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HEALTH BENEFITS OF FERMENTED COLOSTRUM - A REVIEW

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Abstract

Colostrum is the secretion produced by the mammary gland following parturition and transfers the passive immunity gained by the mother to the baby. Colostrum is a mixture of carbohydrates, proteins, growth factors, blood cells and immunoglobulins. Recent studies suggest that in order to improve the biological function of colostrum it is fermented with kefir grains enhanced with selected yeasts, for the development of new nutraceutical and cosmeceutical products. The symbiotic consortia of microorganism produces bioactive peptides with effects against microbial pathogens, cholesterol-lowering capacity and blood pressure-lowering effects, mainly due to inhibition of angiotensin converting enzyme (ACE), antithrombotic and antioxidant activities, opioid, cyto- and immuno-modulatory effects. The present article is a review of the current understanding of the colostrum composition and how it can be improved to an exceptionally safe and useful nutraceutical product.

Key words*: colostrum, milk, kefir, composition, immnunoglobulin.*

INTRODUCTION

In recent years, functional foods have an important role in the development of the food industry (Conte & Scarantino, 2013). The list of functional foods is constantly growing, and colostrum is also gaining popularity due to its benefits (Dzik et al., 2017).

Colostrum is breast milk secreted in the first 48 hours after birth and has a different composition than mature milk.

During breastfeeding, the composition of the breast secretion changes continuously (Ahmadi et al., 2016). Colostrum has the consistency of a dense, viscous, sticky liquid and usually has a color that can vary from yellow to orange (Shrinivas et al., 2010). It is extremely rich in nutrients, such as proteins, fat, lactose, vitamins and minerals and, in addition, it plays a fundamental protection role having an antimicrobial effect, due to immunoglobulins, lactoferrin, lacto- peroxidase, lysozyme and cytokines (Korhonen et al., 2012; Ayar et al., 2016).

Colostrum proteins offer a much lower lactose intolerance than milk, being considered safe and good for consumers healths (Bagwe et al., 2015). Newborns have a very small and immature gastrointestinal system and colostrum provides naturally produced nutrients in a highly concentrated low-volume form. Immunoglobulin A (Ig A) or antibodies present in colostrum not only provide protection to newborns against infectious diseases, but also provide passive immunity and good gastrointestinal development (Shrinivas et al., 2010; Gaspar-Pintiliescu et al., 2019).

Colostrum should not be processed at high temperatures, as its biological activity decreases. It is preferred to dose colostrum in a highly concentrated solid form. It has a short shelf life so the addition of preservatives is a necessity for its storage. (Bagwe et al., 2015)

Many studies have showed the value of colostrum as an agent that provides protection to the newborn against the new environment (Shrinivas et al., 2010).

In the present study we intend to review the main benefits of the colostrum and also, to support with data reports that the biological functions of bovine colostrum can be improved by fermentation and that the functional qualities of the resulted fermented products are important for developing new nutraceutical and cosmeceutical products.

COLOSTRUM COMPOSITION

Recent studies show that colostrum contains over 90 useful components, grouped in three main classes: immune factors, nutritional factors and growth factors: some of such factors are presented in Figure 1 (Shrinivas et al., 2010; Godhia et al., 2013).

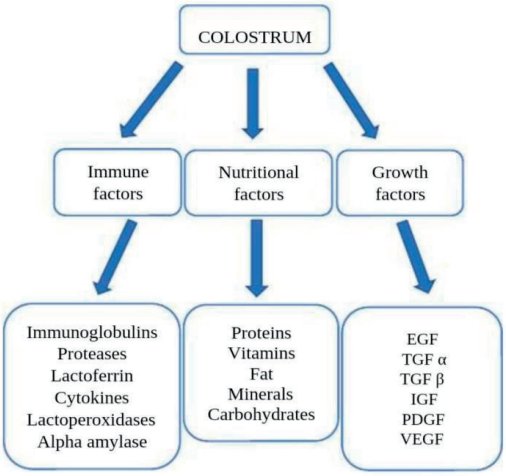

Figure 1. Main immune, nutritional and growth factors in colostrum (EGF: Epidermal growth factor, TGF α: Transforming growth factor, TGF β: Transforming growth factor, IGF: Insulin like growth factor, PDGF: Platelet derived growth factor, VEGF: Vascular endothelial growth factor – according to L.E. Hernandez- (Castellano et al., 2018)

Immune factors

Immunoglobulins are responsible for building the immunity in animals and humans (Bagwe et al., 2015). The immunoglobulins present in bovine colostrum are IgG1, IgG2, IgA, IgM and lactoferrin (Table 1).

Table 1. Immunoglobulins present in bovine colostrum (Bagwe et al., 2015)

Immunoglobulin	mg/mL
IgG1	35.0
IgG2	16.0
IgA	1.7
IgM	4.3
Lactoferrin	0.8

Colostrum is produced in the mammary gland primarily during the last three weeks of pregnancy.

IgG1 immunoglobulins are passively transferred to the mammary gland, and IgG2 immunoglobulins are selectively transferred, resulting in a much higher concentration in colostrum than in serum. The highest concentration of IgG1 in colostrum occurs a few days before calving and then becomes lower, mainly due to an increasing amount of colostrum in the mammary gland (Korhonen et al., 2000).

There is an important group of proteins in terms of the bacteriostatic properties of colostrum and which consist of non-specific antibiotic agents: lysozyme and lactoferrin.

Lysozyme is a cationic protein. Its activity increases in the presence of immunoglobulins (Ganz, 2006).

Lactoferrin it is a glycoprotein present at a concentration of 77g/L in human colostrum. Lactoferrin binds iron, makes it unavailable of *E. coli* in the gut and inhibits bacterial growth (Puppel et al., 2019).

Growth factors

Colostrum contains many hormones like prolactin, oxytocin, somatostatin luteinizing hormone, thyroid stimulating hormone, thyroxine, calcitonin, releasing hormone, progesterone and estrogen. These growth factors are able to stimulate the growth of the intestine and the repair process of the gastrointestinal tract (Godhia et al., 2013).

Epidermal growth factor (EGF) is a 53–amino acid peptide which stimulates the proliferation of different types of cells, fibroblasts and epithelial cells. EGF is present in human colostrum (200 mg/L) and milk (30-50 mg/L) and in many other species but is not found in significant amounts in bovine secretions (Playford et al., 2000).

Transforming growth factor (TGF-α) is present in human colostrum and milk at much lower concentrations than EGF. Instead, TGF-α is produced in the mucosa throughout the gastrointestinal tract.

Therefore, TGF-α may play an additional role to that of TGF-β in controlling intestinal epithelial proliferation and balance (Hoeflich et al., 2017)

Insulin-like growth factors (IGF) IGF-I and IGF-II are polypeptides with a molecular mass of 7.5 kDa (Bączyk et al., 2019).
Platelet-derived growth factor (PDGF) is a suitable mitogen for fibroblasts and arterial smooth muscle cells and administration of exogenous (Hoeflich et al., 2017).
Vascular endothelial growth factor (VEGF) glycoprotein that, induces vascular permeability and promotes monocyte migration (Vuorela et al., 2000).

Nutritional factors

Colostrum contains vitamins that are fat-soluble (retinol, tocopherol, beta-carotene, cholecalciferon, phylloquinone) and water-soluble (niacin, thiamin, riboflavin, vitamin B12, pyridoxal, pyridoxamine, pyridoxine) as it can be seen in Table 2 (McGrath et al., 2016).
The concentrations of riboflavin and retinol higher in colostrum (Calderón et al., 2007).

Table 2. Constituents of water-soluble and fat-soluble vitamins in bovine colostrum (McGrath et al., 2016)

Constituents	Bovine colostrum µg/mL
Water-soluble vitamins	
Niacin	0.34
Thiamine	0.90
Riboflavin	4.55
Vitamin B_{12}	0.60
Pyridoxal	0.15
Pyridoxamine	0.21
Pyridoxine	0.04
Fat-soluble vitamins	
Retinol (Vitamin A)	4.9
Tocopherol (Vitamin E)	2.9
Beta-carotene	0.7
Cholecalciferon (Vitamin D)	0.0305
Phylloquinone (Vitamin K_1)	4.9(µg/L)

Vitamins E and C have an antioxidant effect and help stabilize membranes (macrophages, granulocytes and lymphocytes).
Vitamins A, D and E have a significant role, and their deficiency can have an effect on lowering immunity (McGrath et al., 2016).

Minerals

Colostrum contains 10 times more minerals (except potassium) than milk. The bitter taste of colostrum is given by the mineral content. The amount of minerals in colostrum is shown in Table 3 (Tsioulpas et al., 2007).

Table 3. The content of minerals (%) in colostrum (Tsioulpas et al., 2007)

Minerals	Testing time	
	Calving time	After 11 days
Calcium	0.256	0.130
Magnesium	0.037	0.011
Potassium	0.137	0.153
Sodium Chloride	0.074	0.036
Phosphorus	0.235	0.113
Chloride	0.118	-

The biological and nutritional value of colostrum decreases over the time (Table 4). Colostrum loses its ability to absorb immunoglobulins after the first 6 hours after birth, and after two days an intestinal barrier will appear (Puppel et al., 2019).

Table 4. The composition of colostrum and milk at different hours after calving (Puppel et al., 2019)

Colostrum (h)	Protein %	Casein %	Fat %	Lactose %
0	16.8	4.1	6.7	2.9
6	11.7	3.5	6.1	3.5
12	6.3	3.1	4.4	3.9
24	5.5	2.9	4.1	4.1
48	4.8	2.8	3.9	4.2
Milk	3.2	2.6	3.8	4.6

ADVANTAGES OF COLOSTRUM INTAKE

Colostrum has many therapeutic applications in general health status of consumers. Also, it stimulates the properties of the immune system and contains hormones, growth factors and other bioactive components.
Due to its complex composition, it can be used in combating various diseases (Shrinivas et al., 2010).

Nutritional benefits

As colostrum contains high concentration of carbohydrates, proteins and fats, it delivers its nutrients in very concentrated low volume form (Shrinivas et al., 2010).

Near about twenty times more protein is present in colostrum as compared to the milk produced later (Starton, 2005).

Bioactive compounds in colostrum improve the balance of the intestinal flora, the immune system and tissue regeneration. Autoimmune and cardiovascular diseases are also diseases that can be ameliorated by colostrum (Bagwe et al., 2015).

Colostrum is also rich in polypeptides containing proline, which combat inflammatory response mechanisms. These peptides influence the production of cytokines, the main components of inflammation and inhibit the production of reactive oxygen species, which also cause inflammation (Janusz et al., 2010).

Immune systems benefits

Breastfeeding lays the foundations for good health for all children. One of the greatest significance of colostrum is the fight of the autoimmune diseases and the development of the digestive system. The property of increasing immunity is attributed to molecules called transfer factors.

Some studies (Davison, 2012) showed that colostrum intake can activates the immune system and antimicrobial factors, stimulating the immune functions.

As immune modulator, colostrum can be an important factor in autoimmune diseases (like rheumatoid arthritis) (Godhia et al., 2013).

Wong et al. (2014) demonstrated that a diet supplemented with colostrum improve the immune response to influenza virus. They concluded that bovine colostrum is an important immunomodulator that promotes a good immune response to some infections and that can be used as a therapeutic factor for enhancing immunity, especially in at-risk people.

MICROORGANISMS USED IN THE COLOSTRUM FERMENTATION

Colostrum is an under-used food in the dairy industry (Cotârleț et al., 2020). In order to enhance the benefits of colostrum, it has been fermented with artisanal kefir grains and selected yeasts. The cultures of bacteria and yeasts that act in symbiosis have a greater impact on the health of the consumer (Windayani et al., 2019; Cotârleț et al., 2019)

Kefir it is an old fermented milk product, with a sour taste and refreshing aroma. In Europe and the area of Caucasus Mountains of Russia, is still consumed for its nutritive and functional properties (Cotârleț et al., 2019; Shi et al., 2018).

The kefir grains used for obtaining fermented milk products (known as artisanal cultures grains) represent a complex of proteins, polysaccharides and beneficial microorganisms (lactic acid bacteria, acetic bacteria and yeasts) associated in a natural consortium (Dallas et al., 2016).

The fermentation of colostrum with kefir grains represents a suitable approach to improve the functionality of the obtained product in accordance with the metabolic activity of multiple cultures (bacteria and yeasts) which act in symbiosis. Fermentation also improves the preservation of colostrum, due to the fact that it is very sensitive to microbial contamination and also to heating lability due to the high protein content. (Windayani et al., 2019). During the colostrum fermentation with various microorganism consortia, some bio-peptides (with molecular mass between 1 and 50 KDa) are formed. Bioactive peptides are fragments of protein that bring health to the human body (Shimizu et al., 2007).

These peptides were separated (by ultrafiltration or ultracentrifugation) and tested for their activity *in vitro* (Gaspar-Pintiliescu et al., 2019). Another microorganisms consortia used for colostrum fermentation (in order to enlarge the assortment of dairy fermented products) is a symbiotic association of yeasts and acetic acid bacteria known as “kombucha” (Oancea et al., 2019). It was demonstrated that a symbiosis between microorganisms from kombucha and kefir enhances kombucha fermentation potential, which represents a valuable source of peptides with improved biological activities (Cotârleț et al., 2019; Malbaša et al., 2009; Yang et al., 2008).

HEALTH BENEFITS OF FERMENTED COLOSTRUM AND DERIVED BIOPEPTIDES

A pilot reproducible technology has been developed for bovine colostrum fermentation with symbiotic consortia of microorganism (kefir grains and *Candida lipolytica* selected strain) (Figure 2) (Cotârleț et al., 2019; Cotârleț et al., 2020). By this technology it was obtained a multifunctional, tribiotic product, which includes pre-biotic (bio-peptides with antioxidant effect and polysaccharides from kefiran), pro-biotic (lactobacilli and yeast from kefir grains) and post-biotic (short-chain fatty acids produced by microbial strains and bioactive peptides) (Ricci-Cabello et al., 2012; Cotâleț et al., 2020).

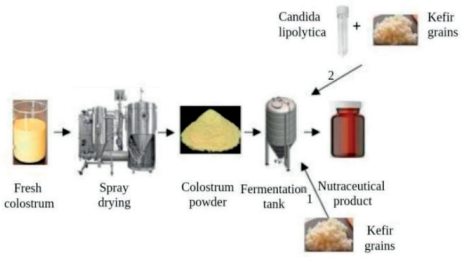

Figure 2. Nutraceutical product obtained by colostrum fermentation technology (Oancea et al., 2019)

Dairy bioactive peptides demonstrated microbicide effects against microbial pathogens, cholesterol lowering ability, and blood pressure lowering effects, mainly due to angiotensin conversion enzyme (ACE) inhibition, antithrombotic and antioxidant activities, opioid, cyto- and immuno-modulatory effects (Mohanty et al., 2016), which recommend them as potential nutraceuticals or therapeutic products for health supporting.

There are reported different benefits of colostrum derived – bioactive peptides on functional or metabolic sides (Figure 3).

Korhonen (2009) studied the effect of various dietary peptides on human health by reducing the risk of chronic diseases, but also by immunizing the immune system. This effect is based on the composition of the peptides and the amino acid sequence. The length of bioactive peptides is generally 2-20 amino acid residues and some peptides may have multifunctional properties (Hartmann et al., 2007).

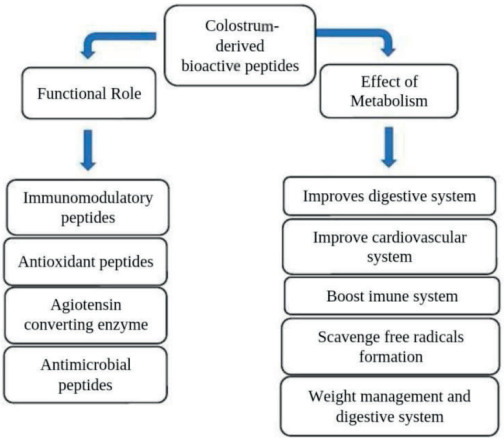

Figure 3. Benefits of colostrum - derived bioactive peptides (Punia et al., 2020)

Colostrum - derived bioactive peptides with antihypertensive effects

Angiotensin converting enzyme (ACE) is a enzyme that controls the arterial blood pressure and electrolyte balance by converting angiotensin I to the vasoconstrictor angiotensin II (Vardanyan el al., 2016). The use of the synthetic drugs for prevention of hypertension may cause serious side effects, such as cough, skin rashes, nausea, vomiting and dizziness (Lin et al., 2012). This has led researchers to search for other, more secure, innovative and cheaper ACE inhibitors (Wijesekara et al., 2011). Food-derived peptides with antihypertensive properties targeting ACE could reduce the risk associated with cardiovascular diseases (Gaspar-Pintiliescu et al., 2019). An important therapeutic strategy is the synthesis and isolation of these biopeptides from various natural sources (Shori et al., 2015). For example, some studies reported a significant variation in the ACE inhibitory activity of peptides derived from kefir-fermented +milk from human, bovine, ovine, buffalo or rat species. A randomized clinical trial recently reported a decrease in blood pressure in prehypertensive adults treated with fermented goat's milk for 8 weeks (Lu et al. 2018).

CONCLUSIONS AND PERSPECTIVES

Colostrum is a safe and useful nutraceutical product for use in a wide range of applications. Colostrum appears to have great potential on human health and this should inspire

researchers to conduct further studies on colostrum fermentation with different consortia in order to analyse the hidden therapeutic and functional properties that have not been revealed to date.

All the data presented in the present work demonstrated that fermented colostrum represents a valuable source of peptides with improved biological activities, compared to those obtained from unfermented (control) colostrum.

Specific bioactivity and functionality of isolated peptides make them suitable as ingredients in functional foods and nutraceuticals and will be further studied.

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ENVIRONMENTAL BIOTECHNOLOGY