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Prashant Tiwari

ICMR–NIHR, Gorakhpur, Uttar
Pradesh, India

Chetna Motla

Pandit Deen Dayal Upadhyaya
Pashu Chikitsa Vigyan
Vishwavidyalaya Evam Go
Anusandhan Sansthan
(DUVASU), Mathura, Uttar
Pradesh, India

Shipra Verma

Acharya Narendra Deva
University of Agriculture and
Technology, Kumarganj,
Ayodhya, Uttar Pradesh, India

Ayush K Singh

Sardar Vallabhbhai Patel
University of Agriculture and
Technology, Meerut, Uttar
Pradesh, India

Rahul Tiwari

ICAR–National Dairy Research
Institute, Karnal, Haryana,
India.

Corresponding Author:

Prashant Tiwari

ICMR–NIHR, Gorakhpur, Uttar
Pradesh, India

Ozone therapy in veterinary medicine: An emerging therapeutic approach

**Prashant Tiwari, Chetna Motla, Shipra Verma, Ayush K Singh and Rahul
Tiwari**

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Abstract

Ozone (O₃) therapy is gaining increasing attention in veterinary medicine as a safe, eco-friendly, and versatile treatment option. It demonstrates a broad range of biological effects, including antimicrobial, antioxidant, immunomodulatory, and microcirculatory actions, making it useful across various clinical settings. Veterinary uses include managing mastitis, promoting wound healing, reproductive medicine, treating osteoarthritis, dentistry, oncology, and supporting care for viral and protozoal infections. Unlike antibiotics, ozone leaves no harmful residues, offering potential benefits in food-producing animals and helping to reduce antimicrobial resistance (AMR). However, despite encouraging results, most veterinary studies are small-scale, and standardized protocols for dosage, duration, and administration routes are still being developed. This review summarizes the mechanisms of action, routes of administration, clinical uses, safety considerations, benefits, limitations, and prospects of ozone therapy, incorporating the latest veterinary evidence.

Keywords: Ozone therapy, veterinary medicine, antimicrobial resistance, mastitis

1. Introduction

Ozone (O₃), a triatomic allotrope of oxygen, was first identified in 1840 by Christian Friedrich Schönbein and derives its name from the Greek word “ozein”, meaning *to smell*, owing to its characteristic pungent odour (Srikanth *et al.*, 2013) ^[1]. The gaseous form of ozone is colourless with a sharp, acrid smell, and in liquid or solid states, it becomes highly unstable and explosive (Elvis & Ekta, 2011) ^[2]. Structurally, ozone possesses a dynamically unstable molecular configuration due to the presence of mesomeric resonance states, which contribute to its strong oxidizing potential.

Naturally, ozone is an essential atmospheric component, distributed unevenly between the stratosphere and the troposphere. In the stratosphere, it forms a critical protective layer that absorbs and filters harmful ultraviolet (UV) radiation, safeguarding terrestrial ecosystems.

Stratospheric ozone is continuously generated via the photodissociation of molecular oxygen (O₂) into atomic oxygen (O), which then combines with O₂ to form O₃ (Hänninen, 2019) ^[3]. This process exists in a dynamic equilibrium with its natural degradation, mediated by UV rays and infrared radiation (Mustafa, 1990) ^[4]. Conversely, in the troposphere, ozone is often regarded as an environmental pollutant. It is produced by photochemical reactions between nitrogen oxides (NO) and volatile organic compounds (VOCs) released from automobile exhausts, power plants, industrial emissions, and wildfires in the presence of sunlight (Lange *et al.*, 2018) ^[5]. While excessive ground-level ozone exposure has adverse effects on human, animal, and plant health, its controlled therapeutic use in medicine has gained significant attention in recent decades.

Over the years, its therapeutic applications have expanded in both human and veterinary medicine due to its unique antimicrobial, antioxidant, and immunomodulatory effects (Bocci, 2011) ^[6]. In veterinary practice, ozone is particularly promising in food-producing animals because of its residue-free profile and potential to reduce antimicrobial usage, thus

contributing to control antimicrobial resistance (AMR). Clinical applications range from managing bovine mastitis and postpartum uterine infections to wound healing, osteoarthritis, dental care, viral and protozoal diseases, and supportive oncology (Ogata & Nagahata, 2000; Escandón *et al.*, 2020; Silva Júnior *et al.*, 2020) ^[7, 8, 9]. Despite its growing adoption, widespread clinical use is still constrained by the absence of standardized veterinary protocols, species-specific dosages, and robust randomized controlled trials. Initiatives like those by the 4th Edition of the Madrid Declaration (2025) provide updated international recommendations on veterinary ozone use, emphasizing species-specific dosing, contraindications, and delivery routes (ISCO3, 2025). These SOP-driven frameworks strengthen your safety section. Recent integrative reviews position ozone as a key residue-free alternative that can significantly reduce antimicrobial usage in dairy and food-producing animals, aligning with One Health AMR strategies (Tomanić *et al.*, 2023) ^[10]. This concise literature review aims to highlight the mechanisms of action, primary therapeutic indications, and the potential applications of ozone therapy across various clinical scenarios in veterinary medicine.

2. Mechanism of Action of Ozone Therapy

Ozone (O₃) exhibits its therapeutic properties through a multifaceted mechanism of action involving controlled oxidative stress, antimicrobial effects, immunomodulation, enhanced oxygen delivery, and tissue regeneration. When administered in precise concentrations, ozone triggers a cascade of biochemical and cellular responses that promote healing and modulate immune function without causing cytotoxicity (Bocci, 2011; Elvis & Ekta, 2011) ^[6, 2].

2.1. Oxidative Preconditioning and Reactive Oxygen Species (ROS) Modulation

Ozone rapidly interacts with biological substrates such as polyunsaturated fatty acids, proteins, and antioxidant molecules, leading to the formation of reactive oxygen species (ROS) and lipid oxidation products (LOPs) (Bocci, 2011) ^[6]. ROS, such as hydrogen peroxide (H₂O₂), act as secondary messengers that regulate various cellular signaling pathways. LOPs exert prolonged systemic effects, including immune modulation and vascular improvement. At therapeutic doses, these effects are controlled and transient, stimulating cellular adaptation rather than causing oxidative damage (Silva Júnior *et al.*, 2020) ^[9]. This phenomenon, called oxidative preconditioning, enhances the organism's antioxidant defense systems by upregulating enzymes like Superoxide dismutase (SOD), Catalase, and Glutathione peroxidase. These enzymes help neutralize excess free radicals and maintain redox homeostasis (Bhatt *et al.*, 2016) ^[11].

2.2. Antimicrobial Action

Ozone exhibits potent broad-spectrum antimicrobial properties against bacteria, viruses, fungi, and protozoa (Elvis & Ekta, 2011; Escandón *et al.*, 2020) ^[2, 8]. Mechanisms include Cell membrane damage through oxidation of phospholipids and lipoproteins, protein denaturation by oxidizing sulfhydryl groups, leading to enzyme inactivation, and nucleic acid disruption by damaging the DNA and RNA of pathogens. This makes ozone therapy particularly effective in managing mastitis, endometritis, infected wounds, and parasitic infections in veterinary practice (Ogata & Nagahata, 2000) ^[7].

2.3. Immunomodulatory Effects

At controlled doses, ozone therapy stimulates cytokine production, including interleukin-2 (IL-2) and interferon-gamma (IFN-γ), and modulates tumor necrosis factor-alpha (TNF-α). It enhances the activity of macrophages and natural killer (NK) cells, thereby improving immune surveillance. Furthermore, it contributes to balancing pro-inflammatory and anti-inflammatory pathways, reducing chronic inflammation while promoting appropriate immune activation (Bocci, 2011; Zeng *et al.*, 2020; Silva Júnior *et al.*, 2020) ^[6, 12, 9].

2.4. Improved Oxygen Delivery and Microcirculation

Ozone therapy helps improve oxygen delivery by increasing 2,3-diphosphoglycerate (2,3-DPG) in red blood cells, which allows more oxygen to reach tissues. It also makes blood flow better by reducing clumping of red cells and improving capillary circulation. In addition, ozone stimulates nitric oxide (NO) production, causing blood vessels to widen and improving microcirculation. These effects are especially useful in treating ischemic wounds, laminitis, and infections in animals where tissues are low in oxygen (Silva Júnior *et al.*, 2020) ^[9].

2.5. Anti-inflammatory and Analgesic Effects

Ozone therapy reduces inflammation through multiple mechanisms, including the downregulation of pro-inflammatory mediators such as prostaglandins, tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β). At the same time, it promotes the upregulation of anti-inflammatory cytokines such as interleukin-10 (IL-10). Additionally, ozone activates endogenous opioid pathways, which contribute to pain relief in musculoskeletal disorders (Escandón *et al.*, 2020) ^[8].

2.6. Tissue Regeneration and Wound Healing

Ozone promotes tissue repair and regeneration by stimulating fibroblast proliferation and collagen synthesis, enhancing angiogenesis (formation of new blood vessels), improving oxygenation at wound sites, and accelerating epithelial regeneration and reducing microbial contamination (Bocci, 2011; Escandón *et al.*, 2020) ^[6, 8].

3. Production of Medical Ozone

Therapeutic ozone is produced by passing pure medical-grade oxygen through ozone generators, resulting in a combined oxygen-ozone (O₂-O₃) mixture. The ozone concentration in this blend typically ranges from 0.05% to 5% (1 to 107 µg/mL), while the corresponding oxygen concentration varies between 99.95% and 95% (Oliveira Junior & Lages, 2012; Schwartz *et al.*, 2020) ^[13, 14]. Ozone generation technologies are well established in both medical and industrial applications. The most commonly used methods include corona discharge, ultraviolet (UV) radiation, cold plasma dielectric barrier discharge (DBD), and electrolytic generation.

Each method differs in principle, efficiency, and suitability for specific therapeutic or industrial purposes.

3.1. Corona Discharge Method

The corona discharge method, also referred to as dielectric barrier discharge (DBD), is the most widely used technique for producing medical-grade ozone. In this method, a high-voltage electrical field (typically 5–20 kV) is applied across electrodes separated by a dielectric material such as glass, quartz, or ceramic. The strong electrical field splits

oxygen molecules (O_2) into atomic oxygen (O), which then combines with O_2 to form ozone (O_3)

This method is considered the gold standard due to its high efficiency, scalability, and ability to precisely control ozone concentrations (Zhang *et al.*, 2025) ^[15]. However, the process generates significant heat, necessitating cooling systems to prevent ozone decomposition and ensure stable output (Oliveira Junior & Lages, 2012) ^[13]. If atmospheric air is used instead of medical oxygen, nitrogen oxides (NO) may form as unwanted by-products, which can be corrosive and $\times$ toxic (Schwartz *et al.*, 2020) ^[14].

3.2. Ultraviolet (UV) Radiation Method

In the UV radiation method, oxygen molecules are exposed to ultraviolet light with a wavelength of approximately 185 nm, which breaks O_2 into atomic oxygen. These atoms then recombine with O_2 to form ozone.

This method has a simpler equipment design and is often used in applications requiring low ozone concentrations, such as surface sterilization or topical therapies. However, it produces relatively low yields of ozone compared to the corona discharge method and lacks precise control at high concentrations (Epelle *et al.*, 2022) ^[16].

3.3. Cold Plasma Method

The cold plasma method, a variation of the dielectric barrier discharge (DBD) system, utilizes non-thermal plasma to produce highly pure ozone. In this technique, a plasma field consisting of micro-discharges is generated, splitting O_2 molecules into atomic oxygen, which then forms ozone.

Cold plasma generators can produce ozone concentrations as high as 24%, offering greater stability and efficiency compared to conventional corona systems (Bocci, 2013) ^[17]. Additionally, the lower operating temperature reduces equipment degradation, making this method particularly suitable for sensitive medical applications. However, the complexity and cost of cold plasma systems limit their widespread use (Martínez-Sánchez *et al.*, 2005) ^[18]. Advancements in cold plasma and dielectric barrier discharge (DBD) generators have improved ozone concentration stability, making therapeutic applications more standardized (Zhang *et al.*, 2025) ^[15].

3.4. Electrolytic (Electrochemical) Method

The electrolytic method involves producing ozone through the electrolysis of water. Using specialized electrodes and catalysts such as lead dioxide or boron-doped diamond, this method generates ozone directly from water without requiring an external oxygen feed.

It can achieve high ozone concentrations (20–30%) in dissolved form and eliminates the risk of producing nitrogen oxides. However, the system has a lower throughput compared to corona discharge and requires expensive, specialized electrodes that may need frequent replacement (Schwartz *et al.*, 2020) ^[14].

4. Mechanisms of Action

The biological effects of ozone therapy are multifactorial and dose-dependent, mediated through antimicrobial activity, oxidative preconditioning, immune modulation, and improved tissue perfusion. As a potent oxidant, ozone disrupts microbial membranes by oxidizing polyunsaturated fatty acids and sulfhydryl groups, leading to structural damage and cell lysis (von Gunten, 2003) ^[19]. It reacts with viral envelope glycoproteins and capsid proteins, inhibiting host-cell attachment and replication, while protozoal cyst walls and key metabolic enzymes are similarly compromised, reducing

infectivity in pathogens such as *Giardia lamblia* and *Cryptosporidium parvum* (Rajabi *et al.*, 2015; Vojtkovská *et al.*, 2023) ^[20, 21]. At therapeutic concentrations, ozone induces a mild, controlled oxidative stress that activates the nuclear factor erythroid 2-related factor 2 (*Nrf2*) pathway, upregulating antioxidant enzymes including superoxide dismutase, catalase, and glutathione peroxidase. This “oxidative preconditioning” enhances cellular resilience and redox homeostasis, protecting tissues from oxidative injury. Recent studies confirm ozone’s hormetic effect by transiently elevating ROS and lipid oxidation products, activating *Nrf2* pathways, and balancing *NF- κ B* signaling, which leads to decreased pro-inflammatory cytokines (*TNF- α* , *IL-1 β*) and increased *IL-10*, thereby enhancing immune regulation and reducing chronic inflammation (Cenci *et al.*, 2022; Silva *et al.*, 2023) ^[22]. Immunomodulatory effects are also significant: ozone stimulates macrophage phagocytosis, neutrophil activation, and natural killer cell cytotoxicity, while balancing pro- and anti-inflammatory cytokines by downregulating tumor necrosis factor- α (*TNF- α*) and interleukin-1 beta (*IL-1 β*) and increasing interleukin-10 (*IL-10*) (Cenci *et al.*, 2022) ^[22]. Furthermore, ozone improves local microcirculation by enhancing erythrocyte deformability and tissue oxygen delivery. It modulates inflammatory pathways by suppressing *NF- κ B* activation and reducing cyclooxygenase-2 (*COX-2*)-driven prostaglandin synthesis, resulting in decreased edema, pain, and inflammatory tissue damage (Chen *et al.*, 2013) ^[23]. Collectively, these mechanisms explain the broad therapeutic potential of ozone therapy in veterinary medicine.

5. Routes of Administration

The route of ozone delivery depends on the disease condition, target tissue, and desired systemic or local effect.

5.1 Major and Minor Autohemotherapy

Major autohemotherapy involves withdrawing venous blood, exposing it to a controlled oxygen-ozone mixture, and reinfusing it intravenously. It enhances immune regulation, improves oxygen utilization, and has shown benefits in systemic infections and as an adjunct in oncology (ISCO3, 2023) ^[24]. Minor autohemotherapy, where a small quantity of ozonated blood is injected intramuscularly, induces localized immune stimulation and has been used in canine mammary tumors alongside chemotherapy to improve oxidative profiles and quality of life (Silva *et al.*, 2024) ^[25].

5.2 Rectal insufflation

Rectal insufflation represents a non-invasive systemic delivery method, with crossover studies in dogs confirming short-term safety and oxidative balance at therapeutic doses (de Oliveira *et al.*, 2024) ^[26]. Rectal ozone insufflation is generally considered safe when used within recommended therapeutic ranges; however, certain conditions require caution. The absolute contraindication is severe anemia, particularly when the hematocrit level is below 20%. Relative contraindications include acute myocardial infarction, pregnancy in the first trimester, uncompensated toxic hyperthyroidism, thrombocytopenia with platelet counts below 50,000 or severe coagulation disorders, severe cardiovascular instability, massive or acute hemorrhage, active convulsive states, hemochromatosis, uncontrolled diabetes mellitus, and patients undergoing copper or iron therapy. Additionally, ozone concentrations above 40 μ g/mL should be strictly avoided, as they may damage the intestinal enterocytes (ISCO3, 2023) ^[24].

Table 1: Indicative Recommended Ozone Doses for Major Autohemotherapy in small Animals (ISCO3, 2023)

Category	Specific Conditions	O ₃ Conc. (µg)	Dose (mL/kg)	Blood Vol. (mL)	Frequency / No. of Treatments
Gastrointestinal	Acute gastroenteritis, canine parvovirus, parasitic & immune-mediated GI diseases, pancreatitis	15–35	1–1.5	8	10 weekly
	Chronic gastroenteritis	15–35	1–1.5	8	8–10
Leishmaniasis	Leishmaniasis	20–35	1–1.5	8	8–10
Hematology (Hct <20% caution)	Anemia, immune-mediated thrombocytopenia	10–35	1–1.5	4	4–8
Liver	Acute & chronic liver diseases	10–35	1–1.5	8	8–16
Nephro-Urology	Acute & chronic kidney diseases	10–35	1–1.5	8	8 / undefined
	Idiopathic feline cystitis	10–25	1	8	8–12
Oncology	Adjuvant/therapeutic	10–35	1–1.5	8	8 / undefined; cycles every 3 months
Dentistry	Periodontal disease, feline gingivostomatitis	15–30	1	8	8–15
Endocrinology	Hypothyroidism, hypoadrenocorticism, diabetes mellitus	15–35	1.5	8	8–20
Ophthalmology	Herpesvirus, calicivirus, papillomavirus, corneal ulcers	10–25	1–1.5	8	8
Cardiorespiratory	Feline asthma, herpesvirus, calicivirus, pulmonary fibrosis, insufficiency	15–30	1	4	4–8
Genitourinary	Prostatitis, BPH, intraprostatic cysts, orchitis, vaginitis, pyometra, endometritis	15–35	1–1.5	4	4–8
Dermatology	Dermatitis (bacterial, fungal, viral, parasitic), immune-mediated dermatitis, vasculitis, hyperkeratosis, anal fistulas	15–35	1–1.5	8	8–10
Neurology	Herniated disc, discospondylitis, immune encephalitis, ischemic vascular alterations, cognitive dysfunction, degenerative myelopathy, neuromuscular disorders	15–35	1–1.5	6	6–15
Traumatology	Osteoarthritis, septic arthritis, osteomyelitis	10–35	1–1.5	6	6–15

Table 2: Indication of recommended doses of ozone for rectal insufflation in small animals (ISCO3, 2023).

Recommendation	Concentration of O ₃ (µg/mL)	Volume (mL/kg)	Frequency of treatment/number of treatments
Acute gastroenteritis, canine parvovirus, parasitic diseases, GI immune-mediated diseases, pancreatitis, chronic gastroenteritis	10-30	3	12
Leishmaniasis	20-35	3	12-15
Immune-mediated anemia and thrombocytopenia	10-35	3	9-12
Acute and chronic hepatic diseases	10-35	3	10-20
Acute and chronic kidney disease	10-35	3	10-20
Idiopathic feline cystitis	10-35	3	10-20
Oncology	10-35	3	10-20
Periodontal disease	20-35	3	8-15
Feline gingivostomatitis	20-35	3	8-15
Hypothyroidism, Hypoadrenocorticism	10-35	3	10-20
Diabetes Mellitus	10-35	3	10-20
Herpesvirus, Calicivirus, Papilloma virus	10-25	3	10-15
Corneal ulcers	10-25	3	10-15
Feline Asthma, Calicivirus Herpes Virus	20-30	3	12-15
Pulmonary fibrosis	20-30	3	12-15
Cardiorespiratory failure	15-35	3	12-15
Prostatitis, BPH cysts, intra-prostatic	15-35	3	12-15
Orchitis	15-35	3	12-15
Vaginitis	15-35	3	12-15
Pyometra, Endometritis	15-30	3	12-15
Dermatitis: bacterial, fungal, viral, parasitic	15-30	3	12-15
Immune-mediated Dermatitis Vasculitis	10-35	3	12-15
Hyperkeratosis Anal fistulas	20-35	3	12-15
Herniated disc, Discospondylitis	10-35	3	9-12
Immune-mediated encephalitis	10-35	3	9-12
Ischemic vascular changes	10-35	3	9-12
Cognitive dysfunction	10-35	3	9-12
Degenerative myelopathy	10-35	3	9-12
Degenerative myopathy	10-35	3	9-12
Osteoarthritis	10-35	3	12-15
Septic arthritis	10-35	3	12-15
Osteomyelitis	10-35	3	12-15

5.3 Intrauterine ozone

In dairy cattle, intrauterine ozone administration has shown promise in managing postpartum uterine diseases by accelerating involution and improving conception rates (Escandón *et al.*, 2020) ^[8].

5.4 Ozone bagging

Ozone “bagging,” where an affected limb or wound is enclosed in an ozone-resistant bag, achieves high local concentrations and promotes healing in ulcers, burns, and hoof lesions (Frezza *et al.*, 2024) ^[27].

5.5 Ozonated oils

Ozonated oils and water are also widely used in dermatological and dental applications. Ozonated olive oil effectively manages ear mite infestations (*Otodectes cynotis*) and chronic dermatitis, while ozonated water serves as a safe irrigant in periodontal care and wound management (Altınok-Yipel *et al.*, 2016; Marchegiani *et al.*, 2019) ^[6, 28]. Ozonated oils such as olive, linseed, hemp, and sunflower, revealing that linseed and hemp oils showed stronger antibacterial activity and higher oxidative stability (Slavinskienė *et al.*, 2024; Repciuc *et al.*, 2025) ^[29, 30].

5.6 Intra-articular ozone injections

Intra-articular ozone injections benefit osteoarthritic joints by reducing synovial inflammation and improving mobility, with canine trials demonstrating significant functional gains when combined with hyaluronic acid (Silva Júnior *et al.*, 2020) ^[9]. Intravenous ozonized fluids, typically prepared using Ringer’s lactate, have been successfully used as supportive therapy in canine parvoviral enteritis, leading to faster clinical recovery (dos Santos *et al.*, 2023) ^[31]. Ozone is combined with hyaluronic acid (HA), showing better pain relief, improved joint mobility, and enhanced cartilage protection compared to HA alone (Akhavanakbari *et al.*, 2025; Unlu *et al.*, 2025) ^[32, 33].

6. Clinical Applications

Ozone therapy has gained recognition in veterinary medicine due to its multifaceted biological effects and diverse therapeutic applications. In dairy practice, intramammary ozone therapy has demonstrated efficacy in reducing bacterial load, lowering somatic cell counts, and improving milk quality in acute bovine mastitis, with Ogata and Nagahata (2000) ^[7] reporting approximately 60% clinical recovery without antibiotics. While randomized trials are limited, ozone’s residue-free nature positions it as a valuable adjunct under antibiotic stewardship programs. Recent reviews position ozone therapy as an antibiotic-sparing adjunct for mastitis management, highlighting its potential role in reducing antimicrobial resistance programs (Tomanić *et al.*, 2023) ^[10].

In wound healing, ozone accelerates granulation, angiogenesis, and epithelialization while exerting strong antimicrobial effects, making it particularly effective in managing contaminated wounds, ulcers, and burns. Experimental studies have demonstrated significant improvements in wound contraction, tensile strength, and vascularization with ozone therapy compared to conventional care (Frezza *et al.*, 2024) ^[27]. Additionally, ozonated oils—particularly linseed and hemp—exhibit stronger antimicrobial activity against *Staphylococcus* spp. and *E. coli*, supporting their inclusion in veterinary wound-care protocols (Slavinskienė *et al.*, 2024) ^[29].

Reproductive medicine has also benefited from ozone therapy. In postpartum dairy cows, intrauterine ozone administration significantly improved uterine involution, reduced endometritis prevalence, and enhanced conception rates compared to standard antibiotic protocols (Escandón *et al.*, 2020) ^[8]. Its residue-free property makes it particularly suitable for food-producing animals. Comparative studies on intrauterine therapies show that ozone provides effective alternatives to antibiotics for treating postpartum endometritis while avoiding drug residues (Menoud *et al.*, 2024) ^[34].

In musculoskeletal disorders, intra-articular ozone therapy has shown promising outcomes. A controlled trial in dogs with naturally occurring hip osteoarthritis demonstrated significant improvements in lameness, mobility, and overall quality of life when ozone was combined with hyaluronic acid compared to hyaluronic acid alone (Silva Júnior *et al.*, 2020) ^[9]. Similar applications in equine practice highlight its potential in laminitis and joint inflammation management.

Ozone also plays an adjunctive role in managing infectious diseases. In puppies with canine parvoviral enteritis, intravenous ozonized fluids significantly shortened hospitalization time and improved clinical recovery when used alongside conventional therapy (dos Santos *et al.*, 2023) ^[31]. Laboratory studies further demonstrate its effectiveness in inactivating protozoan pathogens, including *Giardia lamblia* and *Cryptosporidium parvum*, indicating potential in controlling protozoal infections (Rajabi *et al.*, 2015) ^[20]. Recent shelter studies confirm that gaseous ozone effectively inactivates major veterinary viruses such as feline calicivirus, canine coronavirus, and parvovirus under controlled conditions, supporting ozone’s role in environmental disinfection protocols (Vojtkovská *et al.*, 2023; Catella *et al.*, 2024) ^[21, 35].

In oncology, ozone therapy is being explored as a supportive adjunct to conventional chemotherapy. In dogs with mammary carcinoma, adjunctive ozone therapy improved oxidative profiles and enhanced quality-of-life parameters without replacing standard treatments (Silva *et al.*, 2024) ^[25]. While veterinary oncology evidence remains preliminary, these findings suggest a promising role for ozone in integrative cancer care.

Advantages and Limitations

Ozone therapy offers several advantages in veterinary medicine. Its broad-spectrum antimicrobial activity, lack of harmful residues, immune and antioxidant enhancement, and environmental safety make it highly appealing, especially in food-producing species. Additionally, it may reduce reliance on conventional antibiotics, supporting global efforts to combat antimicrobial resistance.

However, limitations include ozone’s short half-life, requiring on-site generation, the lack of standardized therapeutic protocols across species, limited large-scale clinical trials, and the potential for oxidative damage if administered improperly. These challenges underscore the importance of evidence-based dosing, species-specific guidelines, and monitoring.

Safety Considerations

Safety in ozone therapy relies on strict adherence to standardized protocols established by ISO 3 and other regulatory frameworks. Pulmonary exposure must be avoided due to the risk of respiratory toxicity. Dosage and route should be carefully selected based on clinical indication, species, and health status. Monitoring of oxidative biomarkers is recommended in critically ill patients, and ozone-generating

equipment should be properly calibrated and certified to ensure safe and reproducible outcomes.

Future Prospects

Ozone therapy represents an innovative, eco-friendly adjunct in veterinary medicine with potential applications across clinical disciplines. Future priorities include developing species-specific evidence-based protocols, conducting randomized controlled trials for conditions such as mastitis, postpartum uterine disease, osteoarthritis, and wound management, and integrating ozone therapy into multimodal treatment regimens alongside antibiotics, nutraceuticals, and probiotics. Advances in portable ozone delivery systems and automated generators are expected to expand their field applicability, particularly in food-animal practice, while reducing antimicrobial use and supporting sustainable livestock farming.

7. Conclusion

Ozone therapy is emerging as a promising, versatile, and environmentally friendly therapeutic tool in veterinary practice. Its antimicrobial, antioxidant, and immunomodulatory properties underpin applications in mastitis management, wound healing, reproductive health, osteoarthritis, dentistry, oncology, and adjunctive infectious disease control. While current evidence is encouraging, widespread clinical integration requires robust species-specific trials, standardized protocols, and further mechanistic studies to ensure efficacy and safety. As the demand for residue-free, antibiotic-sparing therapies grows, ozone therapy is poised to play an increasingly important role in integrative veterinary medicine.

Conflict of Interest

Not available

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Not available

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