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Full Length Article

Ameliorative effect of pumpkin oil (*Cucurbita pepo* L.) against alcohol-induced hepatotoxicity and oxidative stress in albino rats

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ARTICLE INFO

Article history:
Received 19 April 2014
Received in revised form
31 July 2014
Accepted 13 August 2014
Available online 1 November 2014

Keywords:
Pumpkin oil-hepatotoxicity
Rattus norvegicus
Oxidative stress

ABSTRACT

Objective: The aim of the present study was to evaluate the protective role of pumpkin oil on experimental alcohol – induced hepatotoxicity.

Materials and methods: Rats are divided into three groups of 10 animals each. Group one (G1) was the control group is orally given distilled water for 4 weeks. Group two (G2) is given absolute ethyl alcohol (10%) in drinking water for 4 weeks. Group three (G3) alcohol–administered rats were pretreated with pumpkin oil (50 mg/kg body weight) three times per week for three weeks and alcohol (10%) three times per week (at the first two weeks of the experiment).

Results: Alcohol caused a marked rise in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (γGT) activities. Concerning oxidative stress and antioxidant defense system, the depleted hepatic glutathione content, glutathione-S-transferase and catalase activities of alcohol-administered rats were potentially increased above normal levels as a result of pretreatment with pumpkin oil. However, while elevated lipid peroxidation was noticed in alcohol treated rats, pretreatment with pumpkin oil produced a detectable decrease in lipid peroxidation level.

Conclusion: The natural plant components found in pumpkin could improve the liver against alcohol-induced liver toxicity and oxidative stress. However, further clinical studies are required to assess the safety and benefits of pumpkin oil in human beings.

1. Introduction

Alcohol is the most psychoactive substance used after caffeine. Chronic alcoholism is a major public health problem and causes disease and toxicity. Accumulating evidence suggest that intermediates of oxygen reduction may be associated with the development of alcoholic disease (Calabrese et al., 2002). Ethanol or its metabolites can prompt a sharp increase of free radicals in the human body (e.g. hepatic cells)

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Peer review under the responsibility of Beni-Suef University.
http://dx.doi.org/10.1016/j.bjbas.2014.08.001
2314-8535/

by acting as a prooxidant or by reducing antioxidant levels and contributing to the progression of a variety of chronic diseases (Clemens and Jerrells, 2004). Reactive oxygen species (ROS) are highly reactive and can damage lipids, proteins and DNA (Arteel, 2003). The ROS, the main culprit, the other one being reactive nitrile species (RNS) are capable of damaging several cellular components such as proteins, lipids and DNA (Koneru et al., 2011).

Liver is the primary organ for the metabolism of ingested alcohol (Shanmugam et al., 2010).The liver is the largest, important organ and the site for essential biochemical reactions in the human body. It has the function to detoxify toxic substances and synthesize useful biomolecules. Therefore, damage to the liver leads to grave consequences. Alcohol induces oxidative stress which is known to cause liver injury that is many biochemical metabolic reactions occur as a result of it. Some of these include redox state changes, production of reactive acetaldehyde, damage to the mitochondria of cells, cell membrane damages, hypoxia, effects on immune system, altered cytokine production, and induction of CYP2E1 and mobilization of iron (Baskaran et al., 2010). Alcoholic liver disease is a worldwide health problem which has three manifestations in form of fatty liver/steatosis, alcoholic hepatitis and liver cirrhosis. At least 80% of chronic alcoholic consumers may develop steatosis, 10–35% alcoholic hepatitis and approximately 10% liver cirrhosis. Intake of alcohol causes accumulation of reactive oxygen species (ROS) like superoxide, hydroxyl radical and hydrogen peroxide in the hepatic cells that oxidize the glutathione which leads to lipid peroxidation of cellular membranes, oxidation of protein and DNA resulting in hepatic damage (Muhammad et al., 2009). Initially, in the liver alcohol is metabolized into the highly toxic acetaldehyde by the enzyme alcohol dehydrogenase. Acetaldehyde is then oxidized to acetate by acetaldehyde oxidase or xanthine oxidase giving rise to ROS via cytochrome P450 2E1. Prolonged consumption of alcohol increases nitric oxide (NO) level which leads to formation of toxic oxidant peroxynitrite. Low capacity of antioxidants in this situation leads to damage of the cells of the hepatic cells and the cell organelles with the release of reactive aldehydes and ROS (Saalu et al., 2012). Treatment options available for common liver diseases such as cirrhosis, fatty liver and chronic hepatitis are inadequate in modern medicine. Conventional drugs used in the treatment of liver diseases such as corticosteroids, antiviral, immunosuppressant may lead to serious adverse effects; they may even cause hepatic damage on prolonged use. Therefore, alternative drugs in the form of herbal medicines which are now used for the treatment of liver diseases are sought instead of currently used drugs of doubtful efficacy and safety (Vetriselvan et al., 2010).

Natural antioxidants are found in many compounds classified as secondary plant metabolites, e.g. in polyphenols (phenolic acids, flavonoids) and terpenoids (carotenoids), and the consumption of foods which contain these compounds in large quantities seems to play an important role in prophylaxis against many diseases. Epidemiological studies have revealed that the incidence of some cardiovascular and cancer diseases is less frequent when fruit and vegetables are consumed regularly (Horubała, 1999), which should be attributed to the large quantities of the phenolics present. Phenolic compounds belong to a numerous group of antioxidants and act via different modes, e.g. by ‘scavenging’ free radicals. Phenolic compounds can also enhance the activity of other antioxidants, for example that of fat-soluble vitamins (Dru_zyń ska et al., 2008).

Pumpkin seeds (Cucurbita pepo L.) are a rich source of unsaturated fatty acids, antioxidants and fibers, known to have anti-atherogenic and hepatoprotective activities (Makni et al., 2008). Pumpkin is one such plant that has been frequently used as functional food or medicine (Caili et al., 2006). Some of its common uses in most countries are for diabetes where it is used internally, as well as externally for management of worms and parasites. Treatment of spontaneously hypertensive rats with felodipine or captopril monotherapy or combined with pumpkin seed oil produced improvement in the measured free radical scavengers in the heart and kidney (Al-Zuhair et al., 2000).

Being rich in unsaturated fatty acids especially linoleic and oleic acid and tocopherols and with very high oxidative stability, pumpkin seed oil is suggested to be a healthy addition towards human diet and have potential suitability for food and industrial applications (Stevenson et al., 2007). In addition to the carotenoids and gamma aminobutyric acids (GABA) found in the fruits (Liu, 2001), there are other biologically active ingredients, which are found in pumpkins (Gossell-Williams et al., 2008) such as, sterols, proteins and peptides, polysaccharides, para-aminobenzoic acid and fixed oils. Essential fatty acids are necessary for human health but the body cannot make them; so they must be taken through food (Eynard et al., 1992). Pumpkin seed oil's main nutrients are: essential fatty acid-omega 6, omega 9, phytosterols, and antioxidants such as carotenoids, vitamin A and vitamin E (Murkovic et al., 1996). Linoleic acid, a polyunsaturated fatty acid present in pumpkin seed oil, is known to increase membrane fluidity and allows for osmosis, intracellular and extra cellular gaseous exchange (Lovejoy, 2002). Pumpkin seed oil includes fatty acids: palmitic (C 16:0), stearic (C 18:0), oleic (C 18:1) and linoleic (C 18:2) (Kulaitiene et al., 2007). Antioxidants are the substances that when present in low concentration significantly delay or reduce the oxidation of the substrate (Halliwell, 2000).

Compared pumpkin oil with another oil, Jia et al. (2011) evaluated the protective effects of almond oil against acute hepatic injury induced by carbon tetrachloride in rats. These result demonstrated that almond oil has potent hepatoprotective effects, and could be developed as a functional food for the therapy and prevention of liver damage. It is well known that almonds contain a wide variety of phenolic acids and flavonoids and the consumption of almonds has been associated with a reduced risk of chronic diseases. (Milbury et al., 2006). The almond contains as much as 50% oil (Zhang et al., 2009). As one of the most popular vegetable oils, almond oil is rich in mono and poly-unsaturated fatty acids, with oleic and linoleic acids as the major constituents, and a number of minor components such as tocopherols and phenolic compounds. Monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA), as well as minor lipid