CHAPTER 1

INTRODUCTION

Mental health statistics reflect the crux of an integrated view of any society's health. A study by a group of researchers show that as of 2018-19, the percentage of college students with depression doubled in the past decade (Duffy et al., 2019). However, mental health issues remain taboo and are often underestimated. Over 90% of psychological counselling centre directors in 2011 reported significant increases in the number of college students with mental health problems out of which 70 % of people chose to suffer in silence (Gallagher, 2011). Interestingly, people's perception about seeking professional help has changed overtime. Penn University report, 2019 states between 2014 and 2019, there was a 35% increase in students reaching out to experts regarding their mental illnesses (Seligman and Schulman, 2019).

Researches have proclaimed stigma to be a ubiquitous barrier in enlisting professional assistance (Knaak et al., 2017). People with experience of a mental illness commonly report that they feel devalued, dismissed, and dehumanized to confront their state in front of society and to approach health professionals (Hamilton et al., 2016).

Mental health is of utmost importance as it determines emotional, behavioural, and cognitive well-being, all of which contribute to maintaining a healthy balance of life activities and obligations while also promoting psychological fortitude, so it should not be taken for granted. Anxiety disorder and depression are two of the most prevalent diagnostic groups that make up common mental diseases. Globally, more than 264 million people of all ages suffer from depression (WHO factsheet, 2020). It is anticipated to be the world's top cause of disability (James et al., 2020). Looking at the rise in the trend of depression among youth there is an urgent need to address the problem by preserving and restoring mental health.

One probable solution lies in the highly dynamic human gastrointestinal tract. While billions of neurons are present in our brain, trillions of 'good' bacteria exist in our intestine. These microbiotas play an important role in maintaining the functionality of

the intestinal barrier which is critical for human mental health (Kelly et al., 2015) making our gut popular as the ‘second brain’. Microbes are thought to communicate directly with the brain labelled as ‘Gut-Brain axis’ through the circular communication loops involving the central nervous system, the enteric nervous system, endocrine and immune signalling mechanisms (De Palma et al., 2014). The activity of 10^{14} intestinal microbiomes aids in the maintenance of normal homeostasis and the synthesis of a diverse range of biologically and neuroactive molecules such as GABA, norepinephrine, dopamine, and short-chain fatty acids, all of which have antidepressant properties. The gut contains 90% of the body's serotonin, which is a key regulator of gastrointestinal motility and the body's feel-good factor (Terry and Margolis, 2017). The vagus nerve is also important in mediating effects on the brain and behaviour (Forsythe et al., 2014). Several clinical findings link the changes in the gut microbial ecology to a variety of psychiatric diseases. The long-held belief that gut microbes interact with the central nervous system (CNS) through influencing brain chemistry and affecting neuroendocrine systems involved in stress response, anxiety, and memory function is the source of much of the enthusiasm around the human microbiome's ability to influence mental health.

Interestingly, biohacking our mental health is possible via the modulation of gut floras to a positive balance. Prebiotics, probiotics, antibiotics, and biogenic metabolites produced by milk fermentation open up new avenues for psychological therapies by altering the intestinal microbiota axis (Carabotti et al., 2015).

Fermentation has the potential to enhance the unique nutritional or phytonutrient content of foods, whose final worth is linked to mental wellness (Selhub et al., 2014). There is a strong link between the consumption of fermented beverages and the reduction of neurodegenerative diseases. Microbes influence the pre-consumption of food items, and these fermented dietary items, in turn, alter our microbiota. One probable reason for the positive effect of fermented milk is the participation of biogenic metabolites, which are created by the action of microorganisms. The proteolytic system of *lactic acid bacteria* operates on casein found in milk and milk derivatives to provide bioactive peptides (Clare and Swaisgood, 2000). These peptides have been shown to improve brain cognitive performance by improving gut-brain connection (Dinan and

Cryan, 2017). Oral administration of biogenic peptide at the rate of 0.1–100 μmol/L to rat pups enhanced the number of goblet cells and Paneth cells along the small intestine (Mann et al., 2017). When compared to controls, biopeptides were found to be significantly more effective than St. John's wort and kava kava in reducing anxiety in one double blind study (Pfluger et al., 2012). There are very limited human studies amplifying the role of biogenic metabolites in improving gut health and managing mental health. Even though most shelf-available fermented beverages are tetra packed, we may still claim the products' health benefits since released biogenic metabolites make the product directly useful without the requirement for live bacteria (Korhonen and Pihlanto, 2003).

Buttermilk is one such fermented dairy product that has long been an important component of a nutritional diet. Probiotic profiling of buttermilk revealed species isolated from *Genus Lactobacillus Lactobacillus acidophilus, Lactobacillus reuteri, Lactobacillus casei* and *Lactobacillus* paracasei. Predominant species isolated from Genus *Bifidobacterium were Bifidobacterium bifidum, Bifidobacterium animalis, Bifidobacterium adolescentis* (Hirdyani and Sheth, 2018). Only a very limited number of scientific reports have been published on the use of buttermilk as a vehicle for improving gut health. *Lactobacillus* and *Bifidobacterium* are the probiotic genera most widely used in the food industry. It is estimated that over 70 products containing *Lactobacillus acidophilus and Bifidobacterium* subsp., including yogurt, buttermilk, frozen desserts and milk powder are produced worldwide (Shah, 2007). However, its potential has not been studied for mental health.

FOS has been recognized for its remarkable potential as a significant food component in enhancing bacterial bionomics, which has shown a direct role in reducing the burden of diseases like CVDs improving glycaemic, lipemic control, and reducing the expression of inflammatory markers (Dehghan et al., 2014). FOS consumption has also been linked to significant reductions in TG, TC, LDL-C, VLDL, and HDL-C, as well as an increase in HDL-C. (Sheth et al., 2015). Many studies have also observed significant reductions in hs-CRP levels and BMI (Sheth and Asudani, 2014; Jain and Sheth, 2017). The ability of prebiotics to regulate the dysbiosis microbiota associated with psychological illnesses such as anxiety, depression, stress, autism, learning, and

memory has also gained traction (Liu et al., 2015). Seeing the health benefits of this prebiotic, it can undoubtedly be claimed that FOS can hold great potential in the nutraceutical industry as a means to manage mental sanity.

Combination of prebiotic added fermented beverages which may have biogenic metabolites in sufficient amounts may trigger the colonization of good bacteria in the gut and thus activate the channels of gut-brain connection to bring about an improvement in the depression status of the individuals. Fermented beverages, prebiotics, and probiotics carry significant implications for research that points the way toward dietary interventions to improve brain function. These foods might be remedy for anxiety and depression and are safer than conventional medication besides providing additional health benefits. The discovery that changing the bacterial environment in the gut can affect the brain has long been surmised in animal data and it looks interesting and suggestive, but still, there is no convincing human study. Therefore, this research was undertaken to ‘Quantify the presence of biogenic metabolites in a prebiotic enriched milk-based fermented beverage (ambil), and to measure if the consumption of ambil, prebiotic (fructooligosaccharide) and buttermilk can associate between gut microbiota and emotional psychiatry. Thereby arriving at the most effective intervention in lowering mild to moderate depression.

Feeding the right gut bacteria for the brain may be a solution to combat mild to moderate depression.