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Kefir: a new role as nutraceuticals

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ABSTRACT

Nutraceutical is the fusion of "nutrition" and pharmaceutical". This products, in broad, are food or part of food that provides medical or health benefits including the prevention and or treatment of a disease. Kefir is renowned nutraceutical dairy products produced through fermentation of bacteria and yeasts and naturally present in grains of kefir. The nutritional attributes are due to presence of vital nutrients such as carbohydrates, amino acids, proteins, minerals, phosphorus, vitamin, calcium, and certain biogenic compounds. Intestinal immunity, antimicrobial, anticarcinogenic, hypocholesterolemic effect, antibiabetic, effect on blood pressure level, antioxidant, wound healing, and lactose intoleran can be achieved using this products. The purpose of this review is to gather information about composition, methods of production, and therapeutic properties of kefir products to provide justification for its consumption. This review confirms that kefir can be a new role of nutraceutical products.

Nutraceutical merupakan perpaduan antara aspek "nutrisi (nutrition) dan farmasi (pharmaceutical)". Sediaan ini, secara luas, didefinisikan sebagai makanan atau bagian dari makanan yang memiliki manfaat terhadap kesehatan, yakni dalam hal pencegahan dan pengobatan penyakit. Kefir dikenal sebagai produk nutraceutical yang berasal dari fermentasi bakteri atau ragi yang secara alami terdapat pada tiap butiran kefir. Kandungan nutrisi pada kefir terdiri dari karbohidrat, asam amino, protein, mineral, fosfor, vitamin, kalsium, dan senyawa biologis lainnya. Imunitas saluran cerna, antimikroorganisme, antikanker, efek hipokolesterolemia, antidiabetes, efek terhadap penurunan tekanan darah, antioksidan, penyembuh luka, dan intoleran laktosa dapat ditangani dengan mengkonsumsi produk ini. Tujuan penulisan artikel ini adalah untuk mengumpulkan informasi terkait dengan komposisi, metode pembuatan, dan karakteristik terapi dari produk kefir pada saat digunakan. Artikel secara keseluruhan menegaskan bahwa kefir dapat berperan sebagai agen nutraceutical.

INTRODUCTION

Nutraceuticals are a diverse product category with various synonyms used internationally. The term nutraceuticals were coined from "nutrition" and "pharmaceutical" by Stephen Defelice MD, founder and chairman of the foundation for innovation in medicine (FIM) Cranford, New Jersy, in 1989. According to Defelice "nutraceuticals are food or part of a food that provides medical or health benefits including the prevention and/or treatment of a disease" [1,2]. Other words used in the context are dietary supplements, functional food, multi-functional food, etc. Functional foods are ordinary foods that have components,

ingredients that incorporated into giving them a specific medicinal or health benefit moreover nutritional effect [3].

NUTRACEUTICAL CATEGORIES

Due to minimal international regulations different types of products fall under the nutraceutical category. Because of this some of them have overlapping definitions. The most usual are herbals, dietary supplements, functional food and products labeled "nutraceutical". These can be grouped into the following three broad categories:

1. Nutrients: Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids.
2. Herbals: Herbs or botanical products as concentrates and extracts.
3. Dietary supplements : Reagents derived from other sources (e.g. pyruvate, chondroitin sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements and meal replacements [4].

Das et al.[5] also organize nutraceutical in several ways depending upon its easier understanding and application, i.e. for academic instruction, clinical trial design, functional food development or dietary recommendations. Some of the most common ways of classifying nutraceuticals can be based on food sources, mechanism of action, chemical nature etc. The food sources used as nutraceuticals are all natural and classified as:

1. Dietary Fibre
2. Probiotics
3. Prebiotics
4. Polyunsaturated fatty acids
5. Antioxidant vitamins
6. Polyphenols
7. Spices

KEFIR

Kefir (or known as kefiran) is an EPS classified as a heteropolysaccharide comprising glucose and galactose in high concentrations, and it is classified as a water-soluble gluco galactan, which makes it suitable to be used as an additive [6] (Fig. 1). Exopolysaccharides (EPSs) of microbial origin are long chain, high-molecular-mass water-soluble polymers which may be ionic or non-ionic and have potential applications in food industries as texturizers, viscosifiers, emulsifiers and syneresis-lowering agents due to their pseudoplastic rheological behaviour and water-binding capacity [7]. Kefiran has excellent rheological properties and can significantly improve the viscosities of lacteous products by favoring and maintaining gel properties and avoiding the loss of water during storage. With respect to the biological activity of kefiran, several studies have demonstrated that this EPS can be used as a nutraceutical [8].

Figure 1. Kefir structure [8]

Origin of kefir

Kefir is a viscous, slightly carbonated dairy beverage that contains small quantities of alcohol and, like yoghurt, is believed to have its origins in the Caucasian mountains of the former USSR. It is also manufactured under a variety of names including kephir, kiaphur, kefer, knapon, kepi, and kippi[9]. It is not clear whether all kefirs originate from a single original starter culture since microbial analyses of kefir samples taken from different locations indicate microflora population differences[10].

Kefiran, which is mainly produced by

homofermentative *Lactobacillus* species and yeasts, is a branched polysaccharide containing equal amounts of glucose and galactose. The kefir grain contains *lactococci, leuconostocs, thermophilic* and *mesophilic lactobacilli*, yeasts (lactose negative and lactose positive), and acetic acid bacteria. These microorganisms maintain a symbiotic life in kefir grain. In this microflora, there are lots of microorganisms such as *Lb. brevis, Lb. kefir, Lb. acidophilus, Lb. bulgaricus, Lb. casei, Lb. kefiranofaciens, Lb. helveticus, Lactococcus lactis subsp. lactis*, and *Lactococcus lactis subsp. Cremoris* [11]. Yeast was isolated from kefir were identified as *Kluyveromyces marxianus, Kluyveromyces wickerhamii, Saccharomyces cerevisiae, Pichia angusta, Pichia guilliermondii, Candida glaebosa*. *Kluyveromyces marxianus* was identified in the isolates from all the kefir samples, followed by *Kluyveromyces wickerhamii*. *Pichia angusta, Pichia guilliermondii, Candida glaebosa* [12].

Kefir production

The traditional way of producing kefir is using raw unpasteurized, pasteurized, or UHT treated milk. The milk is poured into a clean suitable container with the addition of kefir grains, the content is left to stand at room temperature for approximately 24 hours. The cultured-milk is filtered in order to separate and retrieve the milk grains from the liquid-kefir. This fermented milk is appropriate for consumption. The grains are added to more fresh milk and the process is simply repeated. This simple process can be performed on an indefinite basis, since kefir grains are a living ecosystem complex that can be preserved forever as long as it is feeded. As active kefir grains are continually cultured in fresh milk to prepare kefir, the grains increase in volume or in biological mass [13,14] (Fig. 2).

Dailin et al [15] found that the optimum medium for production was composed of (g/L): lactose, 50.0; yeast extract, 12.0; KH_2PO_4, 0.25; sodium acetate, 5.0; Triammonium citrate, 2.0; $MgSO_4.7H_2O$, 0.2; $MnSO_4.5H_2O$, 0.05. This new medium formula not only increased the kefiran volumetric production from 0.23 up to 1.29 g/L but also shorten the production time from 72 hours to only 60 hours. The kefir grain biomass increased significantly by addition of mineral sources and vitamins in conventional medium, using organic milk as culture medium and incubation parameters: 24 hours at 25°C with agitation rate at 125 rpm [16]. Another studies by Purnomo et al[17] and Lengkey et al[18] resulted that the optimum of milk kefir can be prepared with 7% (w/v) and 10% (w/v) Indonesian kefir grains and incubation time of 24 hours.

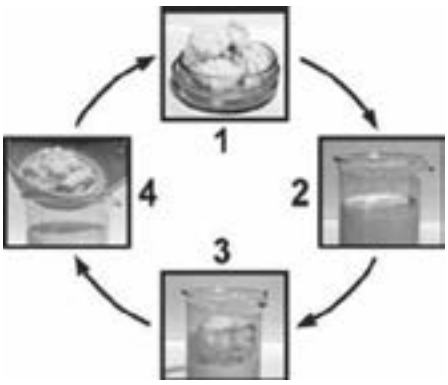

Figure 2. Kefir production. Kefir grains (1) are added to milk, (2) are left to stand at room temperature for fermentation 18-24 h, (3) after which they are filtered, (4) and ready to start another cycle. The fermented milk that results form step 4 is appropriate for consumption[13]

Kefir product also can be made from a mixture of water, dried figs, a slice of lemon and sucrose. The water kefir was prepared in a sucrose solution (100 g/l) in 1 l tap water containing two dry figs and a slice of organic lemon. The predominant genus in water kefirs was Lactobacillus, which the most abundant species were *Lb. hordei* and *Lb. nagelii* followed by considerably lower numbers of *Lb. casei* [19].

Characteristics of Kefir

The kefir grains are insoluble in water and common solvents, gelatinous and irregular in size, varying from 0.3-3.5 cm in diameter. Kefir grains resemble small cauliflower florets: they measure 1-3 cm in length, are lobed, irregularly shaped, white to yellow-white in color, and have a slimy but firm texture (Fig. 3). Grains are kept

viable by transferring them daily into fresh milk and allowing them to grow for approximately 20 hours; during this time, the grains will have increased their mass by 25%. Grains must be replicated in this way to retain their viability, since old and dried kefir grains have little or no ability to replicate [20].

Identification the kefiran (extracted from kefir grains) using FTIR spectroscopy showed that the structural integrity was maintained in biofilms. The best characteristics (transparency and elasticity) obtained from kefiran solution with 7.5% w/w glycerol [21].

Figure 3 Physical appearance of a typical kefir grain [20]

Composition of kefir

Kefir has the high levels of nutritional value, such as amino acids, proteins, minerals, phosphorus, vitamin, and calcium. Suriasih et al. [22] have observed the chemical composition of pasteurised Bali cattle milk. Kefir prepared through 24 hours fermentation showed the highest microbial population, lactose content and pH, but the lowest titratable acidity and protein concentration. There were two species of lactic acid bacteria found in kefir samples, namely, *Lactobacillus paracasei* and *Lactobacillus brevis*, and only one species of yeast, namely *Candida famata* was identified from the kefir samples in this study. *Lactobacillus paracasei* represented the largest and most commonly identified LAB isolates, with 89 of a total of 249 isolates, followed by *Lactobacillus parabuchneri* (41 isolates), *Lactobacillus casei* (32 isolates), *Lactobacillus kefiri* (31 isolates) and *Lactococcus lactis* (24 isolates) in the Brazilian kefir. *Lactobacillus kefiri* is another important bacterium found during kefir fermentation. There are reports on the presence of *Lactobacillus kefiri* as a prevailing member of the lactic acid microbiota in milk kefir [23]. The FAO/WHO (2001) have proposed a definition of kefir based on the microbial composition of both kefir grains (the starter culture used to produce kefir) and the final kefir product (see Table 1).

Table 1 Codex Alimentarius description of kefir

Definition	
Starter culture prepared from kefir grains, *Lactobacillus kefiri*, and species of the genera *Leuconostoc, Lactococcus* and *Acetobacter* growing in a strong specific relationship. Kefir grains constitute both lactose-fermenting yeasts (*Kluyveromyces marxianus*) and non-lactose-fermenting yeasts (*Saccharomyces unisporus, Saccharomyces cerevisiae* and *Saccharomyces exiguus*).	
Composition	
Milk protein (% w/w)	min. 2.8
Milk fat (% m/m)	<10
Titratable acidity, expressed as % of lactic acid(% m/m)	min. 0.6
Ethanol (% vol./w)	not stated
Sum of specific microorganisms constituting the starter culture (cfu/g, in total)	min. 10^7
Yeasts (cfu /g)	min. 10^4

THERAPEUTIC PROPERTIES

Intestinal immunity

Kefir colonizes in the intestine and produces favorable factors (probiotic). To work as probiotic intestinal adhesion to epithelium or/ and transit are vital factors in determining the

host's immune reactivity. *Lactobacillus* species isolated from kefir have the capacity to resist oxgall and many of them are able to adhere to enterocyte like cells[24].

Probiotics are live microorganisms which exert a benefit effects on the host. The Food and Agriculture Organization of the United Nations defines them as "live microorganisms which when administered in adequate amounts confer a health benefit on the host". Members of general Lactobacillus and Bifidobacterium are the most common probiotics used not only for human consumption but also in pharmaceutical preparations or in biomedicine[25]. One of the main criteria for selection of oral administration of probiotics is their ability to adhere to the intestinal mucosa allowing a transitory colonization of the gastrointestinal tract. Probiotics maintain the balance within such complex ecosystem as human intestine in many ways: inhibition of the proliferation of pathogens by competition between bacteria and pathogens for adhesion, suppression of production of virulent factors by pathogens secreting bacteriocins, or modulation of the host immune system via interaction between probiotic bacteria and intestinal epithelial cells [26].

Bekar et al [27] found that kefir improves eradication rates in patients infected with Helicobacter pylori treated by triple therapy during 14-days. This product can enhances the specific intestinal mucosal immune response against cholera holotoxin. Increased immunoglobulin secretion appears to be associated with a higher number of antibody-secreting cells in the gut-associated lymphoid tissues. These probiotic foods may have a common adjuvant effect on the mucosal immune system [28].

Antimicrobial activity

Kefir possesses antimicrobial activity in vitro against a wide variety of Gram-positive and Gram-negative bacteria, as well as some fungi. Some coliforms are actively inhibited by kefir microorganisms, and pathogenic bacteria such as Candida albicans, Salmonella typhi, Shigella sonnei, Staphylococcus aureus, and Escherichia coli [29]. The exact cause of inhibition is not known, but may be due to the antagonist action of various species of LAB (Lactic Acid Bacteria), which are also capable to preventing the adherence, establishment, replication, and/or pathogenic action of certain enteropathogens which related to their function as probiotics [30].

Anticarcinogenic Activity

The anticarcinogenic role of fermented dairy products like kefir, can be attributed to cancer prevention and the suppression of early-stage tumors. The bioactive components in fermented milk have the capacity to prevent the cancer initiation (antimutagenic); these also work by suppressing the initiated tumor growth by hindering certain enzymes so that conversion of procarcinogen to carcinogen is eliminated [31]. Kefir which made from milk and soymilk showed significant antimutagenic by reducing the glutathione peroxidase activity [32]. The other mechanism by which cancer initiation process slows down is the activation of the immune system (Fig. 4).

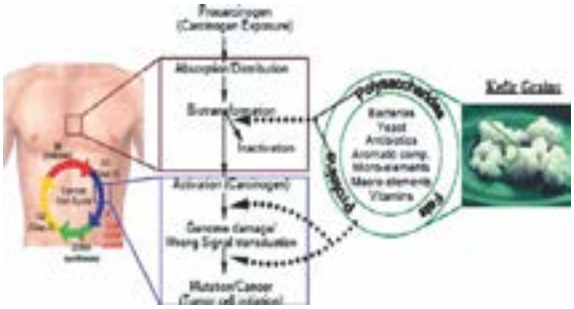

Figure 4 Tumor formation in body and proposed sites of action of kefir [31]

Hypocholesterolemic Effect

Hypolipidemic nutraceuticals help improve serum lipid profiles as reducing total cholesterol, triglyceride, and low-density lipoprotein cholesterol, while elevating high-density lipoprotein cholesterol [33,34]. Possible mechanisms proposed for the hypocholesterolemic activity in kefir may involve different ways: (i) through the binding to and absorption into the cell before it can be absorbed into the body; (ii) producing

free and deconjugating bile acids; (iii) inhibiting the enzyme HMG-CoA reductase.

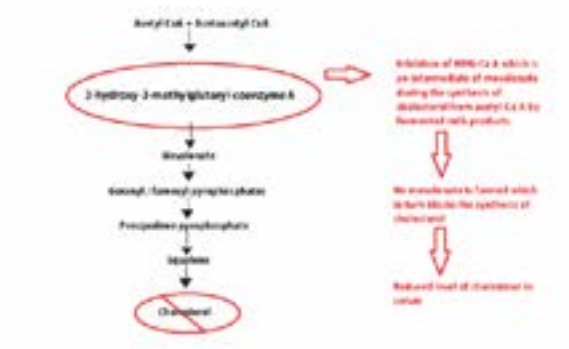

Figure 5 Cholesterol biosynthesis pathway[25]

Two substances, i.e, orotic acids and/or hydroxymethylglutaric are thought to restrict rate-limiting enzyme that is important in synthesis of cholesterol [35] (Fig. 5). The mechanism of deconjugation of bile acids was done by increasing the formation of new bile acids needed to replace those that have escaped the enterohepatic circulation, resulting in the decrease of serum cholesterol levels [36] (Fig. 6). These findings demonstrate that kefir or its components have greater potential to be used as hypocholesterolaemic substance.

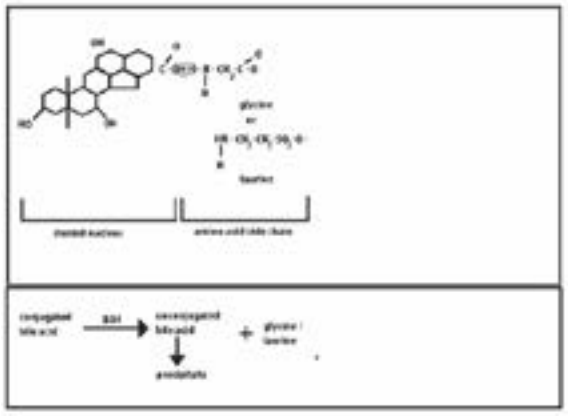

Figure 6 (a) Chemical structure of bile acids. Bile acids are conjugated with either glycine or taurine prior to secretion; (b) Reaction catalyzed by bile salt hydrolase enzymes. BSHs cleave the peptide linkage of bile acids, which results in the removal of the amino acid group from the steroid core. The resulting unconjugated bile acids precipitate at low pH

Antidiabetic activity

Kefir that was produced in conjunction with soymilk and Rhodiola extracts exhibited a better anti-diabetic functionality. This product mobilized the phenolics compounds, which alter the postprandial hyperglycemia [37]. Consumption of probiotic-fermented milk (kefir) in diabetic patients in comparison with conventionally fermented milk decreased the fasting blood glucose and HbA1C levels. These probiotics affected gut bacteria to produce insulinotropic polypeptides and glucagon-like peptide-l so induce uptake of glucose by muscle. As well as liver stimulates the absorption of more blood glucose in the form of glycogen [38].

Effect on blood pressure level

Lactobacillus kefiranofaciens, isolated from kefir grains, produces an extracellular polysaccharide which can decrease the blood pressure in rats after 30 days [39]. A commercial kefir which made from caprine milk can manage blood pressure in the presence of two out of sixteen peptides. This effect on blood pressure may be attributed to suppressing the angiotensin-converting enzyme (ACE). ACE activity influences blood pressure through different means. ACE converts AT I to AT II. AT II is a potent vasoconstrictor and it also stimulates aldosterone in kidney to retain more liquid in the body, thus increases blood pressure [40] (Fig. 7).

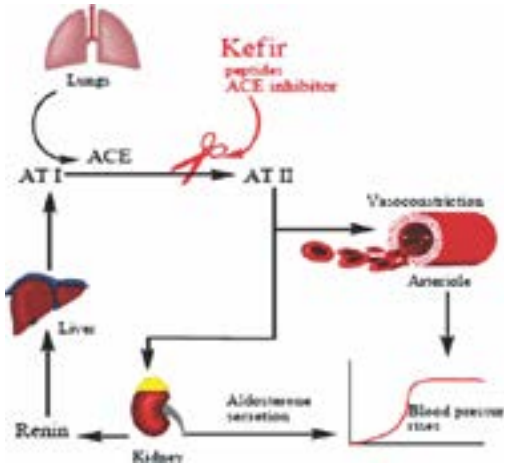

Figure 7 Role of kefir in regulating blood pressure [40]

Antioxidant activity

Kesenkas et al. [41] evaluated antioxidant activity of kefirs produced from full and half fat cow/soy milk mixtures. The inhibition of ascorbate autooxidation from cow/soy milk kefirs ranged from 8.34–17.00%, which related to their reduction activity. Similarly with the ascorbate autoxidation ability and reducing the activity of kefir samples, the superoxide anion scavenging effect of samples showed satisfy results. It has been indicated that some Lactococcus spp. are responsible to expressing antioxidative enzyme superoxide dismutase activity.

Another study possessed that addition of kefir grains to the goat milk, the DPPH radical scavenging activity appeared to have increased. The goat milk-kefir is a good scavenger for DPPH radical; thus, kefir can afford protection against proton free radicals.[42] The fresh water kefir drink showed a high ability for inhibition ascorbate autoxidation, which attributed to its contains of lactic acid, acetic acid bacteria, and yeasts. It can referred to their simultaneously existing, and their intracellular and extracellular metabolites and also to the products of its cell lysis.[43]

Wound healing activity

Kefir gels had a protective effect on skin connective tissue and 7 days treatment enhanced wound healing compared with 5 mg/kg of neomycin–clostebol emulsion [44]. This product which prepared from an extract of continuously cultured kefir grains, resulted the lower inflammation and the higher epithelization and scar formation compared to conventional silver sulfadiazine treatment [45].

Lactose intoleran

The term lactose intolerance indicates that lactose malabsorption causes gastrointestinal symptoms. Lactose malabsorption occurs when a substantial amount of lactose is not absorbed in the intestine. These symptoms are common in the absence of lactose ingestion and are highly susceptible to the placebo effect. The strategy to treat lactose intolerance is to restrict consumption of dairy foods containing lactose. Commercial products developed for lactose-intolerant persons include lactose-reduced milk and lactase supplements taken at the time of milk ingestion, one of them is fermented milk, like kefir [46,47,48].

Kefir can reduce the perceived severity of flatulence by 54% to 71% relative to milk. Abdominal pain and diarrhea symptoms were negligible among the kefir treatment [49]. Many subjects with lactose intolerance can consume milk and dairy products without getting symptoms and fermented milk products may be helpful in improving tolerance. Other individuals do benefit significantly from lactose restriction but care needs to be taken to ensure that calcium intake is sufficient. A greater understanding of the complexity of lactose intolerance, lactase deficiency and symptom generation would help clinicians treat patients more effectively [50].

CONCLUSIONS

Due to high nutraceutical and therapeutic potential, kefir is ranked at top position. The characteristics in kefir are attributed to amino acids, proteins, minerals, phosphorus, vitamin, calcium, and certain biogenic compounds. The microbiota of kefir has especially affected kefir grain from various origins and production methods. The beneficial health associated with kefir are numerous, including, intestinal immunity, antimicrobial, anticarcinogenic, hypocholesterolemic effect, antidiabetic, the effect on blood pressure level, antioxidant, wound healing, and lactose intolerance.

REFERENCES

1. Kalra EK. Nutraceutical-definition and introduction. Aaps Pharmsci. 2003;5(3): 27-35.
2. Palthur MP, Palthur SS, Chitta SK. Nutraceuticals: a conceptual definition. Int J Pharm Pharm Sci. 2010; 2 (3): 19-27.
3. Chauhan B, Kumar G, Kalam N, Ansari SH. Current concepts and prospects of herbal

nutraceutical: A review. Journal of advanced pharmaceutical technology and research. 2013;4(1): 4-8.
4. Dev R, Kumar S, Singh J, Chauhan B. Potential role of nutraceuticals in present scenerio: A review. Journal of Applied Pharmaceutical Science. 2011; 1 (4): 26-28.
5. Das L, Bhaumik E, Raychaudhuri U, Chakraborty R. Role of nutraceuticals in human health. Journal of food science and technology. 2012;49(2):173-256.
6. Giavasis I. Production of microbial polysaccharides for use in food. Microbial Production of Food Ingredients, Enzymes and Nutraceuticals. 2013; 413-481.
7. Patel AK, Michaud P, Singhania RR, Soccol CR, Pandey A. Polysaccharides from probiotics: new developments as food additives. Food Technology and Biotechnology. 2010;48(4): 451-514.
8. Prado MR, Blandón LM, Vandenberghe LP, Rodrigues C, Castro GR, Thomaz-Soccol V, Soccol CR. Milk kefir: composition, microbial cultures, biological activities, and related products. Frontiers in microbiology. 2015;6: 1-10
9. Gaware V, Kotade K, Dolas R, Dhamak K, Somwnshis S, Nikam V, Khadse A, Kashid V. The magic of kefir: a review. Pharmacology online. 2011;1: 376-462.
10. Farnworth ER. Kefir–a complex probiotic. Food Science and Technology Bulletin: Fu. 2006;2(1):1-7.
11. Kesenkas HA, Yerlikaya O, Ozer EL. A functional milk beverage: Kefir. Agro Food Industry Hi Tech. 2013;24: 53-58.
12. Kıvanç M, Yapıcı E. Kefir as a Probiotic Dairy Beverage: Determination Lactic Acid Bacteria and Yeast. International Journal of Food Engineering. 2015;1(1): 55-60.
13. Lopitz-Otsoa F, Rementeria A, Elguezabal N, Garaizar J. Kefir: a symbiotic yeasts-bacteria community with alleged healthy capabilities. Rev Iberoam Micol. 2006;23(2): 67-74.
14. McGrew GN, Barkalow DG, Johnson SS, Record DW, Patel MM, Nimz JD, Zibell SE, Yatka RJ, Greenberg MJ, Aumann RA, Zyck DJ, inventors. Nutraceuticals or nutritional supplements and method of making. United States patent US 6,949,264. 2005; 1-45.
15. Dailin DJ, Elsayed EA, Othman NZ, Malek RA, Ramli S, Sarmidi MR, Aziz R, Wadaan MA, Elenshasy HA. Development of cultivation medium for high yield kefiran production by Lactobacillus kefiranofaciens. International Journal of Pharmacy and Pharmaceutical Sciences. 2015;7(3): 159-163.
16. Pop CR, Apostu S, Salanţă L, Rotar AM, Sindic M, Mabon N, Socaciu C. Influence of Different Growth Conditions on the Kefir Grains Production, used in the Kefiran Synthesis. Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. Food Science and Technology. 2014;71(2): 147-200.
17. Purnomo H, Muslimin LD. Chemical characteristics of pasteurised goat milk and goat milk kefir prepared using different amount of indonesian kefir grains and incubation times. International Food Research Journal. 2012;19(2): 791-794.
18. Lengkey HA, Siwi JA, Balia RL. The effect of various starter dosages on kefir quality. Lucrări Ştiinţifice-Universitatea de Ştiinţe Agricole şi Medicină Veterinară, Seria Zootehnie. 2013;59:113-116.
19. Gulitz A, Stadie J, Wenning M, Ehrmann MA, Vogel RF. The microbial diversity of water kefir. International journal of food microbiology. 2011;151(3):284-292.
20. Prajapat JB, Patel A. Food and health applications of exopolysaccharides produced by lactic acid bacteria. Advances in Dairy Research. 2013; 1(2): 1-7.
21. Pop C, Apostu S, Rotar AM, Semeniuc CA, Sindic M, Mabon N. FTIR spectroscopic characterization of a new biofilm obtained from kefiran. Journal of Agroalimentary Processes and Technologies. 2013;19:157-166.
22. Suriasih K, Aryanta WR, Mahardika G, Astawa NM. Microbiological and chemical properties of Kefir made of Bali cattle milk. Food Science and Quality Management. 2012;6:2225-0557.
23. Magalhães KT, Pereira GV, Campos CR, Dragone G, Schwan RF. Brazilian kefir: structure,

microbial communities and chemical composition. Brazilian Journal of Microbiology. 2011;42(2): 693-702.
24. Otles S, Cagindi O. Kefir: A probiotic dairy-composition, nutritional and therapeutic aspects. Pakistan Journal of Nutrition. 2003;2(2): 54-59.
25. Ciszek, M. Biological function of exopolysaccharides from probiotic bacteria. Central European Journal of Immunology. 2011; 36 (1): 51-55.
26. Arslan S. A review: chemical, microbiological and nutritional characteristics of kefir. CyTA-Journal of Food. 2015;13(3): 340-345.
27. Bekar O, Yilmaz Y, Gulten M. Kefir improves the efficacy and tolerability of triple therapy in eradicating Helicobacter pylori. Journal of medicinal food. 2011;14(4): 344-351.
28. Thoreux K, Schmucker DL. Kefir milk enhances intestinal immunity in young but not old rats. The Journal of nutrition. 2001;131(3): 807-819.
29. Silva KR, Rodrigues SA, Xavier Filho L, Lima ÁS. Antimicrobial activity of broth fermented with kefir grains. Applied biochemistry and biotechnology. 2009;152(2): 316-341.
30. Adriana P, Socaciu C. Probiotic activity of mixed cultures of kefir's lactobacilli and non-lactose fermenting yeasts. Bull. UASVM Agric. 2008;65: 329-363.
31. Ahmed Z, Wang Y, Ahmad A, Khan ST, Nisa M, Ahmad H, Afreen A. Kefir and health: a contemporary perspective. Critical reviews in food science and nutrition. 2013;53(5): 422-456.
32. Liu JR, Chen MJ, Lin CW. Antimutagenic and antioxidant properties of milk-kefir and soymilk-kefir. Journal of agricultural and food chemistry. 2005;53(7): 2467-2541.
33. Chen G, Wang H, Zhang X, Yang ST. Nutraceuticals and functional foods in the management of hyperlipidemia. Critical reviews in food science and nutrition. 2014;54(9): 1180-1381.
34. Chen ZY, Jiao R, Ma KY. Cholesterol-lowering nutraceuticals and functional foods. Journal of Agricultural and Food Chemistry. 2008;56(19): 8761-8834.
35. Leite AM, Miguel MA, Peixoto RS, Rosado AS, Silva JT, Paschoalin VM. Microbiological, technological and therapeutic properties of kefir: a natural probiotic beverage. Brazilian Journal of Microbiology. 2013;44(2):341-350.
36. John SM, Deeseenthum S. Properties and benefits of kefir–A review. Songklanakarin Journal of Science and Technology. 2015;37(3): 275-357.
37. Alsayadi M, Al Jawfi Y, Belarbi M, Soualem-Mami Z, Merzouk H, Sari DC, Sabri F, Ghalim M. Evaluation of anti-hyperglycemic and anti-hyperlipidemic activities of water kefir as probiotic on streptozotocin-induced diabetic wistar rats. Journal of Diabetes Mellitus. 2014; 4: 85-95.
38. Ostadrahimi A, Taghizadeh A, Mobasseri M, Farrin N, Payahoo L, Gheshlaghi ZB, Vahedjabbari M. Effect of probiotic fermented milk (kefir) on glycemic control and lipid profile in type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. Iranian journal of public health. 2015;44(2): 228-237.
39. Maeda H, Zhu X, Suzuki S, Suzuki K, Kitamura S. Structural characterization and biological activities of an exopolysaccharide kefiran produced by Lactobacillus kefiranofaciens WT-2BT. Journal of agricultural and food chemistry. 2004; 52(17):5533-5541.
40. Quirós A, Hernández-Ledesma B, Ramos M, Amigo L, Recio I. Angiotensin-converting enzyme inhibitory activity of peptides derived from caprine kefir. Journal of dairy science. 2005;88(10): 3480-3487.
41. Kesenkas H, Dinkci N, Seckin K, Kinik O, Gonc S.. Antioxidant properties of kefir produced from different cow and soy milk mixtures. Tarım Bilimleri Dergisi. 2011;17(3): 53-55.
42. Yilmaz-Ersan L, Ozcan T, Akpinar-Bayizit A, Sahin S. The Antioxidative Capacity of Kefir Produced from Goat Milk. International Journal of Chemical Engineering and Applications. 2016;7(1):22-26.
43. Muneer AMS, Aldhehar I, Al Jawfi Y, Belarbi M, Sabri FZ. Antioxidant potency of water kefir. The Journal of Microbiology, Biotech-

nology and Food Sciences (Slovak Republic). 2012; 2(6): 2444-2447.
44. Rodrigues KL, Caputo LR, Carvalho JC, Evangelista J, Schneedorf JM. Antimicrobial and healing activity of kefir and kefiran extract. International journal of antimicrobial agents. 2005;25(5):404-412.
45. Huseini HF, Rahimzadeh G, Fazeli MR, Mehrazma M, Salehi M. Evaluation of wound healing activities of kefir products. Burns. 2012;38(5): 719-741.
46. Shaukat A, Levitt MD, Taylor BC, MacDonald R, Shamliyan TA, Kane RL, Wilt TJ. Systematic review: effective management strategies for lactose intolerance. Annals of internal medicine. 2010;152(12): 797-803.
47. Alm L. Effect of fermentation on lactose, glucose, and galactose content in milk and suitability of fermented milk products for lactose intolerant individuals. Journal of Dairy Science. 1982;65(3): 346-397.
48. Nichols AW. Probiotics and athletic performance: a systematic review. Current sports medicine reports. 2007;6(4): 269-341.
49. Hertzler SR, Clancy SM. Kefir improves lactose digestion and tolerance in adults with lactose maldigestion. Journal of the American Dietetic Association. 2003;103(5): 582-589.
50. Lomer MC, Parkes GC, Sanderson JD. Review article: lactose intolerance in clinical practice–myths and realities. Alimentary pharmacology & therapeutics. 2008;27(2): 93-103.