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COLOSTRUM A NATURAL VACCINE : A REVIEW


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ABSTRACT

Colostrum (CLM) is the pre-milk provided by mammal mothers to their newborns. CLM is the first milk produced by mammals for their young ones. This transfers the passive immunity gained by the mother to the baby. CLM is low in volume but high in nutritional value. The CLM is a mixture of carbohydrate, protein, growth factors, blood cells and immunoglobulins. It is yellow, thick and sticky in nature. The bovine CLM has therapeutic potential to the human being as it contains near about 90 useful components. The present article reviews about CLM, its composition, primary role and therapeutic potentials.

Key Words: Colostrum, CLM, mammals, mothers milk, pre-milk growth factors.

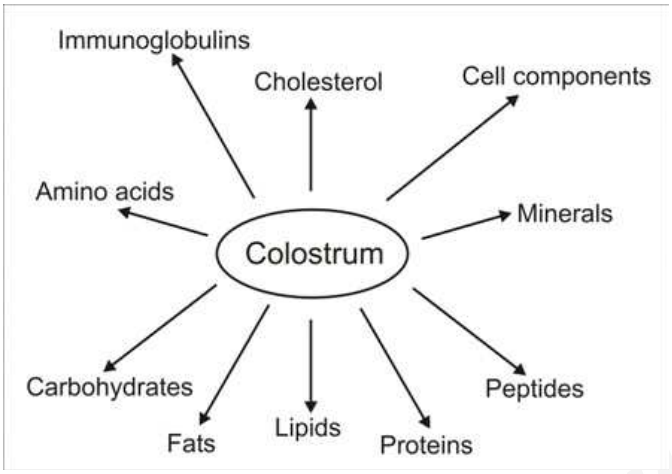
INTRODUCTION

CLM is a form of milk produced by the mammary glands in late pregnancy and continues through the early few days of breast feeding. It is thick in consistency, yellowish to orange in colour and sticky in nature1. The volume of CLM produced per day is very less but its nutritional value is high for the newborn. It is low in fat but high in carbohydrate, protein and antibodies which keep the baby healthy. CLM can be defined as the milk produced in the first 48 hours after delivery which is rich in nutritional value. It contains immunoglobulins, antimicrobial peptides and other bioactive molecules including growth factors. CLM plays an important role in the nutrition, growth and development and also contributes to the immunologic defense of neonates2. Primarily CLM exerts its laxative action for encouraging the evacuation of meconium (Baby's first stool). This clears the excessive bilirubin to prevent jaundice. The immunoglobulin A (Ig A) or antibodies helps to protect the mucus membrane of throat, lungs and intestine of the infant. The white blood cells or leukocytes protect the infant from viral and bacterial infections3. CLM is natural and 100 percent

safe vaccine. Many scientific studies have been reported on the
nutritional and therapeutic importance of CLM (bovine or human). The CLM should not only be considered as nutrient but also an agent providing protection to newborn against new environment4.

COMPOSITION OF CLM

CLM is thick yellow mammary secretion and lasts for 2-4 days after the lactation has started. The scientific literature reveals that Bovine CLM contains around 90 useful components; few of them are presented in Fig. 1. The main two components are immune factors and growth factors. It also contains vitamins, minerals, amino acids, proteins, fats and carbohydrates5**.** CLM is the specific first diet of mammalian neonates. Bovine CLM ultra-filtrate contains 1.16g/L protein, 0.24g/L immunoglobulin G (IgG) and less than 0.24 EU/ml endotoxin6.



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a) Proteins and peptides

Many amino acids, proteins, enzymes and peptides are present in human CLM and milk which plays variety of roles to keep the neonate healthy. The enzymes are α- amylase, lactoperoxidase, protease and vitamin binding protein etc.

Casein*:* Casein in human milk appears to be present almost exclusively in micellar form. Casein is not a single entity but is a group of protein subunits, associated and linked together, with organic and inorganic ions into micelles.

Lactoferrin*:* Lactoferrin, a red-colored iron-binding protein in human milk, was first isolated by Johansson7. Lactoferrin (LF), also known as lactotransferrin (LTF), is a globular multifunctional protein with antimicrobial activity (bacteriocide, fungicide) and is part of the innate defense. It is a glycoprotein present at a concentration of ~7g/L in human CLM8. Lactoferrin facilitate iron absorption, act as an antimicrobial agent and stimulate growth of various cells9. Lactoferrin binds the iron and makes it
unavailable to *E.coli* in the intestine and inhibits bacterial growth10.

Growth factors*:* CLM contains many hormones like prolactin, somatostatin, oxytocin, leutinizing hormone releasing hormone, thyroid stimulating hormone, thyroxine, calcitonin, estrogen and progesterone. These hormones influence thyroid gland,
hypothalamus, sexual gland, adrenal and pancreatic gland11.

Growth hormone (GH) and growth hormone releasing factor (GHRF)*:* GH and GHRF are present in human CLM and bovine CLM. Human CLM contains ~ 41ng/L of GHRF12. Suckling neonates have high circulating concentration of GH13. GH many have direct mitogenic effect14. Peptides growth factors are present
in CLM which can regulate or modulate intestinal growth and development. Non-peptide

trophic factors viz glutamine, polyamines and nucleotides present in colostrum plays an important role in developing and maintaining GI mucosal mass and modulating immune system2.

Epidermal growth factor (EGF): It is a 53-amino acid peptide present in human CLM. Its concentration in human CLM is 200µg/L15.

Transforming growth factor (TGF) α: It is a 50 amino acid molecule present in human CLM at much lower concentration 2.2-7.2µg/L16. TGF-α stimulates gastrointestinal growth and repair, inhibit acid secretion, stimulates mucosal repairing after injury and increases gastric mucin concentration17.

Transforming growth factor (TGF) β: Human milk contained latent, but not free, TGF-beta 1, and especially TGF-beta 2, both of which may be activated by gastric acid pH (18). It is structurally distinct from TGF-α and has many diverse functions. In bovine CLM TGF-β is present in very high concentration (20-40mg/L)1. It is a key component in mediating its ability to maintain GI integrity in suckling neonates19.

Insulin like growth factors (IGF): IGF is also known as somatomedins. Two types of IGF are found in CLM viz. IGF-I and IGF-II. Both have similar structure to proinsulin and it is possible that they exert insulin like action at higher concentration. Bovine CLM contains much higher concentration (500µg/L) of IGF-I than human CLM (18µg/L)20. IGF-I is known to promote protein build-up21. IGF-II is present in bovine CLM at much lower concentration and has anabolic activity22. IGF in bovine and human CLM are present in both free and bound form.

Platelet derived growth factor (PDGF): PDGF present in CLM is a disulphide linked polypeptide consisting of two chains. PGDF is a potent mitogen for fibroblast and arterial smooth muscle cells. Exogenously oral administration of PDGF has been shown to facilitate ulcer healing2.

Vascular endothelial growth factor (VEGF): Human CLM contains VEGF at a concentration of ~ 75µg/L. It is a homodimeric heparin binding glycoprotein with potent angiogenic, mitogenic and vascular permeability enhancing activities23.

Cytokines: CLM contains many cytokines including interleukin (IL) 1β, IL-6. IL-10, tumor necrosis factor α (TNF-α) and granulocyte-macrophage colony stimulating factors. Cytokines trigger acute cellular responses such as chemotaxis, protein synthesis and cellular differentiation in picomolar or nonomolar concentration2.

Colostrinin: Bovine CLM contain a proline rich polypeptide (PRP) complex called colostrinin. The complex shows immunomodulatory actions. It is a cytokine like factor that acts as an inducer of interferon gamma24. Recently it is found that colostrinin have a beneficial effect in Alzheimer's disease25.

Immunoglobulins: Human CLM and mature milk contains high concentration of secretory immunoglobulin-A (S-IgA). S-IgA is quite resistant to trypsin digestion26. The presence of immunologically active cells in CLM which produces antibodies to antigens has profound implications for infant's survival and future health interventions26. The human CLM contains neutralizing antibodies against many infectious agents including entero-viruses. Major portion of the proteins present in CLM consists of immunoglobulins. In human CLM

IgA predominates (120g/L)27**.** IgA acts in the intestine and limit themultiplication of bacterial and viral antigens
Within the digestive tract. Human CLM contains large number of antibodies called secretory immunoglobulin (IgA). CLM actually works as a safe and effective oral vaccine. IgA protect the baby from harmful viruses and bacteria. In human CLM IgA is present in free as well as in association with cellular and non-cellular elements28.

Alpha amylase: The presence of α-amylase in human milk has long been recognized. The concentration of α- amylase is high in CLM and declines rapidly thereafter29.

Lactoperoxidase: Recently Langbakk and Flatmark were able to show that lactoperoxidase is present in human CLM30. The specific assays performed on CLM
and human milk reveals the presence of γ-glutamyl transferase31, acid phosphatase, alkaline phosphotase32, lactic and malic dehydrogenase33, N-acetyl-α-
hexosamidase34, ribonuclease35 and xanthine oxidase36. It is found that activity of some enzymes is higher in CLM than in mature milk.

Protease and protease inhibitor: Human CLM has an inhibitory effect on trypsin activity *invitro*.Themolecular weight of inhibitor found in the CLM is 6000-10000 and is heat and acid stable37.

Vitamin binding protein: Cobalamin (Vitamin B12) for its absorption requires binding protein called cobalamin binding protein (CblBP). The concentration of CblBP is considerably higher in CLM than in mature milk38.

Corticosteroid binding protein: The presence of corticosteroid binding protein in human CLM has been proved by Payne et al. This protein is found in whey
and has a molecular weight of 93000 and its concentration is higher in CLM than in mature milk. It is similar to serum corticosteroid binding globulin39.

Glycoprotein: Glycoprotein from human CLM has been isolated by the researchers40. The non-orosomucoid glycoprotein from CLM and mature milk has
stimulating effect on growth of *lactobacillus bifidus*. This glycoprotein is reported as a proteolyte fragment of human casein.

Biotin and Biotinidase: Human milk contains relatively high concentration of biotin. However the concentration of biotin is much higher in mature milk (0.81µg/100ml) than in CLM41. Biotinidase is present in human CLM and mature milk. The biotinidase activity in CLM is about 5 times higher than that of milk. This enzyme regulates the metabolism of biotin42.

b) Vitamins

Rich alimentary supply of the vitamin is essential in early childhood. Maternal milk; particularly CLM is usually an excellent source of vitamin A and β- carotene in 440 and 428 µg/L concentration respectively43. Human CLM contain β-carotene44. The
concentration of carotenoids in CLM is eight times more than the mature milk10.

Vitamin A: Vitamin A content of CLM and transitional milk is very high and it is found that its concentration is independent of Vitamin A status of mother45.

Cobalamin (Cbl)*:* Sampson and Mc Clelland reported the presence of Cbl in human milk. The Cbl levels found in human CLM was almost eight fold greater

than those of milk collected after a month of lactation46.

Choline: Choline is an organic compound, classified as a water-soluble essential nutrient and usually grouped within the Vitamin B complex. This natural amine is found in the lipids that make up cell membranes and in the neurotransmitter acetylcholine. Adequate intakes (AI) for this micronutrient between 425 to 550 milligrams daily, for adults, have been established. Human CLM contains choline in aqueous as well as in lipid fractions. In aqueous fraction free choline, phosphocholine and glycerophosphocholine are present while lipid fraction contains phosphatidylcholine and sphingomyelin47. Choline is an essential constituent of membrane phospholipids.

c) Miscellaneous

Minerals: Different types of minerals are also present in human CLM. The concentration of few of them viz. copper, iron, selenium and zinc is 400-600, 400-800, 15 and 4000-5000 µg/L respectively48. The ratio of zinc to copper was found to be 13 in human CLM49**.** The same amount of chromium is found in human CLM and mature milk. The average concentration of chromium in breast milk is 0.18 µg/L50. Human CLM contains high concentration of sodium than mature milk10.

Cholesterol: Human CLM and mature milk contain >0.26mmol/L of cholesterol51.

Sialic acid: Sialic acid is a generic term for the *N*- or *O*substituted derivatives of neuraminic acid, a monosaccharide with a nine-carbon backbone. It is *also* the name for the most common member of this group, N-acetylneuraminic acid (Neu5Ac or NANA). Three types of sialic acids are present in human CLM viz. oligosaccharide bond, protein bound and free sialic acid. The concentration of sialic acid is highest in CLM and decreases by nearly 80% over the next three months52.

Fatty acid: Long chain polyunsaturated fatty acid viz. docosahexanoic acid and arachidonic acid are present in human milk and plays an important role in neural maturation of breast feed neonates53. The concentration of total protein, fat and lactose is more in CLM during first 24 hours.

Cellular components: CLM contains two types of macrophages viz macrophages engorged with fat droplets and phagocytic macrophages with abundant lysozymes[54] and synthesizing immunoglobulins55. Human CLM has inherent positive anti-infective properties due to the presence of cellular components.
CLM is rich in cells56 ~3-8x10 cells/ml. The macrophages, neutrophils, T and B-lymphocytes and epithelial cells have been reported in human milk. Tcells comprise more than 50% of the lymphocyte of CLM57.

Others: Human CLM also contains lysozyme58 and corticosteroids59.

GENERAL HEALTH AND THERAPEUTIC BENEFITS OF CLM

CLM because of its versatile composition it can be used in variety of diseases. It has properties to stimulate immune system and also contains hormones, growth factors and other bioactive components required for the body to combat with various diseases. It has been used for various respiratory tract infections, gastrointestinal disorders and rheumatoid arthritis. The medical importance of CLM has been described in ancient ayurveda. In US CLM

was in use for its antibacterial activity before the discovery of antibiotics5. CLM upon contact with stomach acid inhabits and kill *campylobacter, candida, E.coli, colostridium, helicobacter pylori, rotavirus, salmonella, shigella and streptococcus*. CLM is effective in leaky gut, irritable bowel syndrome, colitis, ulcers, chronic fatigue, diabetes, autoimmunity, arthritis, lupus and cancers, improves intestinal assimilation of nutrients, inhibits protein breakdown, shifts energy source from carbohydrate to fat, spur glucose transport in
muscles60. It is now well established fact that ingestion of CLM promotes nutritional, functional and biological activities. Few important benefits and actions of CLM are discussed below

Nutritional benefits
As CLM contains high concentration of carbohydrate, protein and low fat, it delivers its nutrients in very concentrated low volume form. Near about 20 times more protein is present in CLM as compared to the milk produced later61. It is rich in lipids, mineral salts, vitamins and immunoglobulins1.

Role in hyperbilirubinemia
CLM has mild laxative effect which facilitates the passing of meconium (baby's first stool). This process clears excess of bilirubin which is produced in large quantities at birth due to reduction in blood volume and helps to prevents jaundice62.

Shielding action
Immunoglobulin (IgA) present in CLM helps to protect the mucous membrane in the throat, lungs and intestine of newborn. The large number of leukocytes in CLM can destroy disease causing bacteria and viruses62.

Antidiarrheal action
A study on bovine CLM suggests that cryptosporidium (a parasite of human GI tract causing life threatening diarrhea) associated diarrhea in AIDS can be controlled after the treatment with hyper immune bovine CLM63.

Action on immune system
Breast feeding improves the health of children. The greatest significance of CLM is host defense, prevention of autoimmunity, and development of the digestive system; however, the underlying mechanisms for these effects are not well understood.
Based on recent evidence it is found that the cytokines are involved in these processes18. Researchers now believe that CLM may be the jump start; one needs to
fight infection or immune related chronic diseases such as cancer, AIDS etc64. The immune boosting property of CLM is attributed to molecules called transfer factors. CLM also proved to be an effective anti-cancer agent by boosting immune system and by preventing iron from reaching and nourishing cancer cell with the help of phytic acid. Phytic acid is a powerful antioxidant and found in very high concentration in CLM65. Without optimal immune protection we are susceptible to conditions ranging from common cold, flu, various stages of immune deficiency, cancer and even AIDS.

Actions on GI tract
Recent studies suggest that colostral fractions or individual peptides present in CLM will mitigate the symptoms of acid reflex. It might be useful for the treatment of wide variety of gastrointestinal tract disorders7. CLM contains multitude of healthful components that work for adults as well as the newborn. The ingestion
of CLM by newborns helps the profound growth and maturity of esophagus, stomach, small intestine. This is due to the hormones and growth promoting
peptides present in CLM66**.** Healing of tissues damaged by ulcer, trauma burns and surgery can be facilitated using the growth factors present in CLM67.

Antiallergic action

Praline rich polypeptide (PRP) present in colostrums can work as a regulatory substance of the thymus gland. It has been demonstrated that PRP inhibits the overproduction of lymphocytes and T-cells and reduces major symptoms of allergies and autoimmune diseases such as rheumatoid arthritis, lupus, and myasthenia gravis67.

Importance in athletics and body building

Bovine CLM builds muscle and improves athletic performance without side effects. The muscles will become stronger and younger. CLM by nature helps to promote both strength and good health63.

Use in chronic fatigue syndrome

Chronic fatigue syndrome (CFS) is believed to be caused by the Epstein-Barr Virus (EBV). The virus causes an over-reaction of the immune system. The immune system becomes overburdened and immunity is burnout66. The result is feeling of complete exhaustion. CLM is best remedy for CFS as it can boost the immune system.

Miscellaneous uses of CLM

The strengthening of immune system is important in the lyme disease. Lyme disease, or borreliosis, is an emerging infectious disease caused by at least three species of bacteria belonging to the genus *Borrelia*67. Bovine CLM is safe way to enhance immunity. Early diagnosis and treatment with CLM can prevent the complications68. Components of CLM promote the rapid healing, stop bleeding and leave the nostrils clear when applied to bleeding nostrils. CLM is really all-in-one medicine because it has tremendous potential for fight against any diseased condition. It is rich source of carbohydrate, protein, growth factors, blood cells, lysozyme and immunoglobulins.

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