Article

Effect of Terminalia Chebula (Haritaki) on Serum Aspartate Aminotransferase, Alanine Aminotransferase in Paracetemol induced liver damage in Wister Albino Rats

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Abstract

Background: Liver plays a major role in detoxification and excretion of many endogenous and exogenous compounds. Any injury may lead to severe liver damage and impairment of liver function. Harbal plants such as Terminalia chebula (Haritaki) may have free radical scavenging activity thereby can be used for the prevention and treatment of liver damage. **Objective:** To observe the effect of Terminalia chebula on paracetamol induced changes of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in Wister albino rats. **Methods:** This experimental study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka from January to December' 2013. Total 44 rats with age 90 to 120 days, weighing between 150 to 200 gm were selected. After acclimatization for 14 days, they were divided into base line control (BC, n=11), paracetamol treated control (PC, n=11),Terminalia chebula pretreated and paracetamol treated (TCP-PCT n=11) and paracetamol pretreated and Terminalia chebula treated group (PCP-TCT, n=11). All groups received basal diet for 21 consecutive days. In addition to basal diet, rats of BC received propylene glycol (2ml/kg body weight, orally) and PC received single dose of paracetamol suspension (750mg/kg body weight, orally) on 21st day. Rats of TCP-PCT received Terminalia chebula extract (200 mg/kg body weight, orally) for 21 consecutive days and paracetamol suspension (750mg/kg body weight, orally) on 21st day. Again, rats of PCP-TCT received paracetamol suspension (750mg/kg body weight, orally) on the 1st day and Terminalia chebula extract (200 mg/kg body weight orally) for 21 consecutive days. All rats were sacrificed on 22nd day and then blood samples were collected. For assessment of liver function serum AST and ALT levels were estimated by using standard laboratory kits. The statistical analysis was done by one way ANOVA and post hoc Bonferroni test as applicable. **Results:** The mean serum AST and ALT levels were significantly ($p<0.001$) higher in PC in comparison to those of BC. Serum AST and ALT levels of all experimental groups were significantly ($P<0.001$) lower than PC group. **Conclusion:** From the results of this study, it may be concluded that Terminalia chebula may have some hepatoprotective effects in paracetamol induced liver damage in rats.

Keywords: Terminalia chebula, hepatoprotective, paracetamol, aspartate aminotransferase, alanine aminotransferase.

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Introduction

Liver is essential for life as it performs numerous metabolic functions, such as, synthesis of proteins, formation and secretion of bile, regulation of blood glucose level, detoxification of drugs and endogenous compounds and storage of vitamins and minerals[1].Continuous exposure to toxic

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exogenous compounds may lead to liver dysfunction[2]. Liver diseases are major health problem worldwide and highly endemic in developing countries. About 20,000 deaths occur every year due to liver diseases[3]. The modern or synthetic drugs used in the treatment of liver diseases have been reported to cause serious adverse side effects whereas some alternative natural medicinal plants were recommended in Ayurveda for the treatment of liver disorders have less or no side effects[4]. Paracetamol is a very common analgesic and antipyretic drug which is readily available without prescription. Increasing and unregulated use and easy availability of paracetamol have led to over use of this drug and may cause a number of serious clinical problems[5]. Paracetamol is hepatotoxic when used in excessive doses or when used in therapeutic doses for a prolonged period[6,7]. In clinical practice, reliable liver protective drugs are not available but herbs may play an important role in the management of liver disorders[8].

Terminalia chebula have been used as folk medicine throughout the ancient times in India subcontinent. It is locally known as Haritaki and belongs to Combretaceae family. Terminalia chebula is also called as king of medicine because it has been widely used in ayurveda, unani, siddha and homeopathy[9].Terminalia chebula contains tannin, chebulic acid, glycosides, sugar, triterpenoids, steroids and small quantity of phosphoric acid. Many studies reported various therapeutic effects of Terminalia chebula on different diseases[10]. Till today, no side effects of Terminalia chebula are known. Though various researchers investigated the hepatoprotective effects of Terminalia chebula[11] but recently, it has been observed that Terminalia chebula significantly decreased the paracetamol induced elevation of serum AST and ALT in rats[12,13]. Now a day there is increasing need for substances to protect the liver from damage. Modern medicines have more side effects to cure liver diseases but remedies by medicinal plants have lesser side effects for the treatment of liver diseases. Therefore, to investigate the hepatoprotective properties of some natural substances the present study has been designed to examine the hepatoprotective effect of Terminalia chebula on paracetamol induced liver damage in Wister albino rats.

Methods

This experimental study was conducted during 2013 in the Department of Physiology, Dhaka medical college (DMC), Dhaka. Total 44 apparently healthy Wister albino rats, weighing between 150 to 200 grams and age ranging from 90 to 120 days, was used for this study. The rats were purchased from the animal house of Department of Pharmacy, Jahangir Nagar University, Shavar, Dhaka. The protocol of this study was approved by Institutional Ethics Committee (IEC) of DMC. The rats were kept in metallic case in the animal house of Institute of Nutrition and Food Science, University of Dhaka (DU). Before conducting the study, rats were kept in a standard laboratory condition on a 12/12 hour light/dark cycle for 14 days for acclimatization. All the rats received basal diet for 21 days. Total study period was 35 consecutive days. After selection and acclimatization for 14 days, the rats were studied for 21 consecutive days. After acclimatization for 14 days, rats were divided into BC (base line control group, n=11) and PC (paracetamol treated control group, n=11), TCP-PCT (Terminalia chebula pretreated and paracetamol treated group, n=11) and PCP-TCT (paracetamol pretreated and Terminalia chebula treated group, n=11). After grouping, initial body weight of all the rats were measured on 1st day. All groups of rats received basal diet for 21 consecutive days. In addition to basal diet on 21th day, BC received propylene glycol (2ml/kg body weight, orally) and PC received single dose of paracetamol suspension (750mg/kg body weight, orally). In experimental groups, TCP-PCT received Terminalia chebula extract (200 mg / kg body weight, orally) for 21 consecutive days and

paracetamol suspension (750mg/kg body weight, orally) on 21th day. Moreover, PCP-TCT received paracetamol suspension (750mg/kg body weight, orally) on the 1st day and Terminalia chebula extract (200 mg/kg body weight orally) for 21 consecutive days. Powder form paracetamol was purchased from Square pharmaceuticals and 1 gm of paracetamol was dissolved in 9 ml of propylene glycol and form paracetamol suspension. Again, 300 gm Terminalia chebula mixed with 800 ml distilled water for 3 days to form Terminalia chebula extract and it was stored in a refrigerator at around 4^0C and was fed to the experimental rats. Before sacrifice, final body weights of all the rats were measured. On the 22th day, all the rats were anaesthetized with the help of chloroform (30%) and then sacrificed. The blood samples (approximately 5 ml) were collected from the heart by direct puncturing with sterile disposable syringes and taken in separate clean and dry test tubes with proper identification numbers. Then blood was centrifuged at a rate of 4000 rpm for 5 minutes. After that the supernatant serum was separated from the blood, collected in a labeled eppendorf and preserved in a refrigerator at -20°c until analytical measurement of serum for AST and ALT in Department of Pathology, DMC. Data was reported in Mean and ±SD. Statistical analysis was done by One-way ANOVA and post hoc Bonferroni test.

Results

The initial, final and % changes of body weight of all rats were almost similar and showed no statistically significant difference among the groups (Table I).

The mean serum AST and ALT were significantly ($p<0.001$) higher in PC in comparison to that of BC. But these levels were significantly ($p<0.001$) lower in TCP-PCT and PCP-TCT in comparison to that of PC. Again there was no significant difference in those levels between TCP-PCT and PCP-TCT (Table II).

Table I: Initial, final and percent (%) change of body weight in different groups of rats (n=44)

Parameters	BC (n=11)	PC (n=11)	TCP-PCT (n=11)	PCP-TCT (n=11)
Initial body wt(g) Day-1	158.18±6.03	156.45±6.35	161.18 ±14.37	157.91 ±9.85
Final body wt(g) Day-22	163.55±5.96	160.82±8.52	164.45 ±14.69	160.82 ±8.52
% change from final (F) weight to initial (I) weight [F-I/I×100]	3.39 ±1.26	2.80±1.8	2.02±1.25	1.84±2.21

Values are Means ± SD. Statistical analysis was done by one way ANOVA test. n = Number of rats. BC = Baseline control group PC = Paracetamol treated control group TCP-PCT =Terminalia chebula pretreated and paracetamol treated group PCP-TCT = Paracetamol pretreated and Terminalia chebula treated group.

Table II: Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in different groups of rats (n=44)

Parameters	BC (n=11)	PC (n=11)	TCP-PCT (n=11)	PCP-TCT (n=11)
AST (U/L)	40.82±5.95	61.64±13.97***	43.55±5.92¥¥¥	37.45±5.73¶¶¶
ALT (U/L)	42.27±6.44	78.36±8.38***	47.91±7.13¥¥¥	48.09±6.73¶¶¶

Values are Means ± SD. Statistical analysis was done by one way ANOVA test and then Bonferroni test. AST (***p<0.001 BC vs PC) (¥¥¥p<0.001 TCP-PCT vs PC) (¶¶¶p<0.001 PCP-TCT vs PC). n = Number of rats BC= Baseline control group PC= Paracetamol treated control group TCP-PCT= Terminalia chebula pretreated and paracetamol treated group PCP-TCT= Paracetamol pretreated and Terminalia chebula treated group.

Discussion

In the present study, significantly higher serum AST and ALT levels in PC in comparison to that of BC, TCP-PCT and PCP-TCT was observed and it is comparable to others[14,15]. But no significant change was observed by some researchers[13,16,17]. It has been suggested that high doses of paracetamol disrupts the liver cell membrane causing increased release of ALT and AST in the blood which are commonly used marker of liver injury[18,19]. It has also been suggested that metabolism of excess paracetamol in liver imposes oxidative stress by increasing the formation of reactive oxygen species which causes lipid peroxidation and depletion of antioxidant enzymes ultimately leading to destruction of structural and functional organization of cell membrane causing liver cell damage[20]. Moreover, high doses of paracetamol also oxidizes intracellular glutathione (GSH) which causes GSH pool depletion in liver cell leading to liver cell damage[21,22]. In this study, elevated levels of AST and ALT in paracetamol treated rats are suggestive of paracetemol induced liver cell damage. Studies on medicinal plants demonstrated that active compounds of Terminalia chebula increase the activities of antioxidant enzymes which in turn obviously protect liver for oxidative damage[23,24]. Lower levels of serum AST and ALT in TCP-PCT and PCP-TCT rats suggest that Terminalia chebula extract provides protection against paracetamol induced liver injury due to its free radical scavenging activity[10]. However, the exact mechanism involved in the hepatoprotective activity of Terminalia chebula extract against liver damage in rats cannot be explained out from this study as concentration of free radicals was not measured.

Conclusion

From the result of this study, it can be concluded that Terminalia chebula (Haritaki) may have some hepato protective role against paracetemol induced liver damage. Therefore, it may be used to prevent liver damage with hepato toxic drugs.

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Conflict of Interest : None

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