

COLONLUBAN - A NATURAL REMEDY FOR INFLAMMATORY BOWEL DISEASE**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

Inflammatory bowel diseases cover a diverse range of conditions generally grouped into Crohn's disease (CD) or ulcerative colitis (UC) based on clinical, laboratory, radiological, endoscopic, and histological criteria. CD affects the small intestine and large intestine, as well as the mouth, esophagus, stomach and the anus; whereas UC primarily affects the colon and the rectum.^[2-4] The exact cause of inflammatory bowel disease remains unknown. One possible cause is an immune system malfunction. Heredity also seems to play a role in that IBD is more common in people who have family members with the disease. In 2015 an estimated 1.3% of US adults (3 million) reported being diagnosed with IBD (either Crohn's disease or ulcerative colitis). This was a large increase from 1999 (0.9% or 2 million adults). Inflammatory bowel diseases are increasing in Europe. IBS affects 10-25% of the population globally with a slightly higher prevalence in females compared to males. IBD treatment usually involves either drug therapy or surgery. Among drugs used to treat IBD are anti-inflammatory drugs, immune system suppressor, antibiotics, anti-diarrheal, pain relievers, iron supplements. Complementary and alternative medicine approaches have been used in inflammatory bowel disorders such as using *Plantago ovata* and curcumin especially in UC maintenance therapy. We describe in this paper a new oral herbal remedy oral that consists of six monographic herbs with potent anti-inflammatory, immunomodulatory, antioxidant, antibacterial and antispasmodic properties that make it a promising multi-targeted treatment for IBD.

KEYWORDS: *Plantago ovata* and curcumin.**INTRODUCTION**

Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine. Crohn's disease (CD) and ulcerative colitis (UC) are the principal types of inflammatory bowel disease.^[1] CD affects the small intestine and large intestine, as well as the mouth, esophagus, stomach and the anus, whereas UC primarily affects the colon and the rectum. Both diseases may present with any of the following symptoms: abdominal pain, diarrhea, rectal bleeding, severe internal cramps/muscle spasms in the region of the pelvis and weight loss. Anemia is the most prevalent extra intestinal complication of inflammatory bowel disease.^[5,6] The exact cause of inflammatory bowel disease remains unknown. One possible cause is an immune system malfunction.^[2] Heredity also seems to play a role in that IBD is more common in people who have family members with the disease.^[7] However, most people with IBD do not have this family history. IBD resulted in a global 51,000 deaths in 2013 and 55,000 deaths in 1990. The increased incidence of IBD since World War 2 has been linked to the increase in meat consumption worldwide; supporting the claim, that animal protein intake is associated with IBD.^[8,9] Inflammatory bowel diseases are increasing in Europe.

The diagnosis is usually confirmed by biopsies on colonoscopy. IBD fall into the class of autoimmune diseases, in which the body's own immune system attacks elements of the digestive system.^[10] Other forms of IBD, which are not always classified as typical IBD includes, microscopic colitis; diversion colitis, Behcet's disease and the indeterminate colitis.^[11,12] Though both diseases are not medically curable^[13], however, medical treatment of IBD is individualized and the drug of choice for both CD and UC is Mesalazine^[14], which seems to be less useful for CD and more useful in UC. Antibiotics which according to literature effective when used for long-term in CD and not useful for UC.^[15,16] In addition, surgery can be used but often returns following removal of the affected part. However, UC can in most cases be cured by proctocolectomy.^[17,18] In CD, surgery involves removing the worst inflamed segments of the intestine and connecting the healthy regions, but unfortunately, it does not cure Crohn's or eliminate the disease. IBD may also require immunosuppression to control the symptoms, with drugs such as prednisone, TNF inhibitors, azathioprine (Imuran), methotrexate, or 6-mercaptopurine. Deficiencies of B vitamins, fat-soluble vitamins, essential fatty acids, and key minerals such as magnesium, zinc, and selenium are extremely common

and benefit from replacement therapy.^[19,20] Complementary and alternative medicine approaches have been used in inflammatory bowel disorders.^[21] Evidence from controlled studies of these therapies has been reviewed; risk of bias was quite heterogeneous. The best supportive evidence was found for herbal therapy, with *Plantago ovata* and curcumin in UC maintenance therapy. Finally, stem cell is undergoing research as a possible treatment for IBD. A review of studies suggests a promising role, although there are substantial challenges, including cost and characterization of effects, which limit the current use in clinical practice.^[22]

Among the risk factors of IBD are:

- Age. Most people who develop IBD are diagnosed before they're 30 years old. But some people don't develop the disease until their 50s or 60s.
- Race or ethnicity. Although whites have the highest risk of the disease, it can occur in any race.
- Family history. You're at higher risk if you have a close relative — such as a parent, sibling or child — with the disease.
- Cigarette smoking. Cigarette smoking is the most important controllable risk factor for developing Crohn's disease. Although smoking may provide some protection against ulcerative colitis.
- Nonsteroidal anti-inflammatory medications. These include ibuprofen (Advil, Motrin IB, others), naproxen sodium (Aleve), diclofenac sodium (Voltaren) and others. These medications may increase the risk of developing IBD or worsen disease in people who have IBD.
- Environmental factors including a diet high in fat or refined foods, play a role.

Complications

a. Complications found in both UC and AC conditions may include (2)

- Colon cancer. Having IBD increases the risk of colon cancer.
- Skin, eye and joint inflammation.
- Medication side effects. Corticosteroids can be associated with a risk of osteoporosis, high blood pressure and other conditions.
- Primary sclerosing cholangitis. IBD inflammation causes scars within the bile ducts and gradually causing liver damage.
- Blood clots. IBD increases the risk of blood clots in veins and arteries.

Whereas, Complications of Crohn's disease may include:

- Bowel obstruction. Crohn's disease affects the full thickness of the intestinal wall.
- Malnutrition. Diarrhea, abdominal pain and cramping may make it difficult for you to eat or for your intestine to absorb enough nutrients to keep you nourished.

- Ulcers. Chronic inflammation can lead to open sores (ulcers) anywhere in the digestive tract, including your mouth and anus, and in the genital area.
- Fistulas. Sometimes ulcers can extend completely through the intestinal wall, creating a fistula.
- Anal fissure. This is a small tear in the tissue that lines the anus or in the skin around the anus where infections can occur.

b. Complications of ulcerative colitis may include

- Toxic mega-colon. Ulcerative colitis may cause the colon to rapidly widen and swell, a serious condition known as toxic mega-colon.
- A hole in the colon (perforated colon). A perforated colon most commonly is caused by toxic mega-colon, but it may also occur on its own.
- Severe dehydration. Excessive diarrhea can result in dehydration.

Colon Luban

ColonLuban is an herbal-based evidence oral product formulated from six natural, safe and monographic herbal ingredients, which is designed specifically as a remedy for inflammatory bowel diseases. These ingredients include, *Boswellia sacra* gum resin; *Foeniculum vulgare* seeds; *Nigella sativa* seeds; *Silybum marianum* leaves; *Plantago ovata* seeds and *Mentha piperita* leaves extracts mixed in different ratios. ColonLuban possess potential anti-inflammatory, antioxidant, gastroprotective, anti-diarrheal, carminative and with antibacterial and immunomodulatory effects.

Boswellia sacra contain six boswellic and two lupeolic acids and other triterpenoid compounds. It has several therapeutic effects including anti-inflammatory, analgesic, antimicrobial and antioxidant.

Psyllium husk consists of the ground husk of the psyllium seed (*Plantago ovata*), a mixture of polysaccharides composed of pentoses, hexoses, and uronic acids. It is recommended for flatulence and increases significantly in fecal butyrate level in patients with IBD.

Nigella sativa has several therapeutic effects, which are attributed to its constituents like nigellicine, nigellidine, thymoquinone, dithymoquinone, thymol and carvacrol. Several beneficial pharmacological properties of this plant such as anti-oxidant, anti-bacterial, anti-histaminic, anti-inflammatory, immunomodulatory and other effects.

Foeniculum vulgare the major constituent of fennel oil is anethole. Other constituents include alpha pinene, beta myrcene, beta pinene, bitter fenchone, camphene, estragole (methyl-chavicol), fenchone, limonene, p-cymen, and safrole.

Intestinal gas, bloating, loss of appetite, and colic in infants among others.

Silybum marianum the extract consists of about 65–80% silymarin (a flavanolignan complex) and 20–35% fatty acids, including linoleic acid. With several pharmacological benefits such inflammatory bowel disorders and immune problems.

Mentha piperita leaves has 0.3–0.4% of volatile oil containing menthol, menthone, menthyl acetate, menthofuran and 1,8-cineol which blocks calcium channels in smooth muscle, thus producing antispasmodic effects on the gastrointestinal tract.



Figure 1

Gastro-protective compared with some treatments used to treat IBD. The pharmacological action reported by this product indicated its action as multi-targeted agent that can modulate several molecular targets by blocking pro-inflammatory cytokines such as IL-1 β , IL-6, and TNF- α enzyme, transcription factors and other molecular targets beside its analgesic, anti-diarrheal, gastro-protective and antibacterial effect. Therefore, it is a class of product that can be used as a remedy for IBD including UC and CD diseases.

ColonLuban is a very distinguished product that developed after three years of 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- α) and interleukin 6 (IL-6). These studies showed that the product possess significant anti-inflammatory properties. The *in vivo* anti-inflammatory studies of the product were studied in albino rats using two different pharmacological screening tests, these are:

- a) Inhibition of ascites using albino rats.
- b) Freund's adjuvant using albino rats.

ColonLuban 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 ColonLuban was evaluated using two pharmacological screening tests, these are:

- a) Writhing induced by chemicals using albino mice.
- b) Hot plate test using albino mice.

ColonLuban was more potent as analgesic in both tests compared with the reference standard used in the two above tests represented by paracetamol.

The oral acute toxicity of ColonLuban 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 ColonLuban is more than 2000 mg/kg in balb/c mice. Furthermore, a 90 days long-term oral toxicity study of ColonLuban did not result systemic toxicity when administered at up to 1000 mg/kg to *Wistar* rat by oral route.

Healing Paradigm

The healing paradigm of this product (Figure 2) clearly suggest its application for UC and CD and other related IBD diseases.

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 some pro-inflammatory leukotrienes and cytokines.

Psyllium husk consists of the ground husk of the psyllium seed (*Plantago ovata*); a mixture of polysaccharides composed of pentoses, hexoses, and uronic acids. It is recommended for flatulence and increases significantly in fecal butyrate level in patients with IBD.

Black seed, *Nigella sativa* has several therapeutic effects, which are attributed to its constituents like nigellidine, nigellidine, thymoquinone, dithymoquinone, thymol and carvacrol. Several beneficial pharmacological properties of this plant such as anti-oxidant, anti-bacterial, anti-histaminic, anti-inflammatory, immunomodulatory and other effects.

Foeniculum vulgare the major constituent of fennel oil is anethole. Other constituents include alpha pinene, beta myrcene, beta pinene, bitter fenchone, camphene, estragole (methyl-chavicol), fenchone, limonene, p-cymen, and safrole. The pharmacological action documented for *Nigella* showed that it is used for intestinal gas, bloating, loss of appetite, and colic in infants among others.

Silybum marianum the extract consists of about 65–80% silymarin (a flavonolignan complex) and 20–35% fatty acids, including linoleic acid. It is used in inflammatory bowel disorders and immune problems.

Mentha piperita leaves has 0.3–0.4% of volatile oil containing menthol, menthone, menthyl acetate, menthofuran and 1,8-cineol which blocks calcium channels in smooth muscle, thus producing antispasmodic effects on the gastrointestinal tract.

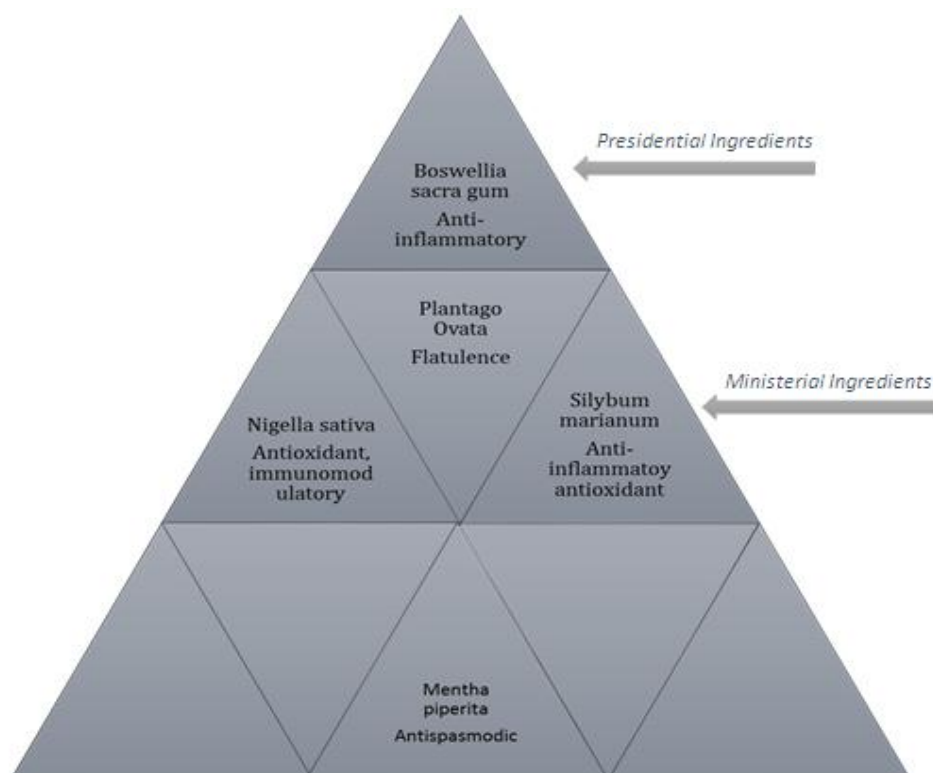


Figure 2

RESULTS

ColonLuban product consists of unique blends of well-researched pharmacopoeia and monographic medicinal ingredients. These are *Boswellia sacra*, *Plantago ovata*, *Foeniculum vulgare*, *Mentha piperita* and *Silybum marianum*. 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, polysaccharides like pentose, hexoses, uronic acids,

nigelone, alpha pinene, silymarin, fatty acids, 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 UC and CD and other IBD, the product exhibited remarkable effect on both UC and CD. They reported simultaneous multiple actions as anti-inflammatory, analgesic, antioxidant, antibacterial and immunomodulatory. 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 Colon Luban

- Help as anti-inflammatory and analgesic.
- Have immunomodulatory effect.
- Help as antimicrobial.
- Have antioxidant property.
- Have antispasmodic, flatulence effect.

Properties of ColonLuban

ColonLuban is a unique natural health product composed of an optimized extract obtained from *Boswellia sacra* gum resin using special extraction procedure 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 *Plantago ovata* seeds consists of a mixture of polysaccharides composed of pentose, hexoses, and acids, Black seed; *Nigella sativa* has several constituents like nigellicine, nigellidine, thymoquinone, dithymoquinone, thymol and carvacrol; *Foeniculum vulgare* seeds which is composed of a major constituent of fennel oil is anethole plus other constituents monoterpenes compounds; *Silybum marianum* which contains about 65–80% silymarin (a flavonolignan complex) and other compounds plus *Mentha piperita* leaves which has 0.3–0.4% of volatile oil containing menthol and other compounds.. The pharmacological action of this product showed potential anti-inflammatory, analgesic, antibacterial, immunomodulatory and antispasmodic effects. Therefore, the medicinal ingredients in ColonLuban 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

1. *Boswellia sacra* extract have potential anti-inflammatory and analgesic effect.
2. *Plantago ovata* has anti-flatulence effect.
3. *Nigella sativa* have antioxidant and immunomodulatory effect.
4. *Foeniculum vulgare* for intestinal gases.
5. *Silybum marianum* have anti-inflammatory and antioxidant effects.
6. *Mentha piperita* have antispasmodic effect.

Side effects

No serious side effects were reported from using this product.

Contraindications

It is contraindicated in patients with hypersensitivity to any of the active substances of the product.
Not to be used during pregnancy.

Direction for use

Three capsules daily in three dividing doses with meals.

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