Research article

Immunomodulators - A Review on Bovine Colostrum

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Abstract.
The COVID-19 pandemic continues to be a global issue that draws worldwide attention. Countries are racing to develop vaccines and drugs to combat the COVID-19 virus. Immunomodulators are used in some of the prevention efforts. Any drug or substance that affects the immune system is classified as an immunomodulator. Bovine colostrum is an example of an immunomodulator. Colostrum is the mammary gland's first secretion after birth, and it differs from mature milk in that it contains more proteins, immunoglobulin-A, vitamins, minerals, bactericides (lactoferrin, lysozyme, and lactoperoxidase), and growth factors. This review examines immunomodulators across various perspectives and characteristics, as an alternative for increasing the body's resistance, and possible mechanisms are discussed. This review thereby facilitates the choice of suitable immune enhancement for the prevention and treatment of COVID-19.

Keywords: Bovine colostrum, Immonumodulator, Covid-19

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1. Introduction

Countries around the world are being hit by cases of acute respiratory disorders, currently known as the Corona virus. Until now, it is still the main headline in most of the world's mass media, especially in Indonesia. The increase in positive cases of COVID-19 is very fast. Now, a very dangerous virus is Covid-19. This is evidenced by a statement from WHO which states that this virus is a global pandemic after the number of infections worldwide reached more than 224 million cases and the number of people who died exceeded 4.6 million cases. With this statement, the current condition should not be allowed to exist because based on history there are only a few diseases that are classified as pandemics [1]. A pandemic is an epidemic that spreads to several countries and infects many people.

The government and religious institutions have made efforts to stop the spread of Covid-19. This is done by issuing several regulations that applied in the community.

Research to date suggests that the possible entry of COVID-19 into cells is similar to that of SARS. This is based on the 76% structural similarity between SARS and COVID-19 [2]. So it is estimated that this virus targets angiotensin Converting Enzyme 2 as an entry receptor and uses transmembrane serine protease 2 for priming S protein, although this still requires further research. The alternative to be able to live life in the meaning of the word ”new normal life” in the COVID-19 pandemic conditions is other than by following the health protocol by using an immunomodulator in the form of cow colostrum probiotics to improve the body’s immune system. Bovine colostrum is yellow liquid which was issued by the parent cows during lactation after giving birth about 24 to 168 hours [3]. According to an international panel of experts, ”probiotics are living microorganisms which, when administered in adequate amounts, confer health benefits on the human body” [4,5]. Strains must be precisely defined (that is, identified and characterized), dosages must be determined, health claims must be demonstrated, and safety must be assessed. The nature of probiotics varies greatly by type. Even the manufacturing process affects the properties of certain strains [6].

A basic portrait of a layered immune system, with multiple levels. The most important thing is the skin as the first barrier against infection. Another form is physiological, where conditions such as body temperature and pH give values that are incompatible with the normal conditions of living organisms. when pathogens successfully enter the body, they are handled by the innate and adaptive immune systems. Both systems consist of many cells and molecules that interact in a complex manner to detect and eliminate pathogens. To eliminate pathogens, it is necessary to detect and eliminate chemical bonds. It can be by binding to various receptors on the cell surface of the immune system, some of which chemically bind to pathogens, while others bind to the immune system or activate complex signaling systems that can elicit an immune response. While immunomodulators themselves are biological or synthetic substances that can trigger, suppress or modulate aspects of the immune system including adaptive and innate substances of the immune system [7].

2. Methodology

The methodology used from several literature studies to produce immunomodulators derived from bovine colostrum probiotics are:

1. Selection of quality cow colostrum

Colostrum comes from dairy cows that give birth and the yellow milk is taken. The microbiological quality of dairy cow colostrum can be influenced by several factors such as sample collection, handling, and milking time.

2. To test the analysis of the microbiological quality of dairy cow colostrum by using microbiological quality measurement indicators, namely the total number of plates.

3. Using pasteurize bovine colostrum using kefir.

4. Then fermented according to various treatments such as (fermentation for 24 hours (T1), 36 hours (T2), 48 hours (T3), and 60 hours (T4)) in a tightly closed place and stored at room temperature and in a light-tight place. Then do the manufacture of kefir grains after fermentation is complete.

5. Then do the delivery of kefir grains after fermentation is complete. After that, the curing is done for 24 hours in the refrigerator.

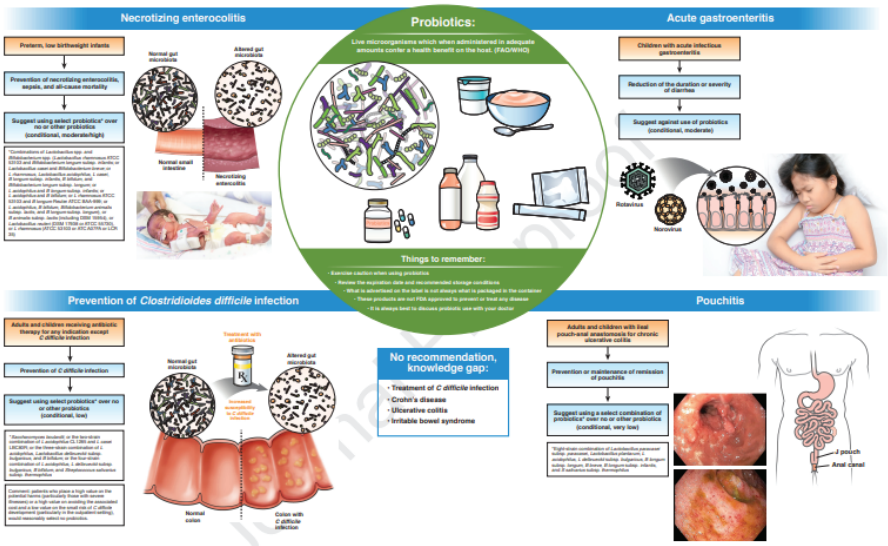

Figure 1: Spotlight: Probiotics Guidelines [8].

3. Result and Discussion

The graph below illustrates how high the level of antibody produced (mg/ml blood serum) against the A antigen. B lymphocyte cells generally take about 5-8 days from the first exposure to respond in the form of increased production of specific antibodies to recognize and neutralize the antigen. . This period is called the “lag phase”. After that the level will continue to rise until it reaches a peak after 2 weeks since the antigen entered and then decreases along with a decrease in the level of the related antigen

in the blood. When the A antigen is re-introduced into the body, the B lymphocyte cells respond by producing antibodies in a shorter time interval and the levels are much higher. If we review, this level will decrease over time as well, but this does not indicate that an individual has decreased immunity. As long as the B lymphocyte cells that produce them are still circulating in the blood or remain in the lymph nodes, they are called memory cells. The ability of the immune system to produce specific antibodies against the associated antigen is still there and ready to fight whenever needed. Over time, the ability of antibodies to recognize the same antigen increases, this phenomenon is called affinity maturation [9].

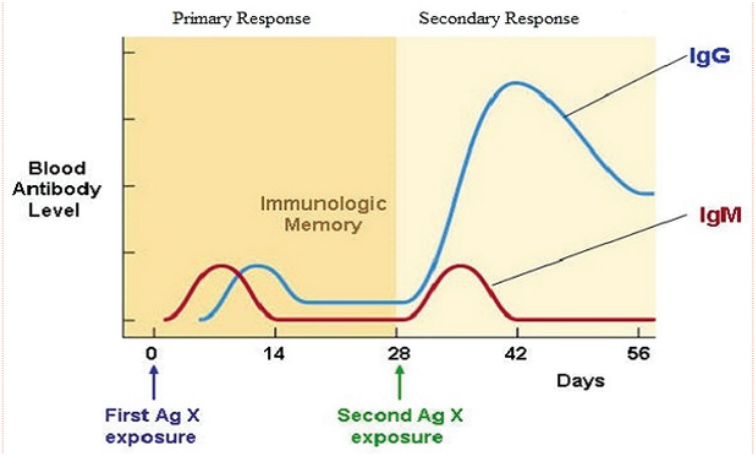

Figure 2: Immune response and secretion of antibodies.

In order to maintain the intestinal barrier, nutritional intervention is necessary, therefore, avoid this complication during and after exercising in the rather limited heat. However, bovine colostrum has been shown to be effective in blunting heat-induced permeability increases in vitro and in vivo in animals and humans [10]. The most important aspects of probiotics is the ability to combine signals and transmit into the immune system in Mucous cells in the human digestive tract locally and systemically. Interactions between probiotics with indigenous microbiota in the intestine, between intestinal epithelial cells and intestinal immune cells to produce an immunomodulatory response that is quite complex and has been extensively studied and reviewed by several previous researchers. [11,12].

The use of live microbiota as a health supplement and even for therapy has skyrocketed today until the term pharmabiotics is known in medicinal products. This phenomenon is related to the need to avoid the toxicity and side effects of chemical compounds as drug raw materials. On the other hand, the target for the effectiveness

of drug use is still a major consideration. One of the living microbes with multifunctionality that do an important role in the formulation of various medicinal preparations is probiotics in the form of monostrain and multistrain.

The Food Agriculture Organization/World Health Organization (WHO) defines probiotics as live microorganisms that can provide benefits to the health of the host when administered in appropriate doses. Some of the health benefits that have been claimed for probiotics include increasing normal microflora, preventing infectious and allergic diseases, lowering cholesterol levels, anti-cancer, stabilizing the intestinal mucosa, influencing immune properties, reducing intestinal disease symptoms, and improving lactose digestion, especially for those who are lactose intolerant hosts [13].

Table 1: Studies Using Bovine Colostrum.

Author/ Co-author	State of the art
Ahmadi *et al* [14]	Yogurt and kefir at dilutions of 8% and 16% (w/w; colostrum/product) provide the benefits of bovine colostrum in nutraceutical products.
Poonia *et al* [15]	This study focused on buffalo and bovine colostrum to study the physico-chemical and sensory properties of the obtained khees.
Saalfeld *et al* [16]	The use of Colostrum as a potential nutrient for probiotics, especially milk and butter drinks.
Mouton *et al* [17]	This study aims to examine the effect of colostrum on the characteristics of ice cream.
Ayar *et al* [18]	The effect of bovine colostrum on the lactic flora of yogurt and kefir. Yogurt and kefir on 8% and 16% (w/w; colostrum/product) dilutions.
Anamika *et al* [19]	This study aims to test the quality of skimmed colostrum powder (curd).
Abdel *et al* [20]	This study aims to produce a new functional yogurt enriched with bovine colostrum and date syrup for children.
Nazir *et al* [21]	This study aims to investigate the sensory quality of colostrum fermented products by mixing various levels of whole milk into colostrum.
Setyawardani *et al* [22]	Characteristic chemical and microbiological properties of kefir made from a mixture of milk, colostrum and milk-colostrum. Kefir is made with several process variables, namely 100% fresh milk, milk-colostrum mixture (20:80%; 40:60%; 60:40%; 80:20%) and 100% colostrum. Fermentation is under room temperature for 24 hours
Silva *et al* [23]	This study aims to develop Greek style yoghurt with bovine colostrum variations. The bovine colostrum variations used were 0%, 10%, 20% and 30% which resulted in four new yoghurt formulations

The latest development of immunomodulators in the pharmaceutical industry is very interesting, because of their comprehensive benefits for the medical world for both preventive and curative purposes.

4. Conclusion

Precautions to improve the human immune system is a a good solution to ward off the body from viral attacks including SARS-CoV-2. Based on research results that probiotics using bovine colostrum has the potential to increase immunity through crosstalk between probiotics and intestinal mucosa. Interaction between probiotic microflora and mucosa intestine can help the formation of lymphocytes. Direct formation of this component will boost the immune system various infectious diseases including COVID-19.

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