Unitary Enterprise
«Unitehprom BSU»

Talker:
Manager, Ph.D., Associate Professor
Bychkovsky Pavel

Minsk, 2014
Enterprise structure:

Scientific-production center of food technologies
Spirometry equipment development laboratory
Scientific-production center of low-tonnage chemistry
  Pharmaceutical service
  Biochemistry applied studies center
  Information-measuring systems center
  Information computation systems center
  Ion-exchange sorption technologies center
Core areas – development of food additives to improve the quality of finished bakery products and enrichment of finished foodstuffs with the required macro-micro-nutrients.

- Processing aids
- Enrichment phyto-additives
- Dry spices «APPETIZING»
- Mixtures for people with protein and carbohydrate metabolism disorders
- Specialized mixture for nutrition of elderly people
- Vitamin mineral premixes
- Antioxidant additives
- Specialized mixtures for schoolchildren nutrition
Processing supplements, corrective properties of flour with reduced baking properties

- series «Paracels»
- series «Slavjanka»
- series «Plissa»
- series «Frigory»

RUE «Vitebskhhlebprom»
CUE «Minskhhlebrom»
Shchychyn DCS
RUE «Mogilevkhlebprom»
Enriching additives – food fibers concentrates

Multi-component powder-like mixtures on the basis of dried and milled Phyto-raw material
Vitamin-mineral premixes

«Arbavit – 1» enriches bakery products with folic acid, iron, B-group vitamins

Town of Baranovichi

«Arbavit – 2» Enriches bakery products with folic acid B-group vitamins

Town of Kobrin

t. Kobrin

t. Vileika

t. Soligorsk
COMPLEX ENRICHING MIXTURES FOR ACTIVE LONGEVITY

to be used when making bakery products, flour sweetness (on the basis of shortbread semi-finished product), tea-cakes on baking powders to enrich them with biologically active substances including vitamins and amino-acids to enlarge the dietary and hero-dietary products’ assortment.

The mixtures are dry powder-like mixtures of grain products, vegetables, fruit, amino-acids with the addition of vitamin-mineral premix «Arbavit – 2», vitamins, including other components.
Laboratory to develop spirometry equipment

Sperometer MAC-1

**Purpose**

Spirometer «MAC-1» - a device to assess human respiratory system

**Features**

Measurement accuracy, functionality, modern design "MAC-1" is not inferior to the best world standards. It measures and calculates over 40 external respiration parameters, compares them with the regulations, issues a medical report, including tests with pharmacological probe.
Application

- functional diagnostics department and outpatient medical facilities
- aerospace medicine
- Sports Medicine
- military, etc.

Used in clinics, spa facilities, rehabilitation and diagnostic centers in practice of pulmonology, allergy, occupational diseases, functional diagnostics, sports medicine, as well as for medical examinations in the medical units of industrial enterprises.

Using of spirometers with an expert assessment of the quality of tests in practice of prophylactic examinations allows create groups of risk on chronic obstructive pulmonary disease.
Optical temperature meter
IT 3CM
aimed for adjustment and subsequent control of complex high thermal processes (measured temperature range from 800 to 1700 °C)

Connected via USB to your laptop or netbook. In stationary mode can be connected to a computer in industrial design. USB cable, standard length of 1.5 to 2.8 m
Pharmaceutical substances and dosage forms developed in the Institute of Physical and Chemical Problems, BSU and produced in UNP RUE "Unitechprom BSU"
SSTP «To create new drugs»
1995 – 2000 years

SSTP «To develop and to master production of actual pharmaceutical forms and pharmaceutical substances in order to meet the needs of healthcare of the Republic of Belarus»
2001 – 2005 years

SSTP «Creating and developing of production of actual drugs on the basis of products of biotechnology and chemical synthesis»
Subprogram «Drugs»
2006 – 2010 years

SSTP «Pharmaceutical substances and drugs»
Subprogram «Drugs»
2011 – 2015 years
Government program of innovation development of the Republic of Belarus (2011-2015 years)

GP «Import-displacement of pharmaceutical products»
«Creating a low-tonnage production of pharmaceutical substances for anticancer, cardiotropic and other drugs based on organizations of the Ministry of Education»
Production of oxidized cellulose
Oxidized cellulose

Johnson & Johnson

Surgicel

Tabotamp

Interceed

Hemostatic

Means for preventing adhesive processes

Hemostatic

Additional effects

Biodegradation

Oxidized cellulose pro-dact and method for preparing the same. Ashton W.H. Пат.США 3364200, 1968


Immunostimulatory


Reparative

Drugs based on oxidized cellulose
- The absence of adverse toxic effects on the body
- Absorption in body tissues
- Complete removal of the polymer itself or its decay products from the body
- The presence of functional groups or structures that achieve the effect of prolonging the action of drugs
BENEFITS OF POLYSACCHARIDES

- High reactivity in the processes of structural and chemical modification;
- Unlimited resource base (reproducibility in nature);
- Natural compounds, macromolecules which contain structural units, causing undesired effects on the body;

PREFERENCE – nitric oxide oxidation products (IV) and esterification with phosphoric acid
The object of modification: cotton cellulose in the form of knitted fabric of oxidized cellulose property

Electron micrograph of cotton cellulose in the form of knitted fabric

Scheme of cellulose oxidation with nitrogen oxide (IV)
Availability of the carboxyl groups, the amount of which depends on the conditions of the oxidation process

- Resorbability when implanted in the body, the terms of which are determined by the content of carboxyl groups

- The absence of any adverse effect on the body (Hazard Class 4 - practically non-toxic compound)

- Availability of antimicrobial, immunostimulatory and reparative properties

- Hemostatic action
Results of the study of processes of interaction of oxidized cellulose with antitumor agents:
Antitumor effects of OT and OT-OC models of sarcoma-180 and Ehrlich ascites carcinoma

<table>
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<th>Drug</th>
<th>Sarcoma-180</th>
<th>Ehrlich ascites carcinoma</th>
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<tr>
<td></td>
<td>Lifespan, days</td>
<td>Index of tumor growth inhibition by period, %</td>
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<tr>
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<td>OC-OT</td>
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**DRUGS PRODUCED BY UNITEHPROM BSU**

**CISPLACEL** – anticancer drug for local chemotherapy of brain tumors and tumors of head and neck

**TEMOZOLEMID** – substance for production of anticancer drug Temobel, capsules 20 mg, 100 mg и 250 mg

**PROSPIDIN** – substance for the production of different pharmaceutical forms (injection, ointment, hydrogel) anticancer drugs

**NITARGAL** – is the original substance for the production of the drug for the treatment of cardiovascular diseases
Indications for use

- malignant brain tumor
- malignant tumors of the neck, mouth, tongue, nose and paranasal sinuses

Pharmacological effect

Intended for local chemotherapy of malignant brain tumors, head and neck area. Prolonged cytostatic effect is due to cisplatin immobilized by oxidized cellulose. The drug inhibits the biosynthesis of DNA, provides targeted traffic cytostatic in the damaged organ.

Using of the «Cisplacel» can reduce the dose of cytostatic and reduce the toxic load on the organism of patient. According to PI «RSPC of Oncology and Medical Radiology им. N.N. Alexandrov» MPH RB local application of drug «Cisplacel» after non-radical resection of primary and recurrent head and neck tumors leads to complete recovery of 51 % of patients, reduce recurrence of by 25-40 % compared with traditional treatment.
Results from clinical trials (malignant tumors in head and neck area) of the drug «Cisplacel»

According to the results of clinical trials implantation of the drug «Cisplacel» in the area of surgically resected low-differentiated gliomas of the brain (Grade III-IV) followed by radiation therapy prolongs life of patients more than 2 times (from 211,0±21,4 to 427,5±28,4 days)

Median survival of patients after local chemotherapy by drug «Cisplacel»
According to PI «RSPC of Oncology and Medical Radiology им. Н.Н. Александров» MPH RB local application of drug «Cisplacel» after non-radical resection of primary and recurrent head and neck tumors leads to complete recovery of 51% of patients, reduce recurrence of by 25-40% compared with traditional treatment.
The drug «Cisplacel» on computer tomography visualized as a band, fitting a remote lodge neoplasms
Comparative evaluation of the effectiveness of local chemotherapy supratentorial glioblastomas

Duration of recurrence-free period statistically reliable increase of more than 50%
Competitive advantage:

compared with traditional treatment:
- cytostatic targeted traffic in the area of the affected organ;
- prolongation of the therapeutic effect;
- effect of radiotherapy potentiation;
- ensuring of hemostasis;
- decrease the total dose of cytostatic and reduction toxic stress on the body;
- full biodegradation after implantation

compared to single imported analogue - drug «Gliadel», produced by «MGI Pharma, Inc.» (USA):
- package price of the drug «Cisplacel» 50 times lower than the price of analogue (cost «Gliadel» of 1 package – U.S. $ 15 000);
- higher stability of the drug during storage;
- does not require the additional application of hemostatic
GLIADEL

CISPLATIN
Cisplacel clinical testing in CIS countries

Armenia
Closed corporation
" A.L. Mikaelian Institute of Surgery. "
0051, Republic of Armenia, Yerevan, str. Hasratian 9
Leader: Kalaydzhyan Andronicus Ishhanovich
Executer: Kirakosyan Avedis Albertovich

Russia
N.N. Blokhin Russian Cancer Research Center,
RAMS
115478, Russia, Moscow, Kashirskoye, 24
www.ronc.ru
Director: Mikhail Davydov
Performer: Fu Radion Ganovich
**TEMOZOLOMID** - substance for production of anticancer drug Temobel, capsules 20 mg, 100 mg и 250 mg, of original pharmaceutical substance and SFF of anticancer drug Temodeks for local chemotherapy of malignant brain tumors (powder for gel preparation)
PROSPIDIN – substance for the production of different pharmaceutical forms (injection, ointment, hydrogel) anticancer drugs
**PHARMACEUTICAL SUBSTANCE**

*NITARGAL* – is the original substance for the production of the drug for the treatment of cardiovascular diseases
Task 01.16. of the subprogram «Drugs»
To develop and to introduce the technology of the production of the Nitargal substance at the Unitary enterprise «Unitehprom BSU» and the technology of the drug Nitargal production at the RUE «Belmedpreparaty»

- the 1-st and 2-nd phases of clinical tests of the drug Nitargal are finished;
- the drug is harmless and well-tolerated;
- the high efficiency of the Nitargal usage for the treatment of the stable stenocardia is shown, treatment effect is manifested in the normalization of blood pressure, reducing of the number of stenocardias attacks;
- the special clinical tests will be conducted for the determination of the safety and tolerability of the drug during chronic administration

Patent RB №8456
Registration certificate MPH RB №10/02/1702
PhAE RB 1389-10 «Nitargal, substance, 100 g in banks, packaged №1»
polysaccharides: dextran, starch, cellulose

PHOSPHORILATION MIXTURES

\[ H_3PO_4 - (C_4H_9)_3PO_4 \]

\[ H_3PO_4 - CO(NH_2)_2 \]

adjustable parameters in the system:
- molar ratio of the components
- temperature
- time
- pressure
As a result it was found that dextran phosphates have the following structure:

\[
R = H; \text{CONH}_2 \text{ или } \text{PO(ONa)}_x(\text{OH})_{2-x},
\]
Electron micrographs of initials of dextran (1) and starch (3) and the esterification products in the system Bu3PO4: H3PO4: P2O5 (2) and phosphoric acid-urea (4)
**THE ROW OF THE DRUGS WHICH WILL BE PRODUCED ON THE BASE OF UNITEHPROM BSU**

*TEMODEX* – is the original substance for the production of the antitumoral drug for the local treatment of brain tumors.

*PROSPIDELONG* – is the hydrogel antitumoral drug with prolonged action for the interperitoneal treatment of the patients with disseminated cancer of the stomach.
**TEMODEX** – is the original substance for the production of the antitumoral drug for the local treatment of brain tumors.
TEMODEX

- A preparation in the form of sterile powders for the preparation of the gel. The product is temozolomide immobilized on a specially synthesized crosslinked gelling dextran phosphate, intended for local chemotherapy of malignant brain tumors. The cavity formed after surgical removal of the brain tumor is filled with the gel. Gelled state provides full access to all areas, providing, at the same time, complete destruction of the remaining tumor cells. Clinical testing of Temodeks as a means of local chemotherapy in patients with cerebral gliomas (Grade II-IV) are carried out.
Performing of surgical stage of local introduction of temodeks

Finished gel-like mass for the interperitoneal treatment

View of the resected tumor cavity filled with a gelatinous mass of temodeks
**PROSPIDELONG** – is the hydrogel antitumoral drug with prolonged action for the interperitoneal treatment of the patients with disseminated cancer of the stomach.
A preparation in the form of sterile powders for the preparation of the gel. Represents prospidium chloride immobilized on a specially synthesized gelling mixed ether of dextrane containing phosphoric acid and carbonates groups. Designed for local chemotherapy of gastric cancer with metastatic lesions of the peritoneum, and in the future tumors at other localizations. According to preclinical testing has a high and sustained anti-tumor activity, characterized by a rather low toxicity parameters. The drug was awarded a Diploma of 1 degree and a gold medal, at "St. Petersburg Technical Fair", St. Petersburg, 2012
PROSPIDELONG PRE-CLINICS

- Toxicology
- Pharmacokinetics
- Specific effects of intraperitoneal and intratumoral injection
Affect of prospidinum and prospidelong on sarcoma tumor growth of M1
Affect of prospidelong on lifespan of tumor-bearing animals
General view of the abdominal cavity of rats vaccinated with Zajdel hepatoma on the 22 day after a single intraperitoneal injection of dextran phosphate (a) prospidinum (b) "prospidelong" (c) – there are no signs of the tumor process in the abdominal cavity
POTENTIAL PLACE OF PROSPIDELONG IN ONCOLOGY

- intraoperative application
- intratumoral administration
- intracavitary application:
  - bladder cancer,
  - abdominal cavity metastases,
  - pleural cavity metastases
Intellectual Property Rights
Research Institute of Physical and Chemical Problems, BSU has patents of Belarus and Russia for manufactured products:
Tsisplatsel, Patents of RB № 6420, 5748
Temozolomide, Patents of RB number 16085, 15961
Prospidelong, Patents of B number 14762, 15136 of Russia number 2455007, 2442586 Nitargal Patent of RB 8456

License agreement has been concluded between the Research Institute for Physical Chemical Problems, BSU and UE "Unitechprom BSU" on the transfer of rights to use the patent number 6420 for the invention of Tsisplatsel. Registered by the World Intellectual Property Organization (Geneva) trademark on Tsisplatsel in Belarus, Armenia, and Ukraine.
Patent of the Republic of Belarus for a process of preparation of «Cisplacel»
Гидрогелевый противопухоловый препарат

№ 2442586
Патент на изобретение
Российская Федерация

Патентообладатель(ы): Учреждение Белорусского государственного университета "Научно-исследовательский институт физико-химических проблем" (НИИ ФХП БГУ) (BY), Общество с ограниченной ответственностью "Биотехнологическая компания ТНК" (RU)

Заявка № 2010134398
Приоритет изобретения 11 ноября 2009 г.
Зарегистрировано в Государственном реестре изобретений Российской Федерации 20 февраля 2012 г.
Срок действия патента истекает 18 августа 2030 г.

Руководитель Федеральной службы по интеллектуальной собственности
В.П. Симонов
Диплом

Степень

Учреждение Белорусского государственного университета "Научно-исследовательский институт физико-химических проблем", УНП РУП «Унитехпром БГУ»

за разработку
ПРОТИВООПУХОЛЕВЫЙ ПРЕПАРАТ "ЦИСПЛАЦЕЛ"
Registration certificate

License for pharmaceutical activity MPH RB
Forms of cooperation

- Manufacturing investment
- Technology sale
- Joint production
- License sale
- Finished product sale
- Joint development of prolonged medical forms on the basis of modified natural polysaccharides
Republican innovation competition “Technosphere -2012"

UE " Unitechprom BSU" is the best innovative company of the year!
The enterprise gained European certificate of quality management system ISO 13485 to develop, sell and service maintenance of automated multipurpose spirometers MAC
PRODUCER

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