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Review Article

The Effect of Nano-Encapsulated Herbal Essential Oils on Poultry' s Health

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Abstract

Diet plays a crucial role in maintaining animal health, productivity, and reproductive performance. Among dietary elements, antioxidants from herbal essential oils are particularly important for stimulating growth performance, reproduction, and immune competence in animal production, especially while their replacement with synthetic antioxidants has no adverse side effects. Recent developments in nanotechnology have improved essential oils' absorption while protecting their bio-compounds. Despite its potential to improve animal health and performance, Nanotechnology has been underutilized in animal nutrition. Nano-encapsulation can cause enhance the herbal essential oil's antioxidant, antimutagenic, anti-inflammatory, and immunomodulatory effects, plus prolonged shelf life, improved physicochemical stability, and controlled release of herbal essential oils. Therefore, herbal essential oils encapsulated with bioactive substances such as phenol, flavonoid, carotenoid, vitamins, and minerals can improve the health and performance of animals. They can be added to both drinking water and feed, where they can be efficiently delivered and fulfill their beneficial effects on the animals. All perspectives on nano-encapsulated herbal essential oils will be discussed in this review, emphasizing their effects on poultry.

Keywords: nanotechnology, essential oil, production, health

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1. Context

Significant potential exists for advances in nanoscience to overcome challenges in the realm of animal health. Numerous mysteries pertaining to animal health, reproduction, productivity, hygienic procedures, and the upkeep of food animals can be resolved in the fruit of Nano-tech. It has been demonstrated that the efficacy of essential oils increases when they are utilized in a protected form, such as an encapsulated form (1). Nanoencapsulation is a novel technology in animal production that protects essential oils from an unfavorable environments, such as high humidity, temperature, and drying (2). Due to the excellent bioavailability of encapsulated herbal essential oils for tissues and their Effect against multidrug-resistant pathogens, nanoencapsulation can enhance growth performance (3).

Some herbal plants such as limes, ginger, garlic, and lemongrass are used not only as common ingredients in feed but also as a treatment for health purposes because of their essential oils and bioactive components such as ascorbic acid, flavonoids, limonoids, saponins, quinones, alkaloids, and carotenoids (4). Essential oil extract has a high antimicrobial effect on many harmful gram-positive, gram-negative, and anaerobic bacteria (5) and many other health-protective effects, such as antioxidant, anti-inflammatory, and other biological properties (6), one of the most well-known natural supplements. In particular, the essential oil of basil has several health benefits, such as enhancing digestion, antimicrobial, antioxidant, anti-inflammatory, chemo-preventive, and anthelmintic properties (7). According to Ndelekwute (8), adding 2% lime extract to the diet increased broiler growth and nutrient digestibility. Lime leaves also have antibacterial, antioxidant, and immunomodulatory properties (9). *in vivo* and *in vitro* studies (10) have demonstrated that lime leaf essential oil possesses antidiabetic and antibacterial properties. In broiler chickens, some herbal essential oils such as garlic, and cumin, particularly in nano-encapsulated form, improved some digestive tract traits (4), including greater villi width and length compared to other treatments and a higher VL: CD - villi length to crypt depth ratio, which affected the *Lactobacilli* population in the ileocecum. Moreover, Granata, Stracquadanio (11) showed that oregano and thyme essential oils, encapsulated in chitosan nanoparticles, are pathogen-effective antimicrobial agents.

Nano-encapsulation has the potential to be an efficient and low-cost method to protect bioactive chemicals and enhance the effects of essential oils in animal nutrition. However, studies on the application of nano-encapsulated essential oils seem scarce; this study targeted to gather and describe all the newest information on the Effect of nano-encapsulated herbal essential oils on growth performance, antioxidant capacity, and immunity of poultry, which will be useful for future research.

2. Evidence Acquisition

The key purpose of this paper is to describe and gather data on the use of new technologies in animal feed. In particular, applying nano-encapsulated essential oil boosts immunity and regulates antioxidant capacity. To collect and analyze the data, the following keywords were selected: "essential oils", "nanoencapsulated essential oils", "nanotechnologies", "encapsulated technology", "antioxidant", "plant oil", "growth", "immunity", etc. The data were collected using the Google Scholar, PubChem, and PubMed databases. All papers were gathered and reviewed. The research team evaluated obtained articles for their relevance before compiling the manuscript. The priority was to obtain published papers or published research from 2017 so far to get the newest information. Almost one hundred publications were found; however, only 50 publications complied with the contexts of this review.

3. Results

3.1. Nano-Encapsulated Technologies

The preservation of essential oils using nanoencapsulation is a well-established method. Improved water solubility, excellent degradation protection, prevention of volatile component evaporation, and controlled and targeted release are just a few of the advantages and effects of essential oils (12). Nanotechnology is the study and technology of entities that are smaller than 100 nanometers in size. Due to their size, nanomaterials may undergo new changes in their chemical and physical structure, indicating greater reactivity and solubility. Nanotechnology represents technological advancements and growth in the molecular, atomic, and macromolecular areas (13). In addition to its high bioavailability and biodegradability, its particular actions provide a scientific edge. All these benefits significantly affect animal productivity, economic losses, and better food and feed creation. Richard P. Feynman, a Nobel Laureate, and physicist at the California Institute of Technology (Caltech), first proposed the concept of nanotechnology in 1959. However, this technology had not been used until 1974 (14). As mentioned above, nanotechnology is the creation of functioning systems at the molecular scale; it involves the application, fabrication, and processing of materials with dimensions of less than thousands of nanometers (14). Nanoencapsulation is a technology for encapsulating compounds in small amounts and refers to bioactive packing on the nanoscale. The particle size directly impacts the distribution of any bioactive substance to distinct body locations. Similar physiological molecules are present on the nanoparticles, which may enable them to employ the same methods for crossing interior barriers (14). In recent years, a detailed investigation into the potential use of appropriately performing nanoparticles for disease control or the detection and treatment of organs protected by internal barriers has advanced (13, 14).

The primary advantages of nanotechnology are decreasing molecular size, which increases bioavailability; 2) improving the solubility of poorly water-soluble ingredients; 3) optical transparency; 4) higher ingredient retention during processing (reduction of volatile organic carbon during spray drying), and 5) homogeneity (15). Encapsulation of herbal essential oils has also been shown to effectively protect antioxidant capabilities and enhance their therapeutic potential by enabling intracellular transport and extending their retention period within the cell (16). In addition, nanoencapsulation has the potential to increase bioavailability, improve controlled release, and enable precise targeting of bioactive substances. Nanocapsules are vesicular systems in which the bioactive chemical is contained within a cavity enclosed by a unique polymer membrane, whereas nanospheres are matrix systems in which the bioactive compound is evenly spread. Nanoencapsulation of medicines improves their efficacy, selectivity, and ability to reach the target (17). It is well known that the synthesis of nanoparticles has two outstanding advantages over conventional/chemical synthesis methods. First, these nanosized particles are more adsorbent across the capillary walls and thus play an essential role in delivering nutrients and therapeutic drugs. Second, this process uses biodegradable materials, eliminating the possibility of accumulation and environmental pollution caused by chemicals (17).

3.2. Modes of Action

Encapsulation has gained popularity in the pharmaceutical industry. Small amounts of bio-compounds are encased in an exterior substance, resulting in particles having bioactive components, such as antioxidants, primarily phenolics, antioxidant enzymes, nutraceuticals, and micronutrients. While microparticles have sizes between 3 and 800 µm, nanoparticles have diameters between 0 and 1,000 nm and can exist as nanocapsules or nanospheres (18). Microencapsulation has the potential to hide the unpleasant flavor of some bioactive substances in food compositions and transform liquid phases into solids. Recently, however, greater focus has been placed on the issue of regulated release. The regulated release process boosts the biochemical response of the living system and ensures optimal nutrition absorption (19).

In animals, nanoparticles are absorbed in various ways, including in the gastrointestinal and respiratory tract. The absorption, distribution, metabolism, and excretion of nanoparticles *in vivo* depend on their physicochemical properties, such as solubility and size. Particle sizes smaller than approximately 300 nm can easily be absorbed into the capillaries, while particles smaller than 100 nm can enter various tissues and organs. Plant leaves exhibit a highly potent antioxidant against numerous oxidative processes (20). Despite its health-related characteristics, plant leaves are rich in bioactive chemicals, as mentioned above, making them one of the most powerful natural antioxidant resources. To deliver these compounds to specific sites of action and increase the utilization efficiency of these compounds, nanoencapsulation technology must be utilized because most bioactive compounds are hydrophobic and easily degraded in the presence of light, air, and high temperatures (21). Encapsulation techniques have also been reported to enhance the antimicrobial efficacy of essential oils. For instance, encapsulated lavender essential oil displayed a threefold enhancement in its antimicrobial potency (22).

3.3. Growth Promoter Function

Direct inclusion of essential oils into animal feed has restrictions due to the bioactive component's reactive, hydrophobic, and volatile nature (2). However, it has been demonstrated that the efficacy of essential oils increases when used in a safe form, such as encapsulation. Table 1 (23-27) highlights some studies using nano-encapsulated herbal essential oils for poultry and swine production. Most studies on nano-encapsulated herbal essential oils showed positive effects on performance by improving weight gain, feed intake, and feed conversion ratio.

Table 1. The application of nano-encapsulated essential oil on animal performance

Animals	Author	Treatment	BWG, g/day	FI, g/day	FCR	Performance
Poultry	Amiri, Afsharmanesh (23)	Control	48.12	91.00	1.89	200 mg/kg cumin NEO improved growth performance
		Cumin NEO	51.51	84.31	1.63	
	Amiri, Afsharmanesh (4)	Control	49.54	88.90	1.79	100 mg/kg garlic NEO improved growth performance
		Garlic NEO	50.97	88.34	1.73	
	Olfati and Hosseini (25)	Control	18.18	29.32	1.63	There was no different at start phase
		Thyme NEO	18.34	29.37	1.61	
	Zuprizal, Yuwanta (27)	Control	578	3155 g/bird	1.82	2% in water improved performance
		Turmeric NEO	644	3393 g/bird	1.76	
	Heydarian, Ebrahimnezhad (24)	Control	2202.20	3699 g/bird	1.67	200 mg/kg Thyme and Oregano NEO improved growth performance
		Thyme and Oregano NEO	2332.75	3744 g/bird	1.61	
Swine	Wang, Xue (26)	Control	421	690	1.64	Encapsulated tea tree oil as a potential feed additive for weaned pigs.
		Tea tree NEO	475	736	1.55	

Note: NEO means nano-capsulated essential oil

Kumar, Singh (28) inferred that the advantages of nanoencapsulation are: protecting bioactive compounds of essential oils from degradation, increasing solubility in an aqueous medium, masking intense aroma, avoiding negative interactions with food components with enhanced bioactivity and targeted delivery, and reducing the effective dose to achieve the preservative and functional Effect of essential oils. The bioactive compounds in nano-encapsulated herbal essential oils may affect the digestive process by stimulating digestive enzymes and maintaining a healthy bacterial population in the intestinal tract. This Effect on the gut and the ingesta may be why nano-encapsulated herbal essential oils could improve animal performance. Furthermore, Risaliti, Kehagia (29) used the freeze-drying method to manufacture a nano-formulation of lemon essential oil, utilizing chitosan and modified starch, to improve the physicochemical qualities and thermal stability of the herbal essential oil. Hasani, Ojagh (30) investigated the anti-inflammatory, antioxidant and antibacterial activities of *Salvia triloba's* and *Rosmarinus Officinalis* essential oils-loaded nanovesicles where he concluded that liposome-based formulations were stable over one month and had significant activities. The bioactive chemicals found in herbal essential oil nano-encapsulation can potentially affect extracellular proteinases and encourage the production and accumulation of the mucin 2 gene in the gastrointestinal tract. Mucin is the primary component of the mucus layer and is crucial in protecting the gastrointestinal system from acidic chyme, digestive enzymes, and infections (23).

Additionally, it lessens the host's competition for the available nutrients, encourages the development of mucosal absorptive cells in the small intestine, and causes the production of enzymes that are naturally involved in digestion (23). Moreover, the essential oils contained chemicals that stimulated the release of digesting enzymes from the intestinal mucosa and the pancreas, such as amylase and trypsin, which led to increased bile acid secretion and a change in the architecture of the intestinal tract (21). Thus, all these functions of nano-encapsulation improve herbal essential oil activities in the animal body, eventually improving poultry performance.

3.4. Antioxidant Role of Nano-Encapsulated Essential Oil in Animals

In general, oxidation is a process that transforms a chemical substance, which generates free radicals (highly reactive molecules) that initiate numerous chain reactions that can destroy cells. The function of antioxidants is to neutralize free radicals capable of preserving optimal cellular functions (31). Both endogenous and exogenous sources produce free radicals, including free radicals such as reactive oxygen and reactive nitrogen groups. By altering the normal redox status, free radicals can affect several important classes of biological molecules, including nucleic acids, lipids, and proteins, increasing oxidative stress (32). Damage to organic substrates caused by free radicals leads to oxidative stress. It is highly damaging at the cellular level and causes degenerative health problems that significantly affect livestock productivity. Thankfully, antioxidants are the solution to these issues.

The oxidation of DNA, proteins, carbohydrates, and lipids is slowed down when these substances are in low amounts (33). Antioxidants can be broken down into three basic categories, which are as follows: first, the antioxidants that make up the initial line of defense, such as catalase (CAT), superoxide dismutase (SOD), and glutathione reductase (GR), as well as minerals such as copper, selenium, zinc, and others; second, the antioxidants that make the second line of defense, such as glutathione (GSH), albumin, vitamin C, vitamin E, flavonoids, and carotenoids; third, the antioxidants that make the third line of defense are a complex group of enzymes that are responsible for the repair of damaged proteins, damaged DNA, peroxides and oxidized lipids. Some examples of these enzymes include protease, lipase, transferases, DNA repair enzymes, and methionine sulfoxide reductase (34).

Antioxidants in the first line of defense work to either stop the production of free radicals or reactive groups within cells or decrease their production. They quickly eliminate free radicals by neutralizing molecules that hold the potential to become unstable. SOD, CAT, and GR enzymes are responsible for transforming harmful hydrogen peroxides and hydroperoxides into harmless molecules (H_2O_2/C_2H_5OH and O_2). Scavenging antioxidants are another common name for antioxidants on the second line of defense against free radicals (35). They do this by removing active radicals from the environment, which stops the chain reaction from the beginning and stops it from spreading. By giving electrons to free radicals, they can scavenge them or neutralize them. However, this action makes them free radicals with less severe side effects. They repair the damage that free radicals cause to biomolecules and reconstruct the damaged cell membrane, particularly proteins, DNA, and lipids, to prevent their accumulation, which can harm human tissues. This protects human tissues from the potentially harmful effects of free radical accumulation (36).

Moreover, the flavonoid, polyphenol, and terpene constituents of leaves such as *Citrus aurantifolia* are responsible for their bioactive activity (11). The antioxidant action of flavonoids may originate from their ability to scavenge reactive oxygen groups directly, chelate redox-active metals to prevent oxidation, and stimulate the production of endogenous antioxidant enzymes (37). According to Liu, Song (38), supplementation with quercetin, one of the flavonoid representatives, improved antioxidant enzyme activity in rats. Dietary flavonoids may be a significant antioxidant source (38). However, flavonoids' *in vivo* antioxidant activity has been less fully proven. Polyphenols other than flavonoids exhibit noteworthy medicinal effects, including antioxidant activity (39). According to Mazur-Kusnirek, Antoszkiewicz (40), the glutathione peroxidase activity of broiler hens fed diets supplemented with polyphenols was elevated. In addition to these chemicals, tannins are one of the bioactive molecules present in leaves. Tannins can be found in various plant species, and excessive amounts of tannins in feed can devastate animal health (41). Adding 0.5% tannin to the feed of broiler chickens aged 1 to 10 days and 1% tannin to broiler chickens aged 11 to 42 days can improve body weight and weight gain (42). In addition, tannins have long been known to have antibiotic properties due to their ability to deprive the growth of bacteria of substrates and metal ions from their cell membranes, resulting in morphological alterations of the cell wall (43). Therefore, plant leaves may provide a viable alternative to natural antioxidants in the future. These chemicals, accompanied by encapsulation technology, can be encapsulated in a carrier for protection, increasing their bioavailability (44). A precise instance can be shown in figure 1, indicating how nanoparticles' antioxidant activity differs from non-nanoparticles. Figure 1 shows the antioxidant activities of clove oil and clove oil nanoparticles at a concentration ranging from 5-100μg/mL, which indicated that nanoparticles had a better performance on antioxidant activities; it seems nanoparticles can improve the antioxidant capacity of herbal oils.

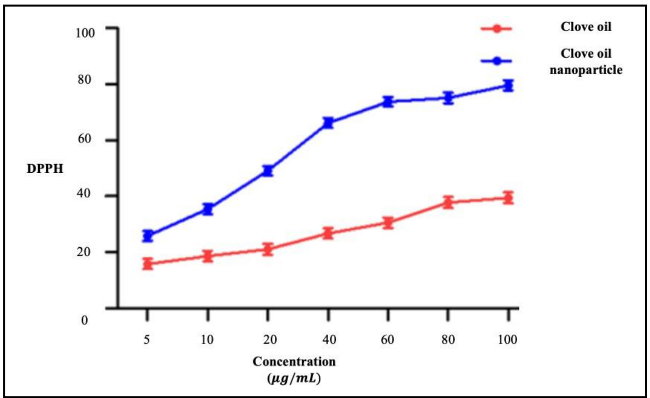

Figure 1. Antioxidant activities of clove oil and clove oil nanoparticles
Source: Nagaraju et al. (37)
Note: DPPH means 1,1-diphenyl picryl hydrazyl

3.5. Immunomodulatory Role of Nano-Encapsulated Essential Oil in Animals

Currently, the disadvantages of nanoencapsulation techniques on immunomodulatory are unknown; most studies just showed the beneficial effects of this technique. As widely studied, the layer-by-layer nano-encapsulation technique is the best method to protect the bio-compounds of herbal essential oils. The ultrathin layers techniques boost the mass transfer of vital nutrients to the islets while reducing the total volume of material and cells implanted (45). The essential oils of cinnamon, clove, basil, oregano, and thyme are characterized by the most important antioxidant properties. Thymol and carvacrol are the most active compounds and are the most beneficial ones in essential oils. Their activity is related to their phenolic structure. These phenolic compounds have redox characteristics and hence play a critical role in the neutralization of free radicals and the decomposition of peroxide (46). Because the diseases may result from cellular damage caused by free radicals (46), essential oils improve animal health. Besides, flavonoid-rich plants raise the vitamin C level of feed and act as antioxidants, which boosts the immune system's overall performance. They may enhance the function of lymphocytes, NK cells, and macrophages; they may also promote phagocytosis and induce interferon synthesis (47).

Additionally, the Effect of essential oil nanoencapsulation on the preservation and protection of active chemicals and their improvement in gut absorption may have contributed to this enhancement (47). The presence of flavonoids and other phenolic compounds in essential oils may enhance the immune-stimulating activity of vitamin C. Amresh, Reddy (48) also reported the antioxidant activity of flavonoids and polyphenolic compounds aids the immune system. Encapsulation preserves the active compounds in essential oils and enhances immune responses (48). The Effect of nano-encapsulated cumin essential oils on the immune response to sheep red blood cells in table 2 can be good evidence for an immune-booster role.

Table 2. The Effect of nano-encapsulated cumin essential oils on the immune response to sheep red blood cells (7 days after injection)

Treatment	1st injection		2nd injection	
	IgG	**IgM**	**IgG**	**IgM**
Control treatment	2.40	0.20	3.20	1.20
100 mg/kg nano-encapsulated cumin EO	3.20	1.20	4.20	1.60
200 mg/kg nano-encapsulated cumin EO	3.20	1.80	5.0	1.00

Source: Amiri, Afsharmanesh (23)

In addition, lymphocytes are crucial in defending against viruses, increasing their number when viral infection occurs. Lymphocytes, particularly Th4 lymphocytes, affect B-cell differentiation into plasma cells by secreting cytokines such as interleukin, IL-2, and IL-4, which are involved in antibody production. When the immune system is overly activated, immune stress may result. Immune stress is primarily caused by the excessive release of inflammatory cytokines, such as TNF-α (tumor necrosis factor-alpha), interleukin-1 (IL-1), and interleukin-6 (IL-6) (49). Amresh, Reddy (48) recorded that the antioxidant activity of flavonoids and polyphenolic compounds in nano-encapsulated essential oils aids the immune system. Encapsulation preserves the active compounds in essential oil and enhances immune responses.

4. Conclusions

In pigs and poultry production, nanoencapsulation of herbal essential oils might be a useful alternative product in the feed. Additionally, both the immunological response and the antioxidant status were enhanced. Through numerous biological activities, this study showed that nano-encapsulated herbal essential oils not only improve productivity but also reveal a potential candidate to replace the antibiotics conventionally used in the livestock industry. This study recommended that the mechanism and the harmful aspects of nano-encapsulated herbal essential oils should be investigated.

Authors' Contribution

Study concept and design: T. L. N. and Q. H. N.

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Acquisition of data: T. L. N. and Q. H. N.
Analysis and interpretation of data: A. T.
Drafting of the manuscript: T. L. N. and Q. H. N.
Critical revision of the manuscript for important intellectual content: T. L. N. and Q. H. N.
Statistical analysis: A. T.
Administrative, technical, and material support: T. L. N., Q. H. N. and A. T.

Conflict of Interest

The authors declare that they have no conflict of interest.

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