JWPR
Journal of World's Poultry Research

2018, Scienceline Publication
J. World Poult. Res. 8(2): 25-30, Jun 25, 2018
Research Paper, PII: S2322455X1800004-8

Hepatoprotective Effects of Cichorium Intybus against Paracetamol Induced Hepatotoxicity in Broiler

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Received: 02 Apr 2018
Accepted: 30 May 2018

ABSTRACT

Hepatic damage in poultry occurs either due to metabolic or nutritional disturbances or chemical intoxication. The absence of reliable liver protective drugs and also consumption of broiler meat, limit us in usage of chemical hepatoprotective agents. The aim of this study is to evaluate the protective effects of CichoriumIntybus (CI) extract in paracetamol-induced hepatotoxicity in broiler chicks. One-day-old Ross chicken broilers were divided into four groups. One group was kept as normal and liver damage were induced in other 3 groups by oral administration of 1 ml/kg body weight of paracetamol for four successive days. Of 3 intoxicated groups one was kept as control and two different medicinal plants extracts were administered 0.2 g/kg of CI and 0.4 g/kg of CI extract. The medicinal plant was administered orally for 14 days after paracetamol administration. Then the blood samples were collected and the chicks sacrificed to histopathological examination. Serum liver markers and histopathological assessment of the livers revealed that Cichoriumintybus has protective activity against hepatic damage specially at a dose of 0.4 g/kg body weight and exhibited anti-hepatotoxic activity in broilers. The present study showed that administration of Cichoriumintybus extract at the doses of 0.2 g/kg/day and 0.4 g/kg/day respectively to Paracetamol intoxicated broilers, mitigates liver toxicity and liver histopathological changes.

Keywords: Cichoriumintybus, Hepatotoxicity, Paracetamol, Broiler.

INTRODUCTION

Nature has bestowed mankind with several plants which contains natural substances which cure diseases & promote health. Due to the limited prevention and treatment options, liver diseases are considered to be one of the most serious health problems in humans and animals. Liver an important organ actively involved in many metabolic functions, the frequent target for a number of toxicants (Jadeja et al., 2017; Meyer and Kulkarni, 2001). Hepatic damage in poultry may occur either due to metabolic or nutritional disturbances or chemical intoxication (Murugesan et al., 2015). Exposure of the liver to the free radicals derived from some xenobiotics and drugs leads to oxidative stress, which is recognized to be an important factor responsible for liver injury or be involved in the pathogenesis of liver disorders (Aseervatham et al., 2018).

In one hand, the absence of reliable liver protective drugs and in the other hand consumption of broiler meat, limit us in usage of chemical hepatoprotective agents. Therefore, herbal therapy seems to be the only logical remedy for liver diseases. A number of plants have shown hepatoprotective effect in Iranian folk medicine (Asadi-Samani et al., 2015). Hepato-protective effect of some plants such as Epaltesdivaricate (Hewawasam et al.,

2004), Aspalathuslinearis (Ulicna et al., 2003), Crassoceplalumcrepidioides (Aniya et al., 2005), Sarcostemmabrevistigma (Singh et al., 2003) and Cichoriumintybushas been well established. Cichoriumintybus is referred to as "kasani" in India and "kasni" in Iran. In some states of Iran the leaves of Cichoriumintybus have been used in drinks and in some other regions for the treatment of liver disorders.

Cichoriumintybus is considered to be folk medicines used for the treatment of liver diseases (Street et al., 2013), and its potent hepatoprotective activity related to antioxidant capacity was demonstrated in previous studies (Casas-Grajales and Muriel, 2015; Gilani et al., 1998; Madani et al., 2008). Esculentin, a compound present in Cichoriumintybus has been observed for its protective effects liver damage (Li et al., 2014). To our knowledge there is no published data on the hepatoprotective effect of Cichoriumintybus in broilers. Considering the fact that the initial event in paracetamol-induced hepatotoxicity is a toxic-metabolic injury that leads to hepatocyte death by necrosis. The aim of this study was to evaluate the protective effects of Cichoriumintybus extract in paracetamol-induced hepatotoxicity in broiler chicks.

MATERIALS AND METHODS

Ethical approval

All experiments in this study were performed in accordance with the guidelines for animal research from the School of Veterinary Medicine, Kerman University, Kerman, Iran. Also, we used the recommendations of European Council Directive (2010/63/EU).

Plants material

The aerial parts of Cichoriumintybus were collected from the local market, dried in room temperature and were powdered. The leaf extract of CI was prepared according to the method of Sadeghi et al (Sadeghi and Yazdanparast, 2003). The therapeutic doses of the extract selected were 0.2 g/kg and 0.4 g/kg b.w (Fallah Huseini et al., 2011).

Experimental protocol

A total of 48 one-day-old Ross chicken broilers were used in this experiment. They were divided into four groups of 12 animals each. One group was kept as normal and liver damage were induced in other 3 groups by oral administration of 1 ml/kg body weight of Paracetamol for four successive days. Of 3 intoxicated groups one was kept as control and two different medicinal plants extracts wereadministered0.2 g/kg of CI and 0.4 g/kg of CI extract. The medicinal plant was administered orally for 14 days after Paracetamol administration.

Serum biochemical and histopathology study

After liver intoxication and medicinal plants extracts treatment, the blood samples were collected and the chicks sacrificed. The serum liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphates (ALP) and total protein were estimated in all groups. The liver tissues were collected and fixed in 10% neutral buffered formalin for histopathological examination. After fixation, the tissue samples were washed, dehydrated by graded ethanol, cleared, embedded in paraffin wax, sectioned at 4-5 µm, stained with haematoxylin and eosin and examined by a light microscope (Olympus, Japan).

Statistical analysis

All the collected data thus obtained was statistically evaluated by ANOVA using SPSS. $P<0.05$ was considered as significant value. All the results were expressed in mean ± Standard Deviation (SD).

RESULTS

Serum liver enzymes

In control group, a significant decrease in Total Protein (TP) levels and increasing in ALT, AST and ALP concentration were recorded after paracetamol administrations compared to the normal group. These disturbances clearly demonstrate the occurrence of hepatic damage. In 0.2 g/kg of CI and 0.4 g/kg of CI extract received groups, the serum ALT, AST and ALP levels were significantly reduced as compared to the control group.

Besides elevation of TP in these treated groups observed. The dose 0.4 g/kg b.w. was proved more effective in its hepatoprotective action as evidenced by remarkable reduction in liver enzymes and increase in TP levels. The statistical results are shown in Table 1.

Histopathological results

Histopathological photomicrographs of liver sections of the chicks treated with paracetamol showed focal necrosis, sever fatty degeneration, and bile pigment retention (Figures 1A, 1B and 1C). Necrosis, which is a more severe form of injury, was markedly prevented by pretreatment with both 0.2 and 0.4 g/kg doses of the CI extract (Figures 1D and 1E).

Table 1. Effects of Cichorium Intybus on biochemical parameters of serum sample collected from broilers with hepatotoxicity at the end of experiment (62 days old)

Enzymes	Group A	Group B	Group C (P+CI 0.2 g/kg)	Group D (P+CI 0.4 g/kg)
ALT (u/l)	(normal)	(Control)	49.1± 0.58**	44.4 ± 1.96**
AST (u/l)	27.1± 0.64	68.2± 1.14*	164.3±7.12**	137.0±1.04**
ALP (u/l)	115.7±5.02	188.6±4.95 *	68.8±4.5	43.6±2.9**
Total protein (g/dL)	31.5±1.9	77.1±2.6*	3.48±0.31**	3.94±0.44**

*Significant level (P<0.05) when compared with group A, ** Significant level (P<0.05) when compared with group B.

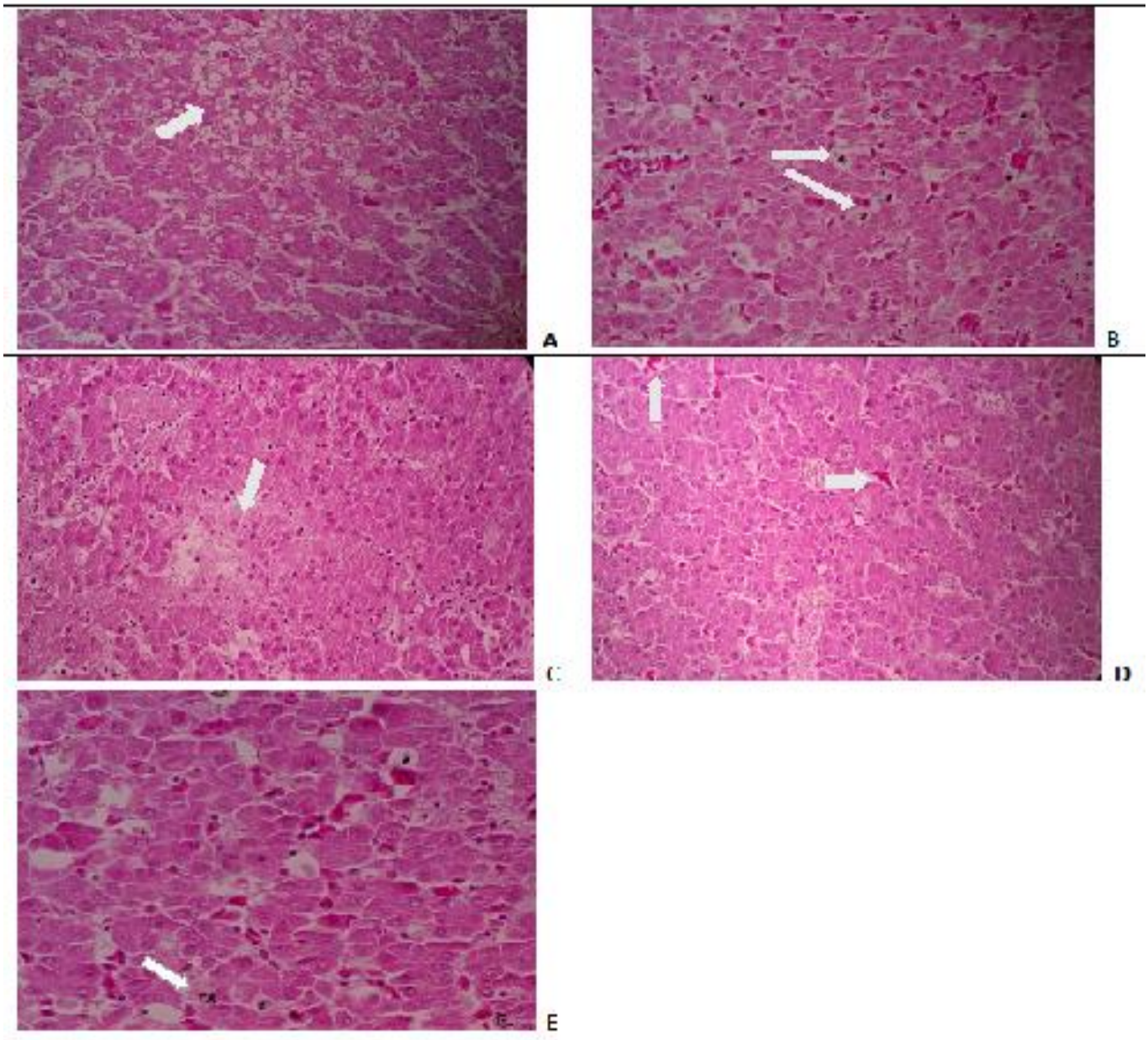

Figure 1. Hepatoprotective effect of CichoriumIntybus in hepatotoxicity of broiler (H&E). A: sever fatty degeneration in paracetamoltoxicated group; B: bile pigment retention in paracetamoltoxicated group; C: focal necrosis in paracetamoltoxicated group; D: congestion in 0.4 g/kg CI treated group; E: mild bile pigment retention in 0.2 g/kg CI treated group

DISCUSSION

Paracetamol (Acetaminophen), a commonly used analgesic, is considered safe at therapeutic doses. However, an overdose can leads to severe hepatotoxicity and necrosis in both humans and experimental animals (Yoon et al., 2016; Elmhdwi et al., 2014). Paracetamol at therapeutic levels, is primarily metabolized by liver through glucuronidation and sulphation; however, a small proportion undergoes cytochrome P450 (CYP450)-mediated bioactivation to N-acetyl-p-benzoquinoimine (NAPQI), which is rapidly quenched by glutathione (GSH) (James et al., 2003). After an overdose of paracetamol, elevated levels of the toxic NAPQI metabolite are generated, and deplete hepatocellular GSH and resulting in hepatocyte death (Tiwari and Khosa, 2010). Although the exact mechanism of cell necrosis is not fully understood, it is generally attributed to lipid peroxidation and oxidative stress (Muriel and Gordillo, 2016).

In the present study, Paracetamol administration to broilers induced hepatic tissue injury as well as significantly changed TP and serum liver enzymes level. Extracts treatment to Paracetamol intoxicated chicks attenuated the liver toxicity as indicated by serum liver enzymes level lowering effect, elevated TP and amelioration in histopathological changes in the liver tissue.

A significant rise in levels of AST, ALT and ALP were observed in hepatotoxicity induced group with paracetamol. This finding is in agreement with the research work reported previously (Hamza and Al-Harbi, 2015; Rajesh et al., 2009) where is observed high AST, ALT and ALP levels after Paracetamol administration. The present results are also similar to the findings of Schmidt and Dalhoff (2002) who reported that administration of Paracetamol can increase the liver enzymes (AST, ALT and ALP) and decrease total protein due to induction of hepatic oxidative stress (Li et al., 2015). The treatment with Cichoriumintybus at doses, 0.2 and 0.4 g/kg b.w. resulted in significant decrease in serum AST, ALT and ALP levels and rise in TP levels which clearly depicts its hepatoprotective action. These findings are in agreement with the findings of Kiran (Butt et al., 2012) who described that Esculetin, a phenolic compound found in Cichoriumintybus has possible protective effects against Paracetamol-induced hepatic damage in rats. Another study demonstrated the hepatoprotective effect of alcoholic extract of Cichoriumintybus (Elgengaihi et al., 2016; Naseem et al., 2009). The results presented also was similar to the study of Jamshidzadeh et al. (2010) that proved the pre incubation of hepatocytes with concentrations between 60 to 600 µg/ml of the Chicory extract for 20 minutes protected hepatocytes against CCl4 -induced cytotoxicity. The protective effect of the Chicory extract in this study was dose-dependent protective effect against CCl4 induced cytotoxicity. It could be due to the presence of Flavonoids and their antioxidant effects (Abbas et al., 2015). In the present study the effective therapeutic dose of Cichoriumintybus for lowering paracetamol induced hepatotoxicity was found 0.4 g/kg as its administration exhibited better reduction in raised AST, ALT and ALP levels while elevation in decreased TP levels.

CONCLUSION

The present findings indicated that, the administration of Cichoriumintybus extract at the doses of 0.2 g/kg/day and 0.4 g/kg/day respectively to Paracetamol intoxicated chicks, mitigates liver toxicity and liver histopathological changes. Further studies are required to evaluate the fractionated extract on hepatotoxicity.

DECLARATIONS

Authors' contributions

R.R., H.Sh., R.Kh. contributed to the conception, design and interpretation of data. H.R. was also involved in the collection of data, statistical analysis and drafting of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

This research was financially supported by grants of Kerman University Research Council.

Competing interests

The authors declare that there is no conflict of interest. This research was financially supported by grants of Kerman University Research Council. All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

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