JSIANE : Vol. 3, Issue 4, 2023, Page 48-50 ISSN (Online) 2583-2093

Journal of Science Innovations and Nature of Earth

Journal homepage : www.jsiane.com

PROTECTIVE EFFECT OF *TRIBULUS TERRESTRIS* ON HEPATO-BIOCHEMICAL PARAMETERS OF ALBINO RAT AFTER TREATMENT WITH DRUG CYPROTERONE ACETATE

[1]Ajay Pratap Singh, [1]P.K. Singh and [2]Harendra Nath Sharma*

[1]Department of Zoology, School of Life Science, Khandari campus, Dr. B.R. Ambedkar University, Agra

*[2]Department of Zoology, S.V. College, Aligarh

Corresponding Author E-mail: ajaypratap1986@gmail.com

https://doi.org/10.59436/76z09z70

Abstract

The study investigates the hepatoprotective effects of *Tribulus terrestris* on albino rats subjected to cyproterone acetate, drug known for their hepatotoxicity. The experiment involved the administration of this drug to induce liver damage, followed by treatment with *Tribulus terrestris* extract. Hepato-biochemical parameters, including serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were monitored to assess liver function and damage. Results showed a significant elevation in ALT, AST and ALP levels in rats treated with cyproterone acetate, indicating liver damage. However, co-administration of *Tribulus terrestris* extract resulted in a marked reduction in these biochemical parameters, suggesting a protective effect on liver function. The study concludes that *Tribulus terrestris* exhibits substantial hepatoprotective and antioxidant effects, potentially mitigating the hepatotoxicity induced by cyproterone acetate. These findings suggest that *Tribulus terrestris* could be considered as a supplementary therapeutic agent to protect against drug-induced liver damage.

Keywords : Tribulus terrestris, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), Cyproterone Acetate,

Received 12.09.2023 **Revised 18.10.2023** **Accepted 24.12.2023**

Introduction

Drugs can have a wide range of side effects on the human body, varying in severity from mild to life-threatening. Common side effects include gastrointestinal issues like nausea, vomiting, and diarrhea; central nervous system effects such as dizziness, headaches, and drowsiness; and allergic reactions, including rashes and anaphylaxis. Long-term use of certain medications can lead to organ damage, such as liver or kidney toxicity, and cardiovascular problems like hypertension and arrhythmias (Stege *et al.* 2000). Psychological effects, including mood swings and depression, are also possible. Monitoring and managing these side effects are crucial for maintaining patient safety and ensuring the therapeutic efficacy of the medications. Cyproterone acetate is used primarily for treating androgen-dependent conditions such as prostate cancer, severe acne, and hypersexuality. Side effects include liver toxicity, fatigue, weight gain, mood changes, and a potential increase in the risk of blood clots (Vejdani *et al.* 2013). Long-term use requires careful monitoring of liver function. *Tribulus terrestris* is known for its protective effects against liver damage, primarily due to its antioxidant properties. It reduces oxidative stress, lowers liver enzyme levels, and improves overall liver function (Goyal *et al.* 2014). Additionally, it may enhance immune response and mitigate inflammation, contributing to its potential as a hepatoprotective agent (Kazemi *et al.* 2018).

Keeping these points in view, the present study is designed to investigate protective effect of *Tribulus terrestris* on side effects of above said drugs on the basis of hepato-biochemical parameters including serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP).

Material and Methods

The male albino rats (Rattus norvegicus) of the wistar strain, weighing around 120±25g, were acquired from the albino rat colony produced at the animal house of the Zoology Department, School of Life Sciences, Khandari Campus, Agra. These rats were employed for experimental purposes. The albino rats were kept in polypropylene cages with dimensions of 45x25x15cm and were maintained at a regulated temperature of 25±20C, humidity of 65±10%, and a perfect circadian rhythm. The animals that had adapted to the environment were separated into several groups according to the experimental procedure for durations of 7, 15, 30, 45, and 60 days. These groups included a control group, a group treated with Cyproterone acetate, a group treated with Cyproterone acetate and Tribulus terrestris, and a group that was kept in separate cages. The subjects were provided with a regular diet, namely Goldmohar brand feed, and had unrestricted access to water.

The drug was given to albino rats in laboratory in form of solution by gavage tube. The dose of Cyproterone acetate was 0.30mg/kg b.wt. The plant extract was prepared in laboratory. The selected dose of *Tribulus terrestris* was 20mg/kg body weight. All treatments of honey were given orally using a syringe and a bent tip canula. The doses were given for 7, 15, 30, 45 and 60 days respectively. The albino rats of all the groups were sacrificed under light anesthesia.

The biochemical parameters were estimated through standard procedures and protocols viz. AST, ALT through Reitman

and Frankel method; and Alkaline phosphatase through Kind and King method. All the data were subjected to statistical analysis through software KY plot version 3.0.

Results and Discussion

The results show significant changes with rice straw smoke exposure from control. The toxic effect in liver is modulated by honey supplementation as shown in Tables and graphs below-

Table-1

Protective Effect of *Tribulus terrestris* on AST after Cyproterone acetate drus treatment for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	104.50±4.28	104.50±4.28	104.50±4.28	104.50±4.28	104.50±4.28
Cyproterone acetate	75.60±2.10***	75.1±2.50***	71.72±1.92***	71.51±1.76***	70.42±1.65***
Cyproterone acetate+*Tribulus terrestris*	105.50±1.90**	104.0±1.60***	105.00±2.10**	104.50±2.00**	103.10±1.40**

NS- Non-significant (p>0.05), *- Significant (p<0.05), **- Highly Significant (p<0.01), ***- Very Highly Significant (p<0.001)

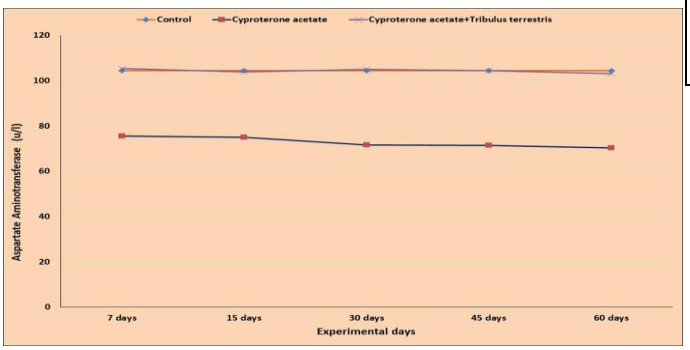

Fig-1

Protective Effect of *Tribulus terrestris* on AST after Cyproterone acetate drug treatment for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	20.5±1.11	20.5±1.11	20.5±1.11	20.5±1.11	20.5±1.11
Cyproterone acetate	16.50±1.69**	16.40±1.50**	16.99±1.10**	15.10±1.05**	14.50±0.99***
Cyproterone acetate+*Tribulus terrestris*	22.01±0.90**	23.50±0.80**	22.99±0.28**	21.06±0.92**	20.21±0.30***

NS- Non-significant (p>0.05), *- Significant (p<0.05), **- Highly Significant (p<0.01), ***- Very Highly Significant (p<0.001)

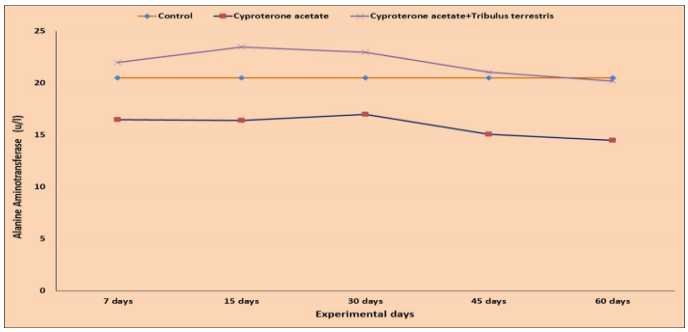

Fig-2

Protective Effect of *Tribulus terrestris* on ALT after Cyproterone acetate drug treatment for 7, 15, 30, 45 and 60 days in Albino rat

Table-3

Protective Effect of *Tribulus terrestris* on ALP after Cyproterone acetate drug treatment for 7, 15, 30, 45 and 60 days in Albino rat

Experimental Sets	7 days (Mean±S.Em.)	15 days (Mean±S.Em.)	30 days (Mean±S.Em.)	45 days (Mean±S.Em.)	60 days (Mean±S.Em.)
Control	135.40±3.30	135.40±3.30	135.40±3.30	135.40±3.30	135.40±3.30
Cyproterone acetate	122.30±2.72*	121.60±2.51**	118.40±1.80***	115.31±0.55***	114.0±0.94***
Cyproterone acetate+*Tribulus terrestris*	130.20±1.73*	134.23±1.30**	131.50±0.81***	133.20±1.05***	134.50±1.50****

NS- Non-significant (p>0.05), *- Significant (p<0.05), **- Highly Significant (p<0.01), ***- Very Highly Significant (p<0.001)

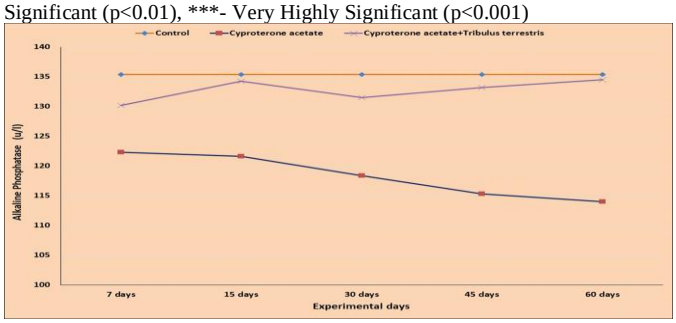

Fig-3

Protective Effect of *Tribulus terrestris* on ALP after Cyproterone acetate drug treatment for 7, 15, 30, 45 and 60 days in Albino rat

Drugs used for prostate problems, such as benign prostatic hyperplasia (BPH) and prostate cancer, are vital for improving patients' quality of life and managing disease progression. Medications like alpha-blockers (e.g., tamsulosin) and 5-alpha-reductase inhibitors (e.g., finasteride) alleviate urinary symptoms by reducing prostate size and relaxing bladder muscles. For prostate cancer, anti-androgens (e.g., flutamide) and hormone therapy help slow cancer growth by inhibiting testosterone effects. These treatments significantly reduce symptoms, prevent complications like urinary retention and kidney damage, and enhance the efficacy of surgical interventions. Careful monitoring is crucial to manage side effects and ensure optimal therapeutic outcomes. Cyproterone acetate works by blocking androgen receptors and inhibiting the action of male hormones (androgens) such as testosterone (Stege *et al.* 2000). This reduces the growth and activity of androgen-dependent cells, which is beneficial in conditions like

prostate cancer and severe acne. Additionally, it suppresses gonadotropin release from the pituitary gland, lowering testosterone production (Vejdani *et al.* 2013). This dual action effectively diminishes androgen effects, alleviating symptoms and slowing disease progression.

Cyproterone acetate may induce liver toxicity, presenting as elevated liver enzymes, hepatomegaly, and cholestatic jaundice. Symptoms include abdominal pain, nausea, and yellowing of the skin. Long-term use can lead to severe liver damage or failure. Regular liver function tests are essential to monitor and manage potential hepatotoxic effects (Strumberg *et al.* 2002). *Tribulus terrestris* exhibits a protective effect on the liver due to its antioxidant and anti-inflammatory properties. It scavenges free radicals, reducing oxidative stress and lipid peroxidation in liver cells (Tajmohammadi *et al.* 2019). Additionally, it enhances cellular defense mechanisms and promotes regeneration of liver tissues. Studies suggest that *Tribulus terrestris* may lower liver enzyme levels, decrease inflammatory markers, and prevent liver damage induced by toxins or drugs (Sharma *et al.* 2021). Its hepatoprotective potential makes it a promising natural remedy for mitigating liver diseases and supporting overall liver health. *Tribulus terrestris* extract acts through various mechanisms to exert its protective effects on the liver. It enhances antioxidant enzymes like superoxide dismutase and catalase, reducing oxidative stress (Chhatre *et al.* 2014). Additionally, it inhibits inflammatory pathways, decreases lipid peroxidation, and promotes liver cell regeneration. These actions collectively contribute to its hepatoprotective properties, guarding against liver damage induced by toxins or drugs and supporting overall liver health. *Tribulus terrestris* extract protects the liver by upregulating antioxidant enzymes, reducing oxidative stress, and inhibiting inflammation. It scavenges free radicals, decreases lipid peroxidation, and enhances liver cell regeneration (Oner *et al.* 2012). These actions collectively mitigate liver damage and contribute to the overall hepatoprotective effects of *Tribulus terrestris* extract.

Conclusion

From this investigation, it could be concluded that the *Tribulus terrestris* is protective in action against the drugs side effect by ameliorating its free radical nature and neutralizing ROS. This study will help the medical field to know about the side effects of steroid prostatic drugs and how to ameliorate the toxicity with *Tribulus terrestris*.

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Cite this article:
Ajay Pratap Singh, P.K. Singh and Harendra Nath Sharma*, 2023, "Protective Effect of *Tribulus terrestris* on Hepato-Biochemical Parameters of Albino Rat after Treatment with Drug Cyproterone Acetate" ***Journal of Science Innovations and Nature of Earth***, Vol. 3(4), page-48-50
https://doi.org/10.59436/76z09z70