Mechanism of action of STW 5 (Iberogast®) and its components on motility and intestinal neurotransmission in “in vitro” model of the human colon.

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**Frequency of Functional Gastrointestinal Diseases**

*30 % of the adult population in western industrialised countries suffer from functional gastrointestinal disorders*

**Among them:**

- 20-30 % show symptoms of an upset stomach (functional dyspepsia)
- These include:
  - approx. 60 % motility disorders
  - approx. 25 % acid-dependent disorders
  - approx. 15 % other functional disorders
- 40-50 % symptoms of an irritable bowel (*Colon irritabile*)
- 30-40 % show both symptoms of dyspepsia as well as of an irritable bowel
- 20-30 % other gastrointestinal diseases
Therapy of Functional Dyspepsia

*Iberogast®* is used since more than 50 years

**Indications:**
Functional and motility-dependent gastrointestinal disorders, Gastritis, gastrointestinal spasms.

**Side effects:**
very rarely allergic reactions

**Interactions:**
None known

**Contraindications:**
known allergy to any of the constituents
Experimental studies in vitro and in vivo on motility, acid production and inflammation

- Modulates gastric tone and contractility.
- Dual principle of action in affecting the contractions of non-stimulated and acetylcholine- or histamine-stimulated small intestine in vitro.
- Binding studies with STW 5 in muscarinic $M_3$, 5-HT$_3$ and 5-HT$_4$ receptors.
- Anti-inflammatory effect (indomethacin controlled experiments in rats).
- Anti-inflammatory and anti-oxidative effects in vitro.
- Antiulcerogenic and acid-reducing effects (cimetidine controlled experiments after Indomethacin ulcer induction in rats).
**100 ml STW 5 (Iberogast®) contain**

<table>
<thead>
<tr>
<th>Alcoholic fresh extract of:</th>
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<tbody>
<tr>
<td><em>Iberis amara</em></td>
<td>STW 6</td>
<td>15 %</td>
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</table>

**Alcoholic extracts of:**

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<thead>
<tr>
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<tbody>
<tr>
<td><em>Peppermint leaves</em></td>
<td>STW 5 K-II</td>
<td>5 %</td>
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<tr>
<td><em>Matricaria flower</em></td>
<td>STW 5 K-III</td>
<td>20 %</td>
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<tr>
<td><em>Liquorice roots</em></td>
<td>STW 5 K-IV</td>
<td>10 %</td>
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<td><em>Angelica roots</em></td>
<td>STW 5 K-V</td>
<td>10 %</td>
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<tr>
<td><em>Caraway fruits</em></td>
<td>STW 5 K-VI</td>
<td>10 %</td>
</tr>
<tr>
<td><em>St. Mary`s thistle fruits</em></td>
<td>STW 5 K-VII</td>
<td>10 %</td>
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<tr>
<td><em>Balm leaves</em></td>
<td>STW 5 K-VIII</td>
<td>10 %</td>
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<tr>
<td><em>Greater Celandine herbs</em></td>
<td>STW 5 K-IX</td>
<td>10 %</td>
</tr>
</tbody>
</table>

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Bittere candytuft
(Iberis amara)
mustard oil glycosides, flavonoids

acts

specifically on the tonus
of the gastrointestinal tract
influences gastrointestinal
peristalsis
Peppermint leaves
(Menthae piperitae folium)
volatile oils (0.7 %), lamiaceae tannins

acts
mildly anesthetic
antiemetic
spasmolytic
carinative
desinfecting
Matricaria flowers
(Matricariae flos)
volatil oils (0.3 - 3 %), flavonoids

acts
anti-inflammatory
 cramp-relieving
 carminative
 ulceroprotective

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Liquorice roots
(Liquiritiae radix)
glycyrrhizinic acid (5 - 15 %), flavonoids, phytosterols, coumarins

acts
antiulcerative
anti-inflammatory
spasmolytic
Angelica roots
(Angelicae radix)
volatile oils (0.35 - 1 %), bitters, flavonoids, coumarins
acts
spasmolytic
carmintive
Caraway fruits
*(Carvi fructus)*
volatile oils (2 - 7 %)

**acts**
carinative
spasmylytic
antimicrobial
St. Mary’s thistle fruits (Cardui mariae fructus)
flavonol derivates, silymarin

acts
antidyspeptic
carminative
hepatoprotektive
STW 5 K-VIII

Balm leaves
(Melissae folium)
volatile oils, lamiaceae tannins, triterpene acids,
bitters, flavonoids

acts
relaxing
carminative
STW 5 K- IX

Greater Celandine herbs
(Chelidonii herba)
alkaloids, flavonoids

acts
spasmolytic
choleckinetic
choleretic
anti-inflammatory
antimicrobial
The current project aims to expand the knowledge gained in animal experiments on human specimens. In the framework of this project, the influence of STW 5 (Iberogast®) and its components on the contractility and neuromuscular transmission of human colon was investigated in vitro.
In organ bath experiments contractions were elicited in human full thickness colonic muscle strips using electrical field stimulation (EFS). STW 5 and its components were tested in a dilution of 1:1000, 1:500, 1:100, and 1:50 in an organ bath and compared to vehicle.
Method 1
Method 2

The effects of these drugs in increasing concentrations were examined on intracellular recordings of inhibitory junctions potentials (IJP) in smooth muscle cells of the circular muscle layer of the human colon.
Method 2

Grass S11 Stimulator

O$_2$/CO$_2$

Kwik Pump 5 ml min$^{-1}$

Isolation unit

Pt-Ir

Ag-AgCl

Thermostat

Sylgard

Duo 733 amplifier

LabVIEW 5.0

Analog-digital Wandler

Faradayscher Käfig
Method 2

- 20 mV
- 60 mV

IJP

5 sek
Results 1

Iberogast® significantly reduced EFS induced cholinergic contractions of human colonic muscle strips (amplitude reduction in % of control: 1:1000 - 67.4±3.0, 1:500 - 43.1±3.9, 1:100 30.8±4.6, and 1:50 14.1±3.4).
Results 1

Iberogast® human colon

control 1:1000 1:500 1:100 1:50

EFS EFS EFS EFS EFS

5 g. 2 g. 30 sec
Results 1

Iberogast® human colon

Amplitude in % of control

- Control
- 1:1000
- 1:500
- 1:100
- 1:50

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**Iberogast®** significantly reduced amplitude of EFS induced IJP (amplitude in mV: control - 22.4±2.3, 1:500 - 20.6 ±1.9, 1:100 17.1±2.7, and 1:50 10.1±2.4) without significant influence on resting membrane potential.
Results 2

**Iberogast® human colon**

Amplitude in mV

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<th>0</th>
<th>10</th>
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<tbody>
<tr>
<td>control</td>
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<tr>
<td>1:500</td>
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<td>1:50</td>
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The individual components of STW 5 had different effects on contractility of human colonic muscle strips

- Extracts of Angelica roots, lemon balm leaves and Greater Celandine herbs significantly reduced the amplitude of EFS induced contractions.

- *Iberis amara* extract increased the amplitude of EFS induced contractions.

- Peppermint leaves, Liquorice roots, Caraway fruits, St. Mary`s thistle fruits and Matricaria flower extracts had no effects.
This investigation shows that STW 5 and its individual components modulate inhibitory neurotransmission as well as amplitude of EFS induced cholinergic contractions of human colonic muscle strips.

The effects of the individual herbal extracts add up to a total effect and the addition of individual effects might be the reason why STW5 is helpful for patients with relieving symptoms of functional gastrointestinal disorders of various origins.
Multiple combination phytomedicines can have advantages in the therapy of functional diseases as they have additive and synergistic effects.

Minimization of side effects by combination therapy

Adapted modulation of different symptoms