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Pathological Changes in Liver Function Induced by Gold Nanoparticles and Protective Role of *Tinospora Cordifolia*: *In Vivo*

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Abstract

Hepatic diseases are a major concern worldwide. Gold nanoparticles (GNPs) are a tremendous scientific achievement of nanotechnology and are used in various fields of medicine. In this study, (24) healthy Albino rats have been divided into 4 groups, 6 animals for each. The control animals included rats without treatment, while the GNPs group rats received 1100 µg/kg of GNPs. In the GNPs +TC group, rats were co-administered with a combination of GNPs at a 1100 µg/kg dose with *Tinospora cordifolia* at a 400 mg/kg dose. The TC group animals were treated with 400 mg/kg of *T. cordifolia*. The levels of serum hepatic parameters including Alanine amino transferase (ALT), Aspartate amino transferase (AST) and Alkaline phosphatase (ALP) have been estimated to detect liver function disorders. Rats treated with GNPs showed significant increase ($P<0.05$) in plasma enzyme levels in comparison to control group. Then, co-administration of *T. cordifolia* along with GNPs exerted a significant recovery effect in liver function disorders. Thus, these results demonstrated that *T. cordifolia* has shown a defensive impact against GNPs induced biochemical changes in liver function of rats.

Keywords: *Hepatic enzymes ,gold nanoparticles, , T. cordifolia.*

Introduction

In modern medicine, nanotechnology and nanoparticles have been shown to be some of indispensable tools for disease treatment and monitoring[1]. At the micro scale size, the Nano materials (NMs) have a much larger surface area than same mass of materials[3], because of their very small sizes (<100 nm)[2]. Because of the increased applications on nanomaterials, concerns have been elevated on their toxicity towards human health[4]. Owing to their high biocompatibility and stability in comparison with other nanomaterials, gold nanoparticles (GNPs) are considered top candidates for biomedical applications[5,6]. More recently, a modern science branch known as nanotoxicology emerged in order to explain the possible effects of nanoparticles and related parameters affecting nanomaterial cytotoxicity[7]. From the toxicologic biomedical point of view, the toxicity of nanoparticles demonstrates the reaction between their natural effects and physico-chemical properties[8,9]. Several available studies reported that GNPs are accumulated in different rat organs[10]. Liver is a main filter in the mammalian's body, which sets along with the circulatory system and captures the circulating exogenous NPs, regardless of their entry route to the body and their physical and chemical structures[11]. Former *in vivo* studies showed that various NMPs types tend to settle down in the liver with severe toxic impacts[,13].

Till now, herbs are used mainly in the treatment in several developing country for primary health care due to their excellent culturing compatibility and acceptance in the human body as well as their lesser side effects[14].

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Tinospora cordifolia is a popular medicinal plant used in many traditional medical fields for curing different diseases[15]. It belongs to the Menispermaceae family [16], and has many therapeutic properties such as hepatoprotective, antidiabetic, anticancer and antioxidant[18]. The present study aims to confirm the deleterious effect of gold nanoparticles on liver biochemical parameters and to assess the protection role of *T. cordifolia* against pathological changes induced by GNPs in the hepatic biomarkers.

Materials & methods

Chemicals

The gold Nano particles were provided by US Research Nanomaterials, Inc. Company (Houston, TX, USA). CAS NO: 7440-57-5, Particle Average Size: 15 nm, spherical, Purity: 99.99 %. GNPs exhibit higher electron densities and are of high homogeneous size & shape. *T.Cordifolia* was obtained from Pure Guduchi Capsules, Plant-Based Supplement, DR WAKDE'S Natural Health Care, London, UK, and dissolved in normal saline.

Animals and treatment groups

In this study, (24) adult male albino rats weighing (200- 215gm) were used. They were provided from the Lab. Animal Centres. The animals have been housed in humidity & temperature controlled ventilated cages on 12 hour light–12 hour dark cycles, with free access to standard lab. water & diet. The animals have been divided randomly into 4 groups (6 animals in each group) and assigned as follows:

- The control group: Healthy rats, without treatment.
- GNPs group: Rats received GNPs at dose of 1100 µg/ kg bw [19].
- (GNPs+TC) group: Rats were co-administered with a combination of gold nanoparticles (1100 µg/kg bw) with *T. cordifolia* at 400 mg/kg bw [20].
- IV (TC) group: Rats which have taken *T. cordifolia* at 400 mg/kg dose alone.

The experimental rats were orally administered all treatments for 42 days, with the aid of gavage tubes. After the experimental period, the rats were sacrificed, blood was collected by cardiac puncture. Blood samples were collected in tubes containing no anticoagulant for biochemical tests.

Biochemical analyses

Rats were euthanized and blood was collected through cardiac puncture. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total protein were estimated according to the instructions of the manufacturer (Roche company).

Statistical analysis

All results have been performed as mean (±) Standard Deviation SD (n=6). All parameters for inter-group variations have been analyzed using the one way analysis of variances (ANOVA) followed by Duncan analysis. The differences between animal groups were regarded as statistically significant at ($p<0.05$).

Results

Results of the experimental groups are presented in figure (1). The rats treated with GNPs showed higher levels of liver enzymes ALT, ALP and AST when compared with the control group animals. The results also demonstrated no effective alteration in all biochemical hepatic parameters in the animals with co-administration of *T.Cordifolia* extract when compared with the GNPs treated rats ($p<0.05$). These results assume that liver could be slightly damaged with the GNP administration, and that liver's function has been immediately affected by GNP.

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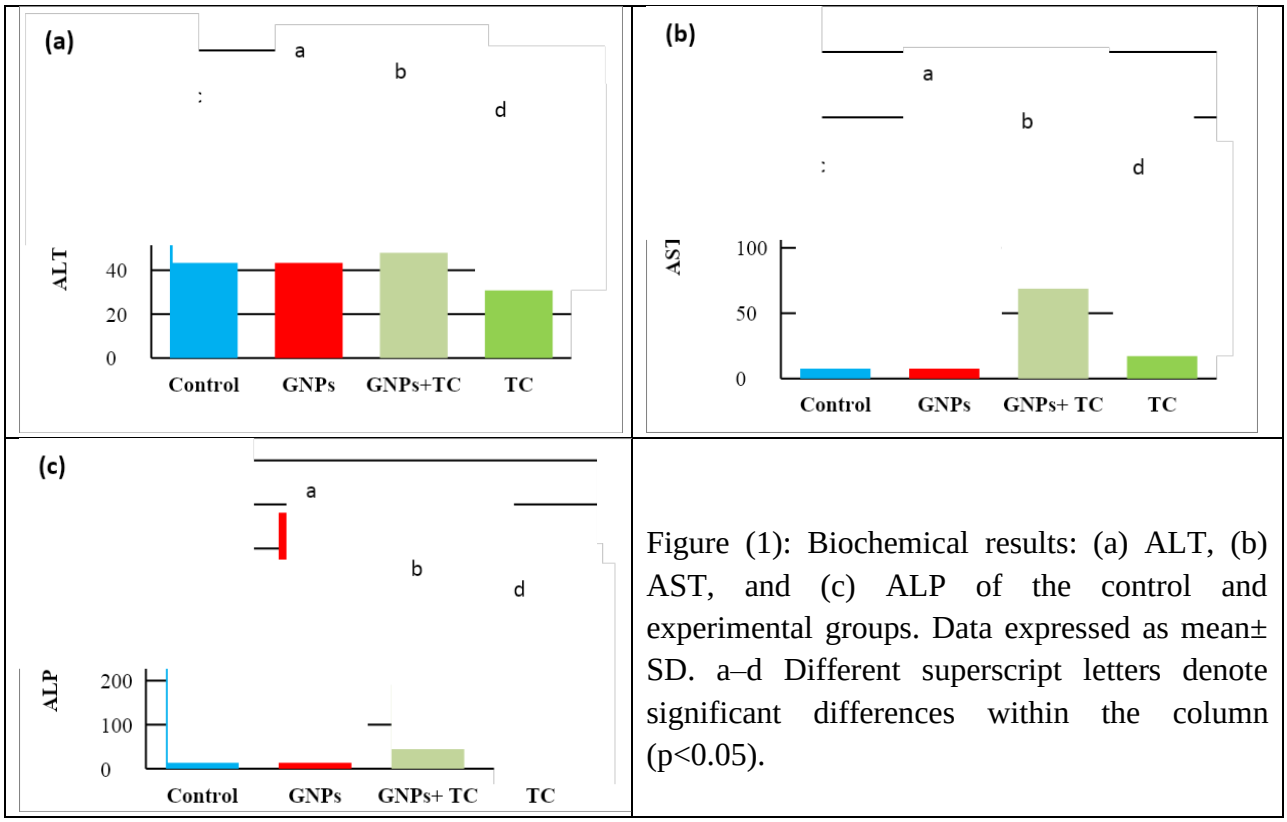

Figure (1): Biochemical results: (a) ALT, (b) AST, and (c) ALP of the control and experimental groups. Data expressed as mean± SD. a–d Different superscript letters denote significant differences within the column ($p<0.05$).

Discussion

The liver functions as a biological barrier by elimination and isolation of different exogenous compounds through phagocytosis. Hepatic diseases very often occur as liver is a primary detoxification organ in the body. Toxic chemicals mainly cause liver disorders. Since nanomaterials are highly accumulated in the liver than other organs, liver is susceptible to metal nanoparticles (MNPs)[21,22]. The MNPs toxicity is basically because of the special chemical and physical properties such as size, surface chemical modification and ion release[23]. The organ distribution of gold Nano particles depends upon size, whereas small gold Nano particles (5–15 nm) size are more widely distributed in the organs than that larger gold nanoparticle of (50–100 nm) [24-27]. The distribution of nanoparticles in the liver can lead to impair its function[28]. Former studies on toxicity demonstrated that gold nanoparticle following oral administration had strong gastro-intestinal persorption impacts. The clinical-chemical body fluid analysis may detect toxic effects on the liver [30].

A significant increase in serum alanine aminotransferase (ALT), alkaline phosphatase (ALP) and aspartate aminotransferase (AST) indicates liver injury. Liver enzyme levels significantly indicate a damage or a destruction in liver cells. Increased or altered levels of these enzymes are correlated with cell content leakage & abnormal functions of that part of liver's cellular membrane. Integrity and stability of hepatic cell membranes is essential for effective liver functioning. Because of their physio-chemical characteristics, Nano particles will definitely disrupt liver's stability and proper functioning[31-34].

These hepatic parameters were shown to be significantly increased in the GNPs + *T.cordifolia* group when they were compared to the GNPs group in our study. This could be attributed to the phytochemical components in the extract as it contains alkaloids, glycosides, sesquiterpenoids, lactones and steroids. In addition, the stem and leaf extracts of *T. cordifolia* were found to have hepato protective impact on male Albino rats against the toxicity induced by Lead Nitrate. The oral plant extract dose in a similar way prevented liver damage induced

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by Lead Nitrate [35,36]. Our results seem to coincide with this claim, and restoration of these functions could entail the existence of the extract of *T. cordifolia* .

Conclusions

Results in this study revealed that gold nanoparticles possess a toxic effect on liver biochemical functional markers. *T.Cordifolia* extracts given to rats improved hepatic enzyme levels in experimental rats. It was effective to protect the liver pathological changes induced by gold nanoparticles. However, there is a need for future studies to prove *T. Cordifolia* as an effective protective agent against liver dysfunction induced by metal nanoparticles.

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Ethical Clearance : No need

Source of Funding: None

Conflict of Interest: The authors have declared no conflict of interest

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