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REVIEW ON KOMBUCHA BEVERAGE AND ITS' PHARMACEUTICALS SCOPE

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ABSTRACT

Kombucha beverage is made by fermenting sugared tea using a culture containing a symbiotic consortium of bacteria and yeasts. Though the origin of Kombucha is obscure, it has gained popularity among consumers as a fermented drink from the last decade. This beverage offers many health benefits including anticancer, hepatoprotective, antimicrobial, antioxidant, probiotics, and many more. Though Kombucha beverage has shown persistent health benefits among the consumer worldwide, there are just a few experimental records to support it. The main purpose of this review is to study the literature available on Kombucha with a pharmaceutical perspective.

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INTRODUCTION

Overview:

Kombucha is a beverage resulting from the fermentation of sweetened tea (*Camellia sinensis*) and added to a culture containing a symbiotic consortium of bacteria and yeasts (SCOBY) [i]. Despite the fact that *C. sinensis* tea is the primary substrate used to make Kombucha, other raw materials have also been employed in studies to make this beverage[ii]. There have been reports of Kombucha culture fermentation on alternative substrates, including herbal infusions[iii], fruit juice[iv], milk[v], soy[vi], and an unconventional food plant like *Malvaviscus arboreus*[vii]. According to reports, they have demonstrated satisfactory results in terms of their kinetics and biological characteristics. These fermented drinks made with other substrates are termed as Kombucha analogs.

Although the history of Kombucha is obscure, there is evidence that it came from the northern Chinese area of Manchuria[viii]. Since last decade, it has been used worldwide for its refreshing and health benefits. It offers a balanced mix of organic acids, cellulose, active enzymes, vitamins, metabolites, proteins, fiber, and other necessary elements[ix]. Kombucha beverage is often referred as a probiotic drink or refreshing beverage. It offers protection from a number of health problems including dyspepsia, cancer, Acquired immune deficiency syndrome (AIDS), anorexia, atherosclerosis, hypertension, and hemorrhoids. Along with the yeast, lactic acid bacteria and acetic acid bacteria are essential for the production of Kombucha. The flavors of the beverage vary based on the type of tea used to make it[x].

Objective of the study:

The main objective behind the study of this review article is to recognize the benefits of Kombucha Beverage as per pharmaceutical aspects and to understand the scope of Kombucha as a forthcoming subject with numerous benefits to human life.

Historical aspect:

In the Tsin Dynasty, 2000 years ago, in Northeast China (Manchuria), Kombucha was first introduced[10], and expanded later to Eastern nations. On the orders of the Japanese Emperor Inkyo, Dr. Kombu imported the beverage from Korea to Japan in 414 AD as a remedy for dyspepsia[xi]. Due to a shortage of sugar and tea, Kombucha consumption decreased during the First World War, but it greatly rose in Italy, France, and Germany[11].

After then, Kombucha beverages became more popular in Asia, Europe, and Russia throughout the 19th and 20th centuries[11]. Many other names for Kombucha have been given to the beverage, including "Manchurian Mushroom Tea," "Tea Fungus," "Kargasok Tea," "Grib tea kvass," "Indian Tea Fungus," "Manchu Fungus," "Teakwass," and "Tea Beer"[11]. Recently, Kombucha has gained popularity as a fermented beverage with low alcohol content and the quickest rate of development. It is notably popular in Brazil[11].

Kombucha is now available commercially and on a small scale across the world. The majority of Kombucha manufacturers and distributors are located in nations like Spain, Canada, the United Kingdom, and North America[11].

Scoby:

SCOBY is gelatinous biofilm which is a symbiotic culture of bacteria and yeast that develops during fermentation on the surface of a polysaccharide matrix (tea)[xii]. By ingesting acetic and lactic acid bacteria, SCOBY aids in the production of cellulose. SCOBY has bacteria including *Acetobacter xylinum*, *Gluconobacter oxydans*, *Acetobacter carboxylic acid*, *Acetobacter pasteurianus* as well as yeasts like *Pichia spp*., genus *Saccharomyces sp*., *Torulopsis sp*., *Zygosaccharomyces bailii*, *Brettanomyces sp*., and *Zygosaccharomyces kombuchaensis*[9].

SCOBY is constantly expanding and becoming denser. It is also known as the "pellicle," which turns teas' sugars into alcohol (low concentration). SCOBY is edible and has several health advantages. It is grown in black, white, and green tea. Black tea is frequently utilized because it creates cellulose more quickly[xiii]. Mother SCOBY create baby SCOBY after fermentation. If there is obvious mold development or a musty smell, SCOBY is either replaced or discarded.

General Procedure for Kombucha tea:

Prepare the infusions by mixing the tea leaves at 10% (w/v) with 20% of sucrose (w/v) in boiling water and steep for 15 min. Then filter out the prepared infusions using filter paper. The clear filtrate that was produced, transfer it into 250 ml Erlenmeyer flasks. Allow filtrate to cool at room temperature, inoculate the flask with an active Kombucha culture. This culture has two parts: a floating cellulose pellicle layer and the liquid broth containing the primary bacteria responsible for the fermentation process. For a period of 8 days to 3 months, the flask has to be covered and incubate at room temperature. Incubation period may vary according to the expected nutritional values.

Black tea liquid broth was historically used to cultivate tea fungus for a period of 14 days. Pour the filtered infusion into a glass jar, add the tea fungal culture that has already been produced, and incubate for 7–14 days at 20–30°C while covering the jar with a clean cloth to prevent contamination. A SCOBY biofilm forms on the surface of fermented tea after a period of 14 days. To separate the SCOBY and fermented drink, the tea is afterwards filtered using cotton or cloth[xiv].

Principle of Kombucha tea fermentation:

During fermentation, sugary tea is transformed into a sour, effervescence, and delightful beverage in presence of SCOBY[9]. Sugary tea, bacteria, and yeast work together to create fermented beverage. Sucrose gets hydrolyzed by yeast, results in the production of glucose and fructose, which further leads to the creation of CO_2 and alcohol. Lactic acid bacteria (LAB) produce lactic acid by consuming glucose and fructose molecules. Alcohol and glucose are used by Acetic acid bacteria (AAB) to produce gluconic acid and acetic acid[9].

METHODOLOGY:

Purpose of Study:

The main purpose of this study is to conduct a systemic literature review as pharmaceutical perspective and to determine in which human health conditions, Kombucha beverage have been used and what could be the scope of it for further research. This was carried out in view of the rising concern over the escalating rates of illnesses in the globe and the potential prospects of Kombucha beverage in terms of pathological condition prevention and/or therapy.

Literature Survey:

Electronic searches on a number of platforms, such as Google Scholar, Web of Science, and PubMed, were used to compile this study. At the first phase, Kombucha and related keywords were searched in order to gather basic knowledge on Kombucha. In the second phase, additional examples of fermented beverage, foods were looked at as well; especially those that were modelled in the industry like yoghurt. At the third phase, researchers were more focused to microbial contribution in the nutraceutical aspects and related topic to see scope for further development.

The electronic search resulted in reach of 456 articles (Identified record N=456). The inclusion and exclusion criteria were used to filter titles, abstracts, and research. After the first screening for duplicate records 210 articles were excluded. The remaining 246 records were undergone second screening, in which 184 articles were excluded based on titles and abstracts. 62 articles went through full text reading. All were compared, and discussed among the reviewers and decided to eliminate 27 articles, leaving 35 papers that met our purpose of the review. Accordingly decisions were made whether the piece of research information should be included in the review.

RESULT AND DISCUSSION:

Pharmaceutical Scope of Kombucha:

Though Kombucha beverage has shown persistent health benefits among the consumer worldwide, there are just a few experimental records to support it. And most of the data have not been supported by scientific data based on human studies. This section reviews several clinical trials and non-human studies that looked at the anticancer, antioxidant, antibacterial, antifungal, hepatoprotective, and other health benefits of Kombucha drinks.

Anticancer Activity:

Though it needs to be researched deeply, Kombucha has been identified to have potential anticancer properties in vitro studies. Kombucha has important ingredients including vitamin C, glucuronic acid, polyphenols, gluconic acid, and lactic acid that help to reduce the risk of stomach cancer[xv]. Tea polyphenols found in Kombucha beverage can suppress gene modification, stop the growth of cancer cells and cause cancer cells to undergo apoptosis. In fact, for cancer patients whose blood pH is 7.56 or higher when unwell, consuming Kombucha tea can be an efficient strategy to rebalance blood pH. Kombucha beverage is also a good option for cancer patients who don't have enough L-lactic acid in their connective tissues because it produces precise L-lactic acid as one of its by-products during the fermentation process[xvi]. In their fascinating study, Srihari et al. looked into the anticancer properties of Kombucha and discovered that it may be a useful tool in the fight against prostate cancer metastasis[xvii]. Numerous studies have shown that tea ingredients, particularly epigallocatechin gallate (EGCG), are anti-mutagenic and anti-inflammatory by preventing the action of oxidants and carcinogens before Deoxy-Ribose Nucleic Acid is damaged[xviii]. Tests on Kombucha tea extracts against human breast cancer and human colon cancer were conducted by Villareal-Soto and colleagues. Their findings indicated that prolonged Kombucha ingestion improved prevention of cancer cell growth[xix].

It may be said that Kombucha is an anticancer agent, however further clinical studies and in vivo research need to be done to emphasise Kombucha's function as an anticancer agent.

Antioxidant Activity:

A number of Kombucha's advantageous constituents with radical scavenging activity properties have been proven to be effective antioxidant, as they have the ability to prevent or postpone the oxidation of the substrate even at low concentration[12]. Principal flavanol category antioxidant constituents in Kombucha beverage are catechins and polyphenols, which efficiently scavenge free radical oxygen species[xx]. Ascorbic acid and D- saccharic-1,4-lactone (DSL), two antioxidants contained in Kombucha, are extremely beneficial for reducing oxidative damage to biological macromolecules like the lipids and proteins found in the blood platelets[xxi].Through two independent techniques, including 2, 2-diphenyl-1-picrylhydrazyl radical (DPPH) and ferric ion reducing power (FRAP), researchers have assessed the antioxidant activity of Kombucha (made with an infusion of rooibos leaves)[xxii]. Due to the absence of catechins in rooibos-infused Kombucha, its antioxidant activity may be lower than that of Kombucha consumed on its own. The beverage's healthful effects come from antioxidant actions that restore the delicate balance between the body's defence mechanisms and free radical generation.

As a consequence, Kombucha can help prevent illnesses including cancer, cardiovascular problems, and neurological conditions[11]. According to study, the antioxidant qualities of these products rely on the type of plant used, the way the tea is brewed, the bacteria that make up the SCOBY, and the fermentation process itself.

Antimicrobial Activity:

It has been demonstrated that Kombucha has an exceptional antibacterial, antifungal impact on a variety of micro-organism[xxiii,xxiv]. The microorganism's ability to proliferate is inhibited by the component of the substrate and by metabolites produced by the bacteria and yeast in the SCOBY. In fact, Kombucha has the power to inhibit the growth of a wide variety of microorganisms, including *Pseudomonas aeruginosa, Agrobacterium tumefaciens, Helicobacter pylori, Enterobacter cloacae, Salmonella enteritidis, Escherichia coli, Yersinia entero*[xxv]. Numerous analysis may had been conducted to show the inhibitory effectiveness against a wide range of microorganisms, including Gram-positive and Gram-negative bacteria[6]. By-products from the acetobacter such as acetic acid and gluconic acid are useful for preventing the growth of several common pathogenic bacteria that are responsible for the stomach discomfort, illness, and diarrhoea associated with food poisoning[xxvi]. Both catechins and acetic acid, which are present in Kombucha, are known to have bactericidal effects. Additionally, it has been claimed that Kombucha contains antibiotic compounds that enhance the antibacterial activity. It has been demonstrated that the acetic acid in Kombucha not only enhances antibacterial qualities but also antifungal properties[9]. The beverage's low pH and high organic acid content has the antibacterial effect against *Shigella dysenteriae*, *Vibrio cholera, Salmonella typhi, and E. coli*. Additionally, neutralised Kombucha was found to prevent the development of bacteria, indicating the bioactive substances such as alkaloids, heterocyclic compounds and esters formed during fermentation are also responsible for the antibacterial effects[9]. Most researchers estimate that acetic acid, which inhibits a variety of bacteria by cytoplasmic acidification and accommodating dissociated acid anion to lethal levels, is the primary cause of Kombucha's antimicrobial effectiveness against foodborne infections[xxvii]. Without harming customers' health, Kombucha might be thought of as an efficient, affordable, and accessible remedy to foodborne diseases.

Hepatoprotective Activity:

It has been demonstrated via research on animal models and cell lines that Kombucha broth has hepatoprotective activity against several environmental pollutants that can induce hepatotoxicity and liver damage[xxviii]. It is researched that it can be used as a protective liver-kidney agent for rats that have been fed a diet that includes Kombucha broth. This study has been conducted on alloxan-induced diabetic mice[xxix]. The acetic acid bacteria present in Kombucha, oxidises glucose to glucuronic acid (GlcUA). GlcUA binds toxins in the liver, allowing for their efficient elimination out of body through excretion. Non-alcoholic fatty liver disease (NAFLD), a condition characterised by aberrant lipid retention in fewer than 5% of hepatocytes (steatosis). If left untreated, NAFLD can proceed to cirrhosis or hepatocellular cancer. According to studies, kombucha influences lipid metabolism and shields hepatocytes from toxicity in mice with NAFLD, and the liver's recovery is aided by the decrease in fibrosis and inflammation.[16,xxx]. Therefore, it is potential that Kombucha can be utilised to control biological factors in liver damage and as a hepatoprotective agent in instances when there's a risk of liver damage. The inclusion of glucoronic acid may contribute to Kombucha tea's hepatoprotective effects by functioning as a robust detoxifying agent. Thus kombucha tea may be useful in protecting the liver against a variety of hepatotoxic substances, including chromat, tert-butyl hydroperoxide, tetrachloride, and lead acetate [xxxi,xxxii].

Probiotic Action:

Probiotic microorganisms are well known for playing a crucial part in maintaining human health. These microbes maintain a balance in the intestinal microbiota, regulating digestive functions, and enhancing the immune system[xxxiii,xxxiv]. The majority of research have claimed that Kombucha functions as a symbiotic, a combination of probiotics and prebiotics, in addition to being just a probiotic[6,xxxv]. The community of beneficial microorganisms found in the human gut are helped by a prebiotic to grow and functions more effectively[28]. The probiotic yeast and bacteria in this beverage work in conjunction with the micro cellulose to aid in the development of beneficial microbes in the gut[xxxvi]. The probiotics are grown in liquid broth but sometimes if not made in particular condition; it may develop harmful bacteria and moulds. This may cause liver problems, Lactic acidosis, allergic reaction and nausea[xxxvii].

CONCLUSION

Kombucha is a beverage made by fermenting sweetened tea (*Camellia sinensis*) that has been mixed with a culture that contains a symbiotic alliance of bacteria and yeasts (SCOBY). Due to its alleged health advantages, this beverage has grown in popularity, been sustained in numerous nations, and is being drank today and distributed all over the world.

During the fermentation process, a number of metabolic events take place that result in the creation of secondary metabolites. The majority of metabolites come from the substrate that is used to produce them. Organic acids, ethanol, carbohydrates, vitamins, and minerals are the primary molecules which are biosynthesized in the beverage. Fermentation can be influenced by a number of variables, including the type and quantity of raw materials, carbon source, starter culture, fermentation time and temperature, pH and oxygen, which can result in beverages with different chemical properties and in turn, alter the biological activity of those beverages.

Although some advantageous benefits have been demonstrated in vitro and in animal models, there is yet no clinical proof of Kombucha's biological activity in people. Consuming Kombucha may have toxic consequences, which require more research and analysis. As a precaution, it should not be advised for those with pre-existing conditions, pregnant women, nursing mothers, and children under the age of four.

These factors influenced the creation of this study, which aims to better understand Kombucha fermented beverages and their potential applications in pharmaceuticals by compiling significant scientific evidence released over the years.

FUTURE SCOPE

Numerous health advantages of Kombucha are studied in non-human subject literature; it is crucial that these claims have to be verified in clinical studies including humans. The possibilities and opportunity for clinical Kombucha investigations are enormous.

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