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HEPATOPROTECTIVE EFFICACY OF OCIMUM CANUM SIMS. ON ISONIAZID INDUCED HEPATOTOXICITY

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ABSTRACT

Liver is the vital organ involved in metabolism and independently involved in many biochemical functions. Liver is the key organ and the principal site where the metabolism of carbohydrate, proteins, lipids and detoxification take place. It is a fifth most common cause of death. The manifestation of drug induced hepatotoxicity is highly variable ranging from asymptomatic elevation of liver enzymes to fulminant hepatic failure. Ocimum canum Sims a large succulent herb with aromatic leaves is known to possess carminative, diaphoretic and stimulant properties. The present study was designed to evaluate the hepatoprotective effect of the aqueous extract of Ocimum canum Sims on isoniazid induced hepatotoxic rats. Wistar strain of albino rats were divided into 6 groups with 6 rats each, group1served as normal control, group 2 served as disease control (54 mg of isoniazid /kg BW p.o once daily for a period of 21 days, groups 3,4&5 were induced with isoniazid and treated with aqueous extract of Ocimum canum Sims. 100, 200, 300mg/kg bw orally for 21 days, group 6 were induced isoniazid and treated with std drug silymarin (50mg/kg BW for 21 days orally). After the experimental period Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma Glutamyl transferase (GGT), Triglycerides, Bilirubin, Protein, Cholesterol, HDL, LDL, VLDL, liver glycogen, antioxidant status were analysed. Disease control rats showed increased levels of ALT, AST, ALP, Bilirubin, LPO and the levels of GSH, SOD, Protein, GP_x, Cholesterol, Glycogen, triglycerides were significantly decreased when compared to normal control rats. The administration of aqueous extract of

Ocimum canum Sims, lead to the restoration of the normal functioning of the liver. The above results reveal the hepatoprotective potentials of Ocimum canum Sims.

KEYWORDS: Hepatic failure, Ocimum canum Sims, Isoniazid, Silymarin, Hepatoprotective.

INTRODUCTION

Liver is a vital organ regulating important metabolic functions and is the second largest organ.[1] It is involved in all the biochemical pathways including growth, immunity, nutrient supply, energy provision and reproduction.[2] It detoxifies the poisonous substances in the body by transforming and removing toxins and wastes.[3] It is the first organ to be exposed to the damaging effects of the newly formed toxic substance during metabolism.[4]

Liver diseases are considered as fatal and life threatening. Liver diseases are due to infection or exposure of liver to various toxic substances such as drugs or alcohol. Liver diseases are considered to be serious health disorders. The liver has one of the highest value of importance for the systemic detoxification of endogenous and exogenous substances.[5]

Isoniazid has been used in the treatment of tuberculosis for a long time. Isoniazid metabolism produces reactive metabolites that bind and damage cellular macromolecules in the liver. This latter interpretation is supported by observations that drugs induce cytochrome p450 levels (including rifampicin which often is prescribed together with isoniazid) appear to increase the risk of isoniazid toxicity.[6]

Modern medicine does not have suitable answers for many conditions such as liver disorders, asthma, cardiovascular disorders etc.,[7] Herbal drugs play a role in the management of various liver disorders most of which speed up the natural healing processes of the liver.[8] So recently there has been a large volume of work aimed at scientific validation of efficacy of herbal drugs used in the traditional medicine.[7] The present investigation focuses on the evaluation of the protective effect of Ocimum canum Sims against isoniazid inducued hepatotoxicity in albino rats.

MATERIALS AND METHODS

Collection of plant material

The plants were collected from in and around Trichy and identified with the help of Flora of Presidency of Madras and authenticated with the voucher specimen deposited at the Rapinat Herbarium, Dept of Botany, St Joseph's College, Trichy.

Preparation of aqueous extract

The aerial parts of Ocimum canum Sims was shade dried and coarsely powdered. The powder was mixed thoroughly with 6 times the volume of water and stirred continuously until the volume reduced to 1/3rd. The extract was filtered with muslin cloth. The residue was re extracted. The filtrate was mixed and evaporated in a water bath till it reached a thick consistency. The extract was stored in refrigerator till further use.

Experimental models

Wistar strains of Albino rats of both sexes weighing 150 – 200g were used for the study. Animals were housed in well ventilated cages in the CPCSEA approved animal house. The protocol was approved by the Institutional Animal Ethics Committee. The animals were fed with pelleted rat chow and water ad libitum and acclimatized to the laboratory conditions for a week before starting the experiment.

Experimental design

The animals were divided in to six groups comprising of six rats each. Hepato toxicity was induced using isoniazid at a dose of 54mg/kg bw p. o once daily for a period of 21 days. Group 1 served as normal control. Group 2 served as disease control (isoniazid at a dose of 54mg/kg bw p. o once daily for a period of 21 days)[9] Group III was induced with Isoniazid and treated with aqueous extract of Ocimum canum Sims. at a dose of 100mg/kg bw orally for 21 days orally. Group IV was induced with Isoniazid and treated with aqueous extract of Ocimum canum Sims. at a dose of 200mg/kg bw for 21 days orally. Group V was induced with Isoniazid and treated with aqueous extract of Ocimum canum Sims. at a dose of 300mg/kg bw for 21 days orally. Group VI was induced with Isoniazid and treated with silymarin 50mg/kg bw at a dose for 21 days. At the end of the experimental period the animals were sacrificed. The blood, serum and liver tissue were used for the studies. All the biochemical parameters such as Bilirubin[11] cholesterol, HDL, LDL, VLDL[12] Triglycerides[13] liver glycogen[14] Protein[15] Enzyme activity as Aspartate transaminase AST,

Alanine transaminase ALT, Alkaline phosphatase ALP, Gamma glutamyl transferase GGT[16] and antioxidant studies as GSH [17] GP_X [18] SOD [19] LPO[20] were measured.

RESULTS

Table 1: Estimation of serum enzyme markers.

Groups/ parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
SGOT	12.34 0.7	201.7±0.076*	104.3±1.22	43.9±0.64	10.31±0.7**	32.25±3.16
SGPT	41.7±0.66	312±0.99*	246.71±0.76	167.7±0.764	78.31±0.55**	75.30±3.21
ALP	597.2±0.8	997.1±0.034*	876.2±0.51	778.32±0.662**	621.52±0.77	326.61±2.10
GGT	34.2±0.301	66.9±0.4*	51.7±0.33	43.1±0.42	37.9±0.52**	30.23±4.12

Values are ± SEM, n = 6;

* When compared with normal control ; ** When compared with disease control.

The group II animals shows the elevation in serum enzyme markers. Treatment with the plant extract of Ocimum canum Sims mediated the restoration of serum marker enzyme to their normal level. The results are depicted in table 1

Table 2: Antioxidant Status in experimental animals.

Groups/ Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
LPO	2.53±0.12	5.1±0.237*	4.81±0.44	3.41±0.72	2.34±0.48**	5.21±2.12
SOD	3.01±0.02	0.87±0.66*	1.36±0.78	1.97±0.34	2.33±0.112**	1.23±0.98
GSH	44.4±0.31	39.5±0.76*	43.1±0.54	46.66±0.033**	48.1±0.011	29.12±4.12
GP_X	47±0.23	27±0.33*	30.9±0.11	40.7±0.12	46.4±0.36**	32.21±4.12

Values are ± SEM, n = 6;

* When compared with normal control; ** When compared with disease control.

Group II animals showed an increase in the level of LPO while GSH, SOD, GP_X, were decreased. After the treatment of plant drug which was restored to near normal in the plant drug treated group. The results are depicted in table 2.

Table 3: Estimation of Protein, Bilirubin and Liver glycogen.

Groups/ Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Protein	7.2±0.03	3.31±0.07	4.95±0.026	6.15±0.023*	7.5±0.052**	6.45±2.12
Bilirubin	0.98±0.045	4.1±0.56*	3.71±0.098	2.23±0.673	1.0±0.007**	1.67±2.01
Liver glycogen	30.4±0.64	14.88±0.62*	19.7±0.65	21.9±0.63**	28.27±0.57	13.45±2.21

Values are ± SEM, n = 6;

* When compared with normal control; ** When compared with disease control.

Group II animals showed an increase in the level of Bilirubin and decrease in the level of liver glycogen and protein. After the treatment of plant drug which was restored to near normal. The results are depicted in table 3

Table 4: Estimation of lipids.

Groups/ parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
VLDL	33.5±0.28	98.3±0.19*	31.4±0.26	31.8±0.29	32.9±0.39**	51.1±1.2
LDL	25.6±0.23	92.7±0.16*	73.09±0.15	55.07±0.21	28.09±0.23	62.45±2.1
HDL	44.5±0.21	24.6±0.18*	33.52±0.12	38.75±0.15	41.57±0.23**	45.2±0.98
CHO	42.0±1.63	78.2±0.67*	58.0±2.16	46.8±1.21**	45.6±1.70	42.8±1.21
TGL	150±0.10	63.1±0.27	113.95±0.29	137.75±0.16	145.82±0.16**	121.2±1.05

Values are ± SEM, n = 6;

* When compared with normal control; ** When compared with disease control.

Group II animals showed an increase in the LDL & VLDL, HDL and cholesterol level were decreased. After the treatment with plant drug the level was restored to normal. The results are depicted in table 4.

DISCUSSION

Isoniazid (isonicotinic acid hydrazide) induced hepatotoxicity is a common complication of tuberculosis therapy that ranges in severity from asymptomatic elevation of serum transaminases to hepatic failure requiring liver transplantation.[6]

The isoniazid has got hepatotoxic potential. Isoniazid metabolite hydrazine plays an important role in inducing hepatotoxicity. Isoniazid hepatotoxicity results in hepatocellular damage.[3] SGOT, SGPT and ALP are enzymes originally present in higher concentration in cytoplasm. In condition of liver damage these enzymes leak in to the blood stream and is proportional to the extent of liver damage. GGT is a sensitive marker of alcohol ingestion and certain hepatotoxic drugs. An elevation in the ALP levels along with an elevation in the GGT levels is a clear indication of a persisiting liver damage.[21]

SOD is a very effective antioxidant enzyme and responsible for catalytic breakdown of highly reactive and potentially toxic superoxide radicals to H_2O_2. H_2O_2 is further metabolized either by catalase or peroxidase.[3]

The GSH antioxidant system is involved in the neutralization of free radical species in human body. Changes in the GSH status of a biological system leads to serious consequences such as

tissue damage that may even lead to death. The increase in lipid peroxide level may be due to the excessive free radical formation and in turn results in hepatic damage. GP_x is involved in the decomposition of lipid hydro peroxides and other reactive oxygen species. GSH conjugates with all free radicals and lipid hydro peroxides to form water soluble products that can be easily excreted.[8]

Measurement of total protein is a suitable diagnostic measure for a variety of hepatic diseases. A decrease in total protein indicates massive necrosis of the liver and disturbances of liver functions.[22]

The serum lipid profile such as total cholesterol, triglycerides, LDL, HDL and VLDL were elevated while HDL level was decreased indicating deterioration in hepatic function due to the damage caused by Isoniazid administration. A number of hepatotoxic agents cause accumulation of fatty deposits predominantly triglycerides in the parenchyma cells of the liver. This accumulation of triglycerides may be the result of an imbalance between the rate of synthesis and the rate of release of triglycerides by the parenchymal cells in to the systematic circulation.[21]

Liver is the vital organ which is involved in synthesis of protein and glycogen. The fatty infiltration of liver causes the reduction in the diffusion of glucose 6 phosphatase and burns all the glucose to acetyl coA.[23] Decrease in the serum protein observed in the isoniazid intoxicated rats may be associated with the decrease in the number of hepatocytes which may result in the decreased synthesis of proteins.[8]

Serum bilirubin is an index of severity of liver damage. Isoniazid injury causes significant degeneration of hepatocytes and blockade of the bile ducts which results in to significant increase in the bilirubin level.[8]

CONCLUSION

Results obtained from the present study suggests that the aqueous extract of Ocimum canum sims possess the protective effect against isoniazid induced hepatotoxicity in experimental animals.

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