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Review

Bovine colostrum: A veterinary nutraceutical

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Colostrum is the lacteal secretion produced after parturition and plays an important role in post-natal health as an immune booster. In addition to nutrients such as proteins, carbohydrates, fats, vitamins and minerals, bovine colostrum contains several biologically active molecules that are essential for specific functions. Bioactive components like growth factors promote the growth and development of the newborn while antimicrobial factors provide passive immunity and protection against infections during the first weeks of life. It has been proven as an effective nutraceutical for the enhancement of immune function in a diverse range of animal species. No side effects or drug interactions have been reported with high quality colostrum supplementation, making it an exceptionally safe and useful nutraceutical product.

Key words: Bovine colostrum, nutrient profile, bioreactive components, functional food.

INTRODUCTION

Veterinary nutraceutical medicine has been defined as 'the use of micronutrients, macronutrients and other nutritional supplements as therapeutic agents' (American Veterinary Medical Association, 1999). Colostrum is used as a nutraceutical for animals of all ages to increase resistance to infection and disease caused by a wide range of pathogens including bacteria, viruses, parasites and fungi. It is used for applications such as healing of intestinal lesions and increasing the absorption of nutrients from the gastrointestinal tract. The components of colostrum that convey its nutraceutical properties are nearly identical in structure and function among different species (Francis et al., 1986; Anderson et al., 1989), thus could be effectively used across the species. It is used in nutraceutical medicine due to the relative ease with which large amounts can be collected and processed, and its proven effectiveness when used to treat a variety of ailments.

Colostrum is the "early" milk produced by female mammals and in case of bovine it is the first four days of milk post parturition (Gopal and Gill, 2000). Colostrogenesis, preceeding lactogenesis and lactation, results in the secretion of colostrum which is unique in composition and function and is supposed to be under endocrine and local control and regulation (Barrington et al., 2001). The role of colostrum for a new born for first few days of life is not only to provide nutrition, but also to provide protection against infection while immune system is still developing. It has a nutrient profile and immunological composition that differs substantially from 'mature' milk. Proteins, carbohydrates, fats, vitamins and minerals included in the nutrient profile are in addition to the growth factors, cytokines and nucleosides. It is rich in oligosaccharides, natural antimicrobials, immune regulation factors (Kelly, 2003) and antioxidative factors. The immunoglobulins are selectively transported to mammary secretion from maternal circulation several weeks before parturition (Butler, 1983).

BOVINE COLOSTRUM AS IMMUNOMODULATOR

In humans, maternal immunoglobulins with specific antimicrobial activity are transferred to the new born via placenta and confer a degree of passive immunity. Contrarily, in animals such as bovines, ovines, caprines and equines, the immunoglobulins are transferred posnatally through colostrum as the placenta does not allow significant transfer of macromolecules. Bovine colostrum contains immunoglobulins such as IgG, IgM, IgA, IgD, and IgE. IgG and IgM function in systemic infections while IgA functions within internal body surfaces such as the intestine (Muller and Ellinger, 1981). When taken orally, the immunoglobins in colostrum are

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not absorbed into the blood stream in case of animals older than 36 to 48 h. However, within the GI tract of animals of all ages they are very effective against pathogenic organisms. Colostral immunoglobins are able to bind and agglutinate invading organisms such as bacteria, viruses, fungi and parasites that enter the intestinal tract, facilitating their removal before they cause infection and diseases (Oyenyi and Hunte, 1978). The immunoglobulins also prevent pathogens from binding to intestinal surfaces (Bitzan et al., 1998) thereby inhibiting an important step in the infection process. Colostrum supplementation in rabbits has shown immunomodulatory potential by enhancing cell mediated immune response without any effect on humoral immune response (Nagaraja, 2010).

The iron binding glycoprotiens, lactoferrin and transferrin, found in colostrum slow pathogen growth by sequestering free iron molecules in the gut and moving the iron in the blood stream (Pakdaman et al., 1998). Lactoferrin attacks pathogens directly by destabilizing the coat membranes of gram negative bacteria (Dionysius and Milne, 1997) which allows the immune system to attack them more successfully. It increases the ability of neutrophils to attack and destroy bacterial invaders (Miyauchi et al., 1998). It may also bind to receptors in the intestine and act as a signal to stimulate the immune system (Miyauchi et al., 1998). It is proven to exhibit antiviral properties most likely by attaching to the virus and preventing it from entering the cells (Sato et al., 1996; Swart et al., 1998).

The cytokines IL-1, IL-2, IL-6, TNF α and IFN γ present in the colostrum are fundamental components of immune system. They enhance B and T cell maturation and increase the level of endogenous antibody production (Watkins et al., 1995). They are required to fight systemic infections and to protect against septic shock. They play a major role in the regulation of epithelial cell growth and development including intestinal inflammation and epithelial restitution following mucosal damage (Elson et al., 1994).

Transfer factors, a family of small oligoribo-nucleopeptides, are known to potentiate the action of T cells (Wilson et al., 1982; Kirkpatrick, 1996). The stimulated T cells produce a secondary immune response upon first exposure to antigens, rather than a primary response that would otherwise be the case. These factors function in a cross species manner (Radesevich et al., 1985).

Proline Rich Polypeptide (PRP) present in colostrum stimulates the weakened immune system and also stabilizes hyperactive immune system due to autoimmune diseases and allergies in the body (Thapa, 2005).

BOVINE COLOSTRUM AS HEALTH PROMOTER

Colostrum contains a number of growth and maturation factors such as somatomedins (IGF-1, IGF-2), somatotrophin, fibroblast growth factor (FGF), transforming growth factor α and β (TGF-α and TGF-β), insulin, platelet derived growth factor (PDGF) and epidermal growth factor (EGF) which form a powerful combination in colostrum (Oda et al., 1989; Ginjala and Pakkanen, 1998). These naturally occurring substances have been shown to enhance the synthesis of DNA, RNA and protein, while at the same time inhibit breakdown of protein (Ballard et al., 1982; Ginjala and Pakkanen, 1998). There are receptors for these compounds throughout the intestinal tract and they are postulated to be mediators of intestinal growth and development (Montaner et al., 1999). They are known to increase cell mass of intestine, influence the composition of absorptive surfaces and may be involved in stimulating wound healing (Hardin et al., 1993). Maturation and proliferation of intestinal cells result in increased absorption of electrolytes and nutrients from intestine (Opleta-madsen et al., 1991; Alexander and Carey, 1999). Bovine colostrum supplementation in rabbits increased body weight gain without any significant effect on biochemical parameters except AST (Dar et al., 2010). Further, the adjunctive therapeutic potential of colostrum along with Ivermectin has been reported against naturally *Psorptes cuniculi* infested rabbit (Dar et al., 2010). Colostrum supplemented calves suffered less diarrhea and received fewer antimicrobial treatments than control and placebo calves (Berge et al., 2009)

Nucleotides and nucleosides in colostrum belong to the group of natural bioactive minor substances. They are not only active as metabolites but seem to be important in the regulation of body functions also. They participate in iron absorption in the gut, desaturation and elongation rates in biosynthesis of fatty acids. Their concentration tends to decrease with time after parturition (Przybylska et al., 2007).

Grehlin, present in colostrum, is an acylated peptide from stomach, which plays a role in stimulating growth hormone release by the pituitary gland and in affecting feeding behavior as stimulator of food intake (Kojima and Kangawa, 2005).

Trypsin and protease inhibitors present in colostrum are highly effective in protecting the immune and growth factors from being broker down in the gastrointestinal tract. They prevent *Helicobacter pylori* from attaching to the walls of the stomach and have a beneficial role in the treatment of peptic ulcers (Bitzan et al., 1998).

Lysozyme is a lytic enzyme of 14.3 kDa. The natural substrate of this enzyme is the peptidoglycan layer of the bacterial cell wall and its degradation product results in lysis of the bacteria (Reiter, 1978). A peculiarity of the lysozyme is its interaction with other factors present in the colostrum. It partly activates lactoperoxidase by forming a complex with it (Hulea et al., 1989). In presence of lactoferrin, the antimicrobial activity of lysozyme against *Escherichia coli* is also enhanced as lactoferrin damages the outer membrane of gram negative

bacteria and the organism becomes susceptible to lysozyme (Yamauchi et al., 1993). It also works in synergy with IgA and complement factors against *E. coli* (Hill et al., 1974). *Lactobacillus bifidus acidophilus*, a friendly bacterium in colostrum, is necessary for the normal digestion of food and its presence is essential to reduce the growth of harmful bacteria in the digestive system. It also effectively combats *Candida albicans*.

BOVINE COLOSTRUM AS AN ANTIOXIDANT

At birth the newborn encounters an environment much richer in oxygen than the intrauterine life and antioxidant defense mechanisms that are poorly developed in the neonatal period may be overcome by the generation of excessive reactive oxygen species thereby exposing the neonate to oxidative stress. Colostrum with a significantly high total antioxidant capacity can be beneficial against this oxidative damage. It is rich in enzymatic as well as non enzymatic antioxidants. The enzymatic antioxidants include lactoperoxidase, catalase, superoxide dismutase and glutathione peroxidase.

Lactoperoxidase, a basic glycoprotein containing a heme-group with Fe^{3+} catalyses the oxidation of thiocyanate (SCN^-) in the presence of hydrogen peroxide (H_2O_2), producing a toxic intermediary oxidation product which inhibits bacterial metabolism via the oxidation of essential sulphahydryl groups in microbial enzymes and other proteins (Pruitt et al., 1985).

$$H_2O_2 + SCN^- \longrightarrow OSCN + H_2O$$

Its biological significance lies in its involvement in the natural host defense system against invading microorganisms, degradation of various carcinogens and protection of animal cells against peroxidative effects. Catalse catalyses the decomposition of hydrogen peroxide.

$$2H_2O_2 \longrightarrow 2H_2O + O_2.$$

Cream and skim milk contains about 60 and 40%, respectively of milk catalase. Most of it in cream is bound firmly to the membranes of fat globules and cannot be released readily into skim milk (Ito and Akuzawa, 1983).

Superoxide dismutase (SOD) catalyses the dismutation of superoxide anion to hydrogen peroxide:

$$2O_2^- + 2H^+ \longrightarrow H_2O + O_2$$

There are three types of SOD which contain either manganese, copper/zinc or iron, respectively. In bovine milk Cu/Zn-SOD is found (Asada, 1976). It is absent in cream and only found in skim milk. The concentration of SOD in milk varies between cows and breeds. In cow's milk it is probably not affected by stage of lactation or age of cow and does not vary between morning and night milking. Glutathione peroxidase (GSH-Px) activity has been detected in bovine milk at levels between 12 and 32 U/ml and correlated significantly with selenium concentration. This suggests that GSH-Px is one of the biologically active forms of selenium in milk (Hojo, 1982; Debski et al., 1987). Both GSH-Px activity and selenium content of milk have been shown to decrease within the time of lactation (Hojo, 1986). It has been found that several seleno compounds may scavenge peroxynitrite radicals (Sies et al., 1997).

The non enzymatic antioxidants in colostum include vitamin E, A, C, lactoferrin, selenium, copper, zinc, cysteine etc.

Vitamin E, an important lipid-soluble membrane antioxidant enhances the functional efficiency for neutrophils by protecting them from oxidative damage following intracellular killing of ingested bacteria. It acts as a radical scavenger and protects from peroxidative damage of all phospho-lipid containing membranes.

Vitamin A has numerous functions that are not fully understood, but its main role is the resistance to infectious diseases particularly mastitis.

Vitamin C is water soluble and is present in the cytosolic compartment of the cell. It serves as an electron donor to vitamin E radicals generated in the cell membrane during oxidative stress. It contributes to maintaining the redox integrity of cells and thereby protects them against reactive oxygen species generated during the respiratory burst and in the inflammatory process.

Lactoferrin provides protection from iron induced lipid peroxidation (Bennett et al., 1986). Its physiological role is the responsibility for primary defense against microbial and viral infection (Masson et al., 1969). It may serve as an antioxidant by binding any catalytic iron generated during the course of cell destruction, minimizing hydroxyl radical mediated tissue injury associated with neutrophil-oxidant production during inflammation. It is able to inhibit Haber-Weiss reaction as well (Ye et al., 2000). The different subfractions of colostrum lactoferrin possess five different enzyme activities: DNase, RNase, ATPase, Phosphatase and malto-oligosaccharide hydrolase.

Selenium is transferred through the placenta and mammary tissue. The mammary-gland regulates mechanisms that control the synthesis and secretion of seleno-compounds throughout lactation with a high total Se level in colostrum that decreases as lactation progresses. It appears in colostrum as a component of specific seleno-proteins and seleno-amino-acids that are well tolerated by infants. Se in colostrum occurs as glutathione-peroxidase (4 to 31% total Se) > selenocyst-amine> selenocystine > Selenomethionine. The wide range of colostrum Se concentration depends on Se consumed in natural foods which reflects the Se contents of the soils where animals are grown. Se prophylaxis, either through the soil Se fertilization or maternal

supplements, is effective in raising colostrum Se concentration (Przyblyska et al., 2007). Se-enriched yeast was much more effective than sodium selenite in increasing the concentration of Se in the blood, colostrum and milk, as well as the GSH-Px activity (Slavik et al., 2008).

Others include Copper, Zinc, Cysteine etc. The former two are necessary for proper activity of antioxidant enzymes besides possessing their own antioxidant properties (Ahmed et al., 2004). The latter is a precursor of glutathione (Goldmas et al., 1986) which is a powerful antioxidant found in colostrum.

Casiens and whey proteins from colostrum exert antioxidant activities measured by reducing power, ferrous ion chelating abilities as well as inhibitory effects on lipid peroxidation (Chiang and Chang, 2005).

Colostrinin, a complex of proline rich polypeptides possesses antioxidant activity besides inducing mitogenic stimulation. It reduces intracellular levels of reactive oxygen species and appears to down regulate 4-hydroxynonen-mediated lipid peroxidation (Bilikiewicz and Gaus, 2004). Colostrum is also capable of spontaneous reduction of cytochrome c, depletion of polymorpho nuclear leukocyte-produced H_2O_2 and protection of epithelial cells from PMN-mediated detachment (Przyblyska et al., 2007).

Published reports have shown that colostrum and its components are effective against a wide range of common pathogens, including *Rotavirus*, *Cryptosporidium* spp., *Staphylococcus aureus*, *Candida* spp., *Clostridium* spp., *Feline immunodeficiency virus*, *Shigella* spp., *Streptococcus* spp. and *E. coli*. It is a proven effective nutraceutical for the enhancement of immune function in a diverse range of animal species including cattle, horse, pig, sheep, cats, mice, hamsters, ferrets and lizards (Taillon and Andreason, 2000).

CONCLUSION

Bovine colostrum can be given alone as a treatment to reduce the length and severity of established infections or it can be used in conjunction with traditional treatments such as antibiotics. There are no reported side effects or drug interactions associated with supplementation with high quality colostrum, making it an exceptionally safe and useful nutraceutical product for use in wide range of applications.

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