

**This is an electronic reprint of the
original article (publisher's pdf).**

Please cite the original article:

Fasse, S., Alarinta, J., Frahm, B., & Wirtanen, G. (2021). Bovine colostrum for human consumption – Improving microbial quality and maintaining bioactive characteristics through processing. *Dairy* 4(2), 556–575. <https://doi.org/10.3390/dairy2040044>



Review

Bovine Colostrum for Human Consumption—Improving Microbial Quality and Maintaining Bioactive Characteristics through Processing

Sylvia Fasse ^{1,2} , Jarmo Alarinta ¹, Björn Frahm ²  and Gun Wirtanen ^{1,*} 

¹ School of Food and Agriculture, Seinäjoki University of Applied Sciences, P.O. Box 412, FI-60101 Seinäjoki, Finland; sfasse@hs-bremerhaven.de (S.F.); jarmo.alarinta@seamk.fi (J.A.)

² Biotechnology and Bioprocess Engineering, Ostwestfalen-Lippe University of Applied Sciences and Arts, Campusallee 12, DE-32657 Lemgo, Germany; bjoern.frahm@th-owl.de

* Correspondence: gun.wirtanen@seamk.fi; Tel.: +358-40-830-0334

Abstract: The main purpose of bovine colostrum, being the milk secreted by a cow after giving birth, is to transfer passive immunity to the calf. The calves have an immature immune system as they lack immunoglobulins (Igs). Subsequently, the supply of good quality bovine colostrum is required. The quality of colostrum is classified by low bacterial counts and adequate Ig concentrations. Bacterial contamination can contain a variety of human pathogens or high counts of spoilage bacteria, which has become more challenging with the emerging use of bovine colostrum as food and food supplements. There is also a growing risk for the spread of zoonotic diseases originating from bovines. For this reason, processing based on heat treatment or other feasible techniques is required. This review provides an overview of literature on the microbial quality of bovine colostrum and processing methods to improve its microbial quality and keep its nutritional values as food. The highlights of this review are as follows: high quality colostrum is a valuable raw material in food products and supplements; the microbial safety of bovine colostrum is increased using an appropriate processing-suitable effective heat treatment which does not destroy the high nutrition value of colostrum; the heat treatment processes are cost-effective compared to other methods; and heat treatment can be performed in both small- and large-scale production.

Keywords: bovine colostrum; bacteria; pathogens; probiotic bacteria; cost-effective processing; heat treatment; pasteurization; contamination control; immunoglobulins; enzymes



Citation: Fasse, S.; Alarinta, J.; Frahm, B.; Wirtanen, G. Bovine Colostrum for Human Consumption—Improving Microbial Quality and Maintaining Bioactive Characteristics through Processing. *Dairy* **2021**, *2*, 556–575. <https://doi.org/10.3390/dairy2040044>

Received: 6 July 2021

Accepted: 30 September 2021

Published: 10 October 2021

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Background on Bovine Colostrum, Contaminants, and Processing

Bovine colostrum is the first milk given by a cow after parturition as nutrition to the newborn calf. This liquid is essential for the conferring of passive immunity to the newborn calves. The newborn calves lack immunization at birth and require the uptake of immunoglobulins (Igs) within 24–36 h after birth. Initial milk is considered bovine colostrum up to 3 days postpartum. Specifically, an elevated concentration of immunoglobulin G (IgG) is characteristic for bovine colostrum, as it is of significance in the transfer of passive immunity [1]. Besides these Igs there are other immune components present, e.g., enzymes or lactoferrin (LF), which act as nonspecific antibacterial factors [2]. Furthermore, healthy cows produce colostrum in excess of the calf's need, which means that the ethical aspects for calves are not impacted [3]. Therefore, there is an increasing interest for the human use of bovine colostrum as a nutraceutical food [4]. Several human studies provide information on treatment or prevention effectiveness in bone development, respiratory, inflammatory, and gastrointestinal diseases, e.g., inflammatory bowel syndrome and *Escherichia coli* induced diarrhea [5–7]. Additionally, improvements in athletes' performances have been confirmed [8].

1.1. Contamination

The microbiology in raw colostrum is expected to be highly diverse. There are risks for the growth of both spoilage and pathogenic bacteria. Therefore, the consumption of raw contaminated colostrum may lead to illnesses in the calves due to spoiled nutrition and to intoxication or infections of *Staphylococcus* spp., *Bacillus* spp., or *Salmonella* spp., etc. in humans [9,10]. Especially well described is the occurrence of infectious bovine diseases, e.g., mastitis. When the calves do not get enough good quality colostrum, the calves can develop microbial diseases due to inadequate passive immunity [11–13]. Specific microbes, e.g., *Mycoplasma bovis* or *Staphylococcus aureus*, in the colostrum provoke the mastitis [14].

The microbes in bovine colostrum have been reported in several papers and they mainly belong to the phyla Firmicutes, Proteobacteria, Bacteroides, and Actinobacteria [14–16]. The harvesting procedure of bovine colostrum is a critical control point, when the occurrence of contamination is to be reduced [15,17].

1.2. Processing

Raw dairy products such as bovine colostrum can be contaminated by several human pathogens during harvesting, which means that there is a need for treatment before consumption [18]. The processing techniques for an efficient inactivation of pathogenic/spoilage bacteria must be applied to obtain health promoting colostrum of good quality. The regulations for marketing dairy products require heat treatment or an equivalently effective treatment to improve the shelf life before selling the product [19]. The design of a heat treatment process for bovine colostrum will be introduced in this review. However, besides a mandatory efficient reduction of the bacterial count, the beneficial constituents in colostrum have to be preserved, not diminished, through the processing. Bioactive components, e.g., Igs, with nutraceutical value for humans are degrading through the high temperature heat treatment of the colostrum [4,20], which means that other feasible methods for the bacterial reduction are of interest to the industry. This review article focuses on specific nutritional values, microbial characteristics, and the basic heat treatment of bovine colostrum to improve its microbial quality and use for human consumption. Examples of food products manufactured from colostrum are given in the chapter “Products of Bovine Colostrum”.

2. Bioactive Components in Colostrum

2.1. Bioactive Compounds

The bioactive compounds in bovine colostrum play a key role in its high nutritional value for human consumers. The list of components with immunomodulatory capabilities comprises direct and indirect powerful mechanisms as well as the adaption of the host's immune response [21,22]. The worldwide market of colostrum has continuously increased between 2014 and 2020 with an estimated value of \$3.046 billion US and it is expected that the market will increase further [23,24]. Predictions indicate an increase by 6.4% per year between 2020 and 2030 on the global market, which can be explained by a rising request for health promoting foods, linked to emerging illnesses and health risks due to improper nutrition [24].

Colostrum and milk contain a variety of nutritious components with chemical/functional activities. The list of these bioactive compounds consists of carbohydrates, proteins, growth factors, cytokines, lipids, enzymes, vitamins, and minerals [22]. Bioactive compounds are molecules needing activation through chemical reactions to perform specific functions. The bioactive components in bovine colostrum (Figure 1) promote health [2,25].

The amount of bioactive compounds in bovine colostrum is significantly higher than in milk [1]. This is proven by an elevated protein concentration, which is 15.9 g/100 g within 24 h postpartum and 3.3 g/100 g after 5 months [26]. Approximately 70–80% of this total protein content in colostrum are Igs, prevalent in concentrations of 30–200 g/L. The Ig concentration declines soon after parturition, being considerably lower in milk with 0.4–1 g/L [1,5]. The subcategory IgG1 accounts for 75% of the antibody content in colostrum, followed by IgM, IgA, and IgG2 [27]. Morrill et al. [11] report that the average

Dairy 2021, 2, x FOR PEER REVIEW IgG concentration is dependent on the number of parities of the cow, in addition to the duration of dry period and breed of the cow [28,29].

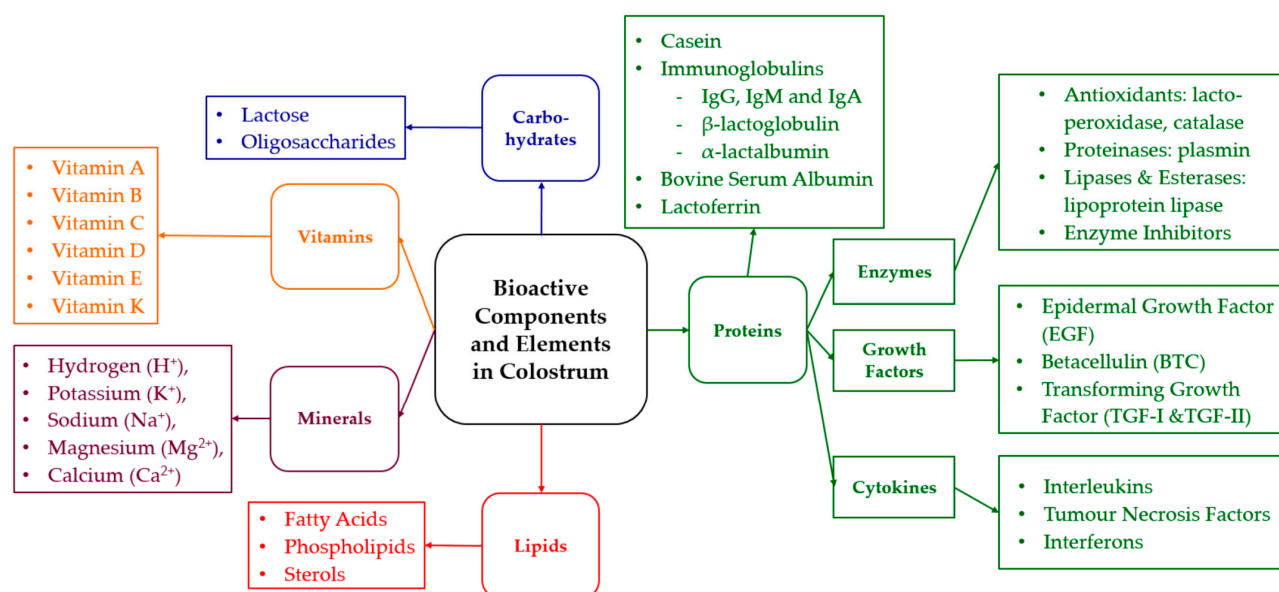


Figure 1. Overview of bioactive components and elements in bovine colostrum based on McGrath et al. [1] and Korhonen [2,25]. The various colors are differentiating groups of constituents: green is used for proteins, blue for carbohydrates, orange for vitamins, lilac for minerals, and red for lipids.

The amount of bioactive compounds in bovine colostrum is significantly higher than in milk [1]. This is proved by an elevated protein concentration, which is 13.9 g/100 g within the postpartum and 0.3 g/100 g after 3 months [26]. Approximately 70% of the tract infections and diarrhea [30,31]. The consumption of bovine colostrum can also lead to changes in the respiratory microbiome, which was shown by nasal swab samples [31].

2.2. Immunoglobulins

Bovine colostrum is dependent on a variety of different parities of the cow, in addition to the duration of dry period [28,29]. The subcategories according to their mode of presence, i.e., monomeric as IgG and IgA, dimeric as IgM, and pentameric as IgG, while the antimicrobial effects are initiated by IgG [2,7,32]. The general operating mechanisms of IgG comprise the prevention of microbes' surface adhesion, inhibition of the bacterial metabolism, agglutination of bacteria, and neutralising toxins and viruses. These mechanisms are performed by IgM antibodies in high efficiency. IgG, which is present in the highest amounts, has versatile functioning mechanisms. It can activate complement-mediated bacteriolytic reactions or induce opsonization by the amplification of the phagocytosis of bacteria by leucocytes. It has additionally been reported that bovine colostrum IgG can retain biological functionality with human digestion. After colostrum consumption, immunological activity in the ileum effluents of adults was discovered [27,33]. Therefore, the ingesting of these colostrum derived IgG can prevent both respiratory and gastrointestinal infections, and is enhanced through improved barrier integrity. By the prevention of respiratory infections, the development of allergies such as allergic asthma can be prevented [34,35].

2.3. Enzymes

According to Fox and Kelly [36,37], about 70 indigenous enzymes have been identified in bovine milk. Both ribonucleases and lysozyme (EC 3.2.1.17) (LZM) are present in higher concentrations in colostrum than in milk. The am extensively elevated concentration of enzymes in the early postpartum periods [1,37,38]. Enzymes have several purposes, e.g., the respiratory and gastrointestinal tract to fulfill their microbial activity in the digestive system or catalyzes other important reactions [2,39].

The LZM plays an undoubtable substantial role in the body's immune system. It provokes bacteriolysis and opsonization having a general higher immune response as well as antiviral and antineoplastic activities [40]. This bacteriostatic effect inhibits the growth of bacteria and shows indirect bactericidal effects potentially effective against udder pathogens [38]. The LZM is effective through exhibiting lytic properties or by complementing the bactericidal action of antibodies [40]. Lie et al. [40] reported LZM activity in colostrum of 0.28 µg/mL on average, which is higher than in milk [39]. The peptidoglycan layer in the bacterial cell walls functions as the substrate for LZM. LZM hydrolyzes the β (1→4)-bond between muramic acid and N-acetylglucosamine in the cell wall [37], which leads to the lysis of bacterial cells [38]. As an example, LZM is effective against *E. coli* and *Pseudomonas aeruginosa* [41].

2.4. Lactoperoxidase

Lactoperoxidase [EC 1.11.1.7] (LPO) is the most common enzyme in milk and one of the major antimicrobial agents in colostrum [38,42]. It was the first enzyme identified in milk in 1881 [36]. It has a broad substrate specificity [42]. The bactericidal mechanism of LPO requires the presence of low levels of hydrogen peroxide and thiocyanate anions. Antimicrobial active short-lived oxidation products, e.g., hypothiocyanites are generated this way. This inhibits the bacterial metabolism based on oxidizing essential sulfhydryl groups in proteins [38]. LPO is relatively heat-resistant and effective against different microbes [42].

The enzyme is produced in the mammary gland [36], where the epithelial cell's gene is expressed encoding for LPO. It also protects the gland from infections, e.g., those caused by pathogenic *Streptococcus* spp., *Listeria monocytogenes*, or *P. aeruginosa* [38]. Meanwhile, LZM makes up 1.25–2.5% of the LPO activity [39]. Korhonen [39] reported an average LPO activity of 37.8 µg/mL. Neither LPO nor LZM accumulates during the dry period. These agents are produced after calving [39].

2.5. Non-Enzymatic Bioactive Components

Lactoferrin (LF), being an iron-binding glycoprotein, is categorized as a multifunctional compound [42]. Both LF and transferrin make iron unavailable for bacteria and prevent bacterial multiplication [43]. LF is also reported to have proteolytic enzymatic activities [44]. LF inhibits the growth of both *E. coli* and *L. monocytogenes*. The mechanism presumably relies on the iron-binding capacity depriving the bacteria of their access to essential iron. The presence of LF enhances the antimicrobial effects of LZM [38]. It also exhibits synergistic effects in combination with LPO and Igs [45].

Both LF and LPO are produced in the mammary gland [39]. The biological activities of LF comprise antimicrobial, anti-oxidative, anti-inflammatory, and anti-carcinogenic as well as immune response properties [42]. It is known to play a key role in the body's inert immune response and simultaneously to increase the susceptibility of bacteria to certain antibiotics, e.g., vancomycin, penicillin, and cephalosporin [25]. Due to the beneficial health effects, bovine LF is gaining attention for being used in functional foods [42]. Bovine LF has also inhibited the growth of lung cancer cells in transgenic mice. Therefore, it could be applied as a therapeutic agent against tumorigenesis by suppressing the inflammation of lung cells [46]. In a study by Kehoe et al. [47], the analysis of 55 colostrum samples revealed an average concentration of LF of 0.82 g/L. In comparison to milk with 0.1 g/L, the concentration of LF is considerably higher in colostrum [45].

Another protein-based ingredient of bovine colostrum is casein, which occurs in higher concentrations postpartum and then decreases to values observed in milk [1,48]. Initially, casein in colostrum is reported to be 9.24%, while it is 2.5–2.8% in milk [49]. Caseins are essential in the digestion of important micronutrients. The formation of micellar structures around minerals or trace elements lead to a better uptake rate within the digestive tract [50,51]. Casein-derived bioactive peptides, which exert anti-oxidative, immunomodulatory activity and cytomodulatory effects, are generated through enzymatic hydrolysis, fermentation, or gastrointestinal digestion [52].

Isaacs [53] described that milk lipids exhibit antimicrobial properties during digestion. Fatty acids such as palmitic (C16) and myristic acid (C14) are the most abundant fatty acids occurring in higher quantities [1,54]. They provide antimicrobial activity released by lipases in the gastrointestinal tract of humans [53]. Microbial bindings to the gastrointestinal tract can be prevented through the attachment of lipids on the bacterial receptors [55]. The summary of these fundamental bioactive components and elements occurring in bovine colostrum is given in Figure 1. The cell types observed in bovine colostrum can synthesize macrophages, monocytes, and T and B lymphocytes, which are immune cells [56]. All these bioactive factors and their effect on human health is well described in several research articles [6,7,42,56].

3. Microbiological Quality of Colostrum

Bacteria in raw colostrum and milk is of vast concern. Pathogenic bacteria present in milk and milk products have been reported to account for 1–5% of bacterial foodborne disease outbreaks in humans in industrialized countries [18]. Bovine milk and colostrum serve as nutritious growth media for bacteria. The psychrotrophic bacteria contaminate milk through both lipolytic and proteolytic activities [57]. The hygiene of the calving cows is crucial, as particularly feces contain several pathogenic bacteria [16]. Furthermore, the storage conditions on the dairy farm as well as before and after processing affect the bacterial loads within the colostrum. At refrigerated temperatures, most bacterial species grow slower, and the storage can be prolonged [17].

The presence of high counts of bacteria is undesirable because they undermine the quality of raw colostrum. Bacteria can grow, digest, and harm colostrum by generating toxic agents or spoilage by-products, which possibly can prevent the beneficial effects of colostrum components [58]. Therefore, this study suggests the heat processing of bovine colostrum. In the following sections, both pathogens and spoilage bacteria as well as typical bacterial infections are described.

3.1. Regulations on Bacterial Counts

For the overall assessment of colostrum quality, the standard plate count (SPC) of raw colostrum samples is of significance. The regulations are the same as for raw bovine milk given for the SPC, the total coliform count (TCC), and stating the absence of other infectious bacteria [19]. Regulation (EC) 853/2004 states that raw milk and colostrum must have a SPC at 30 °C of $\leq 10^5$ CFU/mL [18,19,59]. Eight hundred and twenty-seven (827) samples were analyzed in a survey carried out in the USA by Morrill et al. [11], who found that 43% had a SPC $\geq 10^5$ CFU/mL and 16.9% had $>10^6$ CFU/mL. Godden et al. [60] reported an average count of 4×10^5 CFU/mL in 518 samples tested; meanwhile the study by Houser et al. [10] with 55 samples showed an average count of 10^6 CFU/mL. Half of the colostrum samples should on average be discarded based on the above mentioned regulations, because such products represent a risk when consumed [11,61]. Additionally, raw milk products in general possess a threat due to the contamination with zoonotic pathogens [18].

3.2. Bacteria Occurring in Colostrum

The major zoonotic bacterial species cause diseases in both animals and humans. These are causatives of foodborne diseases and they include *S. aureus*, *Salmonella* spp., *Campylobacter* spp., *L. monocytogenes*, *E. coli*, and *Bacillus* spp. [62,63]. Colostrum along with poor hygiene represent a potential transfer route for both bacterial infections and bacterial intoxications causing diseases [20].

Zoonotic bacteria derived from non-human origin can infect humans with a transferable disease [63]. The microbial contamination has to be monitored to prevent transfers to the human population [10]. In general, disease caused by bacteria in food can be divided into infections and intoxications. Intoxications are evoked by secretion of toxins of specific pathogens, causing food poisoning [63]. These bacterial species include *Staphylococcus*

spp. [64], *E. coli* [19], and *B. cereus* [65]. Infections, on the contrary, are induced by the ingestion of food containing living pathogenic cells [63].

S. aureus of bovine origin, a major zoonotic pathogen, can lead to a wide range of infectious diseases for humans due to its risk to develop antimicrobial resistance [63,66]. Houser et al. [10] found *S. aureus* to be present in 42% of 55 colostrum samples and Fecteau et al. [9] in 7.3% of their 234 samples. Lima et al. [14] performed the identification using a 16S rRNA analysis. Furthermore, Fecteau et al. [9], Lindner et al. [67], and Derakhshani et al. [15] have reported *Staphylococcus* spp. in colostrum. Lindner et al. [67] also reported *S. chromogenes* and *S. pseudintermedius* in colostrum.

Salmonella strains are involved in foodborne outbreaks [63,68] through diverse virulence factors, which cause infections in several host species [69]. Houser et al. [10] discovered the presence of *Salmonella* spp. using a PCR assessment in 15% of 55 raw bovine colostrum samples. The emerging risk of multidrug resistant *Salmonella* strains of bovine origin makes it a threat to human health [68].

L. monocytogenes is a Gram-positive bacterium, which causes the illness listeriosis and seriously affects various human groups with reduced resistance. The fatality rate is reported to be as high as 30%. The presence of *L. monocytogenes* in bovine colostrum has been described. A study in Japan revealed the contamination with *L. monocytogenes* in 7.6% of 210 samples [70].

E. coli strains in bovine colostrum are highly variable and can also be environmental bacteria. Only a few strains cause infections, while others are not pathogenic [66]. According to Fecteau et al. [9], the *E. coli* count exceeded 1000 CFU/mL in 3.8% of the 234 samples.

Bacillus spp. are also considered to be an important zoonotic pathogen in milk [62]. In colostrum, Fecteau et al. [9] detected *Bacillus* spp. presence in 15.4% of 234 to be above 1000 CFU/mL. Lindner et al. [67] identified *B. circulans* in colostrum using a 16S rRNA analysis.

3.3. Bovine Pathogens

Mastitis is characterized as being the inflammation of the mammary gland parenchyma and is considered a highly prevalent infectious disease in dairy cowherds, affecting 95% of American dairy herds [14]. Infection leads to reduced milk yield and changes in milk composition. Furthermore, it shortens the productive life of affected cows [71]. Economically, mastitis is considered a significant burden for the dairy farms [14].

Mastitis causing bacteria include *Streptococcus uberis* [69], *S. agalactiae* [10], *S. dysgalactiae* [69], *Staphylococcus aureus* [72], *Corynebacterium* spp. [15], *Mycoplasma bovis* [73], *E. coli* [66], and *Trueperella pyogenes* [74]. All of the above have been reported to be present in bovine colostrum.

S. uberis is an environmental pathogen [66] and it is reported to be responsible for 20–30% of the clinical mastitis infections [69]. In a study by Fecteau et al. [9], *S. uberis* was detected in 20.5% of 234 colostrum samples. *S. uberis* is strictly an animal pathogen causing mastitis. It has not been found to be harmful to humans [66].

The total *Streptococcus* counts are also monitored, as streptococci can be both environmental and contagious. Houser et al. [10] reported the count of *Streptococcus* spp. to be above 500 CFU/mL in 71% of 55 samples. Studies by Fecteau et al. [9] and Gelsinger et al. [58] found *Streptococcus* colonies in colostrum. Humans should avoid the intake of *S. bovis* because it is associated with bacteremia, meningitis, endocarditis, and colorectal cancer [62]. Its effect is reinforced by the chronic interaction between *S. bovis* and human immune response especially in susceptible hosts [75]. Fecteau et al. [9] reported the occurrence of more than 1000 CFU/mL of *S. bovis* in 7.3% of 234 samples. Furthermore, *S. agalactiae* is known to cause several diseases in humans including gastrointestinal infections in infants, septicemia, urinary tract infections (UTIs), and mastitis in adults [66,76]. Houser et al. [10] revealed the occurrence of *S. agalactiae* in 2% of 55 colostrum samples. In contrast, *S. dysgalactiae* is

regarded as a contagious environmental *Streptococcus* strain not yet reported to be harmful to humans. Fecteau et al. [9] have reported its presence in 1.3% of the 234 colostrum samples.

Lima et al. [14] reported the presence of *Mycoplasma* spp. in bovine colostrum. *M. bovis* is a pathogen, which causes respiratory disease, mastitis, and pneumonia in cows [73]. According to Gille et al. [77], it was detected in 1.9% of 368 colostrum samples.

Fecteau et al. [9], Lima et al. [14], and Derakhshani et al. [15] have described the general occurrence of *Corynebacterium* spp. in bovine colostrum. Fecteau et al. [9] stated that *Corynebacterium* spp. was present in 13.2% of the 234 analyzed colostrum samples. *Corynebacterium bovis* is regarded as a causative agent of mastitis and is described to be a rare human pathogen [78]. As much as 67.5% of the *Corynebacterium* strains from the milk of mastitis-infected cows were identified as *C. bovis* [79].

T. pyogenes causes both bovine mastitis and other bovine diseases [74]. Fecteau et al. [9] reported *T. pyogenes* counts of >1000 CFU/mL in 0.8% of 234 colostrum samples. In humans, *T. pyogenes* can cause endocarditis. The application of antibiotics in the dairy industry facilitates the emergence of multidrug-resistant strains for all hosts [80].

Mycobacterium avium ssp. *paratuberculosis* (MAP) causes paratuberculosis in cows. Paratuberculosis is also referred to as Johne's disease and characterized as being a chronic granulomatous infection of ruminant intestines [81], presenting an economic burden for the dairy industry [82]. Both colostrum and milk act as potential transfer routes in spreading the disease among cattle. The shedding of the bacteria by infected cows mainly happens through feces, but it can also be excreted in colostrum [83]. Besides the threat for bovine health, a likely connection between MAP and Crohn's disease in humans is suspected, but not proven, to be of zoonotic risk [81,82]. In humans, MAP can also cause tuberculosis infection [62,83]. Streeter et al. [84] reported the presence of MAP in 6.4% of 126 colostrum samples, while Pithua et al. [85] discovered it in 33.7% of 205 samples.

Coliforms, a group of bacteria prevalently appearing in human and animal feces, are used as indicators for the occurrence of fecal contamination in milk products [86] and as signs of poor teat treatment or inadequate refrigeration [87]. Dos Santos et al. [88] and Derakhshani et al. [15] have confirmed the presence of Enterobacteriaceae in colostrum. Coliform bacteria, e.g., *E. coli*, can be a source of bovine mastitis infection [89]. Certain coliforms, e.g., enterohemorrhagic *E. coli*, can be pathogenic to humans and others are nonpathogenic [86]. Emerging antibiotic resistance in coliforms of veterinary origin is of special concern for humans [90].

Pseudomonas spp. are non-fermentative Gram-negative rods [9]. Their presence can lead to infection. *P. aeruginosa* has been described as being a pathogen inducing pneumonia, UTI, meningitis, and enterocolitis in humans [64]. *P. aeruginosa* has not yet been reported present in bovine colostrum, but *Pseudomonas* spp. have been found through a 16S rRNA analysis [14,15].

Acinetobacter spp. have been described to be present in colostrum. Both Lima et al. [14] and Derakhshani et al. [15] showed positive results for *Acinetobacter* spp. using a 16S rRNA analysis. Kröger et al. [91] also reported a draft genome sequence of *Acinetobacter junii* MHI21018, which was isolated from bovine colostrum. *A. junii* has been reported to cause septicemia [91]. Additional bacteria, reported to occur in raw colostrum, is summarized in Table 1.

Table 1. Harmful bacteria detected in bovine colostrum with pathogenic potential for humans, which is based on the literature given in the table.

Contaminants	Source	Pathogenic Potential in Humans
Alcaligenaceae	[15]	Wound infection, pneumonia, and sepsis [92]
<i>Brachybacterium</i> sp.	[67]	Thermotolerant spoilage bacterium [93]
<i>Cellulosimicrobium funkei</i>	[67]	Opportunistic pathogen, endocarditis [94]
<i>Cutibacterium acnes</i> (formerly <i>Propionibacterium acnes</i>)	[67]	Endocarditis [76], commensal in human skin microbiome [95]
<i>Enterococcus</i> spp.	[9]	Enterococcal infections, urinary tract infection (UTI), and endocarditis [76]
<i>Fusobacterium</i> spp.	[14]	Endocarditis, UTI, and sepsis [76]
<i>Halomonas</i> spp.	[14]	Bacteremia [96]
<i>Macrococcus caseolyticus</i>	[67]	Close relation to human pathogen staphylococci [97]
<i>Micrococcus</i> spp.	[9]	Endocarditis [76]
<i>Paenibacillus barcinonensis</i>	[67]	No data on effect on humans
<i>Paenibacillus graminis</i>	[67]	No data on effect on humans
<i>Pasteurella</i> spp.	[9]	Empyema, Tularemia, and Brazilian purpuric fever [76]
Porphyromonadaceae	[14]	Empyema and sepsis [76]
<i>Proteus</i> spp.	[9]	Endocarditis and UTI [76]
<i>Stenotrophomonas</i> spp.	[15]	Endocarditis and UTI [76]

3.4. Probiotic Bacteria

Probiotic bacteria are beneficial viable microorganisms employed both in food and drink as well as in medical health products [7,98]. They mainly consist of lactic acid bacteria (LAB), *Bifidobacterium* spp., and *Enterococcus* spp. [64]. The human intestinal microflora mainly consists of *Bacteroides* spp., *Bifidobacterium* spp., *Clostridium* spp., *Eubacterium* spp., *Peptococcus* spp., and *Peptostreptococcus* spp. among others in lower quantities [99].

Bifidobacterium spp. are commonly used as a probiotic strain due to acclaimed health benefits and overall presence in the gastrointestinal tract. There is rising interest especially towards *Bifidobacterium*, as it is a protective agent against infectious diseases. It helps to improve the immune response and to reduce symptoms of irritable bowel syndrome, ulcerative colitis, allergic diseases, and atopic dermatitis associated to immunoglobulin E [100].

Lindner et al. [67] confirmed the presence of *Lactobacillus casei* and *Bifidobacterium pseudolongum* in bovine colostrum. Evaluations of the effects of *L. casei* and *B. pseudolongum* consumption has not yet been reported, but the presence of *Bifidobacterium* spp. in the human intestinal microflora is presumably beneficial in digestion [98]. This can be explained amongst others by the production of conjugated linoleic acid (CLA) isomers, e.g., by *Lactobacillus casei* and several *Bifidobacterium* spp. CLA isomers perform important physiological properties in humans; therefore, the application of those in the dairy industry in probiotic foods or food supplements is of value [101]. More research on probiotic bacteria found in bovine colostrum is needed. These beneficial strains based on these results can be cultured and added in suitable levels to dairy products [99,102]. Lima et al. [14] reported *Bacteroides* spp. in colostrum.

According to Lima et al. [14], an endogenous enteromammary pathway is the reason for intestinal bacteria to be able to migrate to the mammary gland. This most probably facilitates the presence of gut bacteria, e.g., genus *Prevotella* and family Ruminococcaceae in colostrum. Both Ruminococcaceae and *Prevotella* spp. have been discovered in colostrum by a 16S rRNA analysis [14,15]. *Prevotella* spp. as well as Ruminococcaceae bacteria belong to the human gastrointestinal microbiota and they enable the digestion of, for example, plant polysaccharides [103].

LAB strains, which are generally regarded as safe (GRAS) organisms, inhibit coliforms and other bacterial pathogens [18,104]. Santos et al. [88] detected LAB in colostrum samples through culturing. Furthermore, Vivarelli et al. [105] showed that they have anti-carcinogenic effects.

3.5. Bacterial Effects in Colostrum

Certain bacteria can trigger diseases for both animals and humans, and some also deteriorate the product quality. The bacterial count increases rapidly when the colostrum is kept warm. A change in bacterial composition can be problematic and high bacterial counts can lead to a decrease in protein content [58,104]. Cummins et al. [106] reported a decrease in the acidity (pH) of the colostrum with high bacterial counts, especially when it was stored at warm temperatures, i.e., above 4 °C.

On the contrary, there are probiotic species, which secrete beneficial compounds, e.g., *L. casei* strains produce heteropolysaccharides, consisting of sugars and other constituents. Probiotics also synthesize exopolysaccharides or indirectly enzymes synthesizing polysaccharides, which have many health benefits for consumers. LAB also generates lactic acid through the digestion of carbohydrates. The biological activities include anticancer, antimicrobial, immunomodulatory, and anti-inflammatory activity. Probiotics as an ingredient can improve the quality of raw colostrum for human consumption [98–102].

4. Products of Bovine Colostrum

Nowadays, bovine colostrum as food is available on the market. Bovine colostrum for human consumption is collected and frozen on the individual farms and thereafter shipped frozen to processing facilities, where it is pasteurized and further treated through optional fat and lactose removal before spray- or freeze-drying to powder [7]. Available colostrum products include: (1) raw whole colostrum powder, (2) raw skim colostrum powder, and (3) industrially produced colostrum milk protein concentrate [35]. Currently, bovine colostrum is available in liquid form or as spray- or freeze-dried colostrum powder [8,107]. It has also been used as nutraceutical. Whey formulations with high concentrations of bioactive proteins and peptides are accumulating immense interest among human health specialists [108]. The powder can also be marketed as a dietary supplement in the form of sachets, capsules, or chewable tablets [7]. The fractionation of bioactive components out of bovine milk and colostrum yielding health-promoting foods is also gaining attention. This entails the fractionation of caseins or whey proteins as well as the isolation of LF, LPO, or especially bovine colostrum's Igs [45]. There are also dairy products, in which bovine colostrum is used as an additive in cheeses, butter, yogurts, kefir, fermented milk, milk powdered beverages, ice cream, jellies, nutritional bars, and ready-to-drink beverages [6,7].

5. Contamination Control On-Farm and in Processing

5.1. Contamination Risk On-Farm

The harvesting and storage of colostrum are the main factors in determining the microbiological quality during primary production [61]. Pathogenic and spoilage microorganisms can enter the colostrum directly from the udder due to contamination, the environment, workers, and contaminated equipment. Poor hygiene practices increase the risks [109,110]. Microbes may contaminate the colostrum during milking, processing, packaging, storage, and transport [111].

Bacterial counts of colostrum derived aseptically from the udder contain relatively low counts of bacteria. Thirty-nine analyzed samples gave a mean SPC of 30 CFU/mL. The harvesting process is regarded as a critical control point in colostrum production. Especially the pre-treatment of the gland and milking buckets are potential threats [17].

Transmission of bovine infections like mastitis, which is commonly caused by *S. uberis* or paratuberculosis infection by MAP, is described to occur due to the shedding of bacteria from feces [69]. Feces of infected cows may contain MAP in concentrations of $>10^8$ CFU/g [81]. Stewart et al. [17] reported the TCC to be quite low directly on the udder, with the average being 8 CFU/mL in 39 samples. The numbers vastly increase up to 50,000 CFU/mL during further storage without processing. The number of coliforms present is highly variable, ranging between a minimum of zero to a maximum of 4×10^6 CFU/mL [10].

Besides the harvesting, the storage conditions of colostrum are critical [106]. EU regulations state that colostrum must immediately be cooled below 8 °C and stored separately.

During transportation, the temperature must be kept below 10 °C [19]. Phipps et al. [61] stated that the refrigerated storage of colostrum yields lower bacterial contamination counts than storage at ambient temperatures. Cummins et al. [106] analyzed the bacterial counts in colostrum stored at different temperatures, i.e., 4, 13, and 20 °C for 72 h. Six samples were analyzed and showed the most significant increase while stored at 20 °C from the initial 10^6 CFU/mL to 8×10^8 CFU/mL, at 13 °C it reached 10^8 CFU/mL, and at 4 °C it increased to 2×10^6 CFU/mL. Therefore, colostrum should be stored at temperatures ≤ 4 °C, while the first 6 h after milking are critical [106]. Subsequently, colostrum should be cooled as soon as possible after harvest to avoid the fast accumulation of high bacterial loads, which should be monitored accordingly. Morrill et al. [11] confirmed that the counts in refrigerated samples are greater than in frozen samples.

5.2. Risks in Processing of Bovine Colostrum

The following steps affect the colostrum quality prior to and during processing: (1) cow's health status, (2) milking hygiene, (3) chilling practices and efficiency, (4) cleanliness of milking equipment including equipment design, maintenance, cleaning, and disinfection, (5) personnel hygiene, (6)–(8) chill temperatures during packaging, storage, and transportation, as well as (9) heat treatment taking into account the soiling of the heat exchanger plates during use [111,112]. Precautions taken by the dairy farmers cannot completely guarantee that the colostrum is free from harmful bacteria.

The industrial processing of bovine colostrum becomes essential with the consideration of potential pathogens being inherent in raw dairy products [18,20]. The colostrum must be treated either decentral at the dairy farm or central at a dairy processing site (Figure 2). There are several techniques utilized to improve the colostrum quality, e.g., pasteurization either batch wise or continuously with high temperature short time (HTST) or low temperature short time (LTST) pasteurization [20], microfiltration and high-pressure processing [4], and fermentation [113]. More information on the techniques can be found in this chapter.

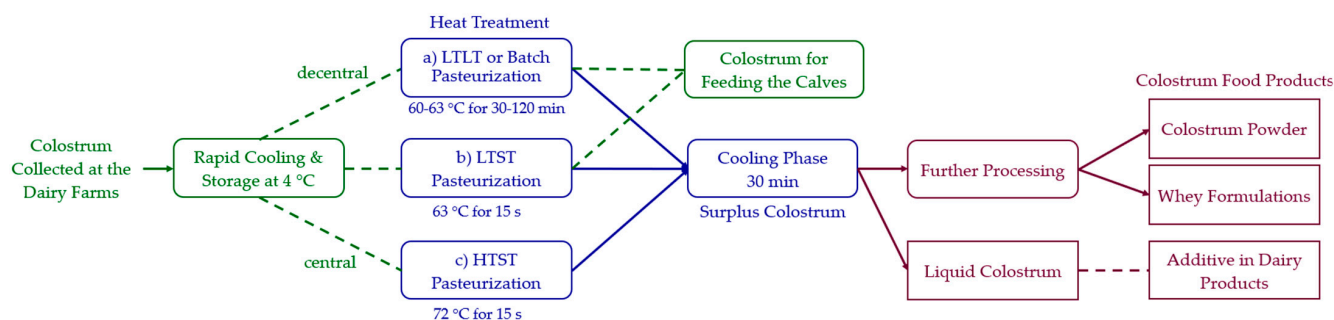


Figure 2. Feasible colostrum heat treatment procedures are either decentral on-farm or central at the dairy. The steps within the boxes display options for heat treatment of colostrum, which can be (1) pasteurized in batches in a low temperature long time (LTLT) pasteurizer (110), (2) continuous, low temperature short time (LTST) pasteurizer (2150), or (3) continuous high temperature short time (HTST) pasteurization. A pasteurization heat-treated colostrum is available for use and collected for the calf. The rest is available for use in food. The green color indicates activities on the farm except heat treatments. All heat treatment alternatives are colored in blue. Further processing of colostrum products and collection of liquid colostrum for human consumption are given in lilac.

5.3. Heat Treatment

Different industrial standards include batch pasteurization in which the colostrum is heated to 63 °C for 30 min, also called LTLT-pasteurization, and can be employed to minimize viable bacterial counts [114]. HTST pasteurization is commonly replacing the batch method. It gives similar effects but more efficiently, e.g., at 72 °C for 15 s. Pasteurization normally involves the rapid heating of liquids to inactivate bacteria. LTLT heat treatment is the most convenient treatment for farms with small amounts of colostrum [18,20,114]. The treatment options are also described with Regulation (EC) No. 853/2004, Annex II, Chapter XI for the treatment of raw colostrum or milk [109]. By the application of these heat treatment methods, the product will not be sterilized, because sterilization entails the killing of all viable bacteria. With pasteurization, most of the harmful organisms in milk will be inactivated or reduced to a secure microbial level in the product [20]. An additional process described for milk heat treatment is LTST pasteurization, in which temperatures

These treatment options are also described in Regulation (EC) No. 852/2004, Annex II, Chapter XI for the treatment of raw colostrum or milk [109]. By the application of these heat treatment methods, the product will not be sterilized, because sterilization entails the killing of all viable bacteria. With pasteurization, most of the harmful organisms in milk will be inactivated or reduced to a secure microbial level in the product [20]. An additional process described for milk heat treatment is LTST pasteurization, in which temperatures between 58–68 °C are used for 15–30 s. The lower the temperature is, the longer time is required. This processing technique focuses on the inactivation of psychrotrophic bacteria, which can release heat-resistant enzymes, e.g., protease and lipase into raw milk. Commonly, this process is followed by consequent further treatments [115].

A report by Johnson et al. [116] stated that the feeding of heat-treated colostrum led to an increased IgG absorption rate, resulting in elevated serum IgG levels. Firstly, this can be explained by the lower microbe concentration of, e.g., coliforms within the colostrum, which could bind free Igs [20,60]. This is prevented by heat inactivation, leaving free Igs. Secondly, a protein denaturation caused by heat processing results in less interference for IgG receptor sites by other proteins [20]. Godden et al. [60] discovered a higher serum IgG concentration in calves fed heat-treated colostrum (18 mg/mL) compared to those being fed fresh colostrum (15 mg/mL) by the analysis of the upbringing of 1071 newborn calves. Whether this phenomenon is also applicable in bovine colostrum digestion in humans remains to be analyzed.

Godden et al. [117] analyzed the batch heat treatment of colostrum inoculated with *M. bovis* (10^8 CFU/mL), *L. monocytogenes* (10^6 CFU/mL), *E. coli* O157:H7 (10^6 CFU/mL), *Salmonella enteritidis* (10^6 CFU/mL), and MAP (10^3 CFU/mL). After keeping the colostrum at 60 °C for 30 min, no *M. bovis*, *L. monocytogenes*, *E. coli* O157:H7, and *S. enteritidis* were detected. Treatment at 60 °C for 60 min additionally inactivated viable MAP. The volume of the batch of colostrum treated was 30 L with a commercial on-farm pasteurizing system [117]. Earlier, MAP was used as an indicator for sufficient inactivation through heat as it is a relatively heat-resistant pathogen [18]. Inactivation of MAP through pasteurization might not be complete, which depends on the initial bacterial count [81].

Further Godden et al. [60] measured SPC and TCC of heat-treated and not heat-treated colostrum samples. An average SPC of 515,000 CFU/mL and TCC of 51,500 CFU/mL was detected for untreated, fresh colostrum, while heat-treated colostrum had an average SPC of 2100 CFU/mL and a TCC of 90 CFU/mL. Heat treatment in this case comprised heating of colostrum in a commercial batch pasteurizer at 60 °C for 60 min [60].

Thermotolerant bacteria, which to varying extents survive the pasteurization, e.g., *Enterococcus* spp. and *Bacillus* spp., are of risk to reduce the shelf life of colostrum and products thereof. Particularly bacteria forming endospores, e.g., *Bacillus* spp., contaminate the colostrum after pasteurization [93]. In that case, pasteurization might not sufficiently eliminate the pathogens and other processing methods should be considered.

The HTST pasteurization can be as efficient, i.e., by keeping the liquid at a higher temperature for a shorter amount of time than in normal pasteurization. Stabel et al. [118] analyzed the inactivation of MAP inoculated colostrum by using a commercial on-farm HTST pasteurization unit. The survival of MAP and remaining IgG concentration were tested and examined at two temperatures. The viable count in colostrum decreased from 10^5 CFU/mL to 2 CFU/mL, when kept at 67 °C for 15 s with a post-pasteurization period of 30 min. At identical conditions, no viable MAP was detected directly after treatment when kept at 72 °C [118].

The bacterial inactivation can be improved, and loss of bioactive agents can be diminished through process optimization, which has been summarized in Table 2. The IgG concentration is given in most articles and therefore used as the immediate comparison value. Regarding most of the other immune components, there is less information available. For example, HTST pasteurization will lead to the inactivation of 50% of the initial LPO activity [42].

Table 2. Summary of the effects of processing methods reported as microbial inactivation or microbial inactivation rate in bovine colostrum. The inactivation rates are given based on the measured reduction as standard plate counts (SPCs) before and after treatment (in log CFU/mL). The detected loss in antibody concentration (IgG) is given in percentage (%) [4,113,117–119].

Method	Inactivation Rate (log CFU/mL)	IgG Concentration Loss (%)
Low temperature long time (LTLT) batch pasteurization, 30 min at 60 °C [117]	Inactivation of <i>Mycoplasma bovis</i> , <i>Listeria monocytogenes</i> , <i>Escherichia coli</i> O157:H7 and <i>Salmonella enteritidis</i> , but <i>Mycobacterium avium</i> ssp. <i>paratuberculosis</i> (MAP) was detected	No significant loss detected
LTLT batch pasteurization, 60 min at 60 °C [117]	Inactivation of <i>M. bovis</i> , <i>L. monocytogenes</i> , <i>E. coli</i> O157:H7, <i>S. enteritidis</i> , and in three of four batches no MAP	No significant loss detected
LTLT batch pasteurization, 120 min at 60 °C [117]	Viable <i>M. bovis</i> , <i>L. monocytogenes</i> , <i>E. coli</i> O157:H7, <i>S. enteritidis</i> , and MAP were not detected	No significant loss detected
High temperature short time (HTST) pasteurization, 15 s at 67 °C [118]	MAP 4	22
HTST pasteurization, 15 s at 72 °C [118]	Inactivation of MAP in colostrum	27
Fermentation with <i>Lactobacillus plantarum</i> LUHS135 [113,119]	3 [113]	No significant loss detected [119]
Fermentation with <i>Lactobacillus paracasei</i> LUHS244 [113,119]	3.3 [113]	22 [119]
Microfiltration (MF) and high-pressure treatment (HPP) [4]	>6	27–64

5.4. Fermentation

A biological preservation method can be the fermentation of colostrum with microorganisms that are GRAS for consumers and are commonly employed in starter cultures [113]. Bartkiene et al. [113] analyzed the effect of fermentation with *Lactobacillus plantarum* LUHS135 and *Lactobacillus paracasei* LUHS244 on the microbial contamination of colostrum in combination with ultrasonication and dehydration. Both organisms are LAB. Fermentation enables biological and gentle preservation, but on the other hand, it can provoke the formation of biogenic amines out of protein. In a current study, Bartkiene et al. [119] measured the effect of fermentation on the concentration of bioactive compounds, as IgA, IgM, and IgG. Fermentation with *L. plantarum* LUHS135 showed no significant loss in IgG concentration. Moreover, during this study, the antimicrobial activity against 15 pathogenic strains, including *P. aeruginosa* and *S. aureus*, was analyzed. The fermentation process in both studies entailed the inoculation of strain cultures and cultivation in a CO₂ incubator for 24 h at 30 °C [113,119]. Fermentation with each of both *Lactobacillus* spp. led to the inhibition of 11 out of 15 studied microorganisms [119].

5.5. Microfiltration, High-Pressure Processing, and Subsequent Processing

It is possible to reduce the bacterial counts in bovine colostrum with various physical methods. Gosch et al. [4] proposed and analyzed the combined treatment by microfiltration (MF) followed by high-pressure processing (HPP). Yet, the employment of crossflow MF includes the risk of forming a fouling layer on the filter membranes. This happens due to the micellar casein structures. Other ingredients besides bacteria are prevented to enter the permeate. Thus, the protein concentration in colostrum is altered, resulting in a loss of serum protein. Therefore, a membrane pore size of 1 µm is suggested, which does not solely lead to a sufficient bacterial reduction. For that reason, HPP at temperatures below 40 °C follows the MF to reach colostrum of quality for human consumption. This HPP was performed at 400 MPa or 500 MPa over a time of 60 s. This treatment reduced the bacterial count by more than 6 log CFU/mL. Further, combined MF with HPP (at 400 MPa) led to the loss of 27–64% of the initial IgG concentration. The comparison of bacterial reduction achieved by MF and HPP to conventional thermal heat processes with simultaneous results reveals less IgG inactivation with the new approach [4]. Another study by Borad et al. [107] described the use of MF followed by the ultrafiltration for the processing of skim colostrum and colostrum whey. Consequently, spray drying was performed with the former addition

of thermal protectants, e.g., sugars. Overall, this method resulted in colostrum powders with 88.5% of the initial Ig concentration but this was only analyzed in a pilot scale [107].

6. Process Design

6.1. Process Synthesis

Processing is described as a systematic series of actions designed to increase the value added to the food product [120]. In the process development system, the configuration of processing steps for desired and safe products is included. When determining the colostrum treatment process, attention is focused on ensuring food safety without destroying biological activity. Typical questions to be answered, when the process is developed, include: Which processing steps are required? What is the best type and size of process to use, and under which operation conditions? A minimum number of process steps is always the goal in an economically viable, efficient process. There are a number of process options, which certify the safety of heat treatment, and among these the most optimal option should be chosen. The first and simplest flow diagram is the block diagram (Figure 2), in which the various unit operations of the process are represented as simple blocks connected to each other by lines representing the process flow from one operation to another. In food processing, two top priority issues are ensuring food hygiene and preventing pollution. Wanniarachchi et al. [121] presented the food processing facility model, which classifies food processing based on activities and risk levels in food processing into five areas, which are primary, secondary, utilities, warehouse, and administration [122].

6.2. Process Alternatives

The first step is a review of colostrum processing choosing between the batch and continuous processes. The batch process has been part of human activity throughout history. It remains used most of the time on a laboratory scale. The batch process is suitable for small-scale manufacturing in capacity. In the small scale, investment in LTLT pasteurization is a possible method for heat treatment. According to the data in Table 2, no significant loss in IgG concentration has been observed for this method [60].

The bovine colostrum is brought from the farm to the dairy for processing. The collection options include refrigeration (4 °C), longer-term freezing, or freeze-drying [3,123]. Refrigeration at 4 °C in plastic containers maintains the Ig properties up to 1 week [124].

For large-scale production, there are several possible thermal treatment processes available. Both LTST pasteurization and HTST pasteurization can be performed efficiently in a continuous plate heat exchanger. Numerical results obtained by Lazaar et al. [125] point out that the turbulence depends on the angle of plate corrugations' inclination. Therefore, in the case of colostrum processing, attention must be paid to the selection of the flow forms of plates of the plate heat exchanger and the distance between the plates, and possibly tested experimentally beforehand. The colostrum feed enters the regeneration section, absorbs heat from the pasteurized colostrum stream, then enters the pasteurization section. Process integration can easily reach a 96% regeneration rate [126].

The use of membrane filtration methods, i.e., microfiltration, requires the separation of fat globules from bovine colostrum, and thus this method brings one more process step. The combination of MF and HPP should be considered as an alternative to the treatment of colostrum and other heat-sensitive raw materials [4].

Meraj et al. [127] have presented a novel pasteurization system for milk. It simulates the thermal modeling system of solar milk pasteurization operated through a number of fully covered semitransparent photovoltaic thermal integrated parabolic concentrators (N/PVT/IPC). Al-Hilphy et al. [128] presented a new non-thermal moderate electric field (MEF) process for milk pasteurization. There is no information on the effect of the two methods, N/PVT/IPC and MEF, on the loss in IgG concentration. In addition, knowledge of the technical maturity of the methods does not yet exist.

6.3. Economic Considerations

The cost estimates in food processing plants are generally based on experience information and are thus less accurate than in chemical process industries [129]. General estimation techniques are used for pre-investigative design. Parin and Zugarramurdi [130] presented an investment analysis for production cost estimates in food plants based on general mathematical clauses. This analysis could be used to compare investment costs in chemical and food processing plants.

From both a financial and profitability point of view, the cost analysis of thermal treatment processes is manageable and scalable both upwards and downwards. A popular method for scaling is to use Guthrie charts of equipment cost versus capacity [131]:

$$C = C_0 \left(\frac{M}{M_0} \right)^n \quad (1)$$

where, C is the equipment cost in capacity M_0 , and C_0 is the equipment cost in capacity M . The scale index, exponent n varies with a type of equipment, i.e., heat exchangers have the value 0.65 for n [129].

6.3.1. Equipment Costs and Efficiency, Non-Dimensional

The key part of the manufacturing costs consists of both equipment and utilities in the process. In a book edited by Bartholomai [132], cost structures of various implemented solutions in food factories were showcased. In this review, costs of equipment in different thermal treatment alternatives were evaluated as dimensionless. For operation costs, the energy cost is comparable between various pasteurization processes. The batch pasteurization process is estimated to be one-tenth of cost of continuous pasteurization. Similarly, the operation cost in terms of energy is five times the cost in batch pasteurization compared to continuous processing. Since there is no significant difference between the methods in the reduction in IgG concentration, optimization can be performed directly based on the amount of processing of colostrum to be treated (Figure 2 and Table 2).

The most reliable cost assessment method for food process equipment is to conduct budget intelligence from key equipment manufacturers or suppliers. However, pricing requires accurate and detailed information about the device sizing, material choices, operating and cleaning conditions, etc. Another way of estimating the prices of food process equipment is to extract the unit processes into small parts and to compile transparent price information for the process device based on standardized parts. Price information on pumps is freely available on the Internet. The operation cost was estimated for the basis of the energy balance of the process and the price of electricity for household consumers in Germany (30.1 cents per kWh) and in Finland (17.3 cents per kWh) in 2019 [133]. Steam as the heating source can be used, if the pasteurization process is part of a large processing plant. In that case, steam could be produced in oil-powered steam generators, in which the energy price was 6 cents/kWh [134]. The equipment cost for the pasteurization process was estimated based on empirical information and the food process solutions presented in the book edited by Bartholomai [132]. Investment costs will increase tenfold when the batch heat treatment becomes continuous. The continuous process allows for a high degree of regeneration of thermal energy, resulting in the cost of energy per unit falling to the tenth. If the energy source is steam, there is an energy cost of 4% more compared to the batch heat treatment process.

6.3.2. Bacterial Inactivation and Loss of Bioactive Agents

Data on the previously described processing techniques regarding the bacterial and IgG inactivation rate have been summarized in Table 2. The IgG concentration is used as an immediate comparison as most data are given. However, the given IgG inactivation rates might not equal the amount of active antibodies, as the processing affects their functionality. Regarding most of the other immune components, there is less information

available. HTST pasteurization, for example, will lead to the inactivation of 50% of the initial LPO activity [42].

7. Conclusions

Bovine colostrum, the milk secreted by cows after giving birth, invigorates newborn calves and supports their immune defense. It contains a variety of different antibodies for conferring passive immunity and for directly combating microbial infection caused by bacteria. Furthermore, about 70 indigenous enzymes have been identified in bovine milk as well as other bioactive components such as carbohydrates, (glycol-) proteins, e.g., lactoferrin and caseins, growth factors, cytokines, lipids, enzymes, vitamins, and minerals.

The amount of bioactive components and elements are significantly higher in colostrum than in milk. Due to the variety of nutritive beneficial components with chemical/functional activities, bovine colostrum is also of interest for human consumption since healthy cows produce colostrum in excess of the calf's need. The use of bovine colostrum as food and food supplements for human consumers is gaining increasing interest. There are benefits for all persons especially those active in athletic performance and for those wanting to prevent or treat gastrointestinal, respiratory, inflammatory, and bone development diseases.

However, there are risks of the growth of both spoilage and pathogenic bacteria in the bovine colostrum, which can lead to the spread of zoonotic diseases from bovine origin. In addition, the product quality is lowered due to the contamination, which can be a result of poor harvesting and subsequent storage conditions. This review outlines the literature on microbial hazards in bovine colostrum, which shows the need for treatment before consumption. There are suitable processing techniques listed in the review. The design of a treatment process contains three options for the heat treatment of bovine colostrum decentral or central. The procedures presented focus on ensuring the food safety and keeping the high nutritional values for consumers. The review pinpoints that the processing of bovine colostrum at the dairy farms with large enough colostrum production can improve the quality and extend the shelf-life of it.

On-farm processing would improve the quality of bovine colostrum used both at home and in small processes, e.g., as ingredients. The traditional pasteurization methods are cost-effective compared with newer processing methods, e.g., HPP. The investment costs of the pasteurization process are adjustable in accordance with the production capacity of the bovine colostrum treated. The pasteurization process does not increase the costs by bringing in other consecutive cost-intensive process steps into the production. Beyond this, studies on more optimized industrial scale heat treatment in combination with the maintenance of nutritional values are required.

Author Contributions: Conceptualization, S.F. and G.W.; writing—original draft preparation, S.F. and J.A.; writing—review and editing, G.W. and S.F.; visualization, S.F. and J.A.; supervision, G.W. and B.F.; funding acquisition, G.W. Finally, all agree on the submission of the review manuscript to the open access MDPI Dairy. Seinäjoki University of Applied Sciences pays the APC fee. All authors have read and agreed to the published version of the manuscript.

Funding: This work was financially supported by Seinäjoki University of Applied Sciences (SeAMK) and Finnish Ministry of Education and Culture. Research material was collected as part of Sylvia Fasse's final thesis performed at SeAMK.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Seinäjoki University of Applied Sciences approved the work to be performed using working hours.

Conflicts of Interest: The authors declare no conflict of interest.

References

- McGrath, B.A.; Fox, P.F.; McSweeney, P.L.H.; Kelly, A.L. Composition and properties of bovine colostrum: A review. *Dairy Sci. Technol.* **2016**, *96*, 133–158. [\[CrossRef\]](#)
- Korhonen, H.J. Bioactive milk proteins and peptides: From science to functional applications. *Aust. J. Dairy Technol.* **2009**, *64*, 16.
- Foley, J.A.; Otterby, D.E. Availability, storage, treatment, composition, and feeding value of surplus colostrum: A review. *J. Dairy Sci.* **1978**, *61*, 1033–1060. [\[CrossRef\]](#)
- Gosch, T.; Apprich, S.; Kneifel, W.; Novalin, S. A combination of microfiltration and high pressure treatment for the elimination of bacteria in bovine colostrum. *Int. Dairy J.* **2014**, *34*, 41–46. [\[CrossRef\]](#)
- El-Loly, M. Bovine milk immunoglobulins in relation to human health. *Int. J. Dairy Sci.* **2007**, *2*, 183–195. [\[CrossRef\]](#)
- dos Santos Oliveira Silva, E.G.; do Nascimento Rangel, A.H.; Mürmam, L.; Bezerra, M.F.; de Oliveira, J.P.F. Bovine colostrum: Benefits of its use in human food. *Food Sci. Technol.* **2019**, *39*, 355–362. [\[CrossRef\]](#)
- Playford, R.J.; Weiser, M.J. Bovine colostrum: Its constituents and uses. *Nutrients* **2021**, *13*, 265. [\[CrossRef\]](#) [\[PubMed\]](#)
- Borad, S.G.; Singh, A.K. Colostrum immunoglobulins: Processing, preservation and application aspects. *Int. Dairy J.* **2018**, *85*, 201–210. [\[CrossRef\]](#)
- Fecteau, G.; Baillargeon, P.; Higgins, R.; Paré, J.; Fortin, M. Bacterial contamination of colostrum fed to newborn calves in Québec dairy herds. *Can. Vet. J.* **2002**, *43*, 523–527.
- Houser, B.A.; Donaldson, S.C.; Kehoe, S.I.; Heinrichs, A.J.; Jayarao, B.M. A survey of bacteriological quality and the occurrence of *Salmonella* in raw bovine colostrum. *Foodborne Pathog. Dis.* **2008**, *5*, 853–858. [\[CrossRef\]](#) [\[PubMed\]](#)
- Morrill, K.M.; Conrad, E.; Lago, A.; Campbell, J.; Quigley, J.; Tyler, H. Nationwide evaluation of quality and composition of colostrum on dairy farms in the United States. *J. Dairy Sci.* **2012**, *95*, 3997–4005. [\[CrossRef\]](#)
- Godden, S.M.; Lombard, J.E.; Woolums, A.R. Colostrum management for dairy calves. *Vet. Clinics. N. Am. Food Anim. Pract.* **2019**, *35*, 535–556. [\[CrossRef\]](#)
- Lora, I.; Gottardo, F.; Bonfanti, L.; Stefani, A.L.; Soranzo, E.; Dall’Ava, B.; Capello, K.; Martini, M.; Barberio, A. Transfer of passive immunity in dairy calves: The effectiveness of providing a supplementary colostrum meal in addition to nursing from the dam. *Animal* **2019**, *13*, 2621–2629. [\[CrossRef\]](#)
- Lima, S.F.; Teixeira, A.G.V.; Lima, F.S.; Ganda, E.K.; Higgins, C.H.; Oikonomou, G.; Bicalho, R.C. The bovine colostrum microbiome and its association with clinical mastitis. *J. Dairy Sci.* **2017**, *100*, 3031–3042. [\[CrossRef\]](#)
- Derakhshani, H.; Plaizier, J.C.; de Buck, J.; Barkema, H.W.; Khafipour, E. Composition of the teat canal and intramammary microbiota of dairy cows subjected to antimicrobial dry cow therapy and internal teat sealant. *J. Dairy Sci.* **2018**, *101*, 10191–10205. [\[CrossRef\]](#)
- Klein-Jöbstl, D.; Quijada, N.M.; Dzieciol, M.; Feldbacher, B.; Wagner, M.; Drillich, M.; Schmitz-Esser, S.; Mann, E. Microbiota of newborn calves and their mothers reveals possible transfer routes for newborn calves’ gastrointestinal microbiota. *PLoS ONE* **2019**, *14*, e0220554. [\[CrossRef\]](#)
- Stewart, S.; Godden, S.M.; Bey, R.; Rapnicki, P.; Fetrow, J.; Farnsworth, R.; Scanlon, M.; Arnold, Y.; Clow, L.; Mueller, K.; et al. Preventing bacterial contamination and proliferation during the harvest, storage, and feeding of fresh bovine colostrum. *J. Dairy Sci.* **2005**, *88*, 2571–2578. [\[CrossRef\]](#)
- Claeys, W.L.; Cardoen, S.; Daube, G.; de Block, J.; Dewettinck, K.; Dierick, K.; de Zutter, L.; Huyghebaert, A.; Imberechts, H.; Thiange, P.; et al. Raw or heated cow milk consumption: Review of risks and benefits. *Food Control* **2013**, *31*, 251–262. [\[CrossRef\]](#)
- Fernandes, R. *Microbiology Handbook: Dairy Products*; Royal Society of Chemistry: Leatherhead, UK, 2009.
- Elizondo-Salazar, J.A.; Heinrichs, A.J. Heat treating bovine colostrum. *Appl. Anim. Sci.* **2008**, *24*, 530–538. [\[CrossRef\]](#)
- Stelwagen, K.; Carpenter, E.; Haigh, B.; Hodgkinson, A.; Wheeler, T.T. Immune components of bovine colostrum and milk. *J. Anim. Sci.* **2009**, *87* (Suppl. 1), 3–9. [\[CrossRef\]](#)
- Park, Y.W.; Nam, M.S. Bioactive peptides in milk and dairy products: A review. *Korean J. Food Sci. Anim. Resour.* **2015**, *35*, 831–840. [\[CrossRef\]](#)
- Grand View Research. Colostrum Market Size, Share & Trends Analysis Report by Product (Whole Powder, Skimmed Powder, Specialty), by Application (Nutritional Supplementation, Animal Feed), by Region, and Segment Forecasts, 2019–2025. 2019. Available online: <https://www.grandviewresearch.com/industry-analysis/colostrum-market> (accessed on 12 November 2020).
- Future Market Insights. Colostrum Market to Surge at 6.4% CAGR, Rising Health Concern due to COVID-19 Will Promote Overall Growth, Says FMI. 2020. Available online: <https://www.futuremarketinsights.com/press-release/colostrum-market> (accessed on 20 December 2020).
- Korhonen, H.J. Bioactive milk proteins, peptides and lipids and other functional components derived from milk and bovine colostrum. In *Functional Foods*, 2nd ed.; Saarela, M., Ed.; Woodhead Publishing Series in Food Science, Technology and Nutrition; Woodhead Publishing: Cambridge, UK, 2011; pp. 471–511.
- Contarini, G.; Povolito, M.; Pelizzola, V.; Monti, L.; Bruni, A.; Passolungo, L.; Abeni, F.; Degano, L. Bovine colostrum: Changes in lipid constituents in the first 5 days after parturition. *J. Dairy Sci.* **2014**, *97*, 5065–5072. [\[CrossRef\]](#)
- Korhonen, H.J.; Marnila, P.; Gill, H.S. Milk immunoglobulins and complement factors. *Br. J. Nutr.* **2000**, *84* (Suppl. 1), S75–S80. [\[CrossRef\]](#)

28. Mayasari, N.; de Vries Reilingh, G.; Nieuwland, M.; Remmelink, G.J.; Parmentier, H.K.; Kemp, B.; van Kneegsel, A. Effect of maternal dry period length on colostrum immunoglobulin content and on natural and specific antibody titers in calves. *J. Dairy Sci.* **2015**, *98*, 3969–3979. [\[CrossRef\]](#)
29. Muller, L.D.; Ellinger, D.K. Colostral immunoglobulin concentrations among breeds of dairy cattle. *J. Dairy Sci.* **1981**, *64*, 1727–1730. [\[CrossRef\]](#)
30. Saad, K.; Abo-Elela, M.G.M.; El-Baseer, K.A.A.; Ahmed, A.E.; Ahmad, F.-A.; Tawfeek, M.S.K.; El-Houfey, A.A.; Aboul Khair, M.D.; Abdel-Salam, A.M.; Abo-elgheit, A.; et al. Effects of bovine colostrum on recurrent respiratory tract infections and diarrhea in children. *Medicine* **2016**, *95*, e4560. [\[CrossRef\]](#)
31. Alsayed, A.; Al-Doori, A.; Al-Dulaimi, A.; Alnaseri, A.; Abuhashish, J.; Aliasin, K.; Alfayoumi, I. Influences of bovine colostrum on nasal swab microbiome and viral upper respiratory tract infections—A case report. *Respir. Med. Case Rep.* **2020**, *31*, 101189. [\[CrossRef\]](#)
32. Kanekanian, A. *Milk and Dairy Products as Functional Foods*; John Wiley & Sons Inc.: Chichester, UK, 2014.
33. Roos, N.; Mahé, S.; Benamouzig, R.; Sick, H.; Rautureau, J.; Tomé, D. 15N-labeled immunoglobulins from bovine colostrum are partially resistant to digestion in human intestine. *J. Nutr.* **1995**, *125*, 1238–1244. [\[CrossRef\]](#)
34. Ulfman, L.H.; Leusen, J.H.W.; Savelkoul, H.F.J.; Warner, J.O.; van Neerven, R.J.J. Effects of bovine immunoglobulins on immune function, allergy, and infection. *Front. Nutr.* **2018**, *5*, 52. [\[CrossRef\]](#)
35. Anderson, R.C.; Dalziel, J.E.; Haggarty, N.W.; Dunstan, K.E.; Gopal, P.K.; Roy, N.C. Short communication: Processed bovine colostrum milk protein concentrate increases epithelial barrier integrity of Caco-2 cell layers. *J. Dairy Sci.* **2019**, *102*, 10772–10778. [\[CrossRef\]](#)
36. Fox, P.F.; Kelly, A.L. Indigenous enzymes in milk: Overview and historical aspects—Part 1. *Int. Dairy J.* **2006**, *16*, 500–516. [\[CrossRef\]](#)
37. Fox, P.F.; Kelly, A.L. Indigenous enzymes in milk: Overview and historical aspects—Part 2. *Int. Dairy J.* **2006**, *16*, 517–532. [\[CrossRef\]](#)
38. Pakkanen, R.; Aalto, J. Growth factors and antimicrobial factors of bovine colostrum. *Int. Dairy J.* **1997**, *7*, 285–297. [\[CrossRef\]](#)
39. Korhonen, H.J. Antimicrobial factors in bovine colostrum. *Agric. Food Sci.* **1977**, *49*, 434–447. [\[CrossRef\]](#)
40. Lie, O.; Solbu, H.; Syed, M. A genetic association between bovine serum and colostrum lysozyme levels. *Anim. Genet.* **1986**, *17*, 39–45. [\[CrossRef\]](#) [\[PubMed\]](#)
41. Reiter, B. Review of nonspecific antimicrobial factors in colostrum. *J. Vet. Res.* **1978**, *9*, 205–224.
42. Korhonen, H.J. Production and properties of health-promoting proteins and peptides from bovine colostrum and milk. *Cell. Mol. Biol.* **2013**, *59*, 12–24. [\[PubMed\]](#)
43. Uruakpa, F.; Ismond, M.; Akobundu, E. Colostrum and its benefits: A review. *Nutr. Res.* **2002**, *22*, 755–767. [\[CrossRef\]](#)
44. Plaut, A.G.; St. Geme, J. Lactoferrin. In *Handbook of Proteolytic Enzymes*, 3rd ed.; Rawlings, N.D., Salvesen, G., Eds.; Academic Press: London, UK, 2013; pp. 3635–3640.
45. Korhonen, H.J.; Pihlanto, A. Technological options for the production of health-promoting proteins and peptides derived from milk and colostrum. *Curr. Pharm. Des.* **2007**, *13*, 829–843. [\[CrossRef\]](#)
46. Tung, Y.-T.; Chen, H.-L.; Yen, C.-C.; Lee, P.-Y.; Tsai, H.-C.; Lin, M.-F.; Chen, C.-M. Bovine lactoferrin inhibits lung cancer growth through suppression of both inflammation and expression of vascular endothelial growth factor. *J. Dairy Sci.* **2013**, *96*, 2095–2106. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Kehoe, S.I.; Jayarao, B.M.; Heinrichs, A.J. A survey of bovine colostrum composition and colostrum management practices on Pennsylvania dairy farms. *J. Dairy Sci.* **2007**, *90*, 4108–4116. [\[CrossRef\]](#)
48. Madsen, B.D.; Rasmussen, M.D.; Nielsen, M.O.; Wiking, L.; Larsen, L.B. Physical properties of mammary secretions in relation to chemical changes during transition from colostrum to milk. *J. Dairy Res.* **2004**, *71*, 263–272. [\[CrossRef\]](#) [\[PubMed\]](#)
49. O’Kennedy, B.T. Caseins. In *Handbook of Food Proteins*; Woodhead Publishing: Cambridge, UK, 2011; pp. 13–29. [\[CrossRef\]](#)
50. Holt, C. Structure and stability of bovine casein micelles. *Adv. Protein Chem.* **1992**, *43*, 63–151. [\[CrossRef\]](#) [\[PubMed\]](#)
51. Lönnerdal, B. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol. Rev.* **1997**, *77*, 643–669. [\[CrossRef\]](#)
52. Phelan, M.; Aherne, A.; FitzGerald, R.J.; O’Brien, N.M. Casein-derived bioactive peptides: Biological effects, industrial uses, safety aspects and regulatory status. *Int. Dairy J.* **2009**, *19*, 643–654. [\[CrossRef\]](#)
53. Isaacs, C. Antimicrobial function of milk lipids. *Adv. Nutr. Res.* **2001**, *10*, 271–285. [\[CrossRef\]](#)
54. Laakso, P.; Manninen, P.; Mäkinen, J.; Kallio, H. Postparturition changes in the triacylglycerols of cow colostrum. *Lipids* **1996**, *31*, 937–943. [\[CrossRef\]](#)
55. Bitzan, M.M.; Gold, B.D.; Philpott, D.J.; Huesca, M.; Sherman, P.M.; Karch, H.; Lissner, R.; Lingwood, C.A.; Karmali, M.A. Inhibition of *Helicobacter pylori* and *Helicobacter mustelae* binding to lipid receptors by bovine colostrum. *J. Infect. Dis.* **1998**, *177*, 955–961. [\[CrossRef\]](#)
56. Sacerdote, P.; Mussano, F.; Franchi, S.; Panerai, A.E.; Bussolati, G.; Carossa, S.; Bartorelli, A.; Bussolati, B. Biological components in a standardized derivative of bovine colostrum. *J. Dairy Sci.* **2013**, *96*, 1745–1754. [\[CrossRef\]](#)
57. Hantsis-Zacharov, E.; Halpern, M. Culturable psychrotrophic bacterial communities in raw milk and their proteolytic and lipolytic traits. *Appl. Environ. Microbiol.* **2007**, *73*, 7162–7168. [\[CrossRef\]](#)

58. Gelsinger, S.L.; Jones, C.M.; Heinrichs, A.J. Effect of colostrum heat treatment and bacterial population on immunoglobulin G absorption and health of neonatal calves. *J. Dairy Sci.* **2015**, *98*, 4640–4645. [\[CrossRef\]](#)
59. European Parliament and the Council of the European Union. Regulation (EC) no 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for on the hygiene of foodstuffs. 2004. Available online: <https://eur-lex.europa.eu/eli/reg/2004/853/oj> (accessed on 10 June 2021).
60. Godden, S.M.; Smolenski, D.J.; Donahue, M.; Oakes, J.M.; Bey, R.; Wells, S.; Sreevatsan, S.; Stabel, J.; Fetrow, J. Heat-treated colostrum and reduced morbidity in preweaned dairy calves: Results of a randomized trial and examination of mechanisms of effectiveness. *J. Dairy Sci.* **2012**, *95*, 4029–4040. [\[CrossRef\]](#)
61. Phipps, A.J.; Beggs, D.S.; Murray, A.J.; Mansell, P.D.; Stevenson, M.A.; Pyman, M.F. Survey of bovine colostrum quality and hygiene on northern Victorian dairy farms. *J. Dairy Sci.* **2016**, *99*, 8981–8990. [\[CrossRef\]](#)
62. Jans, C.; Meile, L.; Kaindi, D.W.M.; Kogi-Makau, W.; Lamuka, P.; Renault, P.; Kreikemeyer, B.; Lacroix, C.; Hattendorf, J.; Zinsstag, J.; et al. African fermented dairy products—Overview of predominant technologically important microorganisms focusing on African *Streptococcus infantarius* variants and potential future applications for enhanced food safety and security. *Int. J. Food Microbiol.* **2017**, *250*, 27–36. [\[CrossRef\]](#)
63. Abebe, E.; Gugsu, G.; Ahmed, M. Review on major food-borne zoonotic bacterial pathogens. *J. Trop. Med.* **2020**, *2020*, 4674235. [\[CrossRef\]](#)
64. Fritsche, O. *Mikrobiologie*; Springer Spektrum: Wiesbaden, Germany, 2016.
65. Hoorfar, J. *Rapid Detection, Characterization, and Enumeration of Foodborne Pathogens*; ASM Press: Washington, DC, USA, 2011.
66. Zadoks, R.N.; Middleton, J.R.; McDougall, S.; Katholm, J.; Schukken, Y.H. Molecular epidemiology of mastitis pathogens of dairy cattle and comparative relevance to humans. *J. Mammary Gland Biol. Neoplasia* **2011**, *16*, 357–372. [\[CrossRef\]](#)
67. Lindner, J.D.D.; Santarelli, M.; Yamaguchi, C.T.; Soccol, C.R.; Neviani, E. Recovery and identification of bovine colostrum microflora using traditional and molecular approaches. *Food Technol. Biotechnol.* **2011**, *49*, 364–368.
68. Lailier, R.; Sanaa, M.; Chadoeuf, J.; Fontez, B.; Brisabois, A.; Colmin, C.; Millemann, Y. Prevalence of multidrug resistant (MDR) *Salmonella* in bovine dairy herds in western France. *Prev. Vet. Med.* **2005**, *70*, 177–189. [\[CrossRef\]](#) [\[PubMed\]](#)
69. Gyles, C.L.; Prescott, J.F.; Prescott, J.F.; Songer, J.G.; Thoen, C.O.; Songer, G. *Pathogenesis of Bacterial Infections in Animals*; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2004.
70. Hasegawa, M.; Iwabuchi, E.; Yamamoto, S.; Esaki, H.; Kobayashi, K.; Ito, M.; Hirai, K. Prevalence and characteristics of *Listeria monocytogenes* in bovine colostrum in Japan. *J. Food Prot.* **2013**, *76*, 248–255. [\[CrossRef\]](#) [\[PubMed\]](#)
71. Janzen, J.J. Economic losses resulting from mastitis: A review. *J. Dairy Sci.* **1970**, *53*, 1151–1160. [\[CrossRef\]](#)
72. Moretti, A.; Pasquali, P.; Mencaroni, G.; Boncio, L.; Piergili Fioretti, D. Relationship between cell counts in bovine milk and the presence of mastitis pathogens (yeasts and bacteria). *J. Vet. Med. B* **1998**, *45*, 129–132. [\[CrossRef\]](#) [\[PubMed\]](#)
73. Maunsell, F.P.; Woolums, A.R.; Francoz, D.; Rosenbusch, R.F.; Step, D.L.; Wilson, D.; Janzen, E. *Mycoplasma bovis* infections in cattle. *J. Vet. Intern. Med./Am. Coll. Vet. Intern. Med.* **2011**, *25*, 772–783. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Zastempowska, E.; Lassa, H. Genotypic characterization and evaluation of an antibiotic resistance of *Trueperella pyogenes* (*Arcanobacterium pyogenes*) isolated from milk of dairy cows with clinical mastitis. *Vet. Microbiol.* **2012**, *161*, 153–158. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Mager, D.L. Bacteria and cancer: Cause, coincidence or cure? A review. *J. Transl. Med.* **2006**, *4*, 14. [\[CrossRef\]](#)
76. Finke, E.-J.; Tomaso, H.; Frangoulidis, D. Bioterrorismus, infektiologische Aspekte. In *Lexikon der Infektionskrankheiten des Menschen: Erreger, Symptome, Diagnose, Therapie und Prophylaxe*; Darai, G., Handermann, M., Sonntag, H.-G., Zöller, L., Eds.; Springer: Berlin/Heidelberg, Germany, 2012; pp. 76–392. Available online: <https://link.springer.com/book/10.1007/978-3-642-17158-1> (accessed on 7 January 2021).
77. Gille, L.; Evrard, J.; Callens, J.; Supré, K.; Grégoire, F.; Boyen, F.; Haesebrouck, F.; Deprez, P.; Pardon, B. The presence of *Mycoplasma bovis* in colostrum. *Vet. Res.* **2020**, *51*, 54. [\[CrossRef\]](#)
78. Bernard, K.A.; Munro, C.; Wiebe, D.; Ongsanoy, E. Characteristics of rare or recently described *Corynebacterium* species recovered from human clinical material in Canada. *J. Clin. Microbiol.* **2002**, *40*, 4375–4381. [\[CrossRef\]](#)
79. Langoni, H.; da Silva, C.; Polo, C.; Troncarelli, M.Z.; Tata, A.; Belaz, K.R.A.; Eberlin, M.N.; Joaquim, S.F.; Guimarães, F.F.; Pardo, R.B.; et al. Short communication: Identification of *Corynebacterium bovis* by MALDI-mass spectrometry. *J. Dairy Sci.* **2017**, *100*, 4287–4289. [\[CrossRef\]](#) [\[PubMed\]](#)
80. Dong, W.-L.; Odah, K.A.; Liu, L.; Xu, Q.-J.; Gao, Y.-H.; Kong, L.-C.; Ma, H.-X. Multidrug resistance genes are associated with a 42-kb island TGI1 carrying a complex class 1 integron in *Trueperella pyogenes*. *J. Glob. Antimicrob. Resist.* **2020**, *22*, 1–4. [\[CrossRef\]](#) [\[PubMed\]](#)
81. Ali, Z.I.; Saudi, A.M.; Albrecht, R.; Talaat, A.M. The inhibitory effect of nisin on *Mycobacterium avium* ssp. *paratuberculosis* and its effect on mycobacterial cell wall. *J. Dairy Sci.* **2019**, *102*, 4935–4944. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Peterz, M.; Butot, S.; Jagadeesan, B.; Bakker, D.; Donaghy, J. Thermal inactivation of *Mycobacterium avium* subsp. *paratuberculosis* in artificially contaminated milk by direct steam injection. *Appl. Environ. Microbiol.* **2016**, *82*, 2800–2808. [\[CrossRef\]](#)
83. Nielsen, S.S.; Bjerre, H.; Toft, N. Colostrum and milk as risk factors for infection with *Mycobacterium avium* subspecies *paratuberculosis* in dairy cattle. *J. Dairy Sci.* **2008**, *91*, 4610–4615. [\[CrossRef\]](#) [\[PubMed\]](#)
84. Streeter, R.N.; Hoffsis, G.F.; Bech-Nielsen, S.; Shulaw, W.P.; Rings, D.M. Isolation of *Mycobacterium paratuberculosis* from colostrum and milk of subclinically infected cows. *Am. J. Vet. Res.* **1995**, *56*, 1322–1324. [\[PubMed\]](#)

85. Pithua, P.; Godden, S.M.; Wells, S.J.; Stabel, J.R. Evaluation of the risk of paratuberculosis in adult cows fed *Mycobacterium avium* subsp. *paratuberculosis* DNA-positive or -negative colostrum as calves. *Am. J. Vet. Res.* **2011**, *72*, 1456–1464. [CrossRef] [PubMed]
86. Gleeson, C.; Gray, N.F. *The coliform index and waterborne disease: Problems of microbial drinking water assessment*; CRC Press: London, UK, 1997.
87. Cockcroft, P. *Bovine Medicine*, 3rd ed.; Wiley Blackwell: Chichester, UK, 2015.
88. dos Santos, G.; da Silva, J.T.; da Rocha Santos, F.H.; Machado Bittar, C.M. Nutritional and microbiological quality of bovine colostrum samples in Brazil. *R. Bras. Zootec.* **2017**, *46*, 72–79. [CrossRef]
89. Nonnecke, B.J.; Smith, K.L. Biochemical and antibacterial properties of bovine mammary secretion during mammary involution and at parturition. *J. Dairy Sci.* **1984**, *67*, 2863–2872. [CrossRef]
90. Wijesooriya, L.I.; Namalie, D.; Sirisena, N.; Sunil-Chandra, N. Antibiotic resistance in coliforms: Human versus livestock infections. *Int. J. Infect. Dis.* **2020**, *101*, S1–S22. [CrossRef]
91. Kröger, C.; Schauer, K.; Clerkin, S.R.; Märklbauer, E.; Fleming, A.B. Draft genome sequence and annotation of *Acinetobacter junii* MHI21018 isolated from bovine colostrum. *Microbiol. Resour. Announc.* **2019**, *8*, e01700–e01718. [CrossRef]
92. Darai, G.; Handermann, M.; Sonntag, H.-G.; Zöller, L. (Eds.) *Lexikon der Infektionskrankheiten des Menschen: Erreger, Symptome, Diagnose, Therapie und Prophylaxe*; Springer: Berlin/Heidelberg, Germany, 2012; pp. 1–31. Available online: <https://link.springer.com/book/10.1007/978-3-642-17158-1>. (accessed on 7 January 2021).
93. Ribeiro Júnior, J.C.; Tamanini, R.; de Oliveira, A.; Alfieri, A.A.; Beloti, V. Genetic diversity of thermophilic spoilage microorganisms of milk from Brazilian dairy farms. *J. Dairy Sci.* **2018**, *101*, 6927–6936. [CrossRef]
94. Petkar, H.; Li, A.; Bunce, N.; Duffy, K.; Malnick, H.; Shah, J.J. *Cellulosimicrobium funkei*: First report of infection in a nonimmuno-compromised patient and useful phenotypic tests for differentiation from *Cellulosimicrobium cellulans* and *Cellulosimicrobium terreum*. *J. Clin. Microbiol.* **2011**, *49*, 1175–1178. [CrossRef]
95. Dréno, B.; Pécastaings, S.; Corvec, S.; Veraldi, S.; Khammari, A.; Roques, C. *Cutibacterium acnes* (*Propionibacterium acnes*) and *acne vulgaris*: A brief look at the latest updates. *J. Eur. Acad. Dermatol. Venereol.* **2018**, *32* (Suppl. 2), 5–14. [CrossRef]
96. Kim, K.K.; Lee, J.-S.; Stevens, D.A. Microbiology and epidemiology of *Halomonas* species. *Future Microbiol.* **2013**, *8*, 1559–1573. [CrossRef]
97. Baba, T.; Kuwahara-Arai, K.; Uchiyama, I.; Takeuchi, F.; Ito, T.; Hiramatsu, K. Complete genome sequence of *Macrococcus caseolyticus* strain JCSC5402, corrected reflecting the ancestral genome of the human-pathogenic staphylococci. *J. Bacteriol.* **2009**, *191*, 1180–1190. [CrossRef] [PubMed]
98. Behera, S.S.; Ray, R.C.; Zdolec, N. *Lactobacillus plantarum* with functional properties: An approach to increase safety and shelf-life of fermented foods. *BioMed Res. Int.* **2018**, *2018*, 9361614. [CrossRef] [PubMed]
99. Parodi, P.W. The role of intestinal bacteria in the causation and prevention of cancer: Modulation by diet and probiotics. *Aust. J. Dairy Technol.* **1999**, *54*, 103–121.
100. Morrin, S.T.; Lane, J.A.; Marotta, M.; Bode, L.; Carrington, S.D.; Irwin, J.A.; Hickey, R.M. Bovine colostrum-driven modulation of intestinal epithelial cells for increased commensal colonisation. *Appl. Microbiol. Biotechnol.* **2019**, *103*, 2745–2758. [CrossRef]
101. Kuhl, G.C.; Lindner, J.D.D. Biohydrogenation of linoleic acid by lactic acid bacteria for the production of functional cultured dairy products: A review. *Foods* **2016**, *5*, 13. [CrossRef] [PubMed]
102. Angelin, J.; Kavitha, M. Exopolysaccharides from probiotic bacteria and their health potential. *Int. J. Biol. Macromol.* **2020**, *162*, 853–865. [CrossRef]
103. Rajilić-Stojanović, M.; de Vos, W.M. The first 1000 cultured species of the human gastrointestinal microbiota. *FEMS Microbiol. Rev.* **2014**, *38*, 996–1047. [CrossRef]
104. Wittanalai, S.; Tanruean, K.; Mapoong, P. Inhibition of coliform bacteria by lactic acid bacteria isolated from nham hed (fermented mushroom). *Appl. Mech. Mater.* **2019**, *886*, 56–60. [CrossRef]
105. Vivarelli, S.; Salemi, R.; Candido, S.; Falzone, L.; Santagati, M.; Stefani, S.; Torino, F.; Banna, G.L.; Tonini, G.; Libra, M. Gut microbiota and cancer: From pathogenesis to therapy. *Cancers* **2019**, *11*, 38. [CrossRef]
106. Cummins, C.; Lorenz, I.; Kennedy, E. Short communication: The effect of storage conditions over time on bovine colostrum immunoglobulin G concentration, bacteria, and pH. *J. Dairy Sci.* **2016**, *99*, 4857–4863. [CrossRef] [PubMed]
107. Borad, S.G.; Singh, A.K.; Meena, G.S.; Arora, S.; Raju, P.N.; Sabikhi, L. Optimization of spray drying of colostrum protein ingredients—A rheological approach. *J. Food Eng.* **2021**, *288*, 110247. [CrossRef]
108. Sats, A.; Kaart, T.; Poikalainen, V.; Aare, A.; Lepasalu, L.; Andreson, H.; Jõudu, I. Bovine colostrum whey: Postpartum changes of particle size distribution and immunoglobulin G concentration at different filtration pore sizes. *J. Dairy Sci.* **2020**, *103*, 6810–6819. [CrossRef] [PubMed]
109. European Parliament and the Council of the European Union. Regulation (EC) no 853/2004 of the European Parliament and of the Council of 29 April 2004 on the Hygiene of Foodstuffs. 2004. Available online: <https://eur-lex.europa.eu/eli/reg/2004/853/oj>. (accessed on 10 June 2021).
110. Dewulf, J.; Van Immerseel, F. (Eds.) *Biosecurity in Animal Production and Veterinary Medicine from Principles to Practice*; Acco: Leuven, Belgium, 2018.
111. Food Standards Australia New Zealand. Primary Production and Processing (PPP) Standards. 2020. Available online: [https://www.foodstandards.gov.au/foodsafety/standards/Pages/Primary-Production-and-Processing-\(PPP\)-Standards-\(Chapter-4\).aspx](https://www.foodstandards.gov.au/foodsafety/standards/Pages/Primary-Production-and-Processing-(PPP)-Standards-(Chapter-4).aspx) (accessed on 28 March 2021).

112. Food Standards Australia New Zealand. Food Safety Hub. 2019. Available online: <https://www.foodstandards.gov.au/foodsafety/Pages/default.aspx>. (accessed on 28 March 2021).
113. Bartkiene, E.; Bartkevics, V.; Ikkere, L.E.; Pugajeva, I.; Zavistanaviciute, P.; Lele, V.; Ruzauskas, M.; Bernatoniene, J.; Jakstas, V.; Klupsaite, D.; et al. The effects of ultrasonication, fermentation with *Lactobacillus* sp., and dehydration on the chemical composition and microbial contamination of bovine colostrum. *J. Dairy Sci.* **2018**, *101*, 6787–6798. [CrossRef] [PubMed]
114. Elizondo-Salazar, J.A.; Jayarao, B.M.; Heinrichs, A.J. Effect of heat treatment of bovine colostrum on bacterial counts, viscosity, and Immunoglobulin G concentration. *J. Dairy Sci.* **2010**, *93*, 961–967. [CrossRef]
115. Lewis, M.J. Thermal processing. In *Food Processing Handbook*; Brennan, J.G., Ed.; WILEY-VCH: Weinheim, Germany, 2006; pp. 33–70.
116. Johnson, J.L.; Godden, S.M.; Molitor, T.; Ames, T.; Hagman, D. Effects of feeding heat-treated colostrum on passive transfer of immune and nutritional parameters in neonatal dairy calves. *J. Dairy Sci.* **2007**, *90*, 5189–5198. [CrossRef]
117. Godden, S.M.; McMartin, S.; Feirtag, J.; Stabel, J.; Bey, R.; Goyal, S.; Metzger, L.; Fetrow, J.; Wells, S.; Chester-Jones, H. Heat-treatment of bovine colostrum. II: Effects of heating duration on pathogen viability and immunoglobulin G. *J. Dairy Sci.* **2006**, *89*, 3476–3483. [CrossRef]
118. Stabel, J.R.; Hurd, S.; Calvente, L.; Rosenbusch, R.F. Destruction of *Mycobacterium paratuberculosis*, *Salmonella* spp., and *Mycoplasma* spp. in raw milk by a commercial on-farm high-temperature, short-time pasteurizer. *J. Dairy Sci.* **2004**, *87*, 2177–2183. [CrossRef]
119. Bartkiene, E.; Lele, V.; Sakiene, V.; Zavistanaviciute, P.; Ruzauskas, M.; Stankevicius, A.; Grigas, J.; Pautienius, A.; Bernatoniene, J.; Jakstas, V.; et al. Fermented, ultrasonicated, and dehydrated bovine colostrum: Changes in antimicrobial properties and immunoglobulin content. *J. Dairy Sci.* **2020**, *103*, 1315–1323. [CrossRef]
120. De Haan, A.B. *Process Technology—An Introduction*; De Gruyter: Eindhoven, The Netherlands, 2015; pp. 11–26. [CrossRef]
121. Wanniarachchi, W.; Gopura, R.; Punchihewa, H. Development of a layout model suitable for the food processing industry. *J. Ind. Eng.* **2016**, *2016*, 1–8. [CrossRef]
122. Bowser, T.J. Food processing facility design. In *Handbook of Farm, Dairy and Food Machinery Engineering*, 3rd ed.; Kutz, M., Ed.; Elsevier Inc.: Cambridge, MA, USA, 2019; pp. 623–649. Available online: <https://app.knovel.com/hotlink/toc/id:kpHFDME01/handbook-farm-dairy-food/handbook-farm-dairy-food> (accessed on 19 February 2021).
123. McGuirk, S.M.; Collins, M. Managing the production, storage, and delivery of colostrum. *Vet. Clin. Food Anim.* **2004**, *20*, 593–603. [CrossRef]
124. Manohar, A.A.; Williamson, M.; Koppikar, G.V. Effect of storage of colostrum in various containers. *Indian Pediatr.* **1997**, *34*, 93–295.
125. Lazaar, M.; Boughanmi, H.; Bouadila, S.; Jarraya, M. Parametric study of plate heat exchanger for eventual use in a solar pasteurization process designed for small milk collection centers in Tunisia. *Sustain. Energy Technol. Assess.* **2021**, *45*, 101174.
126. Tomasula, P.M.; Yee, W.C.F.; MacAloon, A.J.; Nutter, D.W.; Bonnaillie, L.M. Computer simulation of energy use, greenhouse gas emissions, and process economics of the fluid milk process. *J. Dairy Sci.* **2013**, *96*, 3350–3368. [CrossRef]
127. Meraj, M.; Mahmood, S.M.; Khan, M.E.; Azhar, M.; Tiwari, G.N. Effect of N-Photovoltaic thermal integrated parabolic concentrator on milk temperature for pasteurization: A simulation study. *Renew. Energy* **2021**, *163*, 2153–2164. [CrossRef]
128. Al-Hilphy, A.R.; Abdulstar, A.R.; Gavahian, M. Moderate electric field pasteurization of milk in a continuous flow unit: Effects of process parameters, energy consumption, and shelf-life determination. *Innov. Food Sci. Emerg. Technol.* **2021**, *67*, 102568. [CrossRef]
129. Maroulis, Z.B.; Saravacos, G.D. *Food Process Design*; Marcel Dekker: New York, NY, USA, 2003; pp. 21–57.
130. Parin, M.A.; Zugarramurdi, A. Investment and production costs analysis in food processing plants. *Int. J. Prod. Econ.* **1994**, *34*, 83–89. [CrossRef]
131. Couper, J.R.; Hertz, D.W.; Smith, L. Process economics. In *Perry's Chemical Engineers' Handbook*, 8th ed.; Perry, R.H., Green, D.W., Eds.; McGraw-Hill: New York, NY, USA, 2007; 56p.
132. Bartholomai, A. *Food Factories—Processes, Equipment, Costs*; VCH Verlagsgesellschaft mbH: Hemsbach, Germany, 1987.
133. STROM-REPORT. 2021 Strom-Report Blog. Electricity Prices in Europe 2019. Available online: <https://strom-report.de/electricity-prices-europe/> (accessed on 22 February 2021).
134. Rehfeldt, M.; Globisch, J.; Fleiter, T. Fuel choice in industrial steam generation: Empirical evidence reveals technology preferences. *Energy Strategy Rev.* **2019**, *26*, 100407. [CrossRef]