



REVIEW ARTICLE

The multifaceted potential of fennel: From antioxidant to biostimulants

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Abstract

The Apiaceae family, which includes *Foeniculum vulgare* Mill., has several traditional and therapeutic uses. It has been utilized extensively as a vital medication to cure a variety of illness and well-known nutraceuticals worldwide. It has been discovered that many phytochemicals, including anethole, fenchone, limonene, estragole, and p-coumaric acid, fatty acids, flavonoids, phenolic compounds, and volatile compounds are present in different parts of this plant. The two main compounds identified from *F. vulgare* are anethole and fenchone, which have been shown to have significant antioxidant, anticancer, carminative, diuretic, and galactagogue properties. The antioxidant properties of fennel acting as a source of nitric oxide are also documented and make it more suitable for combating oxidative stress. Nitric oxide plays various roles in animals and plants, which makes it a significant universal signaling molecule. At the same time, there is increasing social pressure to reduce the use of antibiotics and substitute them with alternative feed additives for animal husbandry. Consumers believe that phytochemical products are the safest solutions available. Fennel improves health and productivity by acting as a phytochemical feed additive for both humans and cattle. In order to lessen reliance on chemical fertilizers, the agriculture sector is currently using more biostimulants. Fennel is increasingly being used as a biostimulant to a safe and ecologically sound approach for improving crop yields. In order to provide a foundation for future study and development on this medicinal plant, this review outlines its antioxidant properties, biostimulant nature, and possible advantages of employing it as a phytochemical product in animal husbandry.

Keywords: Fennel, Pharmacological action, Antioxidants, Nitric oxide, Phytochemical, Oxidative damage, Biostimulants.

Introduction

There is an urgent need to search for new natural compounds with diverse chemical structures and novel mechanisms of action because there has been an alarming increase in the incidence of new infections and disease. Indeed, natural crude extracts and biologically active compounds from plant species used in traditional medicine may represent valuable sources for such new preservatives. *Foeniculum vulgare*, commonly known as fennel, is a well-known aromatic plant having wide application.

Fennel is regarded as the oldest spice plant and one of the most potent therapeutic herbs in the world because of

its commercial importance and widespread occurrence in arid and semi-arid climates. Because of its anti-inflammatory, antispasmodic, antibacterial, carminative, diuretic, and analgesic qualities, fennel is helpful in the treatment of gastrointestinal diseases. Because of its antioxidant and anti-ulcer properties, it is also used to treat neurological issues (Kooti *et al.*, 2015). This plant is rich in phytoestrogens, which cure various types of diseases (Saharkhiz & Tarakeme, 2011).

Fennel seeds contain volatile essential oils that contain fenchone, anethole, myrcene, limonene, chavicol, cineole, anisic aldehyde, and pinene, as well as amino acids, phenolic compounds, and flavonoids (Ben Abdesslem *et al.*, 2021). Fennel essential oil is used in cosmetics, pharmaceuticals, and perfumery and as a food additive and flavoring agent in food products (Mohamad *et al.*, 2011).

This therapeutic plant contains natural compounds, particularly antioxidants.

These include α -tocopherol, B complex, β -carotene, zinc salts, vitamins, glutamic acid, selenium salts, phosphorus salts, hydrolyzed collagen, magnesium salts, chondroitin sulfate, soy lecithin, and glycosaminoglycan sulfate (Bahmani, Darbandi, Ramshini, Moradi, & Akbari, 2015). According to a recent study, *Fennel* reduced neuronal toxicity by stabilizing the expression levels of oxidative stress indicators and

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amyloid precursor protein isoforms (Özbek *et al.*, 2003). Because of its anti-cholinesterase properties, *Fennel* extract may help people with dementia and Alzheimer's disease to regain their memory. Fennel acts as a source of a signaling molecule called nitric oxide, which helps in the cure of cardiovascular disease to various types of cancer (Ekhlaque A. Khan, 2022). Nitric play an important role in amelioration of oxidative stress caused due to various type of stress. It also play important role in physiological as well as pathological responses in plants (E. A. Khan, Ahmed, *et al.*, 2022; E. A. Khan, M. I. Ahmed, Misra, Sharma, & N. Misra, 2022).

The use of phytochemicals from medicinal plants in animal diets has a greater impact on product quality and consumer health than on output. The use of phytogenic feed additives or herbal plants as antibiotics becomes a viable option because they improve a variety of critical functions in the animal body. Because these phytogenic plants are natural products, consumers may be willing to accept their inclusion in poultry diets. Extensive research has demonstrated that phytogenic plants contain growth-promoting, antimicrobial, antioxidant, and anti-inflammatory effects (Biswas, Ahn, & Kim, 2024). Phytogenic feed additives are supplements that use specific ingredients to improve feed quality, animal health, and animal products.

In order to increase plants' tolerance to stress, an exogenous boosting strategy is required, such as the use of plant extracts as bioactive stimulants (Desoky, Elrys, & Rady, 2019) and nitric oxide. Numerous bioactive substances, including as diverse antioxidants, minerals, and osmoprotectants, are present in a variety of plant extracts. These bioactive components are essential for bolstering plants' defense mechanisms and successfully combating a variety of stressors (Rehman, Alharby, Alzahrani, & Rady, 2018). To help stressed plants, extracts from various plant components are employed as bioactive stimulants. Extracts rich in osmoprotectants, antioxidants (such as proline, free amino acids, soluble sugars, phenolic compounds, glutathione, α -tocopherol, etc.), and other nutritional components can be found in fennel seeds. To the best of our knowledge, however, no research has been done on fennel seed extract as a bioactive stimulant. However, nitric oxide has antioxidant properties and helps in ameliorating the stress of plants (E. A. Khan, Ahmed *et al.*, 2022; E. A. Khan, M. I. Ahmed, *et al.*, 2022; E. A. Khan, Misra, Sharma, & Misra, 2017).

The goal of this review is to focus on the nutritional value and the antioxidant properties of fennel in order to disclose its medical potential and future research directions. This review discusses the potential benefits of using fennel seeds as a phytogenic product in animal husbandry. This review also assess the importance of this herb as a biostimulant for agriculture which is need of time.

Antioxidant activity of Fennel

Reactive oxygen molecules, or reactive oxygen species (ROS), are byproducts of biological reactions and exogenous

factors. They include free radicals such as hydroxyl radicals ($\text{OH}^\cdot$), peroxy radicals ($\text{ROOH}^\cdot$), superoxide radicals ($\text{O}_2^{\cdot-}$, $\text{OOH}^\cdot$), and non-free radicals such as hydrogen peroxide (H_2O_2). Moreover, ROS cause the oxidation of a number of biomolecules within the cell, including proteins, lipids, amines, carbohydrates, and nucleic acids. Ageing and a number of illnesses, including immunodeficiency syndrome, malaria, heart-related issues, cancer, diabetes, and others, are caused by these oxidative damages. The activity of reactive oxygen species (ROS) and antioxidant defense mechanisms are always in balance within biological systems. Overproduction of free radicals causes oxidative stress and lipid peroxidation, which in turn triggers the body's defense mechanism and oxidatively alters components inside the cell or the cell membrane (El-Habit, Saada, Azab, Abdel-Rahman, & El-Malah, 2000). Lipid oxidation during food preparation results in decreased nutritional value, spoiled food taste, and the production of ROS, which initiates unintended chemical reactions (Miller, Diplock, & Rice-Evans, 1995). To delay this auto-oxidation process, conventional antioxidants such as α -tocopherol, tertiary butyl hydroquinone (TBHQ), butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA) are utilized. Nevertheless, they are unstable and may stimulate cancer (Namiki, 1990). Because of their potential for cancer, scientists are now concentrating on safer alternatives, such as naturally occurring antioxidants for use in the food industry and medicinal components.

Fennel may be a rich source of natural antioxidants. This plant can stop free radicals from forming since it has a lot of flavonoids and polyphenols. Phenolic components of this plant, such as "caffeoylquinic acid, rosmarinic acid, eriodictyol-7-orutinoside, quercetin 3-O-galactoside, and kaempferol-3-O-glucoside," demonstrated antioxidant activity. Fennel volatile oil also possesses strong antioxidant qualities.

Antioxidants function as a crucial component to safeguard food and medication by scavenging oxygen, chelating catalytic metals, and interfering with the oxidation process to neutralize these free radicals (Jayaprakasha, Singh, & Sakariah, 2001). We have been using fennel, since ancient times because Anethole, α -pinene, fenchol, limonene, estragole, and fenchone are the principal components of it (Hajalizadeh, Dayani, Khezri, Tahmasbi, & Mohammadabadi, 2019). Due to its anti-inflammatory, anticancer, and antioxidant qualities, fennel is a herbaceous plant that is utilized in home medicines (S. Chatterjee *et al.*, 2012).

Fennel exhibits excellent properties of natural antioxidants, which contribute to the regular antioxidant diet (Shahat *et al.*, 2011). The aqueous and ethanol extract of fennel seeds with antioxidant activity has been detected via several antioxidant methods such as scavenging of free radicals, hydrogen peroxide and superoxide anion radical, metal chelating activity, reducing power and total antioxidants. Due to the antioxidant properties of the essential oils of fennel, it act as natural preservative

for foods with high-fat content like in butter by delaying hydrolytic and oxidative rancidity (Pande & Preetha, 2017). The phenolic content of fennel acetonetic seed extract is high, measuring 0.364 ± 1.1 mg/g tannic acid equivalent in (FACSE).

The flavonoid content of fennel acetonetic seed extract and methanolic seed extract is highest, measuring 0.0449 ± 0.96 mg/g quercetin equivalent in FMSE (fennel methanolic seed extract). Additionally, it has been demonstrated that fennel's methanolic seed extract (FMSE) provides superior defense against DNA damage (Goswami & Chatterjee, 2014). Butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are less potent antioxidants than the acetone extract and essential oils found in Fennel (Ruberto, Baratta, Deans, & Dorman, 2000). In the lipid peroxidation test, Fennel fruit in n-BuOH extract performed mediocely, but at higher tested levels, it demonstrated significant antioxidant activity (De Marino *et al.*, 2007).

Phenolic substances such as kaempferol-3-O-glucoside, eriodictyol-7-rutinoside, and 4-caffeoylquinic acid through the distillation process, essential oils such as 3-caffeoylquinic acid, rosmarinic acid, 1,5-O-dicaffeoylquinic acid, kaempferol-3-O-rutinoside, and quercetin-3-O-galactoside are extracted from the leftover aerial parts of bitter fennel flowers. The potent scavenging action of these essential oils against radicals may be the cause of *F. vulgare's* pharmacological efficacy (Parejo *et al.*, 2004). The antioxidant properties of these substances were contrasted with those of well-known antioxidants such as α -tocopherol, butylated hydroxyanisole, and butylated hydroxytoluene. The results of the study suggest that fennel seed can be a good source of organic antioxidants. Additionally, α -tocopherol (36.1%) and antioxidant activity were 99.1% and 77.5%, respectively, in 100 mg of the ethanol and watery extracts of fennel.

Bioactive compounds of Fennel

Different types of bioactive substances have been found in fennel, including terpenes (myrcene, limonene, and pinene), phenols (phenolic acids, tannins, and flavonoids), coumarins (umbelliferone and scopoletin), essential oils (estragole, fenchone, and anethole), and alkaloids (nicotine and anabasine).

The antispasmodic, sedative, digestive, cardiogenic, diuretic, and tonic properties of essential oils (EOs) derived from medicinal and aromatic plants (MAPs) have made them popular in alternative medicine (Marín, Sayas-Barberá, Viuda-Martos, Navarro, & Sendra, 2016). When these plants and/or their essential oils are grown organically using approved methods, they are frequently added to meals and are generally considered safe. Furthermore, essential oils (EOs) have long been utilized as flavorings in the food sector in addition to several additional uses in fragrances, cosmetics, hygiene products, and medicinal drugs. EOs' inherent antioxidant properties can also be utilized as a substitute for conventional food preservatives (Kalleli *et al.*, 2019).

Fennel as a source of Nitric oxide

Nitric oxide (NO) is a free radical, gaseous multifunctional messenger molecule involved in a wide spectrum of physiological processes from bacteria to humans. It is synthesized by the enzyme nitric oxide synthase (NOS) as well as non-enzymatically (E. A. Khan, Aftab, & Hasanuzzaman, 2023; E. A. Khan *et al.*, 2017). Nitric oxide in animal systems regulates endothelial cell migration, proliferation, extracellular matrix remodeling, and angiogenesis (E. A. Khan & Parwez, 2022). Researchers have confirmed that fennel seeds store nitric oxide in the form of nitrite (Swaminathan *et al.*, 2012).

A study done by E.A.Khan showed that NO plays significant roles in plants including seed dormancy, seed germination, primary and lateral root growth, flowering, fruit ripening, gravitropism, photosynthesis, senescence, programmed cell death, pathogen attack herbicides, abiotic and biotic stress responses. It also regulates antioxidative enzymatic systems, including superoxide dismutases (SOD), catalase (CAT) and peroxidases (PODs) which are involved in the detoxification of superoxide radicals such as (O_2^-), (H_2O_2), (OH) as mentioned by (E. A. Khan, M. I. Ahmed, *et al.*, 2022; Mohamed, Khan, & Misra, 2019). All these antioxidant components must work coordinately to provide a successful response against oxidative stress. Accordingly, the regulation of these antioxidant constituents by an exogenous substance might mediate the plant's tolerance to salt stress. Nitric oxide (NO) is one of the most studied bioactive molecules due to its. Nitric oxide has been reported to alleviate the oxidative stress in plants generated by abiotic stresses (E. A. Khan, Ahmed, *et al.*, 2022; E. A. Khan, M. I. Ahmed, *et al.*, 2022).

Role of fennel seeds in preventing oxidative damage

Various antioxidant compounds—such as α -tocopherol, B complex vitamins, β -carotene, zinc salts, glutamic acid, selenium salts, phosphor salts, hydrolyzed collagen, magnesium salts, chondroitin sulfate, soy lecithin, and glycosaminoglycan sulfate—have been shown alleviate oxidative stress and stress-related conditions (Tripathi, Mehta, Amar, & Gaur, 2006).

A study done by Barakat, H. showed that Fennel seeds (FS) and fennel seed sprouts (FSS) are enriched in volatile and phenolic components with flavonoids as the main antioxidants. By use of various analysis techniques and a test done on rats with 600 mg Kg^{-1} FSS extract, it was concluded that FSS and FS have remarkable properties to reduce oxidative stress related disease. So, it is highly recommendable for good health (Barakat *et al.*, 2022).

Another study on fennel for its pharmacological potential reveals that fennel-based supplements can be used against hepatotoxicity, ulcers, nephron toxicity, and inflammation because in-vivo study reveals the enhancement in antioxidative properties of fennel due to increased activities

of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPX) and biomarker malondialdehyde (MDA) (Singh, Tripathi, & Sharma, 2016; Tanveer, Shehzad, Butt, & Shahid, 2021).

It was also observed that fennel seeds have anti-inflammatory, antioxidant, and antimutagenic effects against γ - irradiation-induced oxidative stress. By using fennel, antioxidant properties of cells get increased like catalase(CAT) and superoxide dismutase (SOD) activities and rise in lactate dehydrogenase (LDH) and also significant increase in (Interleukin) IL-1 β , 6 and 8 to fight again harmful radiation (Farid *et al.*, 2020).

Fennel as a Phytogetic products

Phytogetic feed additives (PFA) are plant-based compounds made from spices and herbs that are fed to cattle and humans to improve health and productivity (R. U. Khan *et al.*, 2021) (Fig 1). In animal husbandry, phytogetic compounds are a great substitute for growth stimulants and antibiotics (A. Khan, Tahir, *et al.*, 2022). Fennel antioxidants reduce acetylcholine and histamine-induced gastrointestinal tract contraction (Kooti *et al.*, 2015). The gastrointestinal tract produces less gas as a result of the action of fennel essential oils on the smooth muscles of the intestine (Kooti *et al.*, 2015).

The enhanced digestion of proteins in FSP-fed animals, such as nursing Frisian cows and Egyptian buffaloes, results in an increase in the total protein (TP) of their blood, improving the quantity and quality of their milk. It is also noted that supplementing their feed with a blend of medicinal plants increased the total proteins (TP) of the serum in Egyptian dairy goats (Author, A, El-Shemy, MAL

Maghraby, & El-Mossalami, 2014). Early lactation crossbreed cows' milk output increases when fennel seed powder (FSP) is added to their diet at a rate of 0.7% for 90 days (Mahmoud, Rahmy, & Ghoneem, 2020). The FSP diet increased milk output and energy-corrected milk (ECM) in early nursing Egyptian buffaloes by 10.5% and 16%, respectively (Fahim, Kholif, & Azzaz, 2022). Giving nursing Holstein cows an FSP supplement equal to 0.03% of their body weight improved their body weight and milk production in 63 days. For two weeks, Holstein calf diets supplemented with 0.4% fennel powder showed improvements in feed conversion, rumen fermentation, daily weight growth, and calf weaning age (Saeedi, Dayani, Tahmasbi, & Khezri, 2017). Short-chain fatty acids (SCFA) and propionate levels rise when FSP is added as a supplement to the food of calves. FSP can be utilized as a source of energy for ruminants since total SCFA production serves as an indicator of rumen fermentation (Saeedi *et al.*, 2017). When 1.5% FSP is added to the entire diet for 80 days during rearing lambs, the yield of muscle tissue, finishing performance, and feed conversion all rise (Hajalizadeh *et al.*, 2019). Temperatures above 30°C cause heat stress in chickens, which has an adverse effect on their ability to produce eggs, their antioxidant system, the quality of their eggs, and their physiology.

Thus, feed limitation, antioxidant-rich food supplements, and electrolyte balance management are necessary for nutrition management (Koppula & Kumar, 2013). Because phytogetic products are natural, plant-based foods, people may accept their usage in poultry diets. Scientists claim that the increased digestibility and antioxidants in fennel seed

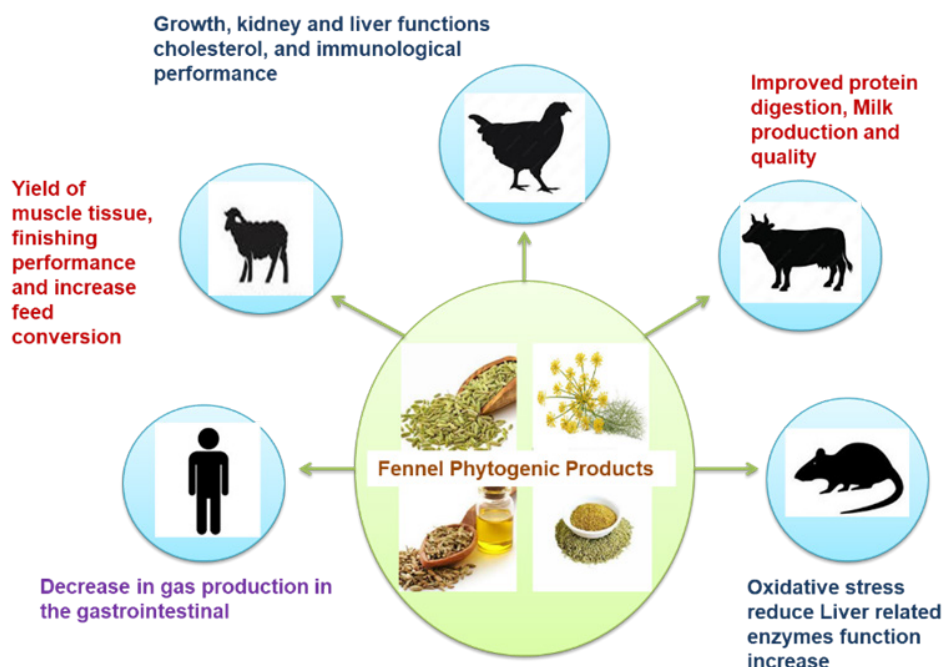


Figure 1: Effect of Phytogetic products

powder and oils improve the performance and quality of carcass chicken (Al-Sagan, Khalil, Hussein, & Attia, 2020). Fennel increased the amount of albumin, globulin, and total plasma proteins in the diet of Japanese quality (Abdel-Latif, Abdel-Daim, Shukry, Nowosad, & Kucharczyk, 2022). By activating the hydroxylase enzyme, fennel extract produces the active form of vitamin D3, which increases the body's ability to absorb calcium through the digestive system and raises blood calcium levels (Badgujar, Patel, & Bandivdekar, 2014).

The effects of supplementing broiler diets with fennel seeds on growth, immunological function, cholesterol, liver and kidney functions were noted (Nassar, El-Sayed, Ouassaf, & Abbas, 2023). Additional studies demonstrate that a fennel diet increased the poultry's appetite and palatability, which increased feed consumption (Ragab, 2007). Furthermore, it was found that fennel supplementation significantly increases the number of liver-related enzymes in rats and protects the liver from oxidative stress (Barakat *et al.*, 2022).

Biostimulants

The definition of the term "plant biostimulant" has been a matter of discussion because several compounds, organic and inorganic, from different biological sources or not (synthetic), may have stimulant plant growth, broadening too much the number of compounds and certainly weakening the definition. It is "a formulated product of biological origin that improves plant productivity as a consequence of the novel, or emergent properties of the complex of constituents, and not as a sole consequence of the presence of known essential plant nutrients, plant growth regulators, or plant protective compounds" (Yakhin, Lubyantsev, Yakhin, & Brown, 2017). Biostimulants can be microorganisms or organic substances which directly affect plant metabolic and physiological processes which results in improvement in growth, crop quality and quantity, nutrient uptake and also improve tolerance of plant to abiotic and biotic stress.

Biostimulants are used in these days in agricultural sector for decreasing dependency on chemical fertilizers. These effectively reduces eutrophication and stress induced due to climate change (Yakhin *et al.*, 2017). Biostimulants helps the plant by improving physiological functions like stress tolerance, improvement in nutrition of crop, increase in crop quality and quantity without any harmful impact on surrounding environment (Barone *et al.*, 2018). Higher plant derived biostimulants (hPDBs) are a class of biostimulants that can be induced from pure metabolites, cell cultures of higher plants, whole plants or particular organs, and extracts from plant by-products. To help stressed plants, extracts from various plant components are employed as bioactive stimulants.

The foliar spray of fennel seed extract which act as biostimulant causes net increase in photosynthesis and

transpiration rate both in controlled and salt stressed condition. Fennel extract biostimulant significantly increases the level of N, P, K⁺ and also the ratio of K⁺/Na⁺ in both controlled as well as salt stressed condition. It has been also observed that concentration of Na⁺ get decreased in salt stressed condition as compared to controlled stress free condition (Desoky *et al.*, 2020). Foliar application of fennel seeds extracts increase the osmoprotectants and photosynthesis pigments which show a decrease due to salt stress (Desoky *et al.*, 2020). Biostimulants reduces the harmful effects of salt stress in cowpea plants by producing osmoprotectants like proline and soluble sugar in large amount. Fennel extracts effects the photosynthetic machinery by effectively effecting PSII reaction centers, ribulose-1,5-bisphosphate regeneration, by decreasing lipid peroxidation and free radical level by initiating the antioxidative defense system (Rady, Semida, Abd El-Mageed, Hemida, & Rady, 2018).

Seeds of fennel (FSE) are important sources of extracts rich in osmoprotectants and antioxidants (e.g., proline, free amino acids, soluble sugars, phenolic compounds, glutathione, α -tocopherol, etc.) and many nutrient elements. However, as far as we know, studies on FSE used as bioactive stimulants have less information (Desoky *et al.*, 2020).

Many plants, including white rocket, lettuce, tomato, sweet pepper, radish, cabbage, rose-scented geranium, lamb's lettuce, and spinach, have been shown to have increased antioxidant activity following biostimulant therapy. Biostimulants often increase the membrane stability index, decrease lipid peroxidation and electrolyte leakage, and increase the amount of antioxidants (like ascorbic acid) and osmoprotectants (like proline and soluble carbohydrates). Reactive chemical species can be reduced by using biostimulants, which can also increase the transcription of genes encoding antioxidant enzymes (such as SOD, CAT, POX, APX, GPX, and GR) and their activity (Hamedani, Rouphael, Colla, Colantoni, & Cardarelli, 2020; Shukla *et al.*, 2023; Zuluaga *et al.*, 2023).

Conclusion and prospects

Fennel is a medicinal and fragrant plant with a wide range of pharmacological applications, particularly in the food sector. Many elements of this plant's studies require further investigation in order to understand its societal benefits. Geographic and seasonal fluctuations, for example, are critical in determining the chemical ingredients responsible for the effect, which can be intriguing. The options for employing phytogenic additions are numerous. Their use does not present as many significant risks as the use of antibiotics or chemical substances. Further research on phytogenic chemicals and their practical use is surely required. Long-term research, however, will be critical in confirming the efficacy of these additives, their safety in terms of animal health, the quality of animal products

and the environment, and, ultimately, their availability in terms of their anticipated regular use. The application of fennel as biostimulants can boost a plant's vigour and nutrient efficiency and stress tolerance, which can ultimately result in crops using less chemical fertilizer and pesticides and making better use of water resources. Fruit yield and nutritional quality can both be enhanced by plant biostimulants. The use of fennel extract as source of nitric oxide is the new way for replacement of chemical based nitric oxide donor. Further research in this direction will lead to a new innovation in future. We were inspired to suggest fennel as a biostimulant. In conclusion, fennel has been the subject of numerous studies, and additional research can be done to determine its potential applications.

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Conflict of interest

The authors declare that they have no conflict of Interest.

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