VISI DAN MISI
PROGRAM STUDI PENDIDIKAN DOKTER
FAKULTAS KEDOKTERAN UNIVERSITAS UDAYANA

VISI :
Menjadi Program Studi Pendidikan Dokter Fakultas Kedokteran Universitas Udayana sebagai lembaga pendidikan kedokteran yang mampu menghasilkan lulusan yang unggul, mandiri, dan berbudaya serta mempunyai daya saing di tingkat nasional dan internasional.

MISI :
1. Misi Umum
Memberdayakan Program Studi Pendidikan Dokter Fakultas Kedokteran Universitas Udayana sebagai perguruan tinggi yang melaksanakan Tri Dharma Perguruan Tinggi berlandaskan pengembangan ilmu pengetahuan dan teknologi dan nilai budaya.

2. Misi Khusus
a. Meningkatkan kegiatan pendidikan, penelitian, dan pengabdian kepada masyarakat bertaraf nasional dan internasional, berlandaskan budaya, moral, dan integritas yang tinggi sesuai dengan tuntutan masyarakat.
b. Mewujudkan program studi yang mandiri dan professional dalam pengelolaan dan pengembangan institusi serta mempunyai tata kelola yang baik (Good Corporate Governance)
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HEPATOPROTECTIVE PROPERTY OF KOMBUCHA TEA

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ABSTRACT

Kombucha tea is made from the fermentation of sweetened black tea (Camelia sinensis L.). It is the product of symbiosis between yeast and acetic acid bacteria. This unique tea might have hepatoprotective properties by modulating oxidative stress induced apoptosis in murine hepatocytes. This may occur due to its antioxidant activity and functioning via mitochondria-dependent pathways. Kombucha tea has a protective effect against tertiary butyl hydroperoxide induced cytotoxicity and cell death in murine hepatocytes. It counteracts the changes in mitochondrial membrane potential and prevents apoptotic cell death of the hepatocytes through formation of antioxidant molecules such as D-saccharic acid -1,4-lactone. D-saccharic acid -1,4-lactone has beta glucoronidase inhibitor activity. Glucoronic acid, has important therapeutic effects by acting as blockers of free radicals. [MEDICINA. 2014; 45:99-101].

Keywords: kombucha, hepatoprotective, hepatotoxicity, glucoronidase inhibitor

INTRODUCTION

Kombucha tea, which is also called tea fungus, is produced from the fermentation of sweetened black tea (Camelia sinensis L.). The nitrogen-fixing Acetobacter nitrogenifigens sp. nov. was isolated from kombucha tea. The yeast species are mainly Brettanomyces bruxellensis, Candida stellata, Schizosaccharomyces pombe, Torulaspora delbrueckii, and Zygosaccharomyces bailii. Kombucha tea is also rich in lysine. Kombucha tea is claimed to have various beneficial effects on human health, however very little scientific evidence is available to support this claim. Research indicates that Kombucha tea might heal liver damage, prevent cardiovascular disease, promote digestion, improve resistance against cancer, stimulate immunity, and reduce inflammation.

In this review, we will discuss about various hepatotoxic agents studies related to kombucha tea treatment in order to see the effect of kombucha tea in depth.

STUDIES OF KOMBUCHA TEA AGAINST VARIOUS HEPATOTOXIC AGENTS

In some studies, tertiary butyl hydroperoxide caused formation of reactive oxygen species, changes in mitochondrial membrane potential, cytochrome c release, activation of caspase (3 and 9), and Apaf-1 on the mitochondrial pathway. Kombucha tea was found to modulate oxidative stress induced apoptosis in murine hepatocytes. This may have occurred due to its antioxidant activity via the mitochondrial dependent pathway. Kombucha tea was significantly more efficient than black tea in reverting carbon-tetrachloride induced hepatotoxicity.

Kombucha tea was obtained from Tamil Nadu. It was a symbiont of Pichia sp. and Zygosaccharomyces sp. First, glass jars were sterilized at 121°C for 20 minutes and then inoculated with 2.5% tea fungus infusion that was cultured for 14 days in 20% fermented liquid tea broth. Then
the cooled black tea was poured into it. Cheesecloth and rubber bands were used to seal the jars for 14 days, in order to make sure the fermentation process goes well.²

Five-week-old male albino rats (150–180 g) were used for the tests. Kombucha tea was given at 2.5 mL/kg body weight after induction with CCl₂ at 2 mL/kg body weight. Control rats were given a normal diet and drinking water ad libitum. Blood samples were taken by puncturing the heart, and the samples mixed with heparin. Each blood sample was centrifuged at 10,000 rpm for 15 minutes, and the levels of aspartate transaminase (AST), alanine transaminase (ALT), and malondialdehyde (MDA) were checked. The liver from each rat was analysed for histopathological study and MDA content. Levels of AST and ALT were estimated by the method of Reitman and Frankel, meanwhile MDA was analysed using Nicchans and Samuelson’s method.²

EFFECT OF KOMBUCHA TEA AGAINST OXIDATIVE STRESS

Oxidative stress is the underlying mechanism for the development of hepatocellular injury. Hepatotoxic agents include arsenic, high doses of paracetamol over an extended period, carbon tetrachloride, and tertiary butyl hydroperoxide. Some research has been conducted on the antioxidant effects of kombucha tea.⁷

Intraxidant intracellular condition and endogenous antioxidants such as catalase, glutathione peroxidase, and superoxide dismutase are important factors in managing oxidative stress.⁸ Inhibition of radical species could be one of the mechanisms involved in hepatoprotective properties.⁹ The presence of glucaric acid and its derivatives could be another reason for the hepatoprotective mechanism.¹⁰ ¹¹

The protective effects of kombucha tea against tertiary butyl hydroperoxide induced cytotoxicity and cell death have been studied in murine hepatocytes.¹¹ Tertiary butyl hydroperoxide disturbed the intracellular antioxidant machines in hepatocytes. This reactive oxygen species inducer disrupts mitochondrial membrane potential and causes apoptosis. Kombucha tea treatment counteracts the changes in mitochondrial membrane potential, and prevented apoptotic cell death of the hepatocytes. Kombucha tea contains D-saccharic acid -1,4-lactone that has beta glucoronidase inhibitor activity. This antioxidant molecule was produced by Gluconacetobacter sp. A4 (G. sp. A4).⁷ ¹¹

The effects of Kombucha on oxidative stress in trichloroethylene-induced rats have been studied. Trichloroethylene may induce oxidative stress that produces free radicals. The Kombucha tea contained acetic acid that was able to conjugate with the toxins, which could subsequently be eliminated easily from the body. Glucaric acid in Kombucha tea also facilitated the detoxification process in the body. Kombucha-treated rats had less total free radicals in their blood compared with the trichloroethylene-induced rats.⁹

EFFECT OF KOMBUCHA TEA TO BIOCHEMICAL MARKERS AND LIVER HISTOPATHOLOGY

Carbon-tetrachloride (CCl₄) induces lipid peroxidation and toxicity. It is metabolized to a highly reactive free radical, namely trichloromethyl. Trichloromethyl will attack the phospholipid membrane. This will cause lipid peroxidation and cell lysis. Carbon-tetrachloride induced damage also alters the antioxidant status of the tissue and causes histopathological abnormalities. As a result of the cell lysis, carbon-tetrachloride releases a cytoplasmic hepatic enzyme into the blood stream. Levels of AST, ALT, and ALP will then increase. As a potent detoxifying agent, the presence of glucaric acid may be one of the reasons for the hepatoprotective properties of kombucha tea. At the end of the study, kombucha tea treatment showed better results for the liver function tests and MDA levels. The group that was treated for ten days was compared to the group that had been treated for 30 days, and the results were as follows: AST levels had decreased from 1,600 IU/L to 1,402 IU/L for the kombucha tea treated group, ALT levels decreased from 1,502 IU/L to 1,425 IU/L, and MDA plasma levels decreased from 2.00 nmol/mL to 1.75 nmol/mL.²

The sucrose in the medium is metabolized to glucose and fructose by yeast invertase and will eventually produce ethanol and glycerol. Acetobacter uses glucose to produce gluconic acid, and ethanol to produce acetic acid.² This agent is one of the organic acids produced during the Kombucha fermentation process, and may improve oxidative metabolism. Uridine diphosphate-glucuronic acid conjugates toxins for subsequent elimination.¹²

Carbon-tetrachloride administration caused vesicle formation in hepatic tissues. Kombucha treatment caused a significantly greater reduction in vesicle necrosis than the black tea and enzyme-prepared tea groups. Gas chromatograph analysis revealed that kumbucha tea contains glucaric acid 0.38 g/100 mL, 1.60 g/100 mL acetic acid, 0.20 g/100 mL gluconic acid, and 0.60 g/100 mL ethanol. Glucaric acid is a potent detoxifying agent, and could be one reason for the hepatoprotective properties of kombucha tea.²

Glucuronidation is the enzymatic addition of a glucuronate ion to organic toxins and other compounds that are being processed for elimination via urine or feces. Glucaric acid is water soluble. This acid is often linked to the xenobiotic metabolism substances such as drugs, pollutants, bilirubin, androgen, estrogen, mineralocorticoids, glucocorticoids, fatty acid derivatives, retinoids, and bile acids to more water-soluble
compounds. The uridine diphosphate glucose -
gluconosyltransferase catalyzes the glucuronidation of the glycosyl 
group of a nucleotide sugar to an 
acceptor compound (aglycone) at a 
nucleophilic functional group of an 
 oxygen (hydroxyl or carboxylic acid 
group), nitrogen (amines), sulfur 
(thiols), and carbons. It involves the 
formation of beta-D- 
glucuronide products.\textsuperscript{13}

Gharib and Fahim\textsuperscript{14} 
conducted similar research on 
carbon-tetrachloride. They found 
increased levels of ALT, AST, ALP, 
gamma glutamyl transferase 
(GGT), and bilirubin. Serum 
levels of AST, ALP, and ALP. 

Jayabalan \textit{et al.}\textsuperscript{5} 
studied the prophylactic and curative effects of 
unfermented black tea and 
kombucha black tea on aflatoxin B\textsubscript{1}, induced liver damage in male 
abino rats. They analyzed 
hepatotoxicity markers (AST, 
ALT, ALP, and GGT), lipid 
peroxidation, reduced glutathione 
and antioxidant enzymes 
(glutathione-S-transferase, 
glutathione peroxidase, glutathione 
reductase, catalase, and 
superoxide dismutase). The 
results of histopathological 
findings and hepatotoxicity 
markers revealed that kombucha 
tea was more potent in preventing 
hepatotoxicity than unfermented 
black tea. It was facilitated by the 
antioxidant properties of 
kombucha tea.\textsuperscript{5}

SUMMARY

Hepatoprotective property of 
kombucha tea can be attained via 
antioxidant activities and 
mitochondria pathways. Kombucha tea can modulate 
oxidative stress because it contains 
glucoronic acid, which was 
obtained via the symbiosis of yeast 
and \textit{Acetobacter} sp in the 
fermentation process. By acting as 
a potent detoxifying agent, the 
presence of glucoronic acid could 
be one reason for the 
hepatoprotective property of 
kombucha tea. Hepatoprotective 
effect of kombucha tea could be 
effective against various 
hepatotoxic agents such as 
chronat, tertier butyl 
hydroperoxide, tetrachloride, and 
lead acetat.

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