Short Communication

Comparison of Cassia fistula leaves and garlic in preventing drug induced liver injury in rats

Nasim Ilyas, Wasif Hassan Awan, Zafar Latif Awan, Zareena Akram, Kashif Rahim, Fouzia Hanif

Poonch Medical College AK, Rai Medical College Sargodha, Maragalla Institute of Health Sciences, Rawal Institute of Health Sciences and Federal Medical Dental College, Islamabad, Pakistan

Objective: To comparison of Cassia fistula leaves and Garlic in preventing drug induced liver injury in rats.

Methodology: Rodents were segregated into Control group (I), Isoniazid group (II), Garlic group (III) & Cassia Fistula group (IV). The control group received only standard diet. The Group II received standard diet along with anti-tuberculous drug. The Group III and IV received standard diet along with INH in addition to Cassia Fistula and Garlic. Blood samples were collected after 1 week of acclimatization and at 30th day.

Results: In group II, elevated serum alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP) and total bilirubin levels were noted. Group III showed values close to normal levels of of liver function, but Group IV showed values within range of normal levels of biochemical indicators of liver function.

Conclusion: Toxic dose of INH caused severe liver injury in group II, while liver injury was prevented in group III and IV receiving CF and Garlic, thus providing hepato-protective effect. (Rawal Med J 202;45:725-727).

Keywords: Hepato-protection, isoniazid, Cassia fistula.

INTRODUCTION

Tuberculosis (TB) is caused by mycobacterium tuberculosis (MT). Commonest mode of transmission is through air by cough, sneeze or contact with saliva. Inhaling fewer than ten bacteria may cause an infection.[1] Nearly 3 million deaths because of TB and 8 million fresh cases occur.[1,2] Anti-tuberculous (ATT) drugs have associated risk of liver injury. The ATT causes production of free radicals, normally they are neutralized by glutathione but prolonged use overwhelms this protective mechanism.[3,4] Isoniazid (INH) is common cause of liver damage.[5,6]

Cassia fistula (CF) commonly called as Amaltas, is a local plant of Pakistan. It has various biomedical uses, such as laxative, antipyretic and analgesic, especially for children and pregnant ladies. Another important property of CF is its hepato-protective effect by preventing lipid peroxidation (LPO).[7] Garlic has been considered as an essential dietary and medicinal product for hundreds of years. Matured garlic extract increases cellular glutathione in a variety of cells (liver and mammary tissue), thus preventing LPO, so considered as antioxidant. Previous studies have also showed its antioxidant effects in in different animal studies.[8,9] This study compared the protective effect of CF and garlic on INH induced liver injury in rats.

METHODOLOGY

The study was carried out at Animal house of NIH for 6 months and included 40 rats. They were segregated into 4 groups, (I, II, III & IV with 10 rats each). One week of acclimatization was done before initiation of experiment. GRP I, II, III, IV were given standard diet only, INH, INH plus CF, INH plus GAR for 4 weeks. The following dosage of INH (50 mg/ kg), CF (500 mg/kg) and garlic (0.25 g/kg) were give through oral route daily. On completion of 4 weeks, blood samples were taken and levels of ALT, AST, ALP and total bilirubin were measured. Data was analyzed using SPSS version 17.0.

RESULTS

Significant increase of serum ALT, AST, ALP and Bilirubin in rats of group II as compared to group I, III and IV were noted (Table).

Table. Hepato-protective effect of Cassia fistula and garlic.

Parameters	Group I	Group II	Group III	Group IV
Serum ALT (u/l)	30.5 ± 0.838	130.9 ± 1.9606*	46.22 ± 814*	36.4 ± 0.6261**
Serum AST (u/l)	101.4 ± 1.8764	272.7 ± 4.4709*	135.06 ± 1.68*	127.4 ± 1.5633**
Serum ALP (u/l)	123.6 ± 1.31	385.6 ± 2.5542*	174.51 ± 1.61*	143.8 ± 1.1827**
Total bilirubin (mg/dl)	0.477 ± 0.0496	2.4673 ±0.1115*	0.48 ± 0.42*	0.629 ± 0.0387**

*Significant difference was observed between group II & Group III ($p<0.05$). **Significant difference was observed between group II & Group IV ($p<0.05$). ***No Significant difference was observed between group III & Group IV ($p>0.05$)

DISCUSSION

INH is known for hepatotoxicity and monitoring of biochemical indicators (ALT, AST, ALP and total bilirubin levels) is necessary for early detection of liver injury.[7] We noted hepato-protective effects of CF in INH hepatotoxicity, markedly raised ALT, AST, ALP and total bilirubin in group II in contract group I. Simultaneous use of CF and garlic with INH in group III and IV, resulted in levels of ALT, AST, ALP, serum total bilirubin remaining within normal range, as compared to group II. Our findings are similar to some of the earlier studies.[6,10]

A previous animal study from Lahore, showed similar results of hepato-protection of CF, INH and RIF induced toxicity. However, methodology was a little different, GAR was not used and there was a comparison of low and high dose of CF.[11] Another study compared hepato-protective role of garlic and silymarin and showed promising results of stopping INH and RIF induced toxicity.[12]

A latest study had reported that the co-treatment of ATT with onion extract, prevented hepatotoxicity of ATT in rats and the biochemical marker remained within normal range.[8] Simultaneous use of garlic and CF played a role in reducing the effect of oxidative stress in group III and IV. Accessible works have revealed that extracts acquired from numerous plants have hepato-protective activities against xeno-biotics (including ATT) induced toxic effects. [12-14] The study had following limitations; exact biochemical ingredient was not identified which provided hepato-protective effort, different parts of both herbs were not separately tested in experimental work and dose dependent effects were not observed.

CONCLUSION

CF and garlic had hepato-protective effect against anti-tuberculosis drugs in rats.

Author Contributions:
Conception and design: Nasim Ilyas, Zareena Akram
Collection and assembly of data: Wasif Hassan Awan
Analysis and interpretation of the data: Wasif Hassan Awan, Zafar Latif Awan
Drafting of the article: Nasim Ilyas, Fouzia Hanif
Critical revision of the article for important intellectual content: Nasim Ilyas, Zafar Latif Awan
Statistical expertise: Zareena Akram, Kashif Rahim
Final approval and guarantor of the article: Nasim Ilyas, Kashif Rahim
Corresponding author email: Nasim Ilyas: biochemistry.iimct@gmail.com
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REFERENCES

1. World Health Organization. (2015). Global tuberculosis report 2015, 20th ed. World Health Organization. https://apps.who.int/iris/handle/10665/191102
2. Singh D, Cho WC, Upadhyay G. Drug-induced liver toxicity and prevention by herbal antioxidants: an overview. Front Physiol 2015;6:363-6.
3. Kumar N, Kedarisetty CK, Kumar S, Khillan V, Sarin SK. Antitubercular therapy in patients with cirrhosis: challenges and options. World J Gastroenterol 2014;20:5760-72.
4. Chowdhury A, Santra S, Kundu S, Mukherjee A, Pandit A, Chaudhuri S, et al., Induction of oxidative stress in antitubercular drug-induced hepatotoxicity. Indian J Gastroenterol 2001;20:97–100.
5. Vuilleumier N, Rossier MF, Chiappe A, Degoumois F, Dayer P, Mermillod B, et al. CYP2E1 genotype and isoniazid-induced hepatotoxicity in patient treated for latent tuberculosis. Eur J Clin Pharmacol 2006;62:423–9.
6. Jeong I, Park JS, Cho YJ, Yoon HI, Song J, Lee CT, et al. Drug-induced hepatotoxicity of anti-tuberculosis drugs and their serum levels. J Korean Med Sci 2015;30:167-72.
7. Ramappa V, Aithal GP. Hepatotoxicity related to anti-

tuberculosis drugs: mechanisms and management. J Clin Exp Hepatol 2013;3:37-49.
8. Sana T, Javed I, Aamir A. Antituberculous treatment induced ALT and ALP derangements and the role of onion extract in male albino Rats. Ann Pun Med Coll 2010;4:33-8.
9. Santosh S, Sini TK, Anandan R, Mathew PT. Effect of chitosan supplementation on antitubercular drugs induced hepatotoxicity in rats. Toxicology 2000;219:53-9.
10. Zhang S, Pan H, Peng X, Lu H, Fan H, Zheng X, et al. Preventive use of a hepatoprotectant against anti-tuberculosis drug-induced liver injury: a randomized controlled trial. J Gastroenterol Hepatol 2016;31:409-16.
11. Jehangir A, Nagi H, Shahzad M, Zia A. The Hepato-Protective Effect of Cassia Fistula (Amaltas) Leaves in Isoniazid and Rifampicin Induced Hepatotoxicity in Rodents. Biomedica 2010; 26:25-9.
12. Tabarsi P, Fahimi F, Heidarzadeh N, Haghgoo R, Kazempour M, Masjedi M, et al. The effect of Garcin® in preventing antiTB-induced hepatitis in newly diagnosed tuberculosis patients. Iran J Pharm Res 2014;13:169-76.
13. Pal R, Vaiphei K, Sikander A, Singh K, Rana SV. Effect of garlic on isoniazid and rifampicin-induced hepatic injury in rats. World J Gastroenterol 2006;12:636-9.
14. Ilyas N, Janghir A, Sadiq M. To Study role of hepatoprotective agents in prevention drug induced hepatotoxicity. Biomedica 2011;27:166-70.