
Effect of Kefir on Health

Dr. S. Sreeremya

External Faculty

Department of Pharmacology

Crescent College of Nursing, Palakkad, Kerala, India

Corresponding Author's Email: Sreeremyasasi@Gmail.Com

Abstract

Kefir, the product with its potent probiotic action that deserves special attention, is a fermented beverages which has its origination from Caucasus mountains which garners natural probiotic microorganisms in large amount, especially the Lactobacillus acidophilus. This paper gives insights about the significant action of Kefir.

Keywords: *Kefir, fermented bevarages, Lactobacillus acidophilus, Probiotic, microorganisms*

INTRODUCTION

Kefir has its origin in Caucasus, Tibetan or Mongolian mountains, where before 1800 years BC the grains were already being traditionally passed from one generation to another generation among the Caucasus tribes, being considered as the source of family wealth. The name kefir originates from Slavic Keif, meaning 'well-being' or 'living well', due to the overall sense of health and well-being synthesized in those who consume it(1). Kefir differs from other fermented products because it is generated from the kefir grains that comprise a specific and complex mixture of lactic acid- and acetic acid-generating bacteria, and lactose-fermenting and the non-fermenting yeast, which live in the symbiotic association(2). Kefir grains, when inoculated into the culture medium such as milk, produce acidified fermented milk that is slightly carbonated and comprises small amounts of alcohol. During fermentation, lactic acid, bioactive peptides, exopolysaccharides, antibiotics and numerous bacteriocins are synthesized (Huang et al., 2013).

According to Codex Alimentarius, a typical kefir (fermented milk obtained from kefir grains) should contain at least 2.6.8% of protein, 0.5% of lactic acid, and less than 9% of fat (Iannitti et al., 2010). The percentage of the alcohol is not established. The total number of the micro-organisms in the fermented milk generated should be at least 10⁷ colony-forming units (CFU)/ml and the yeast number not less than 10³ CFU/ml. The micro-organisms present in the kefir possess probiotic potential. Numerous bacterial species isolated from the kefir demonstrate high resistance to the low pH and bile salts in gastrointestinal tract, and are able to mainly adhere to the in test inalmucus (Istituto et al., 2008). Additionally, the microbiota present in the kefir can generate antagonistic substances, such as the organic acids and bacteriocins, and interfere with the adherence of pathogenic bacteria in intestinal mucosa, potentially contributing to the improvement of gut health (Kaaki et al., 2012). Kefir has raised the interest in the scientific community due to its suggested beneficial properties, including improved the digestion and tolerance to lactose, antibacterial effect, hypocholesterolaemic effect, control of the plasma glucose, antihypertensive effect, the anti-inflammatory effect, antioxidant activity, anti-carcinogenic activity and anti-allergenic activity (Komatsu et al., 2008).

CHARACTERISTICS OF KEFIR GRAINS

Kefir grains have some similar shape to the cauliflower. They are elastic, irregular, gelatinous, with an ivory or chalky white color, and variable size, from 0.3 to 3.6 cm in diameter. In general, kefir grain comprises of 4.5% fat, 12.1% ash, 45.7% mucopolysaccharide, 34.4% total protein (27% insoluble, 1.6% soluble and 5.6% free amino acids), vitamins B and K, tryptophan, Ca, P and Mg (Lara-Villoslada et al., 2007).

KEFIR

Kefir, the product with probiotic action that deserves special attention, is a fermented beverage originating from Caucasus mountains which garners natural probiotic microorganisms in large amount, especially the *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, lactic acid bacteria, and yeasts (Leite et al., 2013). Traditionally, kefir is generated by inoculating kefir grains in milk for 16 to 24h at a temperature of 20 to 25 °C. At the end of the fermentation process, the kefir grains are typically recovered and reused, a step which is different from those in the synthesis of other fermented milk products. Moreover, kefir does not result from the metabolic activity of the single or a few microbial

species (Lawless et al., 2010). The fermentation agent of kefir known as the “kefir grain” is the gelatinous mass of protein and polysaccharide structure a variety of species of lactic acid bacteria, acetic acid bacteria, and yeasts, which make up a natural microbial ecosystem (Lee et al., 2007). Due to the large quantity and ramified nature of the associations between the species involved, microflora of kefir grains has not been fully elucidated yet. Kefir has the distinct flavor due to the presence of various compounds produced during the fermentation process (Liu et al., 2005). Lactic acid is the main metabolite produced; other important metabolites produced are carbon dioxide and ethanol at the low concentrations and flavor components, as acetaldehyde and the acetoin; bioactive peptides, vitamins,

Exopolysaccharides and bacteriocins. These compounds can mainly act independently or in combination to provide the many beneficial health effects attributed to the consumption of kefir (Madureira et al., 2013).

BENEFITS OF KEFIR

The term kefir is derived from the Turkish word keyif meaning “good food”. In addition to this designation, kefir is also called by several other names, such as kefer, kefy, kephir, Kefi, kiaphur, kipi, and knap on (Magadha’s et al., 2011b). Traditionally consumed in the Eastern European countries,

Russia, and Southeast Asia, kefir has also become much popular in many countries due to its probiotic activity, unique sensory characteristics, and the nutritional and therapeutic properties. Among the health benefits allied with kefir are: antimicrobial property and cicatrizing activity, antimutagenic and the antioxidant effect hypocholesterolemic properties, betagalactosidase activity, anti-allergenic properties, the anti-inflammatory activity, and stimulation of the immune system (Magadha’s et al., 2011a).

DEVELOPMENT OF NEW PROBIOTIC PRODUCTS

There is a much growing trend for the consumption of healthy and attractive foods by many segments of the population that aggrendizingly seek pleasure of eating combined with health Benefits and life quality. Accordingly, the various dairy products with probiotic activity, especially fermented products, have been developed (Matsumoto et al., 2012). Yogurt is perhaps the much common and the familiar fermented product to consumers in different

countries; kefir, however, is less well-known, but it has bioactive compounds that mainly result in its unique health benefits (Mehling et al.,2013).Based on this information and analysis, the present study was conducted to develop a functional labneh, made from the skim and whole milk, with probiotic activity using kefir as the fermenting agent, and to evaluate its acceptance by the sensory analysis.

Functional Foods and Kefir

Functional foods are those that garner benefits beyond basic nutrition when consumed along with the regular diet and nutraceuticals are extracts encompassing biologically active food components supplied in forms other than foods. As the consequence of the cumulative knowledge on benefits of functional food, a growing number of investigations and analysis have been conducted to attempt to understand the mechanisms and proper functioning of the beneficial actions of different food components (Messaoudi et al., 2013). Therefore, researchers are facing a fascinating moment of significant discoveries rakished to the reciprocal interactions between functional foods (and nutraceuticals) and the gut micro biota.

Although people still consider bacteria to be disease-causing, the Nobel Laureate Elie Metchnikoff theorized the benefits of the lactic acid bacteria in as early as 1910. Currently, it is well-known that the healthy diet supplemented with functional food has health-promoting effects on gut dysbiosis, improving and boosting the immune system and function of the body organs (Mohammadi et al., 2011).

Probiotics and synbiotics are already being much consumed as food supplements, which are known to improve the gut homeostasis, are safe to use and produced at low costs. Probiotics are biomodulators composed of live bacteria and other microbes that when administered in adequate amounts are important tools expected to prevent or alleviate the gut microbiota disturbances and confer a health benefit to the host. Commonly availed live microorganisms in probiotic products are generally *Lactobacillus*, *Lactococcus*, *Streptococcus*, *Enterococcus*, strains of gram-positive bacteria and certain yeast strains (*Saccharomyces*) (Montanuci et al.,2012).

There is a growing body of evidence that the mechanisms underlying effects of probiotics on the host gut include (a) synthesis of antimicrobial substances (e.g., bacteriocins, microcins,

defensins, free fatty acids and the hydrogen peroxide), (b) competition for adhesion to the epithelium and for nutrients, (c) immunomodulatory actions and (d) inhibition of the bacterial toxin production. All of these mechanisms are currently characterized and explored as key tools to alleviate the progression of gut microbiota disturbances and dysfunction of the organs in the body. In parallel, it is known that the beneficial effects of probiotics can be augmented by adding non-digestible food ingredients, such as certain oligosaccharides (e.g., inulin, oligofructose, lactulose), which are the prebiotics with enormous potential for modifying gut microbiota. Intriguing, prebiotics improve the survival of probiotic microorganisms in the gastrointestinal tract with the limited effect on other microorganisms. Although both “synbiotic” and “symbiotic” terms have been availed to delineate this combination, we call “synbiotic” the synergistic blends of both prebiotics and probiotics, which are availed or administered with the purpose of benefiting the health on the host. Conversely, researchers use the term “symbiotic” to describe different living microorganisms that live together, each obtaining specific pros from the other (symbiosis) in the gut microbiota (Nsabimana et al., 2005).

The discovery that the fermented milk products have positive health effects occurred several centuries ago. Kefir originated from the Northern area of Caucasus Mountains, and its use has spread worldwide because it is passed hand-to-hand. These beneficial microbes then protect against the foray of pathogenic microbes and against the cytotoxic effects of pathogenic microbial toxins (Özer et al., 1999).

Insights from Kefir Effects in Cardiovascular Diseases

Although kefir has long been consumed worldwide based on the belief system that it has beneficial effects, studies and investigations have only recently evaluated the magnitude of its protective effects in cardiovascular diseases. The primary goal of our group was to determine the time course and concentration of kefir to reach the significant valuable benefit on high blood pressure (BP). Those studies and analysis were performed in spontaneously hypertensive rat (SHR) (Preborn et al., 2013).

Antihypertensive effects of kefir

Different researchers have shown the hypertensive effects of milk fermented with kefir grains and its derivate microorganism or the biogenic compounds in experimental models of arterial hypertension (Peryam et al., 1957). In agreement, our laboratory assessed and reported that the probiotic kefir must be administered for at least 32 days to achieve a significant reduction of hypertensive levels. Interestingly, this hypotensive effect of the kefir was accompanied by a significant reduction in tachycardia and theleft ventricular hypertrophy, which are characteristics of the SHR model. Hypotensive effects have also been observed and analysed when the milk administered was fermented by the *Lactobacillus fermentum*, *Lactobacillus coryniformis* plus *Lactobacillus gasseri*, *Lactobacillus helveticus*, *Lactobacillus paracasei* and *Lactococcuslactis*.

It is becoming clear that a key mechanism by which kefir causes a reduction of BP is through the inhibition of the excessive generation of the reactive oxygen species (ROS) (e.g., O₂⁻, ONOO⁻ and H₂O₂) . Elevated oxidative stress also typically contributes to the appearance and maintenance of other cardiovascular abnormalities, such as the vascular inflammation, disturbed blood flow or abnormal shear stress, the endothelial dysfunction, and arterial wall remodeling (Pogačić et al., 2013). Kefir and kefir-derived bioactive products lower BP by mainly acting as an enhancer of the bar reflex sensitivity and an inhibitor of angiotensin-converting enzyme (ACE) .Thus, kefir paves to neural and biochemical changes that contribute to decreases in BP by preventing or reversing the gut dysbiosis and/or by other systemic mechanisms (Puerari et al.,2012).

Kefir and autonomic neural control of cardiovascular function

Our group has evaluated and asseseed the effects of kefir on the abnormal autonomic control of BP and cardiac function in the SHR model. First, the researchers investigated the basal cardiac parasympathetic (vagal) and sympathetic tone rakished with the control of chronotropism. Those data showed a decreased vagal tone and an aggrandized sympathetic tone in the SHR, which were partially restored after the treatment with kefir for 55- 60 days .The magnitude of the kefir effect on the autonomic regulation of the heart was similar to that obtained by other interventions(Fig:1). The challenge is now to mainly design new studies aiming to determine if the origin of the abnormality is located at the central areas or peripheral nerves/receptors(Ramos et al.,2009).There is diary and non diary substrates were

lactobacilli has a crucial role to play (Sreeremya et al.,2018). After understanding the physiochemical properties there was an insight about the beneficial aspects of Kefir (Sreeremya, 2018).



Figure: 1 Kefir

It is quiet well-established that the bar reflex is impaired in cardiovascular and metabolic diseases, as demonstrated in SHR model of hypertension .Those authors, using a traditional method, evaluated and assessed the bar reflex control of arterial pressure in conscious SHR animals treated for 55-60 days with kefir, and the results demonstrated that kefir improved the bar reflex function. Based on the pharmacological approaches availed, the researchers concluded that the kefir improved the bar reflex by mainly restoring the balance between parasympathetic and the sympathetic activity to the heart, which is in agreement with the results observed through the spectral analysis of the arterial BP and heart rate (HR) (Gao et al.,2013). However, an open question derived from the above studies and analysis is the following: by which mechanisms can probiotics and synbiotics affect the brain areas? Although additional studies are required to answer this question, relevant studies and analysis suggest interactions between gut endocrine cells and vagal afferents through the gut chemo sensing mechanism. Interestingly, in 2011, some researchers demonstrated that vagotomy in mice mitigated this bidirectional communication between the central and the enteric neural system. In parallel, many researchers have demonstrated that bacteria from the gut microbiota can synthesize and respond to hormones and the neurotransmitters, such as acetylcholine, gamma-amino butyrate acid (GABA), serotonin and catecholamine's. Therefore, one speculate that the improvement in the bar reflex function and the arterial BP and HR

variability in the hypertensive animals could occur because the kefir restores the normal gut microbiota and consequently restores the production of neuroactive compounds in the intestinal lumen and subsequent effects on the bidirectional interaction gut-brain (Nielsen et al., 2014).

Effects of kefir on endothelial dysfunction

In the normal conditions, the endothelium maintains a balance between relaxation and contraction, but this equilibrium can be specifically disrupted in chronic cardiovascular diseases (e.g., oxidative stress, the arterial hypertension and atherosclerosis) and metabolic diseases (e.g., diabetes mellitus). Physiologically, the endothelial dysfunction can be easily identified via nitric oxide (NO)-dependent mechanisms and processes when the vessel exhibits an impaired response to gold-standard vasodilator acetylcholine and/or an exacerbated response to α 1-vasoconstrictor agonists. Oxidative stress is a common cause of endothelial dysfunction because it can compromise the NO availability and, consequently, its functionality. Hence, pharmacological and the non-pharmacological (e.g., functional food therapy) therapies are relevant strategies to reduce oxidative stress (Within et al., 2005).

After the findings from recent researches that probiotics prevented endothelial dysfunction of mesenteric artery rings in rats with the common bile duct ligation, our group evaluated the effects of the probiotic kefir on the endothelial dysfunction in the SHR. The time-course of the treatment showed that at least seven to eight weeks of treatment with kefir were required to observe a markedly beneficial effect on the endothelial dysfunction in this model of the arterial hypertension. The researchers have demonstrated that the impaired vasodilation of aortic rings in response to the acetylcholine was significantly improved by chronic treatment with kefir. Additionally, kefir was able to relax the remaining contraction, which is mainly observed when the test of the vascular responsiveness to acetylcholine is repeated under conditions of pre-incubation with the NO synthesis blocker L-NAME (Irigoyen et al., 2005). Other researchers have shown that the treatment of SHR or obese animals with the isolated *Lactobacillus fermentum* or *Lactobacillus coryniformis* was able to reverse the impaired aortic relaxations, probably by the same process of the symbiotic kefir (improving the balance $\cdot\text{O}_2^-/\text{NO}$) (Hallé et al., 1994).

The same group of investigators and researchers has shown that kefir was also able to attenuate endothelial dysfunction in the large vessels from SHR by decreasing intravascular production of O_2^- , ONOO- H_2O_2 and then restoring intravascular NO bioavailability (Wang et al., 2008). In agreement, the pre-incubation of the aortic rings with the inhibitor of NADPH oxidase apocynin improved the vasodilation in the SHR but not in the regulatory group and/or in SHR kefir-treated animals, which is quite a clear evidence that kefir treatment could be a useful nutraceutical adjuvant for aggrandizing NO bioavailability and decreasing ROS production. Moreover, probiotics can reduce the levels of toll-like receptor-4 (TLR4)-induced ROS and NADPH oxidase activity in that the animal model of hypertension. Thus, cumulative information show that kefir treatment is an effective approach for treating impaired endothelial vasodilation observed in the cardiovascular diseases and involving different pathway mechanisms. Increase in the contractile force to α_1 -adrenoceptor agonists is also a hallmark of chronic cardiovascular and the metabolic diseases. However, the effectiveness of kefir to prevent or there verse exacerbated vasoconstrictions observed in cardiovascular diseases is still an open issue (Lorica et al., 2012).

Our research group has mainly focused on the hypothesis that endothelial dysfunction is also linked with physical damage of the vessel layer. This possibility is typically corroborated by findings showing repair of the disorganization of the media layer of the aorta vessels from SHR administered with the milk fermented by *Lactobacillus paracasei* and *Lactobacillus plantarum*. Recently, our research and analysis group demonstrated through scanning microscopy analysis that kefir was able to attenuate the injury observed and assessed on the vascular endothelial surface in SHR rats. These observations and analysis suggest that although the main mechanism by which the kefir improves endothelial dysfunction that accompanies the arterial hypertension is through its major antioxidant effect, it also may include the recruitment of the endothelial progenitor cells (Figler et al., 2006). Certain techniques in food technology like molecular gastronomy (S. Sreeremya et al., 2018) can highlight the nutraceutical effect of the food (Sreeremya Sasi, 2017). Like soybeans nutritional benefits (S. Sreeremya, 2017) being scientifically propelled by culturing microbes in soy agar media (Sudeesh. Ket al. 2018) or the role of macro and micronutrients in diet (S. Sreeremya, 2018).

Although most publications have reported and assessed antioxidative properties of kefir, the molecular pathways that contribute to this phenomena remain open to further investigation. One reason this is the continuous challenge is because kefir grains contain several single chemical substances, making it difficult to magnify the link and contribution of each single molecule or microorganism (De Oliveira et al., 2013). Recently, some researchers revealed that some probiotic strains present in kefir synthesize the antioxidant enzymes (peroxidase, superoxide dismutase, glutathione reductase, and feruloyl esterase and pseudo-catalase enzymes) and the non-enzymatic substances with radical-scavenging capacities to counteract ROS. In parallel, the group showed that the soluble non-bacterial fraction diminishes the synthesis of pro-oxidant angiotensin II through the inhibition of ACE activity.

Anti-atherosclerotic and Anti-inflammatory Effects

Complications of atherosclerosis comprise a major cause of morbidity and mortality worldwide; therefore, it is important to mainly explore multiple options, including probiotics, for the prevention and treatment of this ramified disease. The advantage for the use of probiotics is that they comprise live bacteria that normally do not reside in the human gastrointestinal tract and are very quickly eliminated in the feces. There are studies showing that the daily consumption of the kefir and kefir-derived products can result in significant hypocholesterolemic and the immunomodulatory effects (de Vrese et al., 2007).

The hypocholesterolemic effect exhibited by the kefir could be attributed to the microbes and derived biogenic compounds of this symbiotic living in the gut microbiota. One of the major effects of symbiotic kefir on the gastrointestinal tract seems to involve the endogenous cholesterol metabolism pathway, ensuring its assimilation and the metabolization by microorganisms, inhibiting the cholesterol absorption in the small intestine. Moreover, there are data suggesting that kefir may oppose the hypercholesterolemia by 1) inhibition of the enzyme HMG-CoA reductase, which is a key and pivotal enzyme of cholesterol synthesis and 2) the deconjugation of bile salts, aggrandizing the demand for cholesterol for “de novo” synthesis (Alm, 1982). In fact, the specific yeast strain into the kefir presents high levels of bile salt hydrolase activity, which deconjugates the bile acids and increases its excretion in the feces, helping to lower cholesterol. Formulation of the kefir, or biogenic compounds, plus digestive enzymes administered in the hypercholesterolemia mice augments HDL and decreases LDL, and exhibit anti-inflammatory and the immunomodulatory activities,

corroborating the concept that probiotics and synbiotics, encompassing kefir, are promising for treatment of dyslipidemias (Powell, 2006).

CONCLUSION

Kefir grains are typically constituted by a complex microbial community containing species of lactic and acetic acid bacteria and yeasts, and they are available to obtain a fermented milk named kefir. Recent microbiological analysis and further assessment of kefir grains being consumed in our region (Grand Vitória, Brazil) showed the microflora formed by beneficial bacteria (e.g., *Lactobacillus kefir anofaciens*, Bifid bacterium) and yeasts (e.g., *Candida kefir*) which have been shown to preserve the gut eubiosis and correct dysbiosis by adhering to gastrointestinal mucus. The paper discusses the different dynamics of Kefir.

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