in combination with adenosine 5 V-diphosphate (ADP) and ferrous sulfate ($FeSO_4$)	Human spermatozoa	In vitro	-	Protects sperm membrane from the deleterious action of oxidative attack, reducing TBARS formation and LDH release	Exhibited a strong antioxidant activity	[44]

s/*n*	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
8.	Propolis (Czech Republic)	(1 uL) 10 participants		Human spermatozoa (0.1 mL of fresh ejaculate)	In vitro	-	Maintains sperm motility and improves the total mitochondrial respiratory efficiency	Antioxidant property	[45]
9.	Propolis (Egypt)	50 mg/kg bw/day	-	Rats	Oral	Intraperitoneal injection of genta micin (5 mg/kg bw/day)	Improves structure of seminiferous tubules and ↑ daily sperm production	↓ Level of free radicals and lactate dehydrogenase	[46]
10.	Propolis (Egypt)	100, 200, and 300 mg/kg bw/day, respectively for two weeks (one week before and after mating) for five consecutive times	-	New Zealand White (NZW) rabbit		-	Improves all studied traits	Substantial levels of antioxidant nutrients, including vitamins, minerals, phenolic constituents, and enzymes	[47]
11.	Propolis (green brazallian propolis)	3, 6, and 10 mg/kg/day (56 days)	-	Rats	Oral	-	↑ Sperm production and greater epithelium height of the epididymis initial segment and no induction of oxidative stress	Mechanism still under investigation	[48]
12.	Propolis (Egypt)	50 mg kg/bw (4 weeks)	Paclitaxel 5 mg/kg/bw	Rats	Oral	-	↑ Sperm count, motility, viability, and sperm morphology	Scavenging the free radicals and enhancing the antioxidant activities	[8]
13.	Propolis (India)	400 mg/kg bw (5 days a week for 8 weeks)	Mitomycin C (2, 4, and 8 mg/kg bodyweight single dose) (i.p)	Mice	Oral	-	↓ Oxidative stress and DNA damage, ↑ testicular testosterone and inhibin B	Strong antioxidant activity	[50]
14.	Propolis + bee pollen (Turkey)	Propolis (200 mg/kg/day) and pollen (100 mg/kg/day) the last 14 of 28 days	N(ω)-nitro-L-arginine methyl ester (L-NAME) (40 mg/kg, i.p.)	Rats	Oral		↓ TOS, NF-kB, MDA, TAS levels, PON1, and CAT activities in the testis tissue	Protective effect of antioxidant mechanisms against oxidative mechanisms on the reproductive system	[51]
15.	Propolis (Malaysia)	Propolis (300 mg/kg bw for 4 weeks	streptozotocin (50 mg/kg i.v.)	Rats	Oral	Metformin (300 mg/kg/day	↑Testosterone level, steroidogenic and sperm parameters	↑ In peptyl cGMP and serum testosterone levels due to presence of phenols	[49]

2.5. Effects of Royal Jelly on Male Reproductive Parameters

Egyptian bee honey (100 g) mixed with 3 g of royal jelly and 1 teaspoon of bee bread intravaginally in humans shows an increase in pregnancy rate due to increase in sperm capacitation through its antioxidant and scavenging activities against free oxygen species [51]. The administration of Egyptian royal jelly (1 g/kg bw) for 1 month increased the testicular weight and the body of epididymus, sperm count, testosterone hormone, and glutathione level, and it also caused a decrease in sperm deformity percentage, while there were no significant differences in the prostate weight, seminal vesicles, percentage of live sperm, malondialdehyde level, and body weight through the central effect of royal jelly because it contains acetylcholine [52] in hydrogen peroxide (0.5%) in drinking water induced rats. Meanwhile, 100 mg/kg of royal jelly causes a decrease in the toxic effect of cyclosporine in testis of rats due to its antioxidant property [53]. Egyptian royal jelly administered at 200, 400, or 800 mg/kg body weight once a week (6 weeks) significantly boosts testosterone level, ejaculated volume, and semen plasma fructose; improves sperm motility and sperm total output; reduces abnormal sperm and dead sperm due to the presence of vitamin C and amino acids; and increases spermatic concentration [54].

Turkish royal jelly (50 and 100 mg/kg) for 10 days decreases the malondialdehyde level and increases superoxide dismutase, catalase, and glutathione–peroxidase activities and increases the weights of testes, epididymis, seminal vesicles, and prostate along with epididymal sperm concentration and motility in cisplatin-induced in rats. Similarly, 50, 100, or 150 mg of Chinese royal jelly/kg twice per week, respectively, administered over a 20-week period shows a significant increase ($p < 0.05$) in rabbits' sperm concentration, total sperm output, sperm motility, live sperm, and normal sperm in rabbits; it was suggested that amino acids and vitamins might have played a role [55]. Egyptian royal jelly (0.4%) and heparin administered to buffalo induces sperm acrosome reaction but also is effective for the in vitro fertilizing capacity of the cryopreserved buffalo spermatozoa as a result of possessing motility stimulants such as adenosine and adenosine monophosphate [7].

Iranian royal jelly (100 mg/kg bw) increases testicular weight, sperm count, motility, viability, and serum testosterone levels and decreases observed sperm deformity, DNA integrity, chromatin quality, and tissue MDA levels in streptozotocin-induced diabetic rats. This might be because of its antioxidant properties due to the presence of vitamins E and C [56]. Similarly, bleomycin-induced rats treated with Iranian royal jelly (100 mg/kg/day) for 48 days improved sperm parameters and testosterone levels as well as decreased MDA levels due to its antioxidant properties [57]. On the other hand, Iranian

royal jelly of 0, 50, 100, and 150 mg/kg bw increases sperm and causes a significant upregulation of transcription factor E2f1 mRNA in taxol-induced toxicity [58]. Japanese royal jelly of 50 µg/g diet or 500 µg/g diet for 12 weeks increases the intensity of spermatogenesis and testosterone levels in hamsters via its antioxidant activity [59]. Japanese royal jelly (300 mg) administered for 6 months accelerates the conversion of DHEA-S to testosterone [60], while Turkish royal jelly of 400 mg/kg daily for 4 weeks caused caspase-3-positive cells to be significantly decreased in testicular apoptosis via its anti-apoptotic activity [61]. Twenty-eight adult Wistar rats administered with royal jelly (100 mg/kg bw) for 6 weeks showed increases in CAT and FRAP activities [62]. Rats induced with hydroxylurea (225 or 450 mg kg/bw/day) followed by administration of royal jelly (100 mg kg/bw/day) for 60 days revealed improved sperm quality, hormonal, and antioxidant status as well as histology architecture [63] (Table 5).

Table 5. Effects of royal jelly on male reproductive parameters.

s/*n*	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Royal jelly (Iraq)	1 g/kg bw (1 month)	hydrogen peroxide (0.5%) in drinking water		Oral	-	↑ Testicular weight and the body of epididymis, sperm count, testosterone hormone and glutathione levels; ↓ sperm deformity percentage, while there were no significant differences in the prostate weight, seminal vesicles, the percentage of live sperm, MDA level, and body weight	Central effect of royal jelly because it contains acetylcholine	[52]
2.	Royal jelly (Iraq)	100 mg/kg (5, 10, and 15 days	20, 40, and 60 m/kg cyclosporine A for 5, 10 and 15 days (i.p)	Rats	Oral	-	↓ Toxic effect	Antitumor, antioxidant	[53]
3.	Royal jelly (Egypt)	200, 400, or 800 mg royal jelly (RJ)/kg body weight once a week (6 weeks)	-	Rabbits	Oral	-	↑ Testosterone level, ejaculated volume, seminal plasma fructose, improves sperm motility, sperm total output, ↓ abnormal sperm, and dead sperm	Presence of vitamin C and amino acids have increased spermatic concentration	[54]
4.	Royal jelly (Turkey)	50 and 100 mg/kg (10 days)	Cisplatin (single dose of 7 mg/kg i.p)	Rats	Oral	-	↓ MDA level and ↑ SOD, catalase, and glutathione peroxidase activities and weights of testes, epididymides, seminal vesicles, and prostate along with epididymal sperm concentration and motility	Antioxidant property	[64]
5.	Royal jelly (Japan)	50 µg/g diet or 500 µg/g diet for 12 weeks	-	Hamsters	Oral (food)	-	↑ Intensity of spermatogenesis and testosterone levels	Inhibited the age-associated decline and testosterone-secreting cells	[59]

s/n	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
6.	Royal jelly (Turkey)	(400 mg/kg daily for 4 weeks)	a single intraperitoneal injection of STZ (60 mg/kg)	Rats	Oral	-	↓ Caspase-3-positive cells in testicular apoptosis	Estrogenic effect	[61]
7.	Royal jelly (Chinese)	50, 100, or 150 mg of Chinese royal jelly (RJ)/kg twice per week, respectively, over a 20-week period	temperatures ranging from 23 to 36 °C	Rabbits	Oral	-	↑ Sperm concentration, total sperm output, sperm motility, live sperm, and normal sperm	Amino acids and vitamins may play a role	[55]
8.	Royal jelly (Egypt)	100 g of Egyptian bee honey mixed with 3 g of royal jelly and 1 teaspoon of bee bread	Asthenozoospermia	Humans	Intravaginal	-	↑ Pregnancy rate due to ↑ in sperm capacitation	Antioxidant and scavenging activities against free oxygen species	[51]
9.	Royal jelly (Egypt)	0.4% royal jelly + heparin	-	Buffalo (Bubalus Bubalis)	IVF	-	Induces sperm acrosome reaction but also is effective for in vitro fertilizing capacity of the cryopreserved buffalo spermatozoa	Contain motility stimulants such as adenosine and adenosine monophosphate ((AMP) N (1)-oxide)	[7]
10.	Royal jelly (Iran)	100 mg/kg bw	Streptozotocin (STZ) 60 mg/kg body weight (BW) i.p	Rats	Oral	-	↑ Testicular weight, sperm count, motility, viability, and serum testosterone levels and ↑ sperm deformity, DNA integrity, chromatin quality, and tissue MDA levels	Antioxidant activity due to the presence of vitamins E and C	[56]
11.	Royal jelly (Japan)	300 mg (6 months)	-	Human voluntiers	Oral	-	Accelerates conversion from DHEA-S to testosterone	Antioxidant activity	[60]
13.	Royal jelly (Iran)	100 mg/kg daily (48 days)	Bleomycin group (BLG) received BL (10 mg/kg twice a week) with i.p for 48 days	Rats	Oral	-	Improves bleomycin-induced toxicity on sperm parameters, testosterone, and MDA concentrations	Antioxidant activity	[57]
14.	Royal jelly (Iran)	(0, 50, 100, and 150 mg/kg bw)	Taxol 7.5 mg/kg body weight (bw), weekly	Rats	Oral	-	↑ Sperm and significant upregulation of transcription factor E2f1 mRNA	Antioxidant activity	[58]

2.6. Effects of Bee Bread on Male Reproductive Parameters

The administration of 0.5 g/kg/bw Malaysian bee bread for 12 weeks caused increases in testicular antioxidant enzymes, downregulated inflammation and apoptosis, and increased PCNA immunoexpression as well as improved lactate transport, through its antioxidant, anti-inflammatory, and antiapoptotic properties [65][66] (Table 6).

Table 6. Effects of bee bread on male reproductive parameters.

s/n	Bee Products	Dose/Duration of Treatment	Substance Used to Induce Stress	Animal Model Used	Route of Administration	Standard Drug	Effect on Reproductive Function Parameters	Possible Molecular Mechanisms	References
1.	Bee bread (Malaysia)	0.5 g/kg/day bw (12 weeks)	High-fat diet	Rats	Oral	Orlistat	Upregulated testicular antioxidant enzymes, downregulated inflammation and apoptosis, and increased PCNA immunoexpression, as well as improving lactate transport	Antioxidant, anti-inflammatory, and antiapoptotic properties	[65][66]

References

1. Kaškonienė, V.; Katilevičiūtė, A.; Kaškonas, P.; Maruška, A. The impact of solid-state fermentation on bee pollen phenolic compounds and radical scavenging capacity. Chem. Pap. 2018, 72, 2115–2120.
2. Ahuja, V.; Ahuja, A. Apitherapy-A sweet approach to dental diseases. Part II: Propolis. J. Adv. Oral Res. 2011, 2, 1–8.
3. Çelik, K.; Aşgun, H.F. Apitherapy: Health and Healing from the Bees; Tudás Alapítvány: Hódmezővásárhely, Hungary, 2020.
4. Gupta, R.K.; Stangaciu, S. Apitherapy: Holistic healing through the honeybee and bee products in countries with poor healthcare system. In Beekeeping for Poverty Alleviation and Livelihood Security; Springer: Berlin/Heidelberg, Germany, 2014; pp. 413–446.
5. Selamaglu, Z. Apitherapy and biomedical application. Appl. Nat. Sci. 2019 2019, 25.
6. Ratiu, I.A.; Al-Suod, H.; Bukowska, M.; Ligor, M.; Buszewski, B. Correlation study of honey regarding their physicochemical properties and sugars and cyclitols content. Molecules 2020, 25, 34.
7. Abd-Allah, S.M. Effect of royal jelly on the fertilizing ability of buffalo spermatozoa in vitro. J. Buffalo Sci. 2012, 1, 1–4.
8. Abd-Elrazek, A.M.; El-dash, H.A.; Said, N.I. The role of propolis against paclitaxel—Induced oligospermia, sperm abnormality, oxidative stress and DNA damage in testes of male rats. Andrologia 2020, 52, e13394.
9. Abu-Zinadah, O.; Alsaggaf, S.; Shaikh Omar, A.; Hussein, H. Effect of honey on testicular functions in rats exposed to octylphenol. Life Sci. J. Acta Zhengzhou Univ. Overseas Ed. 2013, 10, 979–984.
10. Al-Sayigh, M.A.; Al-Mallah, K.H.; Abdul-Rasoul, E.M.; Al-Sadi, H.I. Effect of Bee Venom on Sexual Efficiency in Normal and Hydrogen Peroxide Treated Adult Male Rats; International Animal Science Congress of Turkish and Relatives Communities: Isparta, Turkey, 2012.
11. Budin, S.B.; Jubaidi, F.F.; Azam, S.N.F.M.N.; Yusof, N.L.M.; Taib, I.S.; Mohamed, J. Kelulut honey supplementation prevents sperm and testicular oxidative damage in streptozotocin-induced diabetic rats. J. Teknol. 2017, 79.
12. Mohamed, N.A.; Ahmed, O.M.; Hozayen, W.G.; Ahmed, M.A. Ameliorative effects of bee pollen and date palm pollen on the glycemic state and male sexual dysfunctions in streptozotocin-Induced diabetic wistar rats. Biomed. Pharmacother. 2018, 97, 9–18.
13. Florea, A.; Puică, C.; Hamed, S.; Tilinca, M.; Matei, H. Histopathological and ultrastructural changes experimentally induced by bee venom in seminiferous epithelium via structural-functional alteration of Sertoli cells. Micron 2017, 102, 1–14.
14. Majid, A.; Durriyah Sharifah, M.; Kamaruddin, M. Effects of Gelam Honey on Sperm Quality and Testis of Rat. Sains Malays. 2011, 40, 1243–1246.
15. Rizk, S.M.; Zaki, H.F.; Mina, M.A. Propolis attenuates doxorubicin-induced testicular toxicity in rats. Food Chem. Toxicol. 2014, 67, 176–186.
16. Agarwal, A.; Virk, G.; Ong, C.; du Plessis, S.S. Effect of oxidative stress on male reproduction. World J. Men’s Health 2014, 32, 1–17.
17. Selmanoğlu, G.; Hayretdağ, S.; Kolankaya, D.; Özkök-Tüylü, A.; Sorkun, K. The effect of pollen on some reproductive parameters of male rats. Pestic. I Fitomed. 2009, 24, 59–63.
18. Bharti, U.; Kumar, N.R.; Kaur, J. Bee Pollen attenuates Rifampicin and Isoniazid in Combination induced Oxidative Stress in Testis of SD Rats. Res. J. Pharm. Technol. 2018, 11, 1159–1163.
19. Bouazza, S.; Demmouche, A.; Toumi-Benali, F.; Zouba, M.; Bahri, M.R.; Agher, N.; Merakchi, N.; El Ahmar, M. Effect of bee pollen extract on lead-induced toxicity in rat testis. South Asian J. Exp. Biol. 2018, 8, 91–102.
20. 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.
21. Blank, J.; Freeman, D. Differential reproductive response to short photoperiod in deer mice: Role of melatonin. J. Comp. Physiol. A 1991, 169, 501–506.
22. Salman, T.M.; Alagbonsi, I.A.; Olayaki, L.A.; Biliaminu, S.A.; Salahdeen, H.M.; Olowu, O.A. Honey increases sperm count in male albino rats by enhancing testosterone production. Biokemistri 2013, 25, 39–44.
23. Tartibian, B.; Maleki, B.H. The effects of honey supplementation on seminal plasma cytokines, oxidative stress biomarkers, and antioxidants during 8 weeks of intensive cycling training. J. Androl. 2012, 33, 449–461.
24. Sharifah, D. Effects of nicotine and Gelam honey on testis parameters and sperm qualities of juvenile rats. Sci. Res. Essays 2011, 6, 5471–5474.

25. EL-Ghait, A.T.A.; Ahmed, O.G. The Actions of Honey on Adult Male Mice Testes Exposed to Carbon Tetra-Chloride (Ccl4): Histological and Physiological Studies. AAMJ 2004, 2.
26. Hadi, I.H. Effect of Honey on Sperm Characteristics and Pregnancy Rate in Mice. Bull. Iraq Nat. Hist. Mus. 2017, 14, 223–233.
27. Mohammed, W.H. Hormonal and Histological Study on the Effect of Honey on Mice Male. Eng. Technol. J. 2014, 32, 862–868.
28. Haron, M.N.; Mohamed, M. Effect of honey on the reproductive system of male rat offspring exposed to prenatal restraint stress. Andrologia 2016, 48, 525–531.
29. Mohamed, M.; Sulaiman, S.A.; Sirajudeen, K.N.S. Protective effect of honey against cigarette smoke induced-impaired sexual behavior and fertility of male rats. Toxicol. Ind. Health 2013, 29, 264–271.
30. Mohamed, M.; Sulaiman, S.; Jaafar, H.; Sirajudeen, K. Effect of different doses of Malaysian honey on reproductive parameters in adult male rats. Andrologia 2012, 44, 182–186.
31. Islam, M.; Zul Izhar, M.; Yatiban, M. A Pilot Study to Compare the Effect of Honey on Spermatogenesis In Rats Exposed to Cigarette Smoke. Malays. J. Med. Sci. 2007, 14, 126.
32. Kadir, E.R.; Ojulari, L.S.; Ibrahim, A.; Ekundayo, O.J.; Jaji-Sulaimon, R.; Jimoh-Abdulghaffaar, H.O. Testicular morphology and seminal fluid parameters of adult Wistar rats following honey administration. Trop. J. Pharm. Res. 2018, 17, 1331–1335.
33. Dare, W.; Igbigbi, P.; Avwioro, O. The effect of chronic honey intake on sperm parameters and fertility potential in adult male wistar rats. World Appl. Sci. J. 2013, 22, 657–661.
34. Igbokwe, V.; Samuel, O. Pure Honey Potent Fertility Booster: Activities of Honey on Sperm. IOSR J. Dent. Med. Sci. 2013, 9, 43–47.
35. Kolawole, T.; Oyeyemi, W.; Adigwe, C.; Leko, B.; Udeh, C.; Dapper, D. Honey Attenuates the Detrimental Effects of Nicotine on Testicular Functions in Nicotine Treated Wistar Rats. Niger. J. Physiol. Sci. 2015, 30, 10–16.
36. 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.
37. Zoheir, K.M.A.; Harisa, G.I.; Abo-Salem, O.M.; Ahmad, S.F. Honey bee is a potential antioxidant against cyclophosphamide-induced genotoxicity in albino male mice. Pak. J. Pharm. Sci 2015, 28, 973–981.
38. Seres, A.; Ducza, E.; Báthori, M.; Hunyadi, A.; Béni, Z.; Dékány, M.; Hajagos-Tóth, J.; Verli, J.; Gáspár, R. Androgenic effect of honeybee drone milk in castrated rats: Roles of methyl palmitate and methyl oleate. J. Ethnopharmacol. 2014, 153, 446–453.
39. Ghazi, A.; Ulaiwi, H.K.; Jary, S. The role of local propolis extract against harmful effects of acrylamide on some male reproductive parameters in rats. AL-Qadisiyah J. Vet. Med. Sci. 2013, 12, 87–95.
40. Attia, A.A.; ElMazoudy, R.H.; El-Shenawy, N.S. Antioxidant role of propolis extract against oxidative damage of testicular tissue induced by insecticide chlorpyrifos in rats. Pestic. Biochem. Physiol. 2012, 103, 87–93.
41. Yousef, M.I.; Salama, A.F. Propolis protection from reproductive toxicity caused by aluminium chloride in male rats. Food Chem. Toxicol. 2009, 47, 1168–1175.
42. Sönmez, M.F.; Çilenk, K.T.; Karabulut, D.; Ünalmış, S.; Deligönül, E.; Öztürk, İ.; Kaymak, E. Protective effects of propolis on methotrexate-induced testis injury in rat. Biomed. Pharmacother. 2016, 79, 44–51.
43. Gulhan, M.F. Therapeutic potentials of propolis and pollen on biochemical changes in reproductive function of L-NAME induced hypertensive male rats. Clin. Exp. Hypertens. 2018, 41, 1–7.
44. Russo, A.; Troncoso, N.; Sanchez, F.; Garbarino, J.; Vanella, A. Propolis protects human spermatozoa from DNA damage caused by benzo [a] pyrene and exogenous reactive oxygen species. Life Sci. 2006, 78, 1401–1406.
45. Cedikova, M.; Miklikova, M.; Stachova, L.; Grundmanova, M.; Tuma, Z.; Vetvicka, V.; Zech, N.; Kralickova, M.; Kuncova, J. Effects of the czech propolis on sperm mitochondrial function. Evid. Based Complement. Altern. Med. 2014, 2014, 248768.
46. Fetouh, F.A.; Azab, A.E.S. Ameliorating effects of curcumin and propolis against the reproductive toxicity of gentamicin in adult male guinea pigs: Quantitative analysis and morphological study. Am. J. Life Sci. 2014, 2, 138–149.
47. Kamel, K.; El-Hanoun, A.; El-Sbeiy, M.; Gad, H. Effect of bee propolis extract (bee glue) on some productive. reproductive and physiological traits of rabbits does and their progenys. In Proceedings of the International Conference on Rabbits Production in Hot Climes, Hurghada, Egypt, 4–7 December 2007; pp. 403–415.

48. 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. Green Brazilian propolis effects on sperm count and epididymis morphology and oxidative stress. Food Chem. Toxicol. 2012, 50, 3956–3962.
49. Nna, V.U.; Bakar, A.B.A.; Ahmad, A.; Umar, U.Z.; Suleiman, J.B.; Zakaria, Z.; Othman, Z.A.; Mohamed, M. Malaysian propolis and metformin mitigate subfertility in streptozotocin-induced diabetic male rats by targeting steroidogenesis, testicular lactate transport, spermatogenesis and mating behaviour. Andrology 2020, 8, 731–746.
50. Kumari, S.; Nayak, G.; Lukose, S.T.; Kalthur, S.G.; Bhat, N.; Hegde, A.R.; Mutalik, S.; Kalthur, G.; Adiga, S.K. Indian propolis ameliorates the mitomycin C-induced testicular toxicity by reducing DNA damage and elevating the antioxidant activity. Biomed. Pharmacother. 2017, 95, 252–263.
51. 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.
52. Hassan, A. Effect of royal jelly on sexual efficiency in adult male rats. Iraqi J. Vet. Sci. 2009, 23.
53. Gawish, A.M.; ElFiky, S.; Therase, M.; AbdElraaof, A.; Khalil, W.; Mohamed, K.A. Sperm abnormality toxicity due to cyclosporine A and the ameliorative effect of royal jelly in male rats. J. Basic Appl. Zool. 2016, 76, 60–73.
54. Elnagar, S.A. Royal jelly counteracts bucks' "summer infertility". Anim. Reprod. Sci. 2010, 121, 174–180.
55. El-Hanoun, A.; Elkomy, A.; Fares, W.; Shahien, E. Impact of royal jelly to improve reproductive performance of male rabbits under hot summer conditions. World Rabbit Sci. 2014, 22, 241–248.
56. Ghanbari, E.; Nejati, V.; Najafi, G.; Khazaei, M.; Babaei, M. Study on the effect of royal jelly on reproductive parameters in streptozotocin-induced diabetic rats. Int. J. Fertil. Steril. 2015, 9, 113.
57. Amirshahi, T.; Najafi, G.; Nejati, V. Protective effect of royal jelly on fertility and biochemical parameters in bleomycin-induced male rats. Iran. J. Reprod. Med. 2014, 12, 209.
58. Delkhoshe-Kasmaie, F.; Malekinejad, H.; Khoramjouy, M.; Rezaei-Golmisheh, A.; Janbaze-Acyabar, H. Royal jelly protects from taxol-induced testicular damages via improvement of antioxidant status and up-regulation of E2f1. Syst. Biol. Reprod. Med. 2014, 60, 80–88.
59. Kohguchi, M.; Inoue, S.-i.; Ushio, S.; Iwaki, K.; Ikeda, M.; Kurimoto, M. Effect of royal jelly diet on the testicular function of hamsters. Food Sci. Technol. Res. 2007, 10, 420–423.
60. Morita, H.; Ikeda, T.; Kajita, K.; Fujioka, K.; Mori, I.; Okada, H.; Uno, Y.; Ishizuka, T. Effect of royal jelly ingestion for six months on healthy volunteers. Nutr. J. 2012, 11, 77.
61. Karaca, T.; Demirtaş, S.; Karaboğa, İ.; Ayvaz, S. Protective effects of royal jelly against testicular damage in streptozotocin-induced diabetic rats. Turk. J. Med. Sci. 2015, 45, 27–32.
62. Ghanbari, E.; Nejati, V.; Khazaei, M. Antioxidant and protective effects of Royal jelly on histopathological changes in testis of diabetic rats. Int. J. Reprod. BioMed. 2016, 14, 519.
63. Tohamy, H.G.; El-Karim, D.R.G.; El-Sayed, Y.S. Attenuation potentials of royal jelly against hydroxyurea-induced infertility through inhibiting oxidation and release of pro-inflammatory cytokines in male rats. Environ. Sci. Pollut. Res. 2019, 26, 21524–21534.
64. Silici, S.; Ekmekcioglu, O.; Eraslan, G.; Demirtas, A. Antioxidative effect of royal jelly in cisplatin-induced testes damage. Urology 2009, 74, 545–551.
65. Suleiman, J.B.; Nna, V.U.; Zakaria, Z.; Othman, Z.A.; Eleazu, C.O.; Bakar, A.B.A.; Ahmad, A.; Usman, U.Z.; Rahman, W.F.W.A.; Mohamed, M. Protective effects of bee bread on testicular oxidative stress, NF-κB-mediated inflammation, apoptosis and lactate transport decline in obese male rats. Biomed. Pharmacother. 2020, 131, 110781.
66. Suleiman, J.B.; Bakar, A.B.A.; Mohamed, M. Malaysian Bee Bread Attenuates Apoptosis and Improves Cell Proliferation in Testis of High-Fat Diet-Induced Obese Rats. Int. J. Hum. Health Sci. 2019, 44.