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


## *Andrei Sibaev*

*Assoc. Prof., MD, Ph.D.*

*Department of Internal Medicine II, Klinikum Grosshadern*
*Ludwig-Maximilians Univesität of Munich, Germany*



The 19th International Congress PHYTOPHAM 2015 July 21-24, 2015 Bonn Germany

# *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

## Experimental studies *in vitro* and *in vivo* on motility, acid production and inflammation

Iberogast®

- ***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

| | | |
|---|---|---|
| *Alcoholic fresh extract of:* | | |
| *Iberis amara* | STW 6 | 15 % |
| *Alcoholic extracts of:* | | |
| *Peppermint leaves* | STW 5 K-II | 5 % |
| *Matricaria flower* | STW 5 K-III | 20 % |
| *Liquorice roots* | STW 5 K-IV | 10 % |
| *Angelica roots* | STW 5 K-V | 10 % |
| *Caraway fruits* | STW 5 K-VI | 10 % |
| *St. Mary`s thistle fruits* | STW 5 K-VII | 10 % |
| *Balm leaves* | STW 5 K-VIII | 10 % |
| *Greater Celandine herbs* | STW 5 K-IX | 10 % |

# *STW 6*

## *Bittere candytuft*

***(Iberis amara)***

*mustard oil glycosides, flavonoids*

## acts

***specifically on the tonus of the gastrointestinal tract influences gastrointestinal peristalsis***

# *STW 5 K-II*

## *Peppermint leaves*

***(Menthae piperitae folium)***

*volatile oils (0.7 %), lamiaceae tannins*

**acts**

***mildly anethetic***

***antiemetic***

***spasmolytic***

***carminative***

***desinfecting***

# *STW 5 K-III*

## *Matricaria flowers*

***(Matricariae flos)***

*volatile oils (0,3 - 3 %), flavonoids*

**acts**

***anti-inflammatory***

***cramp-relieving***

***carminative***

***ulceroprotective***

# *STW 5 K-IV*

## *Liquorice roots*

***(Liquiritiae radix)***

*glyzyrrhizinic acid (5 - 15 %), flavonoids, phytosterols, coumarins*

## acts

***antiulcerative***

***anti-inflammatory***

***spasmolytic***

# *STW 5 K-V*

## *Angelica roots*

***(Angelicae radix)***

*volatile oils (0,35 - 1 %), bitters, flavonoids, coumarins*

**acts**

***spasmolytic***

***carminative***

# *STW 5 K-VI*

## *Caraway fruits*

***(Carvi fructus)***

*volatile oils (2 - 7 %)*

**acts**

***carminative***

***spasmolytic***

***antimicrobial***

# *STW 5 K-VII*

## *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***

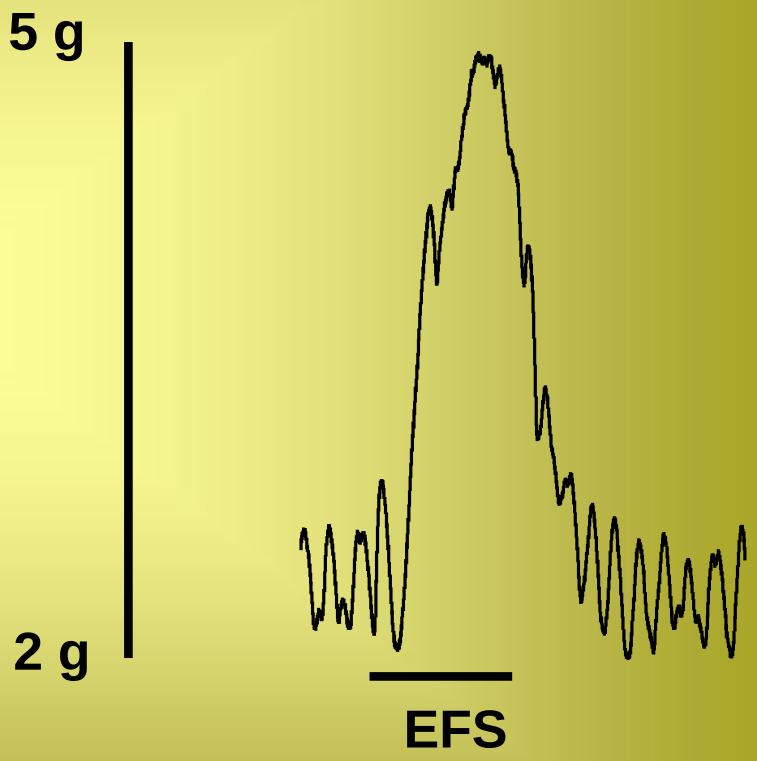
# *Aim*

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.

# *Method 1*

In organ bath experiments contractions were elicited in human full thickness colonic muscle strips using electrical field stimulation (EFS). STW 5 and its components ware tested in a dilution of 1:1000, 1:500, 1:100, and 1:50 in an organ bath and compared to vehicle.

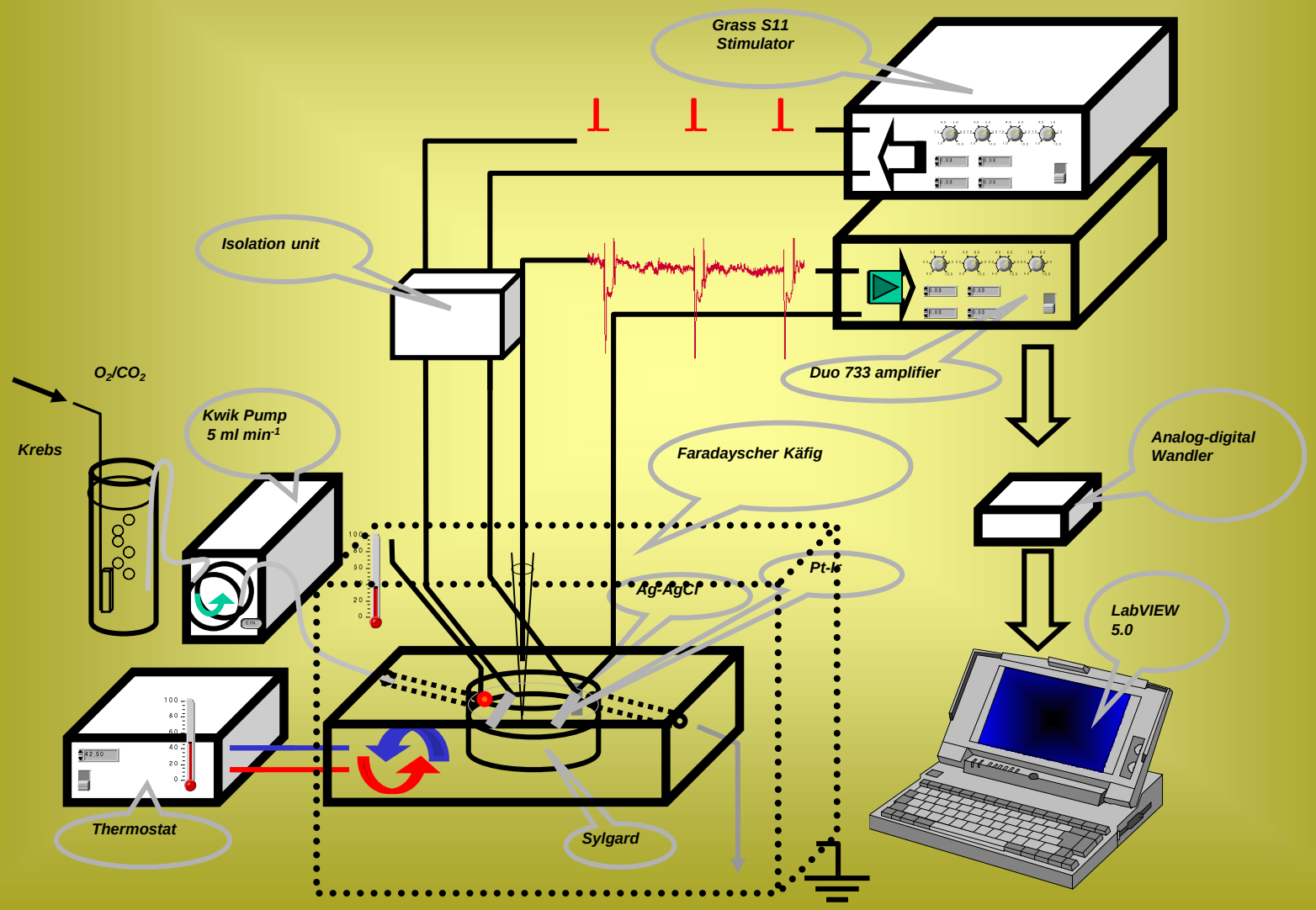
# Method 1



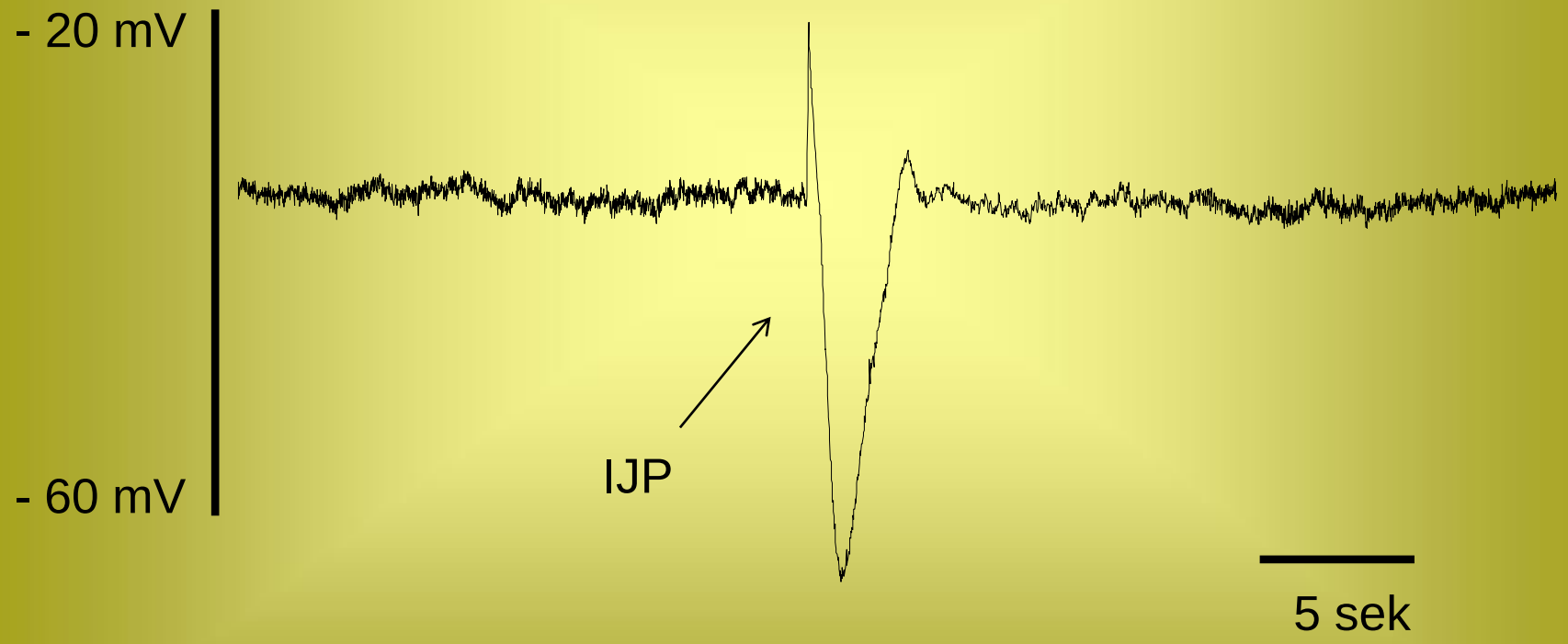
# *Method 2*

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
Isolation unit
Duo 733 amplifier
$O_2/CO_2$
Krebs
Kwik Pump
5 ml min$^{-1}$
Faradayscher Käfig
Analog-digital
Wandler
Pt-Ir
Ag-AgCl
LabVIEW
5.0
Thermostat
Sylgard

# Method 2

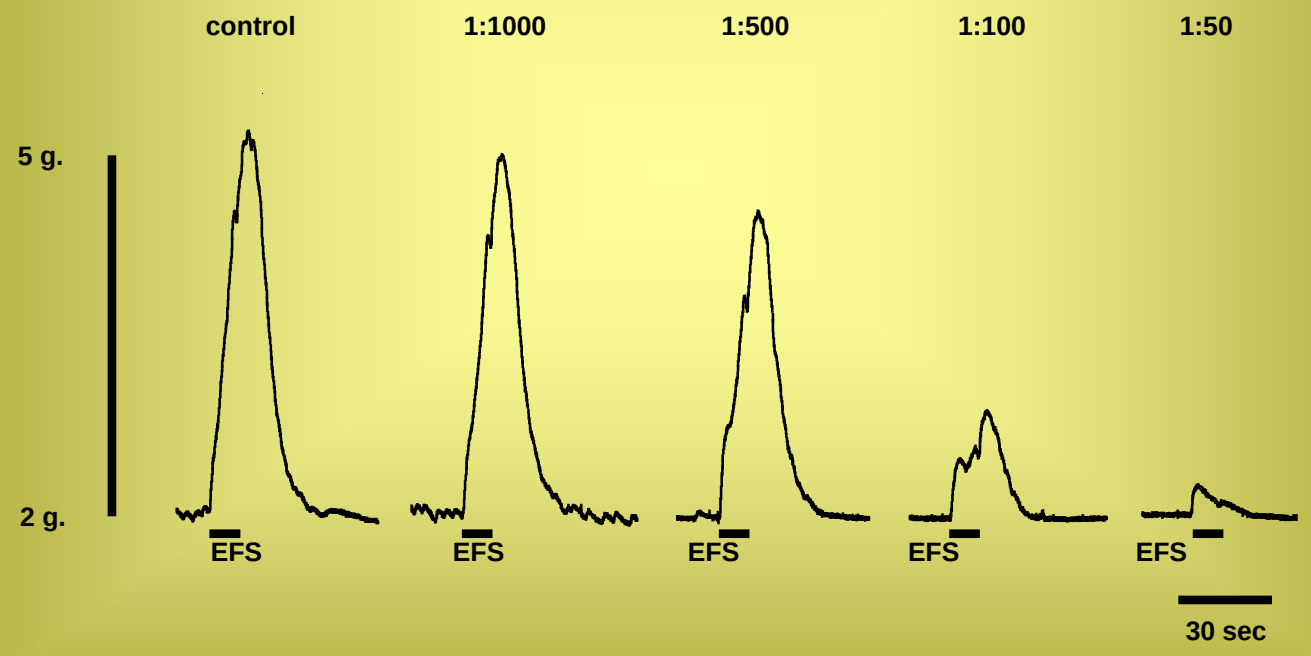


# *Results 1*

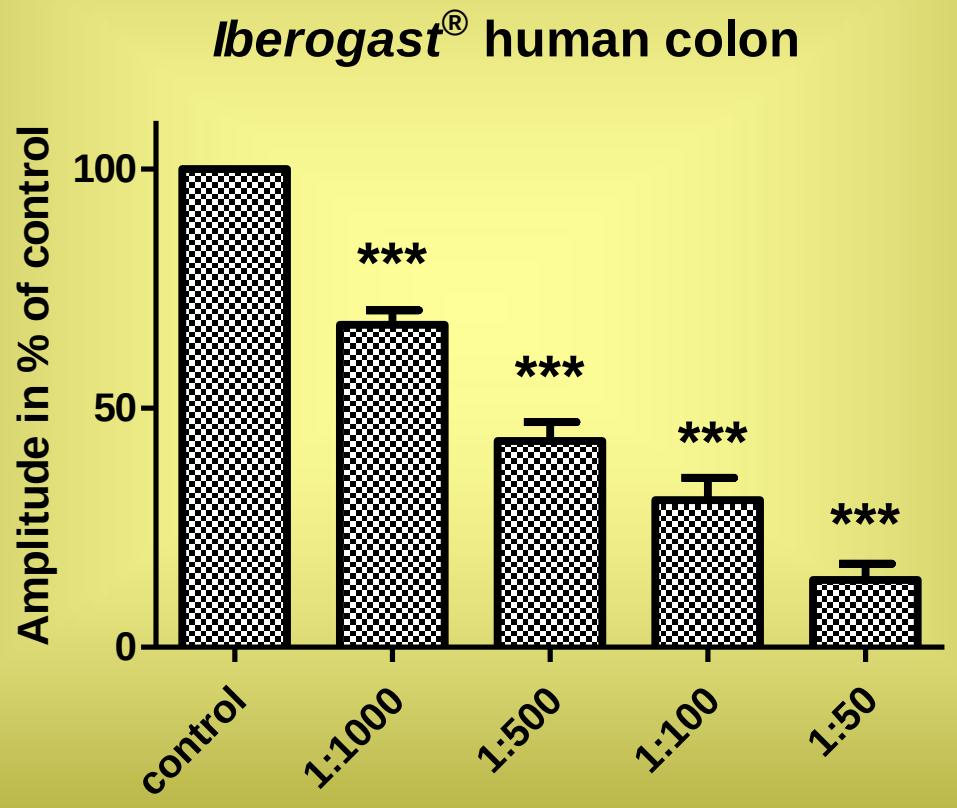
***Iberogast®*** significantly reduced EFS induced cholinergic contractions of human colonic muscle strips (amplitude reduction in % of control: 1:1000 - 67,4±3.0, 1:500 - 43,1±3,9, 1:100 30,8±4,6, and 1:50 14,1±3,4).

# Results 1

***Iberogast®*** **human colon**



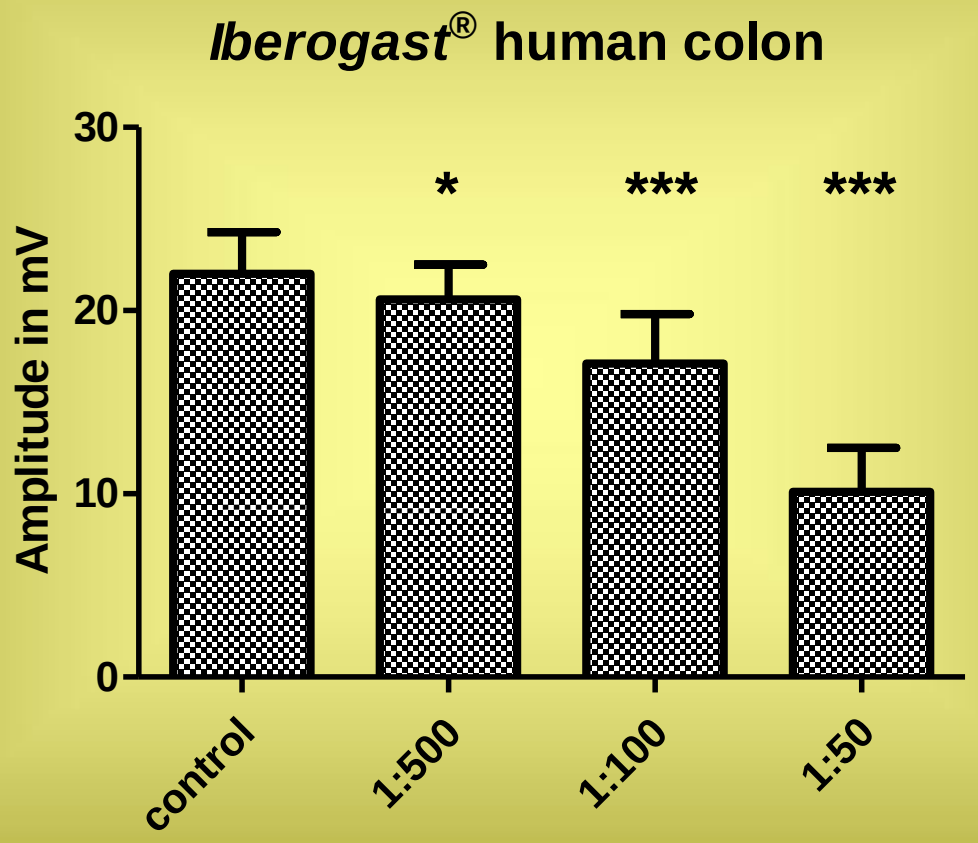
# Results 1


*Iberogast*® human colon
Amplitude in % of control
100
50
0
***
***
***
***
control
1:1000
1:500
1:100
1:50

# *Results 2*

***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
30
20
10
0
*
***
***
control
1:500
1:100
1:50

# *Results 3*

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.

# Conclusion

***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.***

# *Conclusion*

Multiple combination phytomedicines can have advantages in the therapy of functional diseases as they have addiotive and synergistic effects

***Minimization of side effects by combination therapy***

***Adapted modulation of different symptoms***