Review

Lactic Acid Bacteria in Health and Disease

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Abstract

The genera, lactic acid bacteria (LAB) have been used by humans in production of fermented foods since time immemorial and in some ancient communities; consumption of LAB fermented foods products was associated with improved health. Currently there is a keen scientific interest in developed countries on health benefits obtained due to consumption of fermented food products. LAB has been shown to ameliorate immune-mediated health complications such as allergy, atopic dermatitis, rhinitis, oral-tolerance, cancer and inflammatory bowl diseases. Studies have also shown that consumption of LAB fermented food products can lead to control of cardio-vascular diseases and improvement of mental health. Prevention of antibiotic associated diarrhoea, reduction in lactose intolerance, production of conjugated linoliec acid, breakdown of phytic (an inhibitor of mineral absorption in the intestine) acids and improvement of gut-microbial balance have also been linked with increased consumption of LAB fermented foods. Besides, the enormous benefits of consuming LAB fermented food products, there are very few studies conducted to determine the efficacy of traditionally fermented African food products. If conducted such studies may lead to prevention/control of several health complications, reduction in health costs and improved income and livelihoods of communities producing such foods.

Key words: Lactic acid bacteria, probiotics, milk

Introduction

Description of lactic acid bacteria

The lactic acid group is currently composed of 13 genera of Gram-positive bacteria that includes; *Carnobacterium*, *Enterococcus*, *Lactoccoccus*, *Lactobacillus*, *Lactosphaera*, *Leuconostoc*, *Oenococcus*, *Pediococcus*, *Paralactobacillus*, *Streptococcus*, *Tetragenococcus*, *Vagococcus* and *Weissella*. [1] Lactic acid bacteria (LAB) are facultative anaerobes, non-sporulating, and acid tolerant. They are strictly fermentative and have complex, sometimes very fastidious nutritional requirements for carbohydrates, amino acids, produce large amounts of lactic acid and small amounts of other compounds are the products of their carbohydrates metabolism. [2] LABs are non-motile organisms with the exception of *Lactobacillus agilis* and the recently described species *Lactobacillus ghanensis* [3] and *Lactobacillus capillatus*. [4] The heterogeneity of this bacterial group is well expressed in their morphological traits, since they may appear rod or coccal shaped, in single cells or couple, tetrads and short or long chains. [5] LAB is divided into two groups based on the end products of glucose metabolism. Those that produce lactic acid as the major or sole product of glucose fermentation are designated homofermenters meanwhile those that produce equal molar amounts of lactate, carbon dioxide, and ethanol from hexoses are designated heterofermentative. [1] *Bifidobacterium* exists as a separate taxon (*Actinobacteria*) but given their similarities to the genus lactobacillus, bifidobacteria were included into the genus lactobacillus. [2] Bifidobacteria are strictly anaerobic, Gram-positive bacteria, and do not produce gas during its growth, though some *Bifidobacterium* spp. can tolerate O_2 in the presence of CO_2. [2] Bifidobacteria has a characteristic Y-shape, a GC content of about 55-67 mol% and poses fructose-6-phosphoketolase which cleaves fructose-6-phosphate into acetyl phosphate and erythrose-4-phosphate. [2]

LAB influence the flavour, texture, shelf life, nutritive properties, health attributes and commerical value of industrially and traditionally fermented foods. The genera most commonly used in industrial processes are *Lactococcus*, *Lactobacillus*, *Leuconostoc*, *Pediococcus*, *Oenocococcus* and *Streptocococcus*. LAB are normally used to ferment milk, meat, vegetables, cereals and wine and of recently there is keen interest in health promoting effects of LAB. Under the US Food and Adminstration (FDA) guidelines, LAB is generally regarded as safe (GRAS). Implying that they have been proven to be safe for human consumption through scientific procedures or through experience based on common use in food, as based on a substantial history of consumption by a significant number of individuals. [6] Among food fermentations, milk-based fermentations are common in many societies. In Rwanda, sour milk *(Ikivuguto)* is the most popular. Other fermented milk products widely consumed in Rwanda are *amacunda* (whey like product) and *Ikimuli* (traditionally fermented butter).

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Similar products are produced and consumed in African countries like Sudan, Egypt, Ethiopia, Kenya, Uganda, Namibia, South Africa, Zimbabwe, Nigeria and Morococo amongst others.

Although in many African communities it is widely believed that fermented milk products provide health benefits, there are extremely few carefully designed studies demonstrating the health promoting effects of these foods and or microorganisms found in the fermented products. Demonstrating the health promoting effects of LAB fermented foods could lead to increased consumption of fermented milk particularly from those sectors of the African communities that do no like fermented products. Therefore the purpose of this review article is to highlight the recent scientific reports demonstrating the health promoting effects of fermented milk products with the aim of encouraging researchers in Rwanda and the rest of Africa to conduct more studies on the efficacy of traditionally fermented milk products.

Application of lactic acid bacteria in health and disease

The tenet, "Let food be thy medicine and medicine be thy food" was embraced ~2500 years ago by Hippocrates, the father of medicine. However, this "food as medicine" philosophy fell in relative obscurity in the 19th century with the advent of modern drug therapy. In 1908, Élie Metchinkoff, proposed that the acid-producing organisms (lactic acid bacteria) in fermented dairy products could prevent fouling in the large intestine and thus lead to a prolongation of the life span of consumers. Later on the concept of probiotics was introduced and defined [7] as live microbial food supplements, which benefit the health of consumers by maintaining, or improving their intestinal microbial balance. The FAO/WHO definition which states that, "Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit to the host" [8] is the most acceptable at present. The concept of probiotics defines also the use of competitive exclusion for improving a specific ecology. [9] Probiotics are also referred to as functional foods. Functional foods are similar in appearance to conventional foods that are consumed as part of a normal diet and have demonstrated physiological benefits and/or reduce the risk of chronic diseases beyond basic nutritional functions. [10] To date application of probiotics in health has been widely embraced by food processors, nutritionists, medical practitioners and consumers. The fundamental reasons for the development and acceptance of fermented foods can be variably ascribed to preservation, improved nutritional properties, better flavour/aroma, upgrading of substrates to higher value products and improved health aspects. [11] The greatest potential application of LAB in human health relies on its ability to ameliorate immunologic diseases such as allergy, cancer, inflammatory bowel diseases (IBD) such as Chron's disease and ulcerative colitis. In addition, several scientific reports indicate that regular intake of probiotics can restore/maintain microbial balance in the gastrointestinal, uro-genital and respiratory tract which is important in preventing colonization of these niches when inhabited by pathogenic bacteria. Biotransformation of deleterious compounds in the Gastro Intestinal Tract (GIT) to less deleterious compounds and production of other useful compounds such as vitamins and short chain fatty acids (SCFA) by LAB have been reported to lead to improved health. The strong inhibitory effect against the growth and toxin production of most other bacteria [11] was suggested as one of the ways LAB prevents colonization of ecological niches within the human body. The antagonistic activity can be a result of competition for available nutrients, decrease in redox potential, production of acid (lactic acid and acetic acid) resulting in a decrease of pH, production of inhibitory metabolites (hydrogen perioxide and diacetyl) and production of antimicrobial compounds like bacteriocins and antibiotics. [11]

Requirements for lactic acid bacterial strain to be considered a Probiotic

Several properties of selected strains of LAB need to be ascertained in order for the strain to be considered a probiotic and these include;

a) The strain should be considered as GRAS. Thus the probiotic should be of human origin and genetically stable, but more crucial is that it needs to be intrinsically resistant to antibiotics, and the resistance should not be transmissible or inducible. [9] The main concern among lactic acid bacteria is the resistance to vancomycin, especially within the genus *Enterococcus* where the resistance as been shown to be transferable. Phage resistance aids in maintaining genetic stability of the strains.
b) The LAB strain should be able to survive and colonize the GIT. Therefore the probiotic strain should be able to withstand gastric acid and bile. The strains should also be stable against oxygen and enzymes such as lysozymes.
c) Selected LAB strains should be able to exert health promoting effects *in vivo.* Most important is that the efficacy of probiotics must be demonstrated in carefully designed and managed double-blinded, completely randomized and placebo controlled human studies.

d) The strain should be able to adhere to the gastrointestinal tract. This improves persistence and multiplication in the intestine and may promote competitive exclusion of potential pathogens from mucosal surfaces. [6]
e) Probiotics must have good technological properties so that it can be manufactured and incorporated into food product without losing functionality or creating unpleasant flavours. [12] They must be capable of being prepared on a large scale and in a viable manner since it is also very important for probiotics to be viable and active in the specific delivery vehicle. [6]
f) It is essential that probiotics sold with any health benefits meet the criterion of a minimum of 10^6 CFU/ml at the expiry date; because the minimum therapeutic dose per day is suggested to be 10^8-10^9 cells. [13]
g) Probiotics must be safe in food and during clinical use, even in immuno-compromised individuals. [6]

Immunomodulatory effects of lactic acid bacteria

Anti-allergic effects of lactic acid bacteria

Recent studies demonstrate a significant increase in the prevalence of allergic diseases (atopic dermatitis, asthma, allergic rhinitis, allergic eosinophiliac gastroenteritis and hay fever) in industrialized countries. T-helper1/T-helper2 (Th1/Th2) immunobalance has been reported to play an important role in controlling immune diseases including allergy, cancer and autoimmunity. [14, 15] Food allergies involve abnormal immunological responses to substances in foods regarded as harmless in healthy individuals and can be further subdivided into immunoglobulin E (IgE) and cell mediated hyper-sensitivities. [15] One theory of immunoregulation involves homeostasis (Fig. 1) between Th1 and Th2 activity. [16]

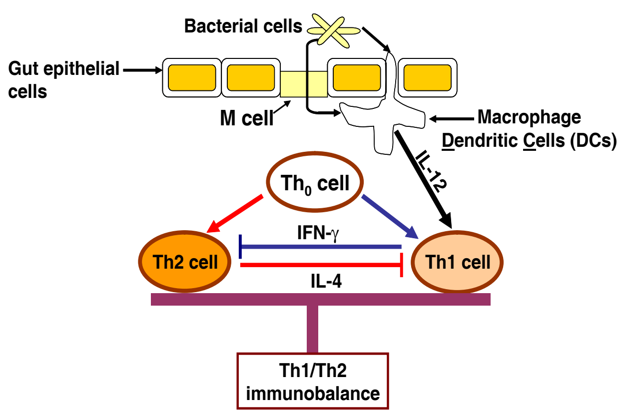

Figure 1: Th1/Th2 immunobalance.

LAB interacts directly with DCs that protrude between gut epithelial cells on indirectly through uptake of bacterial components by M-cells. Interaction between LAB and DCs results into production of IL-12 which enhances Th1 cell proliferation, IFN-γ production and polarisation of naive Th cells (Th_o) into Th1 phenotype. Production of Interferon gamma (IFN-γ) by Th1 cells in turn suppresses Th2 cell proliferation and production of Interleukin 4 (IL-4) which is associated with allergic responses.

Cytokines produced by immunocompetent cells, such as antigen presenting cells (APCs) and T lymphocytes, play significant roles in modulation of allergy. There is a significant positive relationship between eosinophilic infiltration, nasal obstruction, air flow and Th2-derived cytokines such as IL-4, IL-5 and IL-13 in patients with seasonal allergic rhinitis [17]. Furthermore, IL-4 promotes B lymphocyte production of Immunoglobulin E (IgE).[18] In contrast, Th1 lymphocytes secrete IFN-γ, which is responsible for skewing a predominantly Th2 immune profile towards a Th1 profile and acts on B cells to inhibit switching to IgE. [18] IFN-γ promotes the differentiation of naïve Th lymphocytes (Tho) towards a Th1 subset and prevents proliferation of Th2 lymphocytes. In addition, myeloid dendritic cell (DC) subsets have a capacity to produce IL-12 in response to microbial stimuli and, thereby, to induce Th1 development. [19]

The exact mechanism of interaction of LAB and immune cells is not yet well understood. However, there is substantial evidence that recognition of cell wall components (Fig. 2) of Gram-positive and Gram-negative bacteria by Toll-like receptors (TLR) on the surface of DCs is essential for bacteria induced DC maturation. [20]

Peptidoglycans, lipopeptide, are examples of bacterial membrane components that are recognized by DCs. [2-24] Lactobacilli may deliver signals in myeloid DCs through TLR-2, thereby promoting activation of these cells. [25] Because DCs are crucial for the induction of diverse Ag-specific immune responses such as oral tolerance and Th1/Th2 immunity, and bacterial colonization of the gut appears mandatory for development of competent immune function of the host, the presence of probiotic bacteria or components thereof during the development of the DC play a role in determining the outcome of the response. [26] Hence, alteration of the Th2 to Th1 balance in the immune system is considered to be an important strategy in control of allergic diseases.

Changes in the composition of the gut flora as a consequence of an altered life style and diet in industrialized countries may play a role for the higher prevalence of allergy. [27]

A model showing how LAB modulates the immune system is shown in Fig. 3. The model illustrates how *Streptococcus thermophilus* AHU1838 and *Lactobacillus. paracasei* subsp. *casei* AHU1839 enhanced expression of cell surface molecules on dendritics cells which is important for differentiation of naïve T cells towards a Th1 phenotype and inhibition of differentiation of naïve T cells towards a Th2 phenotype. Additionally the selected LAB enhanced production of IL-12 which enhances Th1 cell proliferation and IFN- production. There is mounting evidence that LAB play a key role in modulation of allergy. In a study comparing the intestinal microflora of allergic and non-allergic Estonian and Swedish 2-year-old children, allergic children were less often colonized with lactobacilli and bifidobacteria, as compared with non-allergic children. [28]

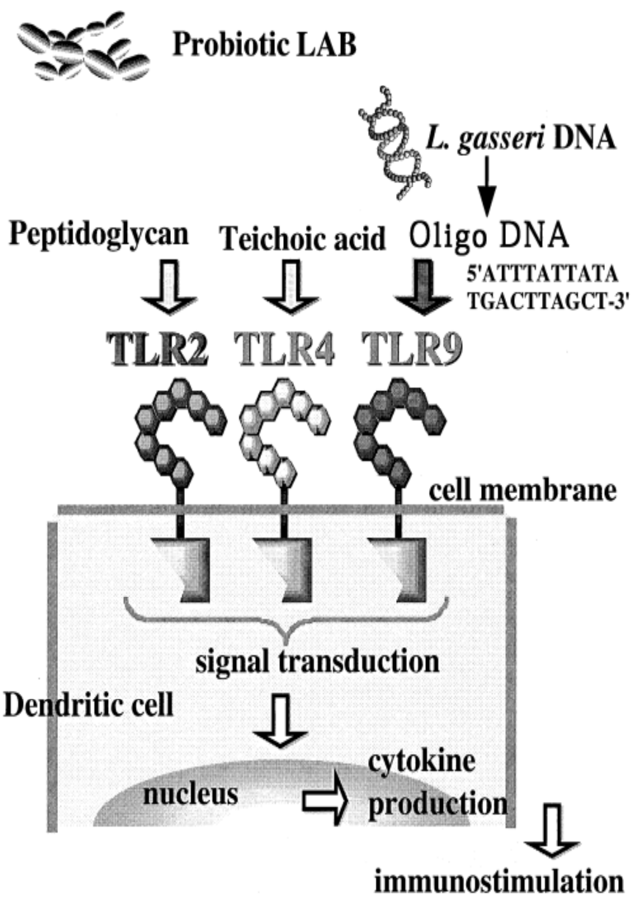

Figure 2: Estimated pathway of immunostimulation reaction by peptidoglycan, teichoic acid and oligo DNA motif from Lactobacillus gasseri (Adopted from Saito, 2004 [21])

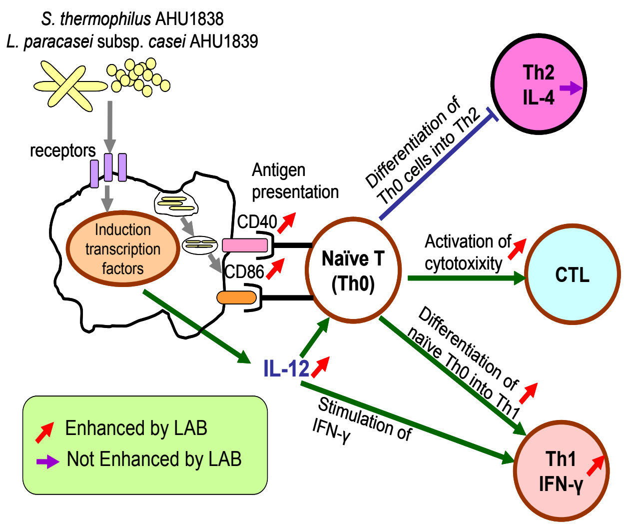

Figure 3: Immuno-modulatory effects of Streptococcus thermophilus AHU1838 and Lactobacillus paracasei subsp. casei AHU1839.

It was also confirmed that lactic acid microflora were more common in Estonian children [28] that have been reported to show less symptoms of allergy. Non-allergic, as compared to the allergic infants had higher levels of propionic, i-butyric, i-valeric and valeric acid in their faeces. [27] The allergic infants had higher levels and a high relative distribution of i-caproic acid in faeces. [27] The higher levels of i-caproic acid among the allergic, as compared to non-allergic infants may therefore indicate a disturbed gut flora with higher counts of *C. difficle* in the former group. [27] High levels of propionic acid have been associated with the presence of LAB in the GIT. Thus the lower levels of propionic acid in faeces from allergic, as compared to non-allergic children may indicate lower counts of lactobacilli. [27]

Effects of lactic acid bacteria intake on atopic dermatitis

Atopic dermatitis is a chronic inflammatory skin disease associated with IL-4 mediated IgE synthesis. Foetal immune responses are constitutively Th2-skewed, and this type of immune responsiveness is considered pivotal in the development of atopy and atopic disease. In a study conducted [29] in children aged 3 it was found that those with eczema had a lower *Bifidobacterium* population in GIT. This indicates that *Bifidobacterium* may play an important role in prevention of eczema in children. In a double-blinded, placebo-controlled trial, [30] involving 159 pregnant women who were fed with *Lactobacillus rhamnosus* GG (ATCC 53103; daily dose 2 X 10^{10} CFU/ml), it was found out that in a subgroup of infants (n = 19) in whom the umbilical cord blood

IgE concentration was above the detection limit (≥ 0.5 kU/l), the concentration of Transforming Growth Factor (TGF)-β2 in the breast milk of probiotic treated mothers was 5085 pg/ml compared with 1138 pg/ml in the case of mothers who received placebo. In another experiment, administration of *L. rhamnosus* GG at 10^{10} CFU/ml twice daily for 4 weeks to nine children aged 7-42 months with atopic dermatitis and cow's milk allergy was found to increase IL-10 levels at late stage. [31] IL-10 inhibits its own cytokine synthesis and synthesis of IL-2, IL-4, IL-6, IL-12, TNF-α and IFN-γ. [32, 33] The anti-CD3 stimulated cultures from these three patients showed a transient up regulation in IFN-γ production in early samples. In patients with atopic asthma who may have diminished IL-10 production, induction of IL-10 is thought to be more advantageous by reasons of its antagonistic effect on eosinophilic inflammation and IgE–dependent activation [32] reduced to a better health score in patients suffering from dermatitis. Administration of probiotics to mothers during pregnancy and breast-feeding appears to be a safe and effective mode of enhancing the immuno protective potential of breast milk and preventing atopic eczema in infants.

Effects of lactic acid bacteria intake on amelioration of milk allergy

Milk allergy affects 1.9% to 2.8% of young children. They may be sensitized to various proteins, mainly bovine β-lactoglobulin (BLG) and casein. Orally administered proteins are subject to degradation in the gastrointestinal tract by digestive enzymes (pepsin, trypsin, and chymotrypsin) and intestinal bacteria. [34] Probiotics colonizing the gut have been shown to contribute to this degradation. The suppression of lymphocyte (Th1 and Th2) proliferation by bovine caseins hydrolysed by *L. rhamnosus* GG enzymes in vitro has been reported, suggesting a potential effect of this strain in the oral tolerance.

Effect of lactic acid bacteria intake on allergic rhinitis

Allergic rhinitis is a common chronic inflammatory disorder and may be mediated by T helper (Th) lymphocytes expressing a Th2 type [35] conducted a randomized, double-blinded, placebo controlled study involving 80 subjects. After intake of a fermented drink (LP-33) containing *Lactobacillus paracasei* (1 X 10^7 CFU/ml) for 30 days, there was improvements in the level of bother caused by nose symptoms and the score for the overall quality of life decreased. A similar clinical study was conducted to determine the effects of *Lactobacillus acidophilus* strain L-92 on allergic rhinitis. [36] Scores of swelling and colour of the nasal mucosa of the L-92 group decreased at week 6 and 8 of ingestion, but not significantly compared with the start date. [36] The anti-allergic effect of L-92 was observed during the later period of ingestion in this study, suggesting that L-92 influences host immune status at a slow and steady pace. [36] It can be concluded that LAB consumption significantly improves the quality of life of allergic rhinitis sufferers but the improvement occurs at slow and steady pace.

Effects of lactic acid bacteria intake on induction of oral tolerance.

Oral tolerance is the specific suppression of cellular and /or humoral immune responses to an antigen by prior administration of the antigen by oral route. [37] Oral tolerance induction to commensal and dietary proteins represents the major immunological event taking place in the gut in physiological conditions. [37] Induction of oral tolerance occurs mainly through a class of T-lymphocyte cells known as regulatory T-cells (Treg). Tregs appear to control the development of autoimmune diseases and transplant rejection, and may also play a critical role in controlling allergic diseases including atopic asthma. [38] Recently, an alternative view has emerged that suggests the importance of reduced immune suppression rather than imbalances in Th1/Th2 cells population. According to this view, the lower microbial burden does not act by inducing a lower production of Th1 inducing cytokines but by decreasing the activity of Tregs. It was proposed that all types of microbial stimulation (both Th1 and Th2 polarizing) induce Tregs that control immune responsiveness through the production of immunosuppressive cytokines such as IL-10 and transforming growth factor-β (TGF-β). [39] These naturally occurring Tregs inhibit T cell proliferation in vitro, and they are important in the control of T-cell responses to self-antigens, thus preventing the development of autoimmune diseases. Most reports detailing the effects of LAB on Tregs are in relation to Treg cell-driven tolerance associated with production of IL-10 and TGF-β.

Anti-carcinogenic effects of lactic acid bacteria

Cancer is now becoming one of the leading causes of death in many parts of the world. Changes in life style have been closely linked with cancer. Unhealthy life style reduces natural killer (NK) cell and lymphokine-activated killer activity. Natural Killer (NK) cells are identified by their ability to kill susceptible lymphoid tumour cell lines in vitro without the need for prior immunization or sensitization. [40] NK cells are activated by cytokines such as IFN-γ and IL-12. A low NK cell activity increases the risk of cancer development. Drinking fermented milk containing *L. casei* strain Shirota by healthy individuals with relatively low NK cell activity resulted into a significant increase in NK cell activity 3 weeks after the start of intake and remained elevated for 3 weeks. [41] In human studies, LAB was reported to increase NK cell activity, which is important for cancer prevention. Similar findings were reported elsewhere whereby there was an increase in NK activity of 147% in subjects who consumed *L. rhamnosus* HN001). [42] The NK activity remained elevated for the next 3 weeks (p = 0.0221). These findings suggest that the continuous intake of the fermented milk containing *L. casei* strain Shirota is effective in augmenting NK cell activity in healthy people. The results further demonstrated that the effect of fermented milk is particularly prominent in individuals who have low levels of NK cell activity.

Anti-carcinogenic effects of lactic acid bacteria in the elderly

Many of the health issues faced by the elderly are linked to age-related decline of immune function (immunosenescence), leading to reduced ability to combat disease. A high proportion of the elderly has a predisposition towards Th2 phenotype expression, and has been reported to be deficient in NK cell activity. In 2001, Gill and others showed that the proportion of peripheral blood cells labelled singly for CD56 (a marker for NK cells) showed small but consistent and statistically significant increases following consumption of *L. rhamnosus* HN001 or *L. rhamnosus* HN019, while proportions of dual labeled T/NK cells did not fluctuate significantly. [43] Consumption of LAB-supplemented milk increased peripheral blood mononuclear (PBMC) cells tumoricidal activity of subjects who consumed HN001 and HN019 to 101 and 62% respectively. [43] The LAB-induced NK cell tumoricidal activity was significantly correlated with increasing age. The senescence of the immune system especially affects cell-mediated immunity with a decrease in lymphocyte proliferation capacity and IL-12 production and has been correlated with a marked decrease in bifidobacteria numbers in the gut. [44]

Anti-carcinogenic effects of lactic acid bacteria intake in habitual cigarette smokers

A reduction of NK activity was strongly associated with smoking, suggesting that recovery of NK activity in habitual smokers may be a valuable way of reducing risk of cancer. [45] The effect of intake of *L. casei* strain Shirota containing fermented milk was assessed by a placebo-controlled, double-blinded test using male smokers (20-60 years old). The results showed that intake of fermented milk containing *L. casei* strain Shirota improved NK cell activity while placebo did not.

Effect of lactic acid bacteria intake on bladder cancer

Bladder cancer is the 9th most common cancer in the world. In Japan the incidence of new cases is estimated to be 9,600 per year. Factors associated with bladder cancer include smoking and occupational exposure to chemicals. It was suggested that drinking Yakult and other fermented products prevented bladder cancer in control subjects, and that this effect was independent of age, sex and areas of residence. [46] Immunomodulation by *L. casei* Shirota may enhance the host immune system via stimulation of macrophages to produce IL-12, which would then stimulate helper T cells to differentiate, produce IFN-γ and promote cellular immunity against tumour cells. Immunomodulation may account for at least some reduction in risk, particularly among people who would otherwise be at a higher risk for bladder cancer because their immune systems are compromised by environmental factors.

Effects of lactic acid bacteria intake on colon cancer

Colorectal cancer is one of the most common forms of malignancy in developed countries and approximately 100 new cases of colorectal cancer are diagnosed daily in the United Kingdom. [6] The basis for the use of probiotics to inhibit cancer development in the colon would be the ability of some lactobacilli and bifidobacteria to lower the level of faecal enzymes implicated in carcinogenesis, and their ability to degrade nitroso-compounds. [9] Change in microflora composition is associated with an increase in faecal enzyme activity, β-glucuronidase, azoreductase, urease, nitroreductase and glycocholic acid reductase. [7] These enzymes convert procarcinogens into carcinogens and may thus contribute to an increased risk of colorectal cancer.

Effect of lactic acid bacteria on inflammatory bowl diseases

Ulcerative colitis, Chron's disease and pouchitis are considered as inflammatory bowl diseases (IBD). The disease is characterized by acute non-infectious inflammation of the intestinal mucosa and submucosa and is usually associated with diarrhoea and rectal bleeding with an excess production of mucus. [6] In western countries the number of individuals suffering from IBD is increasing. Although the aetiology of IBD is unknown, genetic and environmental factors may be involved in IBD pathogenesis. Gut microbial imbalances such as a decrease in microbial diversity and increase in the population of Gram-negative bacteria has been associated with IBD. Probiotics do not cure the disease, but once patients are in remission through treatment with corticosteroids, some probiotics can prolong the remission period, thus reducing the incidence of relapse and the use of corticosteroids leading to improved quality of life of patients. [48]

Other health benefits associated with probiotic strains of lactic acid Bacteria

Prevention of antibiotic-associated complications.

Whereas the discovery and use of antimicrobial agents has been one of medicine's greatest achievements, frequent and lengthy use of antibiotics usually results in alteration in the complexity of the intestinal commensal flora. [49] Reduction in diversity of intestinal microflora can lead to proliferation of opportunistic and deleterious microbial species such as *Candida albicans* and *Clostridium defficle*. Prescribing antibiotics with probiotics could be one of the avenues of prevent colonization of the gut by opportunistic and deleterious microbial strains.

Furthermore intake of probiotics after operation has been shown to improve the immunologic conditions of the patients. In a randomized controlled trial involving perioperative and postoperative biliary cancer subjects who are taking a symbiotic product containing *L. casei* strain Shirota and *B. breve,* had increased NK cell activity, while IL-6 levels decreased after intake of the symbiotic. [50]

Lactose intolerance

More than half of the world's adult population is lactose intolerant. [51] Lactose malabsorption is a condition in which lactose, the principal carbohydrate of milk, is not completely hydrolysed into its component monosaccharides, glucose and galactose. [48] Since lactose is cleaved into its constituent monosaccharides by the enzyme β-D-galactosidase,lactose malabsorption results from a deficiency of this enzyme. [48] The disaccharide lactose can cause severe intestinal distress, characterized by bloating, flatulence and abdominal pain in subjects with low levels of β-galactosidase. [9] The condition increases in severity with age and restricts the use of dairy products. [9] Probiotics can be useful in this condition, as lactobacilli produce lactase, which hydrolyzes the lactose in dairy products. [9] Hydrogen peroxide, the marker for bacteria metabolism of lactose in the large bowel has been shown to be significantly lower in subjects treated with fermented milk than in the group treated with non-fermented milk.

Reduction of high blood pressure and cholesterol

A high serum cholesterol concentration is generally considered as high risk factor in the development of cardiovascular disease. [11] Fermented foods may reduce the serum cholesterol concentration by reducing the intestinal absorption of dietary and endogenous cholesterol, inhibiting cholesterol synthesis in the liver [11] or by deconjugation of bile acids which are eventually excreted in the faeces. Enhanced excretion of bile acids results into reduction in cholesterol levels in the body. Feeding of fermented milk containing very large numbers of probiotic bacteria (10^9 bacteria g/l) to hypercholesterolaemic human subjects has resulted in lowering cholesterol from 3.0 to 1.5 g/l. [48] Probiotic bacteria are reported to de-conjugate bile salts: deconjugated bile acid does not absorb lipid as readily as its conjugated counterpart, leading to a reduction in cholesterol level. [48]

Hypertension is a risk factor for cardiovascular diseases, including coronary heart disease, peripheral arterial disease, and stroke. [52] The cardinal factor in the controlling arterial blood pressure is the rennin-angiotensin-aldosterone-system. Rennin, a proteolytic enzyme is synthesized and stored in the kidney. It hydrolyzes angiotensinogen to angiotensin I, an inactive decapeptide. [53] Angiotensin I is then acted on by a second proteolytic enzyme, angiotensin converting enzyme (ACE), producing the potent octapeptide, angiotensin II which reacts with specific receptors on adrenal cortical cells, leading to the release of aldosterone. [53] Aldosterone release results into retention of sodium, excretion of potassium leading to increased water retention in body and hypertension. Moreover, ACE catalyzes the inactivation of bradykinin, which has an important vasodilation activity. [54] Soluble fraction of milk fermented with a mixture of *Streptococcus thermophilus* CR12, *Lactobacillus casei* LC01 and *Lactobacillus helveticus* PR4 was found to inhibit 82% of ACE in vitro. Therefore, ACE plays an important role in the regulation of arterial blood pressure and inhibition of this enzyme can generate an antihypertensive effect. [54] Drugs that have ACE-inhibitory activity are often used to control arterial blood pressure. LAB has been successfully applied to produce fermented food products that can control blood pressure. In both cases, the peptides Ile-Pro-Pro (IPP) and Val-Pro-Pro (VPP) have been identified as responsible for most of the ACEI activities of these fermented milk samples. [54] Several commercial products containing highly proteolytic strains of *L. helveticus* have been developed and marketed as possessing hypotensive activity, including Calpis® and Evolus®. [48]

Production of vitamins and bioactive compounds

Conjugated linoleic acid: Conjugated linoleic acid (CLA) is a mixture of structurally similar forms of linoleic acid (cis-9, trans-11 octadecadienoic acid). Yoghurt has been shown to have a higher concentration of CLA, a long chain biohydrogenated derivative of linoleic acid. [56] CLA was reported to have immunostimulatory and anti-carcinogenic properties. [57]

Biotransformation of soy isoflavones: Soya beans have the highest concentration of isoflavones. Isoflavones are phytochemicals that exist in two basic categories, the aglycones and the glucosidic conjugates. [58] The main glucosidic isoflavones are daidzin and genistin, and the main aglycones are daidzein and genistein. [58] Isoflavones in soya in form of glucoside conjugates are poorly bioavialable. LAB has been shown to poses β-Glucosidases that can break β-glucoside linkages in glucosidic isoflavones enhancing bioavailability of the soy isoflavones. Phytoestrogens in soy products was reported to have anti-carcinogenic effect and their ant-ioxidative property may help in preventing oxidative damage in tissues. Isoflavones in soy proteins are conjugated with sugars. [59] The β-glucoside forms are not absorbed and require hydrolysis for bioavailability and subsequent metabolism. Hydrolysis of isoflavones takes place in the gastrointestinal tract by action of gut microflora. The β-glucosidase enzymes produced by *Lactobacillus acidophilus*, *Bifidobacterium lactis* and *Lactobacillus casei* were responsible for the breakdown of β-1-6 glucosidic bond, which conjugates the pran ring of isoflavone and the sugar moieties. [59] The breakdown of isoflavone glycosides into sugar moieties and bioactive isoflavone aglycones during fermentation could improve the biological activity of soy milk. [59]

Production of bioactive peptides: Milk proteins are considered as the main source of a range of biologically active peptides (bioactive peptides) defined as specific protein fragments that have a positive impact on body functions or conditions and may ultimately influence health of humans with moderate hypertension. [60] Many bioactive peptides are encrypted within the primary structure of milk proteins, requiring proteolysis for their generation from precursors. [55]

Production of γ-Aminobutyric acid: Gamma-aminobutyric acid (GABA) is a major neurotransmitter widely distributed throughout the central nervous system. [61] Low GABA levels or decreased GABA function in the brain is associated with several psychiatric and neurological disorders, including anxiety, depression, insomnia, and epilepsy and studies indicate that GABA can improve relaxation and sleep. [61] LAB has the capacity to synthesize GABA from L-glutamate through glutamate decarboxylase activity. [5] Naturally GABA is produced via a fermentation process that utilizes *Lactobacillus hilgardii*. [61] *Lactobacillus hilgardii* was identified in traditionally fermented butter similar to *ikimuli*. [62] It is more likely that there is more GABA in *amacunda* than in ghee because heat clarification of butter to make ghee may result into losses in GABA.

Breakdown of phytic acids: Phytic acid, the major anti-nutritional factor that blocks the availability of minerals in soy beans decreases during fermentation because of the action of phytase enzyme. [63] LAB is a major source of this enzyme, as it degrades phytate into myo-inositol and phosphate during fermentation.

Application of lactic acid bacteria in modulation of gut microbial balance

A deranged gut environment has increasingly been recognized as a source of allergic and autoimmune disease, as well as acute and chronic infection particularly in patients undergoing advanced medical and surgical treatment and in patients suffering from various acute diseases. [63] Probiotics can re-establish the lost balance by adhesion to epithelial cells, competing for nutrients, modifying pH and producing antimicrobial substances. [9] It was revealed that faecal microbial composition in healthy adults could be changed by consuming yoghurt with a trend toward a general improvement in gastrointestinal health. [64] Quantitative analysis of faecal samples after yoghurt intake showed a clear reduction in the *Bacteroides* population and a concomitant increase in LAB population. [65] The increase was higher in the group of subjects that initially presented a low density of these organisms. [65] It can be concluded that consumption of yoghurt can lead to modulation of the GIT microbial balance.

Previous studies on African traditional foods

Scientific studies have reported the prescence of enterococci, lactobacilli, lactococci, and streptococci, in African traditional dairy products such as kule naoto, samin, ergo, nyarmie and omashikwa amongs others. [62, 66, 67, 68, 69, 70, 71, 72] Hence it is highly likely that these products could be possesing probiotic effects. For instance, Lactobacillus strains isolated from Maasai traditional fermented milk 'kule naoto' were resistant to gastric juice and bile. [73] Moreover, *L. acidophilus* strains isolated from 'kule naoto' expressed bile salt hydrolase activity and ability to assimilate cholesterol. [73] Several studies have revealed that Maasai pastoralist have low rates of coronary heart diseases despite a diet high in saturated fat. [74] Though not yet clearly clarified, the high consumption rates of fermented milk products amongst the Maasai may be contributing but not entirely on the health of the Maasai. In many parts of Nigeria, nursing mothers do give their babies' ogi liquor (water from fermented cereal pulp) and this causes the termination of their illness. [75] Adebolu *et al.* evaluated the antibacterial activities of ogi liquor from different grains against some common diarrhoeal bacteria in southwest Nigeria and discovered the inhibition of the pathogens by the ogi liquor which contains a variety of organisms including *Lactobacillus* species. [76] In Sudan milk is the traditional weaning food and food for young children. [67] In Sudan the tradition of rural Sudanese nothing parallels a bowl of sorghum or millet porridge consumed with milk, until recently the standard dinner of the average Sudanese. [67] Scenarios similar to those described above exist in several communities in Africa implying the concept of probiosis and synbiosis could have existed in African cultures for centuries. The missing linkage is the application of start-of the-art technologies in describing the efficacy and mode of action of traditional African milk products.

Conclusion

LAB is one of the major inhabitants of the human gastrointestinal tract and is commonly used in fermentation of various kinds of food products. Furthermore there is mounting scientific evidence that LAB fermented food products positively influence the health of humans. Fermented food products such as *ikimuli* (Rwandan traditionally fermented butter), *amacunda* (Rwandan whey like product during traditional butter fermentation process), *ikuvuguto* (Rwandan sour milk) and *ubushera* (a fermented sorghum product of Uganda) are commonly consumed in Rwanda, Burundi and some parts of Uganda. However very few studies have been conducted on identifying and determining mechanism of action of health-promoting compounds in LAB fermented products in Africa. Health problems such as diarrhoea, lactose intolerance, and cancer amongst others are common in many African societies. Therefore, consumption of fermented food products could result into improved health in many low income communities in the developing world.

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