Innovative Gastro-absorption method

A novel cleansing system in prevention and treatment
Detoxifying role of the gut

• The body handles toxic substances (so-called homotoxins) trying to neutralize and output, and in case of failure - will deposit at a specific location (extracellular matrix).

• Major role in the elimination of toxins plays intestine.
History

In ancient America, Egypt, India, Greece and charcoal and clay were used for the treatment of poisoning. Medicine as adding where something is missing, and removing where there is too much (Hippocrates). In the "Canon of Medicine" Avicenna called body cleaning as the basic postulate of the art of health care. Homotoxicology was developed by Dr Reckeweg (Germany) during the 1940’s. Diseases are the result of the body’s attempt to self heal by ridding itself of toxins.
Enterosorption

Definition

Nowadays the method binding of harmful substances in the intestinal lumen by sorbent has a scientific justification and is referred to as ENTEROSORPTION (*intestinal adsorption*).

The substances used for enterosorption are called enterosorbents (*intestinal adsorbents*).
How do sorbents work?

- Adsorption—Adhesion of a Molecule to a Surface
  - Binding occurs as a result of random collisions
  - Generally a reversible, equilibrium process
  - Higher concentration in solution => more solute bound
High Internal and External Surface Area

- Typically porous beads offer extremely large internal surface area (e.g. 300-800 m²/g) for binding.
- Smaller particles offer better transport due to higher external surface area, but higher pressure drop.
The World’s Oldest cleansing method

**Enterosorption** - innovative method of intestinal adsorption is a method of enteral adsorption based on binding of toxic substances by sorbents.

About 3,000 years ago coal, clay have been found empirically able to bind harmful substances in the gastrointestinal tract (Hippocrates of Cos).
A07B intestinal adsorbents

**ALIMENTARY TRACT AND METABOLISM**

A07 **ANTIDIARRHEALS, INTESTINAL**

ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS

Combinations with intestinal antiinfectives are classified in A07A.

A07B **INTESTINAL ADSORBENTS**

A07BB **Bismuth preparations**

A07BC **Other intestinal adsorbents**

http://www.whocc.no/atc_ddd_index/?code=A07B&showdescription=yes

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A07BC01</td>
<td>pectin</td>
</tr>
<tr>
<td>A07BC02</td>
<td>kaolin</td>
</tr>
<tr>
<td>A07BC03</td>
<td>crospovidone</td>
</tr>
<tr>
<td>A07BC04</td>
<td>attapulgite</td>
</tr>
<tr>
<td>A07BC05</td>
<td>diosmectite</td>
</tr>
<tr>
<td>A07BC30</td>
<td>combinations</td>
</tr>
<tr>
<td>A07BC54</td>
<td>attapulgite, combinations</td>
</tr>
</tbody>
</table>

A lot of intestinal adsorbents are available on pharma market.
Charcoal activated (oral use)

- Activated charcoal is used in the emergency treatment of certain kinds of poisoning.
- It helps prevent the poison from being absorbed from the stomach into the body.

Diosmectite

- The diosmectite is a natural clay characterized by a structure of fine overlapping crystalline lamellae which gives a high absorbing power, to make it capable of incorporating the liquids present in the intestinal lumen, increasing stool consistency and slowing expulsion.

A07B intestinal adsorbents

Modern tendencies of Dosage forms

A transition from solid powder and tablets sorbents to liquid forms due to the effect of Herbst-Volkheimer
THE PHENOMENON OF PERSORPTION: PERSORPTION, DISSEMINATION, AND ELIMINATION OF MICROPARTICLES (Herbst-Volkheimer)

Solid particles in the micrometer range regularly pass from the alimentary tract into the organism.

Their microparticles from the blood passage into the alveolar lumen, bile, urine, cerebrospinal fluid, peritoneal cavity, through the lactating mamma into the milk and also the transplacental transfer to the foetal blood circulation.

http://www.old-herborn-university.de/literature/books/OHUni_book_14_article_2.pdf
In the early 60's Greek nephrologist Hippocratos Jatzidis first cleared the blood of uremic patients with activated charcoal (hemocarboperfusion).

But the methods are expensive, complicated, and had not commercial success.
History of the Enterosorption

• Y.M. Lopukhin in 60-70’s, actively promoted the idea in SU.
• He found positive effects of sorption detoxification in various diseases.
• In terms of state regulation the cheapest and easiest method of enterosorption was available for mass use.

Y.M. Lopukhin, MD, professor considered the founder of the sorption methods of detoxification of the body
In the late 70's of the XX century in Russia there was born an idea of creating universal oral detoxification medicine, which could preserve health and prolong lives.
Enterosgel Development

Since all available products did not meet the convincing efficacy and safety requirements, it was decided to synthesize completely new molecule - innovative intestinal adsorbent Enterosgel.

Vladimir Nikolayev, MD, professor, laureate of the State Prize of the USSR in 1979, one of the founders of the method.
Enterosgel® - first intestinal sorbent with predetermined properties

The molecule of Enterosgel was created on assignment of the USSR Ministry of Defense. For the first time in the world, the enterosorbent with predetermined properties has been synthesized, which was capable of eliminating harmful substances from the body.
Graphical abstract

Branched polymethylsiloxane molecules form primary nanoparticles (<10 nm) structured in soft mesoporous/macroporous secondary particles (0.1–5 μm) with textural porosity responsible for adsorption of proteins and other macromolecules.

Comparative characterization of polymethylsiloxane hydrogel and silylated fumed silica and silica gel
V.M. Gun'ko et al. Journal of Colloid and Interface Science
Volume 308, Issue 1, 1 April 2007, P. 142–156
Clinical Trials in USSR

• Enterosgel was tested in four USSR Ministry of Defense hospitals - Tashkent, Kiev, Vilnius, Dushanbe.
• The total number of cases - more than 5,000.
• Studies have been conducted for the treatment of
• hepatitis,
• intestinal infections,
• poisoning,
• postoperative complications
• burns.

Tashkent military hospital, 1988
Enterosgel® in Afghanistan

- Enterosgel demonstrated high efficacy in the treatment and prevention of diseases in the southern regions of the USSR and during military conflict in Afghanistan.
Enterosgel® in Afghanistan

- During the war in Afghanistan sanitary losses from infectious diseases ranged from 45 to 68%.
- Enterosgel has been used successfully in the treatment of infectious diseases.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Structure of infectious diseases, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral hepatitis</td>
<td>40,6-51,2</td>
</tr>
<tr>
<td>Infections of gastrointestinal tract</td>
<td>14,6-20,2</td>
</tr>
<tr>
<td>Typhoid fever and paratyphoid A and B</td>
<td>9,6-26,9</td>
</tr>
</tbody>
</table>

Enterosgel® in Chernobyl

On June 27, 1954, the world's first nuclear power plant to generate electricity for a power grid started operations at the Soviet city of Obninsk.

- In 1986-1988 Enterosgel was used in military personnel aged 30-46 years who were carrying out work in the area of the 4th reactor of the Chernobyl nuclear power plant.
Clinical Trial Results in Chernobyl military personnel (n = 750)

- The therapeutic effect of those who received Enterosgel are good - in 75%, satisfactory in 25%.

<table>
<thead>
<tr>
<th>Group</th>
<th>Blood biochemical markers normalization, days</th>
<th>Duration of rehabilitation, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterosgel</td>
<td>14-16</td>
<td>18±2</td>
</tr>
<tr>
<td>Control</td>
<td>20-30</td>
<td>32±2</td>
</tr>
</tbody>
</table>
Method of removal of radionuclides (radioactive cesium) with Enterosorption

- First prescribe a course of fasting-diet therapy.
- Treatment with Enterosgel performed in therapeutically effective doses to complete starvation period, for 3-10 days.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
<th>Duration, days</th>
<th>Number of cases</th>
<th>Content of radioactive cesium, kBk</th>
<th>Change from baseline, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterosgel</td>
<td>1g/kg</td>
<td>10</td>
<td>12</td>
<td>before: 9.8±1.7, after: 6.5±1.3</td>
<td>-34</td>
</tr>
</tbody>
</table>

Shumilov V., 2003
Method of removal of radionuclides (radioactive cesium) with Enterosorbtion

Case

Patient S., male, Age - 41. Likvidator at the Chernobyl nuclear power plant. After a stay in the 30-km zone could feel fatigue.

Content of radioactive cesium was 9.8 kBq (kilobecquerels).

Has passed the 10-day course of fasting-diet therapy with Enterosgel.

Enterosgel administered orally in a mixture with water during the fasting total dose of 1 g / kg body weight, daily.

Radiocesium content decreased to 6.5 kBq that with respect to the initial value was reduced by 34%. Patient's condition improved, complaints of chronic fatigue is not. Agreed to repeat the course.
In 2003, the Moscow Dolphinarium developed the outbreak of enterovirus infection in dolphins. The prescription of Enterosgel to all the dolphins, helped to eliminate the infection.
ATHLETES & Enterosgel

**Enterosgel** is not prohibited for Athletes

**Enterosgel** was in the first aid kits for athletes Sochi 2014

The logos of the Rio 2016 Olympic Games and Rio 2016 Paralympic Games are pictured next to a message on a screen that reads "Message about Zika" during a media briefing in Rio de Janeiro, Brazil, February 2, 2016. REUTERS/RICARDO MORAES
After the collapse of the USSR, secrecy status has been abolished. Industrial production of Enterosgel has been organized in Russia; and the unique medication has become available for public.
The choice criteria for new facility’s location

1. healing water,
2. qualified staff,
3. logistics
Czech Republic
The world history of medicine

XIX
Priessnitzovy léčebné lázně - Jesenik spa resort (1822)

XX
Classic cleansing by J. Hasek (1923)

XXI
Production of Enterosgel in the Czech Republic (2011)
Enterosgel is the only enterosorbent enriched with the healing properties of unique water from Jesenik spa resort (Czech Republic).
GUNA and Enterosgel

Key partner in Europe - GUNA (Italy).
No specific treatment is available for Zika virus disease

The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes).

Treat the symptoms:
Get plenty of rest.
Drink fluids to prevent dehydration.
Take medicine such as acetaminophen to reduce fever and pain.
The influence of ENTEROSORPTION on the level of proinflammatory cytokines in patients with acute gastroenteritis and measles

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Enterosgel</th>
<th>Control</th>
<th>Before Treatment</th>
<th>After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β</td>
<td>79.12</td>
<td>78.33</td>
<td>59.21</td>
<td>68.72</td>
</tr>
<tr>
<td>IL-6</td>
<td>14.06</td>
<td>13.94</td>
<td>10.41</td>
<td>13.06</td>
</tr>
<tr>
<td>TNF-α</td>
<td>107.64</td>
<td>110.08</td>
<td>62.12</td>
<td>92.16</td>
</tr>
</tbody>
</table>

N.B. Before treatment

Гебеш В.В., Сухов Ю.А., Голуб А.П. http://m-l.com.ua/?aid=947
Conclusions: the Use of Enterosgel in the treatment of flu accelerates clinical recovery: faster stopped the cough and fever normalized indicators of endogenous intoxication and humoral immunity.
Duration of cough in the group of ENTEROSGEL (left) and control (right), %

Cough decreased significantly faster in the group of Enterosgel
• Pneumonia is accompanied by severe intoxication. Pneumonia may be the extraesophageal manifestation of GERD (GERD-associated pneumonia), Features of GERD-associated pneumonia (pathogenic mechanism of aspiration): -lung destruction - episodes of loss of consciousness (chronic intoxication, alcoholism, drug addiction)
Conclusions: the Use of ENTEROSGEL in the treatment of pneumonia accelerates clinical recovery: faster, cropped x-ray and clinical symptoms.

А.А. Матвеев., 2002
The influence of Enterosgel on the growth of *S. aureus* strain 722 produces staphylococcal enterotoxin A (SEA), and delete the SEA from the culture medium.
The influence of Enterosgel on the growth of *S. aureus* strain 722 produces staphylococcal enterotoxin A (SEA), and deletes the SEA from the culture medium.

<table>
<thead>
<tr>
<th>№</th>
<th>The studied samples</th>
<th>The precipitation reaction in the gel</th>
<th>The optical density at 560 nm (1:30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>S. aureus</em> FRI- 722 (control) the Control</td>
<td>+</td>
<td>0,3</td>
</tr>
<tr>
<td>2</td>
<td><em>S. aureus</em> FRI- 722 + 2,0 % Enterosgel filtrate of culture</td>
<td>+</td>
<td>0,3</td>
</tr>
<tr>
<td>3</td>
<td><em>S. aureus</em> FRI- 722 + 10,0 % Enterosgel</td>
<td>—</td>
<td>0,21</td>
</tr>
<tr>
<td>4</td>
<td><em>S. aureus</em> FRI-722 + 20,0 % Enterosgel</td>
<td>—</td>
<td>0,19</td>
</tr>
</tbody>
</table>
Enterosgel eliminates pathogenic intestinal microflora. Enterosgel actively introduced to the cell surface of *Shigella Flexneri*.
Enterosgel penetrates the lipopolysaccharide layer of *Salmonella typhimurium* and destroys the cell wall.

Microbiology Dept, Kiev Med. Academy Postgraduate Education.
Prerequisites:
Enterosgel ideal for detoxification in homeopathic therapy

- it does not contain substances that can penetrate into the bloodstream and other organs or tissues out of the lumen of the gastrointestinal tract.
- it may be used perfectly with homeopathic and AGTT (antihomotoxic) remedies.
- oral detoxification with Enterosgel provides high efficacy and safety of homeopathic and AGTT therapy.
Bioline Products s.r.o.
actively participated in several scientific and practical conferences of homeopathy in Moscow and St. Petersburg (Russia, see next slides).
Enterosgel as a product with great potential has always found great interest a wide audience of physicians (practicing homeopaths and doctors of various specialties who are interested in the techniques of modern homeopathy for the treatment and prevention).
Homeopathy Conference in Moscow (jan. 2013)
Homeopathy Conference in Moscow (jan. 2013)
Antiageing programm (Russia) Homeopahty & Enterosgel

Программа антистарения

I. Детоксикация
- Методы народной медицины
- Синтетические адсорбенты (ентеросгель и др.)
- Гомеопатические комплексы

II. Диета, двигательный режим, релаксация
- Иммуномодуляторы
  - Синтетические
    - Фитокомплексы
      - Гомеопатические
        - АНАБАР ЭДАС-308
        - БЭТ 03-01

III. Активизация систем защиты
- Антиоксиданты
  - Синтетические
    - Фитопрепараты
      - Комплексы ЭДАС
      - КАСКАТОЛ
      - КАСКОРУТОЛ
      - ЧАГАЮКС

IV. Интеграция гомеопатии с современными высокотехнологичными средствами и методами
- Биогенные стимуляторы
  - Синтетические
    - Препараты пчеловодства
      - Комплексы ЭДАС
      - Фитокомплексы
      - РОЗОЛАКРИТ
      - КАРБИОБАД

Гепатопротекторы ГЕПА ЭДАС-933
- Дренаж КАРСАТ ЭДАС-136 (936)
EC CERTIFICATE
No. 11 0058 QS/NB/a


ENTEROSGEL
Manufactured by company:
Bioline Products s.r.o.
Krejčovská 1335/10, 110 00 Praha 1, Czech Republic

The notified body No. 1023 has performed an audit of the above-product manufacturing quality system. The quality system has been assessed, approved and is subject to continuous surveillance according to Annex V, Sections 3.2, and 4. of the Directive 93/42/EEC. The detailed description of the system, its requirements and measures taken by the manufacturer are presented in the Final Report No. 0090100429051 and No. 049000200279, which are annexed to this Certificate.

Condition of this Certificate are as follows:
1. This Certificate applies only to the above-referenced product manufactured by the manufacturer and it does not authorize the change of type-designation procedures, if requested.
2. The Certificate remains valid only if the manufacturing conditions of the quality system are unchanged but until the 24th January 2016 at the latest.
3. The Certificate validity is confirmed by positive results of supervision audits.
4. After fulfilling the relevant EU legislation requirements the manufacturer must refer to each medical device of the above-referenced medical devices by the number of the notified body (according to this protocol).

Institute for Testing and Certification, Inc.
Zlín, Czech Republic - www.itq.cz

Notified Body No. 1023
Institute for Testing and Certification, Inc.
Zlín, Czech Republic - www.itq.cz

EC 1023

Issued in Zlín, on 8th March 2013

RNDr. Radomír Čerčnik
Representative of the Notified Body No. 1023

Replaces the withdrawn EC Certificate No. 11 0058 QS/NB issued on 25th January 2011
Class IIa medical device in Europe: Czech Republic, Belgium, Bosnia and Herzegovina, Estonia, Germany, Holland, Hungary, Italy, Lithuania, Poland, Romania, Slovakia, Slovenia, Croatia, Serbia, UK
Other: New Zealand, Saudi Arabia

a) Medicinal product in CIS: Russia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Uzbekistan.
• SUGAR
• SWEETENERS
• LACTOSE
• GLUTEN
• FATS
• COLORINGS
• FLAVOUR
• ENHANCERS
• PRESERVATIVES FREE
ENTEROSGEL® is not absorbed as it binds and removes toxic substances, pathogenic bacteria and allergens from the body.
ENTEROSGEL® does not cause deficiency in microelements, calcium, vitamins and other essential substances.
Gracias por su atención!