ISSN 2347-2375

UNIQUE JOURNAL OF AYURVEDIC AND HERBAL MEDICINES

Available online: www.ujconline.net

Research Article

EXPERIMENTAL STUDY OF DHATTURA *(DHATTURA ALBA NEES.)* W.S.R. TO ITS CHRONIC TOXICITY

Kumbhojkar Vidyanand Fanchu*

Assistant professor, Dept. of Dravyaguna, Seth Govindji Raoji Ayurved Mahavidyalay, Solapur, Maharashtra, India

Received 31-10-2014; Revised 30-11-2014; Accepted 29-12-2014

*Corresponding Author: **Dr. Kumbhojkar Vidyanand Fanchu**
Assistant professor, Dept. of Dravyaguna, 21/A/13, Seth Govindji Raoji Ayurved Mahavidyalay, Budhwar Peth, Samrat Chowk, Solapur, Maharashtra, 413002
Mobile: 9890469639, 9404130499

ABSTRACT

Ayurveda discribes *Dhattura* as Upavisha (Sub Poison). After *shodhana* (purification) it is used in many clinical entities & medicinal preparations. In this era of globalization of ayurveda there should be support of data on the ayurvedic drugs especially when it is mentioned as toxic one. In this research work an effort has been made to get the data on the chronic toxicity if any produced by *Dhattura (Dhattura alba Nees*.) before & after *shodhana*. Biochemicals as well as histopathological parameters are used to see the toxicity at different dose levels of *Shodhita* as well as *Ashodhita Dhattura* seed extract.

Keywords: Dhattura, Histopathological Parameters, Biochemical Parameters, Shodhana.

INTRODUCTION

Dhattura is described as *upavisa* (sub poison) in ayurveda[1] in modern toxicology also it is described as poisonous[2], it is having alkaloids like hyoscyamine & hyoscine.[3] After *Shodhana* (purification) it is used medicinally in many Ayurvedic preparations. So it becomes necessary to obtain data on its toxicity levels before & after *shodhana*. Present study was undertaken to see the chronic toxicity of Dhattura *(Dhattura alba Nees*.) before & after shodhana.

Objectives

(1) *Shodhna* of *Dhattura* seeds by *Gomutra* (Cows urine).
(2) To see the chronic toxicity on Albino Rats before and after *shodhan.*

MATERIALS AND METHODS

Experimental Study:

Aim- To see the chronic toxicity of *Shodhita Dhattura* seeds water extract & *Ashodhita Dhattura* seeds water extract in the selected Albino Rats.

Collection of Animals:

The Animals of either sex were collected from the animal House of B.L.D.E Medical College, Bijapur. They were exposed to ideal laboratory conditions.

Sample size:

For chronic toxicity study 42 Albino Rats were taken.

Materials:

Material required for present study are Dolayantra, Gomutra, Albino Rats of either sex, Gas burner, 5cc syringes, Rubber catheter, 18 no Metallic needle covered with rubber, Seizer, Scalpel forceps, plastic bottles, Small glass bottles, Cloth, Cotton swabs.

Selection of Animals

Healthy Adult Albino Rats of either sex weighing from 180-250gms were used as experimental model in this study.

Preparation of Animals

For Chronic toxicity study the animals were allowed free access to food & water. Before sacrificing the animals, they were fasted for 18 hours.

Grouping & Dosage of chronic toxicity study

Group	Test Drug	Dose	A. Rats
Group I	Shodhita Dhattura Seed Extract	High (216 mg/kg)	6
		Moderate (130 mg/kg)	6
		Low (43 mg/kg)	6
Group II	Ashodhita Dhattura Seed Extract	High (216 mg/kg)	6
		Moderate (130 mg/kg)	6
		Low (43 mg/kg)	6
Group III	Distilled Water	1 ml	6

Grouping:

Chronic toxicity study:

For chronic toxicity study total 3 groups were made.

Group I – Receiving Shodhita Dhattura seed extract.
Group II – Receiving Ashodhita Dhattura seed extract.
Group III – Receiving Distilled water.
Group I and Group II were again subdivided into 3 subgroups according to the High, Moderate & Low dose.

Methodology:

A) Shodhan of Dhattura seeds[4]

As per classified reference found in Rastarangini, the shodhan of Dhattura seeds (*Dattura alba* Nees.) was carried out in Dr B. N.M.E Trust Ayurvedic Medical College Pharmacy by Dolayantra method. The Dravadravya used was Gomutra.

C) Chronic Toxicity studies[5]:

The aim of present chronic toxicity study was to see effect of Shodhita Dhattura seed extract & Ashodhita Dhattura seed extract on Blood parameters & Histopathological changes in selected organs.

The study was carried out for 40 days & the animals were dosed daily at high, Moderate & Low dose levels according to the grouping on 41th day All the Rats were sacrificed, Blood & organs were collected.

Dose Selection

Animal Dose = Human dose X 0.018= 240mg X 0.018= 4.32mg= 4.32 X 5 = 21.6mg/kg body weight of Albino Rat.

Low Dose

This dose level was twice the Therapeutic Animal Dose
21.6 X 2= 43.2 mg/kg
For practical convenience 43mg/kg was taken

Moderate Dose

This was selected midway between Low Dose & High Dose
= 216 +43=259, 259/2 = 129.5mg/kg
For practical convenience 130mg/kg was taken.

High Dose

The dose level was ten times to the therapeutic animal dose.
= 21.6 mg/kg X 10= 216mg/kg

Route of Drug Administration

The test drugs were administered to Albino Rats by oral route.

Laboratory Investigations

On 41th day of chronic toxicity study the blood was collected by doing heart puncture & sent for Haemoatological & Biochemical analysis, all the animals were sacrificed & dissected the organs were taken out, kept into formalin bottles & sent for Histopathological studies.

Experimental Parameters

Histopathological studies

The following organs were studied for histopathological changes

1) Brain
2) Liver
3) Lungs
4) Kidneys
5) Stomach
6) Spleen
7) Heart

Biochemical Parameters

1) Serum total Bilirubin
2) Serum Globulin
3) Alkaline Phosphtase
4) Serum total Protein
5) S.G.O.T.
6) S.G.P.T.
7) Serum Albumin
8) Blood Urea

OBSERVATIONS

Observation on Experimental Study:

1) Observation on Shodhan of Dhattura Seeds

- The physical waste like stones, dust was removed by using sieve.
- The Shodhan process was carried out by Dolayantra method on mandagni.
- For 500 gms of seeds 4 litres of Gomutra was used.
- After completion of Shodhan process it was observed that the colour of Gomutra was changed from light yellow to Dark Brown.

2) Observation on Selection of Animals:

The healthy as well as nutritional status of Albino Rats was observed

3) Sample Size:

The bifurcation of Albino Rats in their group was observed & recorded.

4) Preparation Of Solution

Extracts of Ashodhita & Shodhita Dhattura seed were dissolved in 1ml of distilled water.

5) Observation on Selected Dose:

The dose was divided according to the body weight of the Albino Rats.

Observation nn Chronic Toxicity Studies:

Group I

The Shodhita Dhattura seed extract was administered in High, Moderate & Low doses. The animals were kept on normal diet & supplied with tap water.

Group II

The Ashodhita Dhattura seed extract was administered in High, Moderate & Low doses. The animals were kept on normal diet & supplied with tap water.

Group III

The Vehicle i.e., Distilled water was administered & the animals were kept on normal diet & supplied with tap water.

The study was carried out for 40 days after giving dose on 40th day the animals were fasted for 18 hrs & on 41st day they were sacrificed.

Observation on laboratory examination

1) Blood was sent for Biochemical analysis. It was collected by doing heart puncture after light ether anaesthesia.
2) After collecting blood the animals were sacrificed, selected organs were taken out & sent for histopathological studies.

RESULTS

Important results are as follows,

Serum Protein

Serum protein value has shown significant decrease in all the dose levels of Group I & Group II when compared with Group III.

Serum Albumin

The data pertaining to the effect of test drugs on serum albumin level has shown highly significant decrease in value at high dose level of Group I & Group II. At moderate dose level of Group I no significant change has been seen. In Group

II moderate dose level there was decrease in the value which was statistically significant. At low dose level of Group I the decrease was significant where as at low dose level of Group II there was highly significant decrease in Albumin level.

Serum G.O.T

The data obtained from the effect of test drugs on serum G.O.T shows highly significant increase in the value of Group I and group II at high dose level. At Moderate dose level no significant change was observed in Group I where as in Group II moderate dose level there was highly significant increase in S.G.O.T value. At low dose level of Group I & Group II no significant change was observed.

Serum G.P.T

The data obtained from the effect of test drug on serum G.P.T shows highly significant increase in the values of high dose levels of Group I & Group II. At moderate dose level the results of Group I were statistically non-significant where as Group II showed highly significant increase in S.G.P.T value. At low dose level of Group I and Group II no significant change was seen.

Serum Alkaline phosphatase

The data obtained from effect of test drugs on Serum Alkaline phosphatase level shows highly significant increase at high dose level of Group I & Group II. In Group I moderate dose level there was no significant change in the Alkaline phosphatase level where as in Group II moderate dose level there was increase in serum Alkaline phosphate level which was statistically highly significant. At low dose levels of Group I and Group II the results were statistically non significant

Results of Histopathological Studies

Liver

Microscopy of Group I showed central congestion in the lobules at high dose level, mild congestion was seen at moderate dose level where as at low dose level no congestion in the lobules was seen. At all 3 dose levels of Group I no necrosis, fatty change & cirrhosis were seen. Microscopy of Group II rats shows moderate fatty changes in hepatocytes along with cell depletion in most of the sections. The lobules showed moderate congestion along with central necrosis in few sections at high dose level. The moderate dose administered rat section showed mild to moderate congestion in the lobules where as mild congestion was seen in few sections at low dose level.

Heart

In Group I the heart section showed myocardial haemorrhage at high dose & moderate dose level in few sections. The low dose level sections showed normal architecture. In Group II the heart sections showed myocardial haemorrhage in almost all sections of high dose level where as at moderate dose level few sections showed myocardial haemorrhage, at low dose level the heart sections showed normal architecture.

Stomach

Microscopy of stomach sections of Group I showed moderate congestion of mucosa where as severe congestion was seen in two rats, mild to moderate ulcerations were seen at high dose level. At moderate dose level mild congestion of mucosal layer was seen along with ulcerations in few rats. At low dose level mild congestion was seen in few rats, remaining showed normal cytoarchitecture.

Microscopy of Group II showed severe congestion of gastric mucosa along with ulcerations at high dose level. At moderate dose level also sever congestion was seen in few rats along with ulcerations in all of them. At low dose level mild to moderate congestion was in all rats but no ulcerations were found.

Lungs

Microscopy of Group I showed mild to moderate congestion at high dose level & Hemorrhage was seen in a rat. At moderate dose level mild congestion was seen in only one rat. Normal cytoarchitexture was seen in low dose administered rats.

Microscopy of Group II showed moderate congestion of alveoli in all rats at high dose level. Mild to moderate congestion was seen at moderate dose level. Whereas low dose level showed normal cytoarchitecture no haemorrhage & infarction was seen in any rat at the high, moderate & low dose levels

Spleen

Microscopy of Group I high dose level showed mild congestion in all rats. There was mild congestion seen in few rats at moderate dose level. Whereas at low dose level most of the sections showed normal architecture

Microscopy of group II at High dose and moderate dose level showed mild congestion in the cytoarchetecture of all the rats. Whereas at low dose level mild congestion was seen in few rats others showed normal cytoarchetecture.

Kidneys

Microscopy of Group I showed glomerular injury along with cloudy tubular swelling where as interstitum showed normal cytoarchitecture at high dose level. At moderate dose level cloudy tubular swelling along with mild interstitial inflammation was seen in few sections. At low dose level the section showed normal cytoarchetector of kidney.

Microscopy of Group II showed tubular injury in form of cloudy swelling along with moderate interstitial inflammation in all the sections at high dose level. At moderate dose level the sections showed moderate cloudy swelling in tubules along with mild interstitial inflammation. At low dose level few sections showed mild cloudy swelling in tubules.

Brain

The microscopy of Brain sections from Group I showed mild haemorrhagic necrosis only in two rats at high dose level there was no evidence of cerebral lesions. At moderate dose level & low dose level. The sections showed normal cytorchetecture.

The microscopy of Brain sections from Group II showed haemorrhagic necrosis in all rats & cerebral lesions in few rats at high dose level. At moderate dose level the few sections showed haemorrhagic necrosis but no cerebral lesions. At low dose level the cytorchetcture of Brain sections was normal.

Microscopy of control group rats showed normal cytoarhitecture in all sections.

DISCUSSION

Healthy Albino rats of either sex were used for chronic toxicity studies weighing from 180-250gms. Total 3 groups were made Group I & Group II were administered Shodhita &

Ashodhita Dhattura seed extract respectively. Both groups were divided into 3 subgroups according to high, moderate & low dose levels so that maximum Biochemical, Hematological as well as Histopathological changes can be observed. Gr. III was control group which was receiving the vehicle distilled water.

Serum proteins are synthesized in liver. The sevear decrease in serum protein level in blood indicates liver damage, it was decreased in both Gr. I & Gr. II

Serum glutamic pyruvic transaminase (S.G.O.T.) level is increased in tissue injury of liver as well as other tissue like myocardium. Serum glutamic oxaloacetic tranaminase (S.G.P.T.) in blood tells little about function of liver. The blood level of S.G.P.T. is increased in conditions in which hepatocytes are damaged or die. Both of these enzymes were increased highly in Gr. II than Gr. I

Albumin is major protein that is circulating in blood. It is synthesized by liver. Low serum albumin level indicates poor liver function. Hypo albuminamia occurs in significant destruction of hepatocytes. This was significantly decreased in Gr.II than Gr.I

Serum Alkaline Phosphatase is produced by many tissues, especially bone, liver intestine & placenta & is excreted in bile. Elevation in blood level of Serum Alkaline Phosphatase is thus can be found in bone disease, liver pathology & in pregnancy. This enzyme was found increased highly in Gr. I than that of Gr. II.No significant changes were found in Gr.III

By seeing histopathological studies of Liver, heart, stomach, lungs, spleen, kidney, brain it can be said that Ashodhita Dhattura has produced sevear histopathological changes at high dose level where as Shodhita dhattura produced comparatively less histopathological changes at high dose level.

At moderate dose level Ashodhita Dhattura produced marked histopathological changes where as changes produced by Shodhita Dhattura were mild.

At low dose level Ashodhita Dhattura affected the cytorchetecture of Liver, Stomach, Spleen, Kidneys, where as Shodhita Dhattura did not produce any histopathological changes.

CONCLUSION

From the data obtained from Chronic toxicity studies of *Dhattura (Dhattura alba Nees*.), by considering biochemical & Histopathological parameters it can be concluded that toxicity of *Dhattura* has reduced reduced after shodhana.

Recommendation For Future Study

(1) Chronic studies may be carried out on no rodents like rabbits or dogs to confirm the toxic effects.

(2) Isolation of extracted fractions by characterization in TLC, UV, & IR methods may be studied.

REFERENCES

1. Chunekar KC, Bhavaprakasha Nighantu, reprint; 2004; Chaukhamba bharti academy, Varanasi; pp. 634.
2. Parikh CK, Textbook of Medicinal Jurisprudence and Toxicology reprint; 1998: CBS publishers and distributors; pp. 660.
3. Rastogi and Mehrotra, Compendum of Indian Medicinal Plants vol-5, 1990-94: Central drug research institute, Luknow; pp. 288.
4. Pandit Kashinath Shastri, Rasatarangini reprint 1994: Motilal banarasidas publication, pp. 153
5. Ghosh MN, Fundamentals of Experimental Pharmacology, 2nd edi; 1994: Scientific book agency Calcutta; pp. 154.

Source of support: Nil, Conflict of interest: None Declared