



Pykure Ointment: A Soothing Solution for Hemorrhoid Relief

Harbans Singh^{1*}, Deepika Sharma²

¹Herbal Body Cure Pvt. Ltd., New Delhi, India;

²Prakhar Group (Regulatory Services & Marketing Consultancies), Mumbai, Maharashtra, India

E-mail: ¹harbansingh278@gmail.com, ²prakharhealthcare@gmail.com

Abstract This study investigates the management of haemorrhoids of poly herbal formulation Pykure Ointment which contains *Achillea Millefolium*, *Calendula officinalis*, *Aloe Barbadensis*, *Azadirachta indica*, *Piper langrum*, *Albizia Labbeck*, *Camphora*, *Curcuma longa*, *Murraya Koenigi*, *Eucalyptus Koenigi*, *Lawsonia Inermis*, *Rosmarinus officinalis*, *Lini Seminalinum*, *Gloriosa Superba*, *Mentha Arvensis*. The formulation Pykure capsule has been found to be an effective drug in anorectal disorders. Pykure Ointment can safely be recommended in bleeding / non bleeding haemorrhoids.

Keywords Pykure Ointment, Haemorrhoids, Management

Introduction

Hemorrhoids are a prevalent ailment that affects the anorectal area, characterized by the symptomatic swelling and downward movement of the typical anal cushions. They have a significant impact on millions of individuals globally and provide a significant medical and social challenge. Various factors have been identified as the causes of hemorrhoid formation, such as constipation and extended periods of straining. The primary observation in haemorrhoidal illness is the aberrant enlargement and deformation of the blood vessels, accompanied by damaging alterations in the connective tissue that supports the anal cushion [1]. Hemorrhoids may exhibit an inflammatory response [2] and an excessive growth of blood vessels [3, 4]. This article initially examined the pathophysiology and clinical context of haemorrhoidal illness, followed by the current methods for non-surgical and operative treatment.

Pathophysiology

The precise pathophysiology behind the development of hemorrhoids remains inadequately comprehended. The belief that hemorrhoids are caused by varicose veins in the anal canal, known as the theory of varicose veins, was once widely accepted. However, it is now considered obsolete as it has been established that hemorrhoids and anorectal varices are separate conditions. Patients with portal hypertension and varices do not experience a higher occurrence of hemorrhoids [5].

Currently, the concept of the sliding anal canal lining is widely acknowledged and embraced [6]. This hypothesis suggests that hemorrhoids occur when the supportive tissues of the anal cushions undergo disintegration or deterioration. Hemorrhoids refer to the abnormal displacement of the anal cushions, resulting in the dilation of veins. This condition is known as a pathological word. There are generally three primary anal cushions positioned in certain areas of the anal canal: the right anterior, right posterior, and left lateral aspects. Additionally, there are several lesser cushions located between these primary cushions. Patients with hemorrhoids exhibit notable pathological alterations in their anal cushions. The observed abnormalities consist of aberrant widening of the veins, formation of blood clots in the blood vessels, degeneration of the collagen fibers and fibroelastic tissues, as well as



deformation and tearing of the muscle beneath the anal lining. Furthermore, haemorrhoidal specimens have shown a significant inflammatory response that affects the vascular wall and the surrounding connective tissue. This reaction is accompanied by mucosal ulceration, ischemia, and thrombosis [2].

Multiple enzymes and mediators that contribute to the breakdown of the supportive tissues in the anal cushions have been examined. Among these, matrix metalloproteinase (MMP), a zinc-dependent protease, is a very potent enzyme that can degrade extracellular proteins such as elastin, fibronectin, and collagen. The expression of MMP-9 was observed to be increased in hemorrhoids, concomitant with the degradation of elastic fibers [8]. Thrombin, plasmin, and other proteinases activate MMP-2 and MMP-9, leading to the disruption of the capillary bed and the stimulation of angioproliferative activity of transforming growth factor β (TGF- β) [9].

A recent study discovered a rise in the number of small blood vessels in haemorrhoidal tissue, indicating that the development of new blood vessels may be a significant factor in haemorrhoidal disease. In 2004, Chung et al [4] discovered that endoglin (CD105), a receptor for TGF- β and a marker for the growth of new blood vessels, was present in over 50% of haemorrhoidal tissue samples, while it was absent in samples taken from the normal anorectal mucosa. This marker was conspicuously detected in venules with a diameter exceeding 100 μm . In addition, these investigators discovered that there was an increase in the number of small blood vessels in haemorrhoidal tissue, particularly when blood clot formation and the presence of growth factors that promote the creation of blood vessels in the connective tissue were observed. Han et al [8] also found evidence of increased expression of angiogenesis-related proteins, such as VEGF, in hemorrhoids.

Aigner et al [3, 10] discovered that in patients with hemorrhoids, the terminal branches of the superior rectal artery that supply the anal cushion have a noticeably larger diameter, increased blood flow, higher peak velocity, and acceleration velocity compared to those of healthy volunteers. This finding pertains to the study of morphology and hemodynamics of the anal cushions and hemorrhoids. Furthermore, there was a strong correlation between the severity of hemorrhoids and both the enlargement of the arteries and the rise in blood flow. The aberrant findings persisted even after the surgical removal of the hemorrhoids, thereby proving the link between hyper vascularization and the formation of hemorrhoids.

In their study, Aigner et al [3] utilized an immunohistochemical method to discover a sphincter-like structure in normal anorectal specimens. This structure was found in the subepithelial region of the anal transitional zone and consisted of a thickened tunica medium with 5-15 layers of smooth muscle cells, positioned between the vascular plexus. In contrast to typical examples, hemorrhoids have significantly enlarged, delicate blood vessels inside the submucosal arteriovenous plexus, with a lack of or minimal sphincter-like constriction on the vessels. The research determined that a smooth muscle sphincter located in the arteriovenous plexus aids in decreasing the flow of blood into the arteries, hence promoting efficient drainage of blood through the veins. Aigner et al [3] subsequently suggested that if this system is disrupted, excessive blood flow to the arteriovenous plexus will result in the development of hemorrhoids.

The presence of aberrant venous dilatation and distortion in hemorrhoids suggests that dysregulation of vascular tone may contribute to the development of hemorrhoids. Vascular smooth muscle is primarily controlled by the autonomic nervous system, as well as hormones, cytokines, and the endothelium that covers it. The presence of an unequal distribution between substances that relax the endothelium (such as nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factor) and substances that constrict the endothelium (such as reactive oxygen radicals and endothelin) leads to various vascular disorders [11]. The enzyme nitric oxide synthase, responsible for the production of nitric oxide from L-arginine, was found to considerably increase in cases with hemorrhoids [8].

Observations have been made regarding several physiological alterations in the anal canal of individuals suffering from hemorrhoids. Sun et al [12] discovered that the resting anal pressure in individuals with non-prolapsing or prolapsing hemorrhoids was much greater than in healthy individuals. However, there was no notable alteration in the thickness of the internal sphincter. Ho et al [13] conducted anorectal physiological investigations on 24 patients with prolapsed hemorrhoids and compared the findings with those of 13 normal volunteers who were matched in terms of sex and age. Prior to the procedure, individuals with hemorrhoids exhibited markedly elevated resting anal pressures, reduced rectal compliance, and increased perineal descent. The aberrations seen returned to the normal



range after 3 months after undergoing a hemorrhoidectomy, indicating that these physiological changes are likely to be a consequence rather than the underlying cause of haemorrhoidal illness.

Achillea millefolium is a significant botanical specimen that possesses various pharmaceutical applications. *Achillea millefolium* has been utilized for centuries to remedy a range of ailments, such as malaria, hepatitis, and jaundice. *Achillea millefolium* is frequently prescribed for the treatment of hepatic disorders. Additionally, it serves as an anti-inflammatory agent and possesses hepatoprotective properties. Supplemental use of *A. millefolium* is deemed safe. Additionally, it possesses antihepatotoxic properties. It is recommended for use as an astringent. It is indicated for the treatment of hemorrhoids, headache, bleeding disorders, bruises, cough, influenza, pneumonia, kidney stones, high blood pressure, menstrual disorders, fever, rheumatoid arthritis, gout, osteoarthritis, hemorrhagic disorders, chicken pox, cystitis, diabetes mellitus, indigestion, dyspepsia, eczema, psoriasis, and boils [14, 15].

Calendula officinalis L. (Marigold) is widely recognized worldwide for its medicinal significance. The substance exhibits numerous significant biological functions, including promoting wound healing, stimulating the immune system, inducing muscle contractions and relaxation, protecting the liver, preventing genetic damage and counteracting genetic damage, inhibiting the enzyme amylase, reducing inflammation and swelling, combating bacterial and fungal infections, acting as an antioxidant, regulating blood sugar levels, inhibiting HIV and cancer growth, protecting the kidneys, preventing inflammation of the mouth and throat, and providing protection for the stomach without causing toxicity [16, 17].

The Aloe vera plant is renowned in history for its ability to heal abrasions and burns when applied topically. It is also valued by the cosmetic industry for its emollient and moisturizing properties. The latex, which exudes from the plant when incised, is topically administered to the skin area. Alternatively, the leaf can be longitudinally divided and either placed directly on the skin or the inner gel can be extracted and applied as an ointment. Aloe vera is found in a wide variety of skincare products, including moisturizers, creams for the face and hands, cleansers, soaps, suntan lotions, shampoos, hair tonics, shaving products, bath products, makeup, fragrance products, and baby lotions and wipes. Aloe vera topical preparations have been utilized for the treatment of frostbite, burns, radiation dermatitis, ulcers, psoriasis, skin infections, and wounds [18-24].

Throughout centuries, every component of *Azadirachta indica* has been utilized for medicinal purposes. Due to its medicinal properties, it has been utilized in Ayurvedic medicine for over 4000 years. The earliest Sanskrit medical texts mention the advantageous properties of *Azadirachta indica*'s fruits, seeds, oil, leaves, roots, and bark. Both have been utilized in Indian Ayurvedic and Unani medicine, and are currently employed in the pharmaceutical and cosmetics sectors. *Azadirachta indica* oil has various applications in pest management, cosmetics, pharmaceuticals, and other fields. *Azadirachta indica* seed cake serves as a natural fertilizer and insecticide. *Azadirachta indica* leaves possess multiple benefits such as alleviating chickenpox, enhancing the body's immune system, reducing malaria-induced fever, treating various foot fungi, combating termites, and relieving neuromuscular pains. *Azadirachta indica* bark and roots have multiple applications, including the management of fleas and ticks on pets, the treatment of various skin infections such as acne, psoriasis, scabies, and eczema. Additionally, *Azadirachta indica* is used in the treatment of diabetes, AIDS, cancer, heart disease, herpes, allergies, ulcers, hepatitis, and various other diseases. *Azadirachta indica* is widely utilized in various Health and Personal Care items, including eczema cream, antiseptic cream, shampoo, hair oils, toothpaste, tea, vegetarian capsules, powders, soaps, insect repellent (spray and lotion), and candles, among others [25, 26].

Albizia lebbek (shirish) is considered a broad-spectrum and widely applicable remedy according to the Charak Samhita. The bark of this plant is utilized as an ointment, known as lepa, for treating skin diseases such as erysipelas. Every component of the plants is recommended for the therapeutic management of snake bites. Panchshirish Agad, a preparation of 5 parts of this is recommended for the treatment of all type of poisoning. Amritaghrita, Gandhasti agad, and Mahagandhasti agad are additional commonly prepared forms of *Albizia lebbek*, which have been utilized to treat various types of poisoning. The text is called "Charak Samhita". The root is utilized in the treatment of hemicranias through the administration of nasya. It is also prescribed as an anthelmintic and for treating rat bites. The leaves possess therapeutic properties for ophthalmic ailments. The text is called "Susruta Samhita". The root possesses astringent properties and is recommended for the treatment of



ophthalmia. The bark possesses antihelminthic properties and provides relief from toothache. Additionally, it strengthens the gums and teeth. It is utilized in the treatment of leprosy, deafness, boils, scabies, syphilis, paralysis, and weakness. Leaves are beneficial for individuals suffering from night blindness. The flowers possess aphrodisiac and emollient properties, and they also act as a maturant. Additionally, their fragrance is beneficial for treating hemicranias. The seeds are aphrodisiac, brain tonic, used for gonorrhea and tuberculous glands; the oil is applied topically in leukoderma. The bark and seeds of this plant are commonly used in IndoChina for their astringent properties. They are often recommended as a treatment for diarrhea, dysentery, and piles. In Madagascar, leaves are administered as a remedy for syphilis. The plant is considered the most potent alexipharmic and every part of it is prescribed for the treatment of bites and stings from venomous animals [27-29].

Curcuma longa (Turmeric) is widely utilized as a spice, food preservative, and coloring agent in India, China, and Southeast Asia. Powder of *Curcuma longa* is primarily recognized as a key component in the production of curry spice, and it imparts a vibrant yellow hue to ballpark mustard. In addition to its culinary applications, turmeric has been extensively utilized in traditional medicine worldwide. Curcumin, which is the primary yellow bioactive compound found in turmeric, has been demonstrated to possess a broad range of biological effects. These activities encompass the anti-inflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic, antibacterial, antifungal, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, hypotensive, and hypocholesteremic properties of the substance. For traditional Ayurvedics, turmeric plant was an excellent natural antiseptic, disinfectant, anti-inflammatory, and analgesic, while at the same time the plant has been often used to aid digestion, to improve intestinal flora, and to treat skin irritations [30-32].

Murraya koenigii Linn commonly known as Meethi neem or Curry Tree. The leaves have traditionally been employed as a spice in curry and other edible dishes. The leaves have traditionally been used as an antiemetic, antidiarrheal, febrifuge, and blood purifier. The entire plant is regarded as a tonic and stomachic. The leaves have been discovered to possess efficacy as an antioxidant, antidiabetic, antibacterial, antihypertensive, cytotoxic, and in the treatment of bronchial respiratory difficulties [33, 34].

Eucalyptus is widely cultivated for the purpose of producing pulp, plywood, and solid wood. Nevertheless, the aromatic oil extracted from its leaves exhibits remarkable and diverse biological properties, such as antimicrobial, antiseptic, antioxidant, chemotherapy, treatment of respiratory and gastrointestinal disorders, wound healing, insecticidal and insect repellent effects, herbicidal and acaricidal properties, as well as its use in perfumes, soap making, and grease removal [35].

Lawsonia inermis L., a highly branched and smooth shrub or small tree, is primarily grown for its leaves. However, the stem bark, roots, flowers, and seeds of this plant have also been utilized in traditional medicine. The plant has been documented to possess analgesic, hypoglycemic, hepatoprotective, immunostimulant, anti-inflammatory, antibacterial, antimicrobial, antifungal, antiviral, antiparasitic, antitrypanosomal, antidermatophytic, antioxidant, antifertility, tuberculostatic, and anticancer properties [36].

Rosmarinus officinalis L. (Rosemary) has extensive applications in both cooking for flavor enhancement, as well as in traditional medicine, where it is highly regarded for its medicinal properties in preventing and treating colds, rheumatism, and muscular and joint pain [37, 38]. Currently, this plant is widely recognized as a prominent source of natural bioactive compounds. It possesses diverse pharmacological properties, including antibacterial [39], antidiabetic [40], anti-inflammatory [41, 42], antitumor [43–45], and antioxidant [46] activities, among others [47].

Gloriosa superba possesses medicinal properties that make it effective in treating various ailments such as arthritis, gout, rheumatism, inflammation, ulcers, bleeding piles, skin diseases, leprosy, impotency, and snakebites. The entire plant of *G. superba* exhibits various biological activities, including antioxidant, antibacterial, antimicrobial, and anthelmintic properties. In addition, *G. superba* is an effective abortifacient, inducing the expulsion of the fetus from the uterus [48, 49].

Mentha arvensis Linn. family Lamiaceae, it is used as a food seasoner, household remedy, and industrial purposes it is traditionally used in hypertension and in patients with ischemic heart disease. The leaf extract is administered to treat diarrhea and dysentery. The leaves medicinally used for stomach problems and allergy. Additionally, it is



employed for the management of hepatic and splenic disorders, as well as asthma and jaundice. The decoction of these leaves is employed for treating indigestion, rheumatic pains, arthritis, and as a remedy for inflamed joints. Menthol derived from its essential oil is used in pharmaceutical, perfumery, and food industries. Menthol possesses antiseptic, carminative, refrigerant, stimulant, and diuretic properties, making it effective against skin infections [50].

Composition

Each 1gm Pykure Ointment contains extract following ingredients

Achillea Millefolium:	1.50mg	Murraya Koenigi:	1.70mg
Calenduls officinalis:	2.00mg	Eucalyptus Koenigi:	1.20mg
Aloe Barbadensis:	1.30mg	Lawsonia Inermis:	1.30mg
Azadirachta indica:	3.00mg	Rosmarinus officinalis:	1.50mg
Piper langram:	1.50mg	Lini Seminalinum:	2.00mg
Albizzia Labbeck:	1.20mg	Gloriosa Superba:	1.20mg
Camphoria:	1.50mg.	Mentha Arvensis:	1.50mg
Curcuma longa:	2.60mg	Petroleum Jelly (BASE):	75.00mg

Aim & Objective

The aim of this study was to evaluate therapeutic value of Pykure Ointment in the patients of Ano-rectal disorders. Present study was undertaken for 22 cases of Haemorrhoids.

Material & Method

22 Patients of Haemorrhoidal disorder were registered for management of the particular condition with Pykure Capsule, Pykure Ointment and Kabzkure Powder. Out of 22 patients, 20 cases completed the full treatment schedule i.e. 90 days while remaining 2 cases left the treatment. However, clinical pattern was studied in all 22 cases for incidence of age, sex, occupation, economical status, educational status, social status and symptoms of piles disorders.

Selection of cases

All patients selected for study were interrogated and detailed history was recorded on prescribed case history sheet. All patients were thoroughly examined and findings were also recorded for establishing the final diagnosis. Routine examination of blood etc were also done, in addition to the observation of subjective features, clinically. All patients included in clinical study were carefully examined physically and records were maintained with clinical history. The individuals who have symptoms of ano-rectal disorders with or without rectal bleeding were subjected to clinical trial.

Method of Drug Administration

Pykure Ointment: suggested to apply before and after passing stool with the help of Nozzle or by finger tips. Each case was followed up at the interval of 15 days for 90 days.

Clinical Pattern:

Present study consists of total 22 registered cases, out of which 2 cases did not complete full course of treatment. So clinical pattern will be discussed on 22 cases, however, results will be analyzed on observations of findings of 20 cases.

Age Incidence:

Patients of present study were from 20 to 60 years of age. Details are presented in Table 1.

Table 1: The incidence of different Age Group



S. No.	Age Group (In Years)	Number of Patients	Percentage
1	20-35 Years	7	31.8%
2	36-50 Years	7	31.8%
3	51 and above	8	36.4%
	Total	22	100.0%

Sex Incidence:

Patients of both sexes were registered for present study. The sex group is given in Table 2

Table 2: The incidence of sex

S. No.	Sex	Number of Patients	Percentage
1	Male	15	68.20%
2	Female	7	31.80%
	Total	22	100.00%

Occupational Incidence:

In present study the patients belonging to various occupations were included and shown in Table 3.

Table 3: The breakup of Piles in patients of different Occupation

S. No.	Occupation	Number of Patients	Percentage
1	Service	7	31.80%
2	Housewife	5	22.70%
3	Businessman	4	18.10%
4	Student	2	9.10%
5	Cultivator	2	9.10%
6	Retired	2	9.10%
	Total	22	100.00%

Educational Status

When educational status shows patients of both literate and illiterate group were found in the study as given in Table 4.

Table 4: The incidence of Educational status

S. No	Occupation	Number of Patients	Percentage
1	Service	7	31.80%
2	Housewife	5	22.70%
3	Businessman	4	18.10%
4	Student	2	9.10%
5	Cultivator	2	9.10%
6	Retired	2	9.10%
	Total	22	100.00%

Rural and Urban incidence

This study includes the patients from Rural & Urban area as shown in Table 5.

Table 5: The incidence of Rural and Urban status



S. No	Occupation	Number of Patients	Percentage
1	Service	7	31.80%
2	Housewife	5	22.70%
3	Businessman	4	18.10%
4	Student	2	9.10%
5	Cultivator	2	9.10%
6	Retired	2	9.10%
	Total	22	100.00%

Incidence of Internal and External Hemorrhoids

Patients included in this study had both types of hemorrhoids which are presented in Table 6.

Table 6: The incidence of Type of Haemorrhoides

S. No	Type of Hemorrhoids	Number of Patients	Percentage
1	Internal Hemorrhoids	11	50.0%
2	External Hemorrhoids	6	27.3%
	Both	5	22.7%
	Total	22	100.00%

Other Types of Ano-rectal Disorders

Patients included in this study found to have different types of ano-rectal disorders as presented in Table 7.

Table 7: The different associated Ano-rectal Disorders in 22 patients of Haemorrhoids

S. No	Type of Anorectal disorders	Number of Patients
1	Hemorrhoids	11
2	Fistula in Ano	2
	Fisture in Ano	7
	Fistula c Fisture	2

Results and Observation

In this study 22 patients of haemorrhoids were included, out of which 2 patients discontinued and 20 cases had completed the treatment schedule of 90 days. Patients were observed in terms of subjective criteria before treatment, during treatment and after treatment.

The response of treatment on subjective criteria and observed before and after treatment as presented in Table No: 11.

Table 11: The response of treatment on subjective features of Ano-rectal disorders

S. No	Symptoms	No. of Patients Before treatment	No. of Patients After treatment			Percentage
			After 1 Month	After 2 Month	After 3 Month	
1	Pain	15	15	10	nil off & 04	100%
2	Bleeding	19	7	8	nil off & 04	78%
3	Pruritus Anii	2	2	nil	2	100%
4	Prolapse Pile mass	5	3	2	4	40%
5	Constipation	20	11	5	2	81.80%
6	Mucous discharge	8	2	4		75%

It is revealed from above table that more than 80% of relief was observed in symptoms like pain in rectum, rectal pruritus and constipation. More than 65% of relief was observed in symptoms like rectal bleeding, rectal prolapse and itching.



Conclusion

The formulation Pykure Ointment has been found to be an effective formulation in anorectal disorders. The result in the trial group has shown encouraging results after 6 weeks of treatment. After 90 days of treatment along with the improvements of the subjective criteria's significant response was also noticed. The active bleeding was found to be absolutely control by 8 weeks in 79% of the cases while 21% cases continued bleeding off and on and the size of pile mass was found to be reduced. Hence, Pykure Ointment can safely be recommended in bleeding / non bleeding haemorrhoids.

Acknowledgement

We are thankful to Herbal Body Care organization (Chhatwal Pharmaceuticals) for arranging the trial drug and necessary support for conducting the study. We are thankful to Mr. A. S. Pandey for his cooperation in the present study. With the results we feel study in larger subjects with long term follow up will be if presented with additional advantage of this combination in patients suffering from various degrees of Haemorrhoids, will be more authentic and paper may be presented in any Anorectal disease conference.

References

- [1]. Loder PB, Kamm MA, Nicholls RJ, Phillips RK. Haemorrhoids: pathology, pathophysiology and aetiology. *Br J Surg.* 1994; 81:946–954.
- [2]. Morgado PJ, Suárez JA, Gómez LG, Morgado PJ. Histoclinical basis for a new classification of hemorrhoidal disease. *Dis Colon Rectum.* 1988; 31:474–480.
- [3]. Aigner F, Gruber H, Conrad F, Eder J, Wedel T, Zelger B, Engelhardt V, Lametschwandtner A, Wienert V, Böhrler U, et al. Revised morphology and hemodynamics of the anorectal vascular plexus: impact on the course of hemorrhoidal disease. *Int J Colorectal Dis.* 2009; 24:105–113.
- [4]. Chung YC, Hou YC, Pan AC. Endoglin (CD105) expression in the development of haemorrhoids. *Eur J Clin Invest.* 2004; 34:107–112.
- [5]. Goenka MK, Kochhar R, Nagi B, Mehta SK. Rectosigmoid varices and other mucosal changes in patients with portal hypertension. *Am J Gastroenterol.* 1991; 86:1185–1189.
- [6]. Thomson WH. The nature of haemorrhoids. *Br J Surg.* 1975; 62:542–552.
- [7]. Lohsiriwat V. (2012). Hemorrhoids: from basic pathophysiology to clinical management. *World journal of gastroenterology*, 18(17), 2009–2017. <https://doi.org/10.3748/wjg.v18.i17.2009>.
- [8]. Han W, Wang ZJ, Zhao B, Yang XQ, Wang D, Wang JP, Tang XY, Zhao F, Hung YT. [Pathologic change of elastic fibers with difference of microvessel density and expression of angiogenesis-related proteins in internal hemorrhoid tissues] *Zhonghua Weichang Waike Zazhi.* 2005; 8:56–59.
- [9]. Yoon SO, Park SJ, Yun CH, Chung AS. Roles of matrix metalloproteinases in tumor metastasis and angiogenesis. *J Biochem Mol Biol.* 2003; 36:128–137.
- [10]. Aigner F, Bodner G, Gruber H, Conrad F, Fritsch H, Margreiter R, Bonatti H. The vascular nature of hemorrhoids. *J Gastrointest Surg.* 2006; 10:1044–1050.
- [11]. Stankevicius E, Kevelaitis E, Vainorius E, Simonsen U. [Role of nitric oxide and other endothelium-derived factors] *Medicina (Kaunas)* 2003; 39:333–341.
- [12]. Sun WM, Peck RJ, Shorthouse AJ, Read NW. Haemorrhoids are associated not with hypertrophy of the internal anal sphincter, but with hypertension of the anal cushions. *Br J Surg.* 1992; 79:592–594.
- [13]. Ho YH, Seow-Choen F, Goh HS. Haemorrhoidectomy and disordered rectal and anal physiology in patients with prolapsed haemorrhoids. *Br J Surg.* 1995; 82:596–598.
- [14]. Akram, M. (2013). Minireview on *Achillea millefolium* Linn. *The Journal of membrane biology*, 246(9), 661-663.
- [15]. Benedek, B., & Kopp, B. (2007). *Achillea millefolium* L. sl revisited: recent findings confirm the traditional use. *Wiener Medizinische Wochenschrift* (1946), 157(13-14), 312-314.



- [16]. Jan, N., Andrabi, K. I., & John, R. (2017, December). *Calendula officinalis*-an important medicinal plant with potential biological properties. In Proc. Indian Natl. Sci. Acad (Vol. 83, No. 4, pp. 769-787).
- [17]. AshwlayanVD, K. A., & Verma, M. (2018). Therapeutic potential of *Calendula officinalis*. *Pharm Pharmacol Int J*, 6(2), 149-155.
- [18]. Miller MB, Koltai PJ. Treatment of experimental frostbite with pentoxifylline and Aloe vera cream. *Arch Otolaryngol Head Neck Surg* 1995;121:678–680.
- [19]. Somboonwong J, Thanamitramanee S, Jariyapongskul A, Patumraj S. Therapeutic effects of Aloe vera on cutaneous microcirculation and wound healing in second degree burn model in rats. *J Med Assoc Thai* 2000;83:417–425.
- [20]. Kaufman T, Kalderon N, Ullmann Y, Berger J. Aloe vera gel hindered wound healing of experimental second-degree burns: a quantitative controlled study. *J Burn Care Rehabil* 1988;9:156–159.
- [21]. Thomas DR, Goode PS, LaMaster K, Tennyson T. Acemannan hydrogel dressing versus saline dressing for pressure ulcers. A randomized, controlled trial. *Adv Wound Care* 1998;11:273–276.
- [22]. Seyger MM, van de Kerkhof PC, van Vlijmen-Willems IM, de Bakker ES, Zwiers F, de Jong EM. The efficacy of a new topical treatment for psoriasis: Mirak. *J Eur Acad Dermatol Venereol* 1998;11:13–18.
- [23]. Roesler J, Steinmuller C, Kiderlen A, Emmendorffer A, Wagner H, LohmannMatthes ML. Application of purified polysaccharides from cell cultures of the plant *Echinacea purpurea* to mice mediates protection against systemic infections with *Listeria monocytogenes* and *Candida albicans*. *Int J Immunopharmacol* 1991;13:27–37
- [24]. Gallagher J, Gray M. Is aloe vera effective for healing chronic wounds? *J Wound Ostomy Continence Nurs* 2003;30:68–71.
- [25]. Hashmat, I., Azad, H., & Ahmed, A. (2012). *Neem (Azadirachta indica A. Juss)*-A nature's drugstore: an overview. *Int Res J Biol Sci*, 1(6), 76-9.
- [26]. Brototi B., and Kaplay R.D., *Azadirachta indica (Neem): It's Economic utility and chances for commercial planned plantation in Nanded District*, *Int. J. Pharma*, 1(2), 100-104 (2011)
- [27]. Mishra, S. S., Gothecha, V. K., & Sharma, A. (2010). *Albizia lebbeck: a short review*. *Journal of herbal medicine and toxicology*, 4(2), 9-15.
- [28]. Kirtikar K.R., Basu B.D., Revised by Blatter, Caius, Mhasker, *Indian Medicinal Plants*;4:1311,(2000)
- [29]. Kumar, A., Saluja, A. K., Shah, U. D., & Mayavanshi, A. V. (2007). Pharmacological potential of *Albizia lebbeck: a review*. *Pharmacognosy Reviews*, 1(1), 171-174.
- [30]. Verma, R. K., Kumari, P., Maurya, R. K., Kumar, V., Verma, R. B., & Singh, R. K. (2018). Medicinal properties of turmeric (*Curcuma longa L.*): A review. *Int. J. Chem. Stud*, 6(4), 1354-1357.
- [31]. Apisariyakul A, Vanittanakom N, Buddhasukh D. Antifungal activity of turmeric oil extracted from *Curcuma longa* (Zingiberaceae). *J Ethnopharmacol*. 1995; 49:163-169.
- [32]. Chandra D, Gupta SS. Antiinflammatory and antiarthritic activity of volatile oil of *Curcuma longa* (Haldi). *Indian J. Med. Res.* 1972; 60:138-142.
- [33]. Ajay, S., Rahul, S., Sumit, G., Paras, M., Mishra, A., & Gaurav, A. (2011). Comprehensive review: *Murraya koenigii* Linn. *Asian J Pharm Life Sci*, 2231, 4423.
- [34]. Goel, A., Sharma, A., & Kulshrestha, S. (2020). A phytopharmacological review on *Murraya koenigii*: an important medicinal plant. *Int J Pharm Sci Rev Res*, 62(2), 113-9.
- [35]. Dhakad, A. K., Pandey, V. V., Beg, S., Rawat, J. M., & Singh, A. (2018). Biological, medicinal and toxicological significance of *Eucalyptus* leaf essential oil: a review. *Journal of the Science of Food and Agriculture*, 98(3), 833-848.
- [36]. Chaudhary, G., Goyal, S., & Poonia, P. (2010). *Lawsonia inermis* Linnaeus: a phytopharmacological review. *Int J Pharm Sci Drug Res*, 2(2), 91-8.
- [37]. Zhang Y, Adalakun TA, Qu L et al. New terpenoid glycosides obtained from *Rosmarinus officinalis L.* aerial parts. *Fitoterapia*. 99, 78–85 (2014).
- [38]. Calvo MI, Akerreta S, Cavero RY. Pharmaceutical ethnobotany in the Riverside of Navarra (Iberian Peninsula). *J. Ethnopharmacol*. 135(1), 22–33 (2011).



- [39]. Bozin B, Mimica-Dukic N, Samojlik I, Jovin E. Antimicrobial and antioxidant properties of rosemary and sage (*Rosmarinus officinalis* L. and *Salvia officinalis* L., Lamiaceae) essential oils. *J. Agric. Food Chem.* 55(19), 7879–7885 (2007).
- [40]. Bakirel T, Bakirel U, Keleş OU, Ulgen SG, Yardibi H. In vivo assessment of antidiabetic and antioxidant activities of rosemary (*Rosmarinus officinalis*) in alloxan-diabetic rabbits. *J. Ethnopharmacol.* 116(1), 64–73 (2008).
- [41]. Yu M-H, Choi J-H, Chae I-G et al. Suppression of LPS-induced inflammatory activities by *Rosmarinus officinalis* L. *Food Chem.* 136(2), 1047–1054 (2013).
- [42]. Takaki I, Bersani-Amado LE, Vendruscolo A et al. Anti-inflammatory and antinociceptive effects of *Rosmarinus officinalis* L. essential oil in experimental animal models. *J. Med. Food.* 11(4), 741–746 (2008).
- [43]. Cheung S, Tai J. Anti-proliferative and antioxidant properties of rosemary *Rosmarinus officinalis*. *Oncol. Rep.* 17(6), 1525–1531 (2007).
- [44]. Tai J, Cheung S, Wu M, Hasman D. Antiproliferation effect of rosemary (*Rosmarinus officinalis*) on human ovarian cancer cells in vitro. *Phytomedicine* 19(5), 436–443 (2012).
- [45]. Yesil-Celiktas O, Sevimli C, Bedir E, Vardar-Sukan F. Inhibitory effects of rosemary extracts, carnosic acid and rosmarinic acid on the growth of various human cancer cell lines. *Plant foods Hum. Nutr.* 65(2), 158–163 (2010).
- [46]. Pérez-Fons L, Garzón MT, Micol V. Relationship between the antioxidant capacity and effect of rosemary (*Rosmarinus officinalis* L.) polyphenols on membrane phospholipid order. *J. Agric. Food Chem.* 58(1), 161–171 (2010).
- [47]. Andrade, J. M., Faustino, C., Garcia, C., Ladeiras, D., Reis, C. P., & Rijo, P. (2018). *Rosmarinus officinalis* L.: an update review of its phytochemistry and biological activity. *Future science OA*, 4(4), FSO283.
- [48]. Jana, S., & Shekhawat, G. S. (2011). Critical review on medicinally potent plant species: *Gloriosa superba*. *Fitoterapia*, 82(3), 293-301.
- [49]. Ashokkumar, K. (2015). *Gloriosa superba* (L.): A brief review of its phytochemical properties and pharmacology. *International Journal of Pharmacognosy and Phytochemical Research*, 7(6), 1190-1193.
- [50]. Thawkar, B. S. (2016). Phytochemical and pharmacological review of *Mentha arvensis*. *International Journal of Green Pharmacy (IJGP)*, 10(2).

