

Functional Properties of Probiotic Kefir: A Review

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ABSTRACT: Kefir is a fermented dairy product that is made up of a combination of probiotic bacteria and kefir grains. Nowadays humans consume fermented dairy products for good health. As compared to any other probiotic products, kefir has good health benefits and also having an anti-functional property. The inclusion of good dietary content in the finished product contributes to the drink's health benefits. Kefir injections improve human metabolism and lactose tolerance. It is often given to hospital patients and is approved for babies and the elderly. In recent year various study reported that the dietary prevalence such as kefir has good prospects for cancer treatment and anti-functional properties. The present study focuses on the kefir and discusses the anti-functional properties of kefir like anticancer, antioxidant, anti-hypertension, antimicrobial, and anti-allergic properties.

KEYWORDS- Anti-functional, Cancer, Health, Properties Kefir, and Probiotic.

I. INTRODUCTION

Fermented milk and milk additives have had a significant impact on wellbeing in recent years. They are thought to be useful because of their medicinal effects and other properties (John et al., 2014). Milk kefir is a traditional Caucasian fermented milk drink. Because of its health-promoting qualities, it is commonly used in human nutrition. Kefir is traditionally made by fermenting milk with kefir grains, which are made up of a variety of microbial species. The inhabitants of milk kefir grains are mostly lactic acid bacteria (LAB), but kefir also includes yeasts and acetic acid bacteria (AAB). The resulting kefir drink is usually acidic, with a clear flavour, partly viscous, and fluffy, depending on its age. Kefir has been credited with many health benefits for decades, and it was also used as a natural remedy (Nejati et al., 2020).

Probiotics are said to have nutritional benefits, so the beverage is drunk. On enteric

bacterial infections, kefir drink has a bactericidal and bacteriostatic impact. On enteric bacterial infections, kefir drink has a bactericidal and bacteriostatic impacts (Gut et al., 2021). Variation in the color, taste, scent and chemical or microbial background of the final product is caused by variations in the microflora of kefir particles, biochemical properties, and microbiological profile of the milk used, or physical or geographical differences in the process used in processing (Noğay 2019).

Kefir has inspired scientific interest due to its purported benefits, which include increased lactose absorption and immunity, antihypertensive, antioxidative, antiallergenic, antitumor, antimicrobial, anti-inflammatory, and cholesterol-lowering activities with possible prebiotic action, are produced during milk fermentation by kefir grains (Amorim et al., 2019; Cotărel et al., 2019). Therefore this reviews aim on analysis is to go over recent research on kefir and to highlight its anti-functional properties and the mechanism of its effect.

FUNCTIONAL PROPERTIES OF KEFIR ANTICANCER PROPERTIES:

As per the old adage, cancer is as old as the human race holds some validity; paleo pathologic evidence suggests that tumors existed in animals long before humans arrived on the scene. Whatever the case might be, ultimate historical dependency necessitates written reports. In medicine, the Edwin Smith Papyrus, written about 3000 BC, contains the first written account of diseases and cancer, a breast cancer. The author came to the conclusion that a bulging breast tumor was a serious illness for which there was no cure (Breasted, J., 1930). The EbersPapyrus, which dates from about 1500 BC, provides the first mention of a soft-tissue tumor, a fatty tumour, as well as references to scalp, uterus, liver, and rectum cancers. The Egyptians used cautery, scissors, and salts to cure tumors and diseases, and introduced

arsenic paste, which was used as "Egyptian ointment" until the 19th century. The Indians, Sumerians, Chinese, Persians, and Hebrews of the same era used herbal medicines like tea, fruit juices, figs, and boiled cabbage, but in severe circumstances, they did not hesitate to use iron, copper, sulphur, and mercury solutions and pastes (Hajdu, S., 2011).

After some decades new technologies and various kinds of therapies are developed for the treatments of a cancer cell. Most exploratory procedures were replaced by ultrasound (sonography), computed tomography (CT scans), magnetic resonance imaging (MRI scans), and positron emission tomography (PET scans) in the early 1970s. Surgeons may extract cancers from the intestine, oesophagus, and bladder by tubes using miniature video cameras and endoscopy. Surgeons introduced innovative cancer management techniques in the last decades of the twentieth century by incorporating surgery with chemotherapy and/or radiation. Roentgen discovered X-rays after anesthesia had been discovered for 50 years. Doctors later discovered that nitrogen mustard can destroy lymphoma cancer cells that are quickly proliferating. The use of a variety of treatment medications has helped in the effective treatment of a variety of cancers over the years (Sudhakar, A., 2009). In this paper, we discussed the mechanisms of suppression of the cancer cell with the help of the probiotic drink kefir.

ANTI - CANCER EFFECT OF KEFIR:

1. Kefir consumption reduces TGF- β , TGF- α , and Bcl2 secretion while increasing bax secretion, resulting in apoptosis induction.
2. Active peptides of kefir cause Ca/Mg-dependent endonucleases for DNA cleavage and induce ROS-mediated apoptosis.
3. In cancerous cells, low secretion of TGF- β and TGF- α causes an antiproliferative effect.
4. Kefir contains sphingomyelins, which boost the production of interferon- γ , an anti-proliferative cytokine (Sharifi et al., 2017).

BREAST CANCER:

In the past few decades, though, the prevalence of breast cancer has risen worldwide (Hortobagyi et al., 2005). Nowadays breast cancer is rising in an Asian countries (Green et al., 2008). The most populous democracy in the world is India, with a population of 1.2 billion. India is a culture that is pluralistic, multilingual, and multiethnic. About 15 native languages and more than 70 dialects are included. While the focus of

public health in developing countries has been primarily on infectious diseases, non-communicable diseases such as cancer often have an increased resource burden (Khokhar., 2012). In India's urban regions, prostate cancer had the largest prevalence of cancer 15 years ago, but breast cancer has overtaken it as the highest incidence. Breast cancer is frequently diagnosed in women (Anderson et al., 2008). Breast cancer is eminently treatable if diagnosed at an early stage, unlike other cancers. There is a need, however, for culturally suitable education and preventive methods for breast cancer (Khokhar., 2012). In the last few years surgery, chemotherapy, radiation therapy, screening, radiotherapy are various methods used for treating breast cancer (Fisher et al., 2002). Like these all therapies, various scientists also noted that, breast cancer also be treated by consumption of kefir. In 2007 Chen et al carried out research on the influence of kefir extract on the MCF-7 cell line, and HMECs (Human Mammary Epithelial Cells) found that kefir suppressed the growth of MCF-7 cells in a dose-dependent manner. De LeBlanc et al., 2006 shown that memory gland and tumor are shown in the study of cytokines that inhibit murine regulation, kefir experimental breast cancer kefir, cell-free fraction modulatory influence on immune response (De LeBlanc et al., 2006). Instead of apoptosis, Kefir extracts disrupt the cell cycle and decrease tumor growth in breast cancer cells, so it may be necessary to deter or treat breast cancer.

COLON CANCER:

The third most prevalent cause of cancer-related deaths worldwide is colon cancer (Pourhoseingholi., 2012). In Asian countries, colorectal cancer has become an important issue. In asymptomatic Asians, the average prevalence of advanced colorectal neoplasm was also shown to be similar to that of other developing countries. Among medical experts, there is also an unproven finding that there is a growing incidence of colorectal cancer in younger people (Yee et al., 2009). There are 1,849,518 expected new (Colorectal cancer) CRC cases and 880,792 CRC-related deaths in 2018, according to the World Health Organisation (WHO) GLOBOCAN database. Regional figures indicate that facilities and 5-year incidence were observed in Asia among half of the new incidents (Wong et al., 2019). High consumption of alcoholic drinks has increased the risk of colon cancer by up to 60%. Other factors were also significant, including obesity, diabetes, high red, and processed meat intake, and cigarette smoking, all of which were associated with a 20

percent increased risk of colon cancer (Huxley et al., 2009). In colon cancer, the primary adjuvant treatment is chemotherapy (Chau et al., 2006). For stage III rectal cancer patients, radiotherapy is typically used in conjunction with chemotherapy (Granados-Romero et al., 2017). Surgical resection, adjuvant therapy, endoscopic resection, neoadjuvant therapy, systemic therapy is also good treatments for colon cancer (Recio-Boileset al., 2019). Like these all therapies, the various scientists suggested that the consumption of probiotic drink kefir is useful for treated colon cancer. (Guzel-Seydim et al., 2016) stated that, in all types of cancer, colon cancer is very popular. Milk and fermented milk products, in particular kefir, have inhibitory activity against *Fusobacterium nucleatum*, a bacterial pathogen of colon cancer. Milk contains calcium, proteins, and carbohydrates that facilitate the proliferation and adhesion of probiotics to the colon, whereas Kefir contains lactic acid bacteria adhering to the colon and special yeast flora. It is understood that *F. nucleatum* causes colon cancer by adhering to the colon epithelium and causing the mutation of the cell.

L. kefir, *L. kefiranoformis* and *L. kefirgranum*, which has been shown to have significant probiotic properties and favorable health effects in recent research, is only found in kefir grain. Showed that the activity of the *F. nucleatum* was suppressed by natural kefir derived from kefir grains. Another study suggested that fermented dairy products kefir and ayran have health-promoting functions and reduce the risk of colon cancer which are responsible for the decrease in DNA damage. Because of high contents of acetic acid and lactic acid present in kefir shows antioxidant property and thus decreases DNA damage in colon cancer (Grishina et al., 2011).

GASTRIC CANCER:

Gastric cancer is the fourth most common cancer worldwide and in Eastern Asia, Eastern Europe, and South America Gastric cancer is one of the second most causes of cancer death in both sexes. In 2012, 720,000 gastric cancer patients died and more than 950,000 new patients are come each year (Van Cutsem et al., 2016, Gao et al., 2013). However, since World War II, the prevalence of gastric cancer has been decreasing globally and it is one of the least frequent cancers in North America. In 2009, there were an estimated 21,130 new cases of gastric cancer in the United States and 10,620 predicted deaths (Ajani et al., 2010) Surgery, radiation therapy, chemotherapy, adjuvant chemotherapy, neoadjuvant chemotherapy are

useful for treated gastric cancer worldwide (Orditura et al., 2014). Like all treatments, researchers work on probiotic products to decrease gastric cancer in human beings. A study of kefir found that, it had a dose-dependent anti-proliferative effect on the gastric cancer cell line SGC7901, kefir demonstrated anti-carcinogenic activity in vitro. A study found that kefir was able to induce programmed cell death (apoptosis) in SGC7901 cells through the regulation of the BAX gene and the promoter of apoptosis and anti-oncogene, and to induce the regulation of the known apoptosis and oncogene inhibitor, the BCL-2 gene. In addition to encouraging cell death of cancer cells, tests of carcinogens have demonstrated antimutagenic effects (García-Burgos et al., 2020). In another study with *Lactobacillus kefir*, a new kefir compound, PFT was shown to induce dose-dependent apoptosis in gastric cancer cells; although apoptosis was correlated with decreased mitochondrial membrane potential (MMP) polarization and decreased Bcl2 expression, PFT was not shown to induce apoptosis in peripheral mononuclear blood cells (PBMCs) or 4T1 breast cancer cell. The findings suggest that white blood cells are healthy for PFT and cause apoptotic effects in gastric cancer cells. Therefore, it has been confirmed that it has the potential for the treatment of gastric cancers (Tasdemiret al., 2020).

GLIOBLASTOMA CANCER:

The human brain contains more than 120 individual tumor forms (Hatzikirou et al., 2005). The most widespread and aggressive type of primary brain tumor is glioblastoma multiform (GBM) (Azzarelliet al., 2021). Glioblastoma (GBM) is the most prevalent malignant primary brain tumor in the United States, affecting about 3 out of every 100,000 people (Mende et al., 2021). The World Health Organization (WHO) classifies glioblastoma (GB) as a category IV astrocytoma. The estimated patient life period is just 16 months, making it the worst primary malignant brain tumor. GBM is now treated mainly with tumour resection followed by radiotherapy and chemotherapy, usually with alkylating agents. Photodynamic therapy, which is dependent on photo oxidative reactions and the aggregation of photo sensitizers in tumor tissue, can be used to aid tumor resection and target cell proliferation (Møller et al., 2013). Like all treatments, researchers work on kefir products to decrease the glioblastoma in human beings. Fatahiet al., 2021 studied the cytotoxic effect of kefir on the growth and increase of glioblastoma cancer cells, the most

extreme type of brain tumors. U87 cancer cell line used in the experiment (glioblastoma). At 24 and 48 hours, the connection of cancer cells with varying amounts of kefir drink and supernatants was studied. The MTT test was used to evaluate the cell cytotoxicity of kefir and the sedimentation of cell lysate and extract after 24 and 48 hours. In contrast to the control sample, the MTT test found that care of the cells with the 48-hour fermented drink caused the most cell cytotoxicity. The toxic effect was dose-dependent in both categories, with cell survival declining significantly as the concentration was increased. The study found that the fermented kefir drink supernatant, when used as a probiotic product, has a higher toxicity and lethality effect on glioblastoma cancer cells. This substance can be used as a cancer drug supplement or as a support.

FREE RADICALS:

Free radicals are highly reactive and unstable molecules formed spontaneously in the body as a by product of metabolism (oxidation) or as a result of exposure to contaminants in the atmosphere such as cigarette smoke and ultraviolet light. Free radicals only last a fraction of a second, but during that time they can destroy DNA (Deoxyribonucleic acid) resulting in mutations that can lead to cancer. In other words, every molecular species capable of autonomous life that includes an unpaired electron in an atomic orbital is referred to as a free radical. The presence of an unpaired electron causes most radicals to have those properties in common. Most radicals are extremely reactive and unstable. They function as oxidants or reductants depending on whether they donate or take an electron from other molecules (Lobo et al., 2010). Oxygen-free radicals, also known as "Reactive oxygen species," (ROS) are the most common free radicals that cause damage to biological structures. These are the major byproducts produced in aerobic organisms' cells, and they can initiate autocatalytic reactions in which molecules they associate with are transformed into free radicals, propagating the damage chain (Rahman K., 2007). Hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radicals, and peroxy nitrite radical are the most important oxygen-containing free radicals in many disease states. There are highly reactive organisms capable of destroying biologically important molecules such as DNA, proteins, sugars, and lipids in the nucleus and cell membranes. Free radicals target essential macromolecules, causing cell destruction and loss of homeostasis. Free radicals target a large variety of molecules in the

body. Lipids, nucleic acids, and proteins are among the most important targets (Young et al., 2001).

GENERATION OF FREE RADICAL:

Free radicals are generated in the cell by enzymatic and non-enzymatic reactions (Bagchi et al., 1998). The respiratory chain, phagocytosis, prostaglandin synthesis, and the cytochrome P450 mechanism are all examples of enzymatic reactions that create free radicals. Several cellular oxidase processes, such as NADPH (Nicotinamide adenine dinucleotide phosphate hydrogen) oxidase, xanthine oxidase, and peroxidases, contain the superoxide anion radical ($O_2^{\bullet-}$). If formed, it undergoes a series of reactions that produce a variety of ROS and RNS (Reactive nitrogen species), including hydrogen peroxide, hydroxyl radical (OH^{\bullet}), peroxy nitrite ($ONOO^-$), hypochlorous acid ($HOCl$), and others. A number of oxidase enzymes, including amino acid oxidase and xanthine oxidase, contain H_2O_2 (a non-radical). The oxidation of hypoxanthine to xanthine and xanthine to uric acid is catalyzed by the last one. The most reactive free radical in vivo, the hydroxyl radical (OH^{\bullet}), is formed when $O_2^{\bullet-}$ reacts with H_2O_2 in the presence of Fe^{2+} or Cu^+ (catalyst). The Fenton reaction is the term for this reaction. Myeloperoxidase, a neutrophil-derived enzyme, produces hypochlorous acid ($HOCl$) by oxidizing chloride ions in the presence of H_2O_2 . The oxidation of L-arginine to citrulline by nitric oxide synthase produces nitric oxide radical (NO^{\bullet}) in biological tissues (Pham-Huyet et al., 2008).

Non-enzymatic reactions of oxygen with organic compounds, as well as those initiated by ionizing radiations, can create free radicals. The nonenzymatic mechanism can also occur in the mitochondria during oxidative phosphorylation (aerobic respiration) (Valko et al., 2007, Droge W., 2002, Willcox et al., 2004).

Some externally generated sources of free radicals are cigarette smoke, environmental pollutants, radiation, certain drugs, pesticides, industrial solvents, ozone wherever some internally generated sources of free radicals are mitochondria, xanthine oxidase, peroxisomes, inflammation, phagocytosis, arachidonate pathways, exercise, ischemia-reperfusion injury (Lobo et al., 2010).

EFFECT OF FREE RADICALS ON THE BODY:

Free radicals are particularly reactive and can damage almost all biomolecules (Proteins, lipids, carbohydrates & nucleic acid). Lipid peroxidation is a mechanism that free radicals may use to damage cell membranes and

lipoproteins. ROS/NOS can also affect proteins, causing structural modifications and the lack of enzyme activity. Free radicals can damage DNA and induce mutagenicity and cytotoxicity, making them important players in cancer growth. ROS is thought to cause mutations and suppress DNA repair, resulting in the inactivation of 17 tumor repressor genes, which leads to cancer (Shinde et al., 2012). Free radicals have an effect on the body by various diseases such as tumors and cancer like lung cancer, leukemia, breast, ovary, rectum cancers, etc. Inflammatory lung conditions such as asthma and chronic obstructive pulmonary disease (COPD) as well as atherosclerosis, ischemic heart disease, coronary hypertrophy, hypertension, shock, and trauma are all cardiovascular diseases (Sen et al., 2010).

ANTIOXIDANTS:

Antioxidants are compounds that can help protect cells from free radical damage. Antioxidants bind with and stabilize free radicals, potentially preventing any of the damage caused by free radicals (Shinde et al., 2012). Oxidation is a chemical reaction that produces free radicals, which can cause chain reactions that damage an organism's cells. Antioxidants including thiols and ascorbic acid (vitamin C) stop these chain reactions from continuing. Plants and animals retain diverse networks of competing antioxidants, such as glutathione and enzymes, to balance oxidative stress (Dabelstein et al., 2000). Antioxidants are maybe vitamins and minerals as well as they are the proteins that are present in the human body. Chronic illnesses such as cancer, diabetes, coronary disease, stroke, Alzheimer's disease, rheumatoid arthritis, and cataracts are thought to be prevented by Antioxidants (Kumar et al., 2017). Antioxidants may be either exogenous or endogenous. There are two forms of endogenous antioxidants: enzymatic and non-enzymatic. Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase 26 (GPx), and glutathione reductase (GR) are antioxidant enzymes (GRx) (Young et al., 2001). The non-enzymatic antioxidant is classified into nutrient antioxidants and metabolic antioxidants. Lipoic acid, glutathione, L-arginine, uric acid, bilirubin, etc. are the metabolic antioxidant while Vitamin E, Vitamin C, carotenoids, trace elements (Se, Cu, Zn, Mn) are the nutrient antioxidant which cannot be formed by the human body (Kohen et al., 2002; Willcox et al., 2004). Peto and his colleagues expanded on the connection between lower serum levels of beta carotene (BC) and cancer in 1981. Beta carotene is a strong anti-oxidant. Some antioxidants include retinol (Vit. A), retinoid, and

tocopherol (vitamin E) is good for the human body (Birangane et al., 2011).

ANTIOXIDANTS PROPERTIES:

Dietary components play a major role in protecting the body against oxidative damage. Kefir contains a series of components that have good antioxidant activity. Kefir comprises a number of elements that have anti-oxidant properties (Chen et al., 2006). In an animal model, (Güven et al., 2003) compared the antioxidative effects of kefir and vitamin E against CCl₄ oxidative disruption. The findings showed that both vitamin E and kefir can protect tissues from CCl₄-induced damage, with kefir providing more protection than vitamin E (Ahmed et al., 2013). Kefir consumption raises glutathione peroxidase levels and lowers malondialdehyde levels, all of which are involved in the regulation of oxidative stress. Kefir, on the other hand, can bind to the 1,1-diphenyl-2-picrylhydrazyl (DPPH) and superoxide radicals, as well as inhibit the peroxidation of linoleic acid. As a result, kefir acts as an anti-carcinogen by acting as an antioxidant and reducing DNA damage (Sharifi et al., 2017).

ANTI-HYPERTENSION EFFECT:

According to some proof, probiotic bacteria or their fermented products play a significant role in blood pressure regulation. Although the evidence is scarce and controversial, anti-hypertensive effects have been observed in laboratory and clinical trials (Rosa et al., 2017). Ebner et al., (2015) identified 236 peptides produced exclusively during kefir development in a recent review. From β -kazein and α 2-kazein, the researchers discovered 12 peptides with ACE inhibitor action. The effects of kefir on animals have been shown to substantially lower blood pressure (Maeda et al., 2004a). Another research looked into the effects of kefir (100 and 300 mg/kg of rat) developed by *Lactobacillus kefir* and of action WT-2BT on rat blood pressure. ACE movements in the serum and thoracic aorta of kefir-an-fed rats were slightly lower than those in the control group, according to researchers (Maeda et al., 2004b). According to Grnnevik et al., (2011), the decarboxylation agent of glutamic acid, γ -aminobutyric acid (GABA), which has a blood pressure-lowering benefit, increased continuously in Norwegian kefir for 8 weeks of storage. Low molecular weight peptides, kefir, and GABA appear to play important roles in kefir's antihypertensive activity. The ACE-inhibitory peptides block the manufacture of the vasoconstrictor angiotensin I and, as a result,

aldosterone, a hormone that stimulates an increase in serum sodium concentration, resulting in a rise in blood pressure. Furthermore, ACE-inhibitory peptides block the degradation of bradykinin, a hormone that has a vasodilator function, resulting in a reduction in blood pressure (Hernández-Ledesma et al., 2011).

ANTIMICROBIAL PROPERTIES

Kefir and kefir-related strains have been found to have a wide variety of antimicrobial properties (Bourriest al., 2016). Kefir's intrinsic formation of amino acids, hydrogen peroxide, acetaldehyde, carbon dioxide, and bacteriocins has an antibacterial activity toward several pathogenic species. For example, from *Lactobacillus Plantarum* ST8KF, 3.5 kD bacteriocin was developed in kefir. Aside from that, hydrogen peroxide, an antimicrobial compound formed by certain bacteria, is another metabolite (John et al., 2015). F1, a bacteriocin developed by *Lactobacillus paracasei* sub sp. *tolerans* strain FX-6 derived from Tibetan kefir grains, is another kefir-derived bacteriocin. *S. aureus*, *Shigella dysenteriae*, and *Aspergillus niger* are among the bacteria and fungi that F1 has been shown to inhibit (Miao et al., 2014).

In another study of disc diffusion tests, kefir fermented milk was shown to have antimicrobial activity comparable to ampicillin, azithromycin, ceftriaxone, amoxicillin, and ketoconazole against a wide variety of pathogenic bacterial and fungal organisms (Bourrie et al., 2016). Both 21 isolates of lactic acid bacteria from Turkish kefir developed hydrogen peroxide (0.04–0.19 g/ml), according to Yuksekdağ et al., 2004a. They later announced that 11 out of 21 strains of kefir Lactococci developed hydrogen peroxide in a later paper (Yuksekdağ et al., 2004).

When screened using an agar spot examination, other *Lactobacillus* species originating from kefir, such as *L. acidophilus* and *L. kefirifaciens*, as well as some *S. thermophilus* strains, showed antimicrobial activity against a wide variety of pathogenic organisms, including *E. coli*, *L. monocytogenes*, *S. aureus*, *S. typhimurium*, *S. enteritidis*, *S. flexneri* (Yüksekdağ et al., 2004; Golowczyet al., 2008; Santos et al., 2003).

ANTI-ALLERGIC PROPERTIES

Food allergies are allergic responses to proteins in foods that can cause a variety of symptoms (wang et al., 2011). Food allergies are most frequent in babies and young children, and their prevalence varies with age. Food allergies affect about 6% of children aged 0–5, compared to

1–2% of adults (Pouloset al., 2007). Egg, milk, peanuts, tree nuts, sesame, fish, shrimp, wheat, and soy are the most widely implicated foods. Reactions usually develop shortly after eating and may include an acute rash around the lips, as well as redness and swelling of the cheeks. Urticarial, angioedema, respiratory difficulties, vomiting, and/or anaphylactic shock are symptoms of more acute responses, which may lead to death. Food allergies can also present as chronic eczema, with or without a clear link to food (Hodge et al., 2009). Nowadays food allergy is a major problem like another allergy. Probiotic drink like kefir has been reported as an anti-allergic agent by the various scientist. The IgE and IgG1 responses are suppressed when kefir milk and soy-based kefir products are consumed regularly. Thus, altering gut micro flora will help us achieve our goals of preventing food allergies and improving mucosal tolerance to gastrointestinal pathogen infection. Kefir also prevents ovalbumin-induced eosinophilia in lung tissue and mucus hyper secretion, according to another study. As a result, kefir has a lot of therapeutic promise for allergic bronchial asthma (Ahmed et al., 2013). In a sample of OVA-sensitized mice fed with heat-inactivated strain M1 of *L. kefirifaciens*, the inactivated M1 was able to lower levels of pro-inflammatory and Th2 cytokines such as IL-4, IL-6, IL13, and ccl20 in both the splenocytes and BALF of the mice while also lowering OVA-specific IgE and the Th17 related cytokines. The M1 therapy also increased the number of regulatory T cells in the body (Bourrie et al., 2016). According to studies like this, kefir can help reduce certain allergy symptoms.

II. CONCLUSION

Kefir is a fermented probiotic milk product which is originated from Caucasian mountain. In the last few years fermented food products have greater interaction with food industries and scientists. Basically, this fermented milk product is good for treating various types of diseases. Like other fermented food products kefir is also safe for human consumption and it is very easy to make in the home, it is a low production cost and the main benefits are, it is easily digested by the human body. Due to the functional properties of kefir, it is very useful to cancer patients for suppressed the cancer cell from breast cancer, colon cancer, gastric cancer, glioblastoma cancer. The health benefits associated with kefir are it works on antiallergic, antimicrobial, antioxidant, antihypertension patients to take care of their health. This fermented milk kefir has

considerable potential for investigating the latent therapeutic and functional properties that have never been identified to date, and this should motivate investigators to do more research on kefir.

REFERENCES

- [1]. Ahmed, Z., Wang, Y., Ahmad, A., Khan, S. T., Nisa, M., Ahmad, H., & Afreen, A. (2013). Kefir and health: a contemporary perspective. *Critical reviews in food science and nutrition*, 53(5), 422-434.
- [2]. Ajani, J. A., Barthel, J. S., Bekaii-Saab, T., Bentrem, D. J., D'Amico, T. A., Das, P., ... & Yang, G. (2010). Gastric cancer. *Journal of the National Comprehensive Cancer Network*, 8(4), 378-409.
- [3]. Amorim, F. G., Coitinho, L. B., Dias, A. T., Friques, A. G. F., Monteiro, B. L., de Rezende, L. C. D., ... & Quinton, L. (2019). Identification of new bioactive peptides from Kefir milk through proteopeptidomics: Bioprospection of antihypertensive molecules. *Food chemistry*, 282, 109-119.
- [4]. Anderson, B. O., & Jakesz, R. (2008). Breast cancer issues in developing countries: an overview of the Breast Health Global Initiative. *World journal of surgery*, 32(12), 2578-2585.
- [5]. Azzarelli, R., Ori, M., Philpott, A., & Simons, B. D. (2021). Three-dimensional model of glioblastoma by co-culturing tumor stem cells with human brain organoids. *Biology Open*, 10(2).
- [6]. Bagchi, K., & Puri, S. (1998). Free radicals and antioxidants in health and disease: A review. *EMHJ-Eastern Mediterranean Health Journal*, 4 (2), 350-360, 1998.
- [7]. Birangane, R. S., Chole, D. G., & Reddy, K. S. P. (2011). A review of antioxidants. *Journal of Indian Academy of Oral Medicine and Radiology*, 23(5), 351.
- [8]. Bourrie, B. C., Willing, B. P., & Cotter, P. D. (2016). The microbiota and health promoting characteristics of the fermented beverage kefir. *Frontiers in microbiology*, 7, 647.
- [9]. Breasted, J. H. (1930). *The Edwin Smith Surgical Papyrus: published in facsimile and hieroglyphic transliteration with translation and commentary in two volumes*.
- [10]. Chau, I., & Cunningham, D. (2006). Adjuvant therapy in colon cancer—what, when and how?. *Annals of Oncology*, 17(9), 1347-1359.
- [11]. Cotârlet, M., Vasile, A. M., Cantaragiu, A. M., Gaspar-Pintiliescu, A., Crăciunescu, O., Oancea, A., ... & Bahrim, G. E. (2019). Colostrum-derived bioactive peptides obtained by fermentation with kefir grains enriched with selected yeasts. *The Annals of the University Dunarea de Jos of Galati. Fascicle VI-Food Technology*, 43(1), 54-68.
- [12]. Dabelstein, W., Reglitzky, A., Schütze, A., Reders, K., & Brunner, A. (2000). Automotive fuels. *Ullmann's Encyclopedia of Industrial Chemistry*, 1-41.
- [13]. 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.
- [14]. Dröge, W. (2002). Free radicals in the physiological control of cell function. *Physiological reviews*.
- [15]. Ebner, J., AşçıArslan, A., Fedorovac, M., Hoffmann, R., Küçükçetin, A., Pischetsrieder, M., 2015. Peptide profiling of bovine kefir reveals 236 unique peptides released from caseins during its production by starter culture or kefir grains. *Journal of Proteomics* 117, 41-57.
- [16]. Fang, Y. Z., Yang, S., & Wu, G. (2002). Free radicals, antioxidants, and nutrition. *Nutrition*, 18(10), 872-ss879.
- [17]. Fatahi, A., Soleimani, N., & Afrough, P. (2021). Anticancer Activity of Kefir on Glioblastoma Cancer Cell as a New Treatment. *International Journal of Food Science*, 2021.
- [18]. Fisher B, Anderson S, Bryant J. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*. 2002;347:1233-1241.
- [19]. Gao, J., Gu, F., Ruan, H., Chen, Q., He, J., & He, G. (2013). Induction of apoptosis of gastric cancer cells SGC7901 in vitro by a cell-free fraction of Tibetan kefir. *International Dairy Journal*, 30(1), 14-18.
- [20]. García-Burgos, M., Moreno-Fernández, J., Alférez, M. J., Díaz-Castro, J., & López-Aliaga, I. (2020). New perspectives in fermented dairy products and their health relevance. *Journal of Functional Foods*, 72, 104059.
- [21]. Golowczyc, M. A., Gugliada, M. J., Hollmann, A., Delfederico, L., Garrote, G. L., Abraham, A. G., et al. (2008). Characterization of homofermentative Lactobacilli isolated from

- kefir grains: potential use as probiotic. *J. Dairy Res.* 75, 211–217. doi: 10.1017/S0022029908003117.
- [22]. Granados-Romero, J. J., Valderrama-Treviño, A. I., Contreras-Flores, E. H., Barrera-Mera, B., Herrera Enríquez, M., Uriarte-Ruiz, K., ... & Arauz-Peña, G. (2017). Colorectal cancer: a review. *Int J Res Med Sci*, 5(11), 4667-4676.
- [23]. Green M, Raina V (2008). Epidemiology, screening and diagnosis of breast cancer in the Asia-Pacific region: current perspectives and important considerations. *Asia Pac J ClinOncol*, 4, 5-13.
- [24]. Grishina, A., Kulikova, I., Alieva, L., Dodson, A., Rowland, I., & Jin, J. (2011). Antigenotoxic effect of kefir and ayan supernatants on fecal water-induced DNA damage in human colon cells. *Nutrition and cancer*, 63(1), 73-79.
- [25]. Grønnevik, H., Falstad, M., Narvhus, J.A., 2011. Microbiological and chemical properties of Norwegian kefir during storage. *International Dairy Journal* 21, 601–606.
- [26]. Gut, A. M., Vasiljevic, T., Yeager, T., & Donkor, O. N. (2021). Kefir characteristics and antibacterial properties-potential applications in control of enteric bacterial infection. *International Dairy Journal*, 105021.
- [27]. Guzel-Seydim, Z. B., Dibekci, M., Cagdas, E., & Seydim, A. C. (2016). Effect of kefir on *Fusobacterium nucleatum* in potentially preventing intestinal cancer. *Functional Foods in Health and Disease*, 6(7), 469-477.
- [28]. Guzel-Seydim, Z. B., Kok-Tas, T., Greene, A. K., & Seydim, A. C. (2011). Functional properties of kefir. *Critical reviews in food science and nutrition*, 51(3), 261-268.
- [29]. Hajdu, S. I. (2011). A note from history: landmarks in history of cancer, part 1. *Cancer*, 117(5), 1097-1102.
- [30]. Hartgrink, H. H., Jansen, E. P., van Grieken, N. C., & van de Velde, C. J. (2009). Gastric cancer. *The Lancet*, 374(9688), 477-490.
- [31]. Hatzikirou, H., Deutsch, A., Schaller, C., Simon, M., & Swanson, K. (2005). Mathematical modelling of glioblastoma tumour development: a review. *Mathematical Models and Methods in Applied Sciences*, 15(11), 1779-1794.
- [32]. Hernández-Ledesma B, Contreras MM & Recio I (2011) Antihypertensive peptides: production, bioavailability and incorporation into foods. *Adv Colloid Interface Sci* 165, 23–35.
- [33]. Hodge, L., Swain, A., & Faulkner-Hogg, K. (2009). Food allergy and intolerance. *Australian family physician*, 38(9), 705-707.
- [34]. Hortobagyi GN, Garza SJ, Pritchard K, et al (2005). The global breast cancer burden: variations in epidemiology and survival. *Clin Breast Cancer*, 6, 391-401.
- [35]. Huxley, R. R., Ansary- Moghaddam, A., Clifton, P., Czernichow, S., Parr, C. L., & Woodward, M. (2009). The impact of dietary and lifestyle risk factors on risk of colorectal cancer: a quantitative overview of the epidemiological evidence. *International journal of cancer*, 125(1), 171-180.
- [36]. John, S. M., & Deeseenthum, S. (2015). Properties and benefits of kefir-A review. *Songklanakarin Journal of Science and Technology*, 37(3), 275-282.
- [37]. John, S. M., & Deeseenthum, S. (2015). Properties and benefits of kefir-A review. *Songklanakarin Journal of Science and Technology*, 37(3), 275-282.
- [38]. Khokhar, A. (2012). Breast cancer in India: where do we stand and where do we go?. *Asian Pacific Journal of Cancer Prevention*, 13(10), 4861-4866.
- [39]. Kohen, R., & Nyska, A. (2002). Invited review: Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods for their quantification. *Toxicologic pathology*, 30(6), 620-650.
- [40]. Kumar, S., Sharma, S., & Vasudeva, N. (2017). Review on antioxidants and evaluation procedures. *Chinese journal of integrative medicine*, 1-12.
- [41]. Lobo, V., Patil, A., Phatak, A., & Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy reviews*, 4(8), 118.
- [42]. Maeda, H., Zhu, X., Omura, K., Suzuki, S., Kitamura, S., 2004a. Effects of an exopolysaccharide (kefiran) on lipids, blood pressure, blood glucose, and constipation. *BioFactors* 22, 197–200.
- [43]. Maeda, H., Zhu, X., Suzuki, S., Suzuki, K., Kitamura, S., 2004b. Structural characterization and biological activities of an exopolysaccharide kefiran produced by *Lactobacillus kefirifaciens* WT-2BT. *Journal of Agricultural Food Chemistry* 52, 5533–5538.

- [44]. Mende, A. L., Schulte, J. D., Okada, H., & Clarke, J. L. (2021). Current Advances in Immunotherapy for Glioblastoma. *Current oncology reports*, 23(2), 1-18.
- [45]. Miao, J., Guo, H., Ou, Y., Liu, G., Fang, X., Liao, Z., et al. (2014). Purification and characterization of bacteriocin F1, a novel bacteriocin produced by *Lactobacillus paracasei* subsp. *tolerans* FX-6 from Tibetan kefir, a traditional fermented milk from Tibet, China. *Food Control* 42, 48–53.
- [46]. Møller, H. G., Rasmussen, A. P., Andersen, H. H., Johnsen, K. B., Henriksen, M., & Duroux, M. (2013). A systematic review of microRNA in glioblastomamultiforme: micro-modulators in the mesenchymal mode of migration and invasion. *Molecular neurobiology*, 47(1), 131-144.
- [47]. Nejati, F., Junne, S., & Neubauer, P. (2020). A big world in small grain: A review of natural milk Kefir starters. *Microorganisms*, 8(2), 192.
- [48]. Noğay, N. H. (2019). Kefir beverage and its effects on health. In *Milk-Based Beverages* (pp. 273-296). Woodhead Publishing.
- [49]. Oreditura, M., Galizia, G., Sforza, V., Gambardella, V., Fabozzi, A., Laterza, M. M., ...& De Vita, F. (2014). Treatment of gastric cancer. *World journal of gastroenterology: WJG*, 20(7), 1635.
- [50]. Pham-Huy, L. A., He, H., & Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *International journal of biomedical science: IJBS*, 4(2), 89.
- [51]. Poulos, L. M., Waters, A. M., Correll, P. K., Loblay, R. H., & Marks, G. B. (2007). Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993-1994 to 2004-2005. *Journal of allergy and clinical immunology*, 120(4), 878-884.
- [52]. Pourhoseingholi, M. A. (2012). Increased burden of colorectal cancer in Asia. *World journal of gastrointestinal oncology*, 4(4), 68.
- [53]. Rahman, K. (2007). Studies on free radicals, antioxidants, and co-factors. *Clinical interventions in aging*, 2(2), 219.
- [54]. Recio-Boiles, A., Waheed, A., & Cagir, B. (2019). Cancer, colon. *StatPearls* [Internet].
- [55]. Rosa, D. D., Dias, M. M., Grzeškowiak, Ł. M., Reis, S. A., Conceição, L. L., & Maria do Carmo, G. P. (2017). Milk kefir: nutritional, microbiological and health benefits. *Nutrition research reviews*, 30(1), 82-96.
- [56]. Santos, A., San Mauro, M., Sanchez, A., Torres, J. M., and Marquina, D. (2003). The antimicrobial properties of different strains of *Lactobacillus* spp. isolated from kefir. *Syst. Appl. Microbiol.* 26, 434–437. doi: 10.1078/072320203322497464.
- [57]. Sen, S., Chakraborty, R., Sridhar, C., Reddy, Y. S. R., & De, B. (2010). Free radicals, antioxidants, diseases and phytomedicines: current status and future prospect. *International journal of pharmaceutical sciences review and research*, 3(1), 91-100.
- [58]. Sharifi, M., Moridnia, A., Mortazavi, D., Salehi, M., Bagheri, M., & Sheikhi, A. (2017). Kefir: a powerful probiotics with anticancer properties. *Medical Oncology*, 34(11), 1-7.
- [59]. Shinde, A., Ganu, J., & Naik, P. (2012). Effect of free radicals & antioxidants on oxidative stress: a review. *Journal of Dental and Allied Sciences*, 1(2), 63.
- [60]. Sudhakar, A. (2009). History of cancer, ancient and modern treatment methods. *Journal of cancer science & therapy*, 1(2), 1.
- [61]. Tasdemir, S. S., & Sanlier, N. (2020). An insight into the anticancer effects of fermented foods: A review. *Journal of Functional Foods*, 104281.
- [62]. Valko, M., Leibfritz, D., Moncol, J., Cronin, M. T., Mazur, M., & Telser, J. (2007). Free radicals and antioxidants in normal physiological functions and human disease. *The international journal of biochemistry & cell biology*, 39(1), 44-84.
- [63]. Van Cutsem, E., Sagaert, X., Topal, B., Haustermans, K., & Prenen, H. (2016). Gastric cancer. *The Lancet*, 388(10060), 2654-2664.
- [64]. Wang, J., & Sampson, H. A. (2011). Food allergy. *The Journal of clinical investigation*, 121(3), 827-835.
- [65]. Willcox, J. K., Ash, S. L., & Catignani, G. L. (2004). Antioxidants and prevention of chronic disease. *Critical reviews in food science and nutrition*, 44(4), 275-295.
- [66]. Wong, M. C., Ding, H., Wang, J., Chan, P. S., & Huang, J. (2019). Prevalence and risk factors of colorectal cancer in Asia. *Intestinal research*, 17(3), 317.
- [67]. Yee, Y. K., Tan, V. P., Chan, P., Hung, I. F., Pang, R., & Wong, B. C. (2009). Epidemiology of colorectal cancer in Asia. *Journal of gastroenterology and hepatology*, 24(12), 1810-1816.

- [68]. Young IS, Woodside JV. Antioxidants in health and disease. *J ClinPathol.* 2001; 54:176–86.
- [69]. Young, I. S., & Woodside, J. V. (2001). Antioxidants in health and disease. *Journal of clinical pathology*, 54(3), 176-186.
- [70]. Yüksesdağ, Z., Beyatli, Y., and Aslim, B. (2004). Determination of some characteristics coccoid forms of lactic acid bacteria isolated from Turkish kefir with natural probiotic. *J. WT-Food Sci. Technol.* 37, 663–667. doi: 10.1016/j.lwt.2004.02.004.
- [71]. Yuksekdağ, Z.N., Beyath, Y. and Aslim, B. 2004a . Metabolic activities of 452 *Lactobacillus* spp. strains isolated from kefir. *Nahrung / Food.* 48, 218-220. 453.
- [72]. Yuksekdağ, Z.N., Beyatli, Y. and Aslim, B. 2004. Determination of some 454 characteristics coccoid forms of lactic acid bacteria isolated from Turkish 455 kefir with natural probiotic. *Lebensmittel-Wissenschaft und-Technologie.* 456 37, 663-667.