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PHARMACOLOGICAL EVALUATION OF SIDDHA FORMULATION KATTU KARUNAI CHOORANAM IN CROTON OIL INDUCED HEMORRHOID IN WISTAR RATS

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ABSTRACT

Hemorrhoids affect about 4.4% of the general population worldwide, irrespective of gender. Pharmacological treatment of haemorrhoid aims at reducing inflammation, pain, and bleeding. Topical dosage forms such as creams, ointments, and suppositories containing steroids (corticosteroids) or nonsteroidal anti-inflammatory agents (NSAIDS: ibuprofen, aspirin, and diclofenac), either alone or in combination with antibiotics or anaesthetics may found effect and offer symptomatic relief but these agent found to elicit life threatening side effects upon long term usage. Hence exploration of viable drugs from alternate source with less side effects are of public interest in recent days. Herbal formulations are highly effective in managing the haemorrhoid and its related complications as it proven to halt the disease pathogenesis by quenching the free radical which accelerates the inflammatory consequences. Kattu karunai chooranam (KKC) is one such siddha herbal drug that is known for the management of hemorrhoidal complication as per siddha literatures. But still now there is no proven research evidencing the efficacy of this formulation, hence the main objective of the present investigation is to evaluate the anti- hemorrhoidal potential of the siddha formulation KKC against croton oil induced hemorrhoid ulcer model in rats. Results of the study advocates increased rectoanal coefficient score of the rats belongs to group II has shown the intensity and severity of hemorrhoid ulcer induction by croton oil preparation in the experimental animals. There was significant decrease in the rectoanal coefficient value observed in trial drug treated rats at the both the dose level of 200 and 400 mg/kg reveals the anti- hemorrhoidal potential of the formulation.

KEY WORDS: ***Hemorrhoid, Siddha, Herbal formulation, Kattu karunai chooranam, Croton oil, Rectoanal coefficient***

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1. Introduction

Today, millions of people are suffering from hemorrhoids and it is more prone as you grow older, and it is becoming a major medical and socioeconomic problem. There are various factors responsible for hemorrhoids like constipation, sedentary life style, pregnancy, low fiber diet, obesity, and so forth. Usually, hemorrhoids develop due to increase in pressure on the veins of the pelvic and rectal region, which causes abnormal dilatation and distortion of the vascular channel, leading to the extravasation of blood around the perianal and anal vein, which results in rectal bleeding [1,2].

Constipation and prolonged straining are widely believed to cause hemorrhoids because hard stool and increased intraabdominal pressure could cause obstruction of venous return, resulting in engorgement of the hemorrhoidal plexus [3]. Defecation of hard fecal material increases shearing force on the anal cushions. However, recent evidence questions the importance of constipation in the development of this common disorder [4, 5].

Management of symptomatic hemorrhoids ranges from nonoperative medical interventions (drugs, dietary, and lifestyle modification) and office-based procedures (rubber band ligation, sclerotherapy, and infrared coagulation) to surgery (hemorrhoidectomy, stapled hemorrhoidopexy, and Doppler-guided haemorrhoid artery ligation) [6]

Pharmacological treatment of haemorrhoid aims at reducing inflammation, pain, and bleeding. Topical dosage forms such as creams, ointments, and suppositories containing steroids (corticosteroids) or nonsteroidal anti-inflammatory agents (NSAIDS: ibuprofen, aspirin, and diclofenac), either alone or in combination with antibiotics or anaesthetics (such as lidocaine, benzocaine, and dibucaine), have been shown to be effective. However, their prolonged use is limited due to the high incidence of side effects [7-9]

Treatment of hemorrhoids in modern medicine is still in infancy. Given the fact that there is no specific drug to treat hemorrhoids, extensive research is ongoing in the field of traditional medicine for utilizing the natural sources for treating haemorrhoids. Kattu karunai chooranam (KKC) is a siddha herbal drug that is known for the management of hemorrhoidal complication as per siddha literatures. But still now there is no proven research evidencing the efficacy of this formulation, hence the main objective of the present investigation is to evaluate the anti-hemorrhoidal potential of the siddha formulation KKC against croton oil induced hemorrhoid ulcer model in rats.

2. Materials and Methods

2.1. Experimental Animals

Healthy adult wistar albino rats of either sex weighing between 200-220 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air handling unit. A 12 light / dark cycle were maintained. Room temperature was maintained between 22 ¬+ 2o C and relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by the Institutional Animal Ethics Committee of Sathyabama Institute of science and technology, Chennai, Tamil Nadu, India with the approval number (SU/CLATR/IAEC/XV/161/2020)

2.2. Experimental Methodology [10,11]

The animals were grouped into four groups of 6 animals each. Group I (Control group) -received normal saline, Group II – Hemorrhoid control rats induced by applying croton oil preparation (deionized water, pyridine, diethyl ether, and 6% croton oil in diethyl ether in the ratio of 1: 4 : 5 : 10). Followed by an overnight fasting, sterile cotton swabs (4 mm diameter) soaked in 100 μL of croton oil preparation will be inserted into the anus (rectoanal portion, 20 mm from anal opening) of all the study animals and kept for 10 seconds. A linear development of edema will be observed up to 7 to 8 hours after the croton oil application. Group III (Low dose treated group): Hemorrhoid rats was treated with 200mg/kg of KKC, p.o for the period of 05 days 1 hr prior to the start of hemorrhoid induction .Group IV (High dose treated group): Hemorrhoid rats was treated with 400mg/kg of KKC, p.o for the period of 05 days 1 hr prior to the start of hemorrhoid induction. At the end of the study animals will be sacrificed for estimation of Rectoanal coefficient and further efficacy of the drug will be ascertained by histological analysis.

2.3. Sample Collection [12]

At the end of the study, before sacrifice, the animals were fasted for overnight with free access to water. Animals were sacrificed with excess anesthesia. Rectoanal tissue was removed weighed and subjected to histological examination. Rectoanal coefficient was carried out according to the method by as given below.

3.Results

3.1. Effect of KKC on Rectoanal coefficient in Croton oil Induced haemorrhoid

Result analysis of the study reveals increased rectoanal coefficient score of the rats belongs to group II has shown the intensity and severity of hemorrhoid ulcer induction by Croton oil preparation in the experimental animals. There was significant decrease in the rectoanal coefficient value observed in trial drug treated rats at the both the dose level of 200 and 400 mg/kg reveals the anti- hemorrhoidal potential of the formulation. As shown in Table 1.

Table 1: Effect of KKC on Rectoanal coefficient in Croton oil Induced hemorrhoid

Group	Group I Normal Control	Group II Croton oil Induced Hemorrhoid	Group III Croton oil + 200 mg/kg of KKC	Group IV Croton oil + 400 mg/kg of KKC
Rectoanal coefficient	1.02 ± 0.022	1.632 ±0.039*	1.42 ±0.023	1.278 ± 0.030*

Values represent mean ± SEM of 6 experimental animals. * P< 0.05

3.1. Effect of KKC on Histology of Rat rectal tissue subjected to the investigation

Prefect alignment of epithelium oriented in the wall of the rectal canal with no signs of degeneration were observed were observed in group I rats. Signs of hemorrhage and degeneration evidence with sever inflammatory changes were observed in sample belongs to group II rats. The continuity of epithelium with occasional signs of inflammation and degeneration observed sample belong to group III animal. Regular arrangement of columnar epithelium were observed in group IV sample. As shown in figure 1.

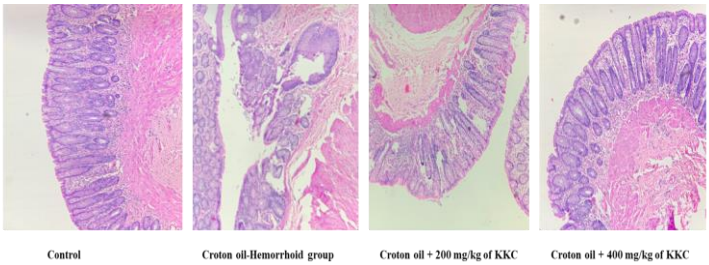

Figure 1: H & E staining of Rectoanal tissue in Control and Treatment Rats

4. Discussion

Hemorrhoids, also called piles, are swollen veins in the anus and lower rectum, similar to varicose veins. Hemorrhoids can develop inside the rectum (internal hemorrhoids) or under the skin around the anus (external hemorrhoids). It occurs frequently as an inflammatory process of the hemorrhoidal plexus [13]. They are often not associated with any symptoms and people may not know they have them. When symptoms do occur, they present as bleeding and/or pain on passing stool, sense of incomplete bowel emptying, a lump around or inside the anus, itchiness or soreness around the anus, and mucus discharge from the anus [14].

Free radical generation is the primary reason for initiation of many physiological and pathological disorders like hemorrhoids. Involvement of free radicals in the precipitation of hemorrhoids is well documented in the literature. It is well known fact that excess concentration of free radicals is a consequence of improper balance between reactive oxygen species and their metabolites [15]. The interplay of herbs and human health has been documented for thousands of years [16]. Herbs have been integral to both traditional and non-traditional forms of medicine dating back at least 5000 years [17]. The enduring popularity of herbal medicines may be explained by the tendency of herbs to work slowly, usually with minimal toxic side effects.

Croton oil has been used as phlogistic agent for experimental induction of hemorrhoids. Croton oil causes inflammation due to release of inflammatory lipid metabolites such as prostaglandins, leukotrienes, TNF-α, nitric acid and bradykinins. These factors alone or in combination regulates the activation of fibroblasts, endothelial cells, macrophages and newly recruited monocytes, lymphocytes, neutrophils and eosinophils which leads to severe inflammation

[18].Result analysis of the study reveals increased rectoanal coefficient score of the rats belongs to group II has shown the intensity and severity of hemorrhoid ulcer induction by Croton oil preparation in the experimental animals. There was significant decrease in the rectoanal coefficient value observed in trial drug KKC treated rats at the both the dose level of 200 and 400 mg/kg reveals the anti- hemorrhoidal potential of the formulation.

Croton oil contains crotonoleic acid, crotonic acid, crotonyl alcohol, 16 kinds of crotonyl alcohol bisester and many kinds of crotonyl alcohol trisester. Also contained in the seed of croton are crotin, cocarcinogen C-3, crotonoside, isoguanine, β-sitosterol, amino acids and many kinds of enzymes. However, the principal component of croton oil possesses multiple drug effects. Croton oil is a stimulant in making inflammatory models, especially in models of skin and mucosal inflammation [19], such as animal models of hemorrhoids, pleuritis, ear edema and uveitis [20].Results of our histological investigation reveals prefect alignment of epithelium oriented in the wall of the rectal canal with no signs of degeneration were observed were observed in group I rats. Signs of hemorrhage and degeneration evidence with sever inflammatory changes were observed in sample belongs to group II rats. The continuity of epithelium with occasional signs of inflammation and degeneration observed sample belong to group III animal. Regular arrangement of columnar epithelium were observed in group IV sample.

5. Conclusion

Therapeutic treatment of hemorrhoids ranges from dietary and lifestyle modification to radical surgery, depending on degree and severity of symptoms. Although surgery is an effective treatment of hemorrhoids, it is reserved for advanced disease and it can be associated with appreciable complication. Currently available therapy for the management of retrograde haemorrhoids are often provides symptomatic relief, where in the higher risk of utilising synthetic agents for long term application will not be advisable. Herbal remedies like Kattu karunai chooranam may grabs the attention of the clinician and researcher in the mean of offering cure for this degenerative disease like haemorrhoids. Results of our study strongly indicates that there was significant decrease in the rectoanal coefficient value observed in Kattu karunai chooranam treated rats at the both the dose levels which reveals the anti- hemorrhoidal potential of the formulation.

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