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**Vitafoods™  
Europe**



**Perilla frutescens extract  
and its immediate, perceptible balancing  
effect on digestive discomfort**

**Dr. S. Buchwald-Werner  
14. May 2013  
Vitafoods Europe Conference**

# Agenda

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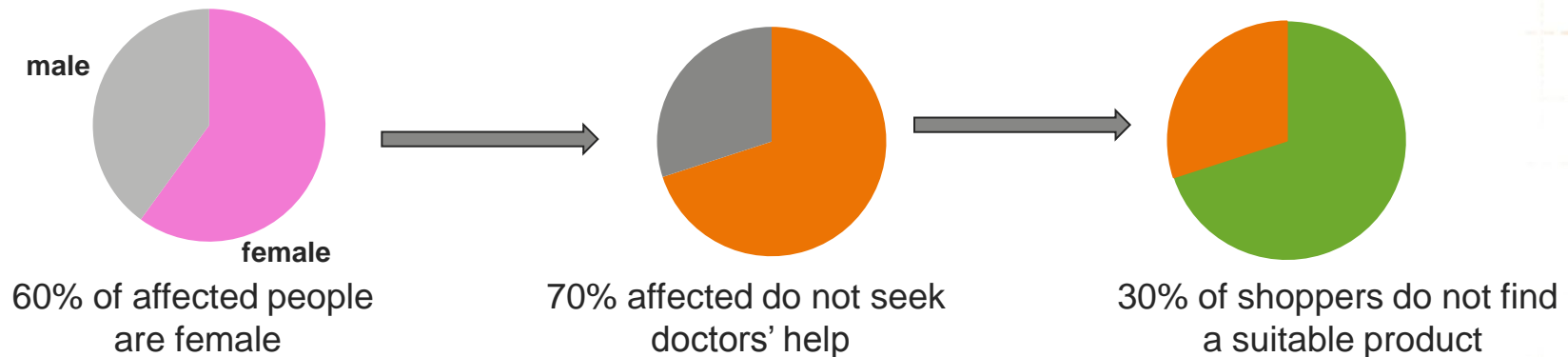
- ✿ Gut health & Consumer needs
- ✿ Development of an innovative gut health ingredient
- ✿ Human study results
- ✿ Product positioning



# Gut health and consumer needs

## The gut health market – consumer insights

- ✿ Approximately 10-20 % of the world population is affected by a digestive disorders
- ✿ Most of them are female and are reluctant to seek doctors' help
- ✿ This demonstrates an interesting business opportunity for gut health ingredients suppliers who are able to educate and create awareness among these consumers



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# Gut health and consumer needs

## Causes for digestive discomfort & beneficial ingredients and its effects

### Causes

- Daily stress
- Food sensitivity
- Allergies
- Infections
- Altered gut flora
- Deregulation of brain-gut cross talk
- Genetic preposition

### Body response

- Ileum contractions
- Unbalanced gut flora
- Unbalanced gut motility
- Inflammations

### Symptoms

- GI discomfort
- Bloating
- Rumbling
- Passage of Gas
- Cramps
- Pain
- Constipation
- Diarrhea
- IBS

### Mode of action

- Antispasmodics
- Anti-inflammatory agents
- Agents to improve brain-gut cross talk
- Stool Volume enhancer
- Growth support to gut flora
- Gut flora substitution

### Ingredients

???

- Fiber
- Prebiotics
- Probiotics



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# Development of a new gut health ingredient

## Origin

- ✿ Extract development based on *Perilla frutescens* (L.) leaves, an annual edible herbaceous plant native to Asia
- ✿ *Perilla frutescens* is a member of the family *Lamiaceae*
- ✿ Its common names are:  
Shiso (Japan), 紫蘇 Zi Su Ye (China)  
Perilla, Japanese Melisse or Japanese Basil (USA, Europe)  
Schwarznessel (Germany)
- ✿ *Perilla* leaves as well as the *Perilla* seed oil is used as food and in traditional medicine
- ✿ In foods the leaves are used fresh or fried as spice, as garnish, salad and in wrappings for sushi
- ✿ Traditional medical applications are all linked of the respiratory tract and the immune system

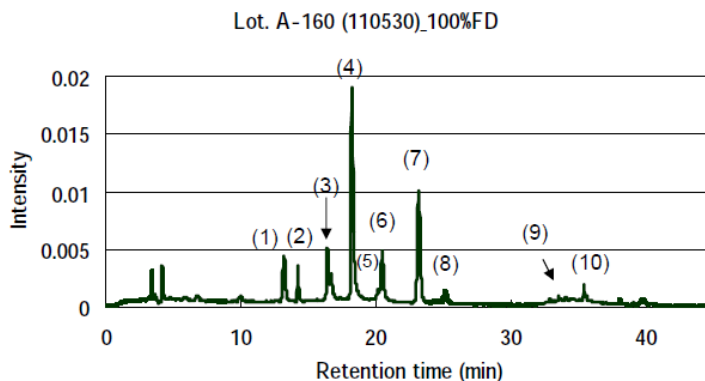
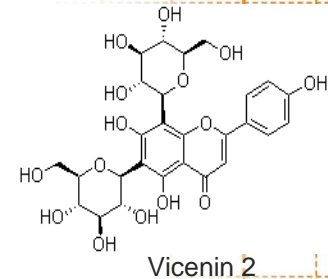


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# Development of a new gut health ingredient

## Extract specifications and “fingerprint”

- Food grade extraction process based on water as extraction solvent
- Phytochemical investigation and identification of Vicenin 2
- Development of a proprietary *Perilla frutescens* leaf extract, standardized on a special flavonoid fractions, including Vicenin 2 and on rosmarinic acid, determined by HPLC



- (1) Caffeic Acid
- (2) Apigenin 6,8-di-C-diglucoside
- (3) luteorin 7-O-[ $\beta$ -glucuronosyl(1 $\rightarrow$ 2) $\beta$ -glucuronide]
- (4) Apigenin 7-O-[ $\beta$ -glucuronosyl(1 $\rightarrow$ 2) $\beta$ -glucuronide]
- (5) luteorin 7-O- $\beta$ -glucuronide
- (6) scutellarein-7-O- $\beta$ -glucuronide
- (7) Rosmaric Acid
- (8) Apigenin 7-O- $\beta$ -glucuronide
- (9) luteolin
- (10) Apigenin



- Perilla frutescens* extract is a water soluble fine beige powder

# Development of a new gut health ingredient

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## Science

Several scientific studies have been carried out using the proprietary Perilla leaf extract as well as isolated Vicenin 2 to investigate the effects on digestive health:

- ✿ ***Ex vivo* human study to test anti-inflammatory and immune effects**
- ✿ ***Ex vivo* animal study to explore anti-spasmodic effects**
- ✿ ***In vitro* study to screen for brain-gut axes activities**
- ✿ **Nutritional human study to investigate effects on GI discomfort**



# Development of a new gut health ingredient

**Ex vivo human study to confirm anti-inflammatory and immune effects for the proprietary *Perilla frutescens* extract within human blood leucocytes from 10 volunteers**

Immune effects	Anti-inflammatory
Stimulation with with Concanavalin A (ConA) and Staphylococcal enterotoxin B (SEB)	Stimulation with lipopolysaccharide (LPS)
<b>Perilla extract showed a low immune modulating efficacy and demonstrated a shift from Th1 to Th2</b> based on the IFN $\gamma$ - IL4 quotient	<b>Perilla extract showed anti-inflammatory properties by the significant reduction of TNF<math>\alpha</math></b>

 The study was conducted by Biotesys, Esslingen, Germany



Fujii H., et al., Investigation of a *Perilla frutescens* special extract. Anti-inflammatory and immune-modulatory properties. Agrofood Industry hi-tech (2012)



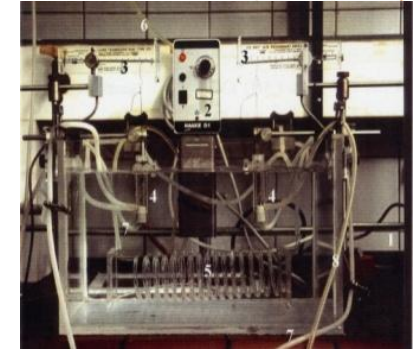
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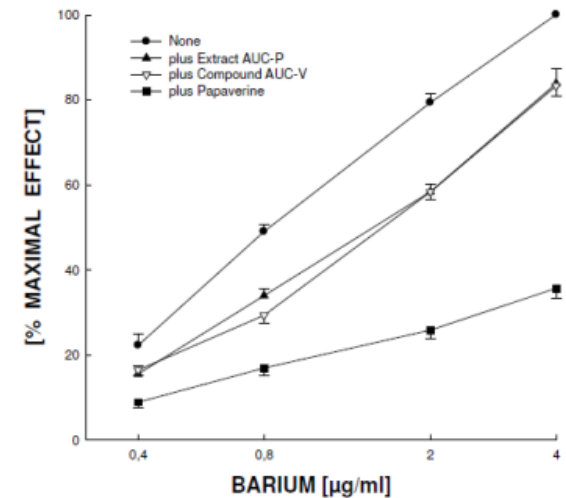
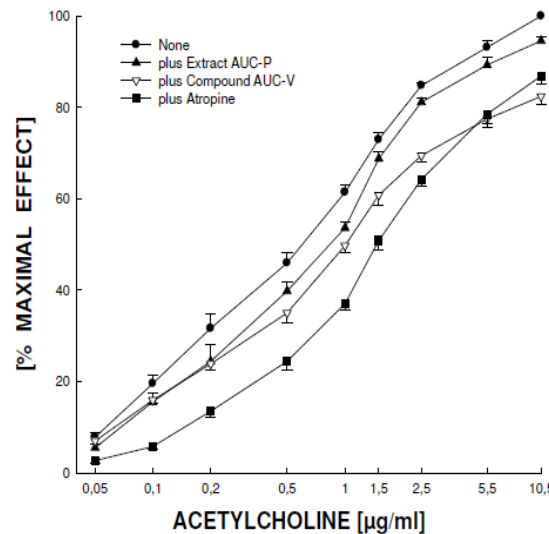
# Development of a new gut health ingredient

## Investigation of antispasmodic activity for application in gut health

- The antispasmodic effect on smooth muscles leads to a relief from gastrointestinal symptoms
- The antispasmodic effect of the proprietary *Perilla frutescens* extract and its key active constituent was investigated on isolated adult male Wistar rats' ileum contraction.



Mode of action	Agonist	Positive control
Neurotropic effect induced by e.g. stress	Acetylcholine	Atropine
Muscolotropic effect induced by e.g. food allergens	Barium	Papaverine



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# Development of a new gut health ingredient

## Investigation of antispasmodic activity for application in gut health

- ✿ Perilla frutescens extract and isolated Vicenin 2 demonstrated antispasmodic, dosage dependent effects inhibiting musculotropic activity and neurotropic, cholinergic activity.
- ✿ Both the extract and the compound have no direct spasmolytic activity. In case of no contraction no activity will be recorded. This behavior demonstrates the safe use of Benegut for application in dietary supplements.
- ✿ The study was conducted by Prof. Verspohl, Westfälische Wilhelms-University, Münster, Germany

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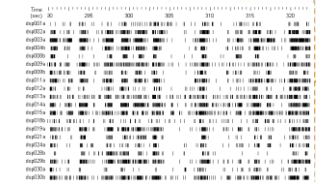
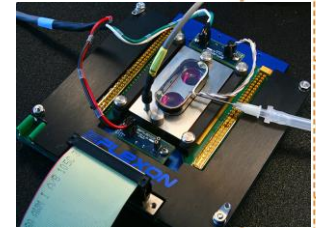
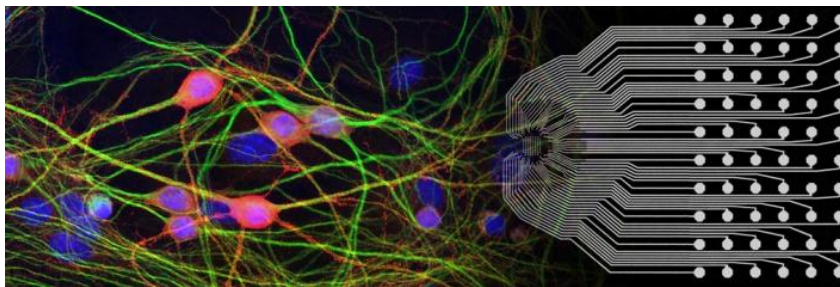
Institut für  
Pharmazeutische und  
Medizinische Chemie  
Abt. Pharmakologie



# Development of a new gut health ingredient

## ***In vitro* study to screen for brain-gut axes activities**

- An acute neuroactive effect of *Perilla frutescens* extract and isolated Vicenin 2 on the neuronal activity of murine frontal cortex networks was tested by means of electrophysiological multi-channel recording in comparison with well-known neuroactive substances.
- *Perilla frutescens* extract and isolated Vicenin 2 act as a reversible cholinesterase inhibitor having prokinetic effect to balance the rhythm and support regularity of the small intestine.
- The study was conducted by Neuroproof, Rostock , Germany



Buchwald-Werner S., Fujii H., Prokinetic and antispasmodic constituent discovered in *Perilla Frutescens* – Development of a gut health ingredient. *Planta medica* (2012)

# Perilla frutescens extract - Human study results

## Nutritional human study to investigate effects on GI discomfort

- ✿ Results of a first nutritional human study showed that daily supplementation with Perilla frutescens extract supports gastrointestinal health.

### Study facts:

- double blind, randomized, placebo-controlled, parallel design human
  - 50 healthy people, ages 30-70, BMI 19-30 kg/m<sup>2</sup>, 41 women & 9 men
  - 150 mg Benegut twice a day for 4 weeks
  - healthy volunteers with GI discomfort and bowel movements between 1.5-3x/week
- ✿ Study population represents the distribution of GI discomfort within the general population
  - ✿ Particularly woman suffer from GI discomfort and reduced bowel movements and are generally more willing to participate in trials
  - ✿ The study was independently conducted by Biotesy, Esslingen, Germany



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# Perilla frutescens extract - Human study results

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## Nutritional human study to investigate effects on GI discomfort

### Challenges:

- ✿ Nutritional human studies investigate effects within healthy people, with the aim to demonstrate an improvement of a physiological status, defined as healthy, that affects quality of life – where improvements range only from slight to moderate
- ✿ GI symptoms show a high fluctuation
- ✿ Gut health studies report high placebo effects
- ✿ This study was designed to take account that GI symptoms a high fluctuation and gut health studies report high placebo effects.



# Perilla frutescens extract - Human study results

## Nutritional human study to investigate effects on GI discomfort

### Study flow

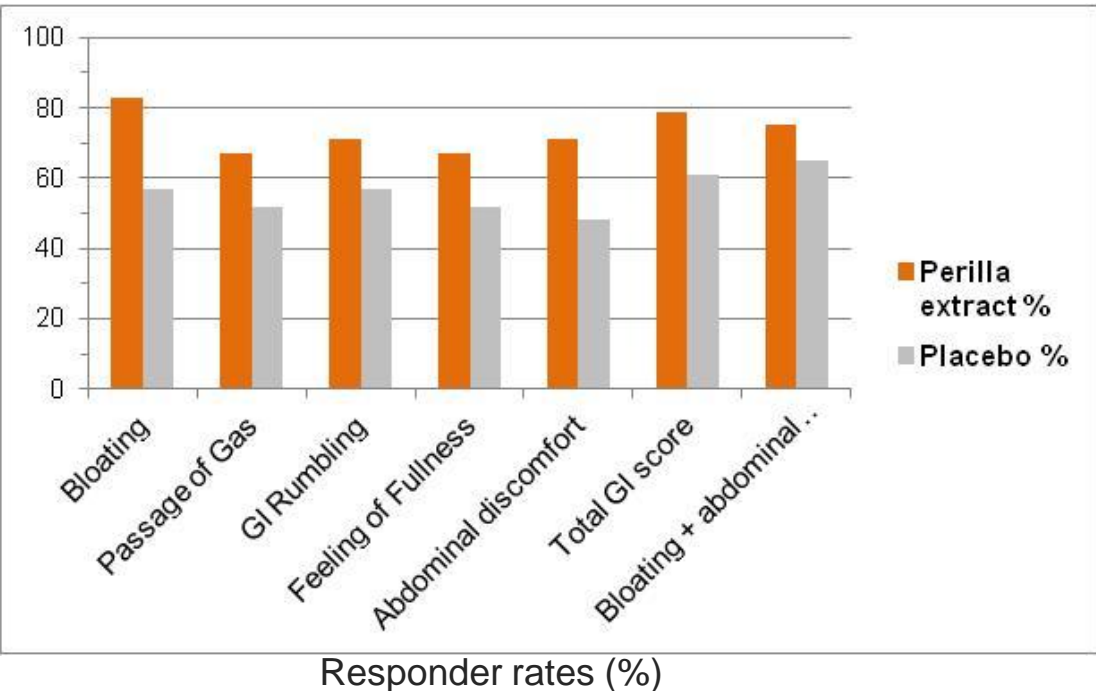
	Screening	Treatment Period		Follow up			
		Whole transit time	Run-In Phase	Visit 1	Visit 2	Whole transit time	Visit 3
Time		1 week prior to run-in	2 weeks	Day 1	Day 29	Day 30 - 38	Day 39
Informed Consent	x						
In- and Exclusion Criteria	x			x	x		
Adverse Events				x	x		x
Anamnesis / Checkup / ECG	x						
Blood Routine Parameters	x						
Gastrointestinal screening module	x						
Questionnaire of bowel movements			x	daily for 28 days			
Questionnaire of stool consistency			x	daily for 28 days			
Questionnaire on daily gastrointestinal characteristics			x	daily for 28 days			
Questionnaire of intestinal symptoms (PAC-SYM) + additional questions				x	x		
PAC-QoL				x	x		
Perceived stress questionnaire (PSQ)				x	x		
Determination of whole transit time		x		Hand in of results		x	Hand in of results
Hand out of study products				x			
Intake of study products				x			
Global assessment					x		



# Perilla frutescens extract - Human study results

## ➔ Perilla frutescens extract is able to reduce GI discomfort

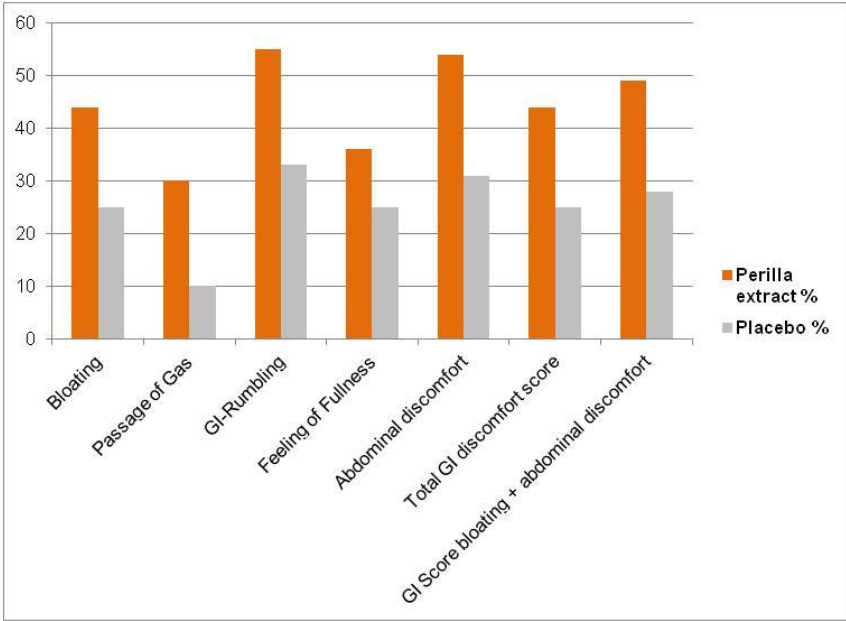
- 🌿 All GI symptoms (bloating, passage of gas, GI-rumbling, feeling of fullness and abdominal discomfort) were significantly improved in healthy people
- 🌿 80% of all volunteers, who took Perilla extract reported substantial improvement of gastrointestinal discomfort.



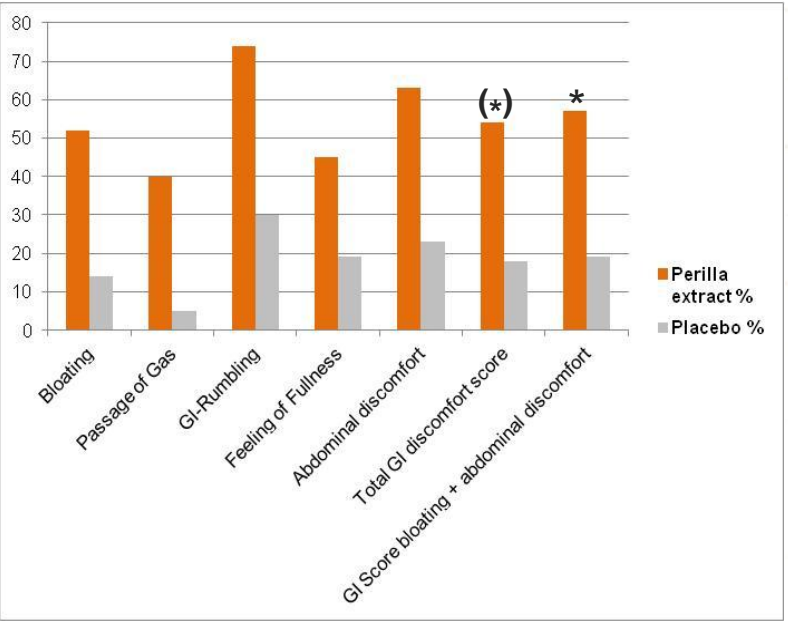
# Perilla frutescens extract - Human study results

## ➔ Perilla frutescens extract is able to reduce GI discomfort

- GI discomfort was reduced leading to an average improved by over 40%
- Perilla was most effective to reduce bloating and abdominal discomfort, particularly in women; Effects were statistically significant against Placebo (p=0.048\*)



GI-discomfort Improvement –all (%)



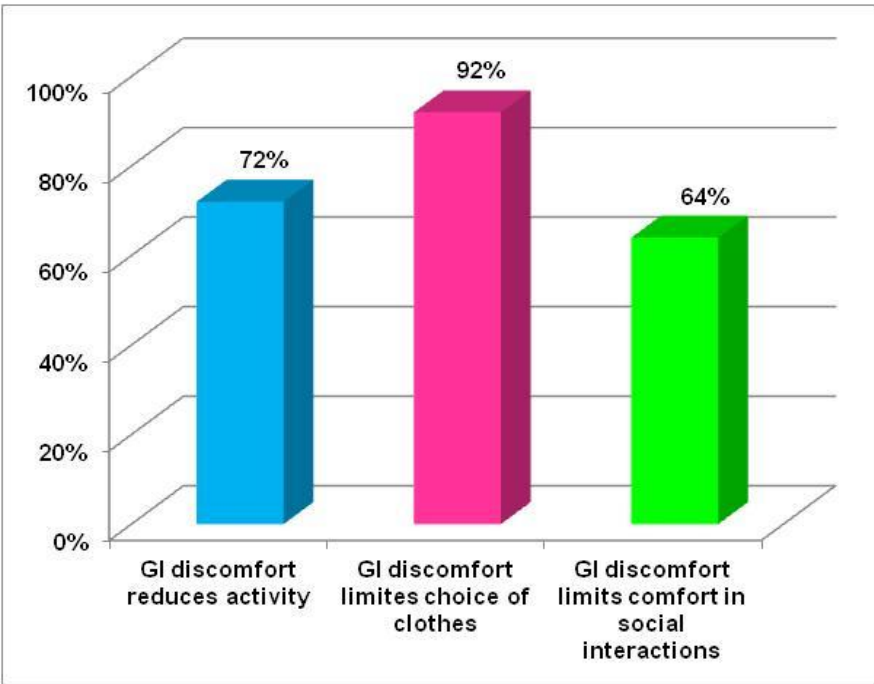
subgroup women %



# Perilla frutescens extract - Human study results

## Study participants were asked how GI symptoms effect their life style

- 92% reported that they feel limited to wear comfortable clothes and they regret that they are not able to wear skinny clothes
- 72% indicated reduced motivation and that they prefer to stay at home and relax on the sofa
- 64% said that they do not feel comfortable to meet with friends or other people



Intake of Perilla extract improved these social contact parameters and contributed to overall quality of life

# Perilla frutescens extract - Human study results

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## **Perilla frutescens extract is able to reduce GI discomfort**

- ✿ Study results confirmed in vitro and ex vivo results, leading to immediate, perceptible relief from GI discomfort. Results confirmed that mode of actions of Perilla extract are prokinetic and anti-spasmodic effects.
- ✿ These study results are very promising, recognizing the challenging set-up of a nutritional human study with healthy volunteers.
- ✿ Perilla frutescens proprietary extract is marketed under the brand name Benegut®

## **Benegut® helps to support...**

- ✿ digestive health.
- ✿ the improvement of gastrointestinal discomfort.
- ✿ the reduction of bloating.
- ✿ the reduction of abdominal discomfort like pain, cramps and inflammations.
- ✿ the freedom to wear the clothes of choice like a skinny jeans.
- ✿ the motivation to have social activities even when suffering from GI symptoms.





## The new intelligent ingredient for gut health

### Benegut® Features:

- ✿ A high quality, sustainable, natural food ingredient and the answer to consumer demands for ingredients with beneficial physiological effects for gut health
- ✿ In vitro, ex vivo studies and human studies now demonstrate that Benegut® uniquely combines prokinetic as well as antispasmodic and anti-inflammatory efficacy leading to an immediate, perceptible relief of gastrointestinal discomfort
- ✿ It is a proprietary *Perilla frutescens* (L.) leaf extract, an annual edible plant native to Asia.
- ✿ Contributes to overall quality of life
- ✿ Has demonstrated scientifically proven effects and is IP protected
- ✿ Approved to be used for dietary supplements in Europe and the U.S.
- ✿ Approved to be used as flavour preparation in Europe



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# The new intelligent ingredient for gut health

## Product positioning

### Causes

- Daily stress
- Food sensitivity
- Allergies
- Infections
- Altered gut flora
- Deregulation of brain-gut cross talk
- Genetic preposition

### Body response

- Ileum contractions
- Unbalanced gut flora
- Unbalanced gut motility
- Inflammations

### Symptoms

- GI discomfort
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### Mode of action

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- Stool Volume enhancer
- Growth support to gut flora
- Gut flora substitution

### Ingredients



- Fiber
- Prebiotics
- Probiotics



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# Bene/gut<sup>®</sup>

The new intelligent ingredient for gut health  
Product positioning

“The skinny jeans drink”



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# Acknowledgement

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## Thank you for your attention!

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