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Milk and Milk products for Enhancing Immunity during Epidemic/Pandemic such as COVID-19

This bulletin includes technical information based on latest developments on products, systems, techniques etc. reported in journals, companies' leaflets and books and based on studies and experience. The technical information in different issues is on different areas of plant operation.

The theme of information in this issue is **"Milk and Milk Products for Enhancing Immunity during Epidemic/Pandemic like situations such as COVID-19".** It may be understood that the information given here is by no means complete.

In this issue:

INTRODUCTION

Milk is a highly nutritious food that contains an array of macro and micro components, scientifically proven to provide required nutrients for growth, development and other biological benefits for human health. More interestingly, the potential of several milk constituents including proteins influences immune and neural networks affecting infection rates and mood. Milk is an excellent source of high-quality protein as it contains the 9 essential amino acids. Milk bioactive peptides which are generated during fermentation by dairy starter cultures, and during enzymatic hydrolysis possess antihypertensive, antithrombotic (reduce formation of blood clots), immunomodulating and antimicrobial properties along with many other biological properties.

The immune system protects the host (human body) from pathogenic organisms (bacteria, viruses, fungi, parasites). To deal with this array of threats, the immune system has evolved to include a numerous specialized cell types, communicating molecules and functional responses. Specific nutrients and the foods play a role in supporting the immune system in order that the host can better defend against infections. Therefore, having a healthy/balanced diet could be an important factor.

Corona virus disease-2019 (COVID-19) highly infectious disease caused by recently discovered strain of novel coronavirus known as severe acute respiratory syndrome CoV-2 (SARS CoV-2). COVID-19 causes acute respiratory tract illness and its transmission in humans (infection route) occurs mainly through mouth and/or nose, by either close contact or through inhalation of spit/ respiratory droplet generated (aerosol) when an infected person coughs or sneezes. The infection can also occur

indirectly through contact with contaminated surfaces. COVID-19 was declared a pandemic by the World Health Organization in March 2020. COVID-19 enters human cells by binding to Angiotensin Converting Enzyme 2 (ACE2) as its receptor (Yan et al., 2020).

Various preventive and therapeutic strategies such as vaccination and use of antibiotics/antivirals are being explored to control the infectious diseases. Despite these measures, we see frequent emergence and re-emergence of the known and novel infections resulting in epidemics or pandemics. The risk of viral infection is a critical issue as viruses undergo mutations rapidly. There is no specific antiviral treatment recommended for COVID-19. In the meantime, to ensure that individuals' immune systems react against viruses, balanced nutrition should be at the forefront of approaches. Professionals are suggesting various alternative medicines like Ayurveda, Siddha, Herbal medicines and other adjunctive therapeutic/prophylaxis methods for combating the effects of COVID-19 infections and or improve the immunity against the novel diseases/infections.

This issue of *Technews* provides a review of the latest information on the role of milk and milk products in boosting human Immunity, particularly in light of current COVID-19 pandemic.

CORONA VIRUS DISEASE-2019 (COVID-19) & ACE2

Corona viruses are enveloped, positive-stranded RNA viruses with nucleocapsid that has spike like projections on its enveloped surface giving it a crown like appearance hence the term Corona virus (Singhal, 2020).

It has been well-known that SARS-CoV-2 appears to be optimized for binding to the human receptor ACE2. The ACE2 system is a critical protective pathway against heart failure, myocardial infarction (heart attack), hypertension, against lung disease and diabetes mellitus (Gheblawi et al., 2020). ACE2 is widely expressed, in the lungs, cardiovascular system, gut, kidneys, central nervous system, and adipose tissue. ACE2 primarily acts to counterbalance the effect of ACE. As ACE generates angiotensin II from angiotensin I, ACE2 generates angiotensin-1-7 from angiotensin II which, after binding to the Mas receptor (MasR) broadly, shifts the balance from vasoconstriction with angiotensin II to vasodilation with Mas receptor activation in the effected vascular bed (See Fig 1).

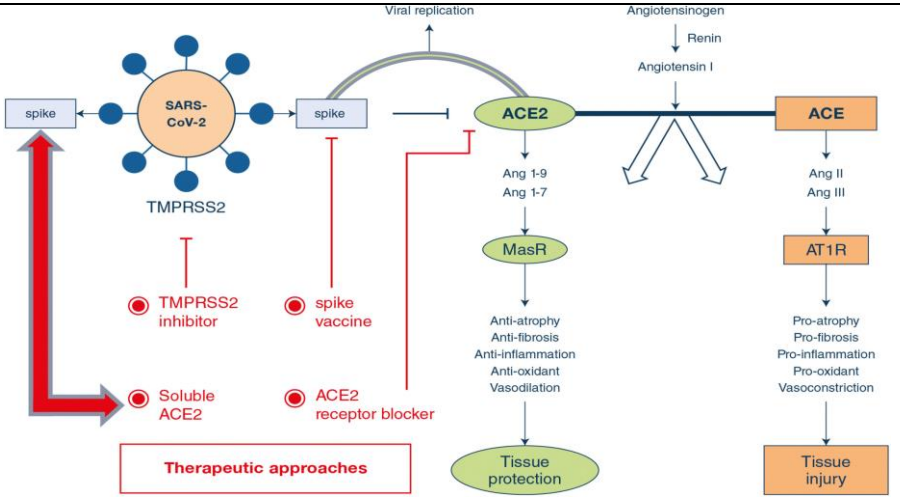

Fig 1 ACE2-mediated SARS-CoV-2 infection

SARS-CoV and likely SARS-CoV-2 lead to down regulation of the ACE2 receptor, but not ACE, through binding of the spike protein with ACE2. This leads to viral entry and replication, as well as severe lung injury.

Ref: H Zhang et al., (2020).

Role of nutrition and diet to enhance immunity is more discussed topic in the recent times in view of costs involved for medication. The food we eat plays a key role in determining your overall health and immunity. Milk and milk products are important in enhancing immunity. People who are deficient in some micronutrients such as vitamin D, vitamin C, or zinc may warrant supplementation or modify their dietary patterns to maintain a nutritional status and immune function.

HUMAN IMMUNE SYSTEM & NUTRITION

Immune System: The immune system comprises a network of organs and cells that are strategically distributed throughout the body. Immunity operates at a number of levels. The main functions of the immune system are to eliminate invading viruses and foreign microorganisms, to rid the body of damaged tissue, and to destroy neoplasms (abnormal growth of cells/tumor) in the body.

The three principal steps in this response are:

1. The recognition of the foreign molecule
2. Destruction of the foreign matter
3. Regulation of the response through multiple feedback controls

Healthy humans have 2 immune mechanisms: acquired (specific) immunity, which responds to specific stimuli (antigens), is enhanced by repeated exposure; and innate (nonspecific) immunity, which does not require stimulation and is not enhanced by repeated exposure. Innate immune mechanisms consist of physical barriers, such as mucous membranes, and the phagocytic and cytotoxic function of

neutrophils, monocytes, macrophages, and lymphatic cells.

Acquired immunity can be classified into 2 types on the basis of the components of the immune system that mediate the response, ie, humoral immunity and cell-mediated immunity.

- Humoral immunity is mediated by immunoglobulins (Igs) produced by bone marrow–derived lymphocytes (B lymphocytes) and is responsible for specific recognition and elimination of extracellular antigens.
- Cell-mediated immunity is mediated by cells of the immune system, particularly thymus-derived lymphocytes (T lymphocytes), that directly kill pathogen infected cells (T-cytotoxic cells, natural killer cells) or that regulate the immune response via cytokines (T-helper cells) (Meydani and Ha, 2000).

Nutrition: The immune system is always active, carrying out surveillance in healthy individuals, this activity is accompanied by an increased rate of metabolism, requiring energy sources, substrates for biosynthesis and regulatory molecules. These energy sources, substrates and regulatory molecules are ultimately derived from the diet. Activation of the immune response induces the production of lipid-derived mediators such as prostaglandins and leukotrienes and of many different types of protein including immunoglobulins, chemokines, cytokines, cytokine receptors, adhesion molecules and acute-phase proteins. These requires availability of the substrate fatty acids and amino acids, respectively.

Various micronutrients (eg, iron, folate, zinc, selenium magnesium) are also involved in nucleotide and nucleic acid synthesis. Some nutrients, such as vitamins A, C, D, E, B2, B6, and B12, and their metabolites are direct

regulators of gene expression in immune cells and play a key role in the maturation, differentiation and responsiveness of immune cells.

The immune impairments and the susceptibility to infection can be reversed by correcting the deficiency (ies). This is recognized by the European Food Safety Authority which permits claims of 'maintenance of functions of the immune system' for vitamins A, B6, B12, C, D and folate (vitamin B9) and for the trace elements zinc, iron, selenium and copper (Calder PC. 2020). As per Food Safety and Standards (Advertising and Claims) Regulations, zinc supports a healthy immune system. In essence, good nutrition creates an environment in which the immune system is able to respond appropriately to challenge, irrespective of the nature of the challenge. Conversely poor nutrition creates an environment in which the immune system cannot respond well.

SIGNIFICANCE OF MILK ON HUMAN NUTRITION

Milk is a widely consumed drink from childhood to adolescence, which is essential to the diet of several millions of people worldwide because it provides significant amounts of fat, protein, micronutrients and unique sugar lactose. Dairy products like milk, cheese and yoghurt contain a range of important nutrients such as protein, bioactive peptides, conjugated linoleic acid, α-linolenic acid, vitamin A, D, B2, B3, B12, calcium, potassium, phosphorus, selenium and much more.

Constituents present in milk product, play a key role in the physiological activities in human body, and act as anti-inflammatory, anti-tumor, antioxidant, antimicrobial hypocholesterolemic and immune boosting. Most of the

constituents in milk do not work in isolation, but rather interact with other constituents. Often, they are involved in more than one biological process.

Milk mediates its protective function by two distinct ways: first by providing passive protection through the transfer of molecules such as antibodies, and secondly by regulating the development of an effective and a balanced immune system. The immunomodulatory effects of milk are attributed to a wide range of milk components, including whey proteins, caseins, lipids, hormones and growth factors. A reduction in respiratory tract infections was also observed in an intervention study with children of 1–6 years of age receiving bovine colostrum that is extremely rich in IgG. In line with these findings, controlled studies in infants with milk components such as lactoferrin, milk fat globule membrane, and colostrum IgG have shown to reduce respiratory infections. In addition, milk proteins contain a host of immunoactive peptides that can be released following enzymatic hydrolysis *in vitro*, commercial processing or normal digestion (Gill, 2000; Gill & Cross, 2000).

Diet plays an important role in shaping the composition of the gut microbiota (gut microbiome is comprised of various types of bacteria, fungi, protozoa, and viruses naturally occurring in humans and animals as normal microflora) thereby influencing host's health status. Literature suggests the therapeutic and beneficial properties of ethnically fermented dairy products and associated microorganisms. The microbiota plays a fundamental role on the induction, training, and function of the host immune system. In optimal conditions, this immune system-microbiota alliance allows the induction of protective responses against pathogens and the maintenance of regulatory pathways. Furthermore,

fermented milk products contain lactic acid bacteria (LAB) that are able to influence a range of host immune responses (Gill and Cross, 2002).

COMPONENTS OF MILK AS IMMUNITY BOOSTERS

Proteins: Milk proteins serve as nutrients for humans with potential physiological effects. Milk protein is a combination of whey (20%) and casein (80%), which plays a role in optimal calcium and phosphate absorption, provides precursors for bioactive peptides. In addition to delivering amino acids, bioactive peptides, are reported to be involved in protection against infections, immune enhancement and development of the gut (Kanwar et al., 2009). Number of health characteristics have been suggested for β-lactoglobulin, including antiviral and anticarcinogenic effects (Chatterton et al., 2006).

Milk proteins are used in a variety of specific functional and nutritional applications and some milk proteins-peptides (bioactive peptides) possess biological activities (see Fig 2). These peptides are inactive within the sequence of precursor proteins, but can be released *in vivo or in vitro* by enzymatic digestion or during fermentation with lactic acid bacteria (LAB) (*Gobbetti* et al., 2000).

During microbial fermentation of milk, proteins are hydrolysed into long oligopeptides by cell wall associated proteinases of LAB, transported into the cell and broken down by intracellular peptidases into a range of peptides with different bioactivities (Nielsen et al., 2009). These milk derived BAPs can function as exogenous regulatory substances such as hormones or drugs, which modulate physiological functions through binding interactions to

specific receptors on target organs leading to induction of physiological responses (Gobbetti et al., 2000).

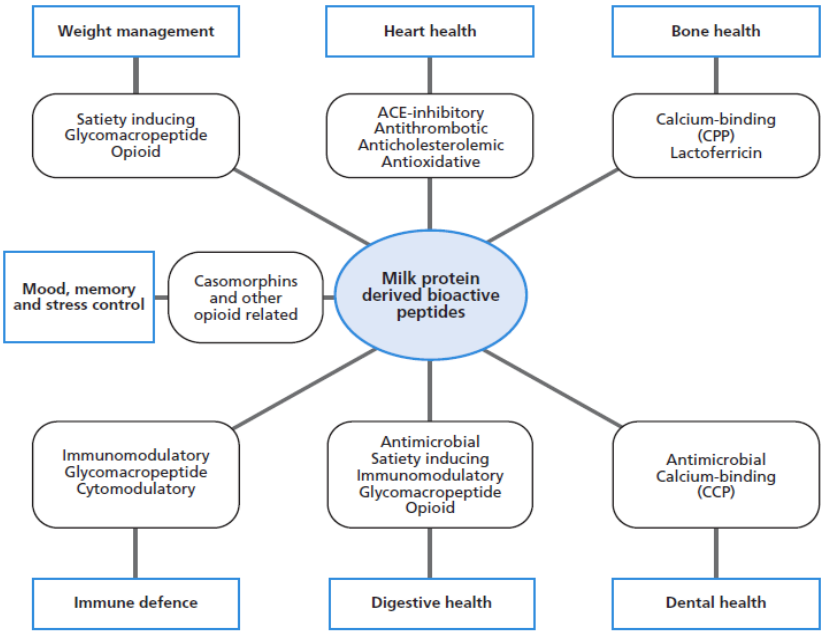

Figure 2. Functionality of milk protein-derived bioactive peptides (BAPS) and their potential health targets.

Among different BAPs, ACE-inhibitory peptides are the most extensively studied group with immunomodulatory, antimicrobial, antithrombotic and mineral binding properties. Studies show that the thermosensitive fraction of the milk (i.e., proteins, most likely whey fraction) is an important driver of the protection against not only allergies and asthma but also viral infections, fever, and inflammatory conditions in the upper airways (Perdijk et al., 2018).

These naturally occurring ACE-inhibitory peptides are reported to be advantageous over the artificially synthesized ACE-inhibitory drugs (vasodilators, diuretics, calcium channel blockers, angiotensin II receptor blockers and ACE-inhibitors such as captopril, enalapril, alecepril, lisinopril). The natural ACE inhibitors are not reported to cause adverse side effects such as hypotension, cough, and increased blood calcium levels, fetal abnormalities, reduced renal function, angioedema and skin rashes (FitzGerald et al., 2004), which are associated with artificially synthesized drugs. Therefore, the concept of functional foods with ACE-inhibitory/antihypertensive activity has attained considerable attention over the past decade as they provide an alternative approach to decrease the requirement of antihypertensive medication.

Most of the milk proteins and peptides that have been identified with antiviral properties are broad spectrum components targeting general features and mechanisms involved in viral infection cycle. Hence, many of these milk proteins do also demonstrate synergy with conventional antiviral drugs (H.Sun and Havard Jenssen, 2012).

Lactoferrin: Lactoferrin (Lf) is an 80 kDa iron-binding highly multifunctional glycoprotein of the transferrin family. It is abundant in milk and in most biological fluids that bridge innate and adaptive immune function in mammals.

It is has been associated with positive antimicrobial effects (antibacterial and antiviral), immune modulation and modulation of the gut microbiota, it also exhibits antioxidant activity and has both anticarcinogenic and anti-inflammatory properties.

The antimicrobial activity of Lf is driven mostly by two mechanisms. The first involves iron sequestration on sites of infection, which deprives nutrient and causes a bacteriostatic effect. The second mechanism is the direct interaction of the Lf molecule with the infectious microorganism. In some cases, positively charged amino acids in Lf can interact with anionic molecules on certain bacterial, viral, fungal and parasite surfaces, causing cell lysis.

One of the proteins in cow's milk that is important for epithelial barrier functioning is TGFβ (Transforming Growth Factor). TGFβ1 is capable of promoting barrier functioning by regulating tight junctions (TJ) expression and proliferation. Interestingly, the production of endogenous TGFβ1 by epithelial cells is regulated by other milk proteins like Lf.

Lf possesses antiviral activity against a broad range of RNA and DNA viruses that infect humans and animals (H.Sun and Havard Jenssen., 2012). de Carvalho CAM et al., 2020 found that bLf (bovine lactoferrin) reduced SARS-CoV-2 progeny virus yield. Regarding *in vivo* responses to CoVs, it is worth noting that genes coding for Lf are highly up-regulated in patients with SARS and the protein may further inhibit virus infection *in vivo* by enhancing natural killer (NK) cell activity and stimulating neutrophil aggregation and adhesion (Reghunathan et al., 2005). DB Kell et al., 2020 noted that Lactoferrin (and more specifically enteric-coated LF because of increased bioavailability) may consequently be of preventive and therapeutic value during the present COVID-19 pandemic.

Immunoglobulin's (Igs): Igs are antibodies that are synthesized by mammals in response to antigenic or immunogenic stimuli such as bacteria and viruses, and

thus provide protection against microbial infections. The main immunoglobulins in milk is IgG1, and others are IgM, IgA and IgG2. In addition to the protection against microbial pathogens, they are responsible for activation of complement, stimulation of phagocytosis, preventing adhesion of microbes, and neutralization of viruses and toxins. They also increase the intracellular levels of glutathione, which is the key cell antioxidant (Bounous and Gold 1991). The secretory IgA (sIgA) prevents adhesion of infectious agents to the mucosal epithelium. The concentration of immunoglobulins is higher in colostrum than milk.

Vitamins:

Vitamin A activity is present in milk as retinol, retinyl esters and as carotenes (see table 1). The concentration of vitamin A and carotenoids in milk is strongly influenced by the carotenoid content of the feed. Vitamin A is important for normal differentiation of epithelial tissue and for immune cell maturation and function. Thus, vitamin A deficiency is associated with impaired barrier function, altered immune responses and increased susceptibility to a range of infections. Vitamin A also supports phagocytic activity and oxidative burst of macrophages, so promoting bacterial killing. Natural killer cell activity is diminished by vitamin A deficiency, which would impair antiviral defenses, predisposes to respiratory infections, diarrhoea and severe measles (Calder PC., 2020).

Vitamin D is often referred to as the sunshine vitamin; occurs in foods of animal origin, it is also found in milk and dairy products (See table 1) or foods fortified with vitamin D, shown to have immunomodulatory effects. Whole cows' milk contains only about 4IU vitamin D per

100 g and 1 litre of milk per day will supply only 10-20% of the recommended daily allowance (RDA). Therefore, milk is often fortified with vitamin D.

Vitamin D itself may exhibit antiviral effects by interfering with viral replication and through its immunomodulatory and anti-inflammatory properties. It is evident that vitamin D3 contributes to epithelial barrier function by regulating TJ (Tight Junction) protein expression. Vitamin D is essential for regeneration of epithelial barrier inside lining of respiratory tract that helps in keeping bacteria and viruses out. With the remarkable potential of Vitamin D in improving cellular immunity, several researchers proposed that Vitamin D supplementation could possibly treat Covid19 or reduce severity, at least.

Table 1. Vitamin A & D in milk and milk products (per 100g)

Products	Retinol (µg)	Carotene (µg)	D (µg)
Cow Milk Whole	150 [a,b]		4[a]
Buffalo milk Whole	240 [a],b		7 [a]
Toned Milk	115 [a,b]		3 [a]
Cow milk skimmed	Tr,[b]		0
Buffalo milk Skimmed	Tr,[b]		0
Butter	3300 [a,b]		92 [a]
SMP	40 [a,b]		Tr
Ghee	3800 [a,b]		99 [a]
Cheese (Surti)	830 [a,b]		20 [a]
Skimmed Pasteurized Milk	1	Tr	Tr
Sterilized whole milk in containers	52	21	0.03
Evaporated Whole Milk	105	100	0.09
Cheddar Cheese	325	225	0.26
Edam	175	150	(0.19)
Gouda	245	145	(0.24)
Processed Cheese Plain	270	95	0.21
UHT, Drinking Yoghurt	Tr	Tr	Tr
Low Fat yoghurt plain	8	5	0.01
Whole Milk yoghurt Plain	28	21	0.04
Ice cream	115	195	0.12

() Estimated Values, a- Values in IU, b- Vitamin A, Tr-Traces
Reference: G P Talwar et al., (2015); P.F.Fox and P.L.H. McSWEENEY (1998).

Vitamin-D deficiencies are significant in elders & they are more susceptible to Covid19. Supportive data for the effective role of vitamin D in decreasing risk of COVID-19 could be highlighted by increased case-fatality rates with chronic disease comorbidity and age, in which lower concentrations of 25(OH)D have been reported. While the natural source of vitamin D is from sunlight exposure, some dietary sources can provide a certain amount of vitamin D, including the fortified cereals and milk (A. Gasmi, et al 2020). Consequently, further research is required before any determination can be made about the prophylactic or therapeutic values of vitamin D against COVID-19.

B-group vitamins involved in intestinal immune regulation, thus contributing to gut barrier function. Folic acid (Vit B9) deficiency in animals' causes thymus and spleen atrophy, and decreases circulating T lymphocyte numbers. Spleen lymphocyte proliferation is also reduced. In contrast, vitamin B12 deficiency decreases phagocytic and bacterial killing capacity of neutrophils, while vitamin B6 deficiency causes thymus and spleen atrophy, low blood T lymphocyte numbers and impaired lymphocyte proliferation and T lymphocyte-mediated immune responses (Calder PC.2020).

Trace elements:

Zinc (Zn) concentration in milk is 3.6 mg/1, but large variations in the zinc content of milk (2.0–6.0 mg/l) have been reported (see table 2). The wide ranging impact of zinc deficiency on immune components is an important contributor to the increased susceptibility to infections, especially lower respiratory tract infection and diarrhoea, seen in zinc deficiency. Read *et* al 2019 provided a very

insightful evaluation of the role of zinc in antiviral immunity. Zinc inhibits the RNA polymerase required by RNA viruses, like coronaviruses, to replicate. Zinc is important element for the maintenance of maintaining T and B lymphocyte numbers. Zn deficiency impairs many aspects of innate and acquired immunity. Zinc also supports the release of neutrophil extracellular traps that capture microbes.

A meta-analysis of oral zinc supplementation studies suggested beneficial effects on the shortened of symptoms and duration of common cold infection. Moreover, research has shown that zinc has antiviral effects, as it improves immune responses. Therefore, the consumption of up to 50 mg zinc per day may provide a protective role against the COVID-19 pandemic, likely by improving the host's resistance against viral infection. (A. Gasmi, et al 2020).

Selenium concentration in cow's milk samples from 15 countries was reported as 10 µg/1 (range 3–40 µg/1) (see table 2). Se deficiency adversely affects several components of both innate and acquired immunity. Lower selenium concentrations in humans have been linked with diminished natural killer cell activity and increased mycobacterial disease. Selenium deficiency leads to mutations and increase virulence of coxsackievirus, polio virus and murine influenza virus (Calder PC.2020).

Table 2: Zinc and Selenium in milk and milk products.

Minerals (per100g)	Cow milk (whole)	Buffalo Milk (Whole)	Paneer	Khoa
Zinc (mg)	0.33±0.03	0.30±0.05	2.74±0.14	2.34±0.15
Selenium (µg)	0.95±0.17	1.45±0.26	23.14±1.37	44.97±13.14

Ref: Indian Food Composition tables., National Institute of Nutrition, 2017

Fermented Dairy Products

Fermented milk products have traditionally been associated with a series of health-promoting properties. The health benefits of dairy products are the result of biologically active components that are present in native milk and also, due to their suitably modulated activities produced through the action of bacteria, in the fermented or sour milk products. These includes certain vitamins, specific proteins, bioactive peptides, oligosaccharides, organic acids (including fatty acids). Some of them are normal milk components, others emerge during digestive or fermentation processes. A number of ACE-inhibitory peptides have been identified from different fermented dairy products such as yoghurt (Chobert et al., 2005), cheese (Smacchi & Gobbetti, 1998; Pripp et al., 2006), dahi and fermented sour milk products with different LAB species such as lactobacilli (*Lb. helveticus, Lb. casei, Lb. plantarum, Lb. rhamnosus, Lb. acidophilus, Lb. delbrueckii subsp. bulgaricus*), lactococci (*L. lactis subsp. cremoris*), *Streptococcus thermophilus* and *Enterococcus faecalis* (Gobbetti et al., 2000; Nielsen et al., 2009). Micro-organisms that perform the fermentation process may produce beneficial metabolites (above biogenic effect) or may themselves interact with the host in a positive manner (the probiotic effect) (Roupas, Williams and Margetts, 2009). In addition to modification of several milk components the probiotics may act also directly as preventive agents, or in therapy of some contagious, atopic, tumor or other severe diseases.

Probiotics

The human gastrointestinal tract (GIT) harbours an extremely complex and diverse microbial ecosystem. The

GIT of an adult human contains approximately 10^{14} cfu bacteria representing over 400 different species. In healthy individuals, there is a definite balance between good and bad bacteria. It is now well recognized that a healthy (balanced) microflora is pivotal to optimum health and that supplementation with probiotics could be used to shift the balance of the gut microflora away from potentially harmful/pathogenic bacteria towards a beneficial or health-promoting microorganisms, like lactobacilli, bifidobacteria.

Probiotics can be used to support general immunity, rather than targeting prevention of a specific disease in the wider population. Most probiotics are LAB, such as lactobacilli and bifidobacteria, commonly consumed with dairy products (including traditionally cultured dairy products and some fermented milks like yoghurt or other fermented products) have multifunctional roles (See fig 3).

Probiotic bacteria compete with some pathogenic bacteria for available nutrients. In addition to these direct interactions between commensal and probiotic organisms on the one hand and pathogens on the other, they can interact with the host's gut epithelium and gut-associate immune tissues. These communications with the host may occur through chemicals released from the bacteria or through direct cell-to cell contact and it is through these interactions that probiotics are thought to be able to influence immune function, even at sites distant from the gut.

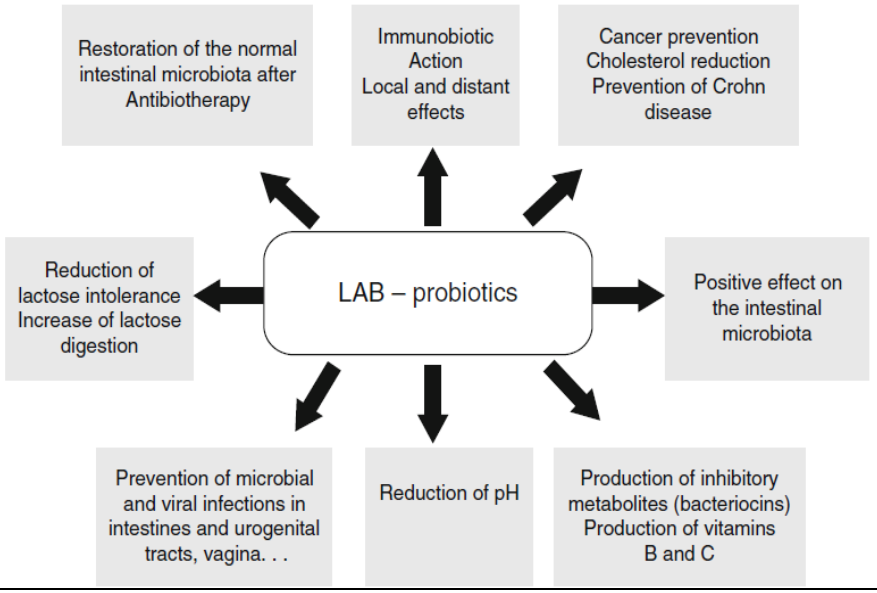

Figure 3. Potential functions attributed to LAB probiotics
Ref: Imad AL KASSAA 2017

Probiotics act on both the innate and acquired immune systems and have the potency to reduce the severity of infections in the gastrointestinal and upper respiratory tracts. Probiotics contain immune stimulatory substances such as lipoteichoic acid, peptidoglycan, nucleic acid, and muramyl dipeptide.

Interestingly, the gut microbiota has been shown to affect pulmonary health through a vital cross-talk between the gut microbiota and the lungs which is referred to as the "gut-lung axis" (Keely et al., 2012). The gut-lung axis is supposed to be bidirectional, meaning the endotoxins, microbial metabolites can impact the lung through blood and when inflammation occurs in the lung, it can affect the gut microbiota as well (Dumas *et al.,* 2018). Gut

microbiota diversity is decreased in old age and Covid-19 has been mainly fatal in elderly patients which again points to the role the gut microbiota may play in this disease. COVID-19 patients shows the gastrointestinal symptoms such as diarrhoea, nausea and vomiting, those patients with gastrointestinal symptoms had overall more severe/critical diseases (Jin et al., 2020; Lin et al., 2020; Ng and Tilg, 2020, Wu et al., 2020).

Antiviral activity of probiotic strains against common respiratory viruses, including influenza, rhinovirus, and respiratory syncytial virus has been reported (Imad Al Kassaa., 2017). Improving gut microbiota profile by personalized nutrition and supplementation known to improve immunity can be one of the prophylactic ways by which the impact of this disease can be minimized in old people and immune-compromised patients. The available evidence suggests a potential role of gut microbiota in the susceptibility of COVID-19 progression and severity.

Milk Beverages with Herbal Extracts

There is a wide class of Indian medicinal plants having potential to cure variety of illness. Commonly used Indian medicinal plants involved in respiratory diseases are mentioned in Table 3. Various *in-vitro* studies has revealed that Indian medicinal plants like *Allium sativum (Garlic), Andrographis paniculata (Kirayat/Kalmegh), Clerodendrum inerme Gaertn (Kundali/Sankuppi), Glycyrrhiza glabra (Yashtimadhu), Sphaeranthus indicus(Mundi), Strobilanthes callosa(Karvy), Strobilanthes cusia (Lesser Kurinji), Vitex trifolia (sambhalu) and Zingiber officinale (Ginger)* are potent against the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV). It has been reported that these

herbs can inhibit/suppress/ reduce the virus (SARS-CoV) growth through the inhibition of protein replication. These herbs and/ or their formulations may show same effects against the SARS-CoV2 (V.Kumar, et al., 2020).

The Ministry of AYUSH, Government of India has issued an Ayurvedic immunity-boosting advisory, listed Golden Milk (Half tea spoon Haldi (turmeric) powder in 150 ml hot milk) as one of the ayurvedic immunity boosting measures for self-care during COVID-19. Cooperative's like Gujarat Cooperative Milk Marketing Federation Ltd. (GCMMF), Karnataka Milk Federation (KMF), Punjab State Cooperative Milk Producers' Federation Ltd, and other federations/affiliated unions launched various milk beverages by incorporating herbal extracts like Turmeric, Tulsi, Ginger, Ashwagandha, Pepper, Clove etc., as immunity boosters.

Table 3. List of commonly used Indian medicinal plants involved in respiratory diseases.

Plant/Herb	Function
Glycyrrhiza glabra (Yashtimadhu)	Immunomodulatory, Anti-inflammatory, Antiviral, Cough and Cold
Caesalpinia crista (kanta karanja)	Anti-viral activity, Immunomodulatory and Bronchial infections
Curcuma longa L. (Turmeric)	Immunomodulatory, Anti-inflammatory, Cough and Cold
Emblica officinalis (Indian gooseberry)	Immunomodulatory, Anti-inflammatory, Antiviral
Piper Nigrum L. (Black pepper)	Immunomodulatory, Anti-inflammatory, Anti-Virus
Tinospora cordifolia (Guduchi)	Immunomodulatory, Anti-inflammatory, Anti-Virus, Antipyretic
Withania somnifera (Ashwagandha)	Immunomodulatory, Anti-inflammatory, Anti-Virus, Antipyretic
Achillea mellefolium (Gandrain, Puthkanda, Bhut Kesi, Rojmaari)	Protects upper respiratory tract from viral infections
Apiumgraveolens (Ugragandhika, Celery)	Anti-bacterial and anti-viral agent

Borassusflabellifer (commonly known as doub palm, palmyra palm, tala palm, toddy palm, wine palm, or ice apple)	Pulmonary infections: anti-bacterial and antiviral activity
Cymbopogon citratus (lemon grass)	Anti-viral infections
Caesalpinia bonduc (gajga, sagaragota)	Treated for asthma (Anti-bacterial and anti-viral agent)
Calotropis gigantea (Safed aak)	Anti-bacterial and anti-viral agent
Crocus sativus (saffron, Kesar)	Treated for asthma and cough
Euphorbia hirta (asthama Plant)	Anti-bacterial and anti-viral agent
Ocimum sanctum (Tulsi)	Anti-viral, Anti-inflammatory, Anti-microbial, Immunomodulatory
Solanum suratens (Kantakaari)	Anti-viral activity
Syzygium aromaticum (Clove)	Anti-viral and Anti-inflammatory activity
Trachyspermum Ammi (Ajwain)	Anti-viral and Anti-microbial activity
Thymus linearis (Jangli ajwain)	Anti-viral activity
Santalum album (Chandan, sandalwood)	Anti- inflammation of the lungs
Zingiber officinale (Ginger)	Anti-viral activity, Immunomodulatory and Bronchial infections
Mucunapruriens X. strumanium, Piper longum, Solanum tornum	Anti-pneumonia drug
Morus laevigata Wall. Brandis, Geranium wallichianum, Micromeriabiflora,	Treated for cough
Primula denticulata Sm.	Treated for cough and bronchitis
Alstonia scholaris L.,	Immunomodulatory Anti-viral, and Bronchial infections
Picrorhiza kurroa,	Immunomodulatory Anti-viral and Bronchial infections
Swertia chirata	Immunomodulatory and Bronchial infections
Achyranthesaspera	Anti-viral activity
Yuthog's Bamboo	Anti-inflammation of the lungs and respiratory tract
Hippophaerhamnoides	Eliminate phlegm, cough, improve digestion
Ref: V. Kumar, et al. (2020)	

Conclusion

Pandemic has pushed the world to the brink. Supportive care/strong immunity remains the most important management strategy for human infection by highly pathogenic CoVs, as there is currently no specific antiviral treatment. While no foods or dietary supplements can prevent COVID-19 infection, evidence shows that a healthy diet and good nutrition play a significant role in building a strong and healthy immune system. Milk and milk products are play a key role in immunity boosting. Elderly, immune-compromised patients and patients with other co-morbidities like type-2 diabetes, cardiovascular disorders fare poorly in combating COVID-19. Research in gut microbiota has propelled knowledge in the field of chronic and infectious diseases. In addition to considering the 'direct' effects of nutrition on the immune system, milk and fermented foods play a role in creating and maintaining a healthy gut microbiota that will also help to support the immune system. A review of countries reporting in the Food and Agriculture Organization (FAO) dietary guidelines database shows that nearly all of them advise consumption of milk and/or dairy foods. This is reflective of the overwhelming scientific evidence that dairy is an important component of a healthy dietary pattern and associated with positive health outcomes (IDF 2020).

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