Ginseng Stem and Leaf Saponins against Newcastle Disease

Umm ul Khair[1], Hurria Ali[1], Mishal Razzaq[1], Muqadas[1,*], Maheen Tahir[2], Khansa Parveen[2], Zuha Fatima[1], Muhammad Abdullah Qureshi[1] and Nimra Imdad[1]

[1]Faculty of Veterinary Science, University of Agriculture, Faisalabad
[2]Faculty of Veterinary Science, Bahauddin Zakariya University, Multan
*Corresponding author: muqadasdh@gmail.com

Abstract

This chapter highlights the importance of ginseng stem-and-leaf saponins as an adjuvant in the vaccine against Newcastle disease (ND). Newcastle is an important poultry disease that causes adverse economic losses to farmers. The satisfactory treatment of viral diseases in animals is not available, vaccination is the ultimate tool to control viral diseases. For effective vaccination, some adjuvants are used, which enhance the efficacy of the vaccines and, as a result, provide longer immunity. Saponins are one of the naturally derived adjuvants from the ginseng plant. It has antioxidants, anti-inflammatory, and immunomodulatory properties. Natural compounds are less expensive and have minimal or no side effects. Saponins are obtained from the ginseng root, stem, and leaf through various extraction methods. Then it is studied in chickens along with vaccination to check the immune response and antiviral effects. Ginseng stem-and-leaf saponins are effective adjuvants when administered orally before vaccination at a dose rate of 5mg/kg, according to studies. There is a need for further studies of ginseng stem and leaf saponins-based vaccines in animal models for large-scale application.

Keywords: Poultry, Ginseng, Saponin, Immunity, Control

Cite this Article as: Khair UU, Ali H, Razzaq M, Muqadas, Tahir M, Parveen K, Fatima Z, Qureshi MA and Imdad N, 2025. Ginseng stem and leaf saponins against newcastle disease. In: Khan A, Hussain R, Tahir S and Ghafoor N (eds), Medicinal Plants and Aromatics: A Holistic Health Perspective. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 90-95. https://doi.org/10.47278/book.HH/2025.204

A Publication of Unique Scientific Publishers

Chapter No: 25-014

Received: 11-Feb-2025
Revised: 25-March-2025
Accepted: 22-Apr-2025

Introduction

Poultry is a big industry that has the highest share in meat production (Istiak & Khaliduzzaman, 2022). Viral diseases with special reference to ND are devastating the poultry industry. It is caused by the Avian Paramyxovirus 1, owned by the *Paramyxoviridae* family, and the *Avulavirus* genus (Saeed et al., 2025). The virus is a negative-sense and single-stranded RNA virus and consists of various genotypes under 2 classes (classes 1 and 2) (Mossie & Wondie, 2022). This virus includes various proteins, i.e., fusion, hemagglutinin-neuraminidase, matrix, large RNA polymerase, phosphoprotein, and nucleoprotein (Wang et al., 2024). The fusion protein is the main pathogenic part of the virus (Zhang et al., 2023). This virus causes disturbance of nervous, gastrointestinal, and respiratory systems (Zhang et al., 2023). It transfers through direct contact with aerosols and by indirect contact via infected premises, feed, water, and feces (Brown et al., 2021). Virulent strains of the ND virus caused many outbreaks and panzootic throughout the world (Moharam, 2021).

The growing threats of Newcastle disease insist that scientists find alternative remedies. Vaccination is the best practice to control viral diseases (Hu et al., 2022). Vaccines cause the release of enough antibodies that can protect the body against the disease (Singh, 2021). These antibodies entangle antigens, minimize the shedding of viruses, and hence control the transmission of disease (Roth et al., 2022). To enhance the efficacy of the concerned vaccines, adjuvants are used, which slowly release the vaccine's active part and provide longer immunity and protection against the disease (Zhao et al., 2023). Various oil-based vaccines are used in the poultry industry, but these cause irritation and granulomatous swelling at the injection site after administration of vaccines (Akache et al., 2022). It also causes undesirable tissue reactions, which disrupt the tissue for a long time. Therefore, the research on potent vaccine adjuvants is the top priority of scientists. The use of plants and plant-derived products is gaining importance in the field of animal diseases because of the reduction in drug resistance and its cheap sources (Ajose et al., 2022). Large-scale medical practitioners use herbal oils and extracts to cure diseases. Various studies prove the use of herbal oils and extracts as prophylactic agents and antiviral agents in the feed of animals (Chaachouay & Zidane, 2024).

Various natural plant-derived components like chitosan, carboxymethyl cellulose, saponins, neem extracts, dextran, hyaluronic acid, alginate, pectin, liposome, and numerous proteins are used in the advanced technology to get up-to-date and best adjuvant (Selvaraj et al., 2024; Velhal et al., 2024). The plant extracts are composed of various organic substances that support positive performance in poultry (Abd El-Hack et al., 2022). Ginseng is a perennial plant and is well familiar with its medicinal properties (Potenza et al., 2023). It lessens pathological conditions, protects from harmful diseases, and enhances health (Flagg, 2021). Ginseng consists of many ingredients, among which saponin is the active ingredient. Saponins obtained from the root, stem, and leaves of *Panax ginseng* constitute various adjuvant properties when administered along with vaccines (El-Sebai et al., 2022; Abbas et al., 2025). In addition to roots, saponins can also be isolated from stems and leaves. Saponins produce both cellular and humoral immunity in the chickens against ND (Li et al., 2021). Ginseng stem-and-leaf saponins can revive immunity in immunosuppressed birds (Kumar & Yadav, 2022). It can also be synergistically used with other compounds to enhance the

immunity in birds, as mentioned in Table 1. In this chapter, we will go through the manufacturing types and chemistry of saponins, the mechanism of action, the antiviral, immunomodulatory, adjuvant, and other miscellaneous effects of saponins, future remarks, and limitations.

Method of Preparation Saponins

Saponins are a structurally broad class obtained from the ginseng plant, and have numerous biological functions, such as antioxidant, immunomodulatory, and antiviral (Geng et al., 2024). Traditionally, the saponins from the *Panax ginseng* are isolated through various techniques, which include heat reflux and Soxhlet extraction (Yang et al., 2021). These methods are time-consuming and have a small extraction efficiency. Several advanced procedures are present that use high pressure and high temperature (Wu et al., 2024). These advanced techniques are supercritical fluid, microwave-assisted, pulse-electric field, and ultrahigh-pressure extraction (Herzyk et al., 2024). The last one is very quick, it does the extraction in a few minutes.

Mechanism of Action

The oral route is the preferred one, as it cannot produce irritation at the injection site. As the mucosal surface is the 1st line of defense against invading pathogens, the production of secretory IgA antibodies provides mucosal immunity (Bhat & Aadıl, 2021). Intraepithelial lymphocytes promote gut mucosal immunity. These intestinal lymphocytes are the immunocompetent cells that make cytokines such as interleukins and interferons, which help in the surveillance of infected cells by cell-mediated cytotoxicity (Mahapatro et al., 2021; Yao et al., 2024). After the administration of these adjuvant-based vaccines, no side effects or change in body weight were observed; it is safe to use (Wang, 2021). In birds with higher levels of maternal antibodies, the antigen can be neutralized, evoking a lesser immune response (Bhat & Aadıl, 2021). This can be checked by the ginseng stem-and-leaf saponins adjuvanted vaccines, which cannot disrupt primary immunity (Zou et al., 2024).

Adjuvant Effects of Saponins

In 2019, the effects of ginseng stem-and-leaf saponins, in addition to selenium, were assessed against ND virus via intranasal and intraocular routes in chickens. The result showed the highest antibody response in chickens against NDV (Ma et al., 2019). Furthermore, in 2020, to check the natural defense mechanism against NDV, chicken ginseng saponins extract, along with sunflower oil, was used, and the result depicted that it is safer to be used against this fatal virus (Alsayari et al., 2021).

Through intramuscular immunization, when the antigen is co-injected with saponins, it induces an effective immune response (Chen et al., 2023). Via intranasal inoculation, saponins, as adjuvant, depicted their effectiveness in increasing both mucosal and systemic immune response (Correa et al., 2022). Saponins increase cytokine production such as IL-1α and β, IL-6, TNF-α, and colony-stimulating factor granulocyte-macrophage by innate cells, which then recruit monocytes and neutrophils to the respiratory tract, promoting their ability to take up more uptake of antigens (Ratan et al., 2021; Wijesekara et al., 2024). Antigen uptake by epithelial cells of the nasal mucosa is promoted by saponin-based adjuvants, the dendritic cells activate both adjuvants and antigens and present them to T-cells (Zhang et al., 2021). After T-cell stimulation, B-cell activation takes place, differentiating into plasma cells, B-cells which secrete IgA antibodies to the nasal mucosa, which provide a target for respiratory pathogens like Newcastle virus (Milicic et al., 2022).

Immunomodulatory Effects of Saponins

In a study, saponins were studied on immunosuppressive chickens, it is administered orally in drinking water before the shot of the ND virus. Lipopolysaccharides (LPS) and Con A induced lymphocyte proliferation in the spleen (Yousefpour et al., 2024). This proliferation leads to higher numbers of intraepithelial lymphocytes of the intestine (IELi) and immunoglobulin A secreting cell (IgA+ cells) in the intestine and serum. LPS stimulates B lymphocytes while Con A activates T lymphocytes (Sharma et al., 2022). It is not clear whether ginseng stem and leaf saponins are involved in increasing the number of B and T cells or enhancing the activities of these lymphocytes (You et al., 2022). In the intestine, a huge amount of IgA+ cells is present in lamina propria, which promotes humoral mucosal immunity, while IgG triggers systemic immunity (Pracht et al., 2023). Secretory IgA antibodies cover the intestinal epithelium from the enteric pathogens and harmful substances like toxins, making a gap between pathogens and their receptors on the intestine, entangle them in mucus, and ultimately discharge by mucociliary or peristaltic movement from the body (Deal et al., 2023). IELi is present on the basolateral side of the epithelium and consists of gamma delta cells and natural killer cells (NK). These cells attack pathogens if they cross the intestinal epithelium. Granules in the cytoplasm are meant for spontaneous cytotoxicity and NK cells' activity and do surveillance by the production of interferon-γ (IFN-γ), IL-2, IL-4, and IL-12 (Ham et al., 2022). Hence, the number of IELi by the histology of cells determines the quantity of mucosal immunity (Hartady et al., 2021).

Antiviral Effects of Saponins

Viruses are infectious parasites that have genetic makeup (DNA or RNA) enclosed inside a proteinaceous coat and can cause many infectious diseases, such as diarrhea, hepatitis, and autoimmune diseases. Rapid viral disease epidemics pose a significant public health threat (Chen et al., 2023). So, the resources are directed to the development of antiviral drugs to treat infections. Only a few viruses are combated by antiviral drugs; therefore, herbal medicines are considered as new antiviral alternatives (Perera et al., 2021). Ginseng extract is an effective immunomodulator for viral infection (Wijesekara et al., 2024). Ginsenosides show both anti-enterovirus and antiviral activity against both coxsachievirus and rhinovirus. Moreover, ginsenosides reduce feline calicivirus titter as well. Two herbs, thyme vulgaris and ginseng, along with adjuvant properties with poultry vaccine, also have anti-inflammatory, antioxidant, and immune stimulant functions (Alghirani et al., 2022). These antioxidant properties help decrease the toxic effects produced by the drugs (Basiouni et al., 2023).

Other Effects of Saponins

The compounds in the ginseng stem and leaf improve the digestibility of feed, utilize nutrients, and elevate animal production of broilers (Zhang et al., 2024). Saponins and flavonoids enhance the immune status and meat quality in quails (Elnaggar et al., 2022). Metabolism and absorption of lipids, starch, and other nutrients are pronounced in broilers (Lee et al., 2021). Saponin improves angiogenesis, which promotes the regeneration of blood vessels and local protection from hypoxia (Li et al., 2022).

Table 1: Different components, their doses and results

Component	Dosage	Route	Time interval	Results	References
Ginseng stem-and-leaf saponins	5mg/kg	PO in DW	7days	High HI titers upon IN Newcastle disease vaccine shock promote the immune response	(Zhai LiJuan et al., 2011)
-do-	-do-	-do-	-do-	Upon IM Newcastle disease vaccine shock, higher antibody titers were estimated	(Zhai et al., 2011)
-do-	-do-	-do-	-do-	immunosuppressed birds by cyclophosphamide administered bivalent vaccine of Newcastle disease and avian influenza via SC route, specific antibody titers produced, ginseng stem-and-leaf saponins can trigger immunity in these birds	(Yu et al., 2015)
Ginseng stem and leaf saponins + Se	-do-	-do-	-do-	Adjuvant effects (IL-4 and IFN-γ) were observed as higher antibody responses, by administering a bivalent vaccine of Infectious bronchitis and Newcastle disease by diluting the components via the IN and IO routes	(Ma et al., 2019)
E515D is a ginseng stem-and-leaf saponin present in sunflower oil	-do-	-do-	-do-	E515D is a fine adjuvant compound, a vaccine of Newcastle disease from an emulsion in this compound	(Yuan et al., 2020)
E515D	-do-	-do-	-do-	Higher HI titers, IL-4, and IFN-γ	(Yuan et al., 2020)
Ginseng oil	200mg/l of water	-do-	12 hours/day	After 35 days, the 0.1ml shot of NDV strain VIId, IM, showed higher HI values, improved 100% mortality, and no presence of viruses in trachea and cloaca	(Hassanin et al., 2024)

PO: per os; DW: drinking water; HI: hemagglutination inhibition; IN: intranasal; Sc: subcutaneous; Se: selenium; IO: intraocular.

Limitations

The hydrophobic region of saponin, after interaction with the red blood cell membrane, leads to hemolysis (Oakenfull & Sidhu, 2023). At high doses, a saponin-based adjuvant may cause an inflammatory response and cellular damage (Shen et al., 2023). Regarding parenteral administration, saponin-based adjuvants are primarily safe to be used; however, somehow associated with adverse effects such as swelling, pain, and redness at the injection site (Nguyen et al., 2023). Concerning intranasal immunization, at high doses, saponin-based adjuvants induce damage in the respiratory tract, so careful evaluation is required in intranasal vaccines (Chen et al., 2023). Saponins obtained from ginseng root are expensive because their harvesting time is 4-6 years, which limits their use in veterinary medicine (Li et al., 2022). But those obtained from stem and leaf are less expensive, which is why it is favorable to use them in medicine.

Future Perspectives and Conclusion

The saponin compound obtained from sunflower oil, E515D, is highly recommended for study as an adjuvant in vaccines used for food animals. The saponins and other natural compounds should be researched further for practical applications on a large scale. Vaccination practices should be opted for along with other cheap adjuvants. The study should be carried out on the extraction of saponins from stems and leaves of the ginseng plant, which are available easily, so that it can become available at a low cost. Various naturally present compounds should be studied as vaccine adjuvants.

ND is causing threats to the economy of the country worldwide. Effective vaccination techniques can reduce the disease load. For increasing the immunity with the vaccines, innovative adjuvants are being researched. Saponins derived from the ginseng plant are studied by many scientists along with vaccination. Effective positive results are obtained when used to immunize against ND. Ginseng stem-and-leaf saponins are used with inactivated single or bivalent vaccines to enhance immunity, as depicted by the information in Table 1. Ginseng stems and leaves at the dose rate of 5mg per kg before immunization or with vaccine orally are very effective in producing mucosal humoral and lymphocyte proliferative immune responses. Saponins are a natural compound and a safe component. It has anti-inflammatory, antiviral, and immunomodulatory properties. This compound could be a potent adjuvant for improving the efficacy of vaccines.

References

Abbas, R. Z., Qureshi, M. A., & Saeed, Z. (2025). Botanical compounds: A promising control strategy against Trypanosoma cruzi. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, 24(3), 308-327.

Abd El-Hack, M. E., El-Saadony, M. T., Salem, H. M., El-Tahan, A. M., Soliman, M. M., Youssef, G. B. A., Taha, A. E., Soliman, S. M., Ahmed, A. E., & El-Kott, A. F. (2022). Alternatives to antibiotics for organic poultry production: types, modes of action and impacts on bird's health and production. *Poultry Science*, *101*(4), 101696.

Ajose, D. J., Abolarinwa, T. O., Oluwarinde, B. O., Montso, P. K., Fayemi, O. E., Aremu, A. O., & Ateba, C. N. (2022). Application of plant-derived nanoparticles (PDNP) in food-producing animals as a bio-control agent against antimicrobial-resistant pathogens. *Biomedicines*, *10*(10), 2426.

Akache, B., Stark, F. C., Agbayani, G., Renner, T. M., & McCluskie, M. J. (2022). Adjuvants: Engineering protective immune responses in human and veterinary vaccines. *Vaccine Design: Methods and Protocols, Volume 3. Resources for Vaccine Development*, 179-231.

Alghirani, M. M., Chung, E. L. T., Jesse, F. F. A., Sazili, A. Q., & Loh, T. C. (2022). The potential use of plant-derived saponins as a phytobiotic additive in poultry feed for production and health advancement: a comprehensive review.

Alsayari, A., Muhsinah, A. B., Almaghaslah, D., Annadurai, S., & Wahab, S. (2021). Pharmacological efficacy of ginseng against respiratory tract infections. *Molecules*, *26*(13), 4095.

Basiouni, S., Tellez-Isaias, G., Latorre, J. D., Graham, B. D., Petrone-Garcia, V. M., El-Seedi, H. R., Yalçın, S., El-Wahab, A. A., Visscher, C., & May-Simera, H. L. (2023). Anti-inflammatory and antioxidative phytogenic substances against secret killers in poultry: current status and prospects. *Veterinary Sciences*, *10*(1), 55.

Bhat, B. A., & Aadıl, S. (2021). Adjuvants used in animal vaccines-their formulations and modes of action: an overview. *Osmaniye Korkut Ata Üniversitesi Fen Bilimleri Enstitüsü Dergisi*, *4*(3), 492-506.

Brown, I. H., Cargill, P. W., Woodland, R. M., & van den Berg, T. (2021). Newcastle disease virus. *Veterinary vaccines: Principles and Applications*, 335-353.

Chaachouay, N., & Zidane, L. (2024). Plant-derived natural products: a source for drug discovery and development. *Drugs and Drug Candidates*, *3*(1), 184-207.

Chen, K., Wang, N., Zhang, X., Wang, M., Liu, Y., & Shi, Y. (2023). Potentials of saponins-based adjuvants for nasal vaccines. *Frontiers in Immunology*, *14*, 1153042.

Correa, V. A., Portilho, A. I., & De Gaspari, E. (2022). Vaccines, adjuvants and key factors for mucosal immune response. *Immunology*, *167*(2), 124-138.

Deal, C. E., Richards, A. F., Yeung, T., Maron, M. J., Wang, Z., Lai, Y.-T., Fritz, B. R., Himansu, S., Narayanan, E., & Liu, D. (2023). An mRNA-based platform for the delivery of pathogen-specific IgA into mucosal secretions. *Cell Reports Medicine*, *4*(11).

El-Sebai, A., Khalifa, H. A., Abd El-Motaal, S., & Hassanin, O. (2022). An Updated Review on the Role of Ginseng and Thyme Vulgaris in the Prevention and Control of Avian Viral Diseases with a Special Reference to Newcastle Disease Virus. *Journal of Advanced Veterinary Research*, *12*(6), 803-806.

Elnaggar, A. S., Ghonem, M., & Abdelkhalek, E. (2022). Impact of ginseng (Panax ginseng) on growth performance, blood biochemical parameters and antioxidative status of Japanese Quail. *Egyptian Poultry Science Journal*, *42*(2), 137-156.

Flagg, A. J. (2021). Traditional and current use of ginseng. *Nursing Clinics*, *56*(1), 109-121.

Geng, X., Wang, J., Liu, Y., Liu, L., Liu, X., Zhao, Y., Wang, C., & Liu, J. (2024). Research progress on chemical diversity of saponins in Panax ginseng. *Chinese Herbal Medicines*.

Ham, H., Medlyn, M., & Billadeau, D. D. (2022). Locked and loaded: mechanisms regulating natural killer cell lytic granule biogenesis and release. *Frontiers in Immunology*, *13*, 871106.

Hartady, T., Syamsunarno, M. R. A. A., Priosoeryanto, B. P., Jasni, S., & Balia, R. L. (2021). Review of herbal medicine works in the avian species. *Veterinary World*, *14*(11), 2889.

Hassanin, O., El-Sebai, A., Abd El-Motaal, S., & Khalifa, H. A. (2024). Experimental trials to assess the immune modulatory influence of thyme and ginseng oil on NDV-vaccinated broiler chickens. *Open Veterinary Journal*, *14*(1), 398.

Herzyk, F., Piłakowska-Pietras, D., & Korzeniowska, M. (2024). Supercritical extraction techniques for obtaining biologically active substances from a variety of plant byproducts. *Foods*, *13*(11), 1713.

Hu, Z., He, X., Deng, J., Hu, J., & Liu, X. (2022). Current situation and future direction of Newcastle disease vaccines. *Veterinary Research*, *53*(1), 99.

Istiak, M. S., & Khaliduzzaman, A. (2022). Poultry and egg production: an overview. *Informatics in Poultry Production: A Technical Guidebook for Egg and Poultry Education, Research and Industry*, 3-12.

Kumar, A., & Yadav, G. (2022). Potential role of medicinal plants for their immunomodulatory activity—a review. *Annals of Clinical Pharmacology & Toxicology*, *3*(1), 1021.

Lee, J.-H., Park, H.-S., Song, J.-Y., Kim, B.-K., Park, H.-B., & Kim, J.-H. (2021). Effects of dietary supplementation of ginseng by-products on growth performance, organ weight and blood biochemical characteristics in broiler. *Korean Journal of Poultry Science*, *48*(4), 267-275.

Li, J., Li, R., Wu, X., Zheng, C., Shiu, P. H.-T., Rangsinth, P., Lee, S. M.-Y., & Leung, G. P.-H. (2022). An update on the potential application of herbal medicine in promoting angiogenesis. *Frontiers in Pharmacology*, *13*, 928817.

Li, P., Liu, Y., Gao, M., Fu, J., & Guo, Y. (2021). Dietary soy saponin improves antioxidant and immune function of layer hens. *The Journal of Poultry Science*, *59*(3), 197-205.

Li, X., Liu, J., Zuo, T.-t., Hu, Y., Li, Z., Wang, H.-d., Xu, X.-y., Yang, W.-Z., & Guo, D.-A. (2022). Advances and challenges in ginseng research from 2011 to 2020: the phytochemistry, quality control, metabolism, and biosynthesis. *Natural Product Reports*, *39*(4), 875-909.

Ma, X., Bi, S., Wang, Y., Chi, X., & Hu, S. (2019). Combined adjuvant effect of ginseng stem-leaf saponins and selenium on immune responses to a live bivalent vaccine of Newcastle disease virus and infectious bronchitis virus in chickens. *Poultry Science*, *98*(9), 3548-3556.

Mahapatro, M., Erkert, L., & Becker, C. (2021). Cytokine-mediated crosstalk between immune cells and epithelial cells in the gut. *Cells*, *10*(1), 111.

Milicic, A., Reinke, S., Fergusson, J., Lindblad, E. B., Thakur, A., Corby, G., Longet, S., Górska, S., Razim, A., & Hu, K. (2022). Adjuvants, immunomodulators, and adaptogens. In *Vaccinology and Methods in Vaccine Research* (pp. 223-280). Elsevier.

Moharam, I. M. A. (2021). *Viral respiratory diseases complex: Investigation on the relevance of Newcastle disease virus in vaccinated poultry flocks in Egypt and characterization of further detected viruses*. Freie Universitaet Berlin (Germany).

Mossie, T., & Wondie, D. A. (2022). A compressive review on Newcastle disease virus in Ethiopia. *Journal of Veterinary Science and Technology*, *13*(6).

Nguyen, P. H. D., Jayasinghe, M. K., Le, A. H., Peng, B., & Le, M. T. N. (2023). Advances in drug delivery systems based on red blood cells and their membrane-derived nanoparticles. *ACS nano*, *17*(6), 5187-5210.

Oakenfull, D., & Sidhu, G. S. (2023). Saponins. *Toxicants of Plant Origin*, 97-142.

Perera, W., Liyanage, J. A., Dissanayake, K. G. C., Gunathilaka, H., Weerakoon, W., Wanigasekara, D. N., Fernando, W. S. K., Rajapaksha, R. M. H., Liyanage, R. P., & Perera, B. T. (2021). Antiviral potential of selected medicinal herbs and their isolated natural products. *BioMed Research International*, *2021*(1), 7872406.

Potenza, M. A., Montagnani, M., Santacroce, L., Charitos, I. A., & Bottalico, L. (2023). Ancient herbal therapy: A brief history of Panax ginseng. *Journal of Ginseng Research*, *47*(3), 359-365.

Pracht, K., Wittner, J., Kagerer, F., Jäck, H.-M., & Schuh, W. (2023). The intestine: A highly dynamic microenvironment for IgA plasma cells. *Frontiers in Immunology*, *14*, 1114348.

Ratan, Z. A., Youn, S. H., Kwak, Y.-S., Han, C.-K., Haidere, M. F., Kim, J. K., Min, H., Jung, Y.-J., Hosseinzadeh, H., & Hyun, S. H. (2021). Adaptogenic effects of Panax ginseng on modulation of immune functions. *Journal of Ginseng Research*, *45*(1), 32-40.

Roth, G. A., Picece, V. C. T. M., Ou, B. S., Luo, W., Pulendran, B., & Appel, E. A. (2022). Designing spatial and temporal control of vaccine responses. *Nature Reviews Materials*, *7*(3), 174-195.

Saeed, Z., Muqadas, R. Z. A., & Qureshi, M. A. (2025) A review on chitosan-based nanovaccines against Newcastle disease in poultry. DOI: 10.2478/aoas-2025-0027

Selvaraj, S., Chauhan, A., Dutta, V., Verma, R., Rao, S. K., Radhakrishnan, A., & Ghotekar, S. (2024). A state-of-the-art review on plant-derived cellulose-based green hydrogels and their multifunctional role in advanced biomedical applications. *International Journal of Biological Macromolecules*, 130991.

Sharma, B. K., Ramakrishan, S., Kaliappan, A., Singh, M., Kumar, A., Dandapat, S., Dey, S., & Chellappa, M. M. (2022). Evaluation of a lipopolysaccharide and resiquimod combination as an adjuvant with inactivated Newcastle disease virus vaccine in chickens. *Vaccines*, *10*(6), 894.

Shen, L., Luo, H., Fan, L., Tian, X., Tang, A., Wu, X., Dong, K., & Su, Z. (2023). Potential Immunoregulatory mechanism of Plant saponins: a review. *Molecules*, *29*(1), 113.

Singh, A. (2021). Eliciting B cell immunity against infectious diseases using nanovaccines. *Nature Nanotechnology*, *16*(1), 16-24.

Velhal, M., Dave, M., Sun, E., Holla, S., & Liang, H. (2024). Plant and animal-based bioderived materials: a review of their antimicrobial mechanisms and applications. *Materials Today Sustainability*, 100885.

Wang, P. (2021). Natural and synthetic saponins as vaccine adjuvants. *Vaccines*, *9*(3), 222.

Wang, Z., Geng, Z., Zhou, H., Chen, P., Qian, J., & Guo, A. (2024). Genetic Characterization, Pathogenicity, and Epidemiology Analysis of Three Sub-Genotype Pigeon Newcastle Disease Virus Strains in China. *Microorganisms*, *12*(4), 738.

Wijesekara, T., Luo, J., & Xu, B. (2024). Critical review on anti-inflammation effects of saponins and their molecular mechanisms. *Phytotherapy Research*, *38*(4), 2007-2022.

Wu, Y., Zheng, H., Zheng, T., Jiang, J., Xu, Y., Jia, F., He, K., & Yang, Y. (2024). Quantitative Changes and Transformation Mechanisms of Saponin Components in Chinese Herbal Medicines during Storage and Processing: A Review. *Molecules*, *29*(18), 4486.

Yang, Y., Ju, Z., Yang, Y., Zhang, Y., Yang, L., & Wang, Z. (2021). Phytochemical analysis of Panax species: a review. *Journal of Ginseng Research*, *45*(1), 1-21.

Yao, Y., Shang, W., Bao, L., Peng, Z., & Wu, C. (2024). Epithelial-immune cell crosstalk for intestinal barrier homeostasis. *European Journal of Immunology*, *54*(6), 2350631.

You, L., Cha, S., Kim, M.-Y., & Cho, J. Y. (2022). Ginsenosides are active ingredients in Panax ginseng with immunomodulatory properties from cellular to organismal levels. *Journal of Ginseng Research*, *46*(6), 711-721.

Yousefpour, P., Zhang, Y. J., Maiorino, L., Melo, M. B., Arainga Ramirez, M. A., Kumarapperuma, S. C., Xiao, P., Silva, M., Li, N., & Michaels, K. K. (2024). Modulation of antigen delivery and lymph node activation in nonhuman primates by saponin adjuvant saponin/monophosphoryl lipid A nanoparticle. *PNAS nexus*, *3*(12), 529.

Yu, J., Shi, F. S., & Hu, S. (2015). Improved immune responses to a bivalent vaccine of Newcastle disease and avian influenza in chickens by ginseng stem-leaf saponins. *Veterinary Immunology and Immunopathology*, *167*(3-4), 147-155.

Yuan, L., Wang, Y., Li, Z., Ma, X., Cui, X., Chi, X., Xu, W., & Hu, S. (2020). Sunflower seed oil containing ginseng stem–leaf saponins (E515-D) is a safe adjuvant for Newcastle disease vaccine. *Poultry Science*, *99*(10), 4795-4803.

Yuan, L., Wang, Y., Ma, X., Cui, X., Lu, M., Guan, R., Chi, X., Xu, W., & Hu, S. (2020). Sunflower seed oil combined with ginseng stem-leaf saponins as an adjuvant to enhance the immune response elicited by Newcastle disease vaccine in chickens. *Vaccine*, *38*(33), 5343-5354.

Zhai, L., Li, Y., Wang, W., & Hu, S. (2011). Enhancement of humoral immune responses to inactivated Newcastle disease and avian influenza vaccines by oral administration of ginseng stem-and-leaf saponins in chickens. *Poultry Science*, *90*(9), 1955-1959.

Zhai LiJuan, Z. L., Li YuTao, L. Y., Wang WeiYu, W. W., Wang YueMin, W. Y., & Hu SongHua, H. S. (2011). Effect of oral administration of ginseng stem-and-leaf saponins (GSLS) on the immune responses to Newcastle disease vaccine in chickens.

Zhang, D., Ding, Z., & Xu, X. (2023). Pathologic mechanisms of the Newcastle disease virus. *Viruses*, *15*(4), 864.

Zhang, P., Zhang, H., Ma, C., Lv, Q., Yu, H., & Zhang, Q. (2024). Effect of ginseng stem leaf extract on the production performance, meat quality, antioxidant status, immune function, and lipid metabolism of broilers. *Frontiers in Veterinary Science*, *11*, 1463613.

Zhang, X., Zhang, Z., Xia, N., & Zhao, Q. (2021). Carbohydrate-containing nanoparticles as vaccine adjuvants. *Expert Review of Vaccines*, *20*(7), 797-810.

Zhang, Y., Zhong, X., Xi, Z., Li, Y., & Xu, H. (2023). Antiviral Potential of the Genus Panax: An updated review on their effects and underlying mechanism of action. *Journal of Ginseng Research*, *47*(2), 183-192.

Zhao, T., Cai, Y., Jiang, Y., He, X., Wei, Y., Yu, Y., & Tian, X. (2023). Vaccine adjuvants: mechanisms and platforms. *Signal Transduction and Targeted Therapy*, *8*(1), 283.

Zou, M., Lei, C., Huang, D., Liu, L., & Han, Y. (2024). Application of plant-derived products as adjuvants for immune activation and vaccine development. *Vaccine*. 42(25).