HEMO- AND ENTEROSORBENTS ON THE BASE OF SPHERICALLY GRANULATED SYNTHETIC CARBONS

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Introduction

The application of carbonaceous adsorbents in medicine has old traditions. Still antique doctors used charcoal for treatment of wounds. To the beginning of ?? century the therapeutic use range of active carbons (? C) essentially has extended as an outside means (treatment of purulent wounds and ulcers, disinfecting in surgical and dental surgery practice), and internal adsorption preparation (enterosorbents) for treatment of acute poisonings and many internal illnesses[1]. More than 30 years ago, due to courageous activity of Greek nephrologist H.Yatzidis, AC have begun to be applied to direct purification of blood - hemoperfusion[2]. The development of the last direction was always conjugate with a solution of a problem of AC hemocompatibility. It means the prevention of coagulation of blood and sharp shift of its electrolyte balance on a layer of adsorbent, minimization of blood platelets and proteins loss, and also migration of carbon microparticles, toxic mineral and organic impurities from the adsorbents in blood. As one from effective solutions actually opened a possibility of broad practical use of hemoperfusion it is necessary to recognize offered by T.Chang a method of AC granule microcapsulation, i.e. their partial or full covering by natural or synthetic biocompatible polymers[3].

It became hereinafter clear that microcapsulation to maintain good hemocompatibility of AC sharply reduces them adsorption and apparently catalytic properties, and consequently worsens therapeutic effect of hemoperfusion.

Alternate direction in hemoperfusion - the use of uncovered AC has received development in the former USSR under the direction of the academician Yu.Lopukhin[4]. A principal point of existence and development of this direction was the obtaining in Ukraine[5] the synthetic active carbons (SAC) from co-polymers and resins - base for preparing of high qualitative biocompatible uncoated hemosorbents as well spherical oral adsorbents (enterosorbents). The technologies of SAC deriving and medicinal means on their basis (hemo- and enterosorbents) are patented in Ukraine and Russia[6].

Characterization of SAC: are prepared by pirolysis and consequent steam activation of spherically granulated industrial porous co-polymers or resins on the base of vinylpyridin or styrene, cross-linked by divinylbenzene or phenol-formaldehyde[7]. Obtained corresponding nitrogen containing (SCN) or pure carbonaceous (SCS) SAC appear as spherical particles with a diameter of 0.25-1.2 mm. They have high mechanical strength on friction (not less than 80%), smooth surface of granules with a metal brightness, low contents of mineral impurities (less than 1%). Their porosity is characterized by developed micropores (Vmi = 0.55-0.85 cm^3/g) and macropores connected with transport channels of mesopore type with diameter 10-40 nm (Vma+me = 0.35-1.25 cm^3/g). As a rule, for SAC in an burn-off interval of 40-75% volumes of adsorption pores on benzene (Ws) are within the limits of 0.6-1.2 cm^3/g, and the specific surface areas on argon (Ssp) are within the limits of 1200-1600 m^2/g. These parameters are much higher, than at used on practice carbon hemosorbents on the base of capsulated AC. So, for example, hemosorbents in "classical" columns have parameters:

"Adsorba 300/150?" (Gambro, Sweden)
Ws = 0.49 cm^3/g, Ssp = 920 m^2/g;
"Hemodetoxifier" (?-D, USA)
Ws = 0.39 cm^3/g, Ssp = 690 m^2/g;
"D??-1" (Kuraray, Japan)
Ws = 0.52 cm^3/g, Ssp = 810 m^2/g.

SAC exhibit more expressed, than traditional AC, catalytic activity in responses of an electronic and acid-basic type. As result of this detoxifying effect when SAC contact with biological mediums can essentially amplify at the expense of catalytic neutralization of some harmful and toxic metabolites (decomposition of peroxides and hydroperoxides, oxidation of nitrogenous slugs, hydrolysis of carbohydrates and fats etc.).

Hemosorbents on the basis of SAC

The fraction of SAC with a diameter of 0.5-1.0 mm is used for preparation of hemosorbents such as SCN and SCS. For a solution of a biocompatibility problem we offer a number of technological receptions, in particular: acid-basic demineralization of a material, recycling washing from colloidal microparticles by the biocompatible surfactants (heparin, albumin etc.), ionic balancing of SAC on a level of its saturation by oxygen, including oxidation of a surface. By special researches was shown that

the primary factor of biocompatibility and anyone AC and SAC in particular is the maintenance of their balancing on oxygen. Without this a carbon hemosorbent is capable to poor sharply blood on oxygen, to increase essentially its anode potential and to shift acid-basic balance of blood, to keep electrostatically the platelets on a surface, to call a rupture of erythrocyte membranes (hemolysis). We reveal experimentally the correlation between a gain of an electrode potential of carbon, ?? shifts of a biological liquid and platelets loss.

Comparative quantitative researches of isotherms and kinetics of adsorption on test substances from model solutions have shown that SAC on specific adsorptive ability exceed the technical capsulated adsorbents in 10-15 times for low-molecular substances (M.M. 100-500) and in 30-40 times for “middle" molecules (M.M. 500-5000). It allows minimizing the volume of perfusion columns with SAC up to 50-200 ml. At this the operational parameters of columns are high enough. Their clearances in test measurements (standard hemoperfusion on experimental animals during 60 min) achieve on medinal 70-80%, on creatinine 80-90% and on "middle" oligopeptides 50-60% from a volumetric velocity of blood. At the same time loss of thrombocytes and leukocytes does not exceed 15% from an initial level, and the gain of free hemoglobin makes less than 100 mg/l. Thus, on SAC the high level of hemocompatibility and detoxifying possibilities under conditions of direct hemoperfusion is obtained.

By us it is shown also that SAC are interesting and are perspective as a matrix for covalent immobilization of various bioligands both deriving of a number biospecific and affine hemosorbents.

Enterosorbents on the basis of SAC

The fraction of SAC with a diameter of 0.25-0.63 mm is used for preparation of enterosorbents such as SCN and SCS. The large clinical experience has shown efficiency of SAC use as antidotes and adsorption preparations. The interest to enterosorption is stipulated that efferent method of treatment is more sparing for an organism, and 3-5 days procedure of enterosorption can give practically same results as one session of hemoperfusion.

For want of deriving of SCN and SCS enterosorbents by us some technological receptions on maintenance of biocompatibility (chemical and microbiological cleanness, holding of pharmacopoeia norms on impurities) also are offered.

The deriving technology of adsorption means of the given type provides updating their surface chemistry and introduction useful macro- (K, Mg) and micro-elements (Zn, Cu, Mn, S? etc.).

Enterosorbents on the basic of SAC are especially effective to treat the ecological dependent diseases stipulated by accumulation in an organism of heavy metals (Hg, Pb, Cd, Ni etc.) and also short- and mid-living radionuclides (^{140}??, ^{140}La, ^{125}Te, ^{131}I, ^{95}Zr, ^{95}Nb etc.) are appeared in an environment after Chernobyl NPP accident. The use of enterosorbents of this type has allowed realizing preventive maintenance and treatment of staff working in zones of liquidation of catastrophe consequences. At preventive application of enterosorbents (before the beginning and during work) it was possible on the order to reduce a level of radioactive contamination of an organism. In curative variant 10-14 days course of enterosorption in 7-8 times accelerated removal of incorporated radionuclides from an organism.

It is essential at usage of enterosorbents on the base of SAC the possibility of adsorption-catalytic deactivation of some radiotoxins (peroxides of lipids, hydroperoxides etc.) and also correction of the biochemical status of an organism on parameters of electrolyte, protein, enzyme and lipid exchanges.

The extensive clinical experience of use SAC as hemo- and enterosorbents gives the basis to recommend them for treatment not only acute poisonings, but also chronic intoxication's (endotoxicosis), diseases of internal organs (first of all, liver and kidneys), and also large group of infection, auto-immune and psycho-neuralgic diseases.

The most impressive data was obtained at treatment of chronic renal insufficiencies as alternative to expensive and complicated methods of hemodialysis and plazmapheresis.

The pilot production of hemo- and enterosorbents of SCN and SCS is organized in Institute for Sorption and Problems of Endoecology, NAS of Ukraine.

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