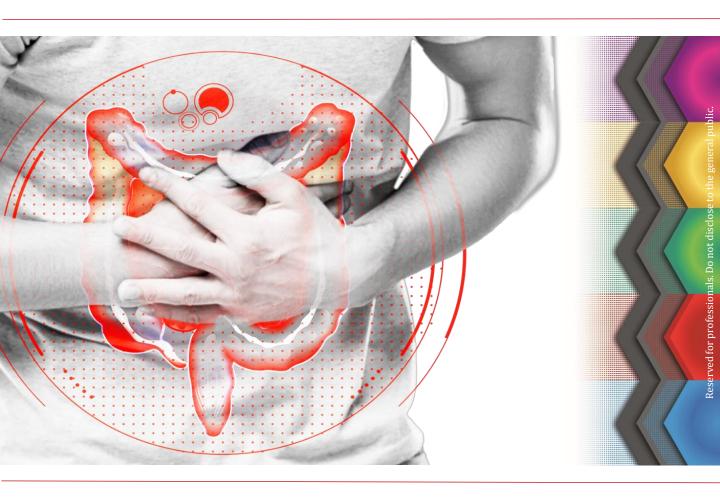
Divertikur line

Innovative food supplemets



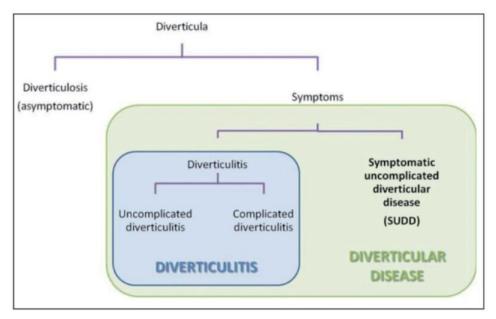
A line of natural products for the treatment of diverticular disease and its symptoms



Diverticulosis and diverticular disease

Diverticulosis is an alteration of the colon wall characterized by the presence of sacs (**diverticula**) that occur when the colon mucosa and submucosa herniate into the muscular layer of the colon wall.

Diverticular disease (DD) is defined as clinically significant and symptomatic diverticulosis. Symptomatic uncomplicated diverticular disease (SUDD) is a subtype of DD in which persistent abdominal symptoms attributed to diverticula in the absence of colitis are present.

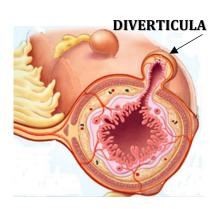


Classification of diverticular disease

SYMPTOMS OF DIVERTICULAR DISEASE

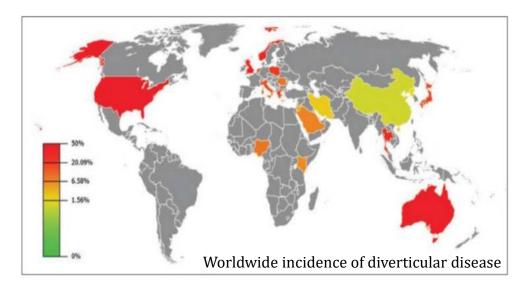
- **Pain** in the lower left part of the abdomen
- Abdominal swelling
- Diarrhea and constipation
- Absence of macroscopic inflammation

The severity and frequency of symptoms can impact daily activities and severely affect quality of life.

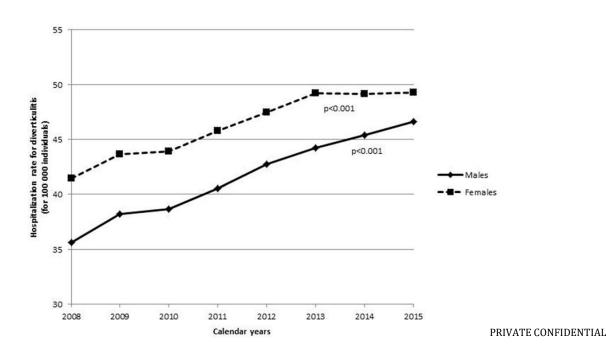


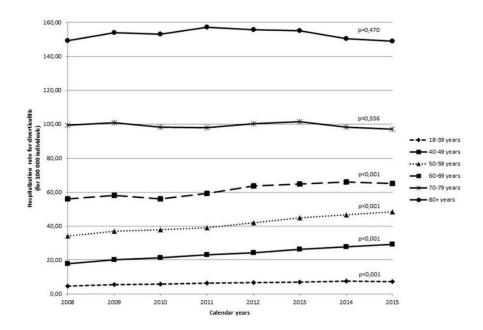
Diverticulosis and diverticular disease

Recent data has revealed an increase of the prevalence of diverticular disease around the world. About 130,000 hospitalizations that occur each year in the United States are attributable to diverticular disease.

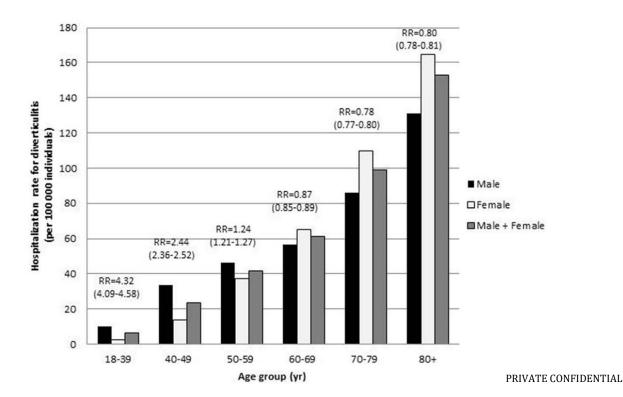


From the data collected in the study "Trends in hospital admission for acute diverticulitis in Italy from 2008 to 2015", the incidence of hospital admissions in Italy, due to this disease, has recently increased. In general, women are more affected, but there is a greater percentage increase for men.





Diverticular disease is traditionally considered a disease that affects the elderly, as its incidence generally increases with age; however, the most recent literature has reported **an increase in the incidence among younger patients compared to previous years**. Incidence rates of hospital admissions increased statistically significantly between groups 18 to 39 (6.6%) and 40 to 49 (7.1%) years of age. Conversely, they are stable in people over 70 years of age.



Diverticulosis and diverticular disease

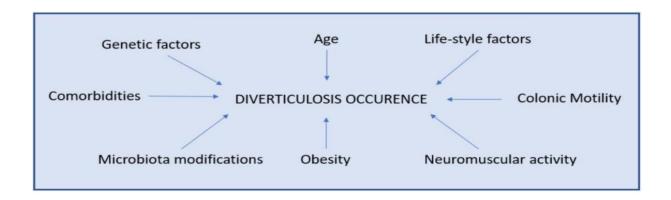
The exact mechanism by which the disease develops is unclear. Studies support the theory of structural changes in the colon wall as a major pathogenic factor. In the intestinal sections of patients with diverticulitis are highlighted some impairment in the collagen fibers linked to cellular aging:

- 1. Decreasing levels of mature type I collagen
- 2. Increasing levels of type III collagen

| | Control (n=14) | Diverticulitis (n=13) | P |
|----------------|----------------|-----------------------|--------|
| Collagen | 3.31±0.42 | 3.24±0.51 | n.s. |
| Collagen I | 1.59±0.31 | 1.37±0.32 | < 0.05 |
| Collagen III | 1.42 ± 0.42 | 1.61±0.32 | < 0.05 |
| Collagen I/III | 1.12 ± 0.31 | 0.86 ± 0.26 | < 0.05 |

MAIN RISK FACTORS

- Age: the incidence of diverticular disease increases with age
- Genetic factors: Ehlers-Danlos, Williams-Beuren, Coffin-Lowry syndrome have extracellular matrix defects in common, suggesting that the impairment of elastin and collagen in smooth muscle may be a prerequisite for diverticula formation
- Obesity / sedentary lifestyle
- Microbiota: bacterial imbalance can play a role in the onset of the disease
- **Diet:** low in fiber
- Increased intraluminal pressure



Divertikur Line

What are the goals of therapy in diverticular disease?

Prevent the progression of diverticulosis and the worsening of the condition



Reduce symptoms such as pain and swelling and improve patients' quality of life



Reduce the use of antibiotics that cause reduction of microbial diversity and persistence of antibiotic resistant genes

Gricar has developed a line of food supplements called **Divertikur** based on natural active ingredients specially designed to improve the symptoms of diverticular disease and to slow down its progression:

Divertikur Rigenera

Divertikur **Dolore**

Divertikur Gonfiore

Divertikur Pulizia

Divertikur **Regola**

Divertikur Rigenera

People with diverticulosis are more likely to have changes in the connective tissue of the intestine, which indicates that changes related to the composition of collagen are an etiological factor of the disease.

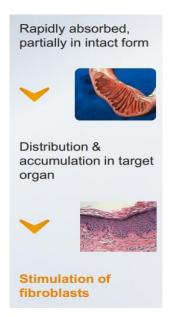
Divertikur Rigenera

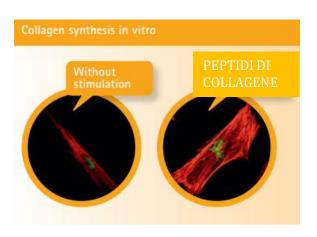
anti-aging action on the colon

Its innovative and exclusive formulation was developed specifically to slow down aging and disorders of the metabolism of the connective tissue of the colon wall in patients with diverticulosis

Peptides from collagen

These are several peptides optimized to maximize the **growth of connective tissue**, **collagen and the synthesis of proteoglycans and fibroblasts**. They are recognized as catabolic fragments of collagen which stimulate the metabolism of collagen to counterbalance its degradation. The result is a significantly higher and uniform production of intestinal collagen in tissue and extracellular matrix.

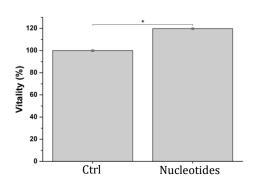


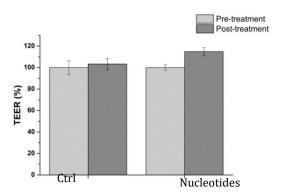


Divertikur Rigenera

Nucleotides

Intracellular compounds that compose the basic units of DNA and RNA. The intestinal mucosa is unable to activate the ex novo synthesis of nucleotides and therefore, for these cells, their exogenous contribution is important. They show a direct effect on **maintaining the integrity of the intestinal mucosa**, promoting the turnover of enterocytes.

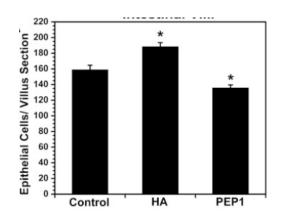




The integration of nucleotides in young rats increases the vitality of the intestinal epithelium and improves the integrity of the barrier

Sodium Hyaluronate

It increases the protein synthesis of keratinocytes, stimulates the production of elastin and **accelerates the healing and tissue rejuvenation processes**. It is a specific combination of **PM fractions** (from 50 to 3000 kDa) that work synergistically, just as it happens in our body naturally.



Exogenous hyaluronic acid increased the number of epithelial cells in the villi and crypts of the rat small intestine

Divertikur Rigenera

DIVERTIKUR RIGENERA

is a food supplement based on Collagen Peptides, Nucleotides, Hyaluronic Acid and Vitamin C. Vitamin C contributes to the protection of cells from oxidative stress.



PACK: 20 sticks

Naturally lactose free Gluten free

DOSAGE: 1 stick / day

HOW TO USE: Pour the contents of a stick into a glass of water, mix well and consume immediately after preparation.

WHEN: Take in the morning, at breakfast.

| NUTRITIONAL VALUES | | | | |
|--------------------|--------------------|-------|--|--|
| INGREDIENTS | Per dose (1 stick) | %NRV* | | |
| Collagen Peptides | 2500 mg | - | | |
| Sodium hyaluronate | 100 mg | - | | |
| Vitamin C | 80 mg | 100% | | |
| Nucleotides 40% | 25 mg | - | | |

*NRV: Nutrient reference values

Divertikur Dolore

Patients with diverticular disease may experience left lower abdominal pain and often have a palpable sigma due to muscle spasms. Such symptoms can impact daily activities and severely affect patients' quality of life. Treating it is therefore essential.

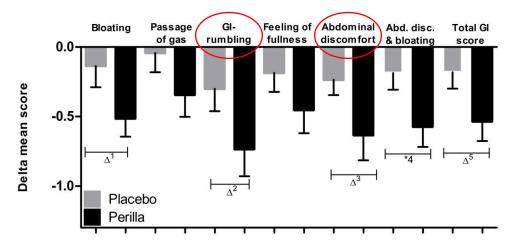
Divertikur Dolore

Its formulation has been specially developed to counteract the painful symptoms associated with diverticular disease

Perilla frutescens



In vitro and ex vivo studies have shown that Perilla frutescens extract combines prokinetic and antispasmodic effects on smooth muscle as well as anti-inflammatory effects. It is able to improve all the symptoms of gastrointestinal discomfort, in particular abdominal discomfort and borborygmi.



Pilot study in which patients consumed in a manner randomized placebo or Perilla frutescens extract for 4 weeks

Divertikur Dolore

Thyme



Thymol (10-64%) is one of the main constituents of thyme essential oils. It exerts an intestinal anti-spasmodic action through its relaxing effect on smooth muscle cells by opposing the activation of Ca2 +. The thymus also regulates gastrointestinal motility and the elimination of gases.

Chamomille



It has carminative potential as it is able to remove the air from the stomach and intestines; decreases abdominal pain and cramps as it relaxes the intestinal muscles: it has antispasmodic properties.

Peppermint



Menthol is the main component of peppermint oil. It works by causing the intestinal smooth muscle to relax by blocking the Ca2 + channels. Since 2000, several clinical studies have been published that have confirmed the effect of peppermint oil on IBS-related abdominal pain symptoms.

Verbena



It has antispasmodic action, reduces abdominal muscle cramps. It also acts as a mild analgesic, digestive and anti-inflammatory.

Divertikur Dolore

DIVERTIKUR DOLORE

is a food supplement based on Verbena and Perilla plant extracts, with essential oils of White Thyme, Chamomile and Peppermint.



DOSAGE: 2 tab/die

HOW TO USE: Swallow with water.

QUANDO: Take preferably 1 tablet after lunch and 1 tablet after dinner.

PACK: 30 tablets

Naturally lactose free Gluten free

| NUTRITIONAL VALUES | | | |
|-----------------------|------------------|--|--|
| INGREDIENTS | Per dose (2 tab) | | |
| Verbena d.e. | 300 mg | | |
| Perilla d.e. tit 2,5% | 200 mg | | |
| Thyme o.e. | 40 mg | | |
| Roman chamomile o.e. | 40 mg | | |
| Peppermint | 40 mg | | |

Divertikur Gonfiore

Patients with diverticular disease often complain of abdominal swelling. The symptom may go away for a while but it can also be constant. Bloating is recognized as a feeling of distended abdomen or abdominal tension due to excessive gas in the abdomen. The aim of the treatment is to alleviate the symptoms and improve the quality of life of the patients.

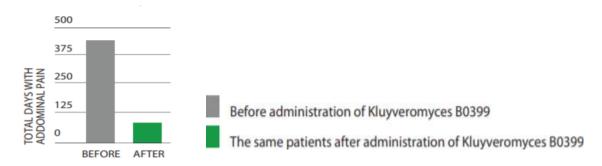
Divertikur Gonfiore

Food supplement with a specific formulation based on enzymes, probiotics and plant extracts capable of promoting the elimination of gas and the reduction of abdominal swelling

Kluyveromyces marxianus fragilis B0399

It is the first non-Saccharomyces yeast approved in food as a probiotic. It ferments lactose. It is resistant to gastric pH, antibiotics and is able to adhere to the intestinal epithelium. All this thanks to a cellular dosage of only 10 million that make it effective without having too much impact on the body. Its administration improves some intestinal disorders such as: bloating, meteorism, abdominal distension, irregular bowel movements.

INTESTINAL DISCONFORT



Divertikur Gonfiore

Enzyme complexes

Concentrated blend of digestive enzymes responsible for the breakdown of carbohydrates, proteins and fats. It includes: amylase, protease, glucoamylase, lipase, cellulase, lactase and pectinase. The complex facilitates the absorption of nutrients by promoting the digestion of macromolecules such as proteins, gluten, caseins, lactose.

Fennel



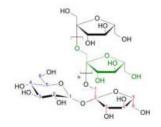
Fennel is known to be the deflationary belly par excellence, as it contains substances that help the fermentation processes in the intestine. It assists the digestive function, regulates gastrointestinal motility and promotes the elimination of gases.

Caraway



Caraway has the ability to reduce the fermentation phenomena that can occur during the digestion of some foods with particular reference to foods rich in sugars, carbohydrates, yeasts and proteins, reducing abdominal swelling. It helps relieve abdominal tension and relieve gastrointestinal symptoms associated with dyspepsia.

Inulin



Soluble fiber, used as a prebiotic. Promotes the selective growth of eubiotic bacteria responsible for the beneficial effects.

Divertikur Gonfiore

DIVERTIKUR GONFIORE

is a food supplement containing a mix of digestive enzymes, Inulin and Lactic Yeast Probiotic® Kluyveromyces marzianus fragilis, with essential oils of Fennel and Caraway. Fennel and Caraway support the digestive function and the elimination of gases. Inulin promotes the balance of the intestinal flora.



DOSAGE: 2 cps/die

HOW TO USE: swallow with water.

WHEN: Take preferably 1 capsule after lunch and 1 capsule after dinner.

PACK: 30 capsules

Naturally lactose free Gluten free

| NUTRITIONAL VALUES | | | |
|----------------------------------|------------------|--|--|
| INGREDIENTS | Per dose (2 cps) | | |
| Inulin | 352 mg | | |
| complexes of Enzyme from | | | |
| fermented vegetable substrates | 200 mg | | |
| Fennel o.e. | 50 mg | | |
| Caraway o.e. | 50 mg | | |
| Kluyveromyces marzianus fragilis | 20 mln UFC | | |

Divertikur Pulizia

The mainstay of treatment of patients with uncomplicated diverticulitis are antibiotics which should be targeted at normal Gram-negative and anaerobic covered enteric bacteria. However, prolonged use of antibiotic therapies can cause reduced microbial diversity and persistence of antibiotic resistant genes, in addition to the common adverse effects.

Divertikur Pulizia

Its formulation was developed specifically to improve the body's natural physiological resistance against pathogens, limiting the use of antibiotics

Grapefruit



Grapefruit Seed Extract is effective against Gram (+) and (-) bacterial strains, viral strains, fungal strains and a large number of parasites. The powerful and almost universal antimicrobial activity attributed to grapefruit seed extract is due to the synthetic preservative agents contained within. It exhibits antioxidant and anti-inflammatory properties.

Tea tree



Malaleuca alternifolia oil (tea tree oil) has a broad spectrum antimicrobial activity. In fact, it is able to inhibit respiration and increase the permeability of the membrane in the microbial cells by alternating them. It has mainly bactericidal action, although it can also be bacteriostatic at lower concentrations.

Divertikur Pulizia

DIVERTIKUR PULIZIA

is a food supplement based on grapefruit plant extract and Melaleuca essential oil.



DOSAGE: 2 cps/die

HOW TO USE: swallow with water.

WHEN: Take preferably 1 capsule after lunch and 1 capsule after dinner.

PACK: 30 capsules

Naturally lactose free Gluten free

| NUTRITIONAL VALUES | | | |
|---------------------|------------------|--|--|
| INGREDIENTS | Per dose (2 cps) | | |
| Grapefruit d.e. 50% | 600 mg | | |
| Malaleuca o.e. | 80 mg | | |

Divertikur Regola

One of the disorders most frequently associated with diverticular disease is intestinal irregularity. Some patients complain of constipation problems, other problems of dysentery, and both symptoms are remarkably annoying in the long run.

Divertikur Regola

Its formulation was developed to improve intestinal function, respecting the natural physiological conditions of the epithelium and intestinal barrier, through the activity of soluble and insoluble natural fibers

Acacia fiber



It is obtained from the sap of carefully selected acacia plants. It oozes from stems and branches and offers a guaranteed minimum of 90% soluble fiber. It is a nondigestible high molecular weight polysaccharide, composed of protein and associated a core polysaccharide fractions. It is non-digestible a carbohydrate with a glycemic index close to zero.

A study performed on this fiber has shown that the following complementary activities can help for a complete reinforcement of the intestinal barrier (microbiota + integrity of the intestinal wall):

- Prebiotic effect (combined with increased shortchain fatty acids and an anti-inflammatory effect)
- Restoration of intestinal impermeability

Divertikur Regola

Boldo



Boldo leaves contain essential oils (cineol and ascaridol); flavonoids and alkaloids (boldin) which give the plant a general detoxifying and cholagogue action, that is, it thins the bile, which increases its secretion and decreases its viscosity.

Its mildly laxative action makes boldo particularly suitable in case of constipation since the increase in bile salts in the intestine favors the enteric function, thanks also to the anti-inflammatory and relaxing effect on smooth muscles.

Plum



The laxative effect of plums is due to the large presence of:

- **Fiber** Insoluble fiber increases fecal volume, the soluble part has a prebiotic effect and feeds healthy bacteria in the digestive system.
- **Sorbitol,** a polyol that has the 'task' of drawing water by thinning the intestinal lumen.

Integration with plum preparations facilitates an emollient laxative activity, which improves the frequency of bowel movement, decreases the length of each movement and decreases pain.

Kiwi



Numerous clinical studies have shown that kiwis help fight constipation and improve intestinal motility. This is due to the high quantity of fibers and the unique properties due to the perfect balance between soluble and insoluble fibers, which work together and simultaneously.

When the soluble fibers move along the digestive system, absorbing water, they give rise to a larger and softer fecal mass, which passes easily into the intestine. Insoluble fibers also contribute to intestinal transit, further increasing the volume of the mass.

Divertikur Regola

DIVERTIKUR REGOLA

is a food supplement based on Acacia Fiber,
Plum, Kiwi and Boldo extract. Plum and Boldo favor the regularity of intestinal
transit.

One stick contains no less than 3 grams of fiber.



PACK: 20 sticks

Naturally lactose free Gluten free

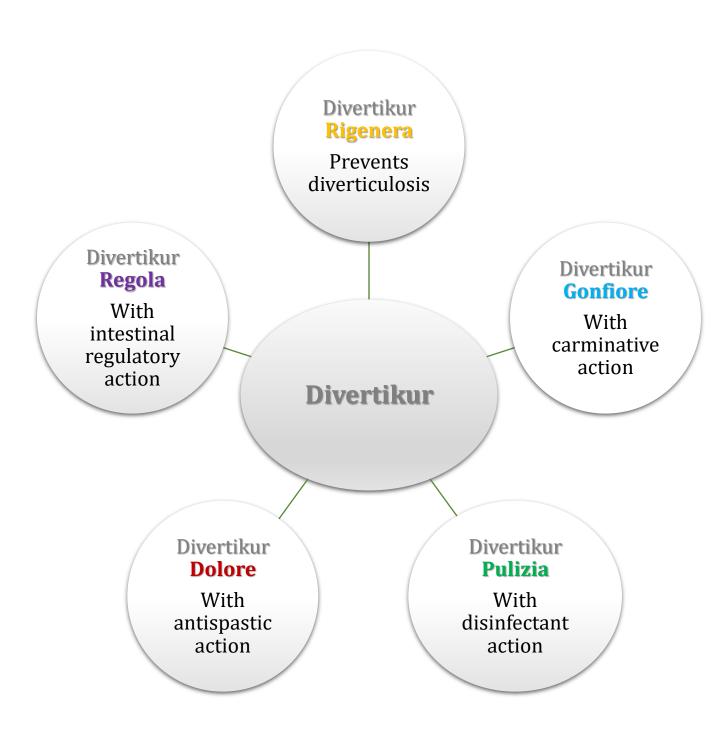
DOSAGE: 1-3 stick/die

HOW TO USE: Pour the content of a stick into a glass of water, mix well for at least 15/20 seconds and consume immediately after preparation.

WHEN: if the intake is 1 stick per day take it preferably in the morning, if you take 3 sticks, spread them over the day.

| NUTRITIONAL VALUES | | | |
|------------------------------|--------------------|--|--|
| INGREDIENTS | Per dose (3 stick) | | |
| Fiber | 9000 mg | | |
| Plum fruit juice concentrate | 300 mg | | |
| Kiwi fruit juice concentrate | 150 mg | | |
| Boldo d.e. tit 0,2% | 225 mg | | |

Linea Divertikur



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