Biospectra : ISSN : 0973-7057, Vol. 15(1), March, 2020, pp. 261-264
An International Biannual Refereed Journal of Life Sciences

18(AS).
Animal Science

ISSN : 0973-7057

Int. Database Index: 663 www.mjl.clarivate.com

Studies on the hepatotoxicity due to prolonged use of colchicine in albino rat

Suman Swaraj*
Department of Zoology, B.N.Mandal University, Madhepura, Bihar, India

Received : 6th December, 2019 ; Revised :15th February, 2020

Abstract : Derived from meadow-saffron plant *Colchicum autumnale,* colchicine is an alkaloid of high potential also called mitotic poison. It is a powerful inhibitor of somatic cell multiplication in mitotically active tissues and organs like liver thereby causing significant hepatotoxicity. In the present article effect of toxic doses of colchicine injected intraperitonially in the albino rats for longer period on the liver functions has been biochemically assayed through standard LFT (liver function tests) package which includes AST(Aspertate aminotransferase test), ALT(Alanine aminotransferase), and ALP(Alkaline phosphatase). Prolonged injection of colchicine resulted in increased concentration of these liver enzymes (AST, ALT& ALP) in the blood of the treated rats. These changes have also led to histopathological abnormalities in the liver such as hepatocyte necrosis, inflammation of central hepatic vein & development of prominent cytoplasmic vacuoles.

Key words: Hepatotoxicity, LFT (AST, ALT, ALP) Colchicine, plant alkaloid, prolonged use

INTRODUCTION

Alkaloids are group of specialized nitrogenous substance having wide range of pharmacological activities. They are usually found in plant world but may be produced by bacteria, fungi, and insects. The colchicine is an important plant alkaloid derived from derived from the meadow saffron plant (*Colchicum autumnale*) and therapeutically used extensively in the treatment of gout, arthritis, Mediterranean fever[1], in the treatment of primary biliary cirrhosis & Behcet disease[2]. Colchicine interferes with the formation of microtubule by binding to microtubular synthesis complex and causing depolymerization of microtubules in diverse functions, including cell movement, vesicle transport and chromosome segregation during mitosis. It has also been reported that colchicine can be either cytotoxic or protective against cytotoxicity. Colchicine has been reported to protect against a variety of hepatotoxic stresses & improves the survival of the rats in a clinical test for alcoholic cirrrhosis.[3] As it has a narrow range of therapeutic index, the overdose of colchicine may lead to high rate of mortality.[4] Studies on the effect of mal absorption on the functions of the small intestine would be greatly facilitated if such states could be routinely induced in the laboratory. A number of efforts to achieve such states in experimental animals have met with little success[5,6] but the use of antimitotic drugs, such as aminopterin and colchicine, cause a pathological villous architecture similar to that found in many types of malabsorption.[6-8] Studies on the effect of colchicine on intestinal absorption have, however, only been carried out in conscious animals[8,9] where absorption depends not only on the activity of the mucosal cells of the intestinal epithelium but also on factors such as gastric

*Corresponding author :
Phone : 9955875200
E-mail : drsumanswaraj@gmail.com

emptying, intestinal motility, blood flow, etc. In order to avoid the influence of a number of these factors the effect of colchicine on intestinal function has been investigated using a recently developed technique in the anaesthetized rat in vivo and on sacs of isolated, everted intestine incubated in vitro.

MATERIALS & METHODS

Thirty adult albino healthy rats weighing (200–250 g) were taken for the study in the laboratory & kept in standard laboratory conditions having free access to water & food. The entire population was dived into three equal groups of 10 individuals and they were marked as -first group as control receiving only distilled water orally; second group, treated with 2 mg of colchicine per kg body weight/day and third group, treated with 3 mg of colchicine per kg body weight/day dissolved in distilled water. The treatment of colchicine concentration in rats of second & third group was done through intraperitoneal injection.

Blood samples from individuals of treated group were collected 24 hours after administration of last dose of colchicine which were centrifuged at 3000 rpm for 10 min to separate the serum.

The separated serum was subjected to biochemical analysis for following liver function tests:

1. Aspartate Aminotransferase Test (AST)

AST was performed by mixing the 5ml serum to 10ml buffered solution of L- aspartic acid and 2-ketoglutarate and then incubated for one hour at 37° C. After incubation, 1 mm of DNPH and 0.4m of NaOH was added.

2. Alanine Aminotransferase Test (ALT)

ALT was performed by mixing 5ml serum to 10 buffered solution of DL- alanine and 2- ketoglutarate, and then incubated for thirty minutes at 37° C. After incubation, 1 mm of DNPH and 0.4m of NaOH was added.

3. Alkaline Phosphatase Test (ALP)

ALP was performed by using p- nitrophenol phosphate as substrate, in alkaline buffer with fresh unhemolysed serum for 45 min at 12°C.

Table 1- Showing results of 3 enzyme biochemical assay test under LFT of albino rat exposed to different concentration of colchicine in group 2 & 3, group 1 being control.

L.F.T Group	ALT (IU/L)	AST (IU/L)	ALP (IU/L)
Group 1	10.16 ± 3.1	30.7±2.8	85.8±5.3
Group 2	22.1±2.1	34.13±1.	89.1±2.3
Group 3	45.9±12.1	51.3±8.2	144.4±9.1

RESULT & DISCUSSION

Liver Examination

Liver of control, untreated rat revealed no morphological changes. But in treated rats belonging to group 2 & 3 with 2 & 3 mg of colchicine per kg body weight/day dissolved in distilled water respectively, marked liver lobe swelling and distention have been noticed. These morphological abnormalities in the liver of rat may be collectively called as fatty liver which is related with internal biochemical changes of the blood existing in the hepatic lumen and the vein nourishing organ.

LFTs-

Significant elevation in the ALT, AST & ALP enzymes concentration have been found in members of group 2 & 3 treatment whose blood biochemical assay were done as per the standard liver function test (Table 1). The ALP concentration in group 3 having 3mg cholchicine exposure dose displayed very sharp rise compared to the control which is metabolically detrimental for related creatinine biosynthesis at kidney level.

DISCUSSION

Colchicine is a safe alkaloid if it is used for short period and under recommended dose. However, its use in the treatment of chronic diseases such as gout and familial Mediterranean fever, the higher recommended dose may be taken for prolonged period of time under clinical supervision.

The present study investigates its toxic effects on liver being metabolically very efficient organ which is also involved in the breakdown and excretion of colchicine when taken in the system. The biochemical assay of the enzymatic concentration of 3 important enzymes synthesized in the liver has been assayed by LFT blood examination of the rats.

The present study showed a statistical significant increase of liver enzymes such as ALT, AST and ALP in third group which received 3mg/kg/day of colchicine in comparison with the control group and the second group which received 2mg/kg/day. Sherlock referred that the use of liver function tests is associated with high specificity

ACKNOWLEDGEMENT

The author is extremely thankful to her guide Dr. R.B.Jha & Prof. Arun Kumar, Head, Department of Zoology, B.N Mandal University Madhepura for their valuable guidance and help in completion of this research paper.

REFERENCE

1. **Zemer D, Revach M, Pras M, 1974.** A controlled trial of colchicine in preventing attacks of familial mediterranean fever. *N Engl J Med* . **291 (18):** 932-4.
2. **Kaplan, MM, Alling, DW, Zimmerman, HJ, Wolfe, HJ, Sepersky, RA, Hirsch, GS, Elta, GH, Glick, KA, & Eagen, KA.1986.** A prospective trial of colchicine for primary biliary cirrhosis. *N Engl J Med*. **315:** 1448-1454.
3. **Maxwell MJ, Muth P and Priiy PE. 2002.** Accidental colchicine overdose. A case report and literature review. *Emerg., Med., J.* **19(3):**265-7.
4. **Lainé M, Mourissoux G and Camou F. 2012.** Early Onset Cardiogenic Shock in Acute Colchicine Overdose. *J., Clinic., Toxicol.*, **2:**2-5.
5 **Althausen, T. L. & Grodsky, G. M. 1961.** Effect of wheat proteins on intestinal absorption in rats. *Gastroenterology*. **40:**665.
6. **Williams, J. N. Jr., & Laster, L. 1963.** Investigation of the use of the albino rat for studying gliadin-induced steatorrhea. *Metabolism*, **12:** 467-471.
7. **Baserga, A., & Morsiani, M. 1958.** Non regenerative enteropathy. *Rass. giul. Med.*, **35:**208-215.
8. **Clark, P. A., & Harland W. A. 1963.** Experimental malabsorption with jejunal atrophy induced by colchicine. *Brit. J. exp. Path.*, **44:**520-523.
9. **Luketic, G. C., and Shapiro, M. 1964.** Effect of colchicine on xylose absorption in dogs. *Clin. Res.,* **12:**31.

***

MS- Young Scientist/ Senior Scientist/Life Time Achivement Award - 2020 Nomination Form

(*Jointly Sponsored by* MADHAWI SHYAM EDUCATIONAL TRUST & ICCB)

"Mandaar-Pushp", Pragatisheel Colony, Chitragupta Nagar,
Baragain,Ranchi - 834009
Jharkhand, India
(Tel. : Mob. : 94313-89253; 94317-08322)

Name of the applicant : .....

Date of birth : .....

Academic Qualifications : .....

.....

Area of Research : .....

No. of research Publications : 1) .....

(Titles of best two) .....

2) .....

.....

Other outstanding Achievements : .....

.....

Place of Working with full .....

address for communication : .....

.....

E-mail : ..... Tel./Mob. : .....

Are you a life member of the Journal or willing to accept the same : Yes / No

Signature of the applicant

Name & Address of 2 Reference : 1)..... 2) .....

....

....

....

Signature & Seal of Referees : ....