

Natural Products in Animal Health: A Narrative Review of Antimicrobial, Anti-Inflammatory, Anticancer, and Anti-Aging Applications

Amer A. Almutairi*

Nursing Unit, King Farhad Medical City (KFMC), Ministry of Health, Saudi Arabia.

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Abstract: Natural products are increasingly explored as complementary tools for improving animal health, particularly in response to antimicrobial resistance, chronic inflammation, cancer, and age-related decline. This narrative review summarizes their antimicrobial, anti-inflammatory, anticancer, and anti-aging applications in experimental and veterinary models. Evidence from in vitro studies, *Caenorhabditis elegans*, rodents, livestock, poultry, aquaculture species, and companion animals shows that natural products may inhibit microbial growth, modulate inflammation, reduce oxidative stress, suppress cancer-related pathways, and support physiological resilience. However, their clinical translation remains limited by variability in composition, inconsistent dosing, poor bioavailability, and insufficient species-specific studies. Overall, natural products represent promising preventive and therapeutic adjuncts, but their use in animal health requires stronger experimental validation, standardized formulations, and controlled veterinary trials.

Keywords: Natural products; Animal health; Antimicrobial activity; Anti-inflammatory agents; Anticancer and anti-aging applications.

Introduction

The health of animals is a critical factor in ensuring global food security, economic prosperity, and public health (1). The livestock and poultry sectors contribute significantly to the Gross Domestic Product of many nations, particularly in developing countries, where they address key agricultural challenges (2). Traditionally, animal health management has relied heavily on synthetic pharmaceuticals, such as antibiotics and anthelmintics, to treat contagious diseases and improve production (1,3). However, the long-term and extensive use of these chemicals has led to serious global issues, most notably the rapid development of antimicrobial resistance and a decline in the therapeutic efficacy of conventional drugs (3,4). This has necessitated a paradigm shift toward alternative, "natural" strategies for animal health management and disease prevention (3).

Natural products, derived from plants, animals, and microorganisms, are increasingly recognized as potent holistic alternatives to synthetic drugs (1,4). These compounds offer a wide range of therapeutic benefits, including antimicrobial, anti-inflammatory, and anticancer properties, often with fewer adverse effects and a lower risk of developing drug resistance compared to synthetic options (1). For instance, extracts from *Eucalyptus globulus* leaves and compounds like ursolic acid have demonstrated significant antibacterial and anti-biofilm activity against drug-resistant mastitis isolates in dairy cows (5). Furthermore, natural products like *Stevia rebaudiana* have been validated as safe feed additives through rigorous toxicological evaluations, providing a scientific foundation for their integration into animal nutrition(5,6).

Beyond antimicrobial applications, natural products are being explored for their anticancer and physiological protective activities.

Phytotherapy is becoming an essential source for modern drug targets, providing supportive treatments for some cancers and acting as growth and health promoters (4). Compounds such as turmeric and aloe vera are utilized for their anti-inflammatory and wound-healing properties, while others like chamomile and lavender are used to manage anxiety and promote physiological well-being in animals (1).

The validation of these natural products requires robust research using experimental models to ensure their safety and efficacy. These models are crucial for understanding the mechanisms of action and the physiological impact of biological controls, vaccines, and botanical medicines (3,4). This paper explores the diverse applications of natural products in animal health, focusing on their antimicrobial, anticancer, and physiological protective activities as demonstrated in experimental models, aiming to provide a comprehensive overview of their potential in modern veterinary therapeutics. This review synthesizes current research on natural product interventions, critically evaluating their promise as sustainable alternatives to conventional treatments in animal husbandry, thereby aligning with the "One Health" initiative for integrated health management (7).

Anti-Inflammatory

Anti-Inflammatory Activities of Natural Products

Inflammation is a complex biological response to stimuli such as pathogens, damaged cells, or irritants (8). In veterinary medicine, chronic inflammatory conditions affecting the musculoskeletal, gastrointestinal, and dermatological systems are common in companion animals like dogs and cats (9). While synthetic agents such as nonsteroidal anti-inflammatory drugs and glucocorticoids are standard treatments, they are often associated with severe side

*Corresponding Author

Amer A. Almutairi*

E-mail: sl_e@hotmail.com

effects, leading to an increased demand for safe and effective natural alternatives (8).

Mechanisms of Anti-inflammatory Action

Natural products derived from plants, animals, and microorganisms interact with diverse molecular targets to modulate the inflammatory cascade (10). Research into these mechanisms has identified several key pathways:

- **Suppression of Pro-inflammatory Mediators:** Many natural extracts inhibit the activation of mediators such as interleukin-1, interleukin-6, and prostaglandin E2 (8). For example, *Moringa oleifera* flower extracts have been shown to suppress these mediators in macrophage models by inhibiting the NF- κ B signaling pathway (8).
- **Modulation of Signaling Pathways:** Plant-derived compounds like curcumin, found in turmeric, and resveratrol, found in grapes and berries, exhibit robust anti-inflammatory effects by interacting with molecular targets involved in the inflammatory response (10).
- **Antioxidant Activity:** Beyond direct pathway modulation, compounds such as resveratrol also mitigate inflammation by reducing oxidative stress (10).

Applications in Veterinary Models

Experimental models are essential for evaluating the clinical relevance and safety of natural anti-inflammatory agents (11). Several compounds have shown promise in specific veterinary contexts:

- **Musculoskeletal and Joint Health:** In an experimental rabbit model of osteoarthritis, chenodeoxycholic acid demonstrated significant therapeutic effects (8). Similarly, herbal medicines are being investigated for their potential to provide benefits in musculoskeletal disorders in small pets (9).
- **Diverse Biological Sources:** In addition to plant metabolites, animal-derived substances like omega-3 fatty acids and bee venom components, as well as microbial-derived probiotics, have been identified as having notable anti-inflammatory properties (10).
- **Pain and Systemic Inflammation:** Animal models of pain and inflammation have been used to evaluate extracts like *Vitis vinifera*, which have been shown to influence biochemical parameters related to inflammatory diseases (12).

Therapeutic Integration and Future Directions

The integration of natural products into veterinary practice often involves their use in multimodal treatment protocols to enhance efficacy and reduce the reliance on synthetic drugs (9). However, the transition from experimental models to clinical use requires standardized drug screening programs that address pharmacokinetics and long-term safety (11). While the anti-inflammatory, antioxidant, and wound-healing effects of these compounds are promising, further robust clinical trials are necessary to consolidate their role in modern veterinary therapeutics(8,9,13).

Antimicrobial

Antimicrobial Activities of Natural Products

The global rise of antimicrobial resistance has drastically reduced the efficacy of conventional drugs, necessitating the exploration of natural compounds as alternative therapeutic strategies (14,15). Natural products, particularly plant-derived antimicrobials, offer a

wide spectrum of activity against fungal and bacterial pathogens in both humans and animals (16–19). Unlike synthetic antibiotics, these natural extracts often possess complex molecular structures for which bacterial resistance is rarely reported, making them vital tools for sustainable infection control (20,21).

Mechanisms of Antimicrobial Action

The antimicrobial efficacy of natural products is primarily attributed to their ability to interfere with vital bacterial components or circumvent resistance mechanisms (22). The most common mechanisms identified in research include the alteration of cell walls and membranes and the inhibition of protein biosynthesis (14). Beyond direct bactericidal effects, many plant compounds exert "anti-virulence" activities, targeting factors such as biofilm formation and quorum sensing that are critical for pathogenicity inside the host (19,21). For instance, flavonoid-type compounds isolated from *Woodfordia uniflora* have been shown to specifically inhibit biofilm formation in methicillin-resistant *Staphylococcus aureus* (23).

Applications in Animal Health Models

Experimental models have demonstrated the diverse utility of natural products across various veterinary sectors:

- **Livestock and Ruminants:** Phytochemicals are used as rumen modifiers to improve feed digestion and growth performance. Supplementing starter diets with essential oils from *Rosmarinus officinalis*, *Zataria multiflora*, and *Mentha pulegium* has been shown to positively impact the growth of suckling calves (24). Additionally, pomegranate byproduct extracts serve as a source of phenolics with inherent antimicrobial and anti-inflammatory activities (24).
- **Poultry and Swine:** The use of plant-based products has proven effective against specific poultry pathogens such as *Salmonella typhimurium* and *Riemerella anatipestifer* (2). In swine, combinations of carvacrol and thymol have demonstrated synergistic potential in controlling microbial populations within the gut (25). These "phytobiotics" are increasingly evaluated as alternatives to antibiotic growth promoters in both conventional and organic production systems (26).
- **Companion Animals:** Natural compounds like antimicrobial peptides and chitosan-based polymers are being developed for therapeutic use in dogs and cats to treat dermatological, gastrointestinal, and systemic infections (20).

Synergy and Therapeutic Enhancement

A significant advantage of natural products is their capacity to act as synergistic enhancers when used concurrently with standard antibiotics (27). This association can restore the antibacterial activity of failing drugs and allow for the use of lower concentrations, which helps address issues related to drug toxicity and overdose (22,27). Furthermore, the integration of natural alternatives in livestock management can reduce environmental contamination and the presence of drug residues in animal-derived food products like meat, milk, and eggs (28). While many of these approaches have been validated through *in vitro* and *in vivo* models, ongoing research using metabolomics is essential to identify the most effective bioactive combinations for clinical veterinary use (15,29).

Anticancer

Anticancer Activities of Natural Products in Veterinary Oncology

The search for novel anticancer agents is increasingly focused on natural products due to their structural diversity and unique biological activities (30). It is estimated that approximately 60% of currently used anticancer drugs, such as vinca alkaloids, are derived from natural sources, including plants, microorganisms, and marine organisms (31). In veterinary medicine, natural products are being explored not only as primary chemotherapeutic agents but also as chemopreventives and chemosensitizers that can enhance the efficacy of conventional treatments (31,32).

Mechanisms of Anticancer Action

Natural compounds exert their anticancer effects through a variety of molecular pathways that target cancer cell survival and progression(33–35). Key mechanisms identified in experimental studies include:

- **Apoptosis and Cell Cycle Arrest:** Secondary metabolites, such as alkaloids and polyphenols, can induce DNA damage and activate apoptosis-inducing enzymes (36,37). For instance, compounds like berberine and evodiamine exhibit anticancer activity by targeting signaling pathways such as PI3K/Akt and Ras/MAP-kinase (36).
- **Anti-Proliferative and Anti-Angiogenic Activity:** Many plant-derived substances inhibit the rapid proliferation of cancer cells and prevent the formation of new blood vessels (angiogenesis) that supply tumors with nutrients (36).
- **Inhibition of Epithelial-Mesenchymal Transition:** Recent research emphasizes the potential of phytochemicals to inhibit EMT, a critical process in cancer metastasis and the development of drug resistance (38).
- **Specific Signaling Modulation:** Compounds such as capsaicin and lycopene have been shown to target the STAT-3 pathway, which is frequently dysregulated in various cancers, including breast and colorectal types (36).

Experimental and Veterinary Models

The evaluation of natural products for cancer therapy relies on both *in vitro* and *in vivo* experimental models:

- **Spontaneous Veterinary Tumors:** Dogs and cats frequently develop spontaneous tumors that closely mimic the biological behavior and complexity of human cancers (39). Unlike chemically induced or transplanted rodent models, these "naturally occurring" models provide a more accurate representation of clinical outcomes and therapeutic responses (39). For example, studies on the latex of *Synadenium grantii* have been conducted using preclinical models of canine prostate cancer to evaluate its antitumor effects (31).
- **Rodent Models:** These remain essential for early-stage toxicological screening and for understanding the optimal therapeutic dose to mitigate side effects on the host (40).
- **Specific Therapeutic Studies:** Research has explored the use of *Artemisia annua* in combination with iron for treating tumors in small pets, highlighting the potential for integrating botanical medicines into veterinary oncology protocols (39).

Synergy and Therapeutic Enhancement

A promising area of research is the use of natural products as adjuvants to reduce the toxicity associated with conventional chemotherapy (32). Combining feed ingredients rich in

polyphenols and carotenoids has shown synergistic potential in reducing canine neoplastic cell proliferation (34). Furthermore, natural products can serve as chemosensitizers, making resistant cancer cells more susceptible to standard drugs, thereby allowing for lower, less toxic dosages (31). While many compounds show potent activity *in vitro*, rigorous *in vivo* testing in complex physiological states is necessary to confirm their safety and clinical efficacy in veterinary patients (32,40).

Antiaging

Antiaging Activities of Natural Products

Aging is defined as a biological process marked by the accumulation of degenerative damage, eventually leading to a decline in physiological function and the death of the organism (41). In animal health research, there is a growing emphasis on extending "healthspan"—the period of life spent in a state of functional homeostasis and stress resistance—rather than solely increasing chronological age (42). Natural products, particularly phytochemicals such as polyphenols, saponins, and polysaccharides, are being investigated for their ability to promote longevity and delay the onset of age-related pathologies (43,44).

Mechanisms of Anti-Aging Action

Natural products exert their anti-aging effects through several conserved molecular pathways:

- **Antioxidant and Anti-inflammatory Properties:** Dietary supplements like polyphenols and alkaloids act as potent antioxidants that protect cells from oxidative stress and DNA damage (44,45). These compounds help mitigate the chronic inflammation and metabolic stress associated with aging (45,46).
- **Nutrient-Sensing and Metabolic Signaling:** Many natural substances act as mimetics of calorie restriction, a known intervention for delaying organ disorders and extending lifespan (45). They modulate nutrient-sensing signals, energy metabolism, and mitochondrial function to improve cellular health (43,45).
- **Xenohormesis Theory:** This theory suggests that naturally occurring metabolites, such as plant polyphenols, serve as evolutionary signals that stimulate protective pathways in the animals that consume them, thereby enhancing their overall healthspan (47).
- **Gene Regulation:** Natural metabolites can influence longevity-related genes and signaling pathways that are evolutionarily conserved across species, from invertebrates to mammals (41,46).

Experimental and Animal Models

The discovery and validation of anti-aging agents rely on diverse experimental models that allow researchers to evaluate safety and efficacy efficiently:

- **Invertebrate Models (*C. elegans* and *Drosophila*):** The nematode *Caenorhabditis elegans* is frequently used as a primary model due to its short life cycle and genetic similarities to humans (48). Studies have shown that whole apple extracts, cocoa supplementation, and oregano-cranberry mixtures can increase lifespan and improve physical biomarkers like mobility in these models(49,50).
- **Mammalian Models:** Systematic reviews of rodent models indicate that natural products can improve healthspan markers such as memory, locomotion, and metabolic homeostasis (42).

These models are essential for translating findings from simpler organisms into potential veterinary treatments (51).

- **Preventive Veterinary Strategies:** Utilizing natural products in the diet is considered an attractive preventive strategy to alleviate age-related degenerative diseases in animals before clinical treatment becomes necessary (52).

Challenges and Therapeutic Potential

Despite the promising potential of natural products, several hurdles remain for their widespread use in veterinary medicine. These include issues with low bioavailability, the need for standardized dosages, and the requirement for more rigorous clinical validation in heterogeneous animal populations (43,46). However, as approximately 60% of existing drugs are derived from natural sources, they remain a vital resource for developing sustainable interventions against aging and its associated diseases (44,46).

Conclusion

Natural products represent a promising and increasingly important resource for improving animal health through antimicrobial, anticancer, anti-inflammatory, anti-aging, and physiological protective activities. Evidence from plant-, animal-, microbial-, and insect-derived products indicates that these compounds can support disease control, enhance immune and antioxidant responses, improve metabolic and functional outcomes, and provide alternative or complementary strategies to conventional pharmaceuticals. Their relevance is particularly strong in the context of antimicrobial resistance, drug residues, chronic inflammation, age-related decline, and the growing demand for sustainable approaches in veterinary medicine and animal production. Experimental models, ranging from invertebrates such as *C. elegans* to rodent, aquaculture, livestock, and companion-animal systems, have been essential for identifying bioactive compounds, evaluating safety, and clarifying potential mechanisms of action. However, despite encouraging findings, the translation of natural products into routine veterinary use remains limited by variability in extract composition, differences in dosage and bioavailability, incomplete mechanistic validation, and the shortage of well-controlled in vivo and clinical studies. Therefore, future research should prioritize standardized preparation methods, dose-response evaluation, long-term safety assessment, and species-specific clinical validation. Overall, natural products should not be viewed as simple replacements for conventional drugs, but as biologically diverse therapeutic and preventive tools that may complement current veterinary strategies. With rigorous experimental validation and careful clinical translation, they have the potential to contribute meaningfully to sustainable animal health management, improved productivity, and broader One Health objectives.

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