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Lycopene stabilizes liver function during D-galactosamine/lipopolysaccharide induced hepatitis in rats

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Abstract

Hepatitis remains as clinical challenge and a problem of great importance in developing and underdeveloped world. Acute hepatitis can have serious health effects including mortality. There is no specific treatment for acute hepatitis. Care is aimed at maintaining comfort and adequate nutritional balance. Lycopene is a potent antioxidant of carotenoid family found in fruits and vegetables. The consumption of lycopene-rich foods, such as tomato paste, chilli sauce, and spaghetti sauce, has been demonstrated to prevent the occurrence of a number of chronic diseases including various types of cancers. Lycopene has been associated with a number of health benefits particularly in regard to prostate, lung, heart and skin health. The present investigation was carried upon to explore the role of lycopene on liver health by analyzing the biochemical parameters and liver marker enzymes during experimentally induced hepatitis in animal model and the findings strongly suggest that lycopene is potential agent of hepatoprotection.

Keywords: Lycopene; Antioxidant; Hepatitis; Galactosamine; Free radical

1. Introduction

The viral hepatitis particularly, Hepatitis B is the most common form of acute hepatitis. Hepatitis B virus (HBV) is a major cause of acute hepatitis, cirrhosis and hepatocellular carcinoma worldwide. HBV continues to be the single most important cause of viral hepatitis in the developing and underdeveloped world. It is estimated that about one-third of the global population, around 2 billion people have been infected with the hepatitis B virus at some stage in their lifetime. Of these, about 360 million people remain chronically infected carriers of the disease. According to World Health Organisation (WHO) report [62], an estimated 600,000 persons die each year due to the acute or chronic consequences of hepatitis B. Hepatitis remains as clinical challenge and a problem of great importance. Acute hepatitis can have serious health effects including mortality. There is no specific treatment for acute hepatitis. Care is aimed at maintaining comfort and adequate nutritional balance [22].

Carotenoids are a class of more than 600 natural pigments that are present in fruits and vegetables [23]. Epidemiological reports demonstrate a clear inverse association between diets high in carotenoid-rich fruits and vegetables and reduced incidence of variety of diseases [59,60]. Lycopene is a potent antioxidant of carotenoid family, and naturally occurring compound that gives characteristic red color to tomato, watermelon, pink grapefruit, orange, and apricot [51]. A number of studies have indicated the health benefits of consuming lycopene and demonstrated its preventive role in

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the occurrence of a number of chronic diseases including various types of cancers [17,24,16,12,1,11,57]. Lycopene is found to be the most effective antioxidant among all the tested carotenes and xanthophylls [36,13]. Among the numerous models of experimental hepatitis, D-GalN induced liver damage is very similar to human viral hepatitis in its morphological and functional features [31]. Administration of a subtoxic dose of galactosamine (GalN) together with or followed by lipopolysaccharide (LPS) induces acute hepatitis and is a well-established model for acute hepatitis [4,63,41]. This liver injury model has been used to evaluate the therapeutic value of flavones, quinines and carotenoids that are known as antioxidants and of other plant products that are claimed to be hepatoprotective [39,19,29].

Despite considerable progress in the treatment of liver diseases by oral hepatoprotective agents, search for newer drugs continues because the existing synthetic drugs have several limitations. Hence crude drugs or natural food diet which possesses antioxidant or free radical scavenging activity has become a central focus for research designed to prevent or ameliorate tissue injury and may have a significant role in maintaining health. The scientific research to date has demonstrated an array of health benefits clearly associated with lycopene. It offers important health benefits particularly in regard to prostate, lung, heart and skin health. In our preliminary investigation we have earlier reported the role of lycopene on liver health in experimental animals [52,49,50]. Thus the present investigation further explores the hepatoprotective role of lycopene by analyzing the biochemical parameters and liver marker enzymes during D-GalN/LPS induced liver injury.

2. Materials and methods

2.1. Chemicals

D-GalN and LPS (Sero type 011.B4 extracted by phenol water method from *Escherichia coli*) were obtained from Sigma Chemical Co. (St. Louis, MO, USA). All other chemicals (acids, bases, solvents and salts) used were of analytical grade obtained from Sisco Research Laboratories Pvt. Ltd., Mumbai, India and Glaxo Laboratoreis, CDH division, Mumbai, India. Jagsonpal Pharmaceuticals, New Delhi, India, kindly provided Lycopene.

2.1.1. Lycopene stock solution

Lycopene (100 mg) was mixed in 2 ml Tween-80 at room temperature until a homogeneous paste was obtained. Physiologic saline at room temperature was added, drop wise and with vigorous stirring, to a final concentration of 10 mg lycopene/ml of suspension [35].

2.2. Animals

Adult male albino rats of Wistar strain weighing around 120–150 g obtained from Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Madhavaram, Chennai, India were used in this study. They were housed in polypropylene cages over husk bedding and a 12 h light and dark cycle was maintained throughout the experimental period. Rats were fed a commercial pelleted diet (Hindustan Lever Limited, Bangalore, India) and water *ad libitum*. The experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and Institutional Animal Ethics Committee guidelines (IAEC No. 01/026/08).

2.3. Experimental design

The animals were divided into four groups of six animals each.

Group 1: Served as vehicle control and was administered with Tween-80 in saline.
Group 2: Rats were given lycopene alone (10 mg/kg body weight for 6 days intraperitoneally).
Group 3: Rats were induced with D-GalN and LPS (300 mg/kg body weight and 30 μg/kg body weight, i.p 18 h before the experiment) [42].
Group 4: Rats were pretreated with lycopene for 6 days prior to the induction of D-GalN/LPS.

2.4. Collection of samples for biochemical analysis

After the experimental period, the animals were anaesthetized by intraperitoneal injection of pentobarbital sodium (30 mg/kg body weight) and sacrificed.

Blood was collected and the liver tissue was excised quickly. The tissues were immediately washed in physiological saline to remove blood clot and other tissue materials and stored at 4 °C until further use.

2.5. Separation of serum

The blood samples collected in plain centrifuge tubes were kept in inclined position to allow complete clotting of blood and then centrifuged at 2500 rpm for 30 min. The resultant clear supernatant was pipetted