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Review

Current Applications and Trends in Rabbit Nutraceuticals

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Abstract: To ensure the sustainability of rabbit production and protect the global rabbit industry, cost-effective and practical strategies for improving rabbit production and meat quality must be developed. Recently, rabbit farming, like other animal farming, has faced feed shortages due to the impact of climate change, high competition among livestock species, and war conditions. The continued use of conventional feed additives in rabbit diets, whether derived from plant or animal sources, has become a critical issue. Furthermore, there is a global trend toward finding natural alternatives to synthetic drugs, such as antibiotics, in rabbit farms. Finding readily available and alternative feed additives is therefore critical to protecting the rabbit industry, particularly in subtropical and Mediterranean-developing countries. Nutraceuticals positively influence several physiological and productive traits in animals, as well as enhancing their health and welfare. The present review aims to provide an overview of previous studies on the potential of using some plant and animal products as nutraceutical alternatives and feed additives in rabbit diets, separately or in combination, to act as natural growth promoters, antioxidants, anti-inflammatory, and antimicrobial agents, and immunostimulants in rabbit farms. From the results, some unconventional plant and animal products, such as spirulina, garden cress, milk whey, and bee venom, can be successfully used as dietary supplements and substitutes in rabbit farms to motivate rabbit growth and reproduction, as well as enhance immunity. These products are rich in minerals, vitamins, enzymes, organic acids, flavonoids, and phenolic acids. These active substances benefit the animal's digestive tract in different ways, including activating the digestive enzymes and maintaining microbial balance, promoting vitamin synthesis. They also improve rabbit production, reproduction, and health.

Keywords: antioxidants; by-products; feed additives; immunostimulants; growth promoters; meat quality; rabbit reproduction

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1. Introduction

Rabbit (*Oryctolagus cuniculus* L.) is a key source of animal protein in certain European, Asian, and North African countries, including Spain, Italy, the Czech Republic, France, China, and Egypt [1]. Rabbit meat has several nutritional benefits, including a high protein content and a low cholesterol level [2,3]. Domestic rabbits are one of the most efficient cellulose converter animal species, ensuring the high production of low-cost meat [4]. Recently, rabbit farming, like other animal farming, has faced feed shortages due to the impact of climate change, high competition among livestock species, and war conditions. The previous factors, apart from the global economic recession, lead to a rise in the price of feedstuffs and livestock final products. It is well known that the diet is considered the most expensive item for livestock projects and the common goal of breeders and producers is to maximize profit and minimize production costs. To protect the global rabbit industry, practical feeding strategies for improving rabbit production and meat quality must be developed. For instance, to maximize the utilization of some by-product compounds, a number of processes, such as extraction, fermentation, drying, and combining with other essential elements like minerals and vitamins, may be carried out. However, it is very important to stop using traditional feed additives, whether they come from animal or plant sources, in rabbit diets and seek readily available and alternative feed additives to sustain the rabbit industry. It is well known that rabbit meat has excellent nutritional value and any significant modification in the diet composition of rabbits can impact their meat nutritional composition and quality preservation. Dietary modifications also are crucial for improving rabbit performance and behavior as well as for reducing the harmful effects of heat stress [5]. Heat stress damage to rabbits can be reduced through nutritional approaches in rabbit farms that face this issue [6].

Nutraceuticals are natural chemical substances that have a good impact on animal physiological and productive characteristics, and they can be divided into plant nutraceuticals such as medicinal herbs and animal nutraceuticals such as bee products, as well as nutraceutical enzymes such as xylanase (Figure 1). Nutraceutical plant products including herb, vegetable, and fruit seeds/leaves/roots belong to the most frequently used nutraceuticals in livestock farms and are recently gaining popularity in rabbit farms because of their nutritional value and therapeutic properties (Table 1) [7–17]. They can be added to rabbit diets, as a natural antioxidant and immunological stimulant, to improve rabbit growth performance and health [18]. Plant products are rich in essential oils and essential fatty acids, which have multiple advantages for the digestive system of animals, such as boosting the digestive enzyme activity and maintaining microbiota balance, thereby improving health and production [19–22]. These products have been shown to stimulate the expression of various genes involved in metabolism, growth, and immunity [23,24]. Additionally, the addition of essential oils to animal diets promoted the expression of some significant genes related to nutrient transportation (such as GLUT2 and SGLT1) [25].

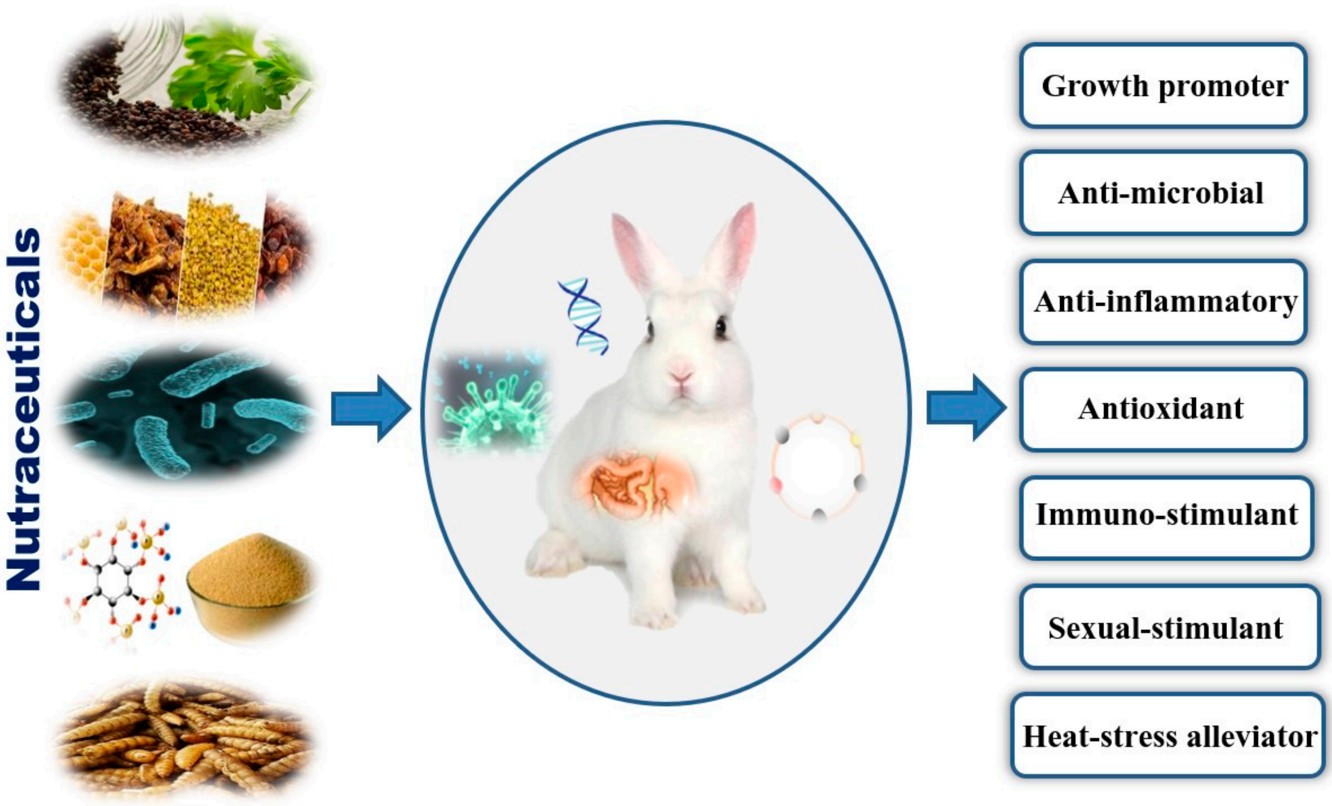

Figure 1. Schematic illustrating the biological functions of different nutraceuticals added to rabbit diets.

Table 1. Summary of some production and health benefits of supplementing rabbit diets with nutraceutical products.

Nutraceutical Products	Studied Traits	Benefits	References
Pumpkin (*Cucurbita* sp.) seed essential oil	Growth, antioxidant status, and immune response	Supplementing growing rabbit diets with pumpkin seed oil up to 2 mL/kg is recommended to improve growth, antioxidative status, and immunological performance, particularly under heat-stress conditions.	[7]
Rosemary essential oils	Growth, antioxidant status, and immune response	Rosemary essential oils can be used, separately or in combination, in rabbit diets to improve antioxidant status and stability, along with improved kidney function, without significant effects on rabbit growth and immunological performances.	[8,9]
Pale purple coneflower (*Echinacea pallida*)	Reproductive performance and hematological parameters	The reproductive and hematological parameters of the does have not been affected by the pale purple coneflower (3 g/kg of diet).	[10]
Goji berries (*Lycium barbarum*)	Body weight, reproductive performance, immune response, and meat quality	Goji berries have been shown to improve rabbit reproductive and productive performance, meat quality, and immunity.	[11]
Fenugreek (*Trigonella foenum-gracum*)	Productive performance and immune response	Fenugreek administration improves milk yield and quality of rabbit does, as well as bunnies' body weight and immunological performance.	[12]
Agro-industrial by-products	Growth performance and carcass quality	The substitution of fenugreek, garden rocket, and mustard seed meals for up to 50% of soybean meal in rabbit diets had positive economical results with no negative effects on growth and carcass.	[13]
Fenugreek seeds and probiotics	Growth performance and carcass quality	Fenugreek seeds and probiotics (15 g/kg of diet and 450 mg/kg of diet, respectively) supplementation improved rabbit growth performance and nutrient digestibility without affecting carcass quality.	[14]
Bee pollen and propolis	Reproductive performance and immune response	Bee pollen and propolis, administered separately or in combination to rabbit does at 150 or 300 mg, improve reproductive performance, milk production, and immune response.	[15]
Milk whey	Growth performance and meat quality	The addition of 2.25% whey powder improved the gut health of growing rabbits and increased their growth performance and thigh muscle quality.	[16]
Insect lipids	Growth performance and gut health	Black soldier flies and yellow mealworm fats can be used as a lipid source to replace soybean oil in rabbit diets without affecting growth performance, digestive process, and gut health.	[17]

Nutraceutical animal products, such as honeybees, worms, eggs, and milk products, could also be used in rabbit feeding to boost animal production and immunity (Table 1). Recently, nutraceuticals are being developed as nano-substances to provide accurate doses and defined effects, as well as treat some animal diseases, including nutritional deficiency. The current review discusses the significant effects of using some available plant and animal products in subtropical and Mediterranean-developing countries as natural and safe feed alternatives to antibiotics in rabbit farms, revealing their properties, doses, biological functions, and welfare impact. Additionally, it presented the feasibility of using agro-industrial by-products as ingredients in rabbit feed to reduce nutrition costs.

2. Effect of Nutraceutical Plant Products on Rabbit Production and Health Status

Rabbits have a short gestation period, rapid growth, and excellent feed efficiency. As a result, rabbits have a higher metabolic rate, which results in the generation of cellular free radicals. These free radicals may affect cellular functioning by increasing oxidative stress, inflammation, and immunosuppression [26]. Researchers recently investigated the ability of various botanical substances and their bioactive components to scavenge free radicals and restore cellular activities required for rabbit production and health.

Plant/botanical products are natural and vital substances widely used as dietary additives in livestock farms. They contain phytobiotics, phenols, flavonoids, tannins, and essential oils, which play a multitude of roles in a rabbit's body. The nutritional and medicinal properties of these substances mainly influence animal performance by improving digestion and enhancing immunity/health [19,20,27]. Additionally, several botanical products, including herbs, are considered phytogenic feed additives for livestock to improve growth performance and health status [28].

2.1. Thyme

Thyme (*Thymus vulgaris* L.) is a popular medicinal plant widely used in livestock farms to improve animal productivity and health due to its antioxidant, antibacterial, and therapeutic properties [29–31]. Dry thyme essential oil (active extract) contains a mixture of monoterpenes, primarily thymol (2-isopropyl-5-methylphenol) and the phenol isomer carvacrol (2-methyl-5-(propan-2-yl) phenol) [32]. Adding plant essential oils to the diet can reduce animal gastrointestinal lesions and enhance the ratio of villus height to crypt depth [33]. Catalase activity was boosted by essential oil phenolic components, which detoxified hydrogen peroxide and converted lipid hydroperoxides to harmless molecules [34]. By breaking up free-radical chains, thyme extracts have the potential to increase the oxidative stability of animal meat. This would provide a product with better oxidative stability [35]. It works by stimulating intramuscular fat and deposition of flavor amino acids. Phytogenic products containing thymol and carvacrol improved animal growth, gut health, and antioxidant enzyme activity [36]. Moreover, thyme extract contains flavonoids (>50%), which are considered antimicrobial and antioxidative agents [37]. Flavonoids increased vitamin C activity, which acts as an antioxidant, as well as improves immunological functions [36,38,39]. Thyme extracts can also reduce bad cholesterols, such as low-density lipoprotein, and this reduction can be related to HMG-CoA reductase activity inhibition which is among the enzymes responsible for controlling cholesterol metabolism in the body [40].

Ezzat Ahmed et al. [41] found that thyme leaf supplementation (4–16 g/kg of diet) can improve the rabbit's appetite, growth performance, and market body weight compared to the control. Thyme's antibacterial activity may be associated with increased rabbit body weight. The feed conversion ratio and weight gain were proportionate to the amount of thyme leaves consumed. Feeding with thyme leaves significantly reduced fecal ammonia [41]. Biomarkers showed that thyme leaves significantly improved liver and kidney function. Furthermore, testosterone levels and sperm quality were significantly higher in the thyme leaf-treated groups when compared to the control [41]. Thus, at an optimum dose of 16 g/kg of diet, thyme leaves could be a beneficial feed addition for rabbits living in hot climes, according to Ezzat Ahmed et al. [41]. In agreement, thyme oil supplementation (up to 150 mg/kg) can improve feed intake and growth performance compared to the control according to Abdel-Wareth et al. [42]. Thyme oil supplementation improved carcass quality by lowering perirenal and scapular fat without damaging internal organs. Thus, thyme oil can be used as an effective feed additive to improve rabbit productivity under hot environmental conditions [42]. Additionally, Benlemlih et al. [43] reported that supplementing rabbit diets with 5% of thyme can reduce mortality rates by 39%. According to Abdel-Wareth and Metwally [44], thyme essential oil levels supplementation (60–180 mg/kg of the diet) significantly improved the feed conversion ratio and body weight gain of treated rabbits compared to the control. This supplementation also significantly increased serum testosterone concentration and decreased aspartate transaminase, alanine transaminase, urea, and creatinine compared to the control group. Furthermore, it enhanced the semen characteristics of male rabbits compared to the control group. Likewise, Abdelnour et al. [5] revealed that thyme essential oil at a level of 100 mg/kg of the diet increased total proteins, albumin, globulin, blood hemoglobin, total antioxidant capacity, hematocrit, and glutathione of treated rabbits while decreasing malondialdehyde level. Immunological variables (IgG and IgM), milk production, and ovulation rate were also improved by this supplementation. Hence, dietary thyme essential oil can alleviate the negative impacts of heat stress on female rabbits by improving their antioxidant and immunological statuses [5]. Generally, plant essential oil supplementation positively influenced animal gut microbiota and boosted crypt depth in the ileum. Moreover, it decreased claudin-1 mRNA expression, as well as increased interleukin-1β and toll-like receptor (TLR) 2 mRNA expression in the ileum [33]. Furthermore, thyme oil significantly improved blood antioxidant capacity and glutathione peroxidase activity in the liver [45]. It also decreased malondialdehyde levels in the duodenal tissue and increased transepithelial electrical resistance values [45].

On the other hand, thyme can be added to the rabbit diet combined with other natural botanical substances to increase the diet's nutritive value or to decrease diet costs. Spirulina (*Arthrospira platensis*) is a unicellular cyanobacterium alga with numerous health benefits, therapeutic properties, and other biological properties [46]. Supplementing growing rabbit diets with 3% thyme (in substitution of alfalfa meal) and 5% spirulina (in substitution of soybean meal) for 3 or 6 weeks did not significantly impact rabbit growth performance and health status, but it reduced diet costs and improved rabbit meat quality [47,48]. Kovács et al. [49] noticed that dietary spirulina supplementation had no discernible effect on rabbits' antioxidant status of blood, but it enhanced immunity by increasing IgG production in the rabbit's body. El-Ratel et al. [50] reported that the combination of spirulina (*Spirulina platensis*) (5 g/kg of the diet) and selenium nanoparticles (0.5 mg/kg of the diet) for 5-week pre-mating significantly increased live litter size and viability rate at birth, hemoglobin and red blood cells, and plasma T_3, T_4, insulin, and total protein compared to the control. Plasma estradiol 17-β (pre-mating), progesterone (mid-pregnancy), and prolactin (day-7 postpartum) were significantly increased by selenium nanoparticles supplementation (0.3, 0.4, and 0.5 mg/kg of the diet). The supplements also reduced white blood cells, cortisol, and lipid profile, and improved liver and kidney functions. Furthermore, superoxide dismutase was increased by selenium nanoparticles supplementation at the levels of 0.4 and 0.5 mg/kg of the diet, whereas malondialdehyde was reduced by 0.3, 0.4, and 0.5 selenium nanoparticles mg/kg of the diet. Sexual receptivity, ovulation rate, and pregnancy rate were significantly increased by increasing selenium nanoparticles above 0.1 mg, whereas embryo yield was increased by >0.2 mg selenium nanoparticles/kg of the diet. Therefore, a combination of spirulina and selenium nanoparticles in combination with thyme could potentially be used as feed additives to rabbit diets to improve heat regulation and rabbit reproduction, particularly in subtropical countries. Working on dietary supplementation of thyme oil (1000 mg thyme oil/kg of the diet) with betaine (1500 mg) and their combination, Abd El-Azeem et al. [51] indicated that feed dry matter digestibility and digestible energy were significantly improved in treated NZW rabbits compared to the control. Hematological parameters, feed intake, and carcass quality were not significantly affected by these supplementations, but daily weight gain was significantly increased in treated rabbits. Feed conversion ratio and economic efficiency recorded the best results with the treated rabbits.

2.2. Garden Cress

Garden cress seed (*Lepidium sativum*) is a valuable medicinal plant product that has recently gained global attention due to its nutritional and pharmaceutical properties, resulting in the development of novel feed additive sources [22]. These seeds have a high protein content (~25%) and are nearly equal in healthy fats. They are also high in vitamins and minerals, which are necessary for animal physiological and biological functions [22,51–53]. Furthermore, they contain phytochemical components that contribute to their high antioxidant properties [52–54]. Polyphenols, flavonoids, antioxidants, and polyunsaturated fatty acids (PUFA) are abundant in garden cress seeds [22]. These substances influence a number of biological processes in an animal's body, including the stimulation of growth genes, the advancement of metabolic processes, and the improvement of product quality by raising PUFA and lowering bad cholesterol levels [23,33,55,56]. They also contain aromatic essential oils that have a variety of therapeutic and nutritional benefits for farm animals. Several types of radicals are lowered by natural vital substances that exist in garden cress oil such as tocopherol (an antioxidant), carotenoid, oleic acid, and α-linolenic acid [57,58]. In addition, it contains α-linolenic acid, which can be converted in the body to eicosapentaenoic acid and docosahexaenoic acid [59]. Therefore, garden cress can be added as a potential feed additive for better biological and productive performance, health status, and economic efficiency [60,61]. El-Gindy et al. [62] reported that including 3% garden cress seeds in the female rabbit diet increased the litter weight of heat-stressed rabbits on the 7th, 14th, and 21st days of age. On the 28th day of weaning, it increased milk yield. Furthermore, blood lipid profile parameters (such as cholesterol and triglyceride levels) and serum urea levels were reduced in the treated rabbits, whereas antioxidant status was improved, particularly with 6% garden cress supplementation. Morshedy et al. [63] reached the same conclusion, recommending 3–4.5% garden cress seeds as a dietary supplement for growing rabbits to improve growth, feed utilization, digestibility, and immune response.

2.3. Azolla

Azolla (*Azolla pinnata*) is a tiny aquatic fern that can withstand high temperatures and lives afloat on the water's surface. It is high in proteins (~30%), vitamins (20–30%), and minerals (10–15%), and has a low fiber content (11–13%) [64–67]. Moreover, it contains a high level of carotenoids, which have beneficial biological properties that support therapeutic benefits, such as immunological, anti-inflammatory, and antibacterial implications, and improve animal growth and productivity [68]. Nonetheless, Azolla can be successfully used as an unconventional feedstuff in livestock diets because of its high nutrient content [69]. Azolla also is an inexpensive alternative protein source for animals, and because of its high nutritive value and low lignin content, it is easily digestible and could increase animal feed efficiency, average daily gain, and milk production by 15–20% [64,70]. The Azolla plant's high antioxidant enzyme content can reduce free radical activity in the animal's body [64]. In general, there are a few articles that discussed using Azolla in rabbit farming. Unfortunately, they offered a different chemical analysis of Azolla. It might relate to employing various Azolla species or where this plant is grown. The main issue with using Azolla on a large scale in livestock farms was the high concentration of water (~88%), but now, there are advanced procedures and inexpensive techniques to address it.

According to Anitha et al. [71], adding fresh Azolla to rabbit diets up to 60% of the basal diet had no impact on the vital organs, carcass traits, and meat chemical composition. Therefore, the unconventional feed Azolla can be recommended for growing rabbit diets and reducing diet item costs. Sireesha et al. [72] concluded that the replacement of conventional protein sources with sundried Azolla in rabbit diets by up to 10% improved the body weight gain and feed conversion efficiency in New Zealand rabbits under tropical conditions. Abdelatty et al. [73] found that incorporating 10% dried Azolla leaf meal into growing rabbit diets improved production performance and meat quality by increasing body weight and modulating the meat amino acid profile. The effect was achieved in part through rapamycin (mTOR) activation (involved in the initiation of protein synthesis). Nevertheless, higher doses of Azolla leaf meal did not appear to have positive effects on growing rabbits. On the other hand, El-Deeb et al. [74] found that the inclusion of dried Azolla substitution of up to 40% of soybean protein in the diet of growing rabbits during 5–14 weeks of age positively affected growing rabbits' productive performance and feeding economic efficiency with no adverse impact on blood biochemical and carcass traits, particularly under Egyptian environmental conditions.

2.4. Turmeric

Turmeric (*Curcuma longa* L.) is a rhizomatous herbaceous plant belonging to the ginger family. It has a significant amount of curcumin, which is frequently used as a spice and food color [75]. Turmeric has been classified as a natural polyphenol nutraceutical and is well known for lowering oxidative stress and repairing the harm that oxidative stress has produced. Therefore, it can be used in animal diets to mitigate heat stress, especially in tropical and subtropical zones where high temperatures can delay growth and impact reproduction [76,77]. According to Sharma et al. [78], curcumin (the active extract of turmeric) has been linked to a number of biological processes, including antioxidant and anti-cancer actions. In addition, numerous scientific investigations have demonstrated the anti-inflammatory and lipid- and cholesterol-lowering benefits of curcumin [79,80]. Alagawany et al. [81] found that turmeric addition (2–6 g/kg) had no effects on rabbit growth, but improved the immunity responses and hepatic antioxidant activity in treated rabbits as well as lowered the lipid profile in the blood and lipid peroxidation in the liver. According to Sirotkin et al. [82], dietary turmeric powder at 5 and 20 g per 100 kg of the diet increases rabbit viability and fecundity (the number of liveborn and weaned pups), as well as the production and growth of ovarian follicles by altering ovarian hormone release and ovarian follicle response to gonadotropin. Moreover, Kaegon et al. [83] revealed that supplementing the growing rabbit diet with turmeric at the levels of 0.5–0.9 g per kg of the diet resulted in beneficial effects on serum metabolites, particularly creatinine, glucose, urea, cholesterol, conjugated bilirubin, total bilirubin, albumin, and total protein. El-Rawi et al. [84] stated that turmeric powder (4–8 g/kg of diet) could improve rabbit growth, digestibility, and some carcass traits. Furthermore, it enhanced immunity and served as an exogenous antioxidant. It can reduce free radicals by activating glutathione (GSH), catalase, and superoxide dismutase (SOD), and limiting ROS-producing enzymes [85,86]. Likewise, turmeric extract (1–2 mg/kg of the diet) improved rabbit productive performance (such as body weight gain and feed conversion ratio), has remarkable antioxidant properties, and can be used in conjunction with a miticide to treat rabbit sarcoptic mange [87]. In agreement, Okanlawon et al. [88] concluded that 1% turmeric supplementation was found to be the most cost-effective level of inclusion for weight gain, efficient feed utilization, optimum profit, and economic benefit.

2.5. Olive

Olive (*Olea europaea* L.) is among the most widely cultivated crops in Mediterranean countries, accounting for more than 95% of global olive production. It provides several by-products, such as leaves, cake, and oil, which are regarded as some of the most significant nutraceutical substances due to their nutritional and healthful properties. Olive leaves, cake meal (olive oil extraction by-product), and oil are employed in animal feeds as a source of energy and antioxidant substances [89]. Olive leaves display excellent preventative effects against oxidation due to their high antioxidant activity, which is derived from phenolics [90,91]. Olive cake meal has a high nutritional value (~10% crude protein and ~15% crude fat) [92,93]. It has a high concentration of non-starch polysaccharides and lignin [89,94]. Moreover, it contains a good amount of vitamin E, calcium, phosphorus, potassium, magnesium, sodium, and iron [95]. The use of olive cake meals as a plant source for animal diets is widespread and available in many nations for an affordable price [96]. The high oleic acid (common monounsaturated fatty acid) concentration of olive oil distinguishes it from other vegetable oils [97]. Polyunsaturated fatty acids, polyphenols, and other vital substances found in olive products increased the animal's productivity and immune response by significantly affecting the metabolism and white blood cells and cytokines production [33,98–102]. The large concentrations of monounsaturated fatty acids and the presence of underrepresented substances such as alpha-tocopherol, phenolics, chlorophyll, and carotenoids provide olive oil its usefulness [103]. The therapeutic effects of olive by-products may be owing to their high quantity of important and biological substances such as monounsaturated fatty acids, polyunsaturated fatty acids, and polyphenols, as well as their strong antioxidant capacity [104]. Additionally, olive oil promotes the absorption of vitamin A (another fat-soluble vitamin) which may raise the level of high-density lipoprotein cholesterol in the blood [105]. Consequently, olive oil is a good vitamin D solvent and can raise the levels of calcium in an animal's body [106]. In this manner, Salama et al. [107] reported that the incorporation of olive cake with the nucleus at the level of 30% of the rabbit diets (by substituting clover hay and provided with 1% bentonite) significantly increased globulin concentration while decreasing the value of plasma cholesterol and total lipids in the treated rabbits, as well as resulting in the best total volatile fatty acids concentration in the cecal. Likewise, Dal Bosco et al. [108] mentioned that olive cakes have a high phenolic concentration and peroxide value and are rich in critical nutrients. They also emphasized the benefit of the stoning procedure, which minimizes the oxidative destruction of phenols in seed, which has the highest peroxide activity. Furthermore, the drying procedure used on the fresh pomaces may have helped to keep them from oxidizing [108]. Consequently, the addition of olive cake to animal diets can impact innate immunity as well as oxidative condition. Therefore, rabbits given a high quality of this by-product had better oxidative damage protection. Younan et al. [109] reported that under Egyptian environmental conditions, dietary supplementation with olive leaf extract at levels of 1 and 1.5 mL/kg of diet could be successfully saved and useful for growing rabbits in terms of improved production performance, alleviation of post-weaning stress, and high profitability. Furthermore, Mattioli et al. [110] investigated the use of selenium-fortified olive leaves (10% olive leaves enriched in selenium (2.17 mg of selenium per kg of dried olive leaves)) as a dietary supplementation for growing rabbits to improve the nutritional characteristics of rabbit meat. They discovered that the meat of rabbits treated with this supplementation had a better oxidative status and nutritive value. The use of selenium-fortified olive leaves improved the lipid oxidative stability of rabbit meat. In addition, Mattioli et al. [111] observed that the combination of selenium and olive leaves in the growing rabbit diet increased plasma selenomethionine and the ferric-reducing ability of plasma and reduced leukocyte DNA damage. Working on dietary polyphenols obtained from the olive oil industry to improve mammalian reproduction, Maranesi et al. [112] found that polyphenolic concentrate (282.4 mg/kg of the diet), obtained from olive mill wastewaters, inhibited inflammatory and apoptotic activities in rabbit ovary by modulating gene and protein expressions of cyclooxygenase-2 and BCL2-associated X protein, which has a significant positive impact on rabbit female reproduction.

3. Effect of Nutraceutical Animal Products on Rabbit Production and Health Status

In order to lower animal diet costs, it becomes critical to use nutraceutical animal products and by-products, such as bee royal jelly and milk whey protein, as healthy/safe nutritious substitutes. By subjecting some animal products to specific procedures, such as fermentation, and combining them with other nutraceuticals, their nutritional value can be increased. The current subtitle indicated that animal nutraceutical products, such as milk and honeybee products, could be used in rabbit diets to improve animal production, reproduction, and immunity.

3.1. Milk Products

Milk products, such as yogurt, casein, skim milk, and fermented milk, have gained popularity among health-conscious consumers due to their nutritional value and health-enhancing properties. Milk by-products, such as whey protein, are substances produced during the manufacturing of various dairy products and contain several essential and vital nutrients required for animal and human growth and health maintenance. Furthermore, lactic acid bacteria produce inhibitory compounds including organic acids, H_2O_2, and bacteriocins which can inhibit several pathogenic organisms' activities [113]. Atallah et al. [114] investigated the effects of supplementing yogurt with 1% whey protein concentrate, Ca-caseinate, and Spirulina platensis on some physiological parameters and meat quality traits of V-line rabbits fed yogurt (at a dose of 5 g/kg body weight/day). They revealed that this combination significantly boosted the growth performance, physicochemical, microbiological, biochemical traits, and meat quality of rabbits. Thus, it can be used as a functional food for rabbits. On the other hand, bovine colostrum is high in nutrients, antioxidants, and antimicrobial agents; thus, it has been used as a beneficial addition to animal nutrition. Castrica et al. [115] reported that the dietary supplementation of colostrum enhanced the oxidative fatty acid capacity of rabbits, but it appears that increasing its percentage of supplementation in the diet up to 5% increased the amount of saturated fatty acids to the disadvantage of monounsaturated fatty acids in rabbit meat. Such a change in fatty acids is clearly undesirable from a nutritional standpoint. Therefore, further studies are needed to determine the optimal colostrum concentration that allows for antioxidant action on meat without compromising health.

Milk whey, a by-product of the cheese industry, has high nutritional and biological value and can be used in animal diets [116]. As it contains a high amount of essential amino acids, whey protein can rapidly increase plasma amino acid concentration to improve the animal body's ability to use proteins [117]. In particular, whey protein contains branched-chain amino acids, especially leucine, which plays a vital role in regulating the initiation translation pathway of muscle protein, as well as modulating the metabolism of muscle protein [118]. Whey powder comprises about 65% lactose, which will promote the development of lactic acid bacteria (natural probiotics) in the animal's gastrointestinal tract. Additionally, the whey proteins' inclusion of β-lactoglobulin and α-lactalbumin can strengthen animals' immunity and increase their chances of surviving [119]. Kishawy et al. [16] investigated the effect of adding graded levels of whey powder to the rabbit diet. They reported that the addition of 2.25% whey powder improved the gut health of growing rabbits while increasing growth performance, nutrient digestibility, and crude protein content of the thigh muscle.

3.2. Honeybee Products

Natural substances produced by honeybees (*Apis mellifera*), such as honey, royal jelly, propolis, bee pollen, and bee venom, have distinctive structures rich in active components of enzymes and peptides that have several pharmaceutical properties [120]. These substances also have a significant impact on the physiological and productive performance of animals in addition to having a high nutritional value. These nutritional and therapeutic alternatives have primarily been employed in China and Egypt for centuries, as well as described in some religious books such as the Quran. In terms of natural medicinal effects, bee products can play an important role as a potential natural contrast to the virus by enhancing human and animal immunity defense [121]. In this view, several studies, such as [122–125], reported that bee products can improve animals' meat quality, apart from the development of their immunological performance, due to their high levels of essential amino acids, active enzymes, vitamins, minerals, antimicrobial, and immunostimulant substances. Bee products can also enhance animal fertility (males and females) by improving cryopreservation of gametes [125].

Working on slum gum as a honeybee product, Ojebiyi et al. [126] discovered that bee slum gum meal can be used as a substitute for maize in growing rabbit diets by up to 25% to reduce diet costs, after which performance starts to decline. On the other hand, Attia et al. [127] found that bee pollen (200 mg/kg body weight), with or without propolis, can increase the productive and reproductive performance, as well as the economic efficiency of rabbit does. A bee pollen and propolis combination positively boosted the body weight of rabbits (17.7%), decreased feed intake (4.49%), and increased litter size (39.4%), as well as the milk yield (43.6%). Furthermore, bee pollen with propolis greatly improved some biochemical parameters, including plasma total protein (43.1%), globulin (41.0), and progesterone (60.5%), as well as decreased plasma cholesterol (31.1%), and the aspartate aminotransferase/alanine aminotransferase ratio (20.3%). The treated rabbit females also had a higher fertility rate (21%) and significantly fewer services per conception (22%) than the control group. According to Zeedan et al. [128], supplementing the rabbit diet with 700 mg bee pollen/kg body weight increased body weight and body weight gain while decreasing daily feed intake due to the improved feed conversion rate of treated rabbits. Additionally, immunological parameters, blood biochemical profiles, and kidney functions were improved in treated groups compared to the control. Working on propolis, Al-Homidan et al. [129] reported that adding propolis to rabbit diets (250–500 mg/kg of diet) had a positive impact on lowering the colonization of *Salmonella* spp. and *Escherichia coli* in the cecum of treated rabbits. They concluded that propolis supplementation can significantly enhance the immunological response of growing rabbits by altering the cecal microbiota in a positive way. Furthermore, Sierra-Galicia et al. [130] indicated that propolis supplementation (50 µL/kg body weight) can serve as a natural growth promoter in rabbits and prevent coccidiosis without impacting rabbit health and meat quality. According to Sierra-Galicia et al. [131], rabbit diets supplemented with bee pollen and propolis have been found to increase weight gain while decreasing the feed conversion rate and raising the overall antioxidant capacity in blood serum. It is known that bee pollen (also known as bee bread) is a raw material collected from some plants and combined with special enzymes and natural substances derived from bee salivary gland secretion. It has been used as natural growth and health promoter in animal farms due to its high content of amino acids, vitamins, minerals, polyphenols, and tannins [132,133]. Abdelnour et al. [134] concluded that bee pollen can increase the animal's body weight gain by improving the feed conversion rate and increasing the intestinal villi surface of the duodenum, jejunum, and ileum [135]. Furthermore, a decrease in fat deposition and an increase in amino acids could be attributed to bee pollen as the underlying mechanism for improving carcass and meat quality. On the other hand, bee propolis (also known as bee glue) is a natural resinous substance rich in active enzymes, vitamins, and minerals [136]. The main substances interacting with propolis' biological properties are aromatic acids, flavonoids, and phenolic compounds [137,138]. The previous findings imply that bee pollen and propolis may be utilized as natural growth promoters and health enhancers. Thus, the results of using bee products are promising for further investigations aimed to improve rabbit productivity, intestinal health, and immunity, as well as save diet expenditures.

Royal jelly is a popular bee product that is widely used as natural food for humans and animals due to its high content of essential nutrients. It is high in Vitamins B and C, folic acid, and phenolic acids. It is also a good source of minerals (macro and micro). It performs numerous vital biological functions in a living being, including acting as an antioxidant, immunostimulant, and growth promoter [139]. The presence of polyphenolic compounds in royal jelly is primarily responsible for its antioxidant activity. It can be used in livestock farms to improve the growth rate, gut health, and immune response, as well as to produce high-quality and safe animal products [139,140]. According to Elnagar et al. [141], administering royal jelly to growing rabbits under heat stress can improve body weight gain and feed conversion ratio as well as alleviate the physiological stress imposed by heat stress. In agreement, El-Hanoun et al. [142] discovered that providing heat-stressed male rabbits with royal jelly (150 mg/kg of body weight) can improve their physiological status, particularly liver and kidney functions, with lower levels of oxidative stress biomarkers, and prevent summer infertility. This treatment has a beneficial impact on libido, sperm quality, sperm production, blood testosterone levels, total proteins, glucose, and fertility. Additionally, concentrations of abnormal and dead sperm were decreased.

Bee venom is another bee product that is produced in the venom gland of honey bees and has a number of pharmaceutical and medical properties [143]. It is made up of a variety of substances, including peptides and enzymes, with melittin being the most effective [144]. It also contains important substances such as apamin and adolapin (polypeptides), which have anti-inflammatory and antibacterial properties [145]. As a result, bee venom can be added to the animal diet to enhance productivity [146] and health status [144], such as disease prevention/treatment. El-Hanoun et al. [147] and Elkomy et al. [148] stated that bee venom can also be an effective and safe alternative to be used in rabbit farms instead of artificial sexual stimulants that can harm the consumer's health. It can promote the reproductive efficiency, serum quality traits, and antioxidant activity of rabbits, as well as enhance their immunological performance by using small doses (0.1–0.3 mg/kg).

3.3. Insect Products

In the development of sustainable feed ingredients for farm animals, insect products are now being considered to supplement/replace conventional feedstuffs. The potential use of insect products in rabbit diets has received little attention and investigation. Kowalska et al. [149] revealed that partially replacing soybean meal with silkworm pupae and mealworm larvae meals in rabbit diets could improve body weight and gain, as well as some carcass characteristics (such as the amount of ether extract in the muscles), without affecting the feed conversion rate. In this manner, Dalle Zotte [150] reported that the inclusion of the black soldier fly (*Hermetia illucens*) has supported animal meats with higher levels of saturated fatty acids, whereas the yellow mealworm has a higher level of monounsaturated fatty acids. The silkworm has a more unsaturated fatty acid profile and is rich in valuable omega-3 fatty acids, but this has rarely changed the related physicochemical variables and the sensory profile of the meat. Consequently, the meat's fatty acid profile can be affected by the insect species in the diet and could be improved by manipulating the insect substrate or using mixtures of insect meal or oil from different insect species [151]. According to Gasco et al. [152], offering two types of insects (mealworms and houseflies) to rabbits resulted in no difference between the control and experimental groups in terms of growth performance, blood metabolites, and mortality. The increase in fats in mealworms and houseflies had no effect on dry matter digestibility, fiber fraction, or energy. Furthermore, the meat of the rabbits fed diets containing insect fat, either from the black soldier fly or yellow mealworm (*Tenebrio Molitor*), was less susceptible to oxidation compared to the control [17]. The use of insect fats increased the saturated fatty acids proportion and the n-6/n-3 polyunsaturated fatty acids ratio of rabbit meat, particularly for black soldier fly fat. The findings of Dabbou et al. [153] demonstrated the potential use of the black soldier fly and yellow mealworm as antibacterial feed ingredients with a positive impact on the rabbit's cecal microbiota. Hence, black soldier flies and yellow mealworm fats may be viable lipid alternatives to soybean oil in rabbit diets.

4. Conclusions

Recent nutraceuticals, such as spirulina, Azolla, garden cress, yogurt, milk whey, and bee venom, can be used successfully as unconventional dietary alternatives in rabbit farming. Due to their nutritional and therapeutic properties, these natural substances are considered functional foods. Based on the previous and current findings, plant and animal products are recommended as natural/safe feed additives and substitutes for any artificial drugs, such as antibiotics, in rabbit farms. These natural substances can be added to the rabbit diet separately or in combination to improve the productive, reproductive, physiological, and immunological performances that impact rabbit welfare and quantitative and qualitative productivity. Additionally, it becomes critical to use plant and animal by-products to reduce animal diet costs. By subjecting them to specific procedures, such as fermentation, and combining them with other nutraceuticals, their nutritional value can be increased. Nutraceuticals are recommended to be used in rabbit farms as promising growth, reproduction, and health promoters for rabbit production sustainability, particularly for temperate and subtropical countries.

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