Current Science International
Volume: 13 | Issue: 04| Oct. – Dec.| 2024

EISSN:2706-7920 ISSN: 2077-4435
DOI: 10.36632/csi/2024.13.4.39
Journal homepage: www.curresweb.com
Pages: 456-464

Prepartum Supplementation of Ginseng to Improve the Reproductive Performance of Dairy Cows

Hazem A. El-Debaky, Amal M. Aboelmaaty and Ahmed M. Nagy

Animal Reproduction and AI Department, Veterinary Research Institute, National Research Centre, Giza, 12622, Egypt

Received: 20 August 2024 **Accepted:** 30 Sept. 2024 **Published:** 10 Oct. 2024

ABSTRACT

Dairy cattle play a crucial role in global milk production, providing a wide range of nutritious dairy products. Increased dairy farms' productivity is accompanied by decreased reproductive performance. Several decades ago, medicinal plants were used extensively to address reproductive disorders. Ginseng contains various bioactive ingredients making it widely used for veterinary purposes. The present study intended to investigate the effect of fresh ginseng supplementation on the reproductive performance of dairy cows during their drying period. This study included pregnant dry cows (n=79) that were divided into a control group (32 cows) and a ginseng-treated group (47 cows) that received 20 gm of ginseng for 30 days. After parturition, these groups were subdivided into cows with normal birth groups and others with retained fetal membranes (RFM). Blood proteins, nitric oxide (NO), haptoglobin (Hp), reduced glutathione (GSH), estradiol (E2), calcium (Ca), phosphorus (P), copper (Cu), and iron (Fe) were measured. The results revealed that milk yield increased in ginseng-treated groups. Parity was significantly low ($P<0.5$) in ginseng-supplemented cows. Control cows with RFM required more ($P<0.5$) services for conception than all other groups. Moreover, serum total protein (TP), albumin (Alb), globulin (Glb), albumin/globulin ratio (A/G ratio), NO, and copper showed non-significant differences between all groups. GSH and Hp declined ($P<0.5$) in ginseng-treated cows with RFM compared to other groups. E2 levels decreased in control cows with RFM ($P<0.5$) than those with normal birth. Serum calcium level declined ($P<0.5$) in control cows with normal birth than in other experimental groups. Iron concentration decreased ($P<0.5$) in ginseng-supplemented cows with normal birth than in other groups. Inversely, ginseng significantly ($P<0.5$) increased serum zinc concentration in cows with normal birth and RFM groups. We concluded that ginseng supplementation improved the reproductive performance, acute phase response, and health status of dairy cows during the drying period.

Keywords: reproductive performance, prepartum, antioxidants, ginseng, dairy cows

1. Introduction

Cattle and buffalo are the main livestock farming livestock in poor countries in the Middle East. Dairy farming represents a main source of animal protein of high nutritious value (meat and milk). They are essential for ensuring food security and self-sufficiency in livestock products which is a crucial goal of most countries in this region.

Increasing the productivity of dairy cattle was primarily directed at milk production through the genetic selection of the flock. It was noticed that dairy cattle with high milk production are associated with inadequate or poor reproductive efficiency and health traits (Weigel *et al*., 2017). Low reproductive performance in dairy farms is the major cause of premature culling of dairy cows, which has a substantial negative impact on their lifetime milk production. Additionally, reproductive inefficiency decreases the number of calves born, limiting the availability of replacements and exacerbating the economic losses caused by infertility (Cardoso *et al*., 2013). Recent advancements in genetic improvement, particularly with the aid of genomic technology, have improved the

Corresponding Author: Amal M. Aboelmaaty, Animal Reproduction and AI Department, Veterinary Research Institute, National Research Centre, Giza, 12622, Egypt.

reproductive potential of modern dairy cows (Cole and VanRaden 2018, Lucy 2019). For optimizing the reproductive potential of high-producing dairy herds, a holistic approach is required to consider various crucial factors such as the breeding program, genetic makeup of the cows, health condition as well as nutritional regimen practices of the flock (Cardoso Consentini *et al*., 2021).

A few decades ago, farmers extensively relied on medicinal plants to improve the reproductive disorders in farm animals. These plants offer several advantages, including minimal side effects, low cost, easy accessibility, and widespread availability (Shai *et al*., 2022). Sarswat and Purohit (2020) recommended some medicinal plants that have widespread use in the veterinary field for various purposes such as ginseng. In animals, all parts of this plant (i.e., roots, leaves, fruit, and stem) possess bioactive properties against many health disorders. Ginseng comprises many compounds including carbohydrates, amino acids, minerals, lipids, proteins, and other bioactive constituents like ginsenosides, acidic polysaccharides, and polyacetylenes which induce the antioxidant effect of ginseng (Choi and Yang, 2012; Jee *et al*., 2014, Yeo *et al*., 2017).

According to the report of the European Medicine Agency of the Committee for Medicinal Products for Veterinary Use, ginseng is safe for human and animal consumption, generally non-toxic, and can be consumed without known side effects (Consultation, 2006).

The dry period of dairy cows is a critical stage for the next lactation cycle. During this period, milk production stops abruptly, and the udder-teat ducts are sealed to avoid the incidence of mastitis due to the entry of pathogens. Covering with antibiotics intramammary is crucial in dairy cows undergoing the drying periods (Vilar *et al*., 2020). In this regard, Ginseng, a natural substance, can help boost the cow's immune system and reduce the risk of mastitis. Ginseng boosts protein metabolism and improves various physiological functions such as reproductive health, antioxidant defence, neurotransmitter activity, and improved muscle fatigue resistance (Bae, 2016). Ginseng showed protective effects on ovarian follicle development by influencing the hypothalamic-pituitary-gonadal (HPG) axis, stimulating growth and development of ovarian somatic cells, reducing lipid peroxidation, and downregulation of apoptotic markers in the ovary (Faghani *et al*., 2022). Panax ginseng improved reproductive performance (Amaefule *et al*., 2019). In steers, red ginseng did not improve growth or alleviate heat stress (Yoo *et al*., 2022).

Though the extracts of *Panax ginseng* decreased milk yield in a dose-dependent pattern and were not recommended as a supplement (Iwuji *et al*., 2018), the supplementation of the fresh plant in dairy animals was not investigated. In dairy cows, ginseng was injected subcutaneously to treat mastitis (Hu *et al*., 2001), improved the oxidative and phagocytic activity of leucocytes in blood and milk (Hu *et al*., 1995), and was used in combination with antibiotics to treat dry cows (Beccaria *et al*., 2021).

This study aimed to determine whether peripartum ginseng supplementation can improve milk yield, reproductive performance, and health status of dairy dry cows by evaluating blood antioxidants, some blood biochemical parameters, trace elements, and estradiol in serum.

2. Materials and Methods

2.1. Animals and grouping

This work was performed following the regulations of the Medicinal Research Ethical Committee of the National Research Centre (MREC). Pregnant Holstein Friesian cows (N= 79) of 3–10 years were kept in open semi-shaded yards and belonged to two private dairy herds. Before conducting the study, the owners of the two dairy farms had permitted and approved the supplementation and the blood sampling of supplemented and control cows. The study followed the international farm animal welfare regulations (Freedom from hunger and thirst, discomfort, pain; injury, and disease) and collected blood samples according to the regulation of the National Research Center Animal and Use Care Committee (MREC-NRC-2022-05-09). Cows were kept in open yards under natural daylight and temperature. The animals were fed a properly formulated ration according to NRC (2001). Rations contained silage in the summer season and the Egyptian green clover (*Trifolium alexandrinum*) during the winter season in addition to the concentrated ration. Cows were milked three times daily.

Late pregnant cows were divided into control (N=32) supplemented with their basal ration the basal diet during the last month before parturition. Control cows were subdivided into cows with normal birth (N=12) and cows with retained fetal membranes (RFM; N=20). Ginseng group (N=47) were supplemented with 20.0 g chopped Ginseng orally for 30 days before the expected date of parturition (Choi *et al*., 1999). Cows supplemented with Ginseng were subdivided into cows with normal birth (N=31) and cows with RFM (N=16).

2.2. Blood Sampling

Blood samples were collected one week before and one week after giving birth from the tail vein, under antiseptic precautions, in sterile blank vacuum tubes. Sera without hemolysis were harvested and preserved at -20°C until the analysis of blood parameters.

2.3. Measurement of antioxidants, blood biochemicals, traces minerals and estradiol

GSH, TP, Alb, NO, calcium, phosphorus, iron, zinc and copper were measured using commercial colorimetric kits (Biodiagnostic, Egypt). The globulins were calculated by subtracting the concentration of Alb from those of the TP. The calcium/phosphorus ratio was counted by dividing the concentration of the calcium on the concentrations of the phosphorus. The corrected calcium concentrations were estimated using the equation (Measured Calcium (mg/dl) - Albumin (g/dl) + 3.5) of Jung (2006). E2 ELISA commercial kit was assayed (E2, DRG®, EIA-2693) which has a sensitivity of 9.714 pg/ mL, intra- and inter-assay precisions of 2.71 and 6.72%. Hp (Ben-Biochemical Enterprise S.r.l.- via Toselli, https://www.ben-srl.com/) was done by an immuno-turbidimetric method by mixing a sample with a precise Antigen to a solution having the corresponding anti-serum (Antibody anti-Hp (goat) in PBS > 25 mmol/L NaN3 < 0.1%) using Multipoint calibrators to prepare a Calibration Curve. The sensitivity limit was 2.9 mg/dL. Within-run precision and Run to Run Precision was 2.1%.

2.4. Statistical analysis

Data are presented as mean± SD (Standard deviation) using SPSS 20. Simple one-way ANOVA was used to study the effect of supplementation and the type of birth (Normal or retention of the fetal membranes) in control on all the studied parameters. Duncan's Multiple Range tests were performed to differentiate between significant means at $P < 0.05$. A Univariate general linear model Two-Way Analysis of Variance was used to study the effect of the birth type (normal/retained) and treatment (control/supplemented).

3. Results

The current study showed that the supplementation with ginseng before parturition lowered the incidence of RFM from 25.32 in the control non-supplemented cows to 20.25% in the supplemented ones (Table 1). As well as, the required number of services per conception during the postpartum period declined in the supplemented cows with RFM (Table 1). Our results revealed no difference in the number of services required for the conception in control and treated cows with normal birth (Table 1). Concerning 35-day milk yield, table (1) pointed out that, ginseng significantly increased ($P<0.5$) milk yield in cows with normal birth or RFM than the controls. Referring to parity, it was significantly lower ($P<0.5$) in both ginseng-treated groups than control ones in normal birth and RFM cows (Table 1). All groups came in the first estrus after parturition before completing 70 days after calving with no significant difference between ginseng treated and control groups.

Table 1: Mean ± SEM (standard error of the Mean) of the reproductive status and milk yield in control and treated cows.

Parameter	Normal birth		RFM		P-value
	Control	Ginseng	Control	Ginseng	
Number (%)	12 (15.19%)	31(39.24%)	20 (25.32%)	16 (20.25%)	**79**
Services/conception	$1.61±0.13^a$	$1.57±0.10^a$	$2.34±0.20^b$	$1.79±0.11^a$	**0.001**
1st PPE	68.26±2.86	67.21±1.85	66.71±1.89	68.83±1.89	**0.870**
Milk yield/ton	$6.33±0.59^a$	$7.79±0.21^b$	$6.88±0.44^a$	$7.94±0.17^b$	**0.001**
Parity	$3.96±0.37^b$	$2.50±0.18^a$	$4.49±0.32^b$	$2.76±0.18^a$	**0.0001**

First postpartum estrus (1st PPE),
Superscript letters (a, b) within row indicate significance at $P <0.5$

Regarding the effect of ginseng on some blood proteins, GSH, and NO, our results revealed that oral supplementation of ginseng did not induce any significant difference in serum concentration of TP, Alb, Glb and A/G ratio compared to control groups in both normal birth and RFM cows (Table 2). The concentration of GSH significantly decreased (P<0.5) in both ginseng-treated groups than control ones. In the same context, serum Hp concentrations declined (P<0.5) in ginseng-treated cows with normal births than controls with either normal birth or RFM cows (Table 2).

Table 2: Mean ± SEM (standard error of the Mean) of the total proteins (g/dl), albumin (g/dl), globulin, glutathione reduced (GSH mg/dl), haptoglobin (Hp mg/dl) and nitric oxide (NO µmol/L) in control and ginseng treated cows.

Parameter	Normal birth		RFM		P-value
	Control	Ginseng	Control	Ginseng	
Total proteins g/dl	5.46±0.10	5.37±0.09	5.52±0.08	5..41±0.09	**0.694**
Albumin g/dl	4.29±0.09	4.10±0.08	4.25±.9	4.13±0.06	**0.377**
Globulin g/dl	1.17±0.12	1.25±0.09	1.27±0.10	1.28±0.09	**0.906**
A/G ratio	3.76±0.32	3.56±0.25	4.71±0.51	3.98±0.31	**0.507**
GSH mg/dl	32.29±3.27^{b}	24.93±1.79^{ab}	31.99±3.12^{b}	24.00±1.88^{a}	**0.022**
Haptoglobin mg/dl	17.80±2.20^{bc}	8.5±1.49^{a}	21.95±2.57^{c}	13.17±1.53^{ab}	**0.0001**
NO µmol/L	27.81±2.63	24.89±2.17	28.91±1.61	27.54±2.29	**0.613**

Superscript letters (a, b, c) within the row indicate significance at P <0.5, glutathione reduced (GSH), albumin/globulin (A/G), nitric oxide (NO)

Regarding estradiol concentrations (Fig. 1), results showed that control cows with retained fetal membranes had the lowest E2 concentrations (P<0.01). Ginseng-treated cows with either RFM or normal birth had higher E2 concentrations groups than those of controls with RFM and non-significantly lower than those of controls with normal birth (Fig. 1). Though no significant difference in serum E2 concentration between both ginsengs treated groups or between ginseng and control groups with normal birth but all the three groups obtained higher E2 concentration than those of the control group with retained placenta.

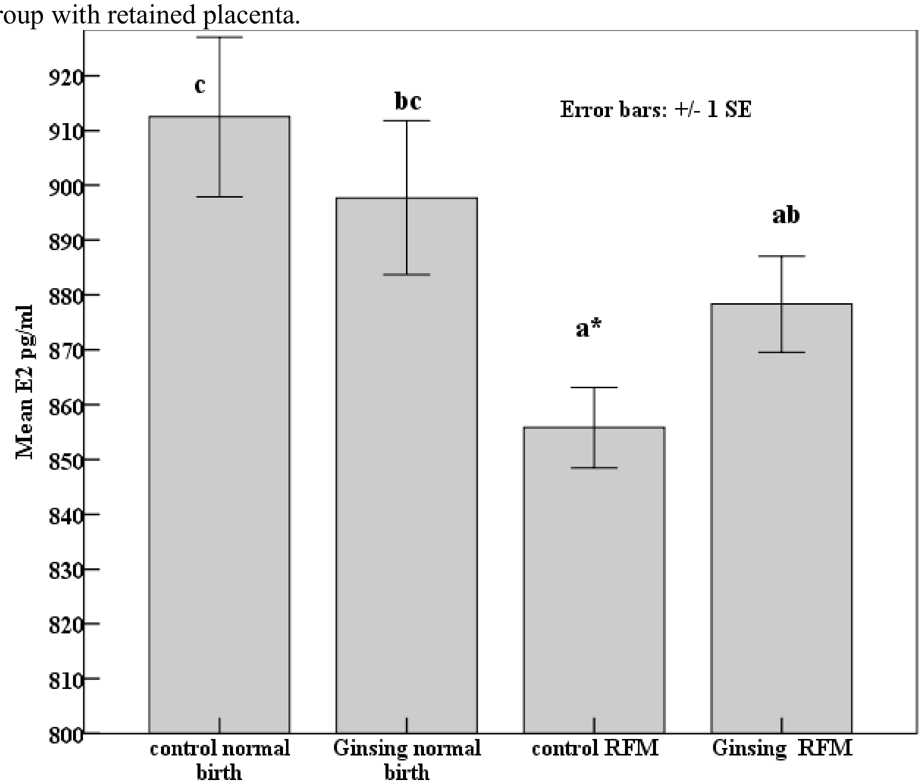

Fig. 1: Mean estradiol (E2) concentrations in treated and control cows with normal birth or retained placenta with standard error bars, superscript means (a, b, c) indicate significant difference at P<0.05, * means significant at P<0.01

Concerning serum concentration of some minerals and ions the results showed that the estimated corrected calcium concentrations in both ginseng-treated groups are higher (P<0.01) than control groups (Table 3). Calcium concentration in both RFM groups and ginseng-treated group with normal birth is significantly higher (P<0.5) than controls with normal birth (Table 3). While, there was no significant difference in phosphorus concentration between the four groups, but a non-significant increase in phosphorus concentrations was noted in the control cows with normal birth. In control cows with normal birth, the calcium/phosphorus ratio was significantly (P<0.05) lower than the other three groups. serum iron concentration (Table 3) presented the lowest concentrations in the ginseng-treated cows with normal birth among the three experimental groups. Also, non-significant low iron concentrations are recorded in the ginseng-treated cows with retained fetal membranes. Moreover, no significant differences in the serum copper concentrations were observed among control and ginseng groups of either normal birth or with RFM. However, ginseng-treated cows had non-significantly low copper concentrations compared to controls. In addition, ginseng-treated groups had higher (P<0.001) serum zinc ion concentrations than control groups.

Table 3: Mean ± SEM (standard error of the Mean) of calcium, phosphorus, iron, copper, and zinc in control and supplemented cows.

Parameter	**Normal birth**		**RFM**		**P-value**
	Control	**Ginseng**	**Control**	**Ginseng**	
Corrected calcium mg/dl	$8.76{\pm}0.19^{a}$	$9.38{\pm}0.11^{b}$	$9.05{\pm}0.16^{ab}$	$9.36{\pm}0.10^{b}$	0.009
Calcium mg/dl	$9.95{\pm}0.14^{a}$	$10.38{\pm}0.10^{b}$	$10.18{\pm}0.11^{ab}$	$10.36{\pm}0.07^{b}$	0.030
Phosphorus mg/dl	4.0±0.03	3.76±0.11	3.96±0.03	3.79±0.10	0.212
Calcium /phosphorus	$2.49{\pm}0.04^{a}$	$2.63{\pm}0.03^{b}$	$2.58{\pm}0.03^{b}$	$2.60{\pm}0.02^{b}$	0.029
Iron µg/dl	$240.6{\pm}17.92^{ab}$	$198.9{\pm}9.72^{a}$	$255.3{\pm}15.86^{b}$	$226.5{\pm}14.21^{ab}$	0.041
Copper µg/dl	$234.8{\pm}7.28^{b}$	$213.5{\pm}9.89^{ab}$	$231.5{\pm}8.32^{ab}$	$209.5{\pm}4.39^{a}$	0.051
Zinc µg/dl	$207.7{\pm}3.24^{a}$	$224.0{\pm}3.15^{b}$	$211.9{\pm}1.55^{a}$	$221.5{\pm}3.47^{b}$	0.001

Superscript letters (a, b) within the row indicate significance at P <0.5

4. Discussion

Dairy farming faces numerous challenges in the reproductive management of dairy cattle to sustain milk production and farm profitability. The profitable operation of dairy farms is influenced by the reproductive performance of the lactating animals.

Bovine reproductive disorders, such as retained fetal membranes (RFM), significantly impact the dairy industry, leading to economic losses (Abdisa, 2018). RFM affects 10% of dairy cows and is considered one of the major health concerns after mastitis and lameness (Suthar et al. 2013). To monitor cow health and prevent such disorders, a comprehensive approach was recommended including pre- and post-calving assessments of milk production, feed intake, body condition, reproductive indicators, and laboratory tests (LeBlanc, 2013). RFMs have direct adverse effects on milk production and the future fertility of animals. Its incidence is affected by some physiological factors such as delayed gestation, forced parturition and early parturition, environmental, or pathological factors due to uterine infection resulting in abortion as well as uterine atony or seasonal and hormonal disorders. In addition to nutritional insufficiency, it is well-known that deficiencies of some vitamins and minerals induce or predispose animals to retention of membrane (placenta) (Yusuf, 2016; Alacam, 2002).

Ginseng is a perennial plant that grows in different areas worldwide. Ginseng contains saponins, antioxidants, peptides, polysaccharides, alkaloids, and lignin. The saponins (ginsenoside) in ginseng are considered to be the main bioactive components (Palazon *et al*., 2003). Saponins in ginseng enhance the immune system and provide pharmaceutical and antioxidant effects in humans and animals (Kim and in, 2010; Yildirim *et al.,* 2013). These positive properties could be explored for better animal productivity. Ginseng improved any disorders in the cardiovascular, endocrine, and immune systems in addition to reproduction (Park *et al*., 2017, Zare and Khaksar 2016).

The increase in milk production in ginseng-treated cows complies with the anti-ageing, antioxidant, and anti-stress properties of ginseng (Kopalli *et al*., 2016, Ramesh *et al*., 2012).

The absence of any significant effect in the NO concentrations in the control and supplemented cows with ginseng whatever with normal birth or RFM confirmed the good reproductive management on the farm that all animals recovered RFM without the development of postpartum subclinical or clinical endometritis or metritis and the effect of supplementation with ginseng in improving the reproductive performance in cows with RFM by decreasing the services required for conception. Contrary to the absence of any significant difference in NO concentrations in control or supplemented dairy cows, NO increased in dairy cows with subclinical endometritis (Xue *et al*., 2015). Panax is one of the famous ginseng species that possesses antioxidant properties, enhanced immune function and synthesis of NO (de Jong *et al.,* 2005; Kim *et al.,* 2005).

The decreased activity of the GSH and Hp concentrations in ginseng-treated cows confirmed the antioxidants (Kitts *et al*., 2000) and the anti-inflammatory (Im, 2020) properties of ginseng and its ability to inhibit metal-induced lipid peroxidation. Similarly, dietary supplementation with ginseng significantly enhanced the antioxidant activity of GSH (Xi *et al*., 2017).

In contrast to our results, NO and polymorphonuclear percentage increased in the uterine secretions of dairy cows with subclinical endometritis compared to those from normal (Xue *et al*., 2015). The absence of any significant differences in NO between cows supplemented with ginseng and their controls could be attributed to its pro-proliferation effects on oocytes, neurons, and endothelial cells (Liu and Zhang 2006, Tan *et al*., 2010).

The increase in estradiol in ginseng-treated groups compared to control cows with retained fetal membranes could be referred to as the modulating effects of ginseng via improving the cellular activity and functions through genomic and non-genomic signaling by binding to the cell surface and nuclear receptors such as estrogen receptors (ER), progesterone receptors (PR), androgen receptors, and proliferator-activated receptors (Seghinsara *et al*., 2018). So, the improvements in the health status of cows delivered with retained fetal membranes could refer to the structural similarity between ginseng and E2 in binding to the E2 receptors (Rietjens *et al*., 2017). In agreement with the increase of E2 levels in ginseng-treated dairy cows of this study, combined ginseng and nicotine increased the level of serum E2 (Faghani *et al*., 2022).

The decrease in the number of services required for conception in the ginseng-treated cows of this study to reach a similar number to control with normal birth could be attributed to the improvement in the maturation of the preantral follicles by the production of steroids and proliferating cell nuclear antigen (Seghinsara *et al*., 2018) and its significant estrogenic activities that regulate the estrous cycle (Xu *et al*., 2014). The high antioxidant properties of ginseng increased the number of ovarian follicles, increased sex hormone concentrations, and reduced the number of antral follicles (Choi *et al*., 2020). The anti-apoptotic, anti-inflammatory, and anti-oxidative effects ginsenoside protected oocytes meiotic maturation against damages (Luo *et al*., 2020). Ginseng prevented ovarian ageing and premature ovarian failure (Zhu *et al*., 2015).

5. Conclusions

The present study pointed out the possible use of ginseng as medicinal plant in improving the reproductive performance of postpartum dairy cows with retained fetal membranes. However medicinal plants, known for their antioxidant and antimicrobial properties, have the potential to address reproductive issues in livestock, including sexual dysfunction and poor reproductive performance.

References

Abdisa, T., 2018. Review on the reproductive health problem of dairy cattle. Dairy Vet. Sci. J. 5: 1–12.

Alacam, E., 2002. The Domestic Animals Obstetrics and Infertility. Medisan Publishing house, Ankara.

Amaefule, B., I. Uzochukwu, N. Ikeh, and E. Ozota, 2019. Reproductive performance and haematology of rabbits fed diet containing korean ginseng. Nigerian Journal of Animal Production, 26-30.

Bae, G.S., 2016. Effect of Supplementing Cultured Wild Ginseng Roots in the Diet of organic saanen dairy goats on milkcomposition and ginsenoside profiles in blood and milk. Korean Journal of Organic Agriculture, 24(3): 485-495.

Beccaria, C., C. Baravalle, P. Silvestrini, M.S. Renna, A.I. Molineri, M.L. Signorini, V.E. Neder, Archilla, G.A.S., L.F. Calvinho, and B.E. Dallard, 2021. Efficacy of Panax ginseng extract combined with cephalexin as a dry cow therapy. Journal of Dairy Research, 88(1): 64-68. doi: 10.1017/S0022029921000017.

Cardoso Consentini, C.E., M.C. Wiltbank, and R. Sartori, 2021 Factors That Optimize Reproductive Efficiency in Dairy Herds with an Emphasis on Timed Artificial Insemination Programs. Animals, 11: 301. https://doi.org/10.3390/ ani11020301.

Cardoso, F.C., S.J. LeBlanc, M.R. Murphy, and J.K. Drackley, 2013. Prepartum nutritional strategy affects reproductive performance in dairy cows. Journal of Dairy Science, 96(9): 5859-5871.

Choi, K.T. and D.C. Yang, 2012. Pharmacological effects and medicinal components of Korean ginseng (Panax ginseng C.A. Meyer). Korean Ginseng Res. Ind. 6: 2–21.

Choi, Y.D, K.H. Rha, and H.K. Choi, 1999. In vitro and in vivo experimental effect of Korean red ginseng on erriction J. Urol., 162:1508-1511.

Choi, J.H., M. Jang, E.J. Kim, M.J. Lee, K.S. Park, S.H. Kim, J.G. In, Y.S. Kwak, D.H. Park, S.S. Cho, and S.Y. Nah, 2020. Korean Red Ginseng alleviates dehydroepiandrosterone-induced polycystic ovarian syndrome in rats via its antiinflammatory and antioxidant activities. J Ginseng Res., 44: 790–8.

Cole, J. and P. VanRaden, 2018. Symposium review: Possibilities in an age of genomics: The future of selection indices. J. Dairy Sci. 101: 3686–3701.

Consultation, E., 2006. Committee for medicinal products for veterinary use (CVMP). European Medicine Agency.

De Jong, J. R., J.W.S. Vlaeyen, P. Onghena, C. Cuypers, M. den Hollander, and J. Ruijgrok, 2005. Reduction of pain-related fear in complex regional pain syndrome type 1: The application of graded exposure in vivo. Pain, 116: 264 – 275.

Faghani, M., S. Saedi, K. Khanaki, and F. Mohammadghasemi, 2022. Ginseng alleviates folliculogenesis disorders via induction of cell proliferation and downregulation of apoptotic markers in nicotine-treated mice. Journal of Ovarian Research, 15(1): 14.

Hu, S., C. Concha, R. Cooray, and O. Holmberg, 1995. Ginseng-enhanced oxidative and phagocytic activities of polymorphonuclear leucocytes from bovine peripheral blood and stripping milk. Vet. Res., 26(3):155-61.

Hu, S., C. Concha, A. Johannisson, G. Meglia, and K.P. Waller, 2001. Effect of subcutaneous injection of ginseng on cows with subclinical Staphylococcus aureus mastitis. J. Vet. Med. B. Infect. Dis. Vet. Public Health., 48(7):519-28. doi: 10.1046/j.1439-0450.2001.00470.x.

Im, D.S., 2020. Pro-Resolving Effect of Ginsenosides as an Anti-Inflammatory Mechanism of Panax ginseng. Biomolecules., 10(3):444. doi: 10.3390/biom10030444.

Iwuji, T.C., U. Herbert, and M.A. Oguike, 2018. Effect of Panax Ginseng Extracts on Milk Yield of New Zealand White Rabbits. Nigerian Journal of Animal Production, 152-154.

Jee, H.S., K.H. Chang, S.H. Park, K.T. Kim, and H.D. Paik, 2014. Morphological characterization, chemical components, and biofunctional activities of *Panax ginseng, Panax quinquefolium*, and *Panax notoginseng* roots: a comparative study. Food Rev. Int. 30: 91–111.

Jung, K., 2006. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Carl A. Burtis, Edward R. Ashwood, and David E. Bruns, editors. St. Louis, MO: Elsevier Saunders, 2448, ISBN 0-7216-0189-8. *Clinical Chemistry*, 52(6):1214-1214.

Kim, D.C. and M.J. In, 2010. Production of hydrolyzed red ginseng residue and its application to lactic acid bacteria cultivation. *J. Ginseng Res.,* 34: 321-326.

Kim, S.H., K.S. Park, M.J. Chang, and J.H. Sung, 2005. Effects of Panax ginseng extract on exercise-induced oxidative stress. Journal of Sports Medicine and Physical Fitness, 45 (2): 178 - 182.

Kitts, D.D., A.N. Wijewickreme, and C. Hu, 2000. Antioxidant properties of a North American ginseng extract. Mol Cell Biochem. 203(1-2):1-10. doi: 10.1023/a:1007078414639.

Kopalli, S.R., K.M. Cha, M.S. Jeong, S.H. Lee, J.H. Sung, S.K. Seo, and S.K. Kim, 2016. Pectinase treated Panax ginseng ameliorates hydrogen peroxide-induced oxidative stress in gc-2 sperm cells and modulates testicular gene expression in aged rats. J Ginseng Res., 40: 185–95.

LeBlanc, S.J., 2013. Managing transition period health for reproductive performance in dairy cows. Cattle Pract. 21:209–215

Liu, H. and C. Zhang, 2006. Ginsenosides promote proliferation of cultured ovarian germ cells involving protein kinase c-mediated system in embryonic chickens. Asian-Australasian J. Anim. Sci., 19: 958–63.

Lucy, M., 2019. Symposium review: Selection for fertility in the modern dairy cow—Current status and future direction for genetic selection. J. Dairy Sci. 102: 3706–3721.

Luo, Z.B., S.U. Rahman, M.F. Xuan, S.Z. Han, Z.Y. Li, X.J. Yin, and J.D. Kang, 2020. The protective role of ginsenoside compound K in porcine oocyte meiotic maturation failed caused by benzo(a)pyrene during in vitro maturation. Theriogenology., 157: 96–109.

NRC 2001. National Research Council. Nutrient Requirement of Dairy Cattle, 7th ed. National Academy Press, Washington, DC.

Palazon, J., R.M. Cusido, M. Bonfil, A. Mallol, E. Moyamo, C. Marales, and M.T. Pinol, 2003. Elicitation of different *Panax ginseng* transformed root phenotypes for an improvement ginsenoside production. Plant Physiol. Biochem., 41: 1019-1025.

Park, J., H. Song, S.K. Kim, M.S. Lee, D.K. Rhee, and Y.J. Lee, 2017. Effects of ginseng on two main sex steroid hormone receptors: estrogen and androgen receptors. J. Ginseng Res., 41:215–21.

Ramesh, T., S.W. Kim, J.H. Sung, S.Y. Hwang, S.H. Sohn, S.K. Yoo, and S.K. Kim, 2012. Effect of fermented Panax ginseng extract (GINST) on oxidative stress and antioxidant activities in major organs of aged rats. Exp. Gerontol., 47: 77–84.

Rietjens, I.M., J. Louisse, and K. Beekmann, 2017. The potential health effects of dietary phytoestrogens. Br. J. Pharmacol., 174: 1263–80.

Sarswat, C.S. and G.N. Purohit, 2020. Use of ethno-veterinary medicine for therapy of reproductive disorders in cattle. J. Entomol. Zool. Stud, 8: 1006-16.

Seghinsara, A.M., H. Shoorei, M.M. Hassanzadeh Taheri, A. Khaki, M. Shokoohi, M. Tahmasebi, A.A. Khaki, H. Eyni, S. Ghorbani, K.R. Rad, and H. Kalarestaghi, 2018. Panax ginseng extract improves follicular development after mouse preantral follicle 3d culture. Cell J., 21: 210–9.

Shai, K., S.L. Lebelo, J.W. Ng'ambi, M. Mabelebele, and N.A. Sebola, 2022. A review of the possibilities of utilising medicinal plants in improving the reproductive performance of male ruminants. All Life, 15(1):1208-1221.

Suthar, V.S., J. Canelas-Raposo, A. Deniz, and W. Heuswieser, 2013. Prevalence of subclinical ketosis and relationships with postpartum diseases in European dairy cows. J. Dairy Sci., 96:2925–2938

Tan, T.Q., C. Ge, Y. Mi, Y. Jin, and C. Zhang, 2010. Ginsenosides promote proliferation of granulosa cells from chicken prehierarchical follicles through PKC activation and up-regulated cyclin gene expression. Cell Biol. Int., 34: 769–75.

Vilar, M.J. and P.J. Rajala-Schultz, 2020. Dry-off and dairy cow udder health and welfare: Effects of different milk cessation methods. Veterinary Journal, 262: 105503.

Weigel, K.A., P. VanRaden, H. Norman, and H.A. Grosu, 2017. 100-Year Review: Methods and impact of genetic selection in dairy cattle—From daughter–dam comparisons to deep learning algorithms. J. Dairy Sci. 100(12): 10234–10250.

Xi, Q.Y., Y. Jiang, S. Zhao, B. Zeng, F. Wang, L.N. Wang, Q.Y. Jiang, and Y.L. Zhang, 2017: Effect of ginseng polysaccharides on the immunity and growth of piglets by dietary supplementation during late pregnancy and lactating sows. Animal Science Journal, 88(6): 863-872.

Xu, Y., J. Ding, X.P. Ma, Y.H. Ma, Z.Q. Liu, and N. Lin, 2014. Treatment with Panax ginseng antagonizes the estrogen decline in ovariectomized mice. Int. J. Mol Sci., 15: 7827–40.

Xue, S., L. De-jun, F. Guo-feng, L. Bei, and L. Yun-feng, 2015. Dynamic analysis of nitric oxide and total oxidant capacity in cow uterine secretion with subclinical endometritis. Journal of Northeast Agricultural University (English Edition), *22*(1): 35-39.

Yeo, C.R., and J.J. Yong, 2017. Popovich DG. Isolation and characterization of bioactive polyacetylenes Panax ginseng Meyer roots. J. Pharmaceut. Biomed. 139: 148–155.

Yoo, D., H. Kim, J. Moon, J. Kim, H. Kim, and J. Seo, 2022. Effects of Red Ginseng Byproducts on Rumen Fermentation, Growth Performance, Blood Metabolites, and mRNA Expression of Heat Shock Proteins in Heat-Stressed Fattening Hanwoo Steers. *Veterinary Sciences*, *9*(5): 220.

Yusuf, J.J., 2016. A review on retention of placenta in dairy cattles. Inter. J. Vet. Sci., 5(4): 200-207.

Zare, A. and Z. Khaksar, 2016. Effects of Panax ginseng alcoholic extract on histomorphometric changes of ovaries in offspring rats from diabetic mothers. Biosci. Biotechnol. Res. Asia., 13: 237–45.

Zhu, L., J. Li, N. Xing, D. Han, H. Kuang, and P. Ge, 2015. American ginseng regulates gene expression to protect against premature ovarian failure in rats. Biomed. Res. Int., 767124.