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Review Article

COLOSTRUM: ALL-IN-ONE MEDICINE

BUMRELA SHRINIVAS*, PATIL RAJESH AND SAXENA MANISHA

Sinhgad Technical Education Society's, Sinhgad Institute of Pharmaceutical Sciences, Kusgaon (Bk), Lonavala. Dist-Pune, MH (India) 410401. e-mail: sbb2000@rediffmail.com

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.

Keywords: Colostrum, composition, therapeutic potential, immunological activity.

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 nature[1]. 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 neonates[2].

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 infections[3]. 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 environment[4].

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 carbohydrates[5]. 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 endotoxin[6].

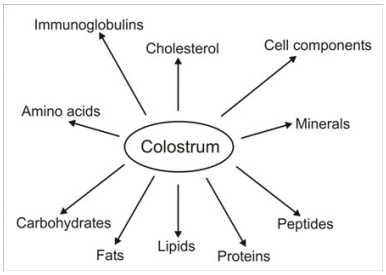

Fig. 1: composition of colostrum

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 Johansson[7]. 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 CLM[8]. Lactoferrin facilitate iron absorption, act as an antimicrobial agent and stimulate growth of various cells[9]. Lactoferrin binds the iron and makes it unavailable to *E.coli* in the intestine and inhibits bacterial growth[10].

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 gland[11.] *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 GHRF[12]. Suckling neonates have high circulating concentration of GH[13]. GH many have direct mitogenic effect[14]. 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 system[2].

Epidermal growth factor (EGF): It is a 53-amino acid peptide present in human CLM. Its concentration in human CLM is 200µg/L[15].

Transforming growth factor (TGF) α: It is a 50 amino acid molecule present in human CLM at much lower concentration 2.2-7.2µg/L[16]. TGF- α stimulates gastrointestinal growth and repair, inhibit acid secretion, stimulates mucosal repairing after injury and increases gastric mucin concentration[17].

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 neonates[19].

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-up[21]. IGF-II is present in bovine CLM at much lower concentration and has anabolic activity[22]. 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 healing[2].

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 activities[23].

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 concentration[2].

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 gamma[24]. Recently it is found that colostrinin have a beneficial effect in Alzheimer's disease[25].

Immunoglobulins: Human CLM and mature milk contains high concentration of secretory immunoglobulin-A (S-IgA). S-IgA is quite resistant to trypsin digestion[26]. The presence of immunologically active cells in CLM which produces antibodies to antigens has profound implications for infant's survival and future health interventions[26]. 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 the multiplication 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 elements[28].

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 thereafter[29].

Lactoperoxidase: Recently Langbakk and Flatmark were able to show that lactoperoxidase is present in human CLM[30]. The specific assays performed on CLM and human milk reveals the presence of γ-glutamyl transferase[31], acid phosphatase, alkaline phosphotase[32], lactic and malic dehydrogenase[33], N-acetyl-α-hexosamidase[34], ribonuclease[35] and xanthine oxidase[36]. 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 *in-vitro*. The

molecular weight of inhibitor found in the CLM is 6000-10000 and is heat and acid stable[37].

Vitamin binding protein: Cobalamin (Vitamin B_{12}) for its absorption requires binding protein called cobalamin binding protein (CblBP). The concentration of CblBP is considerably higher in CLM than in mature milk[38].

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 globulin[39].

Glycoprotein: Glycoprotein from human CLM has been isolated by the researchers[40]. 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 CLM[41]. 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 biotin[42].

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 respectively[43]. Human CLM contain β-carotene[44]. The concentration of carotenoids in CLM is eight times more than the mature milk[10].

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 mother[45].

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 lactation[46].

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 sphingomyelin[47]. 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 respectively[48]. The ratio of zinc to copper was found to be 13 in human CLM[49]. 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/L[50]. Human CLM contains high concentration of sodium than mature milk[10].

Cholesterol: Human CLM and mature milk contain >0.26mmol/L of cholesterol[51].

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 (Table 1) and decreases by nearly 80% over the next three months[52].

Table 1: Sialic acid concentration in human CLM

Type of sialic acid	Concentration (mmol/l)
Oligosaccharide bond	3.72±0.15
Protein bound	1.18±0.09
Free	0.14±0.01
Total Sialic acid	5.04±0.21

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 neonates[53]. 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 immunoglobulins[55]. Human CLM has inherent positive anti-infective properties due to the presence of cellular components.

CLM is rich in cells[56] ~3-8x10 cells/ml. The macrophages, neutrophils, T and B-lymphocytes and epithelial cells have been reported in human milk. T-cells comprise more than 50% of the lymphocyte of CLM[57].

Others: Human CLM also contains lysozyme[58] and corticosteroids[59].

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 antibiotics[5]. 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 muscles[60]. 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 later[61]. It is rich in lipids, mineral salts, vitamins and immunoglobulins[1].

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 jaundice[62].

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 viruses[62].

Anti-diarrheal 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 CLM[63].

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 processes[18]. Researchers now believe that CLM may be the jump start; one needs to fight infection or immune related chronic diseases such as cancer, AIDS etc[64]. 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 CLM[65]. 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 disorders[7].

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 CLM[66]**.** Healing of tissues damaged by ulcer, trauma burns and surgery can be facilitated using the growth factors present in CLM[67].

Anti-allergic action

Praline rich polypeptide (PRP) present in colostrum 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 gravis[67].

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 health[63].

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 burnout[66]. 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

complications[68]. 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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