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Research Article

Effect of Curcumin on ALT, AST and ALP Enzymes in Isoniazid and Rifampicin Given Rats

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Abstract

In this study, the protective potential of Curcumin (CUR) against the Hepatotoxic Effects of Isoniazid (INH) and Rifampicin (RIF), used in the treatment of tuberculosis, was investigated. A total of 60 Wistar albino rats were used in the study. These rats were divided into Control (C), CUR, INH+RIF and INH+RIF+CUR groups. Cur, INH and RIF were administered to the rats at a level of 100mg/kg body weight by gavage. Gavage procedures were performed at the same time every morning. Alanine Transaminase (ALT), Aspartate Transaminase (AST) and Alkaline Phosphatase (ALP) activities were examined in blood samples taken from the rats. The findings show that the combination of INH and RIF significantly reduced liver enzyme activities. As a result, the preventive effects of CUR on liver damage were observed at a visible level.

Keywords: ALT, AST, ALP, Rifampicin, Isoniazid, Curcumin, Hepatotoxicitya

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacterium Mycobacterium tuberculosis and affects millions of people worldwide [1,2]. INH consists of a pyridine ring and a hydrazide group [3]. RIF is approved by the US Food and Drug Administration (FDA) for the treatment of active and latent (TB) [4]. INH and RIF are frequently used first-line drugs in the treatment of TB [5]. However, these drugs can cause hepatotoxicity by affecting liver enzymes [6]. The liver is the largest organ of the human body. Liver Enzymes Alanine Amino Transferase (ALT), Aspartate Amino Transferase (AST), Alkaline Phosphatase (ALP) are generally elevated in acute hepatotoxicity [7]. Natural products and their plant-derived analogues have the potential to alleviate compatibility problems and toxicity during long-term administration. CUR, the bioactive component of the Curcuma longa plant, also known as "Indian Yellow Gold", has been proven to have therapeutic effects against various chronic inflammatory and infectious diseases [8]. At the same time, CUR is known for its hepatoprotective effects due to its antioxidant and anti-inflammatory properties (*Pulido-Moran. et al,)*. The aim of this study was to investigate the preventive effects of CUR on liver damage in rats treated with INH and RIF due to the changes in ALT, AST and ALP enzyme activities.

Material and Method

A total of 60 female Wistar albino rats, 15 in each group (n=15), were divided into four groups:

i. C group (n=15)

ii. CUR group (n=15); 100mg/kg Curcumin was given.

iii. INH+RIF group (n=15); 100mg/kg Isoniazid and Rifampin was given.

iv. INH+RIF+CUR group (n=15); 100mg/kg Curcumin was given in addition to Isoniazid and Rifampin.

The active substances were administered by gavage method at the same time every morning. At the end of 30 days, the rats were sacrificed and blood samples were taken. The obtained blood was placed in yellow-capped biochemistry tubes and centrifuged at 3000rpm for 10 minutes. Thus, the blood was separated into serums.

ALT Activity Determination

The method is based on the recommendations of the "International Association for Clinical Chemistry" (IFCC). ALT transfers the amino group of alanine to 2-oxoglutarate, forming pyruvate and glutamate. The addition of pyridoxal phosphate to the reaction mixture ensures maximum catalytic activity of ALT. Pyruvate undergoes a reaction with NADH, catalyzed by Lactate Dehydrogenase (LDH), and lactate and NAD^+ are released. The decrease in absorbance due to NADH consumption is measured at 340nm and is proportional to the ALT activity in the sample. Endogenous pyruvate is cleared during the incubation period [9].

AST Activity Determination

The method is based on the recommendations of the "International Association of Clinical Chemistry" (IFCC). In this method, aspartate Aminotransferase (AST) catalyzes the transamination of aspartate and 2-oxoglutarate, resulting in the formation of L-glutamate and oxalacetate. The addition of pyridoxal phosphate to the reaction mixture ensures maximum catalytic activity of AST. Oxalacetate is reduced to L-malate by Malate Dehydrogenase (MDH), while simultaneously NADH is converted to NAD^+. The decrease in absorbance due to NADH consumption is measured at 340nm and is proportional to the AST activity in the sample. Endogenous pyruvate is cleared by the LDH reaction during the incubation period [10].

ALP Activity Determination

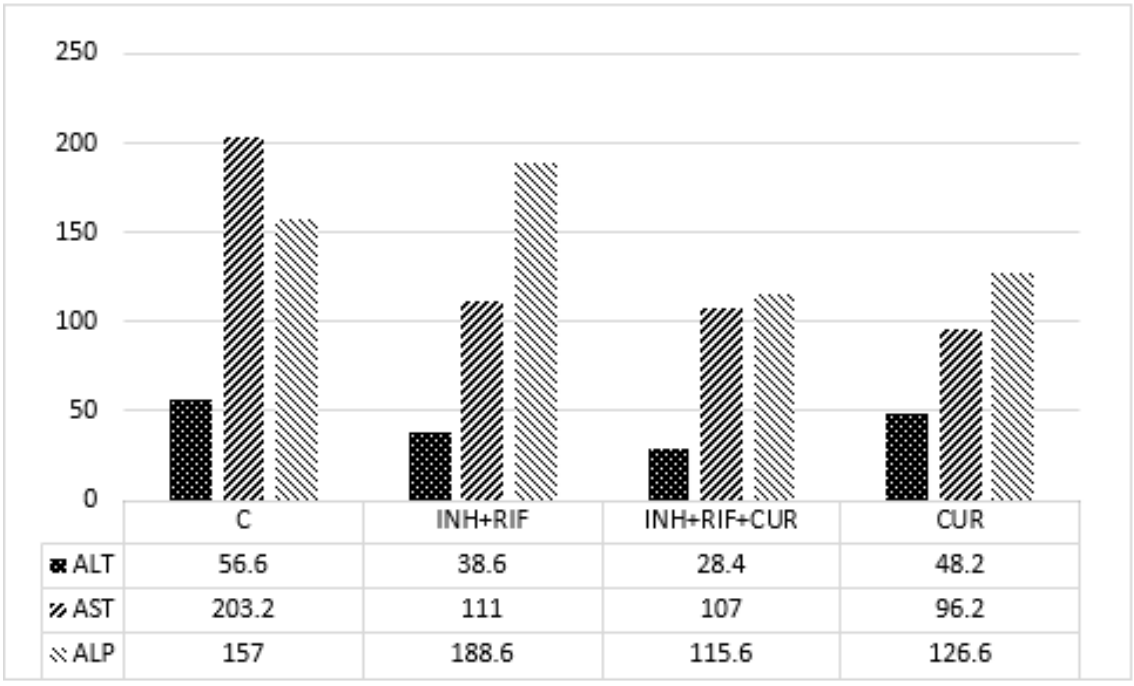
The method is based on the recommendations of the "International Association of Clinical Chemistry" (IFCC). Alkaline Phosphatase activity is determined by measuring the rate of conversion of p-Nitro-Phenylphosphate (pNPP) to p-Nitrophenol (pNP) in the presence of magnesium and zinc ions and 2-Amino-2-Methyl-1-Propanol (AMP) as phosphate acceptors at pH 10.4. The absorbance change rate due to pNP formation is measured dichromatically at 410/480nm and is directly proportional to the ALP activity in the sample [11].

Statistical Analysis

SPSS program was used for statistical analysis. Since the normality assumption was not provided in the analyses, Kruskal Wallis test, which is the nonparametric equivalent of one-way variance analysis, was performed.

Results

The most striking findings of this study show that the INH + RIF combination significantly affected ALT, AST and ALP enzyme activities and that CUR significantly prevented this damage. ALT Enzyme Activity: Although a decrease in ALT levels was observed in the INH+RIF group, maximum inhibition was observed in ALT levels in the INH+RIF+CUR group. When CUR was added to INH+RIF, 35% lower activity was observed. This inhibition was found to be statistically significant ($p=0.019<0.05$). This may indicate that CUR has a significant protective effect on the liver. AST Enzyme Activity: It was observed that all groups caused inhibition in AST levels. However, maximum inhibition was observed in the CUR group compared to the control group ($p=0.017<0.05$). This confirms that CUR is effective against hepatotoxicity. ALP Enzyme Activity: An increase in ALP levels was observed in the INH+RIF group. However, when CUR was added to this group, it was observed that the ALP level decreased by 39% ($p=0.017<0.05$). When CUR was given alone, the ALP level was observed to be 20% lower. These results clearly show that CUR reduces liver enzyme activities and provides effective protection against hepatotoxicity caused by INH+RIF (Figure 1).



	C	INH+RIF	INH+RIF+CUR	CUR
ALT	56.6	38.6	28.4	48.2
AST	203.2	111	107	96.2
ALP	157	188.6	115.6	126.6

Figure 1: Effects of INH+RIF, INH+RIF+CUR and CUR on ALT, AST, ALP enzyme activities.

Discussion

This study clearly demonstrates that CUR plays a strong protective role against INH+RIF-induced liver damage. The antioxidant and anti-inflammatory effects of CUR play a critical role in preventing liver damage. This study confirms that CUR is effective in inhibiting ALT, AST, and ALP enzyme activities. These findings indicate that CUR can be used as a potential supportive therapy to alleviate hepatotoxicity caused by drugs in TB treatment. More comprehensive clinical studies are necessary to confirm these positive effects of curcumin and optimize its dosage.

Conclusion

The findings of this study show that CUR provides significant protective effects against INH+RIF-induced hepatotoxicity. It was observed that liver enzyme activities decreased significantly in the CUR-administered groups. In this context, this study makes a significant contribution to the literature. It is recommended that studies evaluating different doses and durations be continued in order to increase the safety of the application of these results. In conclusion, the use of CUR to reduce liver damage in TB treatment may increase the effectiveness of treatment regimens and improve patient outcomes.

Acknowledgement

None.

Conflict of Interest

None.

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