CHAPTER 33

Ginseng in Veterinary Practice: Benefits and Considerations

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SUMMARY

Plants have been used as medicine for all diseases since the inception of this universe. Plant based preparations and their active single components are widely used as prophylactic and therapeutic agents. The major advantage of plant-based remedies is their least to no side effects. Panax Ginseng is native plant of China, Japan, and Korean peninsula. It is widely used in various forms like tablets, syrups, capsules, jelly, tea and many more. All the parts of this plant are used in herbal medicine; however, the roots of this plant are more enriched in single, active compounds called ginsenosides. This plant is also called a panacea because it has been reported for its unique biological properties like anti-inflammatory, anti-cancerous, anti-microbial, anti-melanogenic, immune booster and many more. Many studies have revealed the beneficial effects of ginseng on laboratory animals for various disease models. Clinical trials on humans have also revealed cardio-protective and libido enhancing effects of ginseng. In animals, ginseng has been reported as immune boosting agent for various viral and bacterial diseases. Our chapter focuses on the diverse application of ginseng in veterinary field for the treatment of various diseases related to ruminants, equines, canines, and poultry.

Introduction

Ethnopharmacology is defined as the scientific study of plants, or any other material used in ethno-cultures as traditional/natural medicines (Patwardhan, 2005). Natural products are the source of common active ingredients used in allopathic medicine. In fact, before the development and evolution of the post-genomic era, more than 80% of chemical drugs were inspired or manufactured from natural compounds. Synthetic compounds with therapeutic potential made from natural/plant materials provide advances in the field of medicine. For example, the use of cinchona, morphine, and digitalis for the treatment of malaria, as well as the advent of aspirin, convinced people as early as the 17th century that flower sources could be used medicinally to treat different diseases (Mukherjee et al., 2010). Furthermore, many contemporary and modern medicines are derived from different plants and fungi, such as streptomycin *(Streptomyces griseus*), penicillin (*Penicillium* spp.), valerian (*Valeriana* spp.), and atropine [*Atropa belladonna*, deadly nightshade (Smith-Schalkwijk, 1999)]. Therefore, it can be said that ethnopharmacology provides a solid foundation and a way forward for the development of new, improved, and effective chemical drugs from plants.

Plants have been utilized by humans and animals since the dawn of this world. They were and are mainly used as food sources by various animals including humans. Many treatments for various diseases depend on particular types of plants. Extensive modernization and civilization have made humans and animals susceptible to all kinds of novel diseases. There are modern allopathic medicines for these diseases and conditions, but their side effects should not be ignored. Therefore, in the past two decades, mankind has once again turned its attention to herbal remedies for various ailments. The same applies to

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animals as well. Most pet owners require and prefer some herbal and allopathic medications (Smith-Schalkwijk, 1999).

Ethnopharmacology of plants helps to identify natural plants with therapeutic potential in specific ethnic or cultural regions. For example, *Trachyspermum ammi* (L.) Sprague ex Turrill or Carom seeds or Ajwain are cultivated in subcontinent regions and are commonly used in the treatment of digestive disorders in humans and animals, leading to inferences about their origin and function (Goyal et al., 2022). Likewise, ginseng, an herbal supplement widely grown and used in Korea, China, and Japan, is rich in biological properties that significantly prolong lifespan, increase libido, suppress cardiovascular diseases, and many more (Yue et al., 2007). There is little concise information on the use of ginseng in veterinary practice, so the purpose of this chapter is to convey and disseminate knowledge about the ethnopharmacological use of ginseng in veterinary practice.

PANAX GINSENG

Panax (*P.*) *Ginseng* Meyer belongs to the floral family of Araliaceae. It is a perennial herb with three to five leaflets. Compared to actively growing plants, ginseng takes around 5-7 years to mature from seed sowing. This long growing season enriches the plant with many beneficial and precious compounds. There are nearly 9 species of ginseng, named according to their geographical locations, such as Asian ginseng (*P. Ginseng*), Japanese ginseng (*P. Japonicus*), American ginseng (*P. Quinquefolium*), and Chinese ginseng [*P. Notoginseng* (Mancuso et al., 2017]. Ginseng is native to Korea and China. There is some debate on the true ethnicity of ginseng from Korea or China. Past literature has shown that ginseng originated from Manchuria and Korea (Yang et al., 2004). Russian Botanist Carl. A. Meyer in 1843 coined the genus name "Panax" to ginseng which is a Greek word meaning "all-healing" (Leung et al., 2013). All parts of this plant (i.e., roots, leaves, fruit, and stem) possess bioactive properties against various disorders in the body Fig 1. The roots of this plant look exactly like a human body and are hence attributed as "Panax" which means cures for all head-to-toe ailments. Overall ginseng exhibits anti-inflammatory, anti-cancerous, anti-diabetic, vasodilating, and anti-allergic properties (Kim, 2018)

The ethnopharmacological significance of this plant lies in the variety of active single compounds called ginsenosides. Ginsenosides are tetracyclic triterpenoids saponins. In addition to saponins, ginseng also contains polyphenolic compounds, polyacetylenes, and acidic polysaccharides. Ginsenosides are divided into three groups based on their chemical structures. The first is protopanaxatriols (Rg1, Rg2, Rf, Re), the second is protopanaxadiols (Rb1-3, Rc and Rd), and the third is oleanane group [Ro (Baek et al., 2012)]. Ginseng is widely consumed in both fresh and processed forms. Fresh ginseng is used as a condiment in many Korean and Chinese dishes and is most commonly used in processed form. Based on processing techniques, ginseng is divided into three types namely Red ginseng (fresh ginseng root steamed and dried for 1 time), white ginseng (naturally dried ginseng), and black ginseng prepared when ginseng root steamed and dried for 3 times (Koh et al., 2015, Lee et al., 2015).

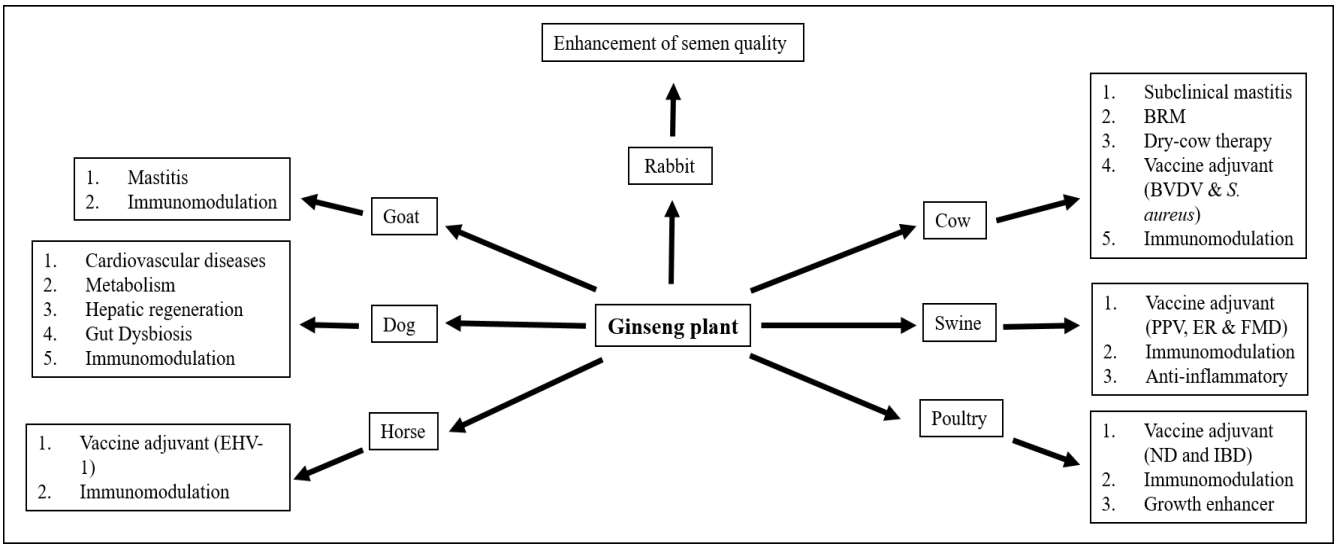

Fig 1. Therapeutic potential of ginseng plant against various diseases.

The most common effects of ginseng are its effects on the nervous system. It is known to enhance mental performance, memory, cognitive learning, sensory alertness, and awareness

(Park et al., 2019). This function is attributed to the availability of saponins present in this herb, which increase the activity of adrenocorticotropic hormone (ACTH) in the brain, thereby mounting mental arousal (Ma et al., 2007). Ginsenoside Re (G-Re) has been reported to elevate acetylcholine and dopamine levels in the brains of rats, thereby enhancing libido in male rats (Shi et al., 2013). The positive effect of ginseng and its ginsenosides on the male reproductive system is what this herb is best known for in the Asian region. Ginsenosides not only enhance libido but also increase serum testosterone levels and spermatogenesis and reduce male infertility (Leung et al., 2013, Sengupta et al., 2022).

GINSENG IN VETERINARY HOMEOPATHY

Generally, homeopathy refers to the treatment of a disease by serial dilution of the pathogen solution or its components that cause the disease, because the undiluted form of that pathogen or its substance might cause symptoms of the disease (Fisher, 2012).

Ginseng is used in veterinary homeopathy as a mother tincture consisting of dried ginseng root. The components of dried ginseng root are ginsenosides (Rg1-content is the most, accounting for about 6%), triterpene saponins, sesquiterpenes, etc. Beta-elemene, eremophilene, polyacetylene, falcarinol, polysaccharides, and essential oils @ 0.05% (Consultation, 2006).

GINSENG IN VETERINARY PRACTICE

Before going into the details about the various uses of ginseng in veterinary, it is necessary to mention that ginseng has been recommended as safe for consumption by humans and in veterinary use according to a European medicine agency report by Committee for Medicinal Products for Veterinary Use (Consultation, 2006). This means that all commercially available ginseng preparations are non-toxic and safe to consume without known side effects. The safety of ginseng use was reported as early as 1983 when a 90-day study of 0, 1.5, 5, and 15 mg of ginseng orally administered [Ginsana (G115)] to 32 beagle dogs reported no toxic effects (Hess et al., 1983).

Immunomodulatory role of ginseng on mastitis in cows

Bovine mastitis is defined as an inflammatory response of the tissue present in the mammary gland, mainly due to physical damage/trauma and infectious pathogens. Mastitis is a widespread disease in large animals that has been of concern due to economic losses in the dairy industry. The economic losses are incurred due to poor quantity and quality of milk (Cheng et al., 2020). According to the severity of inflammation, mastitis is divided into three types: subclinical, clinical, and chronic mastitis. Clinical mastitis, as the name suggests, is characterized by significant signs of inflammation in the udder, with clots and flakes of watery milk. However, subclinical mastitis does not show severe clinical symptoms, but milk production is reduced, and somatic cell count is increased. Bovine production experts agree to the fact that subclinical mastitis accounts for more productive and financial losses in cattle than clinical type (Zhao et al., 2008, Romero et al., 2018). The physical causes for the mastitis include trauma to the udder while milking or dirty environment and sanitation conditions of the cow shed/housing. The pathogenic factors include *Staphylococcus aureus* and *Streptococcus agalactiae*, and less common species like Mycoplasma *bovis* and *Corynebacterium*, which are the natural residents of cow's udder and teat skin (Kibebew, 2017). There are many allopathic treatment options available for mastitis like antibiotic courses, intramammary infusions, and many others. In herbal medicine, ginseng has been reported for the treatment of cows with subclinical mastitis. For example, one study reported that subcutaneous injection of ginseng extract at 8 mg/kg body weight for 6 days activated innate immunity in cows with subclinical mastitis. The number of monocytes and lymphocytes, phagocytes, and oxidative burst activity of neutrophils were significantly increased after ginseng extract treatment (Hu et al., 2001). Furthermore, another study also reported that ginseng extract significantly reduced the internalization of two *S. aureus* strains in bovine mammary epithelial cells (Beccaria et al., 2018).

It has also been reported that ginseng crude extract (GS) and ginsenoside Rb1 (G-Rb1) have excellent adjuvant effects in bovine mastitis S. aureus vaccination by enhancing lymphocyte proliferation and antibody production (Hu et al., 2003). This means that ginseng is not only beneficial for the treatment of mastitis directly but also beneficial for the prevention of mastitis when used in vaccines.

Potential role of ginseng to improve biological response during dry period in cows

The dry period of dairy cows is an important and critical stage in the next lactation cycle. During this time, milk production stops abruptly, and the teat ducts are sealed to prevent the entry of pathogens. Dairy cows undergo dry cow therapy, which includes an application of intramammary antibiotics (Vilar et al., 2020). In this regard, ginseng is used as a biological response modifier. Biological response modifiers (BRM) are agents that modify the host's response to pathogens with resultant beneficial prophylactic or therapeutic effects. A single intramammary infusion of *P. ginseng* extract as an alternative therapy for the control of mastitis has been reported to have a beneficial effect on TNF-α production during the dry period, with higher levels of macrophage/monocyte numbers in cows. In this study, GS extract was used as BRM to maintain low levels of antimicrobial counts in the dry phase of domestic cattle (Baravalle et al., 2011). GS extracts have also been reported to suppress somatic

cell counts, pro-inflammatory cytokine expression, and TNF-α levels in milk during drying-off periods in domestic cattle (Baravalle et al., 2010). Infusion of *P. ginseng* to udder quarters at the time of cessation of lactation resulted in a significant increase in the expression of Toll-like receptors (TLRs) 2, 4, NF-κB, TGF-β1, IL-Iβ, and IL-6. These results suggest that ginseng enhances innate immunity during bovine mammary gland involution (Baravalle et al., 2015).

Use of ginseng for mastitis in lactating goats

Not only whole ginseng extract but single ginsenosides are also effective against mastitis in lactating goats. The lactating goats were given intramammary infusions of liposaccharide (LPS) in one-half of the udder for the development of clinical mastitis. After the bacterial challenge, Ginsenoside Rg1 (G-Rg1) and saline were administered intravenously. The results showed that G-Rg1 treatment reduced rectal temperature, udder skin temperature, udder circumference, and somatic count in milk. Moreover, it also enhanced the levels of milk production, lactose, white blood cells, and blood proteins (Wang et al., 2019). The addition of cultured wild ginseng root (CWGR) to goats' total mixed ration (TMR) increases plasma IgG and protein levels in organic Saanen dairy goats (Bae, 2016).

Use of ginseng in bovine viral diarrhea vaccines in bovine

Bovine Viral Diarrhea Virus (BVDV) is a serious disease condition in cattle causing major economic losses due to severe gastroenteritis and a high mortality rate (Al-Kubati et al., 2021). The glycoprotein E^{rns}, the major envelope protein of the virus, elicits BVDV-associated immunogenicity. *Panax ginseng* has been reported as an alternative plant-based vaccine adjuvant for the expression of the glycoprotein E^{rns} by Agrobacterium-mediated transformation. The glycoprotein E^{rns} was successfully expressed in hairy ginseng roots with potent antigenic and immunogenic properties when evaluated subcutaneously in deer (Gao et al., 2015).

Use of ginseng in rabbit semen

As already given in the previous sections of ginseng, where we have highlighted the remarkable effects of ginseng on the reproductive system of males, Korean red ginseng aqueous extract (KRG) was also reported for its semen quality-enhancing effects in mature Baladi black rabbits. Sperm penetration into estrus cow cervical mucous was highest with 50 µL/mL KRG in semen for artificial insemination. Moreover, sperm motility, percentage of alive spermatozoa, conception rate, kindling rate, and litter size were significantly increased with the use of KRG (Riad et al., 2009).

Use of ginseng as immune booster to Equid Herpesvirus 1 (EHV-1) vaccine in equines

Equine herpesvirus 1 (EHV-1) is also known as the equine abortion virus. It is a highly contagious equine disease characterized by respiratory symptoms, miscarriages, neonatal deaths, and neurological disorders (Yildirim et al., 2015). The best treatment for this disease is prevention through vaccination. In this regard, ground ginseng powder (35 mg/kg body weight) in molasses was administered to horses for 28 days. On day 14, they received the EHV-1 vaccine. An increase in antibody titer was observed in horses that received ginseng as compared to the control group on day 2 post-vaccination. No adverse effects were found in horses supplemented with ginseng, suggesting that the use of ginseng in horse feed is safe (Pearson et al., 2007).

Use of ginseng as an adjuvant for porcine parvovirus, *Erysipelothrix rhusiopathiae,* and Foot and Mouth Disease vaccines in swine

Porcine Parvoviral (PPV) infection is endemic in pig herds. It is the most common cause of reproductive failure in sows (Streck et al., 2020). Erysipelothrix rhusiopathiae (ER) is a gram-positive bacterium which causes a disease called Erysipelas. It causes a disease in pigs called rhombic dermatosis, in which diamond-shaped lesions form on the pig's skin accompanied by fever, depression, anorexia, arthritis, and heart valve disease (Wang et al., 2010). Vaccination is the most important part of the management of PPV and ER infections. In this regard, ginseng has also been reported as a better vaccine adjuvant compared to aluminum hydroxide. Pigs were vaccinated with vaccines adjuvanted with aluminum hydroxide or gensing against porcine parvovirus and *Erysipelothrix*. The ginseng adjuvant antibody titer was higher, which is beneficial to the production of IgG2 antibody. Additionally, adding ginseng to a less immunogenic vaccine converted it into a more potent form (Rivera et al., 2003).

Foot-and-mouth disease (FMD) is also a highly contagious disease of artiodactyls. It is characterized by ulcerative blisters on the mouth, nose, and feet. Foot and mouth disease is highly debilitating to animals and also causes huge economic losses to the owners of pig and cattle farms in terms of animal loss and high disease spread. Vaccination is the last resort for managing FMD in swine or cattle (Stenfeldt et al., 2016). Ginseng leaf and stem saponins (GSLS) have been reported to have beneficial effects on FMD vaccination. Pigs exhibited an enhanced humoral response to FMD infection when injected with the FMD oil-emulsion vaccine supplemented with ginseng leaf and stem saponins (GSLS) at a dose of 40 µg. The addition of GSLS increased the levels of IgG1 and IgG2 (Li et al., 2012).

Korean red ginseng is also reported to enhance the immunity of pigs. A study reported that the fermentation of Korean red ginseng dregs with *Bacillus subtilis* (RGMB) resulted in

increased levels of ginsenoside Rb1. Supplementation of pigs to diets with 1% RGMB resulted in decreased levels of AST, ALT, IL-1β, IL-6, and TNF-α. However, it increased the levels of IgA antibodies. This suggests that RGMB has an immune-enhancing and inflammatory-suppressing effect in pigs (Kim et al., 2018).

Use of ginseng as a feed additive and vaccine adjuvant in poultry

In chickens, ginseng stem and leaf saponins (GSLS) increased growth rate and IgG levels compared to the vaccine control group. This study shows that ginseng is a good candidate as a feed additive for the poultry industry (Park et al., 2015). Oral treatment with GSLS as a vaccine adjuvant has also been reported to provide better protection against lethal infectious bursal disease virus by enhancing humoral and intestinal mucosal immune responses. Results showed significant increases in intestinal intraepithelial lymphocytes, IgA-positive cells, and antibody titers after GSLS treatment before oral IBDV vaccination (Zhai et al., 2014). Not only for IBD but GSLS is also reported for its immune-enhancing effects in chickens vaccinated with the live New Castle disease vaccine (Zhai et al., 2011).

Use of ginseng in companion animals

The effects of Korean ginseng on dogs were reported as early as 1978 and 1981. This study reported that the administration of 40 mg/kg of the ether and ethanol extracts of ginseng resulted in suppression of heart rate, central venous pressure, and mean arterial pressure in dogs under 0.75% halothane anesthesia. Furthermore, the administration of aqueous extracts of ginseng resulted in decreased levels of cardiac output, central venous pressure, and stroke volume. This study demonstrated the alpha-blocker effect of ginseng in canine cardiovascular disease (Lee et al., 1978; Lee et al., 1981). Oral treatment of Korean red ginseng (KRG) in 40% of hepatectomized mongrel dogs resulted in lower AST and ALT levels and higher rates of liver regeneration (Kwon et al., 2003). Metabolic profiling of beagle dogs fed black ginseng for 8 weeks resulted in increased levels of serum biomarkers such as glutamine, histidine, isoleucine, leucine, proline, formate, and valine. These effects confirm the immune-boosting and energy-metabolizing properties of ginseng (Yoon et al., 2020). Supplementation of black ginseng and silkworm in overweight beagle dogs resulted in significant reductions in total cholesterol, triglyceride levels, and obesity-related genes such as NUGGC, EFR3B, RTP4, ACAN, HOXC4, IL17RB, SOX13, SLC18A2, and SOX4 (Park et al., 2021).

Spirocercosis is a parasitic infection caused by the nematode Spirocerca lupi in dogs. The disease can cause digestive symptoms such as cramps and vomiting. A recent study showed that comparative treatment of dogs with ivermectin, ginseng powder extract, and Artemisia powder extract resulted in the absence of eggs in the dog's feces and no recurrence of the disease (Eshkaftaki et al., 2022). A controlled randomized blind study on geriatric dogs revealed that a combination of P. ginseng and brewer's yeast (Gerivet®) improved geriatric symptoms in dogs over 16 weeks study. Senile symptoms are agility, alertness, mental fatigue, responsiveness to stimuli and surroundings, forgetfulness, ambulation, physical activity, and ambulation in relation to the owner's position. These symptoms, especially the mental ones' were improved with supplementation of dogs with P. ginseng and brewer's yeast (Rkman et al., 2007). It was recently reported that red ginseng dregs and steamed red ginseng can enhance the immunity of dogs by increasing the level of interferon-γ released by peripheral blood mononuclear cells in dogs stimulated by IL-2. The dogs were orally treated with red ginseng residue and steamed red ginseng powder for eight weeks (An et al., 2023). Famous traditional Chinese Medicine (TCM) Dendrobium officinale Kimura et Migo (D. officinale) mixed with American ginseng increases the number of short-chain fatty acids producing bacteria to prevent gut dysbiosis. Therefore, this mixture has been recommended as a prebiotic agent for the canine diet (Cheng-Zhi et al., 2020). Juzen-tacho-to, a traditional Chinese medicine with ginseng as an active ingredient, has been reported to have antioxidant effects in healthy beagle dogs (Shinohara et al., 2019).

Not only whole ginseng extracts but individual compounds known as ginsenosides have also been reported to benefit dogs. Ginsenoside Re (G-Re) has been used as a vaccine adjuvant for activated rabies virus vaccines in dogs and cats. The effect of G-Re as an adjuvant was compared with aluminum hydroxide gel (20%) adjuvant in rabies vaccine. Experiments have shown that dogs and cats receiving G-Re adjuvanted rabies vaccine exhibit appreciable amounts of rabies antibodies and a higher level of protection. In addition, G-Re also reduces the protective dose required for the vaccine, thereby increasing productivity (Shendy, 2015).

CONCLUSION

Considering the extensive literature cited and discussed above, the most common effects of ginseng are observed in bovine mastitis, vaccine adjuvant for various bacterial and viral diseases of bovines, equines, swine, canines, and poultry. Therefore, ginseng can be considered an important veterinary ethnopharmacological herb.

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