Submitted: 30 October, 2020 Accepted: 20 November, 2020 Online Published: 13 January, 2021 DOI:10.31083/jomh.2021.008

JOMH Journal of Men's Health

Review

A Review of foods and food supplements increasing testosterone levels

Tomoya Kataoka[1], Yuji Hotta[2], Kazunori Kimura[1,2,*]

[1]Department of Clinical Pharmaceutics, Graduate School of Medical Sciences, Nagoya City University, Japan
[2]Department of Hospital Pharmacy, Graduate School of Pharmaceutical Sciences, Nagoya City University, Japan

*__Correspondence:__ kkimura@med.nagoya-cu.ac.jp (Kazunori Kimura)

Abstract

Androgens are essential for male physical activity. Age-related androgen deficiency, known as late-onset hypogonadism (LOH), is considered a risk factor for several diseases. There are many men's health supplements on the market. Therefore, the purpose of this review is to summarize the food ingredients that have been suggested in published literature to increase testosterone levels. A review of previously reported animal studies suggested that 5 representative nutritional components, 7 food ingredients, and 25 supplements were associated with testosterone. Some food and supplements influence testosterone levels in various animals by directly increasing testosterone or suppressing the decrease in testosterone production due to testicular toxicity. There are three mechanisms by which foods or supplements increase testosterone production: 1) regulating luteinizing hormone, the hormone that stimulates testosterone production, 2) regulating testosterone synthase in the testis, and 3) regulating testosterone-degrading enzymes. In contrast, suppressing the decrease in testosterone depends on the antioxidant effect of the foods. Although detailed mechanistic studies and clinical trials are required to validate these findings, the use of food to regulate testosterone levels is a promising therapeutic option.

Keywords

Testosterone; Nutrition; Supplement; Basic science

1. Introduction

Androgens are essential for male physical activity [1–5]. Age-related androgen deficiency, known as late-onset hypogonadism (LOH), is considered a risk factor for erectile dysfunction (ED) [1, 2]. Several studies have reported that androgen replacement therapy mitigates the symptoms of LOH and ED.

Testosterone deficiency has been reported to be associated with a variety of diseases. In recent years, epidemiologic studies have suggested that obesity is associated with multiple alterations in the gonadal endocrine system and low testosterone levels [6–8]. Type 2 diabetes mellitus (T2DM) is also a risk factor for testosterone deficiency [9, 10]. Interestingly, androgen replacement therapy was effective in restoring testosterone levels in both clinical and basic research [11–13].

There are many men's health supplements for increasing testosterone in the market, some of which have proven useful in human meta-analyses [14, 15]. These health supplements have also been tested in animal studies. Besides, many reports indicate that forages for cows and roosters affect testosterone levels. Therefore, the purpose of this review is to summarize the food ingredients that have been suggested in published literature to increase testosterone levels.

2. Methods

To conduct this review, we performed a search of PubMed.gov (National Library of Medicine) for all English-language literature published on or before June 2020 using the following search terms and their combinations: testosterone, food, and supplement.

TABLE 1. Relationship between Testosterone and Food/Supplement

	Promoting T-production	Inhibiting T-degradation	Alleviating testicular toxicity
Garlic	+ [16–17]	-	+ [18–21]
Ginger	+ [25]	-	-
Lactic acid bacteria	+ [26–28]	-	+ [26–27,29–30]
Soybeans	+ [31]	-	+ [32]
Amino acid	+ [34–36]	-	+ [36]
L-arginine	+ [38–39]	-	+ [39–42]
L-carnitine	+ [43]	-	+ [43–44]
Linoleic Acid	+ [45]	-	-
Selenium	+ [47–49]	-	+ [50–52]
Vitamin (C/E)	+ [53–57]	-	+ [58–62]
Zinc	+ [63–65]	-	+ [66–68]
β-caryophyllene	-	+ [70]	-
Chrysin	-	+ [71]	-
Coenzyme Q10	+ [74–76]	-	+ [77–79]
Cordyceps Militaris	+ [80]	-	-
Curcumin	-	-	+ [81]
Cuscuta chinensis	-	-	+ [82]
Emu oil	-	-	+ [84]
Fish oil	+ [85–91]	-	-
Fucoxanthin	+ [92]	-	-
Geranylgeraniol	+ [95]	-	-
Guarana	+ [96]	-	+ [96]
Hazelnut	+ (Aged only) [97]	-	-
Lutein	-	-	+ [99]
Maca	+ [100]	-	+ [101–102]
Melatonin	+ [103–108]	-	+ [109–112]
Milk thistle seed and rosemary leaf	+ [118]	-	-
Moringa	+ [119]	-	+ [119–120]
N-acetyl-cysteine	-	-	+ [121–125]
Oleuropein	+ [126]	-	-
Piperine	+ [127]	-	-
Propolis and Royal Jelly	+ [128]	-	+ [129–132]
Resveratrol	+ [135]	-	+ [136–141]
Rooibos	+ [142–142]	-	-
Saccharomyces cerevisiae	+ [145]	-	-
Taxifolin	-	-	+ [146]

+ : reported in papers. - : no report.

3. Results

A total of 4158 and 1756 papers were retrieved using the search terms "testosterone and food" and "testosterone and supplement," respectively. These papers included duplicates, which were excluded. We further excluded human clinical trials, cell experiments, and drug-based experiments, and remained with 216 papers on animal experiments. From these papers, we extracted the papers that showed the effect of increasing testosterone (Table 1).

4. Testosterone and food

4.1 Protein and fat

Nutritional status affects testosterone, and nutritional deficiency lowers testosterone levels [16, 17]. Schoech *et al.* reported that feeding male jays a high-protein, high-fat diet increased testosterone levels, whereas estrogen levels did not change in females [18].

4.2 Garlic

Garlic, used in many cuisines around the world, also affects testosterone regulation. Oi *et al.* reported that garlic supplementation increased testosterone levels in mice by raising luteinizing hormone (LH) [19]. McVey *et al.* also reported that garlic increased testosterone in rats [20]. They also reported that garlic has protective effects against lead-mediated oxidative damage, apoptosis, and downregulation of CYP19 gene expression in rat testes. Besides, garlic reduces testicular toxicity and suppresses the decrease in testosterone [19–21].

In contrast, crude garlic-feeding decreased testosterone in rats [22–24]. Hassan *et al.* discussed the effect of crude garlic-feeding on Leydig cells and decreased testosterone levels in rats [20].

4.3 Ginger

Ginger is also used in many cuisines worldwide, and Kandeil *et al.* reported that ginger supplementation increased testes weight and testosterone levels in rabbits [25]. They also reported that a combination of ginger and thyme aqueous extracts increased testosterone and reproductive performance.

4.4 Lactic acid bacteria

Lactic acid bacteria are present in yogurt and are consumed worldwide. Among lactic acid bacteria, *Lactobacillus reuteri* and *Lactobacillus rhamnosus* have been reported to increase testosterone [26–28]. Lee *et al.* reported that *Lactobacillus reuteri* had a protective effect against inflammation in aged mice [26]. Poutahidis *et al.* also reported that *Lactobacillus reuteri* affected Leydig cells and increased testosterone levels in mice [27]. Dardmeh *et al.* reported that *Lactobacillus rhamnosus* increased testosterone and improved sperm motility in obese mice [28].

Moreover, Tian *et al.* reported that *Lactobacillus plantarum* alleviated diethylhexylphathalate-induced testicular damage and suppressed the decrease in testosterone [29]. Xie *et al.* reported that bifidobacteria reversed ciprofloxacin-induced testosterone reduction by alleviating oxidative damage and inflammatory response [30].

4.5 Soybeans (isoflavones/lecithin)

Soybeans are grains containing proteins and various nutrients (isoflavones and lecithin) that are consumed globally. McVey *et al.* reported a dose-dependent increase of testosterone following the consumption of isoflavones by rats [31]. Attia and Kamel reported that soybean lecithin upregulated antioxidant constituents and increased testosterone levels in rabbits [32]. However, Simon et al. reported that both low and high isoflavone levels did not affect testosterone levels in monkeys [33].

5. Testosterone and nutrient

5.1 Amino acid (valine / leucine / isoleucine / threonine)

Branched-chain amino acids (BCAAs), which include valine, leucine, isoleucine, and threonine, have some physical effects. They increase post-exercise testosterone levels in humans [34, 35]. Bahadorani *et al.* reported that BCAA supplementation has a synergistic effect on sperm function and testosterone production in mice [36].

Threonine, an essential amino acid, is associated with the regulation of testosterone. Although there is no study on the direct effect of threonine on testosterone levels, Lin *et al.* reported that threonine protected against testosterone decrease in mice infected with pseudorabies virus [37].

5.2 L-arginine

L-arginine is a semi-essential amino acid that is abundant in eels and garlic. Abbaspour *et al.* reported that L-arginine increased testosterone in old broiler breeder roosters [38]. Stefani *et al.* reported that L-arginine increased testosterone in rats [39]. They also showed that L-arginine alleviated resistance training promoted oxidative stress [39]. Therefore, they reported that L-arginine and resistance training has a synergistic effect on testosterone. Additional studies have reported the effects of L-arginine in reducing testicular toxicity and suppressing the decrease in testosterone [40–42].

5.3 L-carnitine

L-carnitine is a vitamin-like substance that is abundant in meat. El-Sherbini *et al.* reported that L-carnitine increased testosterone in rats [43]. Elokil *et al.* reported that supplementation of food with L-carnitine improved the reproductive activity of aged cock by increasing the expression of gonadotropin-releasing hormone 1 (GnRH1) and melatonin receptors (MT1 and MT2) activities [44]. These studies showed that L-carnitine also had anti-oxidant effects [43, 44].

5.4 Linoleic acid

Linolenic acid is one of the essential fatty acids present in sesame oil and walnuts. Barone *et al.* reported that conjugated linoleic acid upregulated CYP17A1 and stimulated testosterone biosynthesis in mice [45]. In contrast, Abdelatty indicated that high-dose of conjugated linoleic acid might induce testicular tissue apoptosis and reduce sperm quality in male rabbits [46].

5.5 Selenium

Selenium is one of the essential trace elements of living organisms. Selenium supplementation increases goat testosterone levels [47, 48]. Erkekoglu *et al.* reported that selenium deficiency decreased testosterone levels, and selenium supplementation increased testosterone in rats by regulating LH levels [49].

Cao *et al.* reported that selenium had protective effects against aflatoxin-induced testicular toxicity and suppressed the decrease in testosterone in mice [50]. Some studies also reported that selenium maintained testosterone levels in animals by alleviating testicular toxicity [51, 52].

5.6 Vitamin (C/E)

Vitamins are nutrients that are necessary in trace amounts for the survival and growth of living organisms. Some vitamins are associated with testosterone. Harikrishnan *et al.* reported that vitamin C (ascorbic acid) increased testosterone by upregulating LH in pigs [53]. Sonmez *et al.* reported that vitamin C increased testosterone levels and epididymal sperm concentration in rats [54]. Amer reported that vitamin C and glutathione increased testosterone and modulated age-related biochemical changes in aged rats [55]. In contrast, vitamin E in combination with flaxseed oil, increases testosterone in roosters [56, 57].

Vitamin C is an antioxidant vitamin, and some studies have reported that vitamin C suppresses the decrease in testosterone associated with testicular toxicity [58, 59]. Mohasseb *et al.* reported that the combination of vitamin C and vitamin E suppressed diabetes-induced testosterone decrease in rats through an anti-oxidant effect [60]. The combined antioxidant effect of vitamins C and E in improving testosterone levels has also been demonstrated in other studies [61, 62].

5.7 Zinc

Zinc is present in many organs and is a component of different enzymes. Kumar *et al.* reported that zinc supplementation led to a dose-dependent increase in testosterone levels in bulls [63]. The effect of zinc supplementation in raising testosterone levels in various animals has also been demonstrated in more studies [64, 65]. Interestingly, some studies reported the effect of zinc in increasing testosterone levels and protecting Leydig cell from damage [66–68].

6. Testosterone and supplement

6.1 β-caryophyllene

β-caryophyllene is a sesquiterpene contained in spices, herbs, and essential oils of various spices and fruits. β-caryophyllene acts as a selective agonist of the cannabinoid receptor type 2. It is approved by the United States Food and Drug Administration and European agencies as a food additive, taste enhancer, and flavoring agent and termed phytocannabinoid [69]. Fiorenzani *et al.* reported that β-caryophyllene increased testosterone by inhibiting 5α-reductase in rats [70].

6.2 Chrysin

Chrysin is a flavonoid extracted from *Passiflora coerulea* or honeycombs. Altawash *et al.* reported that chrysin increased testosterone in roosters by inhibiting aromatase activity [71]. However, chrysin affects thyroid function [72]. Besides, chrysin can cause cellular toxicity and inhibit DNA synthesis [73]. Due to these side effects, consuming chrysin to increase testosterone levels may not be recommended.

6.3 Coenzyme Q10 (CoQ10)

CoQ10 is a coenzyme that is abundant in the mitochondria and cell membranes. Sharideh *et al.* reported that CoQ10 increased testosterone and improved testicular function in aged roosters [74]. CoQ10 also increased testosterone levels in other animals by increasing LH [75, 76]. Besides, CoQ10 has antioxidant activity, hence suppresses the decrease in testosterone associated with testicular toxicity in rats [77–79].

6.4 Cordyceps militaris

Cordyceps militaris is a fungus belonging to the genus Nomushitake. *Cordyceps militaris* is consumed in East Asia as a crude drug in Chinese medicine or as a medicinal ingredient in Chinese cuisine. Chang *et al.* reported that *Cordyceps militaris* increased testosterone without changing LH, FSH, or prolactin in rats [80].

6.5 Curcumin

Curcumin is a polyphenol compound present in turmeric. Curcumin has antioxidant activity. Ahmed-Farid *et al.* reported that curcumin improved testosterone in rats with reduced testosterone on a protein-restricted diet [81].

6.6 Cuscuta chinensis

Cuscuta chinensis is a parasitic plant in the family Convolvulaceae and is used as a Chinese herb. Wei *et al.* reported a dose-dependent increase in testosterone in rats with reduced testosterone due to the negative effect of bisphenol A on testicular development [82]. They also showed that *Cuscuta chinensis* reduced the methylation level of related genes and protected reproduction.

6.7 Emu oil

Emu, a bird native to Austria, is the source of Emu oil used as a medicine in Austria. Emu oil is obtained from subcutaneous and retroperitoneal fat of the emu, *Dromaius novaehollandiae*, and comprises nearly 98% lipids and 1%–2% natural antioxidants. The major fatty acids present in emu oil are oleic acid (43%–46%), linoleic acid (6%–9%), linolenic acid (6%), palmitic acid (5%–23%), and stearic acid (9%) [83]. Kamalakkannan *et al.* reported that emu oil led to a dose-dependent increase in testosterone levels in diet-induced obese rats with reduced testosterone [84]. The high content of oleic acid in emu oil could have orchestrated inhibition of atheromatous plaque formation in diet-induced obese animals.

6.8 Fish oil(DHA/EPA)omega-3 and omega-6 polyunsaturated fatty acid

Fish oil is rich in omega-3 fatty acids, which are unsaturated fatty acids. Among the omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are widely used as supplements. Fish oil increases testosterone levels in some animals [85–87]. Rossi *et al.* reported that unsaturated fatty acids increased testosterone in bulls [88]. Omega-3 fatty acids also increase testosterone levels in various animals [89, 90]. Kapourchali *et al.* reported that DHA increased serum testosterone and sperm normal morphology in rats [91].

6.9 Fucoxanthin

Fucoxanthin is a major xanthophyll compound obtained from edible brown seaweeds, such as *Sargassum heterophyllum* [92]. and *Sargassum horneri* [93]. Wang *et al.* reported that fucoxanthin increased testosterone levels in rats [94].

6.10 Geranylgeraniol

Geranylgeraniol is a diterpene found in vegetables, fruits, and grains. Ho *et al.* reported that geranylgeraniol increased testosterone levels by up-regulating cAMP in testis-derived I-10 tumor cells [95].

6.11 Guarana (Paullinia cupana var. sorbilis)

Guarana is a plant native to the Amazon basin, and its seed extracts are used in health foods. Leite *et al.* reported that guarana increased testosterone in rats [96]. They also showed that guarana protected against the cadmium-induced testis damage.

6.12 Hazelnut

Hazelnuts are the fruits of deciduous shrubs of the genus Hazel in the family Betulaceae. Kara *et al.* reported that a hazelnut-supplemented diet increased testosterone levels and semen quality parameters in aged rats [97]. In contrast, hazelnut did not change testosterone levels in young rats, implying that this effect might be related to the antioxidant action of hazelnut.

6.13 Lutein

Lutein is one of the most abundant carotenoids in fruits and vegetables with antioxidant properties [98]. Fatani *et al.* reported that lutein could suppress the decrease in testosterone due to testicular toxicity in streptozotocin-induced diabetic rats [99].

6.14 Maca (Lepidium meyenii)

Maca is a perennial plant of the Brassicaceae family that grows in Peru. There are three varieties of Maca, recognizable through their external color (Maca Negro or Black Maca, Yellow Maca, and Red Maca). Ohta *et al.* reported that maca increased testosterone levels by enhancing the steroidogenic ability of Leydig cells in rats [100]. Other studies indicated that maca increased testosterone levels and protected against the testis damage caused by cyclophosphamide in rats [101, 102].

6.15 Melatonin

Melatonin is a hormone present in animals, plants, and microorganisms and is also used as a supplement. Melatonin increases testosterone levels in various animal species [103–108]. Melatonin suppresses the decrease in testosterone levels due to testicular toxicity [109–112]. Interestingly, human clinical trials have reported an increase in testosterone levels following melatonin supplementation [113–116].

6.16 Milk thistle seed and rosemary leaf

Milk thistle seeds contain a type of flavonoid called silymarin. Rosemary is another phytogenic plant, rich in active metabolites such as caffeic acid and rosmarinic acid [117]. Attia *et al.* reported that milk thistle seed and rosemary leaves increased testosterone and sperm quality in rabbits [118].

6.17 Moringa

Moringa is native to the southern foothills of the Himalayas and is widely cultivated in tropical and subtropical regions. Moringa is ingested as a health food. El-Desoky *et al.* reported that moringa increased testosterone in rabbits. Besides, moringa suppresses the decrease in testosterone due to testicular toxicity [119, 120].

6.18 N-acetyl-cysteine

N-acetyl-cysteine is a derivative of L-cysteine. L-cysteine is a natural antioxidant amino acid found in peppers, garlic, and onions. Elnagar *et al.* reported that N-acetyl-cysteine does not increase testosterone, but it suppresses the decrease in testosterone due to testicular toxicity [121]. Some studies have also demonstrated the protective effect of N-acetyl-cysteine for testosterone production [122–125].

6.19 Oleuropein

Oleuropein is a polyphenol contained in olives and privet. Oi-Kano *et al.* reported that oleuropein increased testosterone levels by raising LH in rats [126].

6.20 Piperine

Piperine is a type of alkaloid contained in pepper. Chen *et al.* reported that piperine increased testosterone synthase in the testis and increased testosterone in rats [127].

6.21 Propolis and Royal Jelly

Propolis is a solid substance made by mixing herbs and tree sprouts collected by honeybees with saliva containing enzymatic components. Kumari *et al.* reported that propolis suppressed mitomycin-induced decline in testosterone levels in rats through an anti-oxidant effect [128].

Royal jelly is a substance made by honeybees. Almeer *et al.* reported that royal jelly increased testosterone levels by raising FSH in mice [129]. Royal jelly also suppressed the decrease in testosterone due to testicular toxicity [130–134].

6.22 Resveratrol

Resveratrol is a polyphenolic compound naturally found in peanuts, grapes, red wine, and some berries. Shati reported that resveratrol increased testosterone by raising LH in rats [135]. Resveratrol is an antioxidant [136]. and can suppress the decrease in testosterone due to testicular toxicity [137–141].

6.23 Rooibos

Rooibos is a herb of the genus Aspalathus and the subfamily Papilionoideae native to South Africa. Rooibos contains a large number of flavonoids. Schloms *et al.* reported that

JOMH
Journal of Men's Health

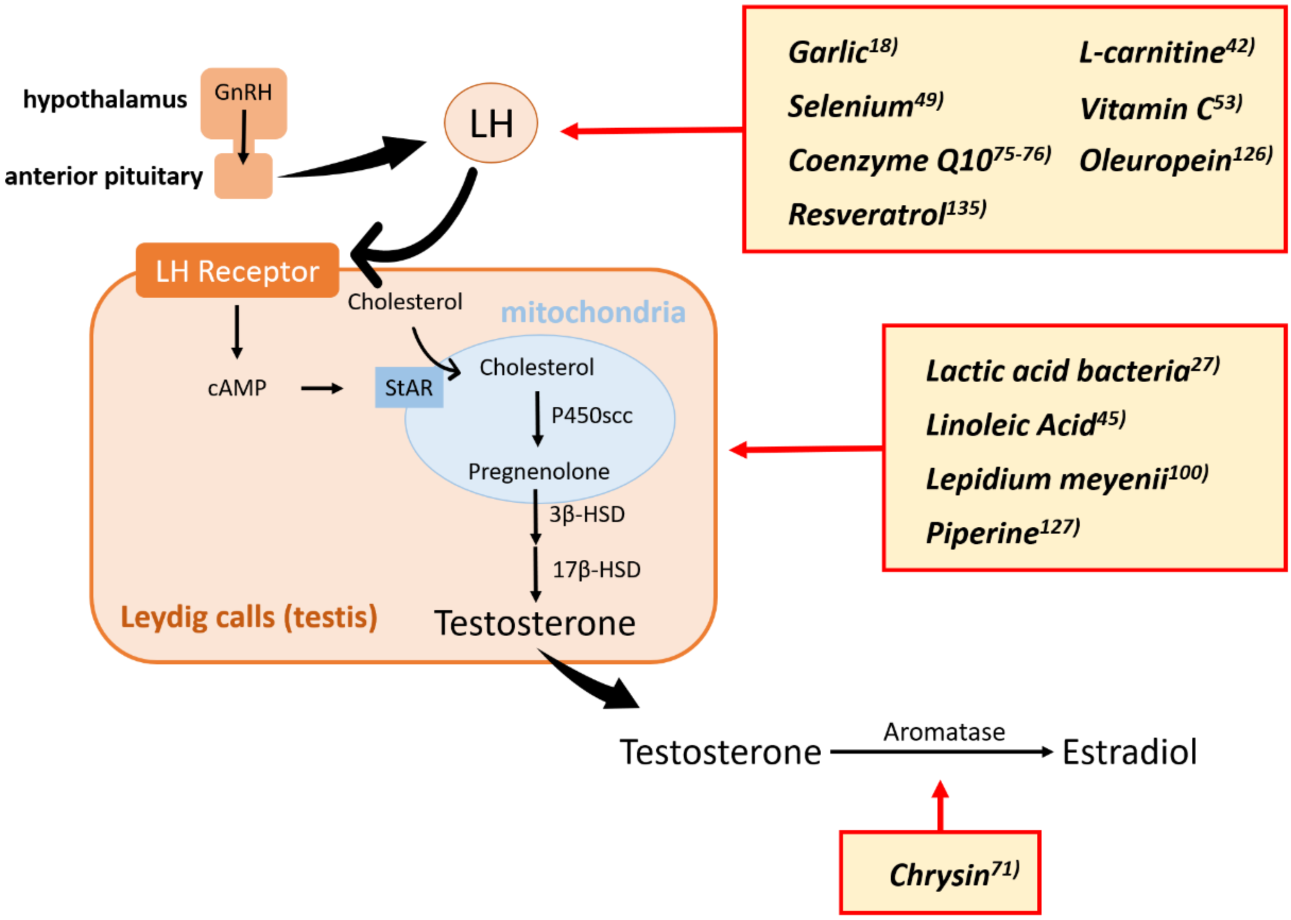

FIG. 1. Targets of testosterone production effected by food or supplements. GnRH: Gonadotropin-releasing hormone, LH: Luteinizing hormone, cAMP: Cyclic adenosine monophosphate, StAR: steroidogenic acute regulatory protein, 3β-HSD: 3β-hydroxysteroid dehydrogenase, 17β-HSD: 17β-hydroxysteroid dehydrogenase.

rooibos increased testosterone and decreased corticosterone levels in rats [142]. Noh *et al.* also reported that rooibos and dandelion increased testosterone and improved sperm quality in rats [143]. Through a clinical trial, Noh demonstrated the effect of MR-10 (a complex of dandelion and rooibos) in increasing testosterone levels [144].

6.24 Saccharomyces cerevisiae

Saccharomyces cerevisiae is a baker's yeast that is widely used as a medicine or supplement. Mannaa *et al.* reported that *Saccharomyces cerevisiae* increased testosterone levels in rats [145].

6.25 Taxifolin

Taxifolin is a flavonoid, usually found in red onions, milk thistle seeds, and Chinese yew. Taxifolin has an anti-oxidant effect. Li *et al.* reported that taxifolin suppressed the decrease in testosterone due to testicular toxicity induced by di-n-butyl phthalate in rats [146].

7. Conclusions

Some foods and supplements influence testosterone levels in various animals. The two main mechanisms are the direct increase in testosterone levels or suppression of the decrease in testosterone production due to testicular toxicity. Foods or supplements raise testosterone production in three ways: 1) regulating LH, the hormone that stimulates the production of testosterone, 2) regulating testosterone synthase in the testis, and 3) regulating testosterone-degrading enzymes (Fig. 1). In contrast, suppression of the decrease in testosterone depends on the antioxidant effect of the foods and supplements.

LH is a gonadotropin that is released by the pituitary glands [147]. Garlic, l-carnitine, selenium, vitamin C, CoQ10, qleuropein, and resveratrol regulate the LH secretion [16, 42, 49, 53, 75, 76, 126, 135]. Secreted LH acts on testis receptors and is involved in the synthesis of testosterone from cholesterol [147]. Lactic acid bacteria enhance testosterone production by increasing Leydig cells in the testis [27]. Linoleic acid, maca, and piperin raise testosterone levels by increasing the levels of enzymes involved in testosterone synthesis [45, 100, 127]. These two pathways of testosterone production would be a promising target for treatment. Foods or supplements that have been shown to increase testosterone might act on these pathways. In contrast, testosterone is metabolized to estradiol by aromatase [148]. Chrysin increased testosterone levels by inhibiting aromatase activity [71]. Although detailed mechanistic studies and clinical trials are required to validate the findings, the effects of these foods on testosterone provide potential therapeutic options.

Acknowledgements

This review was supported in part by Grants-in-Aid for Scientific Research (KAKENHI, 20K09563) from The Japan Society for the Promotion of Science (JSPS).

We would like to thank Editage (www.editage.com) for English language editing.

Conflict of interest

The authors report no conflicts of interest.

References

[1] Meldrum DR, Gambone JC, Morris MA, Esposito K, Giugliano D, Ignarro LJ. Lifestyle and metabolic approaches to maximizing erectile and vascular health. International Journal of Impotence Research. 2012; 24: 61-68.

[2] Isidori AM, Buvat J, Corona G, Goldstein I, Jannini EA, Lenzi A, *et al.* A critical analysis of the role of testosterone in erectile function: from pathophysiology to treatment-a systematic review. European Urology. 2014; 65: 99-112.

[3] Berg WT, Miner M. Hypogonadism and metabolic syndrome: review and update. Current Opinion in Endocrinology, Diabetes and Obesity. 2020; 27: 404-410.

[4] Lapauw B, Kaufman JM. Management of endocrine disease: rationale and current evidence for testosterone therapy in the management of obesity and its complications. European Journal of Endocrinology. 2020; 183: R167-183.

[5] Dandona P, Dhindsa S, Ghanim H, Saad F. Mechanisms underlying the metabolic actions of testosterone in humans: a narrative review. Diabetes, Obesity and Metabolism. 2020 (in press).

[6] Buvat J, Maggi M, Guay A, Torres LO. Testosterone deficiency in men: systematic review and standard operating procedures for diagnosis and treatment. The Journal of Sexual Medicine. 2013; 10: 245-284.

[7] Esposito K, Giugliano F, Martedì E, Feola G, Marfella R, D'Armiento M, *et al.* High proportions of erectile dysfunction in men with the metabolic syndrome. Diabetes Care. 2005; 28: 1201-1203.

[8] Li SY, Zhao YL, Yang YF, Wang X, Nie M, Wu XY, *et al.* Metabolic effects of testosterone replacement therapy in patients with type 2 diabetes mellitus or metabolic syndrome: a meta-analysis. International Journal of Endocrinology. 2020; 4732021.

[9] Hackett G, Cole N, Mulay A, Strange RC, Ramachandran S. Long-term testosterone therapy in type 2 diabetes is associated with decreasing waist circumference and improving erectile function. The World Journal of Men's Health. 2020; 38: 68-77.

[10] Kataoka T, Hotta Y, Maeda Y, Kimura K. Assessment of androgen replacement therapy for erectile function in rats with type 2 diabetes mellitus by examining nitric oxide-related and inflammatory factors. The Journal of Sexual Medicine. 2014; 11: 920-29.

[11] Shamloul R, Ghanem H. Erectile dysfunction. Lancet. 2013; 381: 153-165.

[12] Kataoka T, Hotta Y, Maeda Y, Kimura K. Testosterone deficiency causes endothelial dysfunction via elevation of asymmetric dimethylarginine and oxidative stress in castrated rats. The Journal of Sexual Medicine. 2017; 14: 1540-1548.

[13] Buvat J, Maggi M, Guay A, Torres LO. Testosterone deficiency in men: systematic review and standard operating procedures for diagnosis and treatment. The Journal of Sexual Medicine. 2013; 10: 245-284.

[14] Mansoori A, Hosseini S, Zilaee M, Hormoznejad R, Fathi M. Effect of fenugreek extract supplement on testosterone levels in male: A meta-analysis of clinical trials. Phytotherapy Research. 2020; 34: 1550-1555.

[15] Irani M, Amirian M, Sadeghi R, Lez JL, Latifnejad Roudsari R. The effect of folate and folate plus zinc supplementation on endocrine parameters and sperm characteristics in sub-fertile men: a systematic review and meta-analysis. Urology Journal. 2018; 14: 4069-4078.

[16] McVey MJ, Cooke GM, Curran IHA, Chan HM, Kubow S, Lok E, *et al.* Effects of dietary fats and proteins on rat testicular steroidogenic enzymes and serum testosterone levels. Food and Chemical Toxicology. 2008; 46: 259-269.

[17] McVey MJ, Cooke GM, Curran IHA, Chan HM, Kubow S, Lok E, *et al.* An investigation of the effects of methylmercury in rats fed different dietary fats and proteins: testicular steroidogenic enzymes and serum testosterone levels. Food and Chemical Toxicology. 2008; 46: 270-279.

[18] Schoech SJ, Bowman R, Reynolds SJ. Food supplementation and possible mechanisms underlying early breeding in the florida scrub-jay (Aphelocoma coerulescens). Hormones and Behavior. 2004; 46: 565-573.

[19] Oi Y, Imafuku M, Shishido C, Kominato Y, Nishimura S, Iwai K. Garlic supplementation increases testicular testosterone and decreases plasma corticosterone in rats fed a high protein diet. The Journal of Nutrition. 2001; 131: 2150-2156.

[20] Hassan E, Kahilo K, Kamal T, El-Neweshy M, Hassan M. Protective effect of diallyl sulfide against lead-mediated oxidative damage, apoptosis and down-regulation of cyp19 gene expression in rat testes. Life Sciences. 2019; 226: 193-201.

[21] Abdrabou MI, Elleithy EMM, Yasin NAE, Shaheen YM, Galal M. Ameliorative effects of spirulina maxima and allium sativum on lead acetate-induced testicular injury in male albino rats with respect to caspase-3 gene expression. Acta Histochemica. 2019; 121: 198-206.

[22] Soleimanzadeh A, Mohammadnejad L, Ahmadi A. Ameliorative effect of allium sativum extract on busulfan-induced oxidative stress in mice sperm. Veterinary Research Forum. 2019; 9: 265-271.

[23] Nasr AY. The impact of aged garlic extract on adriamycin-induced testicular changes in adult male wistar rats. Acta Histochemica. 2018; 119: 648-662.

[24] El-Akabawy G, El-Sherif NM. Protective role of garlic oil against oxidative damage induced by furan exposure from weaning through adulthood in adult rat testis. Acta Histochemica. 2017; 118: 456-463.

[25] Kandeil MA, Mohamed AEH, Abdel Gabbar M, Ahmed RR, Ali SM. Ameliorative effects of oral ginger and/or thyme aqueous extracts on productive and reproductive performance of V-line male rabbits. Journal of Animal Physiology and Animal Nutrition. 2019; 103: 1437-1446.

[26] Lee J, Yang W, Hostetler A, Schultz N, Suckow MA, Stewart KL, *et al.* Characterization of the anti-inflammatory lactobacillus reuteri bm36301 and its probiotic benefits on aged mice. BMC Microbiology. 2016; 16: 69.

[27] Poutahidis T, Springer A, Levkovich T, Qi P, Varian BJ, Lakritz JR, *et al.* Probiotic microbes sustain youthful serum testosterone levels and testicular size in aging mice. PloS One. 2014; 9: e84877.

[28] Dardmeh F, Alipour H, Gazerani P, van der Horst G, Brandsborg E, Nielsen HI. Lactobacillus rhamnosus pb01 (dsm 14870) supplementation affects markers of sperm kinematic parameters in a diet-induced obesity mice model. PloS One. 2017; 12: e0185964.

[29] Tian X, Yu Z, Feng P, Ye Z, Li R, Liu J, *et al. Lactobacillus plantarum* TW1-1 alleviates diethylhexylphthalate-induced testicular damage in mice by modulating gut microbiota and decreasing inflammation. Frontiers in Cellular and Infection Microbiology. 2019; 9: 221.

[30] Xie C, Bian Y, Feng H, Zhao Y, Wang L, Li Y, *et al.* Reversal of ciprofloxacin-induced testosterone reduction by probiotic microbes in mouse testes. General and Comparative Endocrinology. 2019; 284: 113268.

[31] McVey MJ, Cooke GM, Curran IHA. Increased serum and testicular androgen levels in f1 rats with lifetime exposure to soy isoflavones. Reproductive Toxicology. 2004; 18: 677-685.

[32] Attia YA, Kamel KI. Semen quality, testosterone, seminal plasma biochemical and antioxidant profiles of rabbit bucks fed diets supplemented with different concentrations of soybean lecithin. Animal. 2012; 6: 824-833.

[33] Simon NG, Kaplan JR, Hu S, Register TC, Adams MR. Increased aggressive behavior and decreased affiliative behavior in adult male

monkeys after long-term consumption of diets rich in soy protein and isoflavones. Hormones and Behavior. 2004; 45: 278-284.
[34] Sharp CPM, Pearson DR. Amino acid supplements and recovery from high-intensity resistance training. Journal of Strength and Conditioning Research. 2010; 24: 1125-1130.
[35] Carli G, Bonifazi M, Lodi L, Lupo C, Martelli G, Viti A. Changes in the exercise-induced hormone response to branched chain amino acid administration. European Journal of Applied Physiology and Occupational Physiology. 1992; 64: 272-277.
[36] Bahadorani M, Tavalaee M, Abedpoor N, Ghaedi K, Nazem MN, Nasr-Esfahani MH. Effects of branched-chain amino acid supplementation and/or aerobic exercise on mouse sperm quality and testosterone production. Andrologia. 2019; 51: e13183.
[37] Lin Y, Wu D, Zeng WX, Fang ZF, Che LQ. Effect of threonine on immunity and reproductive performance of male mice infected with pseudorabies virus. Anima. 2013; 6: 1821-1829.
[38] Abbaspour B, Sharifi SD, Ghazanfari S, Honarbakhsh S, Mohammadi-Sangcheshmeh A. The effect of l-arginine and flaxseed on plasma testosterone concentration, semen quality and some testicular histology parameters in old broiler breeder roosters. Theriogenology. 2019; 128: 101-109.
[39] Stefani GP, Marmett B, Alves JP, Möller GB, Heck TG, Frizzo MN, *et al.* Resistance training and l-arginine supplementation are determinant in genomic stability, cardiac contractility and muscle mass development in rats. PloS One. 2019; 13: e0204858.
[40] Zhang YF, Yang JY, Meng XP, Qiao XL. L-arginine protects against t-2 toxin-induced male reproductive impairments in mice. Theriogenology. 2019; 126: 249-253.
[41] Yang JY, Zhang YF, Nie N, Feng W, Bao J, Meng X, *et al.* Protective effects of l-arginine against testosterone synthesis decreased by T-2 toxin in mouse Leydig cells. Theriogenology. 2019; 134: 98-103.
[42] Jia X, Li Z, Ren X, Dai P, Li Y, Li C. L-Arginine alleviates the testosterone reduction in heat-treated mice by upregulating LH secretion, the testicular antioxidant system and expression of steroidogenesis-related genes. Reproduction, Fertility and Development. 2020; 32: 885-892.
[43] El-Sherbini E, El-Sayed G, El Shotory R, Gheith N, Abou-Alsoud M, Harakeh SM, *et al.* Ameliorative effects of l-carnitine on rats raised on a diet supplemented with lead acetate. Saudi Journal of Biological Sciences. 2019; 24: 1410-1417.
[44] Elokil AA, Bhuiyan AA, Liu HZ, Hussein MN, Ahmed HI, Azmal SA, *et al.* The capability of L-carnitine-mediated antioxidant on cock during aging: evidence for the improved semen quality and enhanced testicular expressions of GnRH1, GnRHR, and melatonin receptors MT 1/2. Poultry Science. 2019; 98: 4172-4181.
[45] Barone R, Macaluso F, Catanese P, Marino Gammazza A, Rizzuto L, Marozzi P, *et al.* Endurance exercise and conjugated linoleic acid (cla) supplementation up-regulate cyp17a1 and stimulate testosterone biosynthesis. PloS One. 2014; 8: e79686.
[46] Abdelatty AM, Badr OAM, Mohamed SA, Khattab MS, Dessouki SM, Farid OAA, *et al.* Long term conjugated linoleic acid supplementation modestly improved growth performance but induced testicular tissue apoptosis and reduced sperm quality in male rabbit. PLoS One. 2020; 15: e0226070.
[47] Mojapelo MM, Lehloenya KC. Effect of selenium supplementation on attainment of puberty in Saanen male goat kids. Theriogenology. 2019; 138: 9-15.
[48] Shi L, Song R, Yao X, Duan Y, Ren Y, Zhang C, *et al.* Effects of maternal dietary selenium (Se-enriched yeast) on testis development, testosterone level and testicular steroidogenesis-related gene expression of their male kids in Taihang Black Goats. Theriogenology. 2018; 114: 95-102.
[49] Erkekoglu P, Zeybek ND, Giray B, Asan E, Arnaud J, Hincal F. Reproductive toxicity of di(2-ethylhexyl) phthalate in selenium-supplemented and selenium-deficient rats. Drug and Chemical Toxicology. 2012; 34: 379-389.
[50] Cao Z, Shao B, Xu F, Liu Y, Li Y, Zhu Y. Protective effect of selenium on aflatoxin b1-induced testicular toxicity in mice. Biological Trace Element Research. 2018; 180: 233-238.
[51] Ibrahim HAM, Zhu Y, Wu C, Lu C, Ezekwe MO, Liao SF, *et al.* Selenium-enriched probiotics improves murine male fertility compromised by high fat diet. Biological Trace Element Research. 2012; 147: 251-260.
[52] El-Mokadem MY, Taha TA, Samak MA, Yassen AM. Alleviation of reproductive toxicity of gossypol using selenium supplementation in rams. Journal of Animal Science. 2013; 90: 3274-3285.
[53] Harikrishnan R, Abhilash PA, Syam Das S, Prathibha P, Rejitha S, John F, *et al.* Protective effect of ascorbic acid against ethanol-induced reproductive toxicity in male guinea pigs. The British Journal of Nutrition. 2013; 110: 689-698.
[54] Sönmez M, Türk G, Yüce A. The effect of ascorbic acid supplementation on sperm quality, lipid peroxidation and testosterone levels of male wistar rats. Theriogenology. 2005; 63: 2063-2072.
[55] Amer MA. Modulation of age-related biochemical changes and oxidative stress by vitamin c and glutathione supplementation in old rats. Annals of Nutrition and Metabolism. 2003; 46: 165-168.
[56] Zanussi HP, Shariatmadari F, Sharafi M, Ahmadi H. Dietary supplementation with flaxseed oil as source of omega-3 fatty acids improves seminal quality and reproductive performance in aged broiler breeder roosters. Theriogenology. 2019; 130: 41-48.
[57] Qi X, Shang M, Chen C, Chen Y, Hua J, Sheng X, *et al.* Dietary supplementation with linseed oil improves semen quality, reproductive hormone, gene and protein expression related to testosterone synthesis in aging layer breeder roosters. Theriogenology. 2019; 131: 9-15.
[58] Zubair M, Ahmad M, Saleemi MK, Gul ST, Ahmad M, Martyniuk CJ, *et al.* Sodium arsenite toxicity on hematology indices and reproductive parameters in Teddy goat bucks and their amelioration with vitamin C. Environmental Science and Pollution Research. 2020; 27: 15223-15232.
[59] Radhakrishnakartha H, Appu AP, Madambath I. Reversal of alcohol induced testicular hyperlipidemia by supplementation of ascorbic acid and its comparison with abstention in male guinea pigs. Journal of Basic and Clinical Physiology and Pharmacology. 2015; 25: 117-124.
[60] Mohasseb M, Ebied S, Yehia MAH, Hussein N. Testicular oxidative damage and role of combined antioxidant supplementation in experimental diabetic rats. Journal of Physiology and Biochemistry. 2011; 67: 185-194.
[61] Sen Gupta R, Sen Gupta E, Dhakal BK, Thakur AR, Ahnn J. Vitamin C and vitamin E protect the rat testes from cadmium-induced reactive oxygen species. Molecules and Cells. 2004; 17: 132-139.
[62] Min Y, Sun T, Niu Z, Liu F. Vitamin c and vitamin e supplementation alleviates oxidative stress induced by dexamethasone and improves fertility of breeder roosters. Animal Reproduction Science. 2016; 171: 1-6.
[63] Kumar N, Verma RP, Singh LP, Varshney VP, Dass RS. Effect of different levels and sources of zinc supplementation on quantitative and qualitative semen attributes and serum testosterone level in crossbred cattle (Bos indicus x Bos taurus) bulls. Reproduction, Nutrition, Development. 2007; 46: 663-675.
[64] Khoobbakht Z, Mohammadi M, Mehr MR, Mohammadghasemi F, Sohani MM. Comparative effects of zinc oxide, zinc oxide nanoparticle and zinc-methionine on hatchability and reproductive variables in male Japanese quail. Animal Reproduction Science. 2018; 192: 84-90.
[65] Arangasamy A, Venkata Krishnaiah M, Manohar N, Selvaraju S, Guvvala PR, Soren NM, *et al.* Advancement of puberty and enhancement of seminal characteristics by supplementation of trace minerals to bucks. Theriogenology. 2018; 110: 182-191.
[66] Aziz NM, Kamel MY, Mohamed MS, Ahmed SM. Antioxidant, anti-inflammatory, and anti-apoptotic effects of zinc supplementation in testes of rats with experimentally induced diabetes. Applied Physiology, Nutrition, and Metabolism. 2019; 43: 1010-1018.
[67] Garcia PC, Piffer RC, Gerardin DCC, Sankako MK, Alves de Lima RO, Pereira OCM. Could zinc prevent reproductive alterations caused by cigarette smoke in male rats? Reproduction, Fertility, and Development. 2012; 24: 559-567.
[68] Sankako MK, Garcia PC, Piffer RC, Dallaqua B, Damasceno DC,

Pereira OCM. Possible mechanism by which zinc protects the testicular function of rats exposed to cigarette smoke. Pharmacological Reports. 2013; 64: 1537-1546.

[69] Sharma C, Al Kaabi JM, Nurulain SM, Goyal SN, Kamal MA, Ojha S. Polypharmacological properties and therapeutic potential of β-caryophyllene: a dietary phytocannabinoid of pharmaceutical promise. Current Pharmaceutical Design. 2017; 22: 3237-3264.

[70] Fiorenzani P, Lamponi S, Magnani A, Ceccarelli I, Aloisi AM. In vitro and in vivo characterization of the new analgesic combination beta-caryophyllene and docosahexaenoic acid. Evidence-Based Complementary and Alternative Medicine. 2014; 2014: 596312.

[71] Amin Altawash AS, Shahneh AZ, Moravej H, Ansari M. Chrysin-induced sperm parameters and fatty acid profile changes improve reproductive performance of roosters. Theriogenology. 2018; 104: 72-79.

[72] Bortolotto VC, Pinheiro FC, Araujo SM, Poetini MR, Bertolazi BS, de Paula MT, *et al.* Chrysin reverses the depressive-like behavior induced by hypothyroidism in female mice by regulating hippocampal serotonin and dopamine. European Journal of Pharmacology. 2018; 822: 78-84.

[73] Tsuji PA, Walle T. Cytotoxic effects of the dietary flavones chrysin and apigenin in a normal trout liver cell line. Chemico-Biological Interactions. 2008; 171: 37-44.

[74] Sharideh H, Zeinoaldini S, Zhandi M, Zaghari M, Sadeghi M, Akhlaghi A, *et al.* Use of supplemental dietary coenzyme q10 to improve testicular function and fertilization capacity in aged broiler breeder roosters. Theriogenology. 2020; 142: 355-362.

[75] El-Khadragy M, Al-Megrin W, AlSadhan N, Metwally D, El-Hennamy R, Salem FE, *et al.* Impact of coenzyme Q10 administration on lead acetate-induced testicular damage in rats. Oxidative Medicine and Cellular Longevity. 2020; 2020: 1-12.

[76] El-Sayed AI, Ahmed-Farid O, Radwan AA, Halawa EH, Elokil AA. The capability of coenzyme Q10 to enhance heat tolerance in male rabbits: evidence from improved semen quality factor (SQF), testicular oxidative defense, and expression of testicular melatonin receptor MT1. Domestic Animal Endocrinology. 2021; 74: 106403.

[77] Ghanbarzadeh S, Garjani A, Ziaee M, Khorrami A. Coq10 and l-carnitine attenuate the effect of high ldl and oxidized ldl on spermatogenesis in male rats. Drug research. 2015; 64: 510-515.

[78] Ghanbarzadeh S, Garjani A, Ziaee M, Khorrami A. Effects of l-carnitine and coenzyme q10 on impaired spermatogenesis caused by isoproterenol in male rats. Drug research. 2015; 64: 449-453.

[79] Fouad AA, Al-Sultan AI, Yacoubi MT. Coenzyme q10 counteracts testicular injury induced by sodium arsenite in rats. European Journal of Pharmacology. 2011; 655: 91-98.

[80] Chang Y, Jeng K, Huang K, Lee Y, Hou C, Chen K, *et al.* Effect of cordyceps militaris supplementation on sperm production, sperm motility and hormones in sprague-dawley rats. the American Journal of Chinese Medicine. 2009; 36: 849-859.

[81] Ahmed-Farid OAH, Nasr M, Ahmed RF, Bakeer RM. Beneficial effects of curcumin nano-emulsion on spermatogenesis and reproductive performance in male rats under protein deficient diet model: enhancement of sperm motility, conservancy of testicular tissue integrity, cell energy and seminal plasma amino acids content. Journal of Biomedical Science. 2017; 24: 66.

[82] Wei Y, Han C, Li S, Bao Y, Shi, W. Cuscuta chinensis flavonoids down-regulate the DNA methylation of the H19/Igf2 imprinted control region and estrogen receptor alpha promoter of the testis in bisphenol A exposed mouse offspring. Food and Function. 2020; 11: 787-798.

[83] Lindsay RJ, Geier MS, Yazbeck R, Butler RN, Howarth GS. Orally administered emu oil decreases acute inflammation and alters selected small intestinal parameters in a rat model of mucositis. The British Journal of Nutrition. 2010; 104: 513-519.

[84] Kamalakkannan S, Tirupathi Pichiah PB, Kalaiselvi S, Arunachalam S, Achiraman S. Emu oil decreases atherogenic plaque formation in cafeteria diet-induced obese rats. Journal of the Science of Food and Agriculture. 2017; 96: 3063-3068.

[85] Lin Y, Cheng X, Mao J, Wu D, Ren B, Xu S, *et al.* Effects of different dietary n-6/n-3 polyunsaturated fatty acid ratios on boar reproduction. Lipids in Health and Disease. 2016; 15: 31.

[86] Safari Asl R, Shariatmadari F, Sharafi M, Karimi Torshizi MA, Shahverdi A. Improvements in semen quality, sperm fatty acids, and reproductive performance in aged Ross breeder roosters fed a diet supplemented with a moderate ratio of n-3: n-6 fatty acids. Poultry Science. 2018; 97: 4113-4121.

[87] Teymouri Zadeh Z, Shariatmadari F, Sharafi M, Karimi Torshizi MA. Amelioration effects of n-3, n-6 sources of fatty acids and rosemary leaves powder on the semen parameters, reproductive hormones, and fatty acid analysis of sperm in aged Ross broiler breeder roosters. Poultry Science. 2020; 99: 708-718.

[88] Rossi G, Dias E, Bastos N, Vrisman D, Rodrigues N, Vantini R, *et al.* Sexual maturity and fertility-related measures in young Nellore bulls receiving long-term dietary supplementation with rumen-protected polyunsaturated fatty acids. Theriogenology. 2019; 139.

[89] Tran LV, Malla BA, Sharma AN, Kumar S, Tyagi N, Tyagi AK. Effect of omega-3 and omega-6 polyunsaturated fatty acid enriched diet on plasma IFG-1 and testosterone concentration, puberty and semen quality in male buffalo. Animal Reproduction Science. 2017; 173: 63-72.

[90] Safari Asl R, Shariatmadari F, Sharafi M, Karimi Torshizi MA, Shahverdi A. Improvements in semen quality, sperm fatty acids, and reproductive performance in aged Ross breeder roosters fed a diet supplemented with a moderate ratio of n-3: n-6 fatty acids. Poultry Science. 2018; 97: 4113-4121.

[91] Kapourchali FR, Louis XL, Eskin MNA, Suh M. A pilot study on the effect of early provision of dietary docosahexaenoic acid on testis development, functions, and sperm quality in rats exposed to prenatal ethanol. Birth Defects Research. 2020; 112: 93-104.

[92] Afolayan AF, Bolton JJ, Lategan CA, Smith PJ, Beukes DR. Fucoxanthin, tetraprenylated toluquinone and toluhydroquinone metabolites from Sargassum heterophyllum inhibit the in vitro growth of the malaria parasite Plasmodium falciparum. Zeitschrift fur Naturforschung. Section C - Biosciences. 2008; 63: 848-852.

[93] Airanthi MKW, Sasaki N, Iwasaki S, Baba N, Abe M, Hosokawa M, *et al.* Effect of brown seaweed lipids on fatty acid composition and lipid hydroperoxide levels of mouse liver. Journal of Agricultural and Food Chemistry. 2011; 59: 4156-4163.

[94] Wang PT, Sudirman S, Hsieh MC, Hu JY, Kong ZL. Oral supplementation of fucoxanthin-rich brown algae extract ameliorates cisplatin-induced testicular damage in hamsters. Biomed Pharmacother. 2020; 125: 109992.

[95] Ho H, Shirakawa H, Giriwono PE, Ito A, Komai M. A novel function of geranylgeraniol in regulating testosterone production. Bioscience, Biotechnology, and Biochemistry. 2018; 82: 956-962.

[96] Leite RP, Wada RS, Monteiro JC, Predes FS, Dolder H. Protective effect of guaraná (paullinia cupana var. sorbilis) pre-treatment on cadmium-induced damages in adult wistar testis. Biological Trace Element Research. 2011; 141: 262-274.

[97] Kara H, Orem A, Yulug E, Yucesan FB, Kerimoglu G, Yaman SO, *et al.* Hazelnut consumption improves testicular antioxidant function and semen quality in young and old male rats. Food Chemistry. 2019; 294: 1-8.

[98] Fatani AJ, Al-Rejaie SS, Abuohashish HM, Al-Assaf A, Parmar MY, Ahmed MM. Lutein dietary supplementation attenuates streptozotocin-induced testicular damage and oxidative stress in diabetic rats. BMC Complementary and Alternative Medicine. 2016; 15: 204.

[99] Sahan A, Akbal C, Tavukcu HH, Cevik O, Cetinel S, Sekerci CA, et al. Melatonin prevents deterioration of erectile function in streptozotocin-induced diabetic rats via sirtuin-1 expression. Andrologia. 2020; 52: e13639.

[100] Ohta Y, Yoshida K, Kamiya S, Kawate N, Takahashi M, Inaba T, *et al.* Feeding hydroalcoholic extract powder of Lepidium meyenii (maca) increases serum testosterone concentration and enhances steroidogenic ability of Leydig cells in male rats. Andrologia. 2016; 48: 347-354.

[101] Onaolapo AY, Oladipo BP, Onaolapo OJ. Cyclophosphamide-

induced male subfertility in mice: an assessment of the potential benefits of maca supplement. Andrologia. 2018; 50.
[102] Lembè DM, Gasco M, Gonzales GF. Synergistic effect of the hydroalcoholic extract from Lepidium meyenii (Brassicaceae) and Fagara tessmannii (Rutaceae) on male sexual organs and hormone level in rats. Pharmacognosy Research. 2014; 6: 80-86.
[103] O'Neill ME, Carroll Y, Corridan B, Olmedilla B, Granado F, Blanco I, *et al.* A european carotenoid database to assess carotenoid intakes and its use in a five-country comparative study. The British Journal of Nutrition. 2001; 85: 499-507.
[104] Alves É R, Ferreira CGM, Silva MVD, Vieira Filho LD, Silva Junior VAD, Melo IMF, *et al.* Protective action of melatonin on diabetic rat testis at cellular, hormonal and immunohistochemical levels. Acta Histochemica. 2020; 122: 151559.
[105] Pool KR, Rickard JP, Pini T, de Graaf SP. Exogenous melatonin advances the ram breeding season and increases testicular function. Scientific Reports. 2020; 10: 9711.
[106] Perumal P, Chang S, De AK, Baruah KK, Khate K, Vupru K, *et al.* Slow release exogenous melatonin modulates scrotal circumference and testicular parameters, libido, endocrinological profiles and antioxidant and oxidative stress profiles in mithun. Theriogenology. 2020; 154: 1-10.
[107] Samir H, Nyametease P, Elbadawy M, Nagaoka K, Sasaki K, Watanabe G. Administration of melatonin improves testicular blood flow, circulating hormones, and semen quality in Shiba goats. Theriogenology. 2020; 146: 111-119.
[108] Abdel-Aziz Swelum A, Saadeldin IM, Ba-Awadh H, Alowaimer AN. Effects of melatonin implants on the reproductive performance and endocrine function of camel (camelus dromedarius) bulls during the non-breeding and subsequent breeding seasons. Theriogenology. 2018; 119: 18-27.
[109] Othman AI, Edrees GM, El-Missiry MA, Ali DA, Aboel-Nour M, Dabdoub BR. Melatonin controlled apoptosis and protected the testes and sperm quality against bisphenol a-induced oxidative toxicity. Toxicology and Industrial Health. 2017; 32: 1537-1549.
[110] Bahrami N, Goudarzi M, Hosseinzadeh A, Sabbagh S, Reiter RJ, Mehrzadi S. Evaluating the protective effects of melatonin on di(2-ethylhexyl) phthalate-induced testicular injury in adult mice. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2019; 108: 515-523.
[111] Mohammadghasemi F, Jahromi SK. Melatonin ameliorates testicular damages induced by nicotine in mice. Iranian Journal of Basic Medical Sciences. 2019; 21: 639-644.
[112] Olukole SG, Ajani SO, Ola-Davies EO, Lanipekun DO, Aina OO, Oyeyemi MO, *et al.* Melatonin ameliorates bisphenol a-induced perturbations of the prostate gland of adult wistar rats. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2018; 105: 73-82.
[113] Olayaki LA, Alagbonsi IA, Abdulrahim AH, Adeyemi WJ, Bakare M, Omeiza N. Melatonin prevents and ameliorates lead-induced gonadotoxicity through antioxidative and hormonal mechanisms. Toxicology and Industrial Health. 2019; 34: 596-608.
[114] Richardson G, Wang-Weigand S. Effects of long-term exposure to ramelteon, a melatonin receptor agonist, on endocrine function in adults with chronic insomnia. Human Psychopharmacology. 2009; 24: 103-111.
[115] Mero AA, Vähälummukka M, Hulmi JJ, Kallio P, von Wright A. Effects of resistance exercise session after oral ingestion of melatonin on physiological and performance responses of adult men. European Journal of Applied Physiology. 2006; 96: 729-739.
[116] Luboshitzky R, Shen-Orr Z, Nave R, Lavi S, Lavie P. Melatonin administration alters semen quality in healthy men. Journal of Andrology. 2002; 23: 572-578.
[117] Herrero M, Arráez-Román D, Segura A, Kenndler E, Gius B, Raggid MA, *et al.* Pressurized liquid extraction-capillary electrophoresis-mass spectrometry for the analysis of polar antioxidants in rosemary extracts. Journal of Chromatography. 2005; 1084: 54-62.
[118] Attia YA, Hamed RS, Bovera F, Abd El-Hamid AEE, Al-Harthi MA, Shahba HA. Semen quality, antioxidant status and reproductive performance of rabbits bucks fed milk thistle seeds and rosemary leaves. Animal Reproduction Science. 2018; 184: 178-186.
[119] Mohamed MA, Ahmed MA, El Sayed RA. Molecular effects of Moringa leaf extract on insulin resistance and reproductive function in hyperinsulinemic male rats. Journal of Diabetes & Metabolic Disorders . 2019; 18: 487-494.
[120] Elblehi SS, El Euony OI, El-Nahas AF. Partial ameliorative effect of moringa leaf ethanolic extract on the reproductive toxicity and the expression of steroidogenic genes induced by subchronic cadmium in male rats. Environmental Science and Pollution Research International. 2019; 26: 23306-23318.
[121] Elnagar AMB, Ibrahim A, Soliman AM. Histopathological effects of titanium dioxide nanoparticles and the possible protective role of n-acetylcysteine on the testes of male albino rats. International Journal of Fertility & Sterility. 2019; 12: 249-256.
[122] El Shehaby DM, El-Mahdy RI, Ahmed AM, Hosny A, Abd El-Rady NM. Neurobehavioral, testicular and erectile impairments of chronic ketamine administration: Pathogenesis and ameliorating effect of N-acetyl cysteine. Reproductive Toxicology. 2020; 96: 57-66.
[123] Malmir M, Soleimani Mehranjani M, Naderi Noreini S, Faraji T. Protective antioxidant effects of n-acetylcysteine against impairment of spermatogenesis caused by paranonylphenol. Andrologia. 2019; 50: e13114.
[124] Jallouli M, El Bini Dhouib I, Dhouib H, Lasram M, Gharbi N, El Fazaa S. Disruption of steroidogenesis after dimethoate exposure and efficacy of n-acetylcysteine in rats: an old drug with new approaches. Environmental Science and Pollution Research. 2016; 23: 7975-7984.
[125] Jana K, Dutta A, Chakraborty P, Manna I, Firdaus SB, Bandyopadhyay D, *et al.* Alpha-lipoic acid andn-acetylcysteine protects intensive swimming exercise-mediated germ-cell depletion, pro-oxidant generation, and alteration of steroidogenesis in rat testis. Molecular Reproduction and Development. 2014; 81: 833-850.
[126] Oi-Kano Y, Kawada T, Watanabe T, Koyama F, Watanabe K, Senbongi R, *et al.* Oleuropein supplementation increases urinary noradrenaline and testicular testosterone levels and decreases plasma corticosterone level in rats fed high-protein diet. The Journal of Nutritional Biochemistry. 2013; 24: 887-893.
[127] Chen X, Ge F, Liu J, Bao S, Chen Y, Li D, *et al.* Diverged effects of piperine on testicular development: stimulating leydig cell development but inhibiting spermatogenesis in rats. Frontiers in Pharmacology. 2019; 9: 244.
[128] Kumari S, Nayak G, Lukose ST, Kalthur SG, Bhat N, Hegde AR, *et al.* Indian propolis ameliorates the mitomycin c-induced testicular toxicity by reducing dna damage and elevating the antioxidant activity. Biomedicine & Pharmacotherapy. 2017; 95: 252-263.
[129] Almeer RS, Soliman D, Kassab RB, AlBasher GI, Alarifi S, Alkahtani S, *et al.* Royal jelly abrogates cadmium-induced oxidative challenge in mouse testes: involvement of the NRF2 pathway. International Journal of Molecular Sciences. 2019; 19: 3979.
[130] Abbaszadeh A, Assadollahi V, Alasvand M, Anbari K, Tavakoli N, Gholami M. Protective effects of royal jelly on testicular torsion induced ischaemia reperfusion injury in rats. Andrologia. 2020; 52: e13716.
[131] Tohamy HG, Gad El-Karim DR, El-Sayed YS. Attenuation potentials of royal jelly against hydroxyurea-induced infertility through inhibiting oxidation and release of pro-inflammatory cytokines in male rats. Environmental Science and Pollution Research. 2019; 26: 21524-21534.
[132] Ahmed MM, El-Shazly SA, Alkafafy ME, Mohamed AA, Mousa AA. Protective potential of royal jelly against cadmium-induced infertility in male rats. Andrologia. 2018; 50: e12996.
[133] 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. International Journal of Fertility & Sterility. 2015; 9: 113-120.
[134] Amirshahi T, Najafi G, Nejati V. Protective effect of royal jelly on fertility and biochemical parameters in bleomycin-induced male rats. Iranian Journal of Reproductive Medicine. 2014; 12: 209-216.

[135] Shati AA. Resveratrol improves sperm parameter and testicular apoptosis in cisplatin-treated rats: effects on erk1/2, jnk, and akt pathways. Systems Biology in Reproductive Medicine. 2019; 65: 236-249.

[136] Salehi B, Mishra A, Nigam M, Sener B, Kilic M, Sharifi-Rad M, *et al.* Resveratrol: a double-edged sword in health benefits. Biomedicines. 2018; 6: 91.

[137] Banerjee B, Nandi P, Chakraborty S, Raha S, Sen PC, Jana K. Resveratrol ameliorates benzo(a)pyrene-induced testicular dysfunction and apoptosis: involvement of p38 mapk/atf2/inos signaling. The Journal of Nutritional Biochemistry. 2016; 34: 17-29.

[138] Banerjee B, Chakraborty S, Chakraborty P, Ghosh D, Jana K. Protective Effect of Resveratrol on Benzo(a)Pyrene Induced Dysfunctions of Steroidogenesis and Steroidogenic Acute Regulatory Gene Expression in Leydig Cells. Frontiers in Endocrinology. 2019; 10: 272.

[139] Guo Y, Wang A, Liu X, Li E. Effects of resveratrol on reducing spermatogenic dysfunction caused by high-intensity exercise. Reproductive Biology and Endocrinology. 2019; 17: 42.

[140] Jalili C, Roshankhah S, Salahshoor MR, Mohammadi MM. Resveratrol attenuates malathion induced damage in some reproductive parameters by decreasing oxidative stress and lipid peroxidation in male rats. Journal of Family & Reproductive Health. 2019;

[141] Abbaszadeh A, Assadollahi V, Alasvand M, Anbari K, Tavakoli N, Gholami M. Protective effects of royal jelly on testicular torsion induced ischaemia reperfusion injury in rats. Andrologia. 2020; 52: e13716.

[142] Schloms L, Smith C, Storbeck K, Marnewick JL, Swart P, Swart AC. Rooibos influences glucocorticoid levels and steroid ratios in vivo and in vitro: a natural approach in the management of stress and metabolic disorders? Molecular Nutrition & Food Research. 2014; 58: 537-549.

[143] Noh Y, Kim D, Kim JY, Park J, Kim OH, Han D, *et al.* Improvement of andropause symptoms by dandelion and rooibos extract complex crs-10 in aging male. Nutrition Research and Practice. 2013; 6: 505-512.

[144] Noh Y. Mr-10 enhances men's health by improving endogenous male sex hormone generation. Journal of Medicinal Food. 2018; 21: 1288-1294.

[145] Mannaa F, Ahmed HH, Estefan SF, Sharaf HA, Eskander EF. Saccharomyces cerevisiae intervention for relieving flutamide-induced hepatotoxicity in male rats. Die Pharmazie. 2005; 60: 689-695.

[146] Li Z, Yu Y, Li Y, Ma F, Fang Y, Ni C, *et al.* Taxifolin attenuates the developmental testicular toxicity induced by di-n-butyl phthalate in fetal male rats. Food and Chemical Toxicology. 2020; 142: 111482.

[147] Desjardins C. Endocrine regulation of reproductive development and function in the male. Journal of Animal Science. 1984; 47: 56-79.

[148] Kacker R, Traish AM, Morgentaler A. Estrogens in men: clinical implications for sexual function and the treatment of testosterone deficiency. The Journal of Sexual Medicine. 2012; 9: 1681-1696.