

STUDY REPORT

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ON ESTABLISHMENT OF LARGE-SCALE PRODUCTION AND HEALTHCARE IMPLEMENTATION OF NOVEL HIGHLY EFFECTIVE POLYORGANOSILOXANE-BASED ADSORBENT DRUGS WITH DETOXIFYING EFFECT

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Novel intestinal and topical adsorbent drugs with detoxifying effect (studies were conducted in 1980-1990 by order of Main Military Clinical Hospital of the Ministry of Defense of Ukraine) were widely evaluated in military medical facilities. The Military Hospital of Kyiv (nowadays the Main Military Clinical Hospital of the Ministry of Defense of Ukraine) participated in the medical and biological evaluation of novel drugs from the beginning of their development (V.N. Fadeev, F.G. Novikov, N.P. Bezlyuda).

Novel medications were specially designed for military use and aimed at the treatment of liver, kidney and gastrointestinal infectious diseases and prevention and therapy of wound infection. Today two drugs are granted authorization for medical use: gel-like intestinal adsorbent Enterosgel and topical adsorbent Immosgent, which is a powder of porous xeroform of polydimethylsiloxane with immobilized antibiotic gentamicin.

The intestinal adsorbent Enterosgel (Temporary Pharmacopoeia Monograph № 42-2074-91) has paste-forming and biogenic properties and does not induce mucosal injury of mouth, esophagus, or intestine. Also, it does not damage parietal digestion, stimulates intestinal peristalsis, and easily eliminated from the body (after 7-8 hours). Compared to the previously described adsorbents with detoxifying effect, Enterosgel has higher adsorption capacity and selectivity to medium-molecular toxic metabolites, full bio- and hemocompatibility, which is caused by organic nature and porous structure. Among the vast patient population Enterosgel was shown to be safe and free of side effects and contraindications. Thus, it was approved for sale without prescription or other restrictions.

Detoxifying effect of Enterosgel is used in mono- and combination therapy in patients with urological diseases (pyelonephritis, polycystic kidney disease, nephrolithiasis, etc.) which are accompanied by chronic kidney disease or toxic liver injuries of infectious origin (toxic hepatitis, viral hepatitis A and B). This drug is also used in cholestasis of different etiology accompanied by liver failure and allergic reactions, gestosis, gastrointestinal

disorders, including diarrhea and food toxicoinfections, gastritis and colitis, purulent septic process and intoxication caused by elephantiasis.

Of particular interest is the ability of Enterosgel to eliminate radionuclides and adjust radiation-induced homeostatic changes. In 1986-1990, Enterosgel was used among the vast majority of militaries aged 30-46 years old involved in Chernobyl disaster clean-up. Treatment course lasted 10 days. The control group was formed by men from the same division with identical work activities. The observations showed the following results: the level of radionuclides decreased to the average value of 60% in the group receiving Enterosgel, while normalization of liver specific biochemical parameters and activity of antioxidant enzymes occurred by 14-16 days after egress from exclusion zone. Normalization of immune status was observed in 750 patients. The average duration of rehabilitation was 18 ± 2 days. In contrast, in the control group internal radiation dose increased, and normalization of liver specific biochemical parameters and activity of antioxidant enzymes occurred by 28-30 days after egress. Normalization of immune status was observed in 12.1% of patients. The average duration of rehabilitation was 32 ± 2 days. Therapeutic effect was observed in 100% of patients receiving Enterosgel, including positive effect in 75% and satisfactory effect in 25%.

Enterosgel was confirmed to have radioprotective effect (according to the data of KGB Hospital of the Ukraine, 1989-1990). Here, total average radionuclide blood activity in militaries not receiving Enterosgel increased 5-fold during 2 weeks in the exclusion zone. At the same period, total blood activity increased only by 0.4% in the group receiving Enterosgel.

Introduction of Enterosgel in the complex therapy of grade 2-3 ARS (according to the data of Institute of Oncology of MH of USSR, 1986) resulted in normalization of biochemical parameters, regression of dizziness, headaches, dyspepsia, and dysbiosis, which was characterized by the development of opportunistic microorganisms (*Neisseria*, *Klebsiella*) in pharynx and catarrh of the upper respiratory tract

Another drug, which is found to be effective in prevention and treatment of wound infections and radiation injuries, is topical adsorbent Immosgent (powder xeroform of Enterosgel containing immobilized antibiotic). The clinical experience was described by the Medical Services of Kiev Military District in the guidelines "Novel method of prevention and treatment of wound infection using immobilized adsorption agents", published in Kiev at 1985. On the basis of Enterosgel, contact adsorbents Furaxan and Anestofuraxan were designed. They contain immobilized antimicrobial agent furazolidone solely or together with anaesthesinum, respectively. These drugs are now used for prevention and treatment of the

purulent inflammatory diseases and postoperative complications. Here, positive effect of topical application is achieved due to the long-term maintaining of therapeutic concentration in wound and simultaneous organophylic matrix adsorption of toxic substances in wound. Medications described reduce pain shock and posttraumatic complications, prevent keloid scars, decrease the duration of therapy by 40-50% as compared to the previously described methods.

Enterogel, Immosgent, Furaxan and Anestofuraxan, are also available in the paste form, made by fine grinding of gel with the immobilized drug. These medications effectively block inflammations occurred in closed cavities; they showed very promising results in the treatment of urological diseases.

Adsorbent agents with detoxifying effect were applied in military operations in Afghanistan, Ufa accident clean-up, Spitak tragedy, Chernobyl disaster, and clean-up of several epidemics in military units; the results suggest using these agents as emergency medications and preparing an appropriate strategic reserve of these medications.

According to our analysis, internal and topical adsorbents with detoxifying effect, which are designed by scientists and physicians on the basis of polyorganosiloxane matrix, are required both for military purposes and rehabilitation of population affected by the Chernobyl disaster. Therefore, establishment of large-scale production is the project of national importance

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