

HISTOPATHOLOGICAL CHANGES IN MUCOSA OF GALL BLADDER IN SWISS ALBINO MICE

(An Experimental Study)

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ABSTRACT –

Gall bladder stone is most common surgical emergency in all over world. Cholesterol & mixed types of gall bladder stones are most common type of Gall Bladder stone. Mixed type of gall bladder stones are also content major percentage of cholesterol. These type of gall bladder stones are mostly developed due to metabolically disturbances. Pigmented gall bladder stones are very less common. In medical sciences, there is no any medicine is available which can dissolve the gall bladder stone without any side effect and recurrence & only surgical removal of gall bladder (either open or laparoscopic cholecystectomy) is the treatment of choice at present era. But *Ayurveda* has kept the potency to dissolve the gall bladder stone and revert back the mucosal changes of gall bladder mucosa without any side effects. For this study, an experimental model was selected, in which first gall bladder stone was developed in experimental model by lithogenic diet than it has to be treated by *Ayurvedic* formulations successfully. It has been found that mucosal changes were also improved by *Ayurvedic* formulations.

Keywords- Gall bladder stone, histopathology, swiss albino mice, *Ayurvedic* formulation etc.

INTRODUCTION-

Cholelithiasis is the most common disorder of the biliary tract ⁽¹⁾. It can cause cholecystitis and may be associated with the appearance of hyperplasia, metaplasia and carcinoma in the gall bladder ⁽²⁻⁵⁾. In the gall bladder, gall stone and inflammation may cause epithelial injury and resultant metaplastic changes ⁽²⁻⁴⁾. In present era only surgical treatment is accepted & successful for chronic cholecystitis & cholelithiasis perhaps few medical treatments are also available in modern science but due to side effects, more expensive, after leaving therapy the recurrence rate is high. So that such medical therapy is not more accepted & frequently used. In *Ayurveda* some drugs are available which work on hepatobiliary system without any side effect in which *Rohitakadhy*a extract & *Phaltrikadi* decoction are used for chronic cholecystitis & cholelithiasis. It is not possible to develop gall bladder stone in patient by given lithogenic diet, then used trial drug (*Rohitakadhy*a extract & *Phaltrikadi* Decoction) to evaluate its effect on gall bladder stone & gall bladder mucosa. So that need of experimental study to evaluate the effect of trial drug on gall bladder stone & gall bladder mucosa of mice, where artificially create gall bladder stone by lithogenic diet.

MATERIAL & METHOD

Experimental animals [Swiss albino mice (*Mus musculus*)] were obtained from central, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The animal study was performed in animal house of Centre of Experimental Medicine & Surgery, IMS, BHU. The Swiss Albino mice were taken both sex female & male & separately kept in poly-propylene cage with stainless steel top grill. The dry paddy husk was used as bedding material and was changed weekly. Before the experimental study, firstly animals were acclimatized for seven days in standard laboratory conditions; 12 ± 01 hour day and night rhythm, maintained at 27 ± 2°C temperature and about 60 % humidity. All Animals were fed with standard & lithogenic diet and water *ad libitum* in respective of there groups. The experimental Protocol used in this study approved by the Institutional Animal Ethics Committee, Institute of Medical Sciences, Banaras Hindu University (Approval number; CAEC/1145-27/04/2015) and the care of animals was taken as per the CPCSEA guidelines

This experimental study divided in four groups-

Group A (Control Negative)- Six mice of weight 24±2 gm of both sex (three male & three female mice) were taken & given standard diet ⁽⁶⁾ for one month.

Group B (Control Positive)- Six mice were taken each of weight 24 ± 2 gm (three male & three female mice) & given Lithogenic diet⁽⁷⁾ for one month to develop gall bladder stone in mice. Lithogenic diet⁽⁷⁾ was freely access to mice for one month.

Group C (Treated Group)- Six mice were selected, each of weight 24 ± 2 gm (three male & three female mice) & given Lithogenic diet for one month to develop gall bladder stone in mice followed by treated with Rohitakadhya Extract for one month. Lithogenic diet⁽⁷⁾ was freely access to mice for one month to develop gall bladder stone & then mice were treated with *Rohitakadhya* extract for one month. The dose of *Rohitakadhya* extract was 5.148 mg per day in divided dose.

Route of drug administration - The drug was administered through oral route by rubber catheter sleeved on to disposable syringe.

Group D- Six mice were selected each of weight 24 ± 2 gm (three male & three female mice) & given Lithogenic diet for one month to develop gall bladder stone in mice followed by treated with *Rohitakadhya* Extract & *Phaltrikadi* Decoction for one month. The dose of lithogenic diet⁽⁷⁾ was freely access to mice. Than mice were treated with *Rohitakadhya extract* (dose- 5.148 mg per day in divided dose)⁽¹⁴⁾ and *Phaltrikadi* decoction (.208ml per day in divided dose)⁽¹⁴⁾ for one month.

DISCUSSION-

In present experimental study, morphological findings of mice gall bladder are normal in group A but in group B where lithogenic diet is given gall bladder become distended & shows presence of sludge's & stone. This study showed that lithogenic diet is responsible for formation of cholesterol stone.

Other hand many researches also have evidence of formation of gallbladder stones because of cholesterol rich diet (lithogenic diet). These studies show that the cholesterol cholic acid-containing diet reduced cholesterol 7α hydroxylase activity by about 80 %. Nakamura-Yamanaka *et al.* (1987)⁽⁹⁾ showed a similar effect on cholesterol 7α -hydroxylase activity in mice fed on a lithogenic diet containing 5g cholesterol/kg and 2.5 g sodium cholate/kg. Since it has been reported that feeding with cholic acid may suppress bile acid synthesis in the rat (Shefer *et al.* 1973; Heuman *et al.* 1988)^(10,11), the present inhibition on bile acid synthesis is most probably due to cholic acid in the diet. Rudling⁽¹²⁾ (1992) reported a suppression of 7α -hydroxylase mRNA in mice when cholic acid was present in the diet and increased mRNA on

feeding pure cholesterol only. This latter effect was seen when the diet contained 17 g cholesterol/kg or more. Similar results were obtained by Spady & Cuthbert (1992)⁽¹³⁾ in rats. Thus the addition of cholic acid to the diet is likely to reduce cholesterol breakdown to bile acids, and consequently increase biliary cholesterol secretion⁽⁸⁾.

Histopathology of excised gall bladder of experimental model, group A shows normal intact single line mucosa, no proliferation seen in mucosa, muscles layer & lamina propria are normal (see figure-1 & 2). In group B (where mice put on lithogenic diet to produce gall bladder stone) histopathology of excised gall bladder of mice shows mucosa becomes proliferated & showing villi projection. In epithelial zone, inflammation with chronic inflammatory cells & oedema present (see figure-3 & 4). In group C, histopathology of excised gall bladder shows there is reduction in inflammation however proliferation less marked. There is reduced edema & congestion in mucosal layer (see figure-5 & 6). In group D, histopathological slides have been showed that inflammatory changes are very less in number, mucosa remained intact, oedema & congestion are not seen.

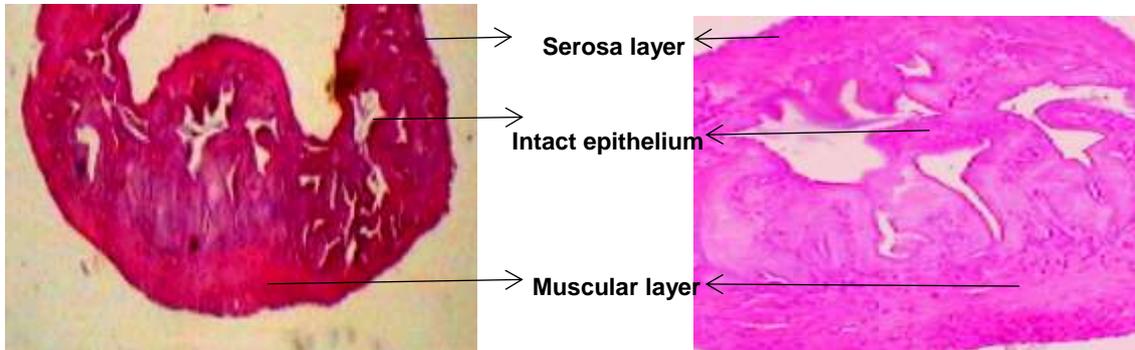
In muscular layer, there is no any congestion, inflammation & oedema seen. The process of destruction of tissue has got either recovered or regenerated after treated by Rohitakadhya extract & Phaltrikadi decoction.

CONCLUSION-

In this study, It has been found that *Ayurvedic* Formulations (Rohitakadhya Extract and Phaltrikadi Decoction) was more effective to dissolve the gall bladder stone and revert back the mucosal changes of gall bladder. Alone Rohitakadhya extract was also effective in dissolving the stone and resolve the mucosal changes but when it was works with Phaltrikadi Decoction than it has produced more satisfactory result as very less number of inflammatory infiltrate, reduce proliferation of mucosa, epithelium becomes intact, oedema of muscular was subsided and serosa layer become intact.

HISTOPATHOLOGICAL STUDY

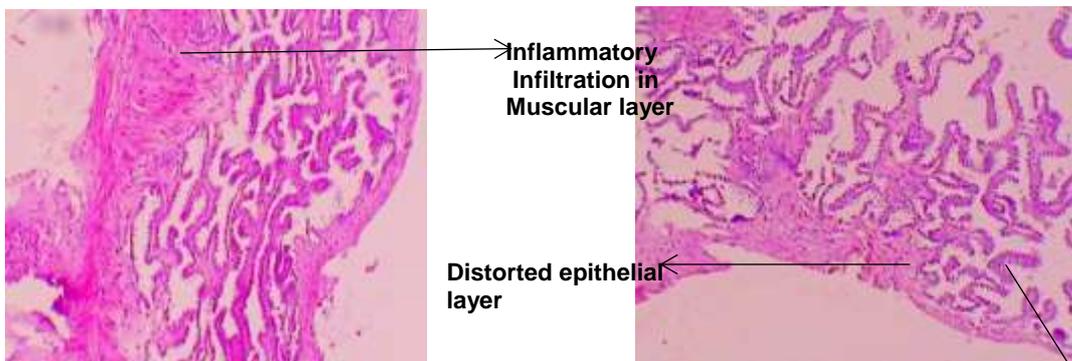
1. Group-A



(Figure-1)

(figure-2)

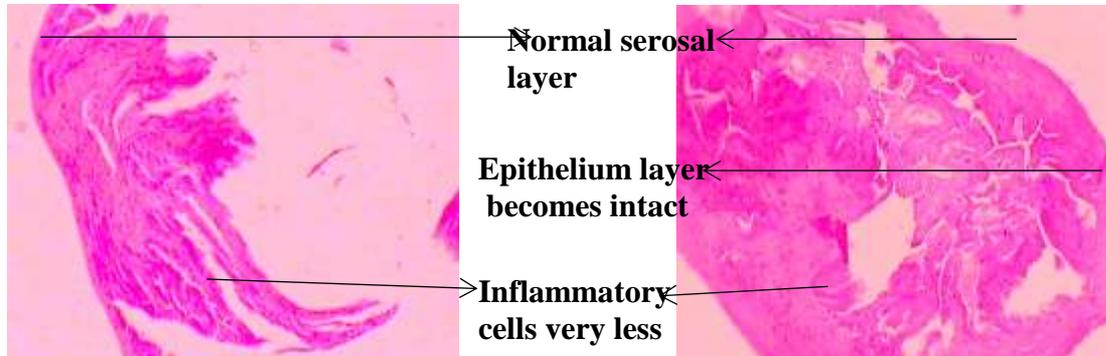
2. Group-B



(Figure-3)

(Figure-4)

3. GROUP- C



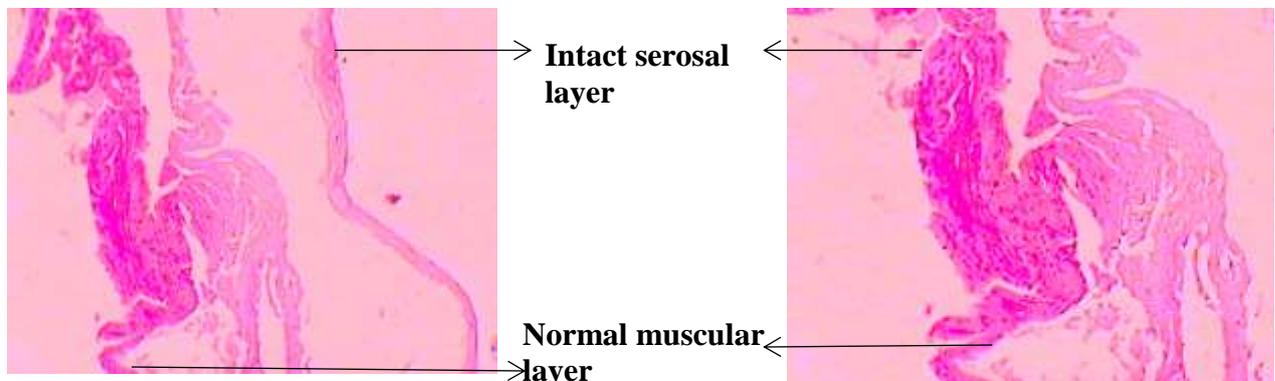
Microscopic Picture Taken Under 10x Magnification

Microscopic Picture Taken Under 40x Magnification

(Figure-5)

(Figure-6)

4. GROUP- D



Microscopic Picture Taken Under 10x Magnification
Under 40x Magnification

Microscopic Picture Taken

(Figure-7)

(Figure-8)

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