

CLINICALLY
PROVEN

benegut[®]
Digestive comfort

Fytexia
an ABF Ingredients Company

FUNCTIONAL DYSPEPSIA & GASTROINTESTINAL DISCOMFORT

Functional dyspepsia

is a term for recurring digestive symptoms that have no obvious cause.

It is defined by the presence of one or more of the following symptoms: **epigastric burning, bloating, early satiety, postprandial fullness**, etc.

(Rome IV criteria)

1/5

of the general population has been estimated to **experience functional dyspepsia.**

Reference: <http://dx.doi.org/10.1136/gutjnl-2014-307843>

GI discomfort impacts daily life



64% of people having GI discomfort said that **they do not feel comfortable meeting with friends or other people.**



92% reported that they feel **limited to wear comfortable clothes and they are not able to wear skinny clothes.**



72% indicated **reduced motivation and that they prefer to stay at home.**

Reference: Clinical study questionnaire 2014

CONSUMER HEALTH CONCERNS

Consumers act on varied health concerns

Have you taken action to improve any of the following health conditions in the past 12 months?

Top responses (Av: 11 countries in 2021)

38% Improve sleep

31% Hydration

30% Immunity

29% Stress/anxiety

27% Gut/digestive health

27% Heart health

Innova Health & Nutrition Survey, 2021

#1 PLANT-BASED & LOW DOSE

A third of the growth of gastrointestinal supplements was attributed to products combining herbal ingredients, making plant-based ingredients a challenger of the star of the category ie. probiotics.

NBJ, condition specific 2021

Benegut® provides a low-dose plant-based approach to the gut health category.

#2 ACUTE BENEFITS

Consumers want to experience the benefits of their supplementation rapidly in this health area.

The new clinical study on Benegut® demonstrates improvement in gastrointestinal comfort after the first intake.

#3 SCIENCE

When considering nutritional supplements, **59% of global consumers want to see scientific evidence supporting efficacy.**

Nutritional Outlook, 2022

Benegut® has been clinically tested on the improvement of the digestive comfort.

#4 EFFICACY

Consumer research indicates that today **third of consumers looking for gut health support do not find an effective product that alleviates their discomfort.**

Nutritional Outlook, 2022

Benegut® is clinically proven to reduce significantly different parameters signing digestive discomfort.

A TRADITIONNAL HERB OF JAPAN



Green perilla leaves

Magnoliopsida > Lamiales > Lamiaceae > Perilla frutescens L.

a.k.a. Shiso (Japan), Japanese Melisse or Japanese Basil (USA, Europe), Schwarznessel (Germany)



An annual edible herbaceous plant native to Asia.

Cultivated in Hokkaido, Japan.



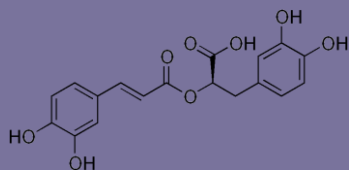
Foods: the leaves are used fresh or fried as spice, as garnish, salad and in wrappings for sushi.

Medicine: traditional medical applications are all linked of the respiratory tract and the immune system.

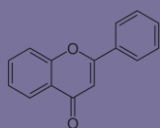


Harvest is done once per year in late summer. Pre-harvest tests are done to set the right harvest time, where Perilla leaves contain the active compounds naturally at the concentration and ratio set for the standardisation.

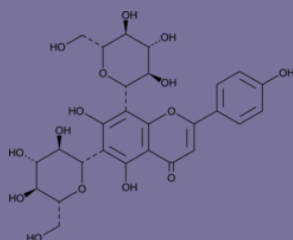
SELECTED COMPOUNDS FOR DIGESTIVE COMFORT



ROSMARINIC ACID



FLAVONOIDS



VICENIN-2

BIOACTIVE COMPOUNDS

Primary active compounds:

Rosmarinic acid	≥ 0.05%
Special flavonoids fraction	≥ 0.18%
incl. Apigenin-6,8-di-C-glucoside (vicenin-2)	≥ 0.007%

BOTANICAL SOURCE

Shiso leaf extract

Perilla frutescens

Annual edible herbaceous plant native to Asia (Hokkaido, Japan)

Water extraction

FORMULATION

Recommended daily dose: 300 mg

No allergens, non-GMO, Halal, Kosher, gluten-free, suitable for vegetarians

Non-irritating: No methyleugenol, Myristicin, Perillaketone detected, tested on each batch.

PATENT

WO2013079623. Vicenin 2 and derivatives thereof
for use as antispasmodic and/or prokinetic agent.

SCIENTIFIC APPROACH

MECHANISM OF ACTION

Ex vivo animal study to explore anti-spasmodic effects

In vitro study to screen for preventive effects on tight junction leakage

CLINICAL BENEFITS

I NEW I

Acute human study on GI discomfort

Chronic human study to investigate effects on functional dyspepsia and associated GI discomfort

SUPPORTING STUDIES *Publications*

CLINICAL TRIAL

Buchwald-Werner *et al.* *BMC Complementary and Alternative Medicine* 2014, 14:173

2023 Publication pending

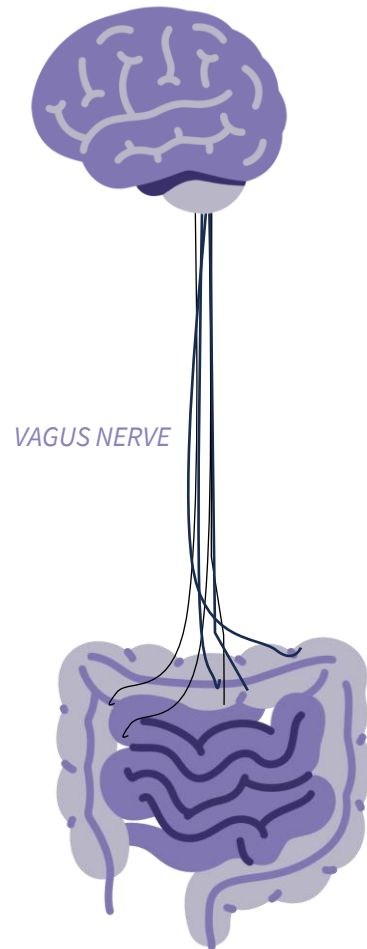
MECHANISTIC STUDIES

J. Verspohl *et al.* *Phytomedicine* 2013, 427–431
Buchwald-Werner *et al.* 2016 *Agro FOOD Industry Hi Tech* - vol. 27(5)



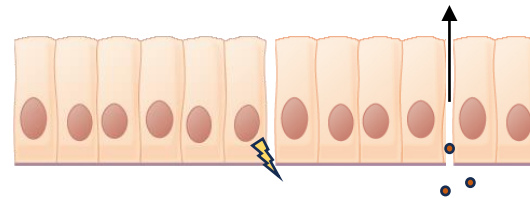
- ✓ No adverse events
- ✓ No side effects

FUNCTIONAL DYSPEPSIA & GI DISCOMFORT



LEAKY GUT

allowing transfer of microbial components hence recruiting mast cells



Acute inflammation

Impaired tight junction

ACTION ON TIGHT JUNCTIONS/INTESTINAL BARRIER

- Apigenin restores the loss of tight junction proteins (occludin, claudin-1)¹;
- Rosmarinic acid promotes mucus secretion (Muc2) enabling maintenance of tight junctions²

ACUTE INFLAMMATION

in intestinal epithelium leading to visceral hypersensitivity

ACUTE ANTI INFLAMMATORY ACTION IN INTESTINAL EPITHELIUM

- Apigenin, Luteolin and Rosmarinic acid have shown inhibitory action on nF-kB thus reducing the secretion of proinflammatory cytokines³

FEELING OF FULLNESS, PAIN PERCEPTION

modulated by gut hormones

ANTI-SPASMODIC EFFECT ON GASTROINTESTINAL RECEPTORS

- Perilla extract and Rosmarinic acid provide antispasmodic effect by inhibiting dopamine D2 receptors in the GI tract⁴;
- Apigenin inhibits Ca²⁺-induced spasms by altering the Ca²⁺ availability in the GI lumen in vitro and in vivo studies⁵

1: <https://doi.org/10.1016/j.jff.2023.105499>

2: <https://doi.org/10.1021/acs.jafc.2c08444>

3: <https://doi.org/10.4049/jimmunol.179.10.7121> , <https://doi.org/10.1016/j.ejphar.2011.04.007>, <https://doi.org/10.1152/ajpgi.00294.2014>

4: DOI:10.1002/tkm2.1296

5: <https://doi.org/10.1016/j.compbimed.2023.106596>, <http://dx.doi.org/10.1016/j.ejphar.2008.09.021>

MAINTAINING INTESTINAL PERMEABILITY

IN VITRO STUDY

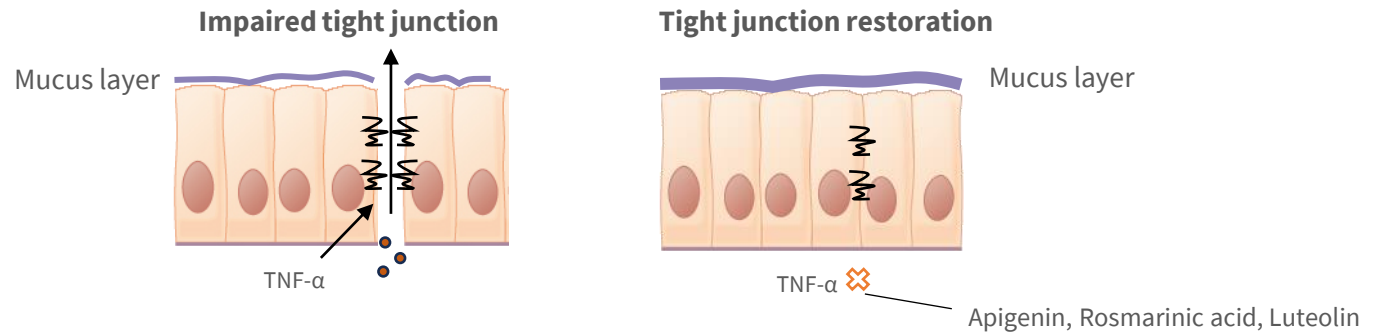
- Human-like model Caco-2 (epithelial cell line)
- 100 µg/mL of Benegut® on Caco-2 cells for 72 hours
- Transepithelial electrical resistance using a cellZScope®

Conducted by the Institute for Pharma Technology,
School of Life Sciences University of Applied
Sciences, Switzerland

REFERENCE

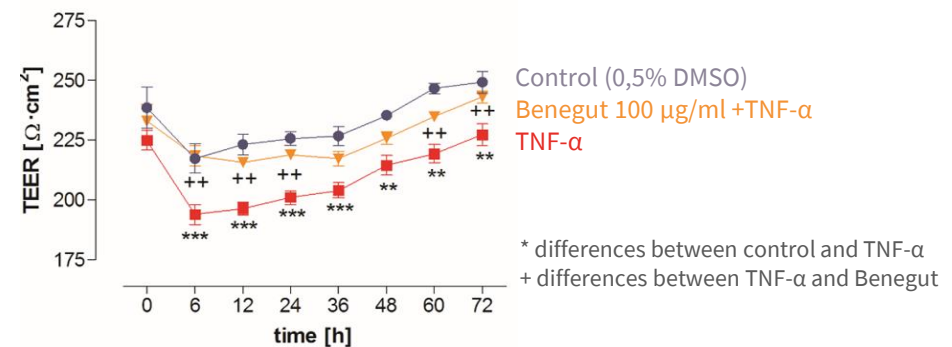
Buchwald-Werner S. *et al.*, 2016, *Agro FOOD Industry Hi Tech* - vol. 27(5)
Perilla Frutescens targets intestinal permeability

Evaluation of intestinal permeability



The effect of Benegut® on TNF α -caused tight junction leakage were investigated on intestinal epithelial cells (Caco-2):

Trans-epithelial electrical resistance



Benegut® showed a significant restorative effect on the tight junctions, after 6 hours until 24h against TNF- α treatment.

ANTI-SPASMODIC EFFECT

EX VIVO STUDY

Experiment on adult male Wistar rat's ileum

Evaluation of the anti-spasmodic effect of

- Benegut®
- Vicenin-2 isolated

Induction of intestinal contraction by spasmodic agents:

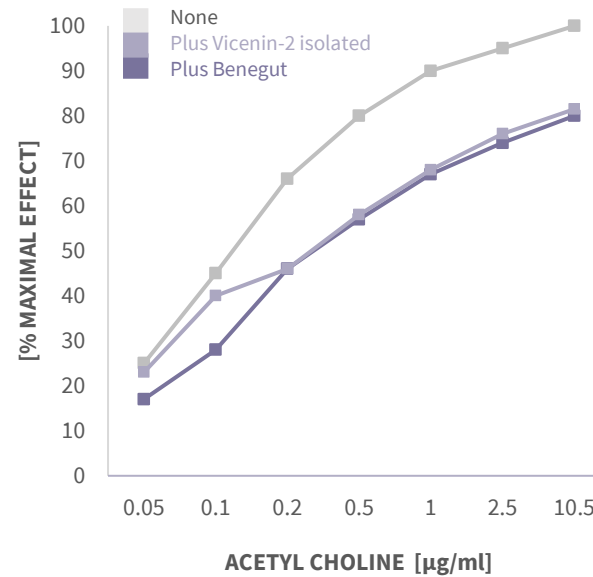
- Acetylcholine, up to 10 g/ml
- Ba²⁺, up to 4 g/ml

Department of Pharmacology, Institute of Medicinal Chemistry, University of Münster, Germany

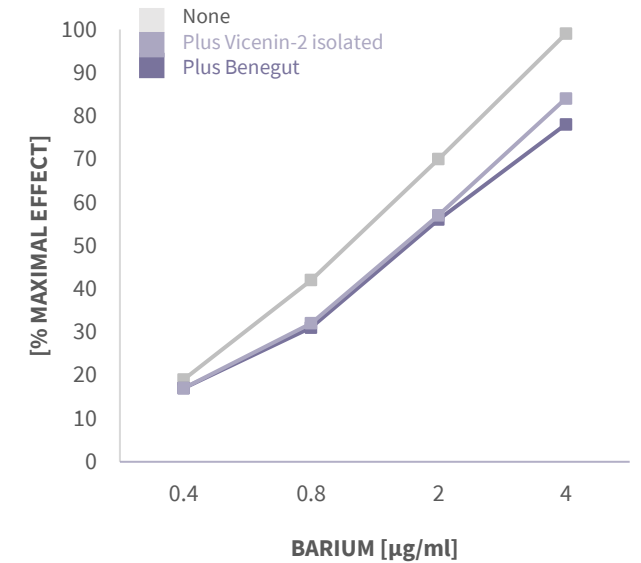
REFERENCE

Verspohl J. *et al.*, 2013, *Phytomedicine*, 427–431
Testing of *Perilla frutescens* extract and Vicenin 2 for their antispasmodic effect

Effects on rat ileum contractions induced by acetylcholine



Effects on rat ileum contractions induced by Barium ion



Curves induced by both Benegut and Vicenin-2 isolated are significantly different from the acetylcholine, Barium curve.

Benegut® & isolated Vicenin-2 decreased significantly acetylcholine- or Ba²⁺ -induced rat ileum contractions indicating an antispasmodic effect.

CLINICAL STUDY

YEAR & DURATION

2012
4 weeks

POPULATION

50 subjects (41 women & 9 men)

Healthy subjects with gastrointestinal discomfort evaluated by a questionnaire

Age: 30-70 years old

BMI: 19-30 kg/m²

PROTOCOL

RUN-IN PHASE

2 WEEKS

BASELINE



SUPPLEMENTATION – INTERVENTION PHASE

4 WEEKS

0 – 15 days: VISIT 1



15- 30 days: VISIT 2



GI symptoms on a scale from 0 to 4 (Daily measure): bloating/distension, passage of gas, GI rumbling, feeling of fullness, abdominal discomfort

Confounding factors monitored: Perceived stress PSQ20 score; stool frequency

INTAKE

CAPSULES

2 x 150 mg/day

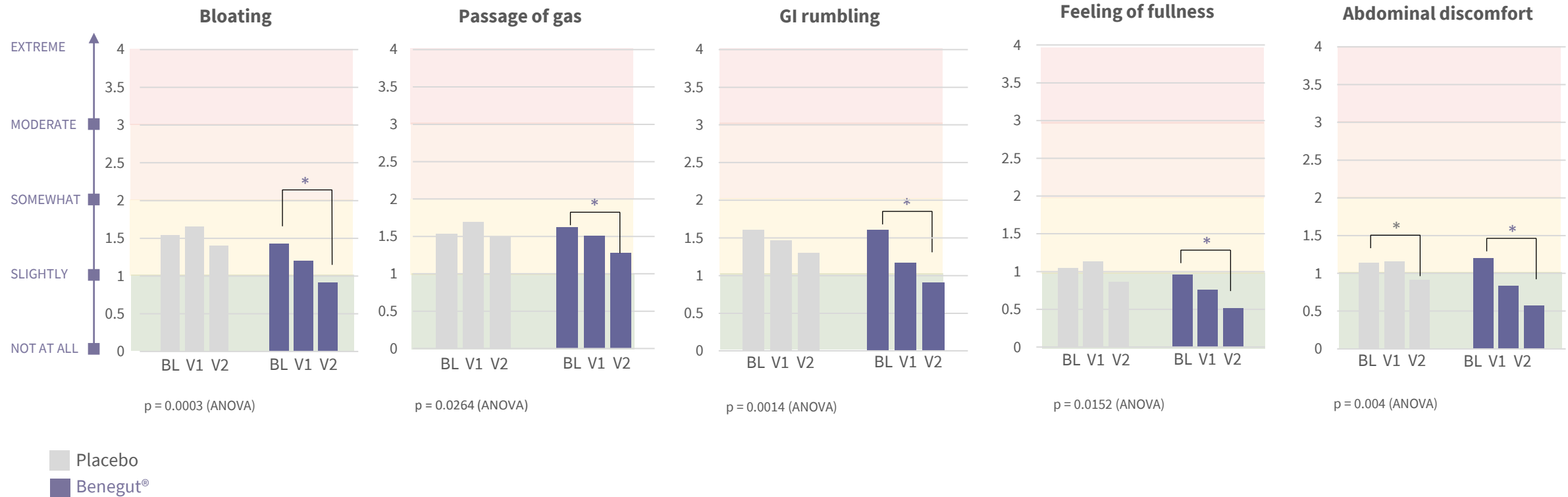
One in the morning and one in the evening before food intake with sufficient water for the 4 weeks duration of the intervention phase.

- Double-blind, randomised, placebo-controlled study
- Registration of clinical trials with ethics committee approval
- Trial registration number: NCT01931930 at ClinicalTrials.gov
- Location: Esslingen, Germany
BioTeSys GmbH

REFERENCE

Buchwald-Werner S. *et al.*, 2014, *BMC Complement Altern Med*, 14:173

GASTROINTESTINAL DISCOMFORT



All GI symptoms were significantly improved over time in the supplemented group.

CLINICAL STUDY

- Acute, Double blind, randomised, powered cross-over trial
- Registration of clinical trials with ethics committee approval
- Trial registration number: NCT05603416 at ClinicalTrials.gov
- Location: Esslingen, Germany
BioTeSys GmbH

YEAR & DURATION

2022

Acute

POPULATION

30 healthy subjects (22 women & 8 men) with overall GI discomfort after a high caloric meal of at least 5 on the VAS scale at baseline visit

Age: 18-30 years old

BMI: 19-30 kg/m²

PROTOCOL

3 groups, in cross-over

- Baseline
- Placebo
- Benegut



Primary outcome: Overall GI symptoms on a VAS scale of 0 to 10

Other outcomes: Individual GI symptoms on Likert scale of 0 to 5
Feeling of fullness, Bloating, Passage of gas, GI discomfort, cramps, pain, Burning GI rumbling, Heartburn, Urge to defecate

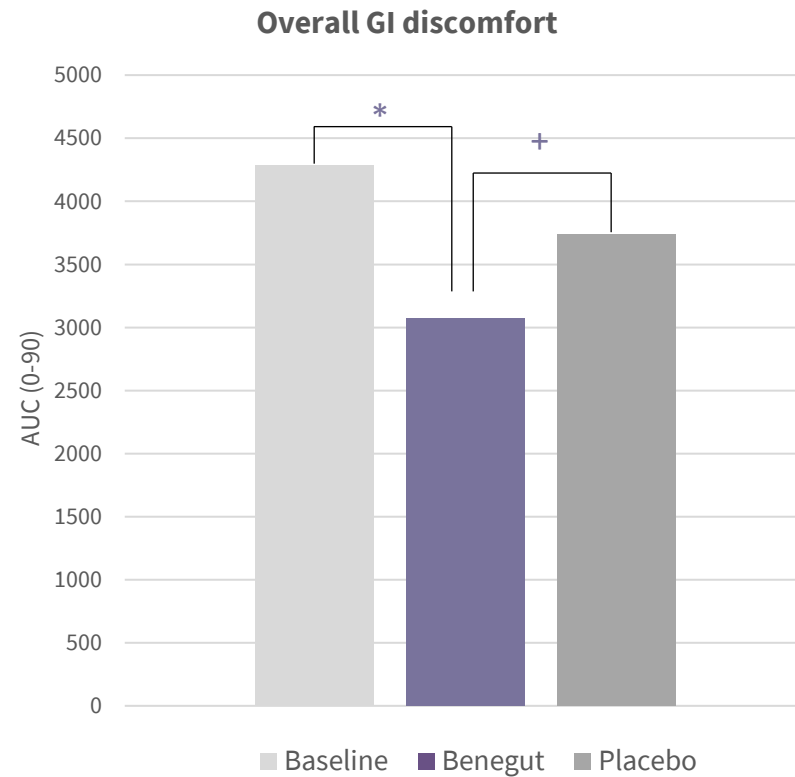
INTAKE

ORODISPERSIBLE STICK PACKS

Stick with peppermint flavor containing 300mg of Benegut or placebo taken immediately after a high caloric meal (single dose)

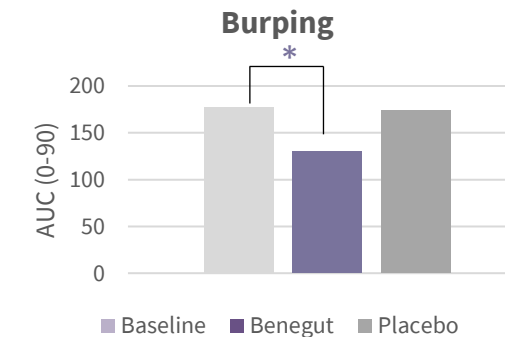
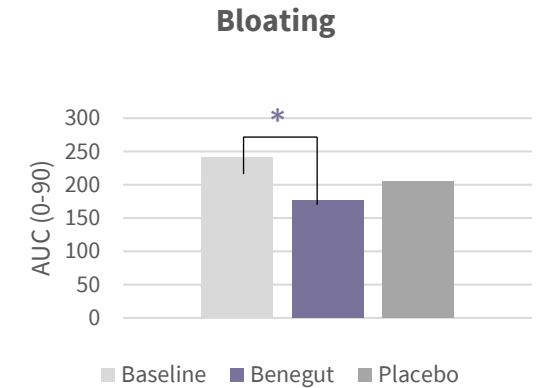
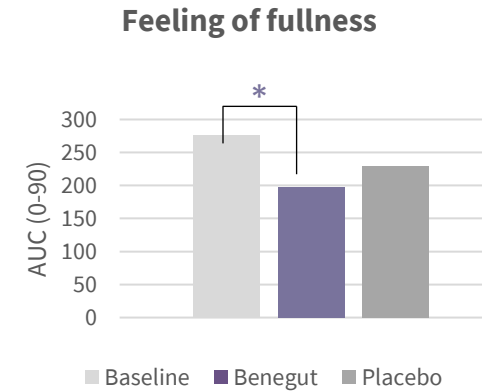
Composition: Sorbitol, Benegut® (Perilla frutescens extract, tapioca maltodextrin) or placebo (300 mg/stick), peppermint aroma, magnesium salts of fatty acids, steviol glycosides

IMPROVEMENT IN OVERALL GI DISCOMFORT SCORE



* Significant differences between Benegut and Baseline

+ Significant differences between Benegut and Placebo

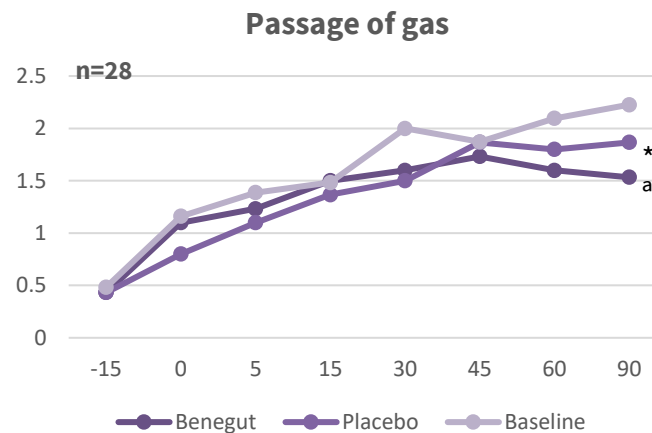
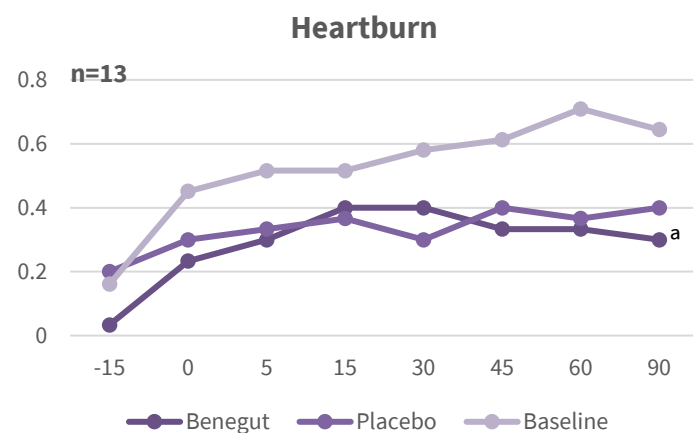
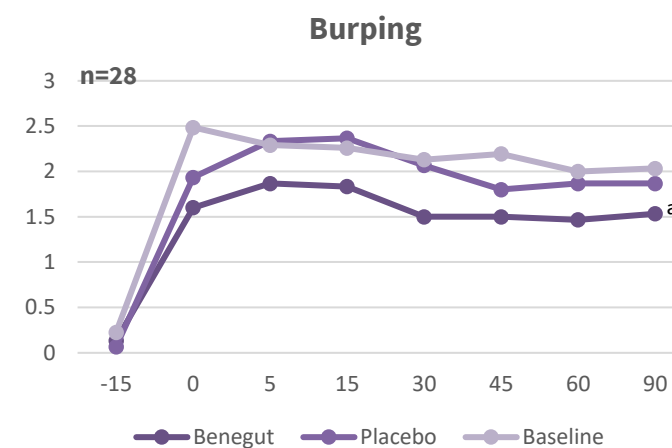
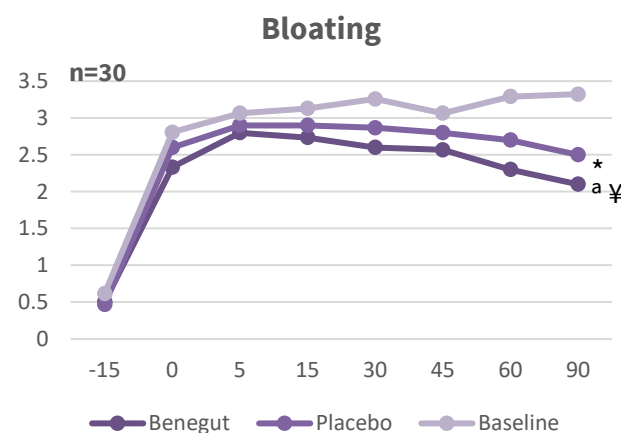
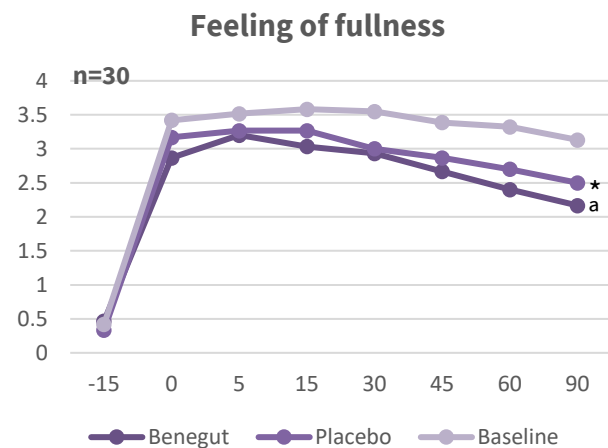


Feeling of fullness, bloating and burping are the 3 main symptoms driving improvement in GI discomfort

Benegut® improves significantly overall GI discomfort compared to baseline and placebo.

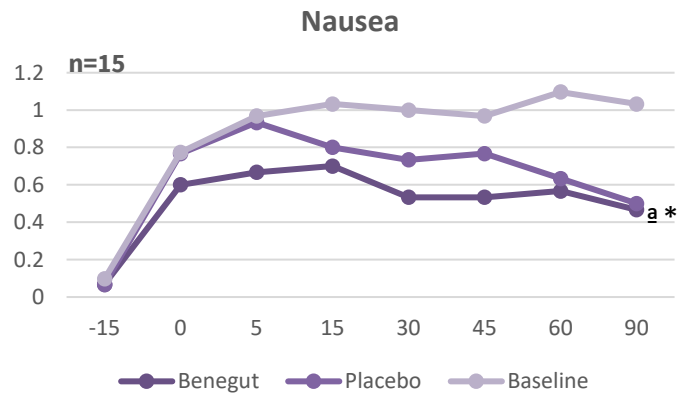
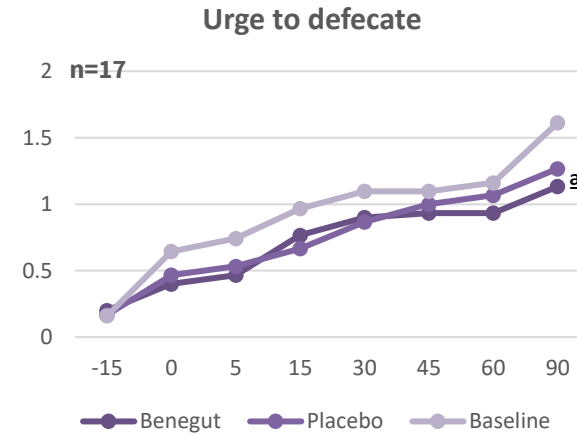
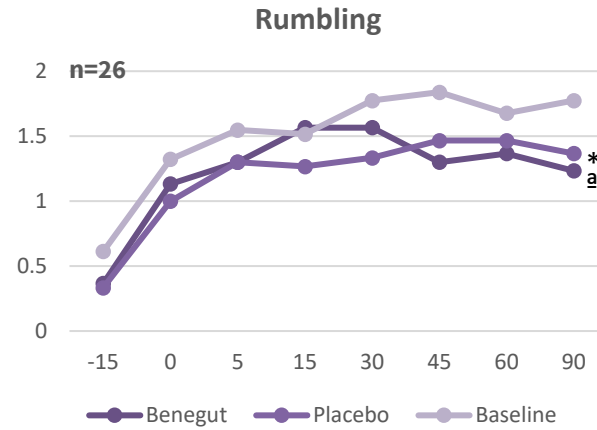
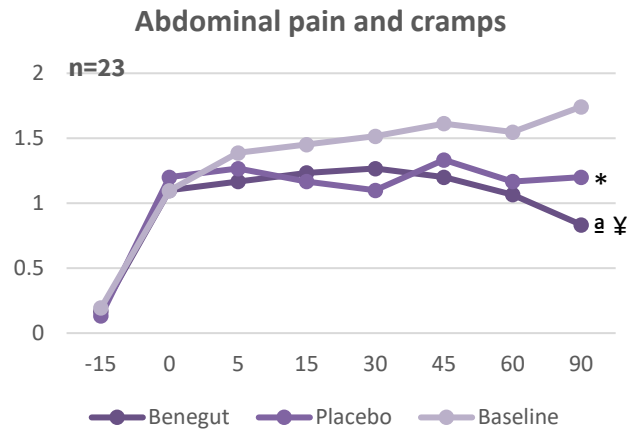
IMPROVEMENT IN SYMPTOMS AFTER 90 MINUTES

All the measured symptoms were significantly reduced in Benegut® group at 90 minutes post high caloric meal consumption compared to baseline.



* Significant difference at end of study (90 min) between Screening and Placebo
^ Significant difference at end of study (90 min) between Screening and Benegut
¥ Significant difference at end of study (90 min) between Placebo and Benegut

IMPROVEMENT IN SYMPTOMS AFTER 90 MINUTES



*Significant difference at end of study (90 min) between Screening and Placebo
^a Significant difference at end of study (90 min) between Screening and Benegut
[¥] Significant difference at end of study (90 min) between Placebo and Benegut

KEY FEATURES

- ✓ Benegut® contributes to the reinforcement of tight junctions of cells.
- ✓ Benegut® shows an antispasmodic effect.
- ✓ Benegut® rapidly reduces overall gastrointestinal discomfort.
- ✓ Benegut® is clinically proven to:
 - Reduces bloating
 - Reduces the passage of gas
 - Reduces GI rumbling
 - Improves the feeling of fullness
 - Reduces overall abdominal discomfort
- ✓ **Clinical results & publications available upon request**

APPLICATIONS

COMMERCIAL NAME

Benegut®

COMPOSITION

Perilla Frutescens (L.) extracts

ACTIVE COMPOUNDS

Rosmarinic acid	≥ 0.05%
Special flavonoids fraction	≥ 0.18%
incl. Apigenin-6,8-di-C-glucoside (vicenin-2)	≥ 0.007%

RECOMMENDED DOSAGE

300 mg/day

APPLICATIONS

Dietary supplements

OTHERS

No allergens, non-GMO, Kosher, Halal, gluten-free, suitable for vegetarians