Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Suppl 3, 2012

Research Article

COMPARATIVE HEPATOPROTECTIVE ACTIVITY OF LIV-52 AND SILYMARINE AGAINST HEPATOTOXICITY INDUCED BY ANTIANDROGEN –BICALUTAMIDE IN RATS

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Received: 29 Dec 2011, Revised and Accepted: 15 Mar 2012

ABSTRACT

Bicalutamide is a nonsteroidal antiandrogenic drug used in treatment of prostate cancer. Bicalutamide is extensively metabolized by liver and reported to have hepatotoxicity. The present study was conducted to compare the hepatoprotective activity of two formulations, Liv-52 and Silymarine against Bicaluatmide induced hepatotoxicity. The serum enzyme level of Glutamate Pyruvate Transaminase (SGPT), Glutamate Oxaloacetate Transaminase (SGOT) and histopathological examination of liver was done after treating the animals for fourteen days. The animals treated with Liv-52 shows a significant decrease in SGPT level and no significant changes in histology of liver. It was concluded from study that Liv-52 has more significant hepatoprotective activity against Bicalutamide in rats in comparison to Silymarine.

Keywords: Bicalutamide, Hepatoprotective, Liv -52, Silymarine, SGPT, SGOT.

INTRODUCTION

Liver play a major role in detoxification and excretion of many endogenous and exogenous compounds. Any type of injury (due to systemic drug, food preservatives, agrochemicals and addiction to alcohol) or impairment of its function may lead to many complications in one's health. There is a no rational therapy available for liver disorders and it is a still challenge to modern medicine[1]. Hepatic injury can be life threatening when the entirely or most of the liver is exposed to any hepatotoxin, including Bicalutamide[2].

Bicalutamide is a nonsteroidal antiandrogenic drug used in treatment of prostate cancer[3]. The most common adverse effects of Bicalutamide are induced by its pharmacological properties of competitive androgen receptor blockade include gynacomastia, hot flashes, fatigue and decreased libido, increased liver function test are seen with Bicalutamide therapy. Regular liver function test are advised during treatment of prostate cancer by anti androgen like Bicalutamide [4, 5].

Present study was conducted to compare the hepatoprotective activity of two marketed formulations Liv-52 and Silymarine against Bicalutamide induced hepatotoxicity in rats.

MATERIALS AND METHODS

Animal

Wister strain male rat having a weight range of 150-180 gm were used for the experiment.

The animals were well housed in polypropylene cage under hygiene condition and maintained at 28 ± 2^{o}C temp. The animals were allowed to have food and water adding *ad libitum*. The animal institutional ethical committee approved the experimental protocol. (Proposal no.416/160/1999/CPCSEA)

Chemicals and drugs

Liv-52 syrup (Himalaya drug company) and Silymarine (Silybon, Micro Labs Limited) were used for hepatoprotective activity and Bicalutamine (Cipla Pharmaceuticals Pvt. Limited) was used to induce hepatotoxicity.

Experimental design

Animals were divided into four groups (n= 6)

Group I (N): Control vehicle i.e. distilled water

Group II (B): Bicalutamide 25mg/kg/day *p.o*[6]

Group III (BL): Bicalutamide 25mg/kg/day and Liv 52 2ml/100gm/day *p.o*[7]

GroupIV (BS): Bicalutamide 25mg/kg/day and Silymarine 50mg/kg/day *p.o*[8 9].

The entire animals were treated for 14 days.

Biochemical estimation

The blood samples were collected on 0th day and on 15th day (24 hrs after last dose) for biochemical study. The blood was obtained from all the animals by puncturing the retro-orbital plexus. The blood samples were allowed to clot for 30 minutes at room temperature. Serum was separated by centrifugation at 2500 rpm for 15 minutes at 30^{0}C and utilized for estimation of various biochemical parameters mainly SGOT and SGPT[10, 11, 12].

Histopathological examination

All the animals were sacrificed on 15th day and livers were removed, washed with saline. The liver pieces were preserved in 10 % formalin solution for histopathological study. The sections were approximately 4-6 micron in thickness. They were stained with hematoxylene and eosin and photographed [13, 14].

Statistical Analysis

The data were expressed as mean ± SD; for obtaining this data biochemical and physiological parameters were statistically analyzed using one way ANOVA followed Dunnet test. For comparison with the control group and Bicalutamide treated group, P< 0.05 set at the minimum level of significance.

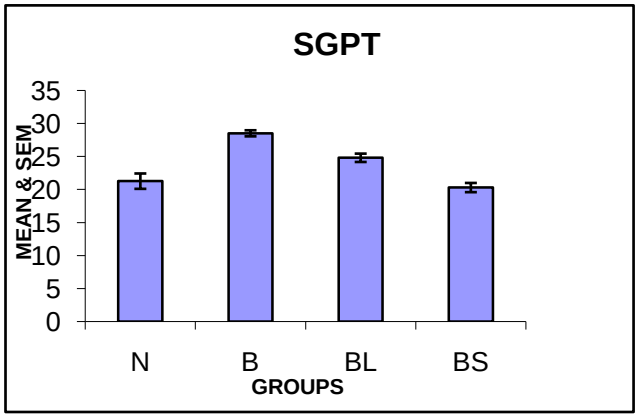
Table 1: Effect of Liv-52 and Silymarine on Bicalutamide induced hepatotoxicity

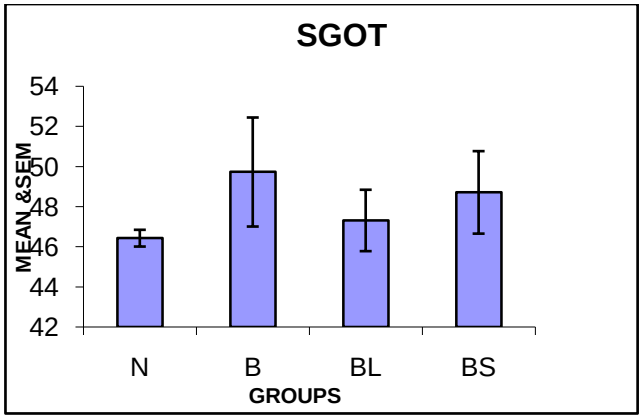
	SGOT(IU/L)	SGPT (IU/L)
Group I	21.26±1.163	46.40±0.4177
Group II	28.51±0.4600	49.33 ±2.719
Group III	24.8±1.550*	47.317±1.531
Group IV	20.29±0.6981	48.717±2.057

Group Biochemical parameters mean ±SEM; *Significant (p <0.05) reduction compare to Bicalutamide

Histopathology of liver

Liver sections of 4-6 micron in thickness were stained with hematoxylin and eosin and observed under H & E x100 resolution of microscope for histopathological changes and photographed.





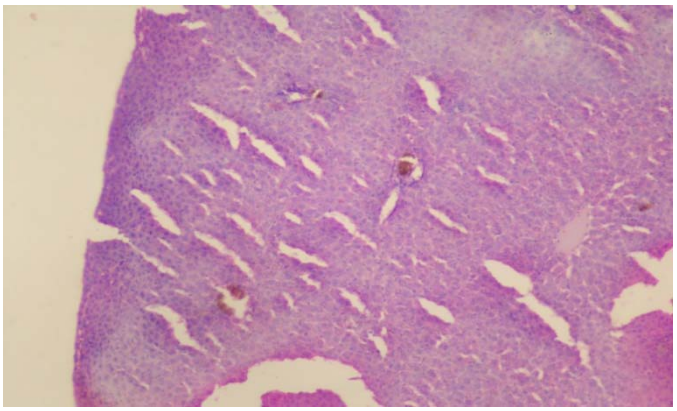


Fig. 1: Control group: No specific change.

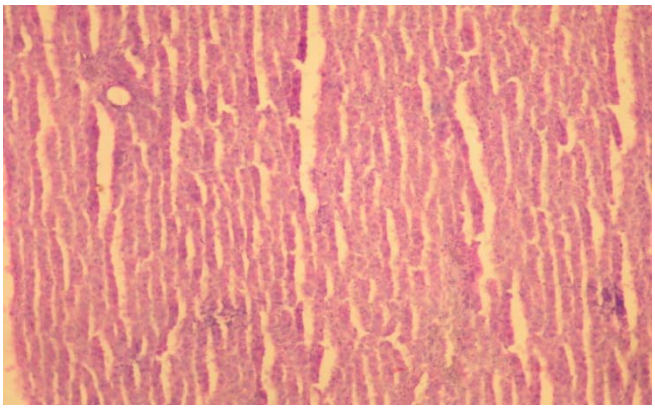


Fig. 2: Bicalutamide-lymphocyte sinusoidal inflammation, Kupffer cell hyperplasic, congested- dilated blood vessels, non necrosis fibrosis.

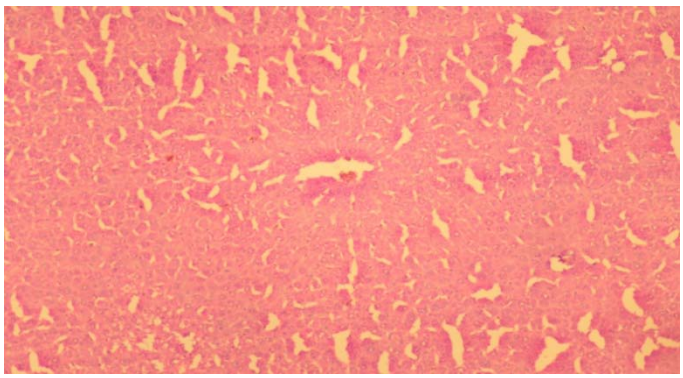


Fig. 3: Bicalutamide with LIV52- Non-specific changes.

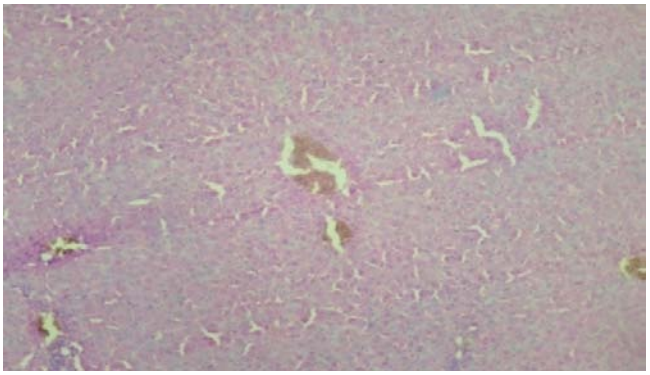


Fig.4: Biclutamide with Silymarin- Focal lymphocyte, Kupffer cell hyperplasic, some congested- dilated blood vessels.

RESULTS AND DISCUSSION

The results of Bicalutamide induced hepatotoxicity are shown in table 1. Bicalutamide intoxication in normal rat significantly elevated the serum levels of SGOT and SGPT. The rats treated with Liv-52 and Silymarine showed reduction in all biochemical parameters.

In histopathological examination of liver sections of control group, (Fig. 1) no specific change was obverse. In the Bicalutamide intoxicated group (Fig. 2), lymphocyte sinusoidal inflammation, Kupffer cell hyperplasic, congested- dilated blood vessels non necrosis fibrosis. In the histopathological profile of Liv-52 treated group (Fig.3), no specific change. In the histopathological profile of Silymarine (Fig. 4), Focal lymphocyte, Kupffer cell hyperplasic, some congested- dilated blood vessels[15, 16, 17].

Liv-52 formulation was able to control this necrotic change that was comparable to that of Silymarine. Thus biochemical observation co-relates well with the histopathology results of the liver samples. These above observations confirmed that the potent hepatoprotective activity of liv52 than that of Silymarine.

In this study rats treated with a repeated dose of Bicalutamide to develop hepatic damage which was observed from a substantial increase in the activity of serum like SGOT and SGPT. Histipathological study is indicative of cellular leakage and loss of the functional integrity of cell membrane in liver.

CONCLUSION

Overall, the result of the present study indicates that Liv-52 demonstrate a significant hepatoprotective activity against Bicalutamide induced hepatotoxicity in rats than silymarin.

ACKNOWLEDGMENT

The authors are thankful to Prof. (Dr.) Madhavan Nirmal, Department of Oral Pathology and Microbiology, Faculty of Dentistry, RMMCH, Annamalai University, Chidambaram, and Prof. (Dr.) Kotheesaravam, Mahatma Gandhi medical college Pondicherry, whose support is significant for the work.

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