



Gastro-AD®: an effective, convenient & natural alternative for heartburn and gastric discomfort

SUMMARY

Heartburn is a growing and widely spread ailment with a global prevalence estimated between 10%-20%, a figure that goes up in westernized countries. There is a need today for natural and effective alternatives that address this growing issue without the side effects of pharmacological solutions. Gastro-AD® is a food supplement based on non-GMO soy fermented by *Lactobacillus* strain *L. delbrueckii* R-187. This supplement has an excellent track-record of safe and effective use for gastric discomfort management and the relief of occasional heartburn, backed by several published studies, involving close to 600 subjects in total. Altogether these studies showed that this fermented soy-based solution was very well tolerated and led to a quick relief of ulcer symptoms including heartburn, pain, vomiting, and constipation.

Now available in orodispersible sticks, Gastro-AD® represents a natural, safe, effective and versatile alternative to heartburn products management with the extra nutritional benefits and healthy image of fermented soy.

Addressing a widespread health issue

The stress of everyday's life, stomach hyperacidity, intake of various drugs, overuse of tobacco and alcohol etc. represent as many aggressions for the stomach and can result in gastric symptoms ranging from heartburn and pain to gastric or duodenal ulcers.

Heartburn is a widely spread ailment and its prevalence has grown dramatically over the past decades. Moreover, it is suggested that the rise of obesity should increase acid reflux prevalence in the coming years. All population groups are affected by this condition: seniors, young active women and men... While overall worldwide prevalence is estimated to 10%-20%, this rate goes up in westernized countries. A 2010 study (Kushner, 2010) reported that an estimated 42% of the United States population has experienced heartburn at

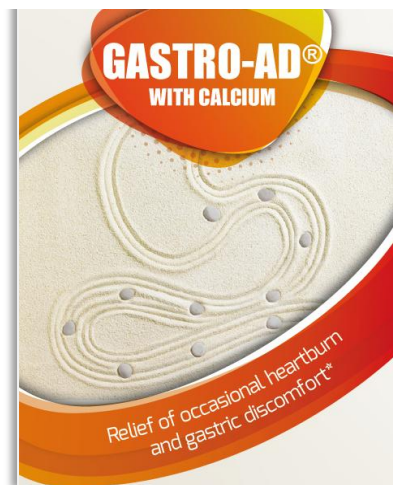
some point. In Europe, a population-based survey in Norway (Ness-Jensen, 2011) showed a substantial rise in gastro-oesophageal reflux symptoms (GORS) in only ten years. Between 1995 and 2006, overall GORS yearly prevalence increased by

30%, from 31.4% to 40.9%, while the prevalence of at least weekly GORS increased by as much as 47%, up to 17.1%. The same study showed that the percentage of spontaneous disappearance of the condition (without medication), was only around 2%.

In terms of **medication**, three main pharmacological approaches are used to alleviate heartburn:

- **Neutralization of stomach acidity:** use of antacids and alkalizing molecules. This approach offers a quick but temporary relief, followed by a reflex increase of acid (HCl) secretion in the gastric juice.
- **Inhibition of acid secretion in the stomach:** use of H₂ receptors antagonists or Proton Pump Inhibitors (PPIs).
- **In the case of *H. Pylori* infection, use of antibiotics.** However, eviction of *H. Pylori* is not sufficient and further actions are necessary to heal stomach ulcer.

However, all these solutions are synthetic drugs and their long-term use poses the problem of



side effects, including the emergence of antibioresistance. The market today demands **natural, convenient and effective alternatives to address the growing issue of heartburn and gastric reflux.**

An effective, versatile, all natural solution

Gastro-AD® is an original food supplement based on non-GMO soy, fermented by a specific lactic acid bacteria strain that was selected and isolated by Dr Bogdanov in the 1950s for its exceptional fermentation capacities: *Lactobacillus delbrueckii* ssp. *lactis* Rosell-187. It contains:

- Natural elements of soybean, widely known for its health benefits and chosen for its nutritional qualities
- Molecules resulting from soy fermentation (peptides, microbial metabolites, etc...)
- *L. delbrueckii* Rosell-187 strain

Gastro-AD® is entirely of biological origin, and does not contain any alkalizing, local anesthetic and/or spasmolytic agents. The gentle processing conditions preserve Gastro-AD®'s biologically active metabolites and soy nutritional qualities (see boxed text about soy).

Until now, Gastro-AD® was available either as a **powder** (recommended intake: 1g/day) or conditioned as **chewable tablets**.

Today, to cater for a wider consumer demand, and tastes, the company has launched unidose



sticks of orodispersible powder: **Gastro-AD® sticks**. Available in various flavours, the sticks can be taken at any time, without water. This new formulation bears very good solubility and taste-masking qualities and benefits from good consumer acceptance. Each stick contains 500mg Gastro-AD®, half the daily recommended dose.

Moreover, Gastro-AD® sticks are available in two forms: traditional and with added calcium carbonate at a concentration of 120mg of Calcium/stick, a sufficient concentration to bear calcium carbonate associated Health Claims in Europe, such as: "*Calcium contributes to the normal function of digestive enzymes*".

Clinically proven efficacy

Gastro-AD® has been tested in several clinical studies, in almost 600 subjects in total: it was shown to be **very well tolerated** and led to a **quick relief of ulcer symptoms including heartburn, pain, vomiting, and constipation.**

- **In 1978, Dr Bogdanov published the first patient study.** The study involved 360 patients suffering from duodenal ulcers (238), gastritis (93), and gastric ulcers (29), for over one year (191 subjects suffered for over 5 years). The symptoms monitored included: acidity, nausea, stomach pains, heartburns.

The subjects were administered 2.5-5g Gastro-AD®, 3 times/day, 30 min before meals, during 30 days.

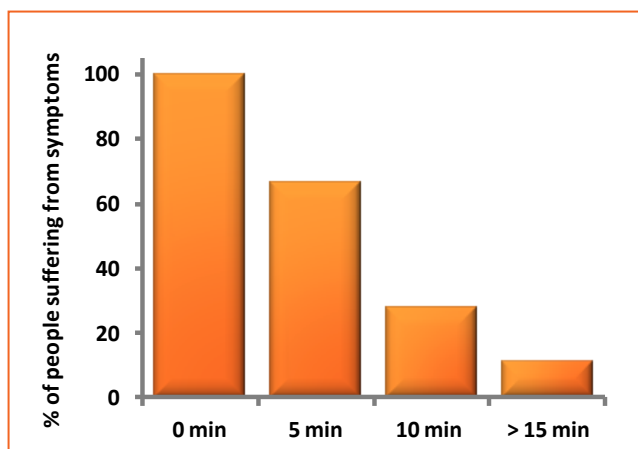


Figure 1: Effect of Gastro-AD® administration on heartburn/pain relief

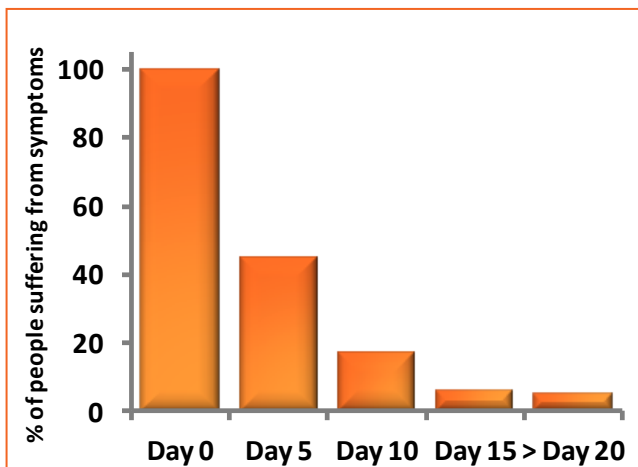


Figure 2: Effect of Gastro-AD® administration on gastric ulcers chronic symptoms (acidity, nausea, stomach pains, heartburns).

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A quick heartburn relief was reported (Fig. 1): 85% of the subjects experienced pain relief in less than 15mn.

At longer term, **chronic ulcers symptoms were reduced** (Fig. 2). It took less than 15 days for 95% of patients to see their symptoms relieved. This study showed that the product was very well tolerated.

- **A second study was conducted on 30 patients** (Daskalov et al., 1994) (26 with duodenal ulcers, 2 with gastritis and 2 with gastric ulcers). The subjects received 6 tablets a day for 10 days, then 3 tablets a day for another 10 days.

Satisfactory to very effective response were observed in 27 patients. In 3 to 10 days, most of the complaints (acidity, pyrosis, pains, and constipation) were relieved. Moreover, X-rays of several patients revealed a disappearance of the ulcerative lesion in 4 patients and a scar tissue formation in 2 others. This study also showed good tolerance by all patients.

- **Another study was conducted on 31 patients** (23 with duodenal ulcers, 6 with gastric ulcers and 2 with duodenal ulcer symptoms) (Yanev, 1994).

Acidity and stomach pains were relieved in less than 30 minutes after Gastro-AD® intake and symptoms disappeared in less than one week treatment in 25 patients.

This study showed that Gastro-AD®, very well tolerated by all patients, led to a quick relief from the main ulcer symptoms.

- **Similar findings were demonstrated in a study involving 47 patients** (Litinskaya, 1981), who have been suffering from duodenal **ulcer** for a period of 3 months to 16 years. All subjects received 2.5 g of Gastro-AD®, 3 times a day during 21 to 25 days, 30 minutes before meals.

In 6 days, a decrease in pain was observed in 44% of the subjects and disappeared completely in 88% at the end of the treatment.

- **Another study (Potashov et al., 1981) was conducted on 105 patients with duodenal ulcers, gastritis, gastroduodenitis, duodenitis and stomach ulcers.** They received 2.5 to 5 g Gastro-AD®, 3 times a day, 30 minutes before meals for one month.

In all patients, symptoms disappeared between the 3rd and 4th day of treatment.

Complaints stopped after 6 days for 55% of patients, after 12 days for 28% of patients, and after 20 days for 11% of patients. Only 6% of patients did not respond to the treatment.

- **In July 2002, a study was conducted in Japan on 12 ambulatory patients suffering from gastritis and other**

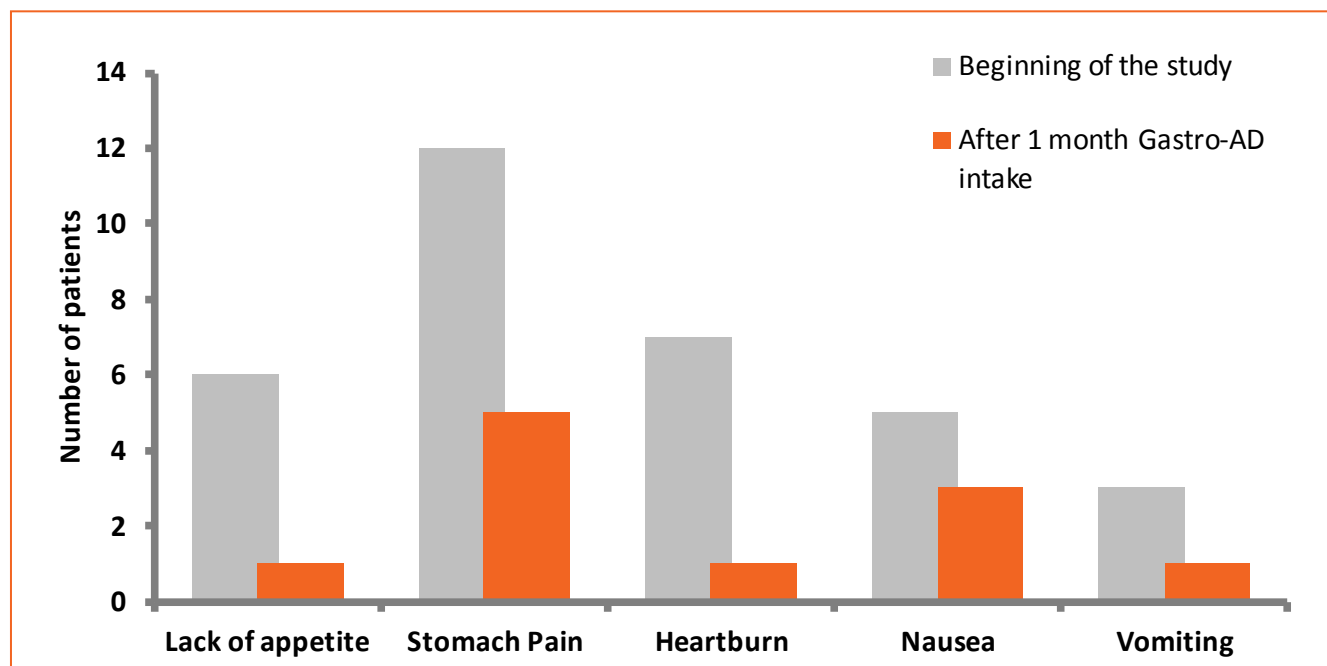


Fig 3: Reduction of most gastroenteropathy symptoms after 30 days of intake of Gastro-AD®

gastroenteropathy. Each patient received 2g Gastro-AD[®], 3 times per day, for 30 days (Hirata and Uchida, 2002).

After one month treatment, significant improvements have been observed in all patients for the various symptoms (Fig 3). In particular, heartburn and lack of appetite.

In the various studies, it appeared that patients who did not respond to Gastro-AD[®] treatment were found to suffer from more severe inflections, such as pyloric stenosis, a penetrating ulcer to the pancreas or a carcinoma.

Altogether, these various trials (almost 600 subjects in total) showed that Gastro-AD[®] is very well tolerated and leads to a quick relief of ulcer symptoms including heartburn, pain, vomiting, and constipation.

Moreover, direct evidence of the supplement's beneficial effects on the healing process were provided by X-ray and gastroscopic examinations showing the disappearance of ulcers and the normalization of the gastric mucosa.

Possible modes of action

Several studies have been conducted to try to elucidate Gastro-AD[®] clinical benefits.

First of all, **the rapid relief of heartburn can**

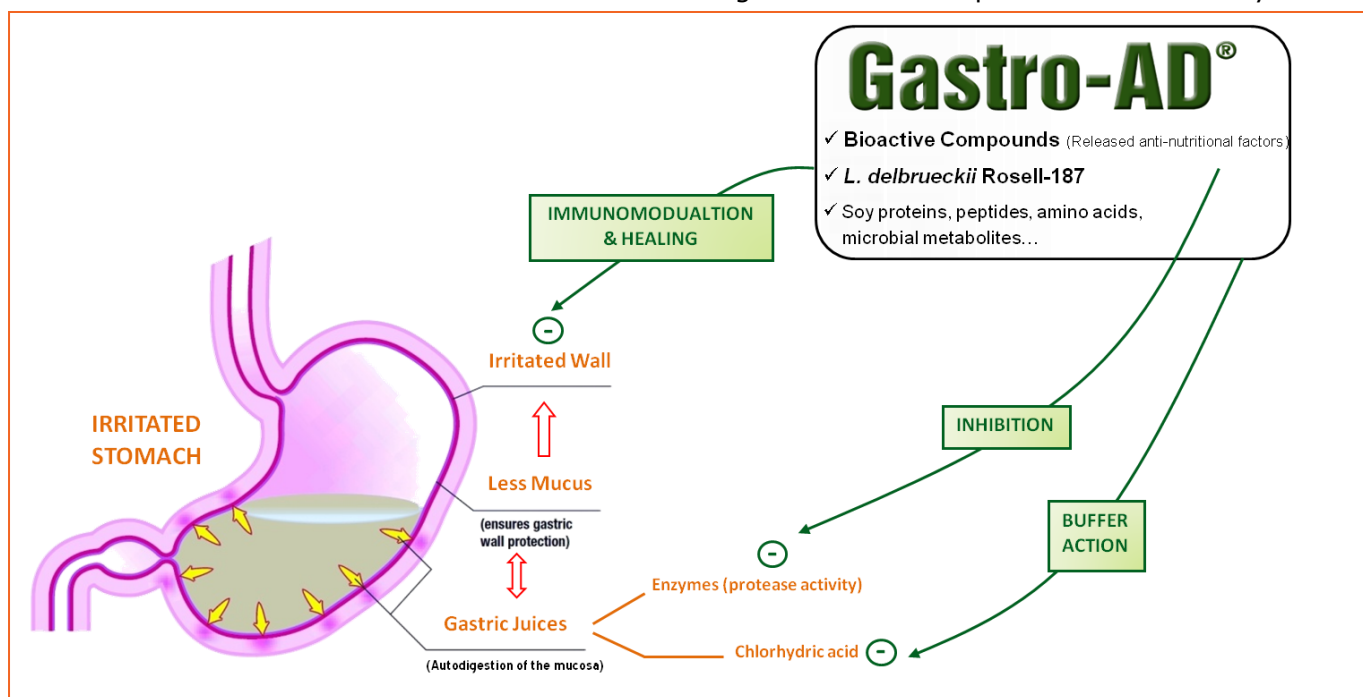
be explained by a buffer effect of the product on the stomach pH. It appears that after intake of Gastro-AD[®], there is a temporary decrease in stomach acidity, which quickly alleviates patients' heartburn and stomach burning sensations. This buffer effect has been shown *in vitro*: Gastro-AD[®] has the ability to neutralize hydrochloric acid. This effect is due to the high concentration of proteins/metabolites in the fermented soy product.

However, if these physico-chemical properties can help explain Gastro-AD[®] symptomatic effects, its effects on gastric healing involve additional mechanisms that contribute to **the restoration of stomach mucosa**. In the past decade, Lallemand R&D laboratories have dedicated some resources to investigate these mechanisms, in particular by examining the peptides and metabolites of soy fermentation by *Lactobacillus delbrueckii* R-187.

Two types of effects were further identified:

- **Inhibition of proteolytic degradation in the stomach through the release of bioactive peptides**

Soy proteins contain regions which have anti-nutritional properties, the "anti-nutritional peptides". When digested and released in the stomach, these factors inhibit the stomach and duodenal proteases that normally aids the degradation of food protein. Because they cannot



Summary of Gastro-AD[®] possible modes of action in the stomach

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be further degraded by the proteinases, they block their active site, thereby inhibiting further action of the enzyme. These peptides are not inhibitory until they are released from the protein.

It was shown (Lallemand Internal Report) that soy fermentation by *Lactobacillus delbrueckii* R-187 releases such anti-nutritional factors, which thus inhibit the action of the enzymes on the stomach lining. As a result, gastric epithelium is protected from the action of the proteases, tissue degradation stops immediately and pain is reduced.

● Immune modulation.

Lactobacillus delbrueckii R-187's ability to moderate the immune response was assessed *in vitro* (Wallace et al., 2003, Easo et al., 2002). The strain was able to down-regulate Interleukin-8 expression by colonic epithelial cells, an inflammatory cytokine. It also had a moderate to weak effect on TNF α expression. These combined actions on proinflammatory cytokines expression could help explain the product effect on gastric ulcerations healing process.

On-going promising investigations should lead to an even better understanding of the molecules involved in Gastro-AD[®] mechanism of action.

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About soy and fermented soy

Soy is considered as an **alternative to animal-based products**, and is highly regarded for its oil and high protein content: soybeans contain 30-46% **proteins** and provides the 8 essential amino acids.

Moreover, soy is associated with many health benefits but certain factors present in soy products can limit its consumption: indigestible carbohydrates, proteins, lectins, allergens.....**Soy fermentation might provide a solution to reduce the negative effects of these anti-nutritional factors**

Fermented soy is recognized as healthy, nutritive ingredient, which has been part of Asian culture for millenaries (e.g. miso, natto, soy sauce...) and associated to many health benefits:

- Prevention of **cancers** (breast, prostate, colon)
- Reduction of **menopausal** symptoms
- **Antioxidant, cholesterol-lowering and anti-allergenic** effects
- Relief of **gastritis** (stomach heartburn & stomach discomfort)

Fermented non GMO soy as found in Gastro-AD[®] represents a natural, nutritional and safe food product.



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