

LUBANOID - A NEW NATURAL TOPICAL FOR ANAL FISSURE**Dr. Luay Rashan¹, Dr. Mohammed Rishan¹ and Dr. Rafie Hamidpour*^{1,2}**¹Biodiversity Center, Medicinal Plants Division, University of Dhofar OMAN.²Department of Herbal Medicine, Pars Bioscience Research Center, Leawood, Kansas, United States.***Corresponding Author: Dr. Rafie Hamidpour**

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ABSTRACT

An anal fissure is a small tear in the thin, moist tissue (mucosa) that lines the anus. An anal fissure may occur when you pass hard or large stools during a bowel movement or frequent diarrhea can also tear the skin around the anus. Anal fissures typically cause pain and bleeding with bowel movements. You also may experience spasms in the ring of muscle at the end of the anus. Anal fissures are very common in young infants but can affect people of any age and it is often seen in infants and young children since constipation is a common problem in these age groups. Other common causes include; straining during childbirth or bowel movements, inflammatory bowel disease, such as Crohn's disease, decreased blood flow to the anorectal area overly tight or spastic anal sphincter muscles. In rare cases, an anal fissure may develop due to anal cancer, HIV, tuberculosis, syphilis and herpes. Anal fissures affect males and females equally; however, an anterior fissure is more likely to develop in women (25%) than in men (8%). Although anal fissures are the most common cause of rectal bleeding in infants, they are primarily seen in young adults. Eighty-seven percent of people with a chronic anal fissure are between the ages of 20 and 60 years. The incidence of anal fissure is around 1 in 350 adults. Anal fissures in children may indicate sexual abuse. Most anal fissures get better with simple treatments, such as increased fiber intake or sit baths. Some people with anal fissures may need medication or, occasionally, surgery. Lubanoid is an herbal-based evidence topical product formulated from six natural, safe and monographic herbal ingredients, which is designed specifically as a remedy for anal fissures, foot fissures, piles and inflamed veins such as varicose and spider veins. Studies conducted in vitro, in vivo and clinically showed that Lubanoid is a novel synergistic composition with potential anti-inflammatory, analgesic and healing effects and found superior in its activity compared with some drugs used currently in the clinics.

INTRODUCTION

Anal fissure (AF) is one of the most common benign anorectal diseases and one of the most common causes of anal pain and anal bleeding (1). AF is a break or tear in the skin of the anal canal that may be noticed by bright red anal bleeding on toilet paper and undergarments, or sometimes in the toilet. Anal fissures usually extend from the anal opening and are usually located posteriorly in the midline, probably because of the relatively unsupported nature and poor perfusion of the anal wall in that location. Anal fissures most often affect infants and middle-age individuals. It is estimated that approximately 235,000 new cases of anal fissure occur every year in the United States (2). The incidence of anal fissures is around 1 in 350 adults. They occur equally commonly in men and women and most often occur in adults aged 15 to 40. The main causes of AF can be divided into the following categories:

1. Common causes include

- Passing large or hard stools
- Constipation and straining during bowel movements
- Chronic diarrhea

- Anal intercourse
- Childbirth

2. Other common causes include

- Childbirth trauma in women.
- Anal sex.
- Crohn's disease.
- Ulcerative colitis.
- Poor toileting in young children.

3. Less common causes include

- Anal cancer
- HIV
- Tuberculosis
- Syphilis

Among signs and symptoms of an AS, include

- Pain, sometimes severe, during bowel movements
- Pain after bowel movements that can last up to several hours
- Bright red blood on the stool or toilet paper after a

- bowel movement
- A visible crack in the skin around the anus
- A small lump or skin tag on the skin near the anal fissures

Some factors may increase risk of developing an AS include

- Constipation. Straining during bowel movements and passing hard stools increase the risk of tearing.
- Childbirth. Anal fissures are more common in women after they give birth.
- Crohn's disease. This inflammatory bowel disease causes chronic inflammation of the intestinal tract, which may make the lining of the anal canal more vulnerable to tearing.
- Anal intercourse.
- Age. Anal fissures can occur at any age, but are more common in infants and middle-aged adults.

Complications

As far as complications of AS can include:

- Failure to heal. An anal fissure that fails to heal within eight weeks is considered chronic and may need further treatment.
- Recurrence. Once you have experienced an anal fissure, you are prone to having another one.

On the other hand, pathogenesis of AF is typically starting with a tear to the anoderm within the distal half of the anal canal. The tear then triggers cycles of recurring anal pain and bleeding, which lead to the development of a chronic anal fissure in as many as 40 percent of patients. The exposed internal sphincter muscle within the bed of the fissure frequently spasms, which not only contributes to severe pain but also can restrict blood flow to the fissure, preventing its healing. Further, there are some criteria to be followed for adults that may help prevent AS. These are:

Avoiding straining when defecating. This includes treating and preventing constipation by eating food rich in dietary fiber, drinking enough water, occasional use of a stool softener, and avoiding constipating agents. Similarly, prompt treatment of diarrhea may reduce anal strain.

- Careful anal hygiene after defecation, including using soft toilet paper and cleaning with water, plus the use of sanitary wipes.
- In cases of pre-existing or suspected fissure, use of a lubricating ointment (It is important to note that hemorrhoid ointment is contraindicated because it constricts small blood vessels, thus causes a decrease in blood flow, which prevents healing. Wiki. Treatment of AF includes:
- Non-surgical treatments are recommended initially for acute and chronic anal fissures. These include topical nitroglycerin or calcium channel blockers (e.g. diltiazem), or injection of botulinum toxin into the anal sphincter.
- Other measures include warm sits baths, topical anesthetics, and high-fiber diet and stool softeners.

- Medication
- Local application of medication to relax the sphincter muscle, thus allowing the healing to proceed, was first proposed in 1994 with nitroglycerine ointment, and then calcium channel blockers in 1999 with nifedipine ointment, and the following year with topical diltiazem.
- A combined surgical and pharmacological treatment may offer up to 98% cure rates.
- Surgery
- Surgical procedures are generally reserved for people with anal fissure who have tried medical therapy for at least one to three months and have not healed. It is not the first option in treatment.
- The main concern with surgery is the development of anal incontinence. Anal incontinence can include inability to control gas, mild fecal soiling, or loss of solid stool. Some degree of incontinence can occur in up to 45 percent of patients in the immediate surgical recovery period. However, incontinence is rarely permanent and is usually mild. The risk should be discussed with one's surgeon.
- Anal dilation, or stretching of the anal canal (Lord's operation), has fallen out of favor in recent years, primarily due to the unacceptably high incidence of fecal incontinence.

Lubanoid is an herbal-based evidence topical product formulated from six natural, safe and monographic herbal ingredients, which is designed specifically as a remedy for anal fissures, foot fissures, piles and inflamed veins such as varicose and spider veins. These ingredients include, Boswellia sacra, Commiphora Myrrha, Aloe Vera extracts, menthol oil, honey and sesame oil.

Lubanoid possess potential anti-inflammatory, healing, analgesic and antibacterial effects. It shows superior activity anti-inflammatory and analgesic action compared with both standard drugs used in the Study, these are phenylbutazone, brufen, aspirin and paracetamol. The pharmacological action reported by this product indicated its action as multitargeted agent that can modulate.

Several molecular targets by blocking pro-inflammatory enzymes and other molecular targets beside its analgesic, healing and antibacterial effect. Therefore, it is a class of product that can be used as a remedy for different types of fissures including anal fissures, piles, spider veins and other inflammatory conditions.



(Figure1).

Description

Lubanoid is a very distinguished product that developed after careful preclinical and clinical studies (Figures 1&2). Several *in vitro* and *in vivo* studies were conducted to study the efficacy and safety of this product both *in vitro* and *in vivo*. For *in vitro* anti-inflammatory effect, several human and murine cell lines were used including primary murine microglia, raw mouse macrophages, primary human monocytes and primary human fibroblasts to see its effect on prostaglandin E₂, interleukin 1-beta (IL-1 Beta), tumor necrosis factor (TNF alpha) and interleukin6 (IL6). These studies showed that the product possess significant anti-inflammatory properties. For *in vivo* anti-inflammatory studies, the activity of the product was studied in albino rats using two different pharmacological screening tests, these are:

- Inhibition of ascites using albino rats.
- Freund's adjuvant using albino rats.
- Lubanoid exhibited potential anti-inflammatory activity compared to phenylbutazone, brufen and aspirin drugs in causing a diminution of ascites fluid and reducing the inflammation at the paw of rats. Further, the analgesic property of Lubanoid was evaluated using two pharmacological screening tests, these are:
 - Writhing induced by chemicals using albino mice.
 - Hot plate test using albino mice.

Lubanoid was more potent as analgesic in both tests compared with the reference standard used in the two above tests represented by paracetamol. On the other hand, the healing efficacy of Lubanoid was studied using albino rabbits of both sexes where incisions (1-2 cm in diameter) were made on the ventral side of the abdominal cavity. The efficacy of Lubanoid was tested after the application of this product for five successive days. The animals were carefully grossly examined every day for six days and it was observed that bleeding stop after 48 hours of applying Lubanoid topical and wound healing occurred in 8 out of 12 rabbits. Further, the healing process was delayed in two rabbits and this process was completed after two weeks of treatment with Lubanoid,

whereas, no healing occurred in the other two rabbits even after four weeks of treatment with Lubanoid. The results of the present studies showed that:

- Lubanoid Ointment has a potential healing effect that could reach up to 80%.
- Lubanoid Ointment has a vasoconstrictor effects on blood vessels and that was evident after 84 hours.
- Both preparations of Lubanoid Ointment (fresh and old preparations) have more or less the same efficacy.

The oral acute toxicity of Lubanoid was investigated *in vivo* utilizing healthy experimental mice as a model. A single dose was administered to the animals followed by monitoring for a period of 14 days after dosing and recording death and changes in animal behavior and any other physical variables.

The results obtained indicated that the oral LD₅₀ of Lubanoid is more than 2000 mg/ kg in Balb/c mice. In addition, Lubanoid neither induced any death nor caused any abnormal behavior when tested at a dose of 2000 mg/ kg. The skin sensitivity of Lubanoid was studied in guinea pigs. The animals were carefully observed for six weeks for the accumulation purposes. The followings scores were measured to see the effect of intradermal irritation of the Lubanoid:

- Degree of erythema.
- Presence of erythema.
- Behavioral of the erythema.
- Food and water intake.
- Average body weight.

In addition, both gross and microscopic examinations were done on most of the important organs (liver, kidney, skin). No changes in the color of the skin of the animals were recorded when compared with the untreated control and no edema was observed in the skin of the experimental animals. This indicates that Lubanoid has no irritation effect on the skin of guinea pigs. Further, no gross or pathological findings were observed in biopsies taken from the liver, kidney and skin in the experimental animals compared to the untreated controls. Furthermore, the effect of Lubanoid was studied on the structure and function of the eye of rabbits to see if this topical has any effect on the eye. The results also showed that Lubanoid has no irritation or inflammatory effect on the eyes of rabbits indicating that it has no toxic effects when applied topically. Finally, the efficacy of Lubanoid in wound healing was studied in albino rabbits. The results of the present studies showed that:

- Lubanoid has a potential healing effect that could reach up to 80%.
- Lubanoid has a vasoconstrictor effects on blood vessels and that was evident after 48 hours of treatment.

Finally, the product showed significant antibacterial effect against many gram-positive and gram – negative

bacteria including *Staphylococcus aureus* ATCC 25923, ATCC 6538, *Staphylococcus epidermis* ATCC 12228

and *Staphylococcus hominis* ATCC 27844.

Healing Paradigm

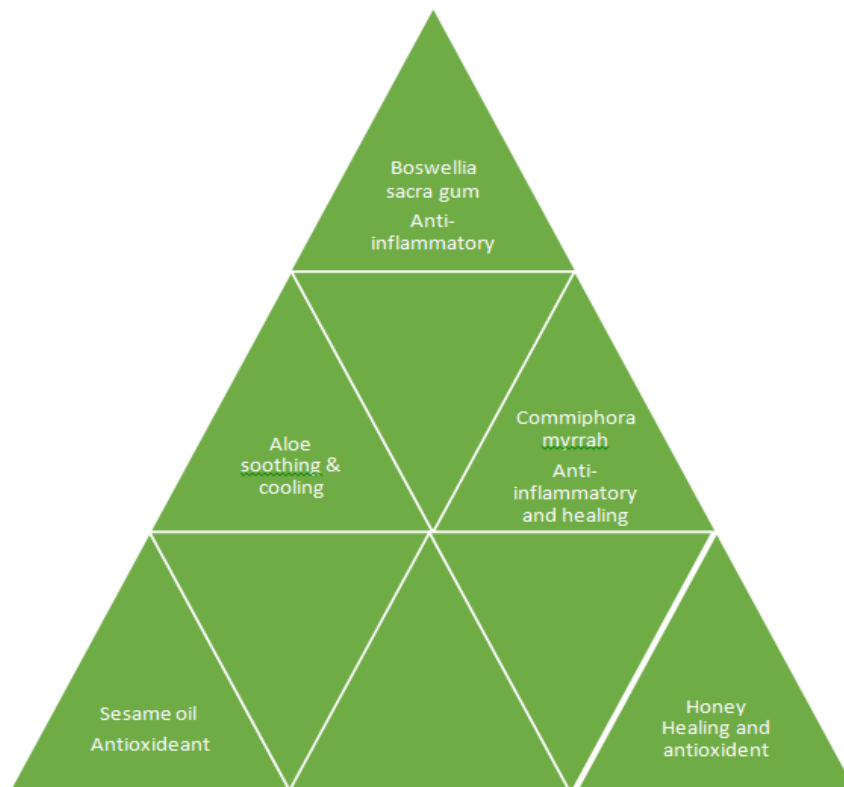


Figure (2).

The healing paradigm of this product (Figure 2) clearly suggest its application for anal fissures, piles, varicose and spider veins.

Frankincense contains six boswellic and two lupeolic acids and other triterpenoid compounds. The pharmacological action documented for boswellic acids, which play a very significant anti-inflammatory role by inhibition the production of inflammatory leukotrienes.

Myrrh resin is made up of alpha-, beta-, and gamma-commiphoric acids, heeraboresene, alpha-, and beta-heerabomyrrhols and commiferin (Hoffmann), plus the soluble gum or mucilage compound mainly of acidic polysaccharide with galactose, 4-O-methyl glucuronic acid, and arabinose in a ratio 8:7:2. It is to be used as an effective antimicrobial agent, useful for the treatment of boils and arthritis and for healing wounds and abrasions.

Sesame oil contains fatty acids such as oleic, palmitic, stearic and linoleic acids. It is also very high in vitamins A and E and contains antioxidants and sesamol, which counteract free radicals (a primary cause of aging).

Aloe contains many compounds such as anthraquinones (Aloin and emodin), polysaccharides (glucmannans/polymannose, acemannan), minerals, enzymes, vitamins, fatty acids and others. It is effective

in reducing postoperative pain both on resting and during defecation both, has cooling, soothing, healing and analgesic effective.

Honey contains many compounds like carbohydrates (sugars), flavonoids and phenolic acids and other compounds; it helps as antioxidant, anti-inflammatory and healing agent.

The medical and non-medical ingredients in Lubanoid work in an effective and synergistic way to support each of the claims, which on the other hand, support the healing paradigm.

RESULTS

Lubanoid topical product consists of unique blends of well-studied pharmacopoeial and monographic medicinal ingredients. These are *Boswellia sacra*, *Commiphora Myrrha*, *Aloe Vera*, sesame oil and honey. It showed a wide range of multi-targeted and multi-channel activities both in vitro, in vivo and in clinical tests. This product contains six boswellic and two lupeolic acids, diterpenoids, triterpenoids, steroids, lignans, aloin, emodin, sugars, flavonoids, phenolic compounds and others. This unique combination of ingredients potentiates their synergistic effect on the body. According to feedback received from clinician's who tested this product on patients suffering from burns and /

or wounds, the product have remarkable effect in both burns and wounds. They reported simultaneous multiple actions as anti-inflammatory, analgesic, antioxidant, antibacterial and healing benefits. It seems logical to interpret these findings based on the multiple ingredients present in this product, which work in an effective way to support each claim, which on the other hand, support the healing paradigm.

Therapeutic values of Lubanoid Ointment

- Help as anti-inflammatory and analgesic.
- Fissures and wound healing abrasions.
- Help as antimicrobial.
- Have antioxidant property.
- Have cooling and soothing effect.

Properties of Lubanoid

Lubanoid is a unique natural health product composed of an optimized extract obtained from *Boswellia sacra* gum resin using special extraction procedure (38) and was characterized using HPLC/MS/MS method. It contains six boswellic acids, two lupeolic acids, and other triterpenoid compounds. In addition, the product contains Myrrh extract plus sesame oil and honey. The pharmacological action of this extract showed potential anti-inflammatory, analgesic, antibacterial and healing effects. Therefore, the medicinal ingredients in Lubanoid work in an effective and synergistic way to support each of the claims, which on the other hand, support the healing paradigm.

Recommended use of purpose

- *Boswellia sacra* extract have potential anti-inflammatory and analgesic effect.
- Sesame oil has antioxidant effect.
- Peppermint oil have an aesthetic and natural analgesic agent.
- Honey has healing and antioxidant effects.
- Aloe has soothing and cooling effects.

Side effects

No serious side effects were reported from using this product.

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