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AMELIORATIVE EFFECT OF *TRIBULUS TERRESTRIS* ON LIVER BIOCHEMICAL PARAMETERS IN ALBINO RAT AFTER TREATMENT WITH DRUG FLUTAMIDE

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Abstract

Chemicals that lessen the harmful effects of hepatotoxic substances on the liver are known as hepatoprotective agents. While some researchers thought of strengthening, tonic, and fortifying. Tribulus terrestris, a leafy herb used in folk medicine, has shown hepatoprotective effects in several studies. The experiment involved the administration of 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 flutamide. 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 clearly states that *Tribulus terrestris* extract exhibits hepatoprotective and effect, mitigating the hepatotoxicity induced by flutamide. These findings suggest that *Tribulus terrestris* could be considered as a supplementary agent to protect against drug-induced liver damage during long term treatments.

Keywords : Flutamide,-*Tribulus terrestris*, ALT, AST, ALP, Albino Rat, hepatotoxic

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Introduction

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. 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. Monitoring and managing these side effects are crucial for maintaining patient safety and ensuring the therapeutic efficacy of the medications. Flutamide is used to treat prostate cancer by blocking androgen receptors. Common side effects include gastrointestinal distress, liver toxicity, gynecomastia, and hot flashes (Saberi-Karimian et al. 2019). It can also cause fatigue, diarrhea, and an increased risk of cardiovascular issues. Regular liver function monitoring is essential due to potential hepatotoxicity (Žaja et al. 2015). *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 drug on the basis of liver biochemical parameters including serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP).

Material and Methods

The experimental goal involved using male albino rats (Rattus norvegicus) of the wistar strain, which were produced at the anima house of the Zoology Department at the School of Life Sciences in Agra. The rats weighed between 120±25g. The albino rats were kept under tightly regulated conditions, including a temperature of 25±20C, humidity of 65±10%, and a correct circadian rhythm, in polypropylene cages that measured 45x25x15cm. Following the methodology, the acclimated animals were split into several groups and kept in separate cages for7,15,30,45, and 60 days of the experiment. These groups included a control set, a set treated with flutamide, and a set treated with flutamide plus Tribulus terrestris. Their normal diet consisted of Goldmohar brand feed and water available whenever they needed it.

The drugs were given to albino rats in laboratory in form of solution by gavage tube. The dose of Flutamide was 1.125mg/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 Flutamide 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	104.50±4.28	104.50±4.28	104.50±4.28	104.50±4.28	104.50±4.28
Flutamide	77.20±1.15***	77.14±1.50***	76.70±1.56***	76.00±1.99***	74.90±1.65***
Flutamide +*Tribulus terrestris*	106.60±2.96**	106.0±1.80***	107.60±4.55**	107.50±3.50**	105.00±2.43**

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

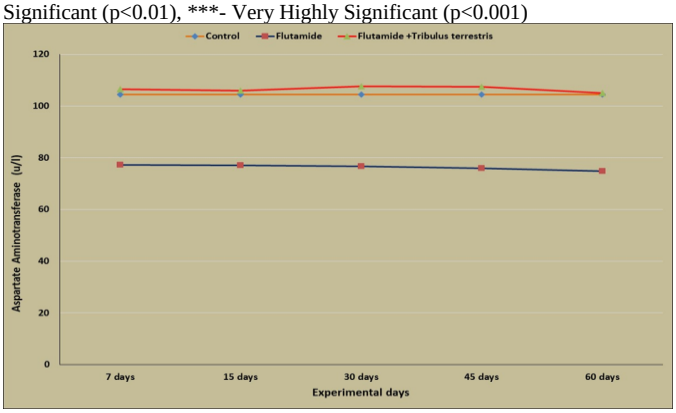

Fig-1

Protective Effect of *Tribulus terrestris* on AST after Flutamide drugstreatment for 7, 15, 30, 45 and 60 days in Albino rat

Table-2

Protective Effect of *Tribulus terrestris* on ALT after Flutamide 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
Flutamide	14.60±0.99***	14.40±0.50***	13.50±0.10****	13.10±0.75****	12.50±0.67****
Flutamide +*Tribulus terrestris*	23.05±0.53**	23.06±0.61**	22.40±0.76***	22.05±0.43***	20.05±0.56***

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

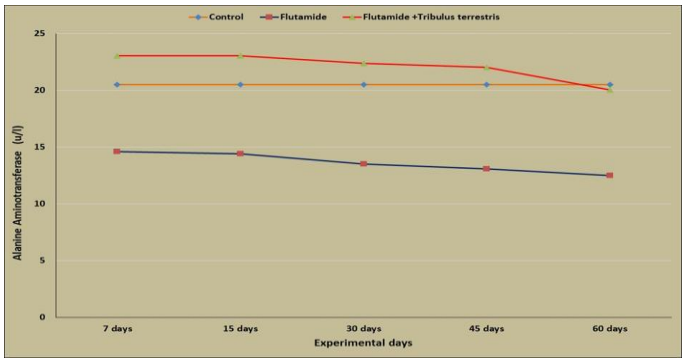

Fig-2

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

Table-3

Protective Effect of *Tribulus terrestris* on ALP after Flutamide 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
Flutamide	121.10±1.70**	120.20±1.50**	116.10±0.80****	112.30±0.50****	110.2±0.90****
Flutamide +*Tribulus terrestris*	131.50±1.70*	132.20±1.35**	132.50±0.85***	133.80±1.05***	135.50±1.18****

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

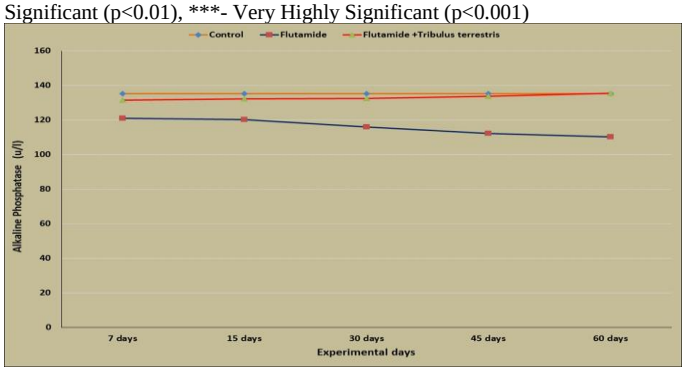

Fig-3

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

Tribulus terrestris extract has protective effects against non-alcoholic toxicity to liver by changing biomarkers of liver tissue results in normalization of parameters as shown in tables and graphs. 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. Flutamide operates as a non-steroidal anti-androgen by competitively inhibiting androgen receptors. It prevents testosterone and dihydrotestosterone (DHT) from

binding to these receptors, thereby blocking androgen effects in tissues such as the prostate. This action inhibits the growth of androgen-dependent prostate cancer cells, reducing tumor progression and alleviating related symptoms, making it an effective treatment option in prostate cancer management. Flutamide can cause significant liver toxicity, leading to elevated liver enzymes, jaundice, and, in severe cases, hepatic failure (Žaja et al. 2015). Symptoms include abdominal pain, fatigue, and dark urine. Due to these potential risks, regular liver function monitoring is crucial during treatment to detect and manage liver-related side effects promptly (Saberi-Karimian et al. 2019).

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). Additionally, it enhances cellular defense mechanisms and promotes regeneration of liver tissues. 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). *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 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. These actions collectively mitigate liver damage and contribute to the overall hepatoprotective effects of *Tribulus terrestris* extract. It scavenges free radicals, decreases lipid peroxidation, and enhances liver cell regeneration (Oner et al. 2012).

Conclusion

From this investigation, it could be concluded that the *Tribulus terrestris* is protective in action against the drug 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 non steroid prostatic drugs and how to ameliorate the toxicity with Tribulus terrestris.

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