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Fermented Foods: The Pharmacological and Anticancer Therapeutic Potential

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Abstract: Globally, dietary and environmental changes have been recognized as major causes of noncommunicable diseases such as malignancies, with ongoing research on modifiable risk factors, including eating habits, estimating that 30–40% of cancer formation can be avoided with behavioral adjustments. According to estimates from the World Health Organization (WHO), cancer is the second leading cause of death worldwide, with 9.6 million fatalities projected in 2018. Cancer accounts for nearly 1 in every 6 deaths especially in females. In a survey of year 2019 within Indian subcontinent about 20% (one in five) female suffers from one of the symptoms of ovarian disorders which further turns into tumors such as ovarian epithelial cells, endometriosis. More effective cancer treatments with lower toxicity are required. Natural foods have become increasingly popular in the treatment and prevention of cancer. Some nutrient components in fermented foods are referred to be "naturally fortified functional nutrients" because they assist to maintain a healthy gut microbiome, which protects against disease and physiology and could prove to be boon for those females by boosting metabolism because such women have lower healthy gut microflora as compared to other females as fermented foods have higher probiotic value which enhance the gut flora. The epidemiological studies suggest the evidences that lactic acid bacteria present in fermented foods plays an important role in preventing breast cancer. This review article summarizes the health benefits of fermented food to certain cancer which has been scientifically proven.

Keywords: Fermented foods, Endometriosis, Microbiome, Cancer, Microflora

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Introduction

Fermentation is a process in which microorganisms consume susceptible organic substrate as part of their own metabolic process. The study of fermentation is called Zymology by Robert *et al.* (2005). The term “ferment” derived from the *fervere*, a Latin word means to “boil it”. Louis Pasteur (1850-1860) was the one who discovered the process of fermentation. Eduard Buechner (1897) had clarified the chemistry of fermentation i.e. reaction mixture of sugar solution and yeast for the very first time. His invention opened a new door in biochemistry and selected for Nobel Prize in Chemistry 1907 (Helmenstin, 2020) It is one of the oldest and natural methods of preserving food before refrigeration. Fermentation Technology is an emerging field in Food microbiology (Sande, 1997; Terefe *et al.*, 2022). With the increasing population food scarcity is also a major issue and this led to malnutrition due to lack of healthy balanced diet. Fermented foods are rich in vitamins and essential amino acids. Therefore, it can fulfill the urge of nutritional deficiency and has the potential to reduce several diseases like hypertension, high cholesterol, diabetes, obesity and mental anxiety (Some and Mandal, 2020).

Most prominent group is of adolescent girls (14-18 years) in which symptoms of ovarian disorders are found, one out of three girl suffering from Polycystic ovarian syndrome or disease (pcod or pcos) which causes gain in weight or obesity (Pirrotta *et al.*, 2022), acne and facial hair problems (Raak *et al.*, 2014). In adult females it causes severe problems such as diabetes (type 1 and type 2), cardiovascular diseases, high cholesterol level, thyroid, anxiety - depression and mood swings sometimes pain in lower abdomen region, cancers and infertility. There are some scientific reasons behind using fermented foods in curing or reducing the chances of ovarian disorder. There is a positive link between dairy consumption and acne and hormone influx in females who are suffering from ovarian disorders (Burris *et al.*, 2013).

Scientific Reasons:

Improves digestive issues and maintains gut flora:

Since fermented foods like yoghurt are good sources of probiotics helps in killing harmful bacteria present in gut. Bloating could be avoided by taking fermented foods in daily diet. If gut flora is healthy then there would be no problem of lactose intolerance, gluten sensitivity and allergies (Ridaura *et al.*, 2013).

Prevent chronic diseases:

Diseases like diabetes, cancer are linked to gut microbes. There is no such medication or vaccination that could completely finishes diabetes but it has been reported that including fermented foods in daily diet helps to control blood-glucose level and helps in preventing gastric cancer by suppressing *Helicobacter pylori*. It has seen that patients who are under observation during this experiment has shown certain changes in gut bacteria and helps in boosting up immunity (Zhao, 2013).

Fermented foods help to feel happy:

Ovarian disorders are caused due to hormonal imbalance and stress could be one reason for hormonal influx. In a survey, females suffer from mental stress and depression more than males. According to doctors females should avoid mental stresses who are suffering from this problem. *Lactobacillus plantarum* (Raak *et al.*, 2014) is a bacteria present in sauerkraut which have shown to produce neurotransmitter that helps to reduce depression and females who consume fermented food in comparison with those who does not are physically and mentally healthy.

Reduces Allergies:

Female's especially adolescent girls suffer from facial problems like acne and hairs on face and sometimes food allergy (Yazdanbakhehsh *et al.*, 2002). In fermented food presence of lactic acid bacteria is associated with changing gut bacteria to be favorable for reducing allergies.

There are some known fermented products (Table 1) which will definitely bring better results in curing ovarian disorders.

Yoghurt:

Yoghurt is made up of bacterial fermentation of milk by adding yoghurt culture (*Lactobacillus bulgaricus* and *Streptococcus thermophiles*) and a probiotic which is good for gut microflora (Ardo *et al.*, 2006; Hao *et al.*, 2011). Dairy consumption seems to be most discussed topic for females who are diagnosed with ovarian diseases. Milk consumption in these patients lead to increase in androgens and insulin levels (Burris *et al.*, 2013). Body needs calcium and vitamin D especially in women after the age of 30 as their bone density starts decreasing. Yoghurt contains higher protein and lower carbohydrates (low glycemic index) which is again helpful in weight loss. *Lactobacillus*, *Leuconostoc*, *Pediococcus*, *Streptococcus*, *Micrococcus* and *Bacillus* species are common fermentation microorganisms. *Paecilomyces*, *Aspergillus*, *Fusarium*, *Cladosporium*, *Penicillium* and *Trichothecium* are examples of fungus (Gupta and Abu-Ghannam, 2012).

Probiotic cultures are thought to minimise exposure to chemical carcinogens. By altering the intestinal environment and thereby lowering the population or metabolic activity of bacteria capable of producing carcinogenic compound (Saxami *et al.*, 2017), detoxifying carcinogens (Lili *et al.*, 2018), producing metabolic products such as butyrate, which increases apoptosis ability (Parvez *et al.*, 2006), and stimulating the immune system against cancer cell IFN- γ , TNF- α , and cytokines are examples of cytotoxic mediators (Kinouchi *et al.*, 2012). Another proposed mechanism, according to Parvez *et al.* (2006), is that probiotics can reduce the number of carcinogens in the intestine by limiting the bacterial growth that modifies the carcinogens. Probiotics also have antimutagenic, antimicrobial, anticarcinogenic, antidiarrheal activity, advancement in lactose intolerance, decrease in serum cholesterol level, immune system

stimulation, and suppression of *Helicobacter pylori* infection (Walia *et al.*, 2015).

Yoghurt could be used in preventing lung cancer, with the combination of dietary fibers (prebiotics) and yoghurt (probiotic) not only enhance gut microflora ecosystem but also act as immunomodulator which secretes cytokine which proliferates immune cells. Bacterial strains *Lactobacillus* and *Bifidobacterium* change the gut and lung ecosystem (Trompette *et al.*, 2016)

Sauerkraut:

Sauerkraut or kimchi are fermented cabbage leaves which convert natural sugars to lactic acid. It contains *Lactobacillus plantarum* which helps in reducing depression, anxiety and inflammation in gastrointestinal tract (Levit *et al.*, 2017). In binary logistic regression study 81 women were assessed using the statistical analysis by using SPSS ver.13 (SPSS Inc. Chicago, Ill, USA). The results showed that about 38.6% suffered from anxiety and 25.7% were suffering from depression and diagnosed with ovarian disorders symptoms.

On contrary, Kimchi is an Asian version of sauerkraut, fermented cabbage with daikon, radish, ginger, garlic and spices. According to a Korean medical report, regular consumption of kimchi by a group of obese women showed changes in gut bacteria that leads to weight loss (Han *et al.*, 2015). Sauerkraut is rich in antioxidants, calcium, magnesium, vitamin C, vitamin D, vitamin K and dietary fibers. Consumption of sauerkraut foods either during adolescence or adulthood significantly reduced breast cancer risk among Polish migrant women (Pathak *et al.*, 2021).

However, it should be consumed in limited amount as it contains high amount of histamine which may increase allergy problems (Katrina Pace, 2017). The kynurenine concentration was decreased by *Lactobacillus plantarum* 299v (LP299v) while this bacterial strain improves cognitive functions in patients with major depression. Placebo controlled study (a double-blind, randomized) was conducted in Medical

University of Bialystok, Poland by Rudzki *et al.* (2019). In this study 79 patients were randomized with major depressive disorder (MDD). Patients received either a Selective serotonin reuptake inhibitors (SSRI) with the placebo of the probiotics (n=39) or SSRI with the LP299v (n=40) for a period of 8 weeks. The severity was assessed by using three parameters like Perceived Stress Scale (PSS-10), hamilton depression rating scale (HAM-D 17) and symptom checklist (SCL-90) while cognitive functions were assessed by using several parameters viz., stroop test parts A and B, attention and perceptivity test (APT), trail making test (tmt) parts A and B, ruff figural fluency test (RFFT), and california verbal learning test (CVLT). Many biochemical parameters were assessed such as kynurenine (KYN), anthranilic acid (AA), tryptophan (TRP), tumor necrosis factor- α (TNF- α), kynurenic acid (KYNA), 3-hydroxy anthranilic acid (3HAA), cortisol plasma concentrations, 3-hydroxykynurenine (3HKYN), interleukin 6 (IL-6) and interleukin 1-beta (IL-1b). After 8 weeks out of 60 patients, 30 in the LP299v group and 30 in the placebo group finished the study and were analyzed. There was a significant decrease in KYN concentration in the LP299v group while significant increase in 3HKYN:KYN ratio in the LP299v group compared with the placebo group was recorded. ANOVA studies revealed a significant effect but there were no significant changes in concentrations of TNF- α , IL-6, IL-1b and cortisol in neither LP299v nor placebo groups. Hence, this study concluded that LP299v decreased KYN concentration and improved cognitive performance in MDD patients due to probiotics bacteria. Decreased concentration of KYN could contribute to the improvement of cognitive functions in the LP299v group compared to the placebo group.

Kefir:

Kefir was originated in Russia, this is a traditional drink made by fermentation of milk. Fermentation is done by clusters of bacteria called “grains” which are matrix of polysaccharides, proteins and lipids containing bacteria (*Leuconostoc acetobacter*,

Lactobacillus kefir and *Lactobacillus kefirianofacines*) and yeast (*Candida kefir*) and digest lactose while the remaining liquid gives slight sour and fizzy in taste which makes kefir drink lactose free (Angulo *et al.*, 1993; Marquina *et al.*, 2002; Latorre-Garcia, 2007; Disoma *et al.*, 2013). Kefir helps to prevent diabetes and reduce cardiovascular diseases (WHO, 1982) and oxidative stress and has antioxidant capacity. Kefir is capable of having anti-carcinogenic effect because of its antioxidant and reducing DNA damage property (Grishina *et al.*, 2011). It increases the glutathione peroxidase and decreases malon-dialdehyde level which controls oxidative stress. Kefir inhibits the linoleic acid peroxidation by binding DPPH (1,1-diphenyl-2-picrylhydrazyl) and superoxide radicals (Cevikbas, 1994). It is suggested that bacteria in kefir reduces allergies in body as well as change the immune signals sent out by body (Bourrie *et al.*, 2016). University of Medical Sciences, Dezful, Iran conducted the work on anti-carcinogenic properties of Kefir. It is capable to prevent cancer in females such as breast cancer and colon cancer. One of the most common cancers among women is breast and ovarian epithelial cancer and the treatment as well as prevention are very substantial. Sharif *et al.* (2017) and Chen *et al.* (2007) showed that kefir extracts induce apoptosis, cell cycle which reduces tumor growth in breast cancer cells which is a strong method of preventing breast cancer. The supernatants of kefir contained high amounts of acetic and lactic acid and showed meaningfully antioxidant capacity and this evidence suggests that kefir can decrease DNA damage, which might be due to their antioxidant properties and its anticancer potential on CRC cell line (Caco -2 and HT -29) at G-1 phase arrest cell cycle. In addition, kefir decreases the expression of Transforming Growth Factor (TGF- β 1) and (TGF- α) in human colorectal adenocarcinoma cell line (HT-29 cell line). It has also been reported that kefir can reduce sleep disturbance in patients treated for colorectal cancer.

Kombucha:

Kombucha is a kind of black tea fermented together by using Symbiotic Culture of Bacteria and Yeast (SCOBY). This special type of black tea has antioxidant as well as antimicrobial properties (Chakravorty *et al.*, 2016; Kaewkod *et al.*, 2022) and also helpful to reduce gastric ulcers, diabetes risk and cholesterol because this drink contains polyphenols and organic acid all of which could affects digestion (Banerjee *et al.*, 2010; Aloulou *et al.*, 2012). This could be easily made at home by keepinf 7 to 10 days for fermentation and then it is served. Tea fungus makes black tea ingredients to undergo various progressive modification (Blanc, 1996). The main metabolites identified in the Kombucha beverage are glucuronic acid, gluconolactone, glucaric acid, gluconic acid, 2-keto-D-gluconic acid and usnic acid (Fig. 1). The composition of metabolite as well as concentration depends on the source of tea fungus, concentration of sugar and the fermentation time. There are different ways to prepare. Glucose and fructose are formed from sucrose because yeast cells hydrolyze and produce ethanol. In the study, LAB (lactic acid bacteria) produces lactic acid and acetic acid and vitamin B complexes and folic acid are produced by the fermentation. If organic acid content increases during the fermentation process then pH of kombucha decreases simultaneously.

Since 1852, mainly in Europe Kombucha has been studied and reviewed by Allen (1998) which proved that kombucha reduce menstrual disorders and menopausal hot flashes, improve hair, skin and nail health, stress and nervous disturbances, insomnia, help for headaches, improve eyesight problems and also enhance general metabolism. Kombucha has anti-carcinogenic effect in body because of tea polyphenols and metabolites like oxalic acid, lactic acid, citric acid (Watawana *et al.*, 1998). Kombucha also inhibit rapid multiplication of cancer cells, induce cancer cell apoptosis, gene mutation and ability to end metastasis and in cancer patients it prevents stomach cancer. Kombucha contains D-saccharic acid-1,4-lactone (DSL) which is helpful in boosting the activity of

doxorubicin antitumor agent in colorectal cancer (Watawana *et al.*, 1998).

Soy based food:

Soy (*Glycine max*) comes from soyabeans originated from China, which can be consumed in the form of soy protein, fiber and contains many essential amino acids that is complete protein source (Shurtleff *et al.*, 2007). Soy contains isoflavones which is converted into phytoestrogens in human body. These phytoestrogens are similar in molecular structure to estrogens (Toi *et al.*, 2013).

Genistein, Daidzein and Glycitein are the soy isoflavones. Daidzein and genistein are the prominent in soy products. Genistein is obtained through diet in soy products like tofu, tempeh exists as conjugated form, genistin in the primary chemical form (Zhang *et al.*, 2013). This is an active flavonoid which participates in the activity of altering estrogen related malignancies which is related to apoptosis, cell cycle and inhibition of metastasis which helps in preventing cancer cells and also shows synergistic properties with anticancer drugs such as doxorubicin for therapy. Caspases, Bcl2-associated X protein, Bcl-2, kinesin-like protein 20A, extracellular signal-regulated kinase 1/2, nuclear transcription factor B (NF-B), mitogen-activated protein kinase, inhibitor of NF-B, Wingless and integration 1 -catenin, and phosphoinositide 3 kinase/Akt signaling pathways have all been implicated in the anticancer and therapeutic effects of genisten (Sarkar *et al.*, 2003; Spagnuolo *et al.*, 2015). Its ability to inhibit NF-B is particularly essential because this inhibits inflammation. Both the NF-B and the serine/threonine-specific protein kinase Akt keep a homeostatic equilibrium between cell survival and apoptosis in place.

Soy isoflavones, particularly genistein, decrease cell growth and facilitate apoptosis and cell cycle arrest in the G2/M phase in patients with colon cancer (Zhang *et al.*, 2013). As shown by quantitative polymerase chain reaction and immunoblotting, cell cycle arrest in the G2/M

Table 1: Mechanism of fermented foods in cancer patients

Fermented foods	Anticancer component	Types of Cancer	Binding sites	Mechanism	References
Yoghurt	Lactobacillus and Bifidobacterium	Gastric cancer and Lung cancer	IFN- γ , TNF- α , and cytokines	Binding the cancerous cells and act as immune-modulator	Nout <i>et al.</i> (2005)
Soy Tofu and Tempeh	Genistein and daidzein	Colon cancer and Breast cancer	Caspases, Bcl2-associated X protein, Bcl-2, kinesin-like protein 20A, extracellular signal-regulated kinase 1/2, nuclear transcription factor B (NF-B), mitogen-activated protein kinase, inhibitor of NF-B, Wingless and integration 1 - catenin, and phosphoinositide 3 kinase/Akt	Genistein triggered G2/M cell cycle arrest in a p53-dependent manner, implying that the ATM/p53-p21 cross-regulatory network is critical in mediating genistein's anticarcinogenic activity as well as binding the Tyrosine Protein Kinase responsible for transduction cell growth factor	Zhang <i>et al.</i> (2013); Cappelletti <i>et al.</i> (2000)
Kefir	Lactic acid	Breast cancer and colon cancer	CRC cell line (Caco - 2 and HT-29) at G-1 phase arrest cell cycle.	It increases the glutathione peroxidase and decreases malon-dialdehyde level which controls oxidative stress. decreases the expression of Transforming Growth Factor (TGF- β 1) and (TGF- α) in human colorectal adenocarcinoma cell line (HT-29 cell line),	Chen <i>et al.</i> (2007); Sharifi <i>et al.</i> (2015)
Kombucha	D-saccharic acid-1,4-lactone (DSL)	Colon Cancer		Strengthen antitumor agent doxorubicin and inhibits the multiplication of cancer cell ,gene mutation	Watawana <i>et al.</i> (2015)

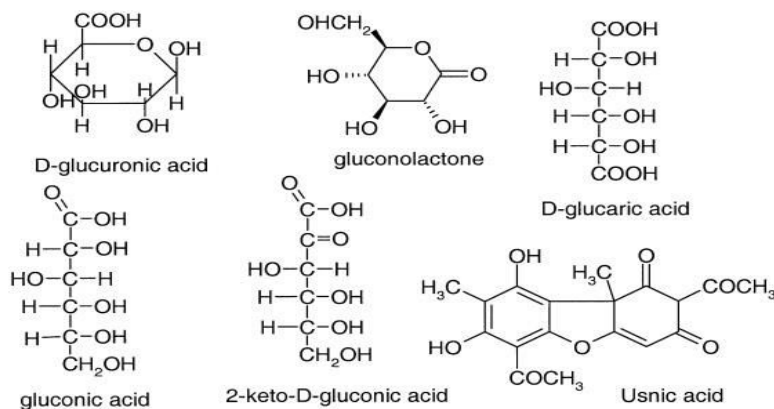


Fig. 1: Chemical structure of Kombucha constituents (source: Dufresne and Farnworth, 2000).

phase is associated with activation of ATM/p53, p21waf1/cip1 and GADD45, as well as downregulation of cdc2 and cdc25A. Genistein triggered G2/M cell cycle arrest in a p53-dependent manner, implying that the ATM/p53-p21 cross-regulatory network is critical in mediating genistein's anticarcinogenic activity. Genistein was discovered to work with the histone deacetylase inhibitor vorinostat to promote cell death in PCa cells (Phillip *et al.*, 2012). This significant isoflavonoid has recently been found to boost radiosensitivity of PCa cells in a synergistic manner.

Another study revealed that high concentrations of probiotics may alter the metabolism of isoflavones. The consumption of beverages containing *L. casei* Shirota (probiotic bacteria) and soy isoflavone was inversely associated with the incidence of breast cancer in Japanese women consuming such beverages regularly since adolescence and has least chance of breast cancer. Then this incidence evaluated through rat carcinogenic model by taking soy isoflavone supplement like soymilk and observed that it prevented the development of mammary tumors (Kaga *et al.*, 2013).

There is another setup that looked at the relation of soy phytoestrogen intake in 315 women undergoing infertility treatment with assisted reproductive technology (ART) (Vanegas *et al.*, 2015). As per this study soy not only improved the fertility rate but also improves pregnancy and birth rate. Hence, we could conclude that soy reduces the chances of infertility as well in women who are diagnosed with ovarian disorders.

Tofu and Tempeh:

Tofu is a processed fermented curdled bean form of soy. It contains isoflavones which possess both dependent and independent characteristics which restricts the development of breast cancer. The mechanism of isoflavones in inhibiting is by competitive binding of estrogen receptors (Jamilian *et al.*, 2016). Genistein, an isoflavonoid found in soy is another inhibitory factor of tumor

growth in various breast cancer through the restriction of TPK (Tyrosine Protein Kinase) which is responsible for transduction cell growth factor (Cappelletti *et al.*, 2000; Zhang *et al.*, 2013). Tofu is a staple food in western Asian countries, therefore probably females in western countries reports more cases of breast cancer comparatively the western Asian females. Soy helps in reducing cholesterol, triglycerides, inflammatory markers and hormone influx. It has low calorie count, high protein and little fat but good source of iron, calcium and magnesium.

Tempeh is the best alternative of protein for females who are non – vegetarian, dietary fibers and vitamins to control cholesterol to avoid obesity or weight gain. It is originated from Indonesia and made from fermented soybeans like tofu but differ in nutritional properties and textural feature. It is made by a natural culturing and controlled method of fermentation that binds soybeans in cake form. The starter culture used is *Rhizopus oryzae* (Shurtleff and Aoyagi, 2007).

It has been found that tempeh can help in restricting breast cancer being a fermented form of soy which has abundant isoflavones-- Genistein and Daidzein. These isoflavonoids has the potential to inhibit the angiogenesis, since proliferation of cancer cells depends on adequate amount of oxygen and nutrients by restricting the oxygen demand to cancerous cells growth of breast cancer cells could be terminated to certain extent (Nishida *et al.*, 2006; Varinska *et al.*, 2015).

Conclusion

With the growing population, fermented foods demand also increasing in India. Fermented foods are not new generation food but it is an ancient practice of preserving food, increases nutritive value, flavours and reduces cooking times. Moreover, fermented foods are functional food which helps in curing or helps in reducing the adverse effects of ovarian disorders along with medical prescription. The foods which are discussed here are easily available in market and could be used in daily life. Apart from this it is

necessary to give time on physical exercise and adapt healthy eating pattern such as fresh fruits, green leafy vegetables and keep mind stress free.

References

- Allen CM. (1998) Past research on Kombucha tea. The Kombucha FAQ Part 6. Research and tests results. http://persweb.direct.ca/chaugen/kombucha_faq_part06.html
- Aloulou A, Hamden K, Elloumi D, Ali MB, Hargafi K, Jaouadi B and Ammar E. (2012) Hypoglycemic and antilipidemic properties of kombucha tea in alloxan-induced diabetic rats. *BMC Complement Altern Med* 12(1): 1-9.
- Angulo L, Lopez E and Lema C. (1993) Microflora present in kefir grains of the Galician region (North – West of Spain). *J Dairy Res*. 60: 262-267.
- Ardo Y. (2006) Flavour formation by amino acid catabolism. *Biotechnol Adv*. 24(2): 238-242.
- Banerjee D, Hassarajani SA, Maity B, Narayan G, Bandyopadhyay SK. and Chattopadhyay S. (2010) Comparative healing property of Kombucha tea and black tea against indomethacin-induced gastric ulceration in mice: possible mechanism of action. *Food Funct*. 1(3): 284-293.
- Blanc PJ. (1996) Characterization of the tea fungus metabolites. *Biotechnol Lett*. 18(2): 139-142.
- Bourrie BC, Willing BP and Cotter PD. (2016) The microbiota and health promoting characteristics of the fermented beverage kefir. *Front Microbiol*. 647. <https://doi.org/10.339/fmicb.2016.00647>.
- Burris J, Rietkerk W and Woolf K. (2013) Acne: the role of medical nutrition therapy. *J Acad Nutr Diet*. 113(3): 416-430.
- Cappelletti V, Fioravanti L, Miodini P and Di Fronzo G. (2000) Genistein blocks breast cancer cells in the G (2) M phase of the cell cycle. *J Cell Biochem*. 79(4): 594-600.
- Cevikbas A, Yemni E, Ezzedenn FW, Yardimici T, Cevikbas U and Stohs S. (1994) Antitumoral, antibacterial and antifungal activities of kefir and kefir grains. *Phytother Res*. 8(2): 78-82.
- Chakravorty S, Bhattacharya S, Chatzinotas A, Chakraborty W, Bhattacharya D and Gachhui R. (2016) Kombucha tea fermentation: Microbial and biochemical dynamics. *Int J Food Microbiol*. 220: 63-72.
- Chen C, Chan HM and Kubow S. (2007) Kefir extracts suppress in vitro proliferation of estrogen-dependent human breast cancer cells but not normal mammary epithelial cells. *J Med Food*. 10(3): 416-422.
- Disoma G, Romanin DE, Rey-Burusco MF, Londero A and Garrote GL. (2013) Yeasts from Kefir grains; isolation, identification and probiotics characterization. *World J Microbiol Biotechnol*. 30(1): 43-53.
- Dufresne C and Farnworth E. (2000) Tea, Kombucha, and health: a review. *Int Food Res J*. 33(6): 409-421.
- Grishina A, Kulikova I, Alieva L, Dodson A, Rowland I and Jin J. (2011) Antigenotoxic effect of kefir and ayran supernatants on fecal water-induced DNA damage in human colon cells. *Nutr Cancer* 63(1): 73-79.
- Gupta S and Abu-Ghannam N. (2012) Probiotic fermentation of plant based products: Possibilities and opportunities. *Crit Rev Food Sci Nutr*. 52 (2): 183-199.
- Han K, Bose S, Wang JH, Kim BS, Kim MJ, Kim EJ and Kim H. (2015) Contrasting effects of fresh and fermented kimchi consumption on gut microbiota composition and gene expression related to metabolic syndrome in obese Korean women. *Mol Nutr Food Res*. 59(5): 1004-1008.
- Hao P, Zheng H, Yu Y, Ding G, Gu W, Chen S and Zhao G. (2011) Complete sequencing and pan-genomic analysis of *Lactobacillus delbrueckii* subsp. *Bulgaricus* reveal its genetic basis for industrial yogurt production. *PloS One* 6(1): e15964.
- Helmenstin AM. (2020) What Is Fermentation? Definition and Examples. <https://www.thoughtco.com/what-is-fermentation-608199,2019>.
- Jamilian M and Asemi Z. (2016) The effects of soy isoflavones on metabolic status of patients with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 101(9): 3386-3394.
- Kaga C, Takagi A, Kano M, Kado S, Kato I, Sakai M, Miyazaki K, Nanno M, Ishikawa F and Ohashi Y. (2013) *Lactobacillus casei* Shirota enhances the preventive efficacy of soymilk in chemically induced breast cancer. *Cancer Sci*. 104(11): 1508-1514.
- Kaewkod T, Sangboonruang S, Khacha-Ananda S, Charoenrak S, Bovonsombut S and Tragoolpua Y. (2022) Combinations of traditional kombucha tea with medicinal plant extracts for enhancement of beneficial substances and activation of apoptosis signaling pathways in colorectal cancer cells. *Food Sci Technol*. 42: e107521.
- Kinouchi FL, Maia DCG, de Abreu Ribeiro LC, Placeres MCP, de Valdez GF, Colombo LL and Carlos IZ. (2012) A soy-based product fermented by *Enterococcus faecium* and *Lactobacillus helveticus* inhibits the development of murine breast adenocarcinoma. *Food Chem Toxicol*. 50(11): 4144-4148.
- Latorre-Garcia L, del Castillo- Agudo I and Polaina J. (2007) Taxonomical classification of yeasts isolated

- from kefir based on the sequence of their ribosomal RNA genes. *World J Microbiol Biotechnol* 23(6): 785-791.
- Levit R, GS de Giori A, de Moreno de Leblanc and Leblanc JG. (2017) Evaluation of effect of soymilk fermented by a riboflavin producing *Lactobacillus plantarum* starin in murine model of colitis. *Benef Microbes* 8(1): 65-72.
- Lili Z, Junyan W, Hongfei Z and Baoqing Z. (2018) Bolin detoxification of cancerogenic compounds by lactic acid bacteria strains. *Critical Rev Food Sci Nutr* 58(16): 2727-2742.
- Marquina D, Santos A, Corpas I, Munoz J, Zazo J and Peinado JM. (2002) Dietary influence of Kefir on microbial activities in the mouse bowel. *Lett Appl Microbiol* 35(2): 136-140.
- Nishida N, Yano H, Nishida T, Kamura T and Kojiro M. (2006) Angiogenesis in cancer. *Vasc Health Risk Manag* 2: 213-219.
- Nout MJ, Robert Vos M, de Willem and Zwietering HM. (2005) *Food Fermentation*, The Netherlands: Wageningen Academic Publishers, Wageningen.
- Pathak DR, Stein AD, He JP, Noel MM, Hembroff L, Nelson DA and Willett WC. (2021) Cabbage and sauerkraut consumption in adolescence and adulthood and breast cancer risk among US-Resident Polish migrant women. *Int J Environ Res Public Health* 18(20): 10795.
- Parvez S, Malik KA, Kang S and Kim HY. (2006) Probiotics and their fermented food products are beneficial for health. *J Appl Microbiol* 100(6): 1171-1185.
- Phillip CJ, Giardina CK, Bilir B, Cutler DJ, Lai YH, Kucuk O and Moreno CS. (2012) Genistein cooperates with the histone deacetylase inhibitor vorinostat to induce cell death in prostate cancer cells. *BMC Cancer* 12(1): 1-11.
- Pirotta S, Lim SS, Grassi A, Couch LM, Jeanes YM, Joham AJ and Moran LJ. (2022) Relationships between self-management strategies and physical activity and diet quality in women with polycystic ovary syndrome. *Patient Education Counseling* 105(1): 190-197.
- Ridaura VK, Faith JJ, Rey FE, Cheng J, Duncan AE, Kau AL, Griffin NW, Lombard V, Henrissat B, Bain JR, Muehlbauer MJ, Ilkayeva O, Semenkovich CF, Funai K, Hayashi DK, Lyle BJ, Martini MC, Ursell LK, Clemente JC, Van Treuren W, Walters WA, Knight R, Newgard CB, Heath AC and Gordon JL. (2013) Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science* 341(6150): 1241214.
- Terefe NS. (2022) Recent developments in fermentation technology: toward the next revolution in food production. *Food Engineer Innov Across Food Supply Chain* 2022: 89-106.
- Rudzki L, Ostrowska L, Pawlak D, Małus A, Pawlak K, Waszkiewicz N and Szuk A. (2019) Probiotic *Lactobacillus Plantarum* 299v decreases kynurenine concentration and improves cognitive functions in patients with major depression: A double-blind, randomized, placebo controlled study. *Psychoneuroendocrinol* 100: 213-222.
- Sande de. (1997) Socioeconomic pitfalls of enhancing indigenous capabilities in house – hold fermentation. *Food Control* 8(5-6): 303-310.
- Sarkar FH and Li Y. (2003) Soy isoflavones and cancer prevention. *Cancer Invest* 21: 744-757.
- Saxami G, Karapetsas A, Chondrou P, Vasiliadis S, Lamprianidou E, Kotsianidis I and Galanis A. (2017) Potentially probiotic *Lactobacillus* strains with anti-proliferative activity induce cytokine/chemokine production and neutrophil recruitment in mice. *Benef Microbes* 8(4): 615-623.
- Sharifi M, Moridnia A, Mortazavi, D, Salehi M, Bagheri M, abdSheikhi A. (2017) Kefir: a powerful probiotics with anticancer properties. *Med Oncol* 34(11): 1-7.
- Shurtleff W and Aoyagi A. (2007) *History of Soybeans and Soyfoods 1100BC to the 1980s*, Soyinfo Centre, Lafayette California. http://www.soyinfocentre.com/HSS/soybean_crushing1.php.
- Some S and Mandal AK. (2020) Fermented foods for health: Processes and prospects. In: *Microbial Fermentation and Enzyme Technology*, CRC Press, pp. 73-84.
- Spagnuolo C, Russo GL, Orhan IE, Habtemariam S, Daglia M, Sureda A and Nabavi SM. (2015) Genistein and cancer: current status, challenges, and future directions. *Adv Nutr* 6(4): 408-419.
- Toi M, Hirota S, Tomotaki A, Sato N, Hozumi Y, Anan K, Nagashima T, Tokuda Y, Masuda N and Ohsumi S. (2013) Probiotic beverage with soy isoflavone consumption for breast cancer prevention: A case-control study. *Curr Nutr Food Sci* 9(3): 194-200.
- Trompette A, Gollwitzer ES, Yadava K, Sichelstiel AK, Sprenger N, Ngom-Bru C and Marsland BJ. (2014) Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. *Nat Med* 20(2): 159-166.
- Vanegas JC, Afeiche MC, Gaskins AJ, Mínguez-Alarcón L, Williams PL, Wright DL and Chavarro JE. (2015) Soy food intake and treatment outcomes of women undergoing assisted reproductive technology. *Fertil Steril* 103(3): 749-755.

- Varinska L, Gal P, Mojzisova G, Mirossay L and Mojzis J. (2015) Soy and breast cancer: focus on angiogenesis. *Int J Mol Sci.* 16(5): 11728-11749.
- Walia S, Kamal R, Kanwar SS and Dhawan DK. (2015) Cyclooxygenase as a target in chemoprevention by probiotics during 1, 2-dimethylhydrazine induced colon carcinogenesis in rats. *Nutr Cancer* 67(4): 603-611.
- Watawana MI, Jayawardena N, Gunawardhana CB and Waisundara VY. (2015) Functional Food Product Development Project 2015, National Institute of Fundamental Studies, Kandy, Srilanka. Health, Wellness and Safety Aspects of the Consumption Kombucha, 11: 3-4.
- Yazdanbakhehsh M, Kremsner PG and Van Reek. (2002) Allergy parasites and the hypothesis. *Science* 296(5567): 490-494.
- Zhang Z, Wang CZ, Du GJ, Qi LW, Calway T, He TC and Yuan CS. (2013) Genistein induces G2/M cell cycle arrest and apoptosis via ATM/p53-dependent pathway in human colon cancer cells. *Int J Oncol.* 43(1): 289-296.
- Zhao L. (2013) The gut microbiota and obesity from correlation to causality. *Nat Rev Microbiol.* 11(9): 639-647.