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A THERAPEUTIC APPROACH TOWARDS PAINFUL AND IRREGULAR MENSES IN RELATION TO PROSTAGLANDINS

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ABSTRACT

The quality of life of adolescents and young adult women are commonly affected by menstrual disorders. Among them painful menses comprises of 87.7% of Indian females of reproductive age group. It has a negative effect on a woman's life. The woman may confine to bed due to severe pain. It refers to the occurrence of painful menstrual cramps of uterine origin. This gynaecological condition has considerable morbidity. The aim of the study is to alleviate the pain during menses by Ayurvedic Therapy which will impart easy, effective and less side effect producing care and can be easily administered on proper counselling and well accepted by the patient. A study was conducted in 75 females of reproductive age group, diagnosed with painful and irregular menses. Patients data were collected by direct history and from the old medical records of the patients, the prescriptions about different modern medical treatment taken for their disease and considering them the patients were registered. To have the idea of complete efficacy, 3 groups were taken for study. A group of oral Guduchyadi Vati, another group of Guduchyadi taila Uttar Basti (i.e Intra uterine instillation) and third as a combined one with both oral and intra uterine instillation. In above three group an experimental analysis was done by assessment of Endometrial Prostaglandins (causative agent of pain) before and after

treatment through Histopathology and Immunohistochemistry with COX 2 antibody so as to see the exact effect of drug on Prostaglandins. The Experimental study on Histology of Endometrium showed the decrease in inflammatory markers before and after treatment but there was significant decrease in markers in group III (oral tablet and intrauterine oil instillation), moderate in group II (only intrauterine oil instillation) and least in group I only oral tablets). In Immunohistochemistry of endometrium before and after treatment, there was significant decrease in COX 2 expression in Group III patients followed by group II and then in group I.

KEYWORDS: painful, irregular menses, endometrium, prostaglandins, COX-2, Ayurveda.

INTRODUCTION

Its rightly said by Sir John Lennon that, "One thing you can't hide is when you're crippled inside". This conveys that 'pain' is such a symptom which cannot be neglected. Sympathy can be charming for sometime, but it does not make up for pain.

One of the commonest problem in women of reproductive age is pain during menses. The initial therapy of choice in patients with presumptive painful menses in Modern system of Medicine are Nonsteroidal anti-inflammatory drugs. But the effect is limited till the tablet is taken. Oral contraceptives and depomedroxyprogesterone acetate are also used in treatment. If there is persistence of pain, then pelvic ultrasonography and referral for laparoscopy is considered to rule out secondary causes. The patients may be rarely advised for hysterectomy as the last choice. Patients of pain during menses may suffer from disruption of social support networks, depression, and anxiety There is an association between painful menses and poor self-rated overall health.[1]

Hence it was the need of time to search an effective treatment for these patients which is easily administered, cost effective and with less side effects. Guduchyadi taila Uttar Basti (intra uterine instillation) and Guduchyadi Vati is said to normalise Vata Dosha[2] (significant cause of pain).

Drugs like Guduchi,[3] Rasna,[4] Bala,[5] Madhuka,[6] Chitrak,[7] Kantakari,[8] Devadaru[9] (the ingredients in tablet and oil) are said to have anti-inflamatory and analgesic properties. Hence the combination of these dravyas might have an effect on Prostaglandins.

A wide variety of cells consist a class of substances named Prostaglandins. The secretory endometrium of patients release excess Prostaglandins PGF2α and PGE2 during painful menses. Spasm of uterine muscles are caused by these prostaglandins during menses, leading to ischeamic pain.[10] The inflammatory response is generated mainly by Prostaglandins. They contribute to the development of the cardinal signs of acute inflammation. In inflammation, PGE_2 is involved in all processes leading to the classic signs of inflammation: redness, swelling and pain.[11] There is increased blood flow into the inflamed tissue through PGE_2-mediated augmentation of arterial dilatation and increased microvascular permeability. $PGF_{2\alpha}$ plays an important role in contraction of uterine smooth muscle and initiation of parturition. These Prostaglandins PGF2α and PGE2 are released in excess amount from secretory endometrium of patients during painful menses which cause uterine muscles spasm, leading to ischeamic pain.

So to authenticate the study, a Premenstrual Endometrial Biopsy was taken before and after treatment in patients of each group for Histopathological changes and also effect on COX-2 Signalling in endometrium by Immunohistochemistry.

Guduchi, Malti, Rasana, Yashtimadhu, Chitraka Moola, Kantakari, Devadaru, Yuthika. These nine dravyas are used in Guduchyadi taila and Vati. Cow's milk, Cow's Urine and tila taila is also used to prepare oil.

Guduchyadi Vati

Drugs 1 part(12 gms each)	=	108gms
Water	=	16 times

1 part of drug and 16 times of water were subjected to agni. When it reduced to ¼, decoction was extracted from the drugs and then a clean decoction again subjected to agni till it became solidified to form tablets. In this way ghanavati was prepared**.**

Mode of Administration

The drug was given orally 2 tablets each of 500mg twice daily for 2 months. Observations were made by assessing the differences in subjective and objective parameters at subsequent follow ups with standard statistical method for final conclusion.

Guduchyadi Taila(Cha. Chi. 30/59-61)

A medicated oil was prepared by taking -

(1) Tila Taila – 750ml

(2) Cow's milk - 1.5ltr

(3) Cow's urine – 1.5 ltr

(4) Paste of each drug (12gm)

Now this mixture was prepared by the standard method of oil preparation and oil thus prepared was used for Experimental trial.

Plan of Study

The subjects included in this study were registered from Outpatient Department of Prasuti Tantra, S.S. Hospital, Banaras Hindu University. The subjects having irregular menses with pain during menses were selected for the study. The subjects were divided into 3 groups for the Experimental study. Each group consisted of 25 patients.

The patients included were with symptoms related to vataja yoni vyapada who were married and under the reproductive age group.

Subjects with any diagnosed uterine organic pathology like uterine fibroid, adenomyosis were excluded from study. Also Subjects with systemic diseases like hypertension, diabetes mellitus or with coagulopathy, anemia, thyroid dysfunction were also excluded. Subjects with malignancy or undiagnosed neoplasm, with history of recent delivery or abortion and patients of genital tuberculosis were excluded from the study.

The subjects were divided in 3 groups

Group I: Subjects were given Guduchyadi Vati 500mg 2 tablets twice a day for 2 months.

Group II: Subjects were given Guduchadi taila Uttar Basti (intrauterine instillation) in 3 sittings after menses for 2 months.

Group III: Subjects were given Guduchyadi Vati for 2 months alongwith Guduchyadi taila Uttar Basti in 3 sittings for 2 months.

Plan of Uttarbasti (IntraUterine Instillation)

Intrauterine medicated oil was given in Ritukala1[12] (after completion of menses preferably on 7^{th}, 8^{th} and 9^{th} day). Patients were called after their menstrual bleeding has been stopped.

Patients were kept nil orally 3 hours prior and after the Uttarabasti procedure. Before starting with the Basti, the needed medicines, instruments and assisting staff was confirmed. Intrauterine procedure needs major aseptic precautions, so all the instruments and oil was autoclaved before use.

Plan for Endometrial Biopsy

Patients were called for Endometrial Biopsy between 22-24th day[13] (Secretory phase) of previous cycle. Proper Counselling was done. All the instruments (Sim's speculum, Anterior Vaginal wall retractor, Vulsellum, Uterine sound, Dilators, Endometrial biopsy curette, gauze pieces, Cut sheets were autoclaved. Assisting staff was confirmed before procedure. The removed tissue was kept in Bouin's solution. The tissue was taken to laboratory, where it was processed for Histopathology and Immunohistochemistry. It was then read microscopically and the diagnosis was made.

Plan for Assessment of Prostaglandins

Endometrial tissue collected for Histology was taken to pathology laboratory and blocks were prepared. A cut section of 2-3µwas taken from block on albumin coated slides. These slides were then stained with Haematoxylin and Eosin stain as per standard method and Histology slides were prepared.

Similar 2-3µ section was taken on Poly-L-Lysine coated slides and after antigen retrieval in Citrate buffer, the slides were treated with COX 2 antibody. Slides were mounted with DPX. Brown ppt. on tissue represented our desired antigen.

Observations

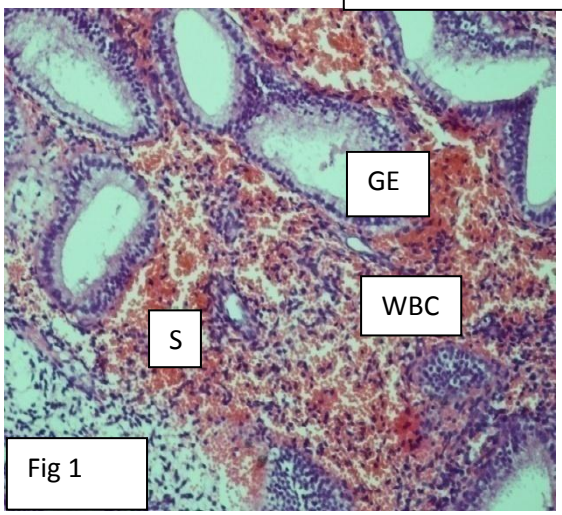
Majority no. of patients in all groups were between 24-29 years of age. In relation with occupation, dietetic status, socioeconomic status all three groups were homogenous without any statistical significance.

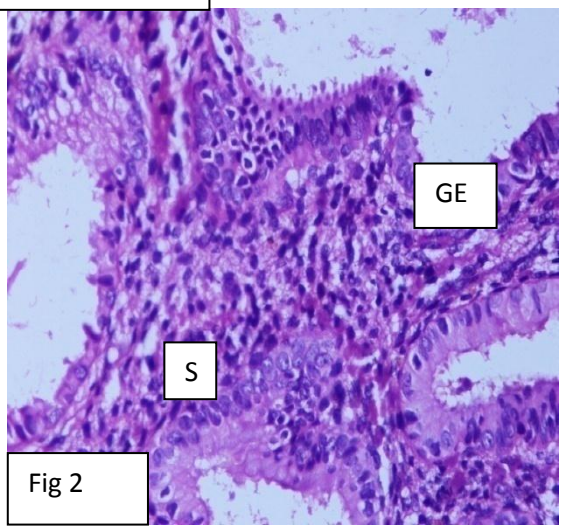
All the subjects negative for HIV, HBSAg, VDRL were taken in study. Alteration in Thyroid Profile is also a cause of irregular menses, so patients with normal thyroid values were registered.

Experimental Observations

Group I

Group I – Oral Guduchyadi Vati



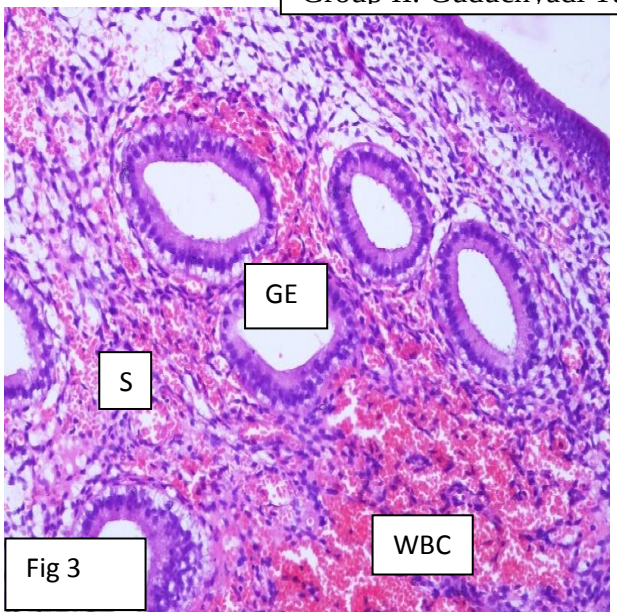


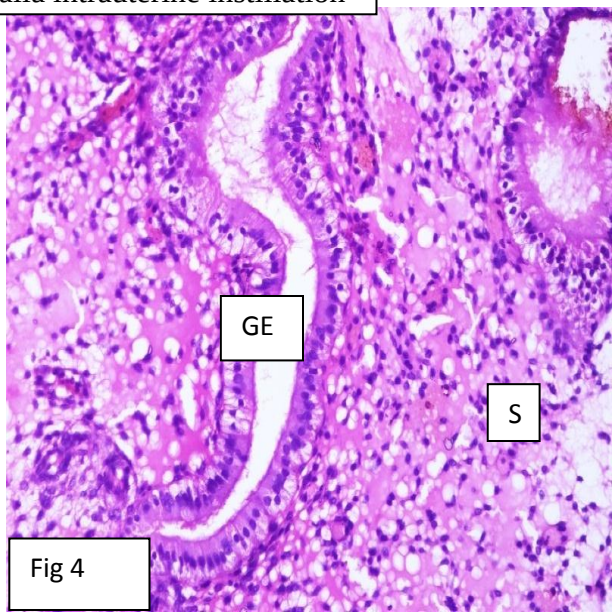
Before Treatment **After Treatment**

The acute phase of inflammation is characterized by the rapid influx of blood granulocytes, typically neutrophils[14] in stroma which can be seen in fig 1. During the resolution of inflammation, granulocytes are eliminated and macrophages and lymphocytes return to normal pre-inflammatory numbers in stroma. These inflammatory markers are reduced in treated patients as evidenced by fig 2. But the endometrium still appears irregular in pattern.

Group II

Group II: Guduchyadi Taila intrauterine instillation

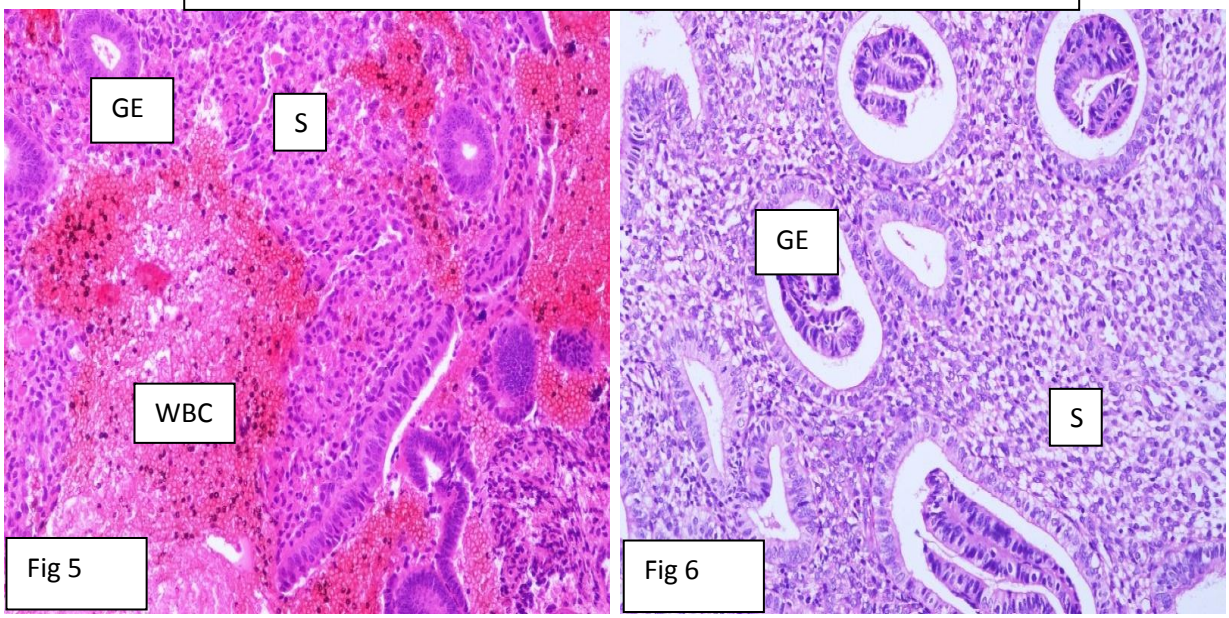




Before Treatment **After Treatment**

The inflammatory markers are reduced in treated patients as evidenced by fig 4 in comparison to fig 3. The pattern of endometrium appears somewhat regular in comparison to fig 3.

Group III Oral Guduchyadi Vati and Intrauterine instillation of Guduchyadi Taila

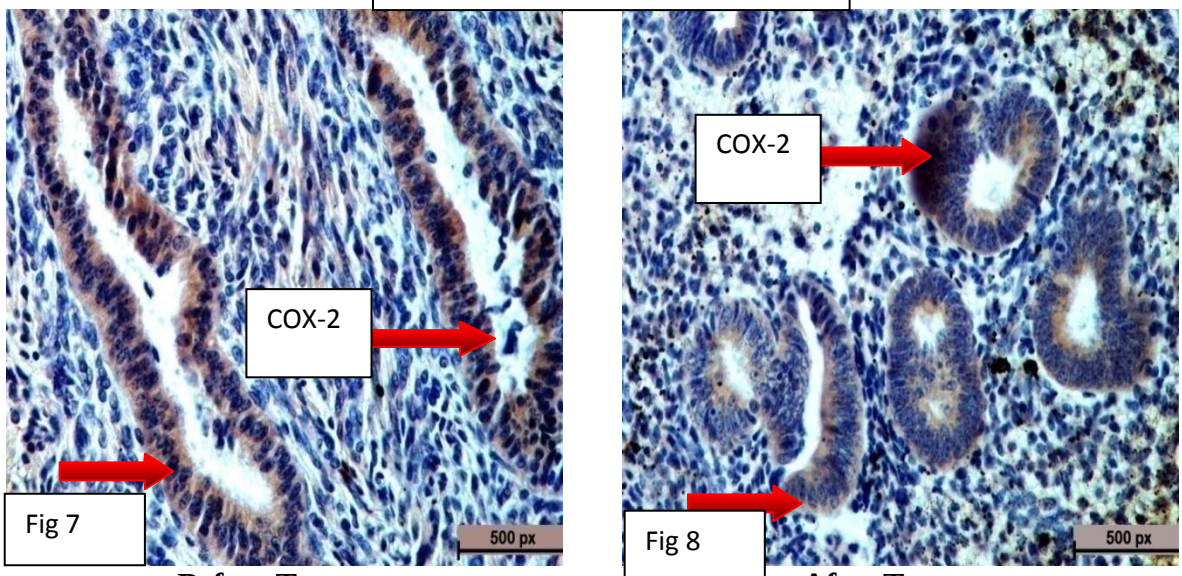


Before Treatment **After Treatment**

The inflammatory markers are significantly reduced in treated patients as evidenced by fig 6 in comparison to fig 5. The pattern of endometrium appears regular like histology of a normal endometrium.

Immunohistochemistry Observations

Group I – Oral Guduchyadi Vati



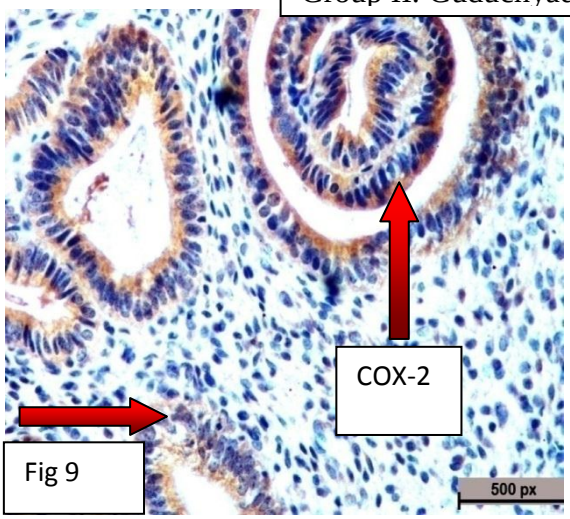
Before Treatment **After Treatment**

The biosynthesis of Prostaglandins is significantly increased in inflamed tissue and they contribute in the development of the cardinal signs of acute inflammation.

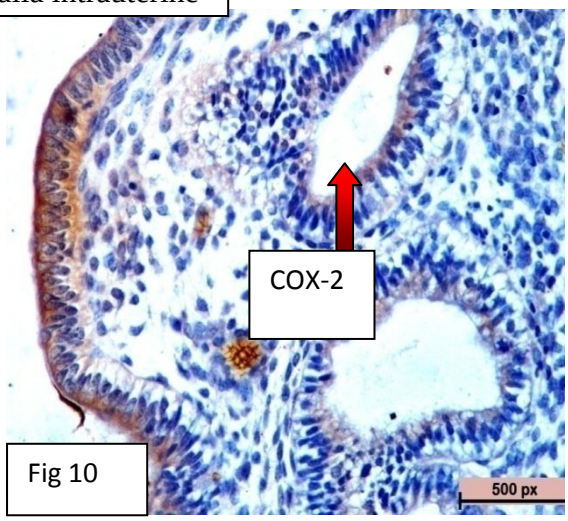
The most important source of prostanoid formation in inflammation is COX-2 which is induced by inflammatory stimuli, hormones and growth factors. Brown precipitate in glandular epithelium shows expression of COX-2.

In Fig 7, the Expression of COX-2 in glandular epithelium is almost same as fig 8 of same patient after treatment indicating no improvement on tissue level.

Group II: Guduchyadi Taila intrauterine



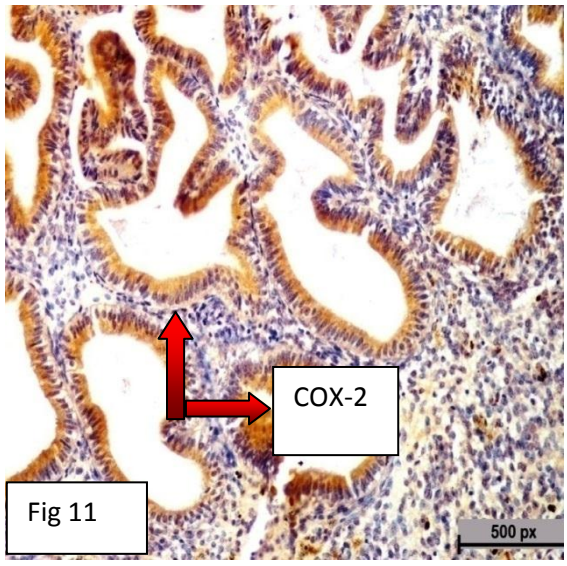
Before Treatment



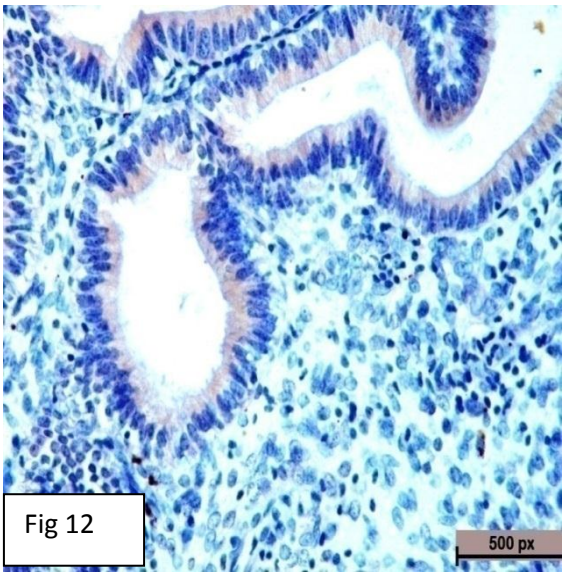
After Treatment

In Fig 8, the Expression of COX-2 in glandular epithelium is moderately reduced in comparison to fig 9 of same patient after treatment.

Group III: Oral Guduchyadi Vati and Intrauterine instillation of Guduchyadi Taila



Before Treatment



After Treatment

In Fig 9, the Expression of COX-2 in glandular epithelium is significantly reduced in comparison to fig 10 of same patient after treatment.

DISCUSSION

The nature's earliest signs of morbidity and one of the commonest presentation seen in medical practise is pain. The equilibrium state of a person is altered through pain. In order to manage such condition there are good number of drugs available in modern medical field but they have potential side effects.[15]

In experimental study related to Histology of endometrium, there was decrease in inflammatory markers in treated patients in all groups, but was significantly evident in Group III endometrium, followed by group II and then group I (Fig.1,2,3,4,5,6). In Group III, the endometrium almost resembled a normal endometrium after treatment.In Immunohistochemistry, the endometrium after treatment in group III showed significant decrease in expression of COX 2, hence Prostaglandins. In group II there was mild improvement but no improvement in patients of Group I (Fig.7,8,9,10,11,12). This clearly says that local treatment with oil alongwith tablet is necessary for reducing pain and proper rejuvenation of endometrium.

CONCLUSION

1) Guduchyadi Vati and Guduchyadi Taila showed beneficial effect in restoration of normal physiology of menstruation, helped to cope up with the minor ailments during menses.
2) 7 constituents (Guduchi, Rasna, Bala, Madhuka, Chitrak, Kantakari Devadaru) are proven anti-inflamatory and analgesic dravyas, hence a combined drug of these constituents has served as a potent anti-inflammatory.
3) The dominant source of prostaglandin formation in inflammation is COX-2. In Immunohistchemistry of all 3 groups, it is clearly evident that there is substantial decrease in COX2 expression after treatment. The effect is best seen in patients treated with both Oral and Uttar Basti, followed by group II and then group I.

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