

The Promising Connection Between Gut Microbiota and Mental Health: Overview of Kefir in Relation to Mental Health

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ABSTRACT

Kefir, along with other fermented foods, have health benefiting traits and properties towards the gut microbiota. There continues to be much to discover about the microbiota as new research indicates that it connects with the brain. There have been numerous studies done on kefir's impact on mental health showing that kefir could potentially treat mental health symptoms. However, some studies contradict that claim indicating that kefir does not affect mental health. Anxiety, depression, attention-deficit/hyperactivity disorder (ADHD), stress, among others, were the mental health issues explored in these studies. Presently, there is not enough evidence to make a feasible claim that kefir can improve mental health. However, promising results from kefir are possible as new research indicates that kefir could impact mental health positively.

Keywords: Behavioral and Social Sciences; Neuroscience; Fermented Foods; Kefir; Mental Health

INTRODUCTION

Kefir could potentially have a positive effect on mental health. This could contribute to a large change in the medical field as there will be more efficient ways to treat mental health disorders. In today's world, mental health is a prominent issue in society, and for the most part, there is not a set cure for mental illnesses. This is why kefir could be very impactful in the field of medicine as it could be used as a treatment for mental health issues. Numerous studies in different organisms already show

how kefir can affect mental health. For example, many studies in rodents show that kefir has improved attention-deficit/hyperactivity disorder (ADHD), stress, depression, and anxiety (1-5). However, there are some contradicting studies which claim that kefir does not improve mental health disorder symptomatology (6). More evidence can help impact the medical and pharmaceutical field. This is why it is important to review the effects that kefir has on mental health, as it could be beneficial to the medical field later on. Mental health sometimes has insufficient treatments where patients are not always treated well, and they might continue to suffer from mental health disorders. Probiotics are live organisms that help improve the gut of a patient (13). However, there is evidence that probiotics could improve mental health in patients as well. Fermented foods are types of probiotics and they contain probiotic effects. Kefir is one example of a fermented drink and many studies have been conducted on kefir to

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determine its effects on mental health. However, although there are studies that claim that kefir does improve mental health, there are some contradicting studies that counter this claim. Although more evidence is needed, kefir is a promising therapy to improve and treat mental health disorders. Some studies in rodents show that kefir does ameliorate ADHD, depression, anxiety, stress, and behavior in rodents (1-5). These studies use the Elevated Plus-Maze Test (EMPT), the Forced Swimming Test (FST), The Tail Suspension Test (TST), and the Open Field Test (OFT) as tests on rodents to determine kefir's effects on mental health. In the majority of these studies, a different type of kefir was given to the rodents for each study, whereas other studies just used the consumption of kefir itself. For example, in one study, researchers isolated a probiotic strain from kefir and gave it to the rodents for their consumption (3). In another study, the authors gave the rodents kefir peptides instead of the normal kefir drink.¹ No matter what form was used, all studies had positive results where kefir improved the rodents' mental health. However, in rodents, there was one contradicting study that also used a similar procedure as the other tests (6). This study used the EMPT, FST, and OFT but the results showed that the rodent's anxiety and depression did not improve. However, results did show that kefir improved the rodent's social recognition. Although this study does display positive results about kefir, it also counters other results that suggest that kefir can affect anxiety and depression (6). Still, overall, studies using the EMPT, FST, TST, and OFT on rodents display positive effects of kefir towards mental health disorders.

There were human studies as well which mostly showed positive results from kefir (7-12). Specifically, mental health concerns such as depression, anxiety, ADHD, quality of life, stress, and sleep quality were measured with the Beck Depression Inventory, spatial reconstruction tasks, Depression Anxiety Stress Scales-42 (DASS-42), Generalized Anxiety Disorder-7 test (GAD-7), Functional Assessment of Cancer Therapy-General (FACT-G), and the MSAS-PSYCH. These studies show that kefir could potentially improve mental health, as numerous tests and illnesses were measured (7-12). However, one study counters the fact that kefir improves mental health in humans (12). In this study, a questionnaire was given to workers and secondary school graduates. The Depression Anxiety Stress Scale (DASS-21) was used in one part of the questionnaire. The results show that kefir had a negative correlation with the DASS-21 scores (12). From these studies, it should be considered that kefir could have the ability to improve mental illnesses but low evidence

and contradicting evidence should be taken into account as they oppose this idea. However, even though there are contradicting studies, many studies show that kefir has the ability to treat mental health disorders such as depression, anxiety, stress, and more.

Introduction to Microbiota

Switching focus from mental health, the microbiota is a composition of all microbes (such as viruses, bacteria, and fungi) in our bodies. The gut microbiota is important for processes in the body, such as influencing the body's behavior (13). The gut microbiome is vital in the human body because some of the main processes, such as metabolic function, occur in the gut microbiota (14). This is one of the many reasons why the gut microbiota is so important. Recent research also shows that the gut microbiota can also possibly correlate with the brain as well. There has been ongoing research on the microbiota's relation to mental health (13-16). New research has the possibility to change the perspective on how mental health may be impacted by the gut microbiota. Although there have been many new therapeutic options for the treatment of mental health, like using microbiota, the use of microbiota to be used for diseases like depression would most likely not replace the current pharmacological devices (13). However, new research shows that there could be a potential relation between the gut and brain.

Specifically, It has been observed by the intake of antibiotics that the vulnerability of the microbiota results in numerous disorders in modern day society (15). This is just one of the many reasons on how the microbiome can affect overall health. The microbiome is composed of many different things, such as metabolites, microorganisms, and microbes (13). Metabolites in the microbiota could be the variable which connects the brain and the gut (13). This means that metabolites could be used in therapeutic treatments for issues relating to the gut and/or brain. These pieces of evidence provide information on the microbiota as a whole, and how there are new studies supporting its connection with mental health effects.

Introduction to Probiotics

As mentioned before, probiotics are live microorganisms in the form of dietary supplements or functional foods. When consumed, they may result in a health benefit to the host (17). Probiotics change the intestinal microbial communities, which may lead to a suppression of pathogens. Probiotics may be involved in immunomodulation the protecting the intestinal barrier (17).

Not only can probiotics treat gut health, but some believe they can also treat mental health concerns (13). The gastrointestinal tract contains a neural network known as enteric nervous system, which is responsible for the regulation of the physiological functions of the gut, as well as modulating communication between the gut and the central nervous system (CNS) (17). It was discovered that disruptions in the gut-brain axis are connected with psychological symptoms such as anxiety as well as gut-related systems such as irritable bowel syndrome (IBS) (17).

Properties of Kefir

Originating from Caucasus, kefir is a fermented drink that has the ability to be used to treat gut diseases and illnesses such as IBS (18). In one study, it was shown that kefir also demonstrates pharmacological effects and shows positive health benefits such as a decrease in obesity, hyperlipidemia, digestive disease, allergies, and asthma.¹ It can also increase the speed of wound healing and prevent hypertension and ischemic heart disease. Kefir, along with other fermented foods, contain antihypertensive and antioxidant properties, which may modulate the gut microbiota (Figure 1) (1). In another study, mice with

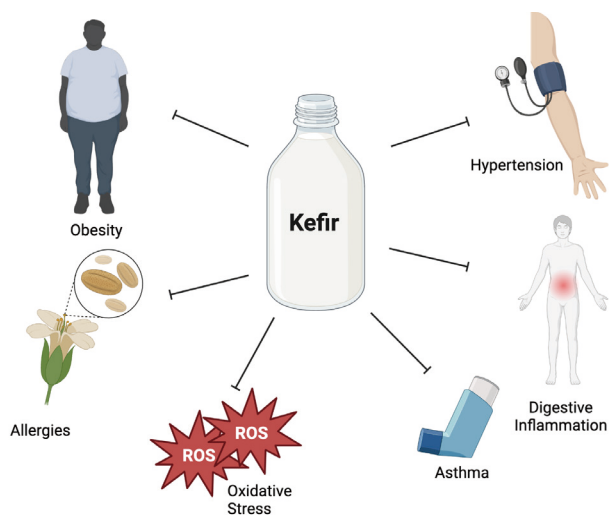


Figure 1. Kefir's positive health benefits and its properties. First, kefir reduces hypertension in the body and lowers the blood pressure and kefir is known to reduce obesity and oxidants. In addition, kefir is also known to reduce digestive disease (e.g., treatment of IBS).. Lastly, kefir contains properties which reduce allergies and asthma. Overall, although it is not prescribed by doctors and physicians, kefir has the ability to act as a treatment towards these health issues.

oxidative stress consumed PFT (probiotics fermentation technology), a kefir product over the duration of 6 weeks (19). Antioxidant status, lipid peroxidation, and protein oxidation were all studied in the brain, liver, and blood. Results show that the novel kefir product PFT reduced oxidative stress in mice (19).

Kefir's Impact on Mental Health

As previously stated, kefir could potentially positively impact mental health (13). Since fermented foods like kefir are probiotics, there is a possibility that they can modify gut bacteria. Probiotics like kefir can benefit the gut by changing microbial communities, strengthening tight junctions in the gut, and increasing mucin production (17). As well as benefiting the gut, probiotics can also benefit the brain (13). Although research evaluating kefir's impact on mental health is scant, kefir's properties and function suggested it may have benefits.

Results in Rodents

Multiple studies have been conducted on rodents testing kefir's effects on mental health (1-6). Kefir itself has been shown to reduce anxiety and depression-like behavior in mice exposed to stress. Other studies have capitalized on these data to try to find more efficient methods of treatment. For example, one study isolated kefir peptides and found similar results.¹ In this study, mice consumed 150 mg of kefir peptides for 8 days and it was reported that they were more active and mobile in the EMPT, the OFT, the FST, and the TST (Figure 2) (1). This means that the rate of mice's anxiety and depression lowered after consuming the kefir peptides. Further, both kefir peptides and kefir delivered orally have been found to decrease time spent immobile in the forced swimming test when compared to controls in mice with genetic predisposition for anxiety and mice exposed to chronic stress respectively (1-2). Another study isolated specific probiotics from kefir called *Lactobacillus kefiranofaciens* CGMCC2809 (ZW3) (3). In this study, mice consumed this probiotic strain of kefir and it was found that ZW3 improved depression-like behaviors in mice with chronic unpredictable mild stress. In different study, mice were given 100g of body weight kefir for 30 days and the EPMT and the FST were used to evaluate depression- and anxiety-like behavior (2). Overall, rodents who consumed kefir demonstrated positive health effects, such as a decrease in depression, anxiety, and stress, among other mental health benefits.

In contrast, some studies had contradicting claims which countered the idea that kefir improves anxiety and depression in mice. It was reported that the mice were

more resistant to stress as they were more active during these tests. In a different study, a variety of tests were used, such as the EPMT, OFT, TST, and the FST (6). This study contradicts kefir's benefits to anxiety and depression and the results of these tests show that the mice's depression and anxiety levels did not improve. However, the mice did show improvement in social recognition (6). In another study, a specific type of kefir strain called UK4 was given to mice and it was reported that kefir modulates repetitive and reward-seeking behavior.⁴ However, once again, it was reported that kefir did not have any effect on depression or anxiety in mice with the use of the EPMT, OFT, TST, and FST (4). In a different study focused on anxiety with a pharmacological origin, rats were given 6mg of nicotine and kefir for 17 days (5). The tests used were the EPMT, OFT, and the FST and it was reported that their anxiety and depression scores improved which shows that kefir

can benefit by improving anxiety and depression levels caused by nicotine in rats (5). Overall, six studies have demonstrated kefir's positive effects on stress responses in rodents while two studies have found that there may be no effect at all. In conclusion, these data suggest that there may be some mental health benefits and more studies are needed.

Results in Humans

Multiple studies have been tested on humans to determine kefir's positive effects on mental health (7-12). In one study, adult patients diagnosed with non-alcoholic fatty liver disease (NAFLD) and other comorbid disorders participated in a study to determine the effects of diet on liver health (7). They consumed a low calorie diet as well as 500cc of kefir daily for eight weeks and reported depression symptoms using the Beck Depression Inventory as a secondary outcome. While patients drinking the kefir did not differ significantly from the diet-only control group, they did improve their reported depression after eight weeks of treatment which supports that kefir did improve perceived depression in patients (7). In a different study, adult participants consumed an 8oz fermented beverage containing kefir cultures for four weeks to test kefir's effect on negative mood states (anxiety and depression), stress, and hippocampal memory performance (8). The hippocampal memory performance was tested using a spatial reconstruction task while anxiety and depression were assessed using the Depression Anxiety Stress Scales-42 (DASS-42). Results showed that the dairy beverage increased a variety of microorganisms in the gut. More importantly, the dairy beverage improved rational memory in fit adults (8). In another study, an online survey was conducted with adult participants on their fear and anxiety from the COVID-19 Virus in Turkey (9). These participants also consumed many different foods such as kefir, as well as yogurt, cheese, and nut-seeds. There was a shown improvement in symptoms on the Generalized Anxiety Disorder-7 (GAD-7) when kefir was consumed (9). This means that kefir slightly improved anxiety in adult humans. In an additional study, *Lactococcus lactis* subsp. *cremoris* (YRC3780), a bacteria strain isolated from kefir, was given to patients for severe psychological stress in adult men (10). The diurnal rhythm of the hypothalamic pituitary adrenal (HPA) axis activity and gut microbiome were assessed and compared. Results show that these bacteria strains from kefir lowered cortisol levels and improved mental health and sleep quality (10). An alternate study demonstrates kefir's effects on quality of life (QOL) for people with cancer (11). Cancer patients

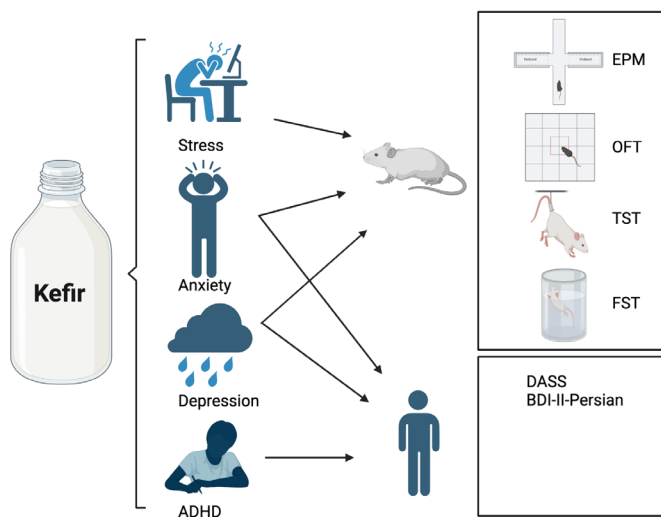


Figure 2. Methods for testing Kefir in humans and mice.

Studies show that kefir can treat anxiety and depression along with ADHD and stress in animal models and people. The tests to measure these conditions in mice are the Elevated-Plus Maze Test (EPMT; anxiety), the Forced Swimming Test (FST; depression), the Tail Suspension Test (TST), and the Open Field Test (OFT). In human studies, kefir can treat anxiety, depression, ADHD, and stress; however, its effects have not been examined beyond clinical studies. Methods for measuring these outcomes in humans include the Depression, Anxiety, Stress Scale (DASS) and the Persian Beck Depression Inventory II (BDI-II-Persian). In the future it is likely that kefir may be used as a treatment for these mood disorders.

consumed 500ml of kefir per day for seven days and the Functional Assessment of Cancer Therapy-General (FACT-G) was used to evaluate the QOL of patients. The MSAS-PSYCH evaluated patients' overall symptom distress of chemotherapy. Results show that the MSAS-PSYCH scores increased in the experimental group where kefir was consumed, which means that the symptoms of chemotherapy improved after consuming kefir (11).

A contradicting study consisted of a questionnaire that was asked to healthcare workers and secondary school graduates (12). In one part of this questionnaire, the Depression Anxiety Stress Scale (DASS-21) was used. Another question included foods they liked and did not like and then correlated these with DASS-21 scores. Results showed that probiotic foods such as kefir along with kombucha had a negative correlation with the DASS-21 scores (12).

In conclusion, there are many studies that show that kefir demonstrates positive effects towards humans. However, there are still some contrasting studies, so it cannot be fully determined yet. Many methods were used to assess kefir's effects on the brain, such as the DASS-21 scale and the Beck Depression Inventory, among others. Overall, kefir's effects on humans are not yet fully known and there is a need for further research in this area.

Results in Other Organisms

Multiple studies used organisms other than humans and rodents to determine kefir's impact on mental health (20-21). In one study, kefir's effects were tested on fly models with Alzheimer's disease (20). The Rapid Iterative Geotaxis (RING) assay was used to test neurodegeneration in flies. Results show that kefir improved flies' Alzheimer's disease as it was tested using the RING assay (20). In another study, zebrafish consumed kefir associated with soybean germ (KSG) which was evaluated in a gastrointestinal digestion model in vitro (21). KSG and the fermented solution of kefir (FSK) were evaluated in anxiety and depression models of kefir. To determine antidepressant activity, a tank dive test was performed. For the KSG, a decrease in intestinal and colon phases were demonstrated. Overall, the experiments demonstrated that both FSK and KSG demonstrated anxiolytic and antidepressant effects (21).

Other Fermented Foods

Like kefir, other fermented foods could also possibly serve as treatment for mental health. These fermented foods include kombucha, yogurt, and cheese. Starting with kombucha, it is very similar to kefir because it contains

similar properties, such as antioxidant, antihyperlipidemic, and antihypertensive properties (22). In kombucha, there is a metabolite called glutamate which is one of the most important neurotransmitters in the brain and is connected to learning, memory, and brain development. Because of this, a connection can be made with kombucha and mental health, as it does have glutamate which is a neurological agent. However, the role of glutamate in kombucha has not yet been fully studied and is therefore unknown (22). It is clear that kefir and kombucha are similar in terms of impacting mental health, as they both demonstrate positive effects towards it. Although there are still limited studies on both fermented foods and their impact on mental health, such research is promising for the future.

As mentioned before, fermented foods, yogurt and cheese, also demonstrate positive effects on mental health. Similar to other fermented foods, yogurt is already used as treatment in the gut but is yet to be used as treatment for mental health. In one study, healthy women consumed yogurt twice a day for a month (23). These women were shown pictures of actors with angry expressions. These pictures would normally signal parts of the brain to make the person feel alert and people who had anxiety feel sensitive towards these images. However, the consumption of yogurt allowed women to portray a less reflective response by fMRI (23). This shows that the consumption of yogurt can reduce anxiety and make people feel calmer. In a double-blind study, patients were given 100g of probiotic yogurt a day and DASS scores were measured (24). In this study, they found an improvement of DASS scores in the probiotic yogurt. In other words, yogurt reduced depression, anxiety, and stress in these patients (24). In conclusion, yogurt is another fermented food that can impact mental health. Along with kefir and kombucha, new research in the future could indicate that these fermented foods can be used as treatment for mental health symptoms.

Although there is not a lot of evidence on the effects of cheese on mental health, there are a few studies describing their results. In one study, women who had poor mental health were compared to healthy women who did not have healthy foods such as cheese in their diet (24). Although not much can be determined from this experiment, there is a chance that cheese could have been a possible factor for reducing mental health issues in women in this experiment. It is clear that all of these other fermented foods still need more research done, including kefir. It cannot be determined for sure that these fermented foods contain the ability to help with mental health disorders but evidence like such in the future is promising (24).

CONCLUSIONS

As a probiotic, kefir has many health benefits. It is able to treat obesity, allergies, oxidative stress, hypertension, asthma, and digestion inflammation, among others. However, it is not yet used as a cure yet clinically for mental health disorders, but can be used as a treatment. Although there are numerous studies that show that kefir can treat anxiety and depression, there are still some studies that contradict that claim. Therefore, it cannot be confirmed that kefir can treat mental health disorders such as anxiety and depression. Also, there are studies across different organisms in which they mostly have different results. From that, it cannot be claimed that kefir does have an overall benefiting effect on mental health. However, kefir being used as a treatment for mental health is promising because of the numerous research being conducted. The current lack of studies on kefir and mental health highlights a need for more testing. Likely, probiotics and kefir will prove to be important therapies for patients with mental health disorders.

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