Med Oncol (2017) 34:183
DOI 10.1007/s12032-017-1044-9

REVIEW ARTICLE

Kefir: a powerful probiotics with anticancer properties

Mohammadreza Sharifi[1] · Abbas Moridnia[2] · Deniz Mortazavi[1] · Mahsa Salehi[1] · Marzieh Bagheri[1] · Abdolkarim Sheikhi[2]

Received: 26 June 2017 / Accepted: 23 September 2017 / Published online: 27 September 2017

Abstract Probiotics and fermented milk products have attracted the attention of scientists from various fields, such as health care, industry and pharmacy. In recent years, reports have shown that dietary probiotics such as kefir have a great potential for cancer prevention and treatment. Kefir is fermented milk with Caucasian and Tibet origin, made from the incubation of kefir grains with raw milk or water. Kefir grains are a mixture of yeast and bacteria, living in a symbiotic association. Antibacterial, antifungal, anti-allergic and anti-inflammatory effects are some of the health beneficial properties of kefir grains. Furthermore, it is suggested that some of the bioactive compounds of kefir such as polysaccharides and peptides have great potential for inhibition of proliferation and induction of apoptosis in tumor cells. Many studies revealed that kefir acts on different cancers such as colorectal cancer, malignant T lymphocytes, breast cancer and lung carcinoma. In this review, we have focused on anticancer properties of kefir.

Keywords Kefir · Probiotics · Cancer · Anticancer

✉ Mohammadreza Sharifi
mo_sharifi@med.mui.ac.ir

Abbas Moridnia
a_moridnia@med.mui.ac.ir

Deniz Mortazavi
deniz.mo68@yahoo.com

Mahsa Salehi
sm.salehi@resident.mui.ac.ir

Marzieh Bagheri
m.bagheri@resident.mui.ac.ir

Abdolkarim Sheikhi
Sheikhi@queensu.ca

[1] Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan 81744-176, Iran

[2] Department of Immunology, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

Introduction

In recent studies, the role of probiotics in health care is getting more attention and has been shown that lactic acid bacteria (LAB) as probiotics have a therapeutic effect in different diseases such as rheumatoid arthritis and cancer [1, 2]. The previous studies suggest that the probiotics, especially LAB, in addition to inducing apoptosis, have different anticancer properties including anti-proliferative, anti-inflammatory, antioxidative and anti-mutagenic effects [3–9]. Kefir is made of small cauliflower floret-like grains added to the fresh milk. The grains are a mixture of yeasts and lactic acid bacteria within a polysaccharide and protein matrix, in a symbiotic community [10, 11]. The main ingredients of kefir are lactic acid, ethanol and CO_2 [12]. The components of kefir complex are involved in the synthesis of anticancer bioactive components including peptides, polysaccharides and sphingolipids, playing vital roles in different signaling pathways and biological cell processes such as apoptosis, proliferation and transformation [1, 10, 13]. Therefore, kefir can act as an effective agent in cancer treatment and prevention. In this review, we discuss about the anticancer properties of kefir and the mechanism of its effect.

Probiotics and Kefir

Probiotics contain live bacteria, which are useful for health [14]. In another word, a probiotics is a live

microbial food supplement that beneficially affects the host, by improving the microbial balance [15]. Based on the definition of Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO), probiotics are "live microorganisms, conferring health benefit on the host when administered in adequate amounts" [16]. Probiotics microorganisms are sensitive to various physicochemical stresses such as pH, acidity, temperature and preservatives [17, 18]. Kefir is one of the most favorite probiotics, considered as a powerful supplement, originating from the Balkan–Caucasian region [8, 9, 19].

Kefir is acidic, partly effervescent, slightly alcoholic, milk foamy and viscous beverage with a uniform creamy and elastic consistency and sour taste, which can be easily digested [20]. It is made from the fermentation of both traditional and commercial shapes of kefir grains with any type of semi-skimmed or skimmed pasteurized milk (goat, sheep, cow, camel, buffalo) [8, 19, 21]. Kefir grains composed of different microflora that is accumulating on matrix polysaccharide and protein, including lactic acid bacteria (*Lactobacillus paracasei*, *Lactobacillus kefiri*, *Lactobacillus parabuchneri* and *Acetobacter lovaniensis*) and yeast such as *Saccharomyces cerevisiae* and *Kluyveromyces lactis* [22]. The bacteria convert the lactose to lactic acid, decreasing the milk pH, and yeasts produce ethanol and CO_2 from lactic acid [9, 22].

In terms of nutritional value, kefir contains at least 2.7% of protein, 0.6% of lactic acid and less than 10% of fat [22]. Kefir is a rich source of vitamins (carotene, vitamins A, K, B_1, B_2, B_5, C, B_{12} and folic acid) and amino acids (ammonia, serine, lysine, alanine, threonine, tryptophan, valine, lysine, methionine, phenylalanine and isoleucine) and mineral compositions (Mg, Ca, P, Zn, Cu, Mn, Fe, Co and Mo) [17]. It is important to note that the quality of the milk used in the process, preparation method and the presenting microorganisms in the kefir grains determine the quantity and the type of vitamin and mineral compositions [8, 22, 23].

Evidence shows the main polysaccharide of kefir, kefiran, has very important physicochemical properties that increase the viscosity and viscoelasticity of acid milk gels, and kefiran can improve the rheological properties and increase the viscosity [9, 19, 24]. In addition, kefiran can be used as an antioxidant [25], anti-tumor and antimicrobial agent. On the other hand, kefir has positive effects on the immune system and cholesterol metabolism [26], improvement of bone health and lactose tolerance [27]. Consequently, it is favorable that kefir intake may have a potential role in cancer prevention and treatment.

Kefir and cancer

Cancer cells are highly proliferative and resist apoptosis. Most of the cancer arises from unhealthy and unbalanced diets; therefore, investigation about dietary factors is vital and extremely important. One of the important dietary factors is probiotics, such as kefir.

A hallmark of neoplastic progression includes the ability of tumor cells to evade immune response [28, 29]. Studies suggest that probiotics bacteria are able to stimulate effector functions of the immune system. Indeed, cytokine profiles in co-cultures of the probiotics bacteria with peripheral blood mononuclear cells (PBMC) are an indication of this phenomenon [30].

Several studies displayed that kefir can interact with several cellular pathways and regulate biological processes including antioxidative process, apoptosis and proliferation (Fig. 1) [31, 32].

The mechanisms of effect of kefir as an anticancer agent are as follows.

Immunomodulatory and anti-inflammatory effect of Kefir

Since cancer is a consequence of dysregulation of the immune and inflammatory system, the immunomodulatory and anti-inflammatory properties of kefir are very appealing and significant and it will be effective via following mechanisms (Fig. 2):

1. Bioactive peptides in kefir induce activation of macrophages and phagocytosis and nitric oxide (NO) production [33].
2. The secretion of TNF-α and cytokines such as IL-5 [34], IL-6 [35], IL-1β [35, 36], IL-12 [36] is increased, and secretion of IL-8 is decreased. High level of IL-5 and TNF-α will lead to high level of IgA secretion. The decreased level of IL-8 may control inflammatory response by suppressing chemotaxis and activation of neutrophils [34].
3. Suppressed T helper 2 immune response and activated T helper 1 immune response induce anti-allergic effect [37, 38].

Anti-carcinogenic effect of Kefir

Two mechanisms through which kefir induces anti-carcinogenic effect are as follows (Fig. 2) [39–41]:

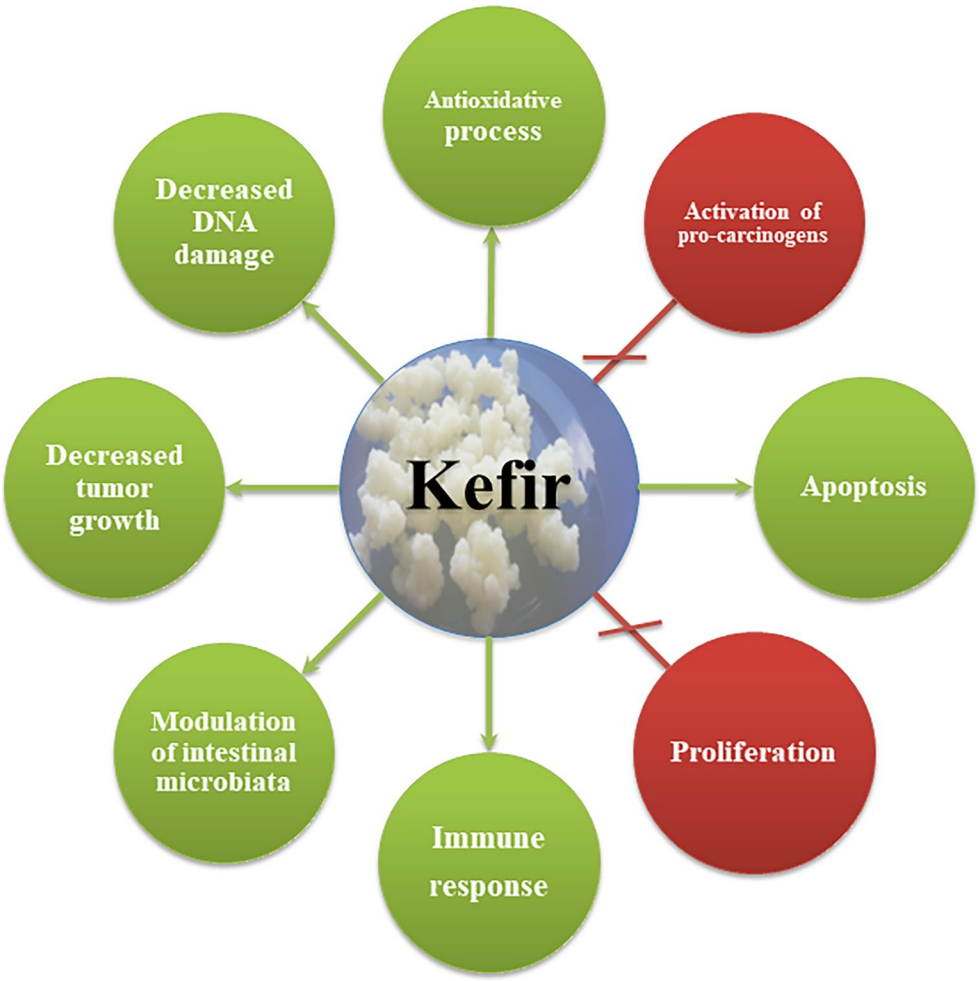

Fig. 1 Anticancer properties of kefir

1. Kefir intake decreases the secretion of TGF-α, TGF-β and Bcl2 and increases the secretion of bax leading to induction of apoptosis.
2. Active peptides of kefir induce ROS-mediated apoptosis and activate Ca^{-}/Mg^{-}-dependent endonucleases for DNA cleavage.
3. Low secretion of TGF-α and TGF-β induces the anti-proliferative effect in cancerous cells.
4. Sphingomyelins in kefir increase secretion of interferon-β, an anti-proliferative cytokine.

Antioxidative effect of Kefir

Kefir intake increases the level of glutathione peroxidase and decreases the level of malondialdehyde, involved in the control of oxidative stress. On the other hand, kefir can bind to 1,1-diphenyl-2-picrylhydrazyl (DPPH) and superoxide radicals and also inhibit the linoleic acid peroxidation [42, 43]. As a result, kefir exerts an anti-carcinogenic effect through an antioxidative property and reducing the DNA damage (Fig. 2) [44].

Anti-mutagenic effect of Kefir

High levels of conjugated linoleic acid isomers and butyric, palmitic, palmitoleic and oleic acids in kefir may contribute to lower induced mutagenicity by methyl methanesulfonate, sodium azide and aflatoxin B1. In addition, kefir has a protective effect against radiation-induced damage (Fig. 2) [45–47].

The mechanism of effects of kefir on different types of cancer cells

Kefir and breast cancer

Previous studies displayed the role of kefir in anti-tumor process in different cancers. Breast cancer is one of the most common cancers among women; therefore, treatment and prevention are very substantial. In 2007, Chen et al. [13] performed a study on effect of extracts of kefir on MCF-7 and HMECs cell lines and demonstrated that kefir depressed MCF-7 cell growth in a dose-dependent manner. In the

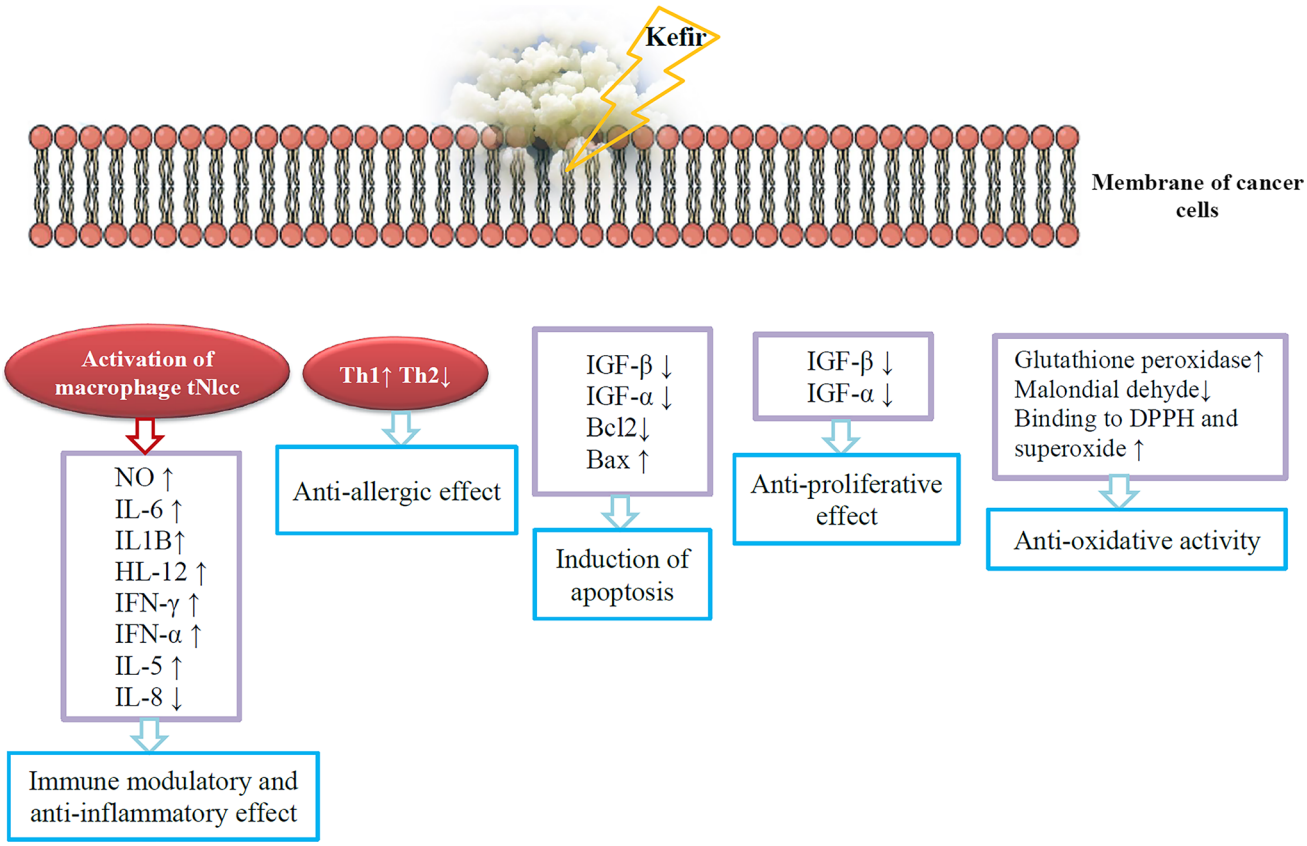

Fig. 2 Mechanisms through which kefir induces anticancer effects

study of cytokines involved in the prevention of a murine experimental breast cancer by kefir, the modulatory capacity of kefir cell-free fraction (KF) on the immune response in mammary glands and tumors was demonstrated [48]. According to previous studies, kefir extracts induce apoptosis, cell cycle arrest and reduce tumor growth in breast cancer cells [4]; therefore, it may be suitable in the prevention or treatment of breast cancer.

Kefir and leukemia

In leukemia, kefir intake has led to increased apoptosis and decreased cell proliferation [9]. In 2011, Maalouf et al. had demonstrated a significant decrease in cell proliferation in CME and Jurkat (human T lymphotropic virus type I-negative malignant T lymphocyte cell lines), in dose- and time-dependent manner. Kefir displayed an anti-proliferative effect by upregulating TGF-β1 and downregulating TGF-α expression [49]. In a study by Rizk et al., anti-proliferative effect of kefir on HuT-102 malignant T lymphocytes was demonstrated and the decrease in proliferation was significant and also dose and time dependent. Kefir has caused downregulation of TGF-α, which is one of the cytokines, inducing cell proliferation and replication [50].

Probiotics fermentation technology (PFT) on kefir grain product is a natural mixture composed primarily of *Lactobacillus kefiri* P-IF strain. The apoptotic effect of PFT on human multidrug-resistant myeloid leukemia (HL60/AR cell line) indicated that PFT induced apoptosis in the HL60/AR cell line in a dose-dependent manner. Apoptotic induction was associated with caspase 3 activation, downregulation of Bcl-2 and lower polarization of mitochondrial membrane potential MMP [51].

Kefir and skin cancer

According to a study regarding the effects of kefir on skin cancer cells, it has been shown that kefir suppressed morphological alterations in melanoma cell lines (HMV-1 and SK-MEL and TIG-1), caused by UVC irradiation. In addition, kefir extract application after UVC irradiation of HVM-1 cells resulted in a notable reduction in intracellular reactive oxygen species (ROS), increased by exposure to UVC irradiation. Also it prevented the generation of thymine dimer, suppressed the apoptosis and rescued HMV-1 cells from cell death caused by UVC irradiation, concluding that application of kefir can inhibit UV damage [52].

Kefir and gastric cancer

Study of assessment of the effect of *Lactobacillus kefiri*, a kefir product, on gastric cancer cells (AGS) by Ghoneum and Felo, revealed apoptosis induction in AGS cell line. Apoptosis was associated with declined polarization of mitochondrial membrane potential (MMP) and reduced Bcl2 expression. Downregulation of Bcl-2 and decrease in the MMP in AGS cells may lead to release of pro-apoptotic molecules and subsequently activation of caspases, causing apoptosis [53]. In 2013, in a study by Gao, the anti-proliferative effect of the KF in SGC7901 cell line was assessed and it was shown that kefir halts G1/S phase transition in SGC7901 cell line and induces apoptosis through downregulation of bcl-2 and overexpression of bax [54].

Kefir and colon cancer

Recently, fermentation of dairy products and their bacterial components has been recommended, which have health-promoting functions and reduce the risk of colorectal cancer. In a study, it has been shown that kefir and ayran intake significantly decrease the DNA damage and the effect of ayran was dose dependent. The supernatants of kefir and ayran contained high amounts of acetic and lactic acid and showed meaningfully antioxidant capacity. The evidence proposes kefir and ayran can decrease DNA damage, which might be due to their antioxidant capacities [44]. Kefir anticancer potential property on CRC cell lines (Caco-2 and HT-29) exhibits the ability of kefir to induce cell cycle arrest at the G1 phase. In addition, kefir decreases the expression of TGF-β1 and TGF-α in HT-29 cell line. Upregulation of the Bax/Bcl-2 ratio supports the pro-apoptotic effect of kefir and increase of p53 independent-p21 expression [55]. Also, reported that kefir can reduce sleep disturbance in patients treated for colorectal cancer [56].

Kefir and sarcoma

According to the previous studies, anti-tumor properties of kefir were demonstrated in diverse types of sarcoma cells [34, 57]. The anti-tumor effects of soy milk kefir and milk kefir by oral administration on mice-bearing sarcoma tumor cells show that tumor growth was inhibited 64.8% in the tumor-bearing group with milk and 70.9% in soy milk kefir group, compared with the controls group [34]. Cevikbas et al. investigated about different forms of sarcoma cells in mice. The results revealed the beneficial therapeutic effects of kefir in decreasing tumor size following treatment with kefir, compared with the saline administrated controls [57]. In another study, the potential anticancer effect of kefir and some kefir products was examined in human sarcoma cell line. Results established the anticancer efficacy of kefir and kefir products. The most effective product on sarcoma cells was alkaline kefir (AK), followed by exo-polysaccharides (EPS), alkaline exo-polysaccharides (AEPS) and kefir, respectively. Proposed AK can be used in the treatment of human sarcoma since kefir is a conventional beverage, and the addition of sodium bicarbonate as the food additive is harmless [58].

Conclusion

In recent decades, probiotics and fermented milk products have attracted great attention between scientists from various fields, such as the food industry, health care, industry and pharmacy. Traditionally, kefir as an effective agent was used in the prevention and treatment of various diseases including gastrointestinal, hypertension and allergies [14, 17].

Many studies revealed promising results, using kefir both in vivo and in vitro, as an anti-tumor, anti-proliferating and inducer of apoptosis in different cancers such as colorectal cancer [59], malignant T lymphocytes [49], breast cancer [48] and lung carcinoma [60]. Perhaps kefir can be used as an effective treatment with the least side effect.

According to the evidence in the literature, we can ascertain that kefir is one of the best therapeutic natural ingredients, applying its anticancer effect through different cellular and molecular pathways.

Kefir is likely to be recognized for effective treatment of malignancies and as an anticancer agent in the near future.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent None.

References

1. Furuya H, Shimizu Y, Kawamori T. Sphingolipids in cancer. Cancer Metastasis Rev. 2011;30(3–4):567–76.
2. Marco ML, Pavan S, Kleerebezem M. Towards understanding molecular modes of probiotic action. Curr Opin Biotechnol. 2006;17(2):204–10.
3. Veer VT, Van Leer EM, Rietdijk A, Kok FJ, Schouten EG, Hermus RJ, et al. Combination of dietary factors in relation to breast-cancer occurrence. Int J Cancer. 1991;47(5):649–53.
4. van't Veer P, Dekker JM, Lamers JW, Kok FJ, Schouten EG, Brants HA, et al. Consumption of fermented milk products and breast cancer: a case-control study in The Netherlands. Can Res. 1989;49(14):4020–3.

5. Le MG, Moulton LH, Hill C, Kramar A. Consumption of dairy produce and alcohol in a case-control study of breast cancer 2. JNCI: J Natl Cancer Inst. 1986;77(3):633–6.
6. Cramer D, Willett W, Bell D, Ng W, Harlow B, Welch W, et al. Galactose consumption and metabolism in relation to the risk of ovarian cancer. Lancet. 1989;334(8654):66–71.
7. Biffi A, Coradini D, Larsen R, Riva L, Di Fronzo G. Antiproliferative effect of fermented milk on the growth of a human breast cancer cell line. Nutr Cancer. 1997;28(1):93–9.
8. Rosa DD, Dias MM, Grześkowiak ŁM, Reis SA, Conceição LL. Maria do Carmo GP. Milk kefir: nutritional, microbiological and health benefits. Nutr Res Rev. 2017;30(1):82–96.
9. Jalali F, Sharifi M, Salehi R. Kefir induces apoptosis and inhibits cell proliferation in human acute erythroleukemia. Med Oncol. 2016;33(1):7.
10. Garrote GL, Abraham AG, De Antoni GL. Microbial interactions in Kefir: a natural probiotic drink. In: Biotechnology of lactic acid bacteria: novel applications. Wiley-Blackwell; 2010. P. 327–36.
11. Farnworth ERT. Handbook of fermented functional foods. New York: CRC Press; 2008.
12. Magalhães KT, Pereira GVdM, Campos CR, Dragone G, Schwan RF. Brazilian kefir: structure, microbial communities and chemical composition. Braz J Microbiol. 2011;42(2):693–702.
13. Chen C, Chan HM, Kubow S. Kefir extracts suppress in vitro proliferation of estrogen-dependent human breast cancer cells but not normal mammary epithelial cells. J Med Food. 2007;10(3):416–22.
14. Salminen S, Bouley C, Boutron M-C, Cummings J, Franck A, Gibson G, et al. Functional food science and gastrointestinal physiology and function. Br J Nutr. 1998;80(S1):S147–71.
15. Gorbach SL, Newton I. The discovery of lactobacillus GG. Nutr Today. 1996;31(6):5S.
16. Hotel ACP, Cordoba A. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. Prevention. 2001;5(1):1–10.
17. Otles S. Cagindi Oe. Kefir: a probiotic dairy-composition, nutritional and therapeutic aspects. Pak J Nutr. 2003;2(2):54–9.
18. Terpou A, Gialleli A-I, Bekatorou A, Dimitrellou D, Ganatsios V, Barouni E, et al. Sour milk production by wheat bran supported probiotic biocatalyst as starter culture. Food Bioprod Process. 2017;101:184–92.
19. Prado MR, Blandón LM, Vandenberghe LP, Rodrigues C, Castro GR, Thomaz-Soccol V, et al. Milk kefir: composition, microbial cultures, biological activities, and related products. Front Microbiol. 2015;6:1177.
20. Nielsen B, Gürakan GC, Ünlü G. Kefir: a multifaceted fermented dairy product. Probiotics Antimicrob Proteins. 2014;6(3–4):123–35.
21. Baschali A, Tsakalidou E, Kyriacou A, Karavasiloglou N, Matalas A-L. Traditional low-alcoholic and non-alcoholic fermented beverages consumed in European countries: a neglected food group. Nutr Res Rev. 2017;30(1):1–24.
22. Gemechu T. Review on lactic acid bacteria function in milk fermentation and preservation. Afr J Food Sci. 2015;9(4):170–5.
23. Sarkar S. Potential of kefir as a dietetic beverage–a review. Br Food J. 2007;109(4):280–90.
24. Diosma G, Romanin DE, Rey-Burusco MF, Londero A, Garrote GL. Yeasts from kefir grains: isolation, identification, and probiotic characterization. World J Microbiol Biotechnol. 2014;30(1):43–53.
25. Chen Z, Shi J, Yang X, Nan B, Liu Y, Wang Z. Chemical and physical characteristics and antioxidant activities of the exopolysaccharide produced by Tibetan kefir grains during milk fermentation. Int Dairy J. 2015;43:15–21.
26. da Silva Fernandes M, Lima FS, Rodrigues D, Handa C, Guelfi M, Garcia S, et al. Evaluation of the isoflavone and total phenolic contents of kefir-fermented soymilk storage and after the in vitro digestive system simulation. Food Chem. 2017;229:373–80.
27. Fiorda FA, de Melo Pereira GV, Thomaz-Soccol V, Rakshit SK, Pagnoncelli MGB, de Souza Vandenberghe LP, et al. Microbiological, biochemical, and functional aspects of sugary kefir fermentation-a review. Food Microbiol. 2017;66:86–95.
28. Sheikhi A, Jafarzadeh A, Kokhaei P, Hojjat-Farsangi M. Whole tumor cell vaccine adjuvants: comparing IL-12 to IL-2 and IL-15. Iran J Immunol. 2016;13(3):148.
29. Sheikhi A, Jafarzadeh A. A new therapeutic potential for cancers: one CAR with 2 different engines! Hum Vaccin Immunother. 2017;13(8):1786–8.
30. Sheikhi A, Shakerian M, Giti H, Baghaeifar M, Jafarzadeh A, Ghaed V, et al. Probiotic yogurt culture bifidobacterium animalis subsp. lactis BB-12 and lactobacillus acidophilus LA-5 modulate the cytokine secretion by peripheral blood mononuclear cells from patients with ulcerative colitis. Drug Res. 2016;66(06):300–5.
31. Daniluk U. Probiotics, the new approach for cancer prevention and/or potentialization of anti-cancer treatment. J Clin Exp Oncol. 2012;1:2.
32. Kumar M, Nagpal R, Verma V, Kumar A, Kaur N, Hemalatha R, et al. Probiotic metabolites as epigenetic targets in the prevention of colon cancer. Nutr Rev. 2013;71(1):23–34.
33. Adiloğlu A, Gönülateş N, Işler M, Senol A. The effect of kefir consumption on human immune system: a cytokine study. Mikrobiyoloji bulteni. 2013;47(2):273–81.
34. Liu J-R, Wang S-Y, Lin Y-Y, Lin C-W. Antitumor activity of milk kefir and soy milk kefir in tumor-bearing mice. Nutr Cancer. 2002;44(2):183–7.
35. Tellez A, Corredig M, Brovko LY, Griffiths MW. Characterization of immune-active peptides obtained from milk fermented by Lactobacillus helveticus. J Dairy Res. 2010;77(2):129–36.
36. Jain S, Yadav H, Sinha PR, Marotta F. Modulation of cytokine gene expression in spleen and Peyer's patches by feeding dahi containing probiotic Lactobacillus casei in mice. J Dig Dis. 2009;10(1):49–54.
37. Hong WS, Chen YP, Chen MJ. The antiallergic effect of kefir Lactobacilli. J Food Sci. 2010;75(8):H244–53.
38. Díaz-Ropero M, Martin R, Sierra S, Lara-Villoslada F, Rodriguez J, Xaus J, et al. Two Lactobacillus strains, isolated from breast milk, differently modulate the immune response. J Appl Microbiol. 2007;102(2):337–43.
39. Ahmed Z, Wang Y, Ahmad A, Khan ST, Nisa M, Ahmad H, et al. Kefir and health: a contemporary perspective. Crit Rev Food Sci Nutr. 2013;53(5):422–34.
40. Pepe G, Tenore GC, Mastrocinque R, Stusio P, Campiglia P. Potential anticarcinogenic peptides from bovine milk. J Amino Acids. 2013;2013:1–7.
41. Khoury N, El-Hayek S, Tarras O, El-Sabban M, El-Sibai M, Rizk S. Kefir exhibits anti-proliferative and pro-apoptotic effects on colon adenocarcinoma cells with no significant effects on cell migration and invasion. Int J Oncol. 2014;45(5):2117–27.
42. Ozcan A, Kaya N, Atakisi O, Karapehlivan M, Atakisi E, Cenesiz S. Effect of kefir on the oxidative stress due to lead in rats. J Appl Anim Res. 2009;35(1):91–3.
43. Liu J-R, Lin Y-Y, Chen M-J, Chen L-J, Lin C-W. Antioxidative activities of kefir. Asian-Aust J Anim Sci. 2005;18(4):567–73.
44. Grishina A, Kulikova I, Alieva L, Dodson A, Rowland I, Jin J. Antigenotoxic effect of kefir and ayran supernatants on fecal water-induced DNA damage in human colon cells. Nutr Cancer. 2011;63(1):73–9.
45. Güzel-Seydim Z, Grene A, Tas T. determination of antimutagenic properties of some fermented milks including changes in the total fatty acid profiles including CLA. Int J Dairy Technol. 2006;59(3):209–15.

46. Teruya K, Myojin-Maekawa Y, Shimamoto F, Watanabe H, Nakamichi N, Tokumaru K, et al. Protective effects of the fermented milk kefir on X-ray irradiation-induced intestinal damage in B6C3F1 mice. Biol Pharm Bull. 2013;36(3):352–9.
47. Matsuu M, Shichijo K, Okaichi K, Wen CY, Fukuda E, Nakashima M, et al. The protective effect of fermented milk kefir on radiation-induced apoptosis in colonic crypt cells of rats. J Radiat Res. 2003;44(2):111–5.
48. de LeBlanc AdM, Matar C, Farnworth E, Perdigon G. Study of cytokines involved in the prevention of a murine experimental breast cancer by kefir. Cytokine. 2006;34(1):1–8.
49. Maalouf K, Baydoun E, Rizk S. Kefir induces cell-cycle arrest and apoptosis in HTLV-1-negative malignant T-lymphocytes. Cancer Manag Res. 2011;3:39.
50. Rizk S, Maalouf K, Baydoun E. The antiproliferative effect of kefir cell-free fraction on HuT-102 malignant T lymphocytes. Clin Lymphoma Myeloma. 2009;9:S198–203.
51. Ghoneum M, Gimzewski J. Apoptotic effect of a novel kefir product, PFT, on multidrug-resistant myeloid leukemia cells via a hole-piercing mechanism. Int J Oncol. 2014;44(3):830–7.
52. Nagira T, Narisawa J, Teruya K, Katakura Y, Shim S-Y, K-i Kusumoto, et al. Suppression of UVC-induced cell damage and enhancement of DNA repair by the fermented milk. Kefir Cytotechnol. 2002;40(1):125–37.
53. Ghoneum M, Felo N. Selective induction of apoptosis in human gastric cancer cells by Lactobacillus kefiri (PFT), a novel kefir product. Oncol Rep. 2015;34(4):1659–66.
54. Gao J, Gu F, Ruan H, Chen Q, He J, He G. Induction of apoptosis of gastric cancer cells SGC7901 in vitro by a cell-free fraction of Tibetan kefir. Int Dairy J. 2013;30(1):14–8.
55. Rizk S, El Khoury N, El-Hayek S, Tarras O, El-sibai M, El-Sabban M. Kefir exhibits anti-proliferative and pro-apoptotic effects on colon adenocarcinoma cells with no significant effects on cell migration and invasion (647.24). FASEB J. 2014;28(1 Supplement):647–724.
56. Can G, Topuz E, Derin D, Durna Z, Aydiner A. Effect of kefir on the quality of life of patients being treated for colorectal cancer. Oncol Nurs Forum. 2009;36(6):335–42.
57. Cevikbas A, Yemni E, Ezzedenn FW, Yardimici T, Cevikbas U, Stohs S. Antitumoural antibacterial and antifungal activities of kefir and kefir grain. Phytother Res. 1994;8(2):78–82.
58. Alsha'ar IA, Aloklah B, Al-Deen RB, Aljamali M, Alkadry R, Albiski F. In vitro anticancer properties of kefir and kefir products produced by a novel method in Syria. IJPSI. 2017;6(5):1–6
59. Topuz E, Derin D, Can G, Kürklü E, Çınar S, Aykan F, et al. Effect of oral administration of kefir on serum proinflammatory cytokines on 5-FU induced oral mucositis in patients with colorectal cancer. Invest New Drugs. 2008;26(6):567–72.
60. Furukawa N, Matsuoka A, Takahashi T, Yamanaka Y. Anti-metastatic effect of kefir grain components on lewis lung carcinoma and highly metastatic B 16 melanoma in mice. J Agric Sci-Tokyo-Univ Agric. 2000;45(1):62–70.