ENTEROSORBENT SILICS PROPERTIES AND CLINICAL APPLICATION

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Abstract

As a result of the complex physico-chemical and medico-biological studies conducted by the Institute of Surface Chemistry of the NAS of Ukraine together with a number of research institutes and clinics of the Ministry of Public Health of Ukraine a new enterosorbent Silics has been developed and introduced into medicinal practice. This synthetic highly dispersed silica with an extended specific surface is characterized by its chemical purity, stability, and physiological innocuousness. The regular structure of its surface as well as the presence of a large number of surface reactive sites insure a high adsorptive capacity of Silics with respect to water, protein molecules, toxins, pathogenic microorganisms, and viruses. At present new technologies are being described for application of Silics as an individual medicinal preparation of sorptive action and as an active basis for a novel generation of composite drugs.

Introduction

In recent years the efferent methods of treatment which are based on the removal of toxic and ballast substances of exo- or endogenous origin from an organism have developed into an independent trend of modern pharmacotherapy. Medicinal sorbents differ considerably in their chemical nature and production process and include various modifications of activated charcoal, ion-exchange resins, silicas, polymers, and other natural and synthetic substances.

Scientific workers of the Institute of Surface Chemistry of the NAS of Ukraine and Vinnytsya State Medical University named after M.I. Pyrogov have designed a new enterosorbent SILICS and introduced it into medicinal practice. The enterosorbent is a synthetic amorphous highly disperse silica (HDS). Owing to salient features of its surface HDS is employed not only as a sorbent with biocorrecting properties but also as a matrix used in the capacity of a carrier of composite medicinal agents [1].

From the chemical standpoint a nucleus of an HDS particle is a three-dimensional polymer whose structural units are silicon-oxygen tetrahedra bonded by disiloxane bridges Si–O–Si. On the surface of HDS particles there are groups O–H chemically bonded with silicon atoms (silanol groups SiOH). The hydroxylic cover of HDS gives rise to a high hydrophilicity of its surface and, correspondingly, to its ability to sorb polar molecules, especially water molecules. The surface of HDS has weak proton-donating properties. Its isoelectric point is attained at pH = 2. The surface of HDS enters into an adsorption interaction with charged molecules and substances capable of forming hydrogen bonds O–H···O. The mechanism of adsorption is to a great extent dependent on pH of medium [2].

The main salient feature of HDS which is brought about by its physico-chemical properties is a high protein-sorbing (proteinonektonic) ability that forms the basis of application of HDS for removal of exotoxins, endotoxins, pathogenic immunocomplexes, products of degradation of necrotic tissues, and other harmful substances of protein origin from an organism as well as for fixation of microorganisms [3].

I. Mechanism of Biological Activity of Highly Disperse Silica (HDS)

The biological activity of SILICS is based on the following properties of HDS which are brought about by the chemical nature of its surface:

1. High hydrophilicity of the surface of HDS;
2. High biosorbing activity
3. Fixation of large amounts of microorganisms and microbial toxins;
4. Adsorption of low-molecular substances.

Let us consider these properties in detail.

1. High hydrophilicity of HDS is due to the presence of a hydroxylic cover and electron-accepting silicon atoms of silanol groups. The surface of HDS is able to sorb polar molecules. Water wets the surface of HDS well, which leads to formation of thin slurries (suspensions) or gels of various consistencies depending on the ingredient ratio.

The hydrophilic properties of HDS have found application to eliminate edemas and to decrease exudation in the case of local treatment of wounds at a stage of inflammation, to bind and structurize water in the intestine of a patient suffering from diarrhea. Besides, HDS is widely used as a drying agent in dermatological practice.

2. High protein-sorbing activity of HDS is effected through all reactive sites of silica (hydroxyl groups, silicon atoms of silanol groups, and electron-donating oxygen atoms of siloxane bonds), and, probably, through co-ordinatively bound water. There are three types of interaction between protein molecules and silica surface, namely electrostatic interactions, hydrogen bonding, and hydrophobic interactions. Adsorption of protein molecules on HDS can be interpreted applying a theoretical model based on interaction of a polyelectrolyte with a charged surface of HDS. According to this model, the affinity of a protein to the surface is determined mainly by electrostatic forces. This inference is corroborated by the dependence of adsorption value for the protein on pH of medium, with the dependence graph displaying a maximum at the isoelectric point (IEP) of the protein [3,4].

Thus, in the situation with serum albumin (IEP is equal to about 5.0) the mutual interaction is observed over the pH interval from the zero-charge point of the surface (pH 2.0) and to the protein IEP when interacting agents bear different charges. At pH values that do not fall within this interval the affinity will be determined by other factors, namely by hydrogen bonds and hydrophobic interactions. The adsorption value maximum at the albumin IEP is attributed to the fact that uncharged globules of the protein have minimal size and a unit surface may accommodate a larger number of them.

A study has been made of adsorption of proteins on HDS within the scope of the model of interaction between the silica sorbent and biologic fluids of an organism (wound exudate, blood serum, etc.). The model proteins have been bovine serum albumin (BSA), egg albumin, dried human blood plasma, horse hemoglobin, gelatin. The kinetic tests have indicated that the main mass of the protein (not less than 90 %) is adsorbed on HDS from solution within the first 10 min of the contact, with the adsorption rate being independent of type of protein. A similar high adsorption rate may be attributed to the fact that HDS has a nonporous structure. As regards the influence of acidity of medium, the researches conducted have shown that the maximum adsorption of proteins on HDS is observed at pH values close to the corresponding IEP of these proteins. For instance, in the case of the bovine serum albumin the maximum adsorption value is attained at pH 5.0 (IEP = 4.8).

The results presented in Table 1 give evidence for the fact that the protein-adsorbing capacity of HDS substantially exceeds the corresponding capacity of other familiar sorbents applied in the medicinal practice. With increasing ionic strength of solutions the adsorption value increases. Besides, the adsorption value also increases as pH of solutions approach the IEP of the albumin.

Table 1
Degree of removal (in %) of proteins from an aqueous medium by HDS and other medical sorbents

Sorbent	Protein Preparation	Degree of Removal, %		
		Distilled Water, pH 6.5	0.9 % NaCl Solution, pH 6.5	0.1 M Phosphate Buffer, pH 5.7
HDS	BSA	27	60	62
	Plasma	64	90	95
SUGS	BSA	1.8	2.4	3.0
	Plasma	0	5.4	4.6
SKN	BSA	4.0	0	0
	Plasma	6.0	6.0	5.3
AUVM Dnipro-MN	BSA	9.2	5.2	6.4
	Plasma	10	12	14
Debrizan	BSA	0	0	0
	Plasma	0	1.4	1.5

Of interest is also the following adsorption potentiality of HDS. In the case of polymer-containing disperse systems with a certain ratio of a solid phase and adsorbate one can observe flocculation that involves merging of disperse particles through formation of bridges with polymer molecules. The flocculation process results in large aggregates that quickly precipitate. The process is especially characteristic of protein-containing systems, which is due to polyvalence of protein macromolecules.

A study has been made of the aggregative stability of colloidal solutions of HDS as a function of concentration of a protein in the solution. It has been found that the presence of a protein at concentrations lower than 4 mg ml^{-} does not affect the stability of a colloidal solution of HDS because such a low amount of protein molecules is not sufficient for coalescence of silica particles into aggregates. At a high concentration of a protein (5 mg ml^{-1} and more) the colloidal solution is stable owing to the colloid protection effect. The lower and upper limits of the dispersion stability make up an interval of concentrations (equivalence zone) suitable for flocculation of a colloidal solution of HDS to take place. In this case a colloidal solution of HDS possesses a higher proteinonektonic ability in comparison with an ordinary dispersion [5].

The results achieved when studying the specificity of interaction between HDS and human blood plasma *in vitro* give evidence for an increased affinity of disperse silica to lipoproteids in comparison with proteins that do not contain lipids (Table 2).

It can be seen that degrees of fixation of lipids components of blood serum by the sorbent amount to 90 % an more (cholesterin: 77 – 78 %) while that of the total protein amount to only about 26 %. The increased sorption of lipid-containing proteins on the silica surface is attributed to fixation of a whole lipoproteid particle (micelle) whose lipid phase content is predominant in comparison with the content of other phases and whose external surface is covered by proteins and phospholipids that possess an increased affinity to HDS. The data collected give grounds to infer that it will be possible to apply HDS for extracorporal hemosorption in the case of hyperlipidemia [6].

On the basis of the above-outlined observations one can, to some extent, explain hypolipidemic activity of HDS in the case of its peroral application because lipids in a gastrointestinal tract are in the form of micelles consisting of proteins, phospholipids, and bile acids. The sorbent provides fixation of food fats and lipid components that appear in an intestine as a result of hepatoenteric recirculation, which interferes with their

d other medical

	1 M Phosphate Buffer, pH 5.7
	62
	95
	3.0
	4.6
	0
	5.3
	6.4
	14
	0
	1.5

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Table 2
Content of proteins, lipoproteids, and cholesterin in blood serum before and after treatment with HDS and corresponding adsorption values (percentage of adsorbed substance)

Serum Components		Time of Contact with the Sorbent (min)			
		0	15	30	60
Total protein	g l^{-1}	74.00	58.60	56.1	54.8
	%		20.80	24.2	25.9
Low-density lipoproteids	g l^{-1}	6.50	0.38	0.13	0.10
	%		94.20	98.00	98.50
Total lipids	g l^{-1}	9.40	2.20	1.50	1.30
	%		76.60	84.00	86.20
Phospholipids	g l^{-1}	2.81	0.20	0.13	0.08
	%		92.90	95.4	97.20
Triglycerides	g l^{-1}	1.93	0.38	0.28	0.18
	%		80.30	85.50	90.60
Total cholesterin	mmol l^{-1}	11.00	2.30	2.50	2.40
	%		78.00	77.00	78.00

absorption. It has been shown that ingestion of a medicinal agent developed on the basis of HDS by patients who suffer for disturbances of metabolism of lipids already within 3 – 4 weeks brings about a substantial decrease in the level of cholesterin in blood serum, and this decrease is the greater, the higher was the initial level of cholesterin at the beginning of the treatment.

As is known, sorbents of medicinal specification must meet certain requirements, with one of the most important being their physico-chemical stability especially their inertness with respect to the internal medium of an organism. Such a sorbent should not be dissolved when in contact with biologic fluids (exudate of a wound, content of a digestive tract). From the results achieved during experiments with test animals (rats and rabbits) it follows that after a single intragastric administration of even a large dose of HDS (1 g kg^{-1}) any statistically reliable variations in concentration of silicon in blood are not revealed. It has been found that rats which were given the above-said dose of HDS for 30 days display a tendency towards increasing in excretion of silicon. However, in this case any reliability of disagreements has not been verified either. One of the causes of the absence of any marked absorption of HDS in a digestive tract may be its low solubility over the pH interval from 2 to 8. It is also possible that there is a specific physiologic mechanism which prevents penetration of silica microparticles through intestine walls. Thus, it has been shown that HDS satisfies one of the most important requirements to sorbents of medicinal specification, namely it possesses a high physico-chemical stability and is not dissolved in the internal medium of an organism [6].

The high protein-sorbing ability displayed by HDS makes the basis for its application for fixation and removal of bacterial toxins, pathogenic immuno-complexes, products of decomposition of necrotic tissues, and other injurious substances of protein origin from an organism.

3. The protein-sorbing properties characteristic of HDS impart preparations on its basis the ability to fix microorganisms. The interaction between silica and microorganisms is not distinguished for any specific nature. It is attributed to the affinity

of silica particles to glycoproteid structures and to phospholipids in membranes of microbe cells.

A research has also been made into interaction of HDS with enteropathogenic *Escherichia coli*, *Staphylococcus aureus*, *Proteus vulgaris*, *Bacillus pynocyaneus* [7]. The procedure is as follows. A certain amount of HDS is added to 3 ml of a diurnal culture of microorganisms, the mixture is stirred for 2-3 min and filtrated, following which the filtrate is quantitatively sowed on a nutrient medium. After incubation for 24 h at 37 °C a count is taken of the colonies grown, with their number being equal to the number of bacteria that were not fixed by the sorbent. The results of the researches show that even at low concentrations of HDS (0.33-1.33 %) practically all the microorganisms which were in the solution (up to 3.5 milliard of microbial bodies per gramme of the sorbent) are fixed, with the fixation value being virtually independent of type of microorganisms. The interaction of the microorganisms with HDS is distinguished for some particularities. Firstly, sizes of HDS particles (4 – 40 nm) are considerably smaller than those of microorganisms (1 – 10 μm), so that HDS seems to bring about the effect of agglutination, which substantially increases its adsorptive capacity with reference to microorganisms. Thus, since HDS particles are much smaller than microbial cells, it is the sorbent particles that are sorbed on microbial cells and not vice versa. Even at a low concentration, HDS particles are able to agglutinate microorganisms, i.e. to act in the capacity of a glue that unites microorganisms into a conglomerate. Evidently, it is this phenomenon of agglutination of microorganisms by particles of HDS which explains its unique ability to bind enormous amounts of microorganisms in comparison with other sorbents. Secondly, it has been found that after a contact of microorganisms with HDS they vary some of their properties. For example, they become more sensitive to antibiotics, especially to erythromycin, gentamycin, and streptomycin (from 40-60 % to 100 %). Thirdly, after a contact with HDS the microorganisms become sensitive to the action of proteolytic enzymes and cationic and anionic SAS, such as bile acids and phospholipids, i.e. to natural components of intestinal and gastric juices. The high affinity of HDS to microorganisms and its influence on processes of vital activity of microorganisms provide an explanation for mechanism of its curative effect because possibility of appearance of infectious diseases and gravity of their progress are directly dependent on values of contagious dose, number of bacteria that are accumulated in an intestine in the course of colonization.

4. Adsorption of low-molecular substances. Of interest also are researches into regularities of adsorption of medicinal substances on HDS because the results of such researches form a scientific basis for development of preparations with a modulated pharmakinetics. A study has been made of adsorption of orthophen, quinidine, scopolamine, amphotericin, and some vitamins on HDS from aqueous solutions [8].

By way of example, it has been shown that in the case of slightly soluble antibiotic amphotericin B it is possible to increase the rate of absorption of the curative substance by simultaneous introduction of the substance and HDS into an intestine. When amphotericin B (at a dose of 3 – 7 g) is administered perorally, its concentration does not exceed 0.3 mg ml^{-1} and the biologic availability makes up only 3 %. The experiment was carried out on 56 rats subdivided into 6 groups. The first group included animals that were administered 2 ml of 0.2 % solution of the preparation (4 mg). The rats of groups II – VI were administered 2 ml of a mixture which contained 4 mg of amphotericin B and different amounts of HDS. The control group was given 2 ml of distilled water. For the half of the animals the experiment was terminated in 4 h (for the rest of them in 24 h). The results achieved are presented in Table 3.

From the data presented it is clear that introduction of the antibiotic simultaneously with an aqueous suspension of HDS leads to an increase in the maximum concentration of the preparation in blood from 2 μg ml^{-1} to 21 μg ml^{-1}. The sharp

Table 3
Variations in concentration of amphotericin B in blood of rats in the case of its simultaneous introduction together with HDS

Group of Animals	Concentration ($\mu g\ ml^{-1}$)	
	4 h	24 h
I. Amphotericin 4 mg + water, 2 ml	2.0±0.1	0.9±0.4
II. Amphotericin 4 mg + HDS, 60 mg kg^{-1}	21.2±0.5	5.4±1.9
III. Amphotericin 4 mg + HDS, 50 mg kg^{-1}	19.1±0.3	6.0±2.5
IV. Amphotericin 4 mg + HDS, 30 mg kg^{-1}	14.7±0.2	4.9±1.2
V. Amphotericin 4 mg + HDS, 20 mg kg^{-1}	9.6±0.3	4.1±1.3
VI. Amphotericin 4 mg + HDS, 0.2 mg kg^{-1}	2.1±0.1	0.9±0.3

increase in the absorption of the curative substance provides an increase in its biologic availability. Analogous effects were observed for substances of other classes, such as alkaloids (quinidine), carbohydrate (xylose), organic substances (voltarene). Thus, the studies of absorption showed that maximum concentration of quinidine in blood increased from 2.6 to 4.6 $\mu g\ ml^{-1}$ and that of voltarene (anti-inflammatory agent) from 16 to 26 $\mu g\ ml^{-1}$.

Further, a study has been conducted of the release of quinidine (common antiarrhythmic preparation) from various medicinal forms produced by immobilization of quinidine and its complexes with surface active substances or protein on HDS. On the basis of the results of the comparative analysis of the data of biopharmaceutic and pharmacokinetic researches it was inferred that the requirements to medicinal agents of prolonged action are most fully met by the preparation produced by coprecipitation of complexes of quinidine with molecules of serum albumin on the surface of HDS. Administration of this preparation does not give rise to any sharp peak of concentration of quinidine in blood and a slow decrease in concentration during a long term is observed. Besides, administration of this medicinal form makes it possible to provide the maximim bioavalability of quinidine.

The results of the comprehensive and thorough researches into physico-chemical and biological properties of HDS conducted at the Vinnytsya State Medical University named after M.I. Pyrogov and at other medical institutions of Ukraine gave grounds to infer that HDS is an active medicinal substance which on its own can function as a therapeutic agent. Sorptive detoxication with the aid of HDS brings about a profound effect in the case of acute intestinal infections, diarrheas of various genesis, viral hepatitis, as well as in the situation of local treatment for pyo-inflammatory diseases and purulent wounds. The pharmacotoxicological trials of HDS have substantiated innocuousness of its enteral and applicative usage at doses more high than those permitted for its application as an ancillary substance. Thus, the maximum dose of HDS (10 g per kg of a test animal body mass) which was introduced into the stomach of an animal proved to be nontoxic. Single and repeated peroral administration of HDS at a dose of 100 and 300 mg kg^{-1} for two species of animals (rabbits and rats) did not lead to any deviation of biologic, immunologic, pharmacologic or morphologic indices [1,4].

II. Clinical Application of SILICS

The data about fields of application of HDS SILICS at polyclinics for treatment for infectious diseases are presented in Table 4.

It is seen that the sphere of application of SILICS is rather large and covers both intestinal infections and toxicosises which victimize infants, as well as viral hepatitises, botulism.

Table 4
Clinical application of SILICS for treatment for infectious diseases

Field of Application	Pathologic Syndrome	Pharmacologic Effect	Particularities of Application	Number of Patients
Intestinal infections (toxicoinfections, salmonellosis, shigellosis, cholera, etc.)	Diarrhea, intoxication, dyspepsia	Fixation of microorganisms and their toxins, normalization of absorption and secretion in GIT	Monotherapy.	54
			Combination with antibacterial agents and agents for rehydration	224
Intestinal toxicosis in children	Dehydration, diarrhea, intoxication, dyspepsia	Sorption of toxins, normalization of absorption and secretion in GIT	Monotherapy.	30
			Combination with antibacterial agents and agents for rehydration	144
Viral hepatitises	Cholestasis, cytolysis of hepatocytes, intoxication	Sorption of viruses, bile acids, and bilirubin	Monotherapy.	33
			Combination with hepatoprotectors	181
Botulism	Neurotoxicosis, dyspepsia	Sorption of toxins, enhancement of action of immunopreparations	Combination with specific serums	103

By way of illustration some concrete data are presented in Table 5. From the data it is clear that inclusion of SILICS into complex treatment of patients suffering from salmonellosis, dysentery, and intestinal toxicosis accelerates normalization of clinic manifestations of these diseases by a factor of two and more. In the case of botulism the normalization of symptoms characteristic of lesions of nervous system is shortened by almost 4 days. If intestinal infections are not severe, SILICS can be recommended as a single therapeutic agent. In the case of a considerable diarrheal syndrome it is more expedient to use it together with rehydration substances.

Inclusion of SILICS into a complex of therapeutic agents for patients suffering from viral hepatitises accelerates substantially recovery rates of patients so that their normal level of bilirubin and activity of alanine aminotranspherase are recovered within shorter periods of time.

The mechanism of the therapeutic effect of HDS on treatment for intestinal infections seems to involve the following major aspects [1].

1. ***Influence on intestinal microflora:***

A) Direct influence:

* fixation of bacteria and their removal from an organism with stools; sorption of microbial toxins of protein nature and other pathogenic proteins (neuraminidase, hyaluronidase, contact hemolysins) that promote pathogenic action of microorganisms;
* bactericidal effect is possible (in the presence of bile acids and proteolytic enzymes);

B) Indirect influence:

*creation of conditions unfavourable for vital activity of pathogenic microorganisms (concentration of microorganisms on the sorbent results in a local deficit of nutrients that are necessary for them, fixation of hemoglobin sets a limit on iron that is necessary for microorganisms, etc.);
* adjuvant action (concentration of microbial cells and their toxins on the sorbent enhances the antigenic action and immune response of an organism).

Table 5
Duration of symptoms of intestinal infections in the course of treatment with the aid of SILICS (M±m)

Duration of Symptoms (days)	Traditional Treatment	Traditional Treatment + SILICS
	Salmonellosis	
Diarrhea	5.60±0.31	2.00±0.45
Normalization of coprogrammes	5.60±1.06	2.60±0.35
	Dysentery	
Diarrhea	7.00±1.50	2.30±0.43
Normalization of coprogrammes	7.20±1.21	4.00±1.25
	Intestinal toxicosises in children	
Intoxication	2.70±0.13	1.80±0.12
Dehydration	3.70±0.18	2.10±0.12
Disturbances of microcirculation	3.80±0.21	2.10±0.35
	Botulism (severe case)	
Neurotoxicosis	13.80±1.39	9.90±0.78

Dynamics of biochemical indices in the course of treatment of patients suffering from hepatitis (M±m)

Indices	Traditional Treatment		Traditional Treatment + SILICS	
	Before Treatment	In 7 – 10 Days	Before Treatment	In 7 – 10 Days
Bilirubin (μmol l^{-1})	264±9.7	192±15.9	244±28.7	151±22.8
Alanine aminotransferase (μmol l^{-1})	3.20±0.65	2.20±0.19	3.00±0.73	1.50±0.28

2. Interaction of HDS with intestinal walls and intestine content:
* blocking of receptors of the mucous membrane of the stomach which are responsible for adhesion of microorganisms and fixation of toxins; intensification of transport of water, electrolytes, and other substances from the intestine into internal medium; modelling of baroreceptors and chemoreceptors of intestinal walls which are responsible for motility;
* clearance of intestinal juice from toxic substances (products of vital activity of microorganisms and of microbial putrefaction of proteins), toxic metabolites of endogenous origin (bilirubin, bile acids, micelle complexes, medium-molecular peptides, etc.);
* fixation of cholesterin and other non-polar lipids being members of complexes with proteins and phospholipids;

*the sorbent particles perform the role of sites of concentration and transport of ingredients of the intestine content so that the sorbent acts as a coenzyme thereby favouring the interaction between metabolites and accelerating the natural course of the process of their transformation, which leads to a decrease in the amount of intermediate products with toxic properties;

* the enterosorbents present in the gastrointestinal tract induce immobilization of digestive enzymes and intensifies digestion (in particular hydrolysis of proteins), which reduces irritation of immune system and activates reactions of oxidation, decomposition of peroxide compounds, transamination, etc.

In the course of the above-mentioned reactions HDS remains unchanged and, correspondingly, preserves its activity within all the time of its residence in the intestine.

Besides, SILICS may have much promise and potentiality in clinical treatment for internal diseases. The major lines of researches into application of this preparation in the relevant therapy are presented in Table 6.

Table 6
Application of SILICS for clinical treatment for infectious diseases

Fields of Application	Pathologic State	Pharmacologic Effect	Particularities of Application	Number of Patients
Disturbances of lipoid metabolism	Hyperchol-esterinemia	Reduction of absorption and synthesis of cholesterin	Monotherapy.	29
			Combination with statines	42
	Hypertriglyceri-demia	Reduction of absorption and synthesis of triglycerides	Combination with nicotinic acid and fibrates	43
				33
Thrombocytarno-coagulative homeostasis	Hypercoagulation	Retardation of aggregation of thrombocytes	Monotherapy.	29
			Combination with aspirin	118
Allergology	Bronchial asthma, food allergy, psoriasis, eczema	Detoxication, sorption of immune complexes	Monotherapy.	138
			Combination with antihistaminic preparations, steroids	97
				49
				250
				160
Correction for effect of toxicity of medicinal agents	Insufficient efficiency, side effects	Acceleration of absorption, decrease in dosage, detoxication	Amiodarone, nicotinate, symvastatine, orthophen, quinidine	43
				32
				25

Of significance is the ability of SILICS to lower levels of cholesterin and triglycerides as well as to retard aggregation of thrombocytes. Thus, with the help of SILICS it becomes possible to correct main pathogenic factors of atherosclerosis, namely hyperlipidemia and hypercoagulation. In the case of profound disturbances of lipoid metabolism it proved advantageous to employ SILICS together with other hypolidemic agents. The use of the complexes SILICS-symvastatine (synthetic inhibitor of biosynthesis of cholesterin) makes it possible to decrease the dose of the latter by a factor of two without lowering of the intensity of hypolipodemic action. Positive results have

also been achieved with reference to reduction of allergic complications induced by symvastatine and of its hepatotoxic action.

SILICS has also been successfully employed for treatment of patients suffering from allergic diseases (such as bronchial asthma), chronic obstructive lesions of lungs, food allergies, psoriasis, eczema. The profound detoxication effect of SILICS and its high affinity to proteins and medium-molecular peptides form the foundation for its application for treatment of patients of this profile. The remote results of such a treatment have shown that the use of SILICS for treatment of patients suffering from chronic obstructive lesions of lungs makes it possible to produce a more complete and more prolonged curative effect in comparison with the traditional treatment.

Important fields of application of SILICS are surgery, stomatology, oncology, obstetrics, and gynecology (Table 7). As far as these fields are concerned, there are two directions of application of SILICS, namely as an enterosorption agent and as an agent for local (apllicative) use.

Table 7
Application of SILICS in surgery, oncology, stomatology, obstetrics, and gynecology

Fields of Application	Pathologic State	Pharmacologic Effect	Particularities of Application	Number of Patients
Operative surgery	Hemorrhages	Hemostasis	Applications	66
Purulent wounds, destructive peritonitis, ileus, purulent pleurisy,	Localized aerobic and anaerobic infections	Sorption of microorganisms, endo- and exotoxins, dehydration	Applications, drainage of cavities	91 56 36 25
Oncology	Intoxication syndrome	Sorption of endo- and exotoxins, chemopreparations	Enterosorption	312
Stomatology	Pyo-inflammatory processes	Sorption of microorganisms, endo- and exotoxins, dehydration, abrasive action	Applications, drainage of cavities	156 286
Gynecology	Endometritis, vaginitis, pelvioperitonitis	Sorption of microorganisms, endo- and exotoxins	Applications, lavage	83 56
Operative obstetrics	Hemorrhages, pyoinflammatory processes	Hemostasis, sorption of microorganisms, endo- and exotoxins, localized dehydration	Applications, lavage, combination with antibacterial agents	62
Pregnancy	Gestosises of pregnancy	Detoxication	Monotherapy. Combination with antioxidants	45 72

Local applicative use of SILICS may have much promise in treatment for purulent wounds, destructive pancreatitis, peritonitis, purulent pleurisy, odontogenous phlegmons.

The mechanism of the curative action resides in sorption of pathogenic microorganisms and microbial toxins, in dehydration of wound tissues. The local applicative use of SILICS reveals one more salient feature of the preparation, namely its hemostatic effect. It has been proved that HDS activates the first phase of coagulation of blood, so that it can be employed in the case of moderate external or internal hemorrhages. Depending on localization of a hemorrhage, SILICS is used for applications or for drainage and insufflation. Hemostasis is usually attained after 1 – 2 treatment procedures involving the sorbent.

When SILICS is used for treatment of purulent wounds or odontogenous phlegmons, it exerted a marked effect on all the phases of a disease process, which manifests itself in acceleration of healing of wounds, with the time interval necessary for restoration of the function of an organ that was injured being shortened by 3 – 4 days.

It is also possible to employ SULICS for treatment in the case of puerperal infections occurring after cesarean sections. Lavage and drainage of the cavity of the uterus shortened the duration of fever, which, in its turn, decreased the time span of antibacterial therapy. SILICS in the capacity of applications or as an ingredient for drainage is also successfully employed for treatment for gynecologic diseases proper (such as vaginitis, endometritis, pelvioperitonitis).

The general detoxicating action of SILICS manifests itself in the case of its use for treatment of oncologic patients. SILICS seems to decrease levels of endogeneous intoxication that was a side effect of application of chemotherapeutic preparations and radiation therapy, with the efficiency of enterosorption being comparable to that of plasmapheresis.

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