# INTERACTION OF BIOACTIVE COMPOUNDS WITH HIGHLY DISPERSE OXIDES IN AQUEOUS SUSPENSION

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## Abstract

Interaction of polymers (albumin, gelatin, polyvinylpyrrolidone) and some drugs with fumed silica in aqueous dispersions was studied using adsorption, <sup>1</sup>H NMR, photon correlation spectroscopy, electrophoresis and thermally stimulated depolarization methods. The impact of polymers on the structural and adsorptive properties of suspended-dried fumed silica was explored using nitrogen adsorption method with the regularization procedure.

### Introduction

Highly disperse oxides such as silica, alumina, titania, etc. can be used as medicinal sorbents or drug fillers, additives and carriers and features of their interaction with dissolved or immobilized drugs and the corresponding media determine their efficiency. This interaction depends not only on pH or the concentration of inert electrolytes in a solution but also the availability of compounds, e.g., proteins, interacting with the oxide surface more effectively than relatively small drug molecules [1,2]. Also, drugs can strongly interact with some biopolymers, e.g., transporting proteins. Therefore, the investigations of drug interaction with the oxide surface with the presence of proteins are of profound importance to elucidate the stages of transport and desorption mechanism of immobilized drugs. Usually bovine (BSA), human serum albumin (HSA), egg albumin and gelatin are used to study protein interaction with different solid surfaces. A maximal adsorption of BSA or HSA onto the oxide surface is observed at pH close to their isoelectric point (IEP) when the molecules have the smallest cross-section area on surface [1,2].

Aqueous suspensions of fumed silica, possessing typically multimodal particle size distributions (PSD), are very stable and do not lose the adsorptive ability (tested using proteins) during a long storage period. Modification of the oxide surface or immobilization of polymers on particle swarms can be responsible for alterations in the hydrogen bond network, free energy of interfacial water, surface charge distribution, etc., which can affect the dispersion stability and other characteristics. Study of interaction between fumed silica suspended in water and dissolved polymers with the linear molecular size close or larger than that of primary silica particles is of interest, as such compounds can influence the dispersion stability, structure of particle swarms, rheological and other properties of the silica dispersions in different liquids [1-11]

The aim of this work was to study features of interaction of albumins, gelatin, polyvinylpyrrolidone (PVP) and substituted aromatic drugs with the surface of individual and binary oxides such as fumed silica, alumina, titania, alumina/silica and titania/silica depending on pH and the concentrations of the components.

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## Experimental

Funed silica (Aerosil A-300, 99.5% purity, and the specific surface area ( $S_{BET}$ ) approximately 300 m<sup>2</sup> g<sup>-1</sup>), fumed alumina ( $S=150 \text{ m}^2 \text{ g}^{-1}$ ), fumed titania ( $S=50 \text{ m}^2 \text{ g}^{-1}$ ) and binary fumed silica/titania (ST) at  $C_{TiO2}=9$  (ST<sub>9</sub>), 20 (ST<sub>20</sub>), and 36 (ST<sub>36</sub>) wt% (S=215, 70, and 90 m<sup>2</sup> g<sup>-1</sup>, respectively) and silica/alumina (SA) at  $C_{AI2O3}=1.28$  (SA<sub>1</sub>), 3 (SA<sub>3</sub>), 23 (SA<sub>23</sub>) and 30.6 (SA<sub>31</sub>) wt% and S=220, 180, 170 and 170 m<sup>2</sup> g<sup>-1</sup>, respectively, and fumed Al<sub>2</sub>O<sub>3</sub>/SiO<sub>2</sub>/TiO<sub>2</sub> (AST) ( $\approx 22 \text{ wt.\% Al}_2O_3$ ,  $\approx 28 \text{ wt.\% SiO}_2$ ,  $\approx 50 \text{ wt.\% TiO}_2$ ) (Pilot Plant of Institute of Surface Chemistry, Kalush, Ukraine) were used for preparation of aqueous suspensions. For initial suspensions, oxide samples (weighting 4 g) were stirred with 200 ml of distilled water during 48 h or a week. In addition, an aqueous suspension of fumed silica (6 wt%) treated in a ball mill during 7 h (mechanochemically activated (MCA) suspension) was used. Also, ball-milled suspension was aged during two months. Proteins BSA (Reachem), HSA (Reanal), gelatin (pharmaceutical purity, molecular weighting  $\approx 3.4 \times 10^5$ ), and egg albumin (pharmaceutical purity, molecular weighting  $\approx 4.3 \times 10^4$ ) were used as received.

PVP (pharmaceutical purity) (-CH<sub>2</sub>CHR-)<sub>n</sub>, where R = NC<sub>4</sub>H<sub>6</sub>O,  $n \approx 100$ , molecular weight of 12600±2700, was used as received. PVP was added to the aqueous suspension of silica, which then was treated in a ball mill during a few hours. In another case, PVP was added to the aged aqueous suspension of silica. The ratio between their concentrations  $\gamma = C_{PVP}/C_{SiO2}$ was between 0 and 1. The values  $\gamma \leq 0.1$  correspond to practically irreversible adsorption of PVP on the silica surface [1]. Additionally, PVP was used in the physiological buffer solution (PBS) with NaCl (5.5 g), KCl (0 42 g), CaCl<sub>2</sub> (0.5 g), MgCl<sub>2</sub> (0.005 g), and NaHCO<sub>3</sub> (0.23 g) per litre of the distilled water.

To estimate the amounts of PVP strongly bound to the silica surface at  $\gamma \approx 0.1$ , temperature-programmed desorption (TPD) of PVP was performed in air over the 293-1273 K range using differential thermogravimetry (TPD-DTG) with a Q-1500D (Paulik & Paulik) DTG apparatus. The PVP/silica suspension was centrifugalized at 8000 rpm, then the separated liquid was removed and the residue of PVP/silica was dried at 333 K. A major desorption in the TPD-DTG spectra was observed over the 550-850 K range, where two maxima at ~610 K and ~770 K corresponded to PVP decomposition. The amount of PVP estimated from the TPD-DTG data corresponded to  $\gamma = 0.094$ . After repeated washing and drying of the PVP/silica residue, firstly dried at 333 K, calculation of the amount of PVP based on the TPD-DTG data gave  $\gamma = 0.092$ ; *i.e.*, polymer molecules were not washed off practically from the silica surface. Statistical monolayer coverage corresponds to  $\gamma \approx 0.18-0.19$ .

Propranolol hydrochloride (Anapriline) is a nonselective adrenaline blocking compound (noradrenaline antagonist). Ethmosine is an anti-arhythmical drug, which inhibits the sodium transportation through the sodium channels in the cell membranes. Verapamil hydrochloride is a calcium antagonist blocking the "slow" channels with the cell membrane proteins [3b]. All studied drugs used against the heart diseases were studied in well-dissoluble forms of hydrochlorides (*i.e.*, cation forms) as the neutral forms are poorly dissoluble in water. The wavelength of a maximal UV absorbance is 268 nm for Ethmosine, 278 nm (Verapamil hydrochloride) and 289 nm (Propranolol hydrochloride). The concentration of drugs (pharmaceutical purity) dissolved in distilled water was measured spectrophotometrically using a Specord M-40 (Karl Zeiss, Germany) spectrophotometer.

Aqueous suspension of oxide (10 ml) and 10 ml of drug solution were mixed and the pH value was adjusted by addition of 0.1 M HCl or NaOH solutions to a desired value. Thereupon the suspension was stirred for 1 h, then centrifuged at 5000 rpm for 15 min and the

concentration of drug in separated solution was measured. Steady-state adsorption of drug was calculated from the difference between its initial and final concentrations in the solution. The steady-state adsorption of albumin onto the surface of oxides was investigated by an analogous technique. BSA, egg albumin, and gelatin were used to study their adsorption onto oxides and HSA was used upon simultaneous adsorption with Verapamil onto the silica surface. Measurements of the pH values of solutions and suspensions were performed using an Ionometer EV-74 apparatus before and after adsorption. The pH changes due to adsorption were  $\pm 0.2$  (proteins) and  $\pm 0.05$  (drugs). The ultimate pH values for the equilibrium states (relatively to adsorption and pH values) of the oxide suspension/protein (drug) solution were used in all represented dependencies of adsorption on pH.

Adsorption of egg albumin and gelatin was studied without oxide pretreatment and with no addition of electrolyte buffer solution. Oxide powder (40 mg of oxide per 5 ml of protein solution) was added to protein solution (0.6 wt%) and adsorption was measured after exposure for hour (enough to reach the plateau adsorption value) and the suspension was centrifuged to determine adsorption.

Photon correlation spectroscopy. Electrophoretic investigations were performed using a ZetaPlus (Brookhaven Instruments)  $\zeta$  potential apparatus or a Zetasizer 3000 (Malvern Instruments) apparatus based on the photon correlation spectroscopy (PCS). Deionized distilled water and different amounts of oxide per litre of the water was used for suspension preparation in the ultrasonic bath for  $t_{us} = 1-9$  h (fresh suspensions) or the suspensions were ultrasonicated for 5 min using an ultrasonic disperser (Sonicator Misonix Inc.) (500 W, frequency 22 kHz). The ball-milled aqueous suspensions of pure fumed silica (5-6 wt. %) were studied as obtained (aged suspensions, as the storage periods were 1-3 months). The ballmilled suspensions of PVP/silica were studied as prepared if  $C_{SiO2} < 6$  wt. %, but at  $C_{SiO2} = 6$ wt. %, the suspension was diluted by half before the measurements. The pH values measured by a precision digital pH-meter were adjusted by addition of 0.1 M HCl or NaOH solutions. Particle sizing was carried out using photon correlation spectroscopy (PCS) with a Brookhaven MAS OPTION particle sizer (accuracy of ±1-2% with monodisperse samples, repeatability of ±1-2% with dust free samples). To compute the particle size distributions (PSDs), Def (average hydrodynamic diameter, i.e., the particle diameter plus the electrical double layer or the double shear layer thickness:  $d_{PCS} = d_{real} + \Delta d$  at  $\Delta d \approx 2\kappa^{-1}$ , where  $\kappa$  is the Debye-Huckel parameter) and polydispersity (PD), the Brookhaven ZetaPlus Particle Sizing software (versions 2.17 and 1.31) was utilized, assuming that particles were spherical. To characterize the PSD uniformity, the polydispersity values can be used, and monodisperse particles correspond to PD < 0.02, and PD = 0.02-0.08 represents narrow distributions. The turbidity ( $\tau$ ) of the dispersions was determined spectrometrically at  $\lambda = 540$  nm.

*Rheology.* Rheological investigations of the ball-milled or sonicated suspensions of PVP/silica were performed using a Rheotest 2.1 (VEB MLW Prufgerate-Werk Medingen Sitz Ftreital, Germany) rotary viscometer with a cylinder-cylinder system at the clearance between the cylinders of 0.4 mm. The effective viscosity ( $\eta$ ) was determined at the shear rate  $\beta_s = 1312$  c<sup>-1</sup> at 293 K.

Nitrogen adsorption. Nitrogen (spectranalyzed grade) adsorption-desorption isotherms were recorded at 77.35 K using a Micromeritics ASAP 2010 (V-2.00) adsorption analyser. The specific surface area ( $S_{BET}$ ) was computed using standard BET equation. The pore volume ( $V_p$ ) was estimated from adsorption at  $p/p_0 \approx 0.98-0.99$  converting the volume of adsorbed nitrogen to the volume of liquid one

<sup>1</sup>H NMR. The <sup>1</sup>H NMR spectra were recorded using a high-resolution WP-100 SY

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(Bruker) NMR spectrometer with a bandwidth of 50 kHz. Relative mean errors were  $\pm 10\%$  for signal intensity and  $\pm 1$  K for temperature. The calculation technique of changes in the free energy ( $\Delta G$ ) of interfacial water in the aqueous suspensions of oxides using freezing out of the

bulk water was described in detail elsewhere [3-6,10-14]. The amount of fumed silica in the suspensions was  $\approx 6$  wt. % and  $C_{PVP}$  was changed over the 0.3 - 5 wt. % range. The amounts of unfrozen water  $(C_{ufw})$  in the frozen aqueous suspensions were calculated by comparing the signal intensity (I) for the interfacial liquid water and water adsorbed on silica powder from the gas phase using the calibrating graph  $I = f(C_{ufw})$ .

Thermally stimulated depolarisation (TSD) method. The tablets (diameter 30 mm, thickness ~1 mm) with frozen aqueous suspension of fumed silica or PVP/SiO2 were polarized by the electrostatic field with intensity  $F \sim 2 \times 10^5$  -  $5 \times 10^5$  V/m at 263 K then cooled to 100 K with the field still applied and reheated without the field using the linear heating rate  $\beta$  of 0.05 K/s. The current evolving due to sample depolarisation is recorded by an electrometer having the 10<sup>-15</sup>-10<sup>-5</sup> A range Relative mean errors for measured TSD current are  $\delta_l = \pm 5\%$ ,  $\delta_r = \pm 2$ K for temperature,  $\delta_{\beta} = \pm 5\%$  for the temperature change rate. The TSD spectra parameters have been calculated in accordance with the equation describing dependence of the TSD current on temperature

 $I_m = s\omega_o TP_o exp(-E/kT - \omega_c k/(E\beta) * (T^2 exp(-E/kT) - T_o^2 exp(-E/kT_o)))$ where s is the surface area of the electrodes, P is the frozen polarization, E is the activation energy of depolarisation,  $\tau_o = I/\omega_b$  is a pre-exponential factor, and  $T_o$  is initial temperature [5,15].

Computing. The adsorption free energy distribution was calculated with the Langmuir equation

$$\Theta = \frac{bC}{1+bC} \tag{2}$$

where  $b = e^{-RT}$ ,  $\Delta G$  is the Gibbs free energy change due to adsorption, R is the gas constant, having regard to lateral interactions (z) between PVP assuming z = 2RT (this z value is close to  $\Delta G$  at monolayer coverage), as a kernel in the overall adsorption equation in the form of Fredholm integral equation of the first kind

$$\Theta(T,p) = \int_{x_{min}}^{x_{max}} \Theta_i(T,p,x) f(x) dx$$
(3)

where f(x) is the unknown distribution function of a given parameter x. To calculate the f(x)function, the regularization method can be used, as solution of Eq. (3) is well known ill-posed problem due to a strong influence of noise components on experimental data, which do not allow one to effectively utilize exact inversion formulas or iterative algorithms. Monolayer coverage estimated with Eq. (2) corresponds to  $\gamma = C_{PVP}/C_{SiO2} \approx 0.18-0.19$ . To compute the activation depolarisation energy distribution  $f(E_a)$  on the basis of TSD current measurements, Eq. (1) was used as a kernel of Eq. (3). The regularization procedure was also used to calculate the pore size distributions  $f(R_p)$  for powders prepared from dried aqueous suspensions of silica, PVP/silica and protein/silica utilizing the overall adsorption isotherm equation described in details elsewhere [9].

# **Results and Discussion**

At pH<4.5, adsorption of all the studied drugs onto oxides is less than 30 % of their





Fig. 1. Adsorption of (a) Propranolol hydrochloride, (b) Ethmosine, and (c) Verapamil (in percent of the initial concentration) onto silica,  $SA_{31}$ , and  $ST_{20}$  at the concentration of oxides of 1 wt% and drugs of 0.001 M. (d) Adsorption of Verapamil onto silica in aqueous suspension stirred during a week (star-like symbols) and 48 h (open cycles) and at 0.1 M NaCl (rhomb-like symbols) and mixed adsorption of Verapamil ( $\Delta$ ) and HSA ( $\blacktriangle$ ); (e) adsorption (in  $\mu g$  per m<sup>2</sup> of the surface area) of Propranolol hydrochloride (A), Ethmosine (E), and Verapamil (V) onto the different oxide surfaces at 0.001 M of drug and 1 wt% of oxide.

initial concentration. However, adsorption increases with increasing pH (Fig. 1) due to the basic properties of the drugs (attachment of protons to N atoms as these drugs are used as



dissoluble hydrochlorides) and acidic properties of silica (=SiOH groups) or binary oxides  $(\equiv SiO(H)M\equiv)$ . With increasing pH above IEP<sub>SiO2</sub> ( $\approx 2.2$ ), a magnification of the negative charge of the silica surface occurs and attractive interaction with positively charged drugs increases. For the alumina (for pure alumina IEP $\approx$ 9.8) and titania (IEP<sub>TiO2</sub> $\approx$ 6) phases in binary oxides X/SiO<sub>2</sub>, which possess acidic properties (however, the IEP<sub>X/SiO2</sub> is lower than IEP<sub>SiO2</sub> [1]), the charge distribution is non-uniform and strongly differs from one for silica with changing pH However, zeta potential or electrophoretic mobility of ST and SA in aqueous suspensions depends slightly on the nature and the concentration of the second oxide phase and they are close to that for fumed silica [1,4]. Therefore, the characteristics of binary oxides X/SiO2 depend on the properties of silica and the interface more strongly than of the second X component. Due to the changes in the interface of X/SiO2 for different X, significant variations in the adsorption of drugs onto SA, ST, and silica surfaces are observed. For example, SA can better adsorb drugs than ST (Fig. 1), this can be explained from the higher acidic properties of Brønsted acid sites (B-sites) of silica/alumina (AlO(H)Si) and larger S value in comparison with silica/titania [4,8,12]. Ethmosine does not adsorb practically onto the  $ST_{20}$  surface at pH<4.5 when the titania phase in ST has a positive charge. However, at the same pH values, its adsorption onto silica surface possessing negative surface charge is approximately 20 % and depends slightly on alkalizing solution (Fig. 1b). Ethmosine adsorption onto the SA<sub>31</sub> surface depends on a pH near linearly. The difference in adsorption of Propranolol hydrochloride onto X/SiO<sub>2</sub> is smaller (Fig. 1a), but at pH>5, adsorption onto ST is less than onto SA and silica. At pH<5, the concentration of Verapamil adsorbed onto SA31 is higher than that in the other cases.

If the adsorption is calculated in g per  $m^2$  of the oxide surface area a maximal value is observed for Verapamil adsorbed onto  $ST_{20}$  (having a small *S*), however, the value is close to its adsorption onto  $SA_{31}$  (Fig. 1e). Drug adsorption (in µg per  $m^2$  of the oxide surface area) onto the silica surface is relatively low (Fig. 1e). Consequently, adsorptive ability and efficiency of fumed oxides in aqueous suspension related to adsorption of the studied substituted aromatic drugs depend not only on the oxide nature (*e.g.*, availability of Brønsted or Lewis acid sites, *etc.*) but also their specific surface area (primary particle size distribution).

Upon joint adsorption of HSA and Verapamil onto the silica surface from solution, the influence of protein is relatively small (Fig. 1d), however, the concentration of the drug in this experiment was lower than upon its adsorption without HSA and the curve slope slightly increases. This can be explained by adsorption of the drug onto both the silica surface and albumin, as HSA is the main transportation protein in blood and drug transportation in the human body can occur with its participation. Additionally, maxima of adsorption of Verapamil and HSA are not coincident (Fig. 1d) as the pH(IEP) values of these compounds differ (typically, adsorption of charged particles or molecules strongly increases at a pH near IEP due to disappearance of the electrostatic repulsive interaction). Also, at pH>IEP<sub>SiO2</sub>, protein can effectively interact with the oxide surface through amino groups with attached protons. Also, - COO<sup>-</sup> groups of HAS turned into the bulk solution can strongly interact with protons attached to amino groups of the drug, which is dissolved poorly in the molecular state and used only as hydrochlorides. Consequently, adsorption of protonated drugs or proteins onto the oxide surface depends mainly on the difference between a given pH value of the suspension and pH(IEP) of these compounds (Fig. 1).

The comparison studies of BSA adsorption on the surface of fumed silica, titania, alumina and mixed oxides show the highest adsorption (in mg per m<sup>2</sup>) onto alumina/titania/silica (Fig. 2) having the smallest  $S_{BET} = 38 \text{ m}^2/\text{g}$ . For ST, a maximal adsorption value (in mg/g) increases with decreasing S. For different SA, such an effect is not marked as

erapamil (in on of oxides in aqueous 0.1 *M* NaCl disorption (in the (E), and exide.

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the difference in the S value is smaller than that for different ST and adsorption onto silica or SA is close to that for ST<sub>9</sub> having the specific surface area close to  $S_{S4I}$ . However, the efficiency of adsorption of BSA (in %) from solution is the greatest for silica possessing the largest S value from the studied oxides (Fig. 2). The differences in the adsorptive ability (in both % and mg m<sup>-2</sup>) of ST and SA at a low concentration ( $C_x$ ) of the second phase is small. This effect is caused by relatively uniform distribution of the minor phase (small  $C_x$ ) in the silica matrix and the similarity in the properties of X/SiO<sub>2</sub> and silica, *e.g.*, in  $\zeta$  as a function of pH [1,4].



Fig. 2. Adsorption of BSA in (a) mg per  $m^2$  of the surface or (b) per g of different oxides as a function of pH.

Adsorption of BSA onto oxides at low concentrations of oxides  $(C_{\alpha x})$  in suspension increases exponentially with decreasing  $C_{\alpha x}$  and slightly depends on the nature of oxides (Fig. 3). However, reduction in  $C_{\alpha x}$  is accompanied by a strong decrease in the efficiency of protein adsorption (Fig. 3b). The difference in the adsorption in percent of the initial concentration of BSA is larger than that in mg per g of oxide (Fig. 3) especially for MCA-suspension of fumed silica aged during two months.

Protein adsorption on oxides in the untreated suspensions (Tables 1 and 2) decreases in comparison with adsorption of BSA or HSA after relatively long stirring of the dispersion (Fig. 2). This difference can be caused by a lower

accessible surface area of oxides in untreated suspensions for biopolymers as large oxide agglomerates (>10  $\mu$ m) remain in suspension in contrast to the fumed oxide suspensions after long MCA, stirring or ultrasonic treatment [1]. Relative stability of agglomerates can be linked with increasing apparent density of the powders (Table 1) that correlate with a decrease in protein adsorption. The relative difference in adsorption of gelatin and egg albumin is lower than the relative difference in their molecular weight due to differences in their forms, as egg albumin is a globular protein but gelatin is ellipsoidal with a large axial ratio.

A maximal adsorption of the last proteins is observed for  $SA_{23}$  which has the maximal number of  $\equiv$ Si-O-Al $\equiv$  and  $\equiv$ Si-O(H)-Al $\equiv$  bridges (*i.e.*, Brønsted acid sites, which can strongly interact with basic amino groups of proteins) at the interface. Pure fumed titania gives a relatively great value of adsorption of gelatin that is in agreement with the large adsorption of BSA by this oxide (Fig. 2) and the ratio in adsorption of gelatin and egg albumin by ST<sub>9</sub> and ST<sub>20</sub> (Table 1) is close to that upon adsorption of BSA. Consequently, adsorptive ability of fumed oxides depends on the oxide treatment but the relationship between protein adsorption by oxides of the different origin is kept and depends on the concentration of the second oxide phase and characterize the nature of surface sites (mainly B-sites).



Fig. 3. BSA adsorption in (a) mg per g of different oxides and in (b) percent of the initial concentration in the solution as a function of the concentration of oxide in aqueous suspension.

Table 1
Plateau Adsorption of Egg Albumin and Gelatin anta Indiating the second
without Pretreatment of Aqueous Suspension of Oxides

Ovida	American				
UNIUE	Apparent Density	Egg Albumin		Gelatin	
0.0	<u>g l</u> -1	$mg g^{-1}$	$mg m^{-2}$	$mgg^{-1}$	$m\alpha m^{-2}$
$SIO_2$	38	270	0.90	360	1.20
$Al_2O_3$	147	87	0.59	500	1.20
TiO <sub>2</sub>	86	26	0.38	84	0.56
SA:	28	30	0.72	93	1.86
SA	20	180	1.0	300	1.67
0A23	32	330	1.94	380	2.24
519	33	180	0.84	200	1.25
ST <sub>20</sub>	75	72	1.0	290	1.35
		· / / ·	1.0	130	1.81

An increase in S enhances the adsorption (in mg/g) of both proteins (Table 2); however, adsorption in mg/m<sup>2</sup> goes down with S due to reduction of  $C_{OH}$  (silanols are the main adsorption sites) and a possible increase in the stability of swarms (interacting with proteins) with decreasing primary particle size. Protein adsorption rises with  $C_{OH}$  independently on the protein nature.

PVP having polar bonds N-C=O in the basic side groups enhances pH(IEP) of the isoelectric point (IEP) nearly linearly with  $C_{PVP}$ , as well as the  $\zeta$  potential is reduced with  $C_{PVP}$  at a constant  $C_{SiO2}$  in MCA-silica/PVP suspension (Table 3). The large number of polar N-C=O bonds in PVP molecules is responsible for irreversible adsorption of PVP on silica surface due to hydrogen, polar, and electrostatic bonding. PVP molecules can also hold protons or metal cations, whose interaction with the silica surface negatively charged at pH > pH(IEP<sub>siO2</sub>) enhances the adsorption energy determined mainly by the hydrogen bonds. Additionally,



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interaction between O and N atoms from PVP and  $\equiv$ SiOH groups can cause buildup of the surface charge density on silica particles, which depends on  $C_{PVP}$  and the concentration of electrolytes in the solution [1], but strong adsorption of PVP molecules on silica particles results in increase in pH(IEP) and decrease in  $\zeta$  due to shielding of the oxide surface by polymer molecules.

ra	cterist	ICS OI F	unieu Silieu	Albumin		Gelatin	
	No	$S^{i}$	Сон	Albumin l	$ma m^{-2}$	$m\sigma \sigma^{-1}$	$mg m^{-2}$
		$M^2/g$	µmol m <sup>-</sup>	mg g	1 06	170	1.67
	1	102	4.8	200	1.90	243	1 62
	2	148	3.8		1.04	245	1 49
	3	197	3.6	210	1.06	295	1.04
	4	192	3.5	230	1.19	200	1.01
	5	270	3.2	310	1.14	275	1.09
	6	293	2.9	280	0.95	320	1.02
	7	300	2.9			340	1.15
	0	275	3.0			315	1.14
	0	208	3.0	320	1.03	307	1.0
	9	200	3.0	350	1.14	380	1.23
	10	269	2.6	380	1.03	250	0.68
	11	308	2.0	450	1.17	420	1.09
	12	384	2.0	410	1.05	470	1.21
	13	390	2.0	430	1.05	450	1,10
	14	410	2.4	380	0.92	200	0.48
	15	411	2.4	300			

Table 2	aut and Plateau Adsorption of Albumin and Gelati	n
Characteristics of Fumed	Silicas and Flatcau Flatcau Gelatin	

Table 3	E Duro DVP	Fumed	Silica and F	VP/Silica
Parameters of Aqueou	s Suspensions of Pule I VI	, <u>rumer</u> nH	$D_{ef}$	PD

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Sample	$C_{PVP}$	CSiO2	5	P	um	
- •	wt%	wt%	mv	( )7	>50	
DVD	5	-	1.5	0.27	070	0.440
PVF		5	-15.1	5.21	0.78	0.440
$SiO_2 (A-300)^{*}$	-	5	120	5 43	0.76	0.299
$SiO_2 (A-300)^{b}$	-	2	•12.9	5.93	0.50	0.323
SiO <sub>2</sub> /PVP <sup>a</sup>	0.13	5	-0.0	5.55	0.47	0 217
	0.25	5	-15.6	6.10	0.47	0.270
$S_1O_2/PVP$	0.20	5	-122	6,16	0.37	0.319
SiO <sub>2</sub> /PVP <sup>a</sup>	0.38	2	14.1	6.07	0.34	0.343
SiO <sub>2</sub> /PVP <sup>a</sup>	0.5	5	-14.1	5.70	031	0.180
	25	5	-7.1	5.72	0.51	0.005
$S_1O_2/PVP$	2.0	5	-62	5.75	0.36	0.005
SiO <sub>2</sub> /PVP°	5.0			1	Fresh sus	nension son

<u>SiO<sub>2</sub>/PVP</u><sup>c</sup> 5.0 5 -0.2 5.0 5 suspension sonicated Note. <sup>a</sup>MCA-suspension ball-milled for 5 h and stored for 1 month; <sup>b</sup>fresh suspension sonicated for 9 h; <sup>c</sup>PVP addition to the same MCA-suspension of silica before (5 min) the measurements (non-sonicated samples).

Multimodal PSD is observed for silica dispersions (Figs. 4 and 5) having agglomerates at  $d_{PCS} \approx 1-10 \ \mu\text{m}$  and several types of aggregates, however, the lion's share of the particles has the size  $\approx 60 \ \text{nm}$  (Figs. 5 and 6a). Notice that primary particles of A-300 have the size mainly over 5-15 nm range, i.e.  $D_{min}$  (average diameter for the first peak) corresponds to small

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aggregates. Immobilization of low amounts of PVP changes the PSDs (Figs. 4-7), and the size of large swarms decreases (Table 3,  $D_{ef}$ ), but  $D_{min}$  grows (Fig. 8a). Consequently, PVP molecules disrupts agglomerates and, in part, aggregates (Fig. 4) and the monomodal PSD (PD = 0.005) is observed at  $C_{PVP}$  = 5 wt. % ( $\gamma$  = 1) and nearly monodisperse distribution is observed at lower PVP amounts (Figs. 6c and 6d).  $D_{min}$  growing with  $C_{PVP}$  (Fig. 8a) is maximal at  $C_{PVP} = 0.24$  wt.% ( $\gamma = 0.048$ ), which is lower than  $C_{PVP}$  required for statistical monolayer coverage ( $\gamma \approx 0.18-0.19$ ) or  $C_{PVP}$  for PVP strongly bound ( $\gamma \approx 0.09$ ) to the silica surface. However, average diameter for all paricles  $(D_{ef})$  decreases with  $C_{PVP}$  (Table 3) due to reduction of the size of large swarms.

The suspension turbidity (1) (Fig. 8a, curve 1), as well as  $D_{min}$ , rises due to PVP aggregation with small oxide aggregates with simultaneous decomposition of large agglomerates with increasing  $C_{PIP}$  to 0.4 wt.%; however,  $\tau$  changes slightly with subsequent enhancement of  $C_{PVP}$  to 1.2 wt.%. The sediment volume formed during 10 days depends on  $C_{PVP}$  (Fig. 8b, curve 3). The PVP/SiO<sub>2</sub> suspension is stable at  $C_{PVP} = 0.12-0.24$  wt. % and does not practically exfoliate for 10 days. At the last  $C_{PVP}$  value, a maximal viscosity is observed (Fig. 8b, curve 2) due to suspension structurization on suspension aging Formed structures are disrupted on rheological investigations and decomposition of inter-particle bonds with increasing shear rate  $(\beta_s)$  gives deviation of the curves from those for Newton liquid flow. If the rate of rearrangement of decomposed bonds is less than that of their decomposition that the viscosity tapers off (during the rheological measurements) until equalization of the rates of direct and reverse processes. This equilibrium comes quickly for pure silica suspension, which shows its relatively low thickening, which markedly increases due to addition of PVP. It should be noted that the rheopexy effect is observed at  $C_{PVP} > 0.6$  wt.% ( $\gamma > 0.1$ ) for aged suspension corresponding to an enhancement of the viscosity during the measurements due to a greater rate of bond rearrangement than decomposition [11]. The viscosity dependence on  $C_{PVP}$  at maximal  $\beta_s = 1312 \text{ c}^{-1}$  changes due to aging of the suspension. For suspension aged for 3 months,  $\eta$  has a higher maximum at  $C_{PVP} \approx 0.2$  wt.% and lower values at  $C_{PVP} > 0.4$  wt.% (Fig. 8b, curve 2) than that for freshly prepared suspension (Fig. 8b, curve 1), as dispersion structurization is a long process, which can result in alterations in the structure of both dense adsorbed layer and inter-particles bonds with  $C_{PVP}$ .

Calculations of changes in the free energy due to PVP adsorption (Figs. 10a and 10b) and the corresponding derivative (Fig. 9a, dashed line) using equation

$$\Delta G = -RT\ln K$$

where K is the equilibrium constant, show that the strong adsorption of PVP on silica is observed at the equilibrium concentration  $C_{PVP,e} \le 0.1$  wt.%. The  $f(\Delta G)$  peaks between -9 kJ/mol and -17 kJ/mol (Fig. 9c) are linked with such an interaction at low PVP concentration. It should be noted that observed scatter in  $\Delta G$  (Fig. 9b) and  $f(\Delta G)$  (Fig. 9c) computed using PVP adsorption isotherms recorded under the same conditions is due to complexity of PVP/SiO2 suspensions as fumed silica possesses four-stepwise structural hierarchy [1], which changes on PVP adsorption due to decomposition of large agglomerates and rearrangement of aggregates. The  $\Delta G$  value is close to zero at  $C_{PVP,e} \approx 0.75$  wt.% (Fig. 9) and  $f(\Delta G)$  peaks at  $\Delta G$  $\rightarrow$  0 corresponding to weakly adsorbed PVP (great  $C_{PPP}$ ), which is in agreement with rheological investigations showing diminution in PVP interaction with the silica surface at overall concentration  $C_{PVP} > 0.24$  wt.%.

![](_page_9_Picture_7.jpeg)

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![](_page_9_Picture_9.jpeg)

![](_page_10_Figure_0.jpeg)

Fig. 4. Particle size distribution in (a) the MCA (for 5 h) suspension of silica; (b) freshly prepared silica suspension sonicated for 9 h; (c-f) MCA (for 5 h) suspension of PVP/silica at  $C_{PVP} = 0.13$  (c), 0.25 (d), 0.38 (e) and 0.5 wt. %; PVP addition ( $C_{PVP} = 2.5$  (g) and 5 wt. % (h)) to MCA-suspension of silica previously treated for 5 h;  $C_{SiO2} = 5$  wt. % (a-h) (ZetaPlus apparatus).

![](_page_11_Figure_0.jpeg)

Fig. 5. Particle size distributions in respect to the light scattering (solid lines), particle volume (dashed lines) and particle number (dot-dashed lines) for the aqueous suspensions of fumed silica A-300 sonicated for 5 min at  $C_{S1O2} = 0.25$  (a) and 1 (b, c, d) wt.% and pH = 8.92 (a), 7.03 (b), 8.8 (c), and 5.3 (d) (Zetasizer 3000 apparatus).

![](_page_11_Figure_2.jpeg)

Fig. 6. Particle size distribution (as relative number N of particles with a given diameter) for MCA-suspensions at  $C_{SiO2} = 5$  wt.% (a) pure silica (light histogram) and PVP/SiO<sub>2</sub> at  $C_{PVP} = 0.06$  wt.% (dark histogram); (b)  $C_{PVP} = 0.12$  wt.% (light histogram) and  $C_{PVP} = 0.24$  wt.% (dark histogram) (c)  $C_{PVP} = 0.18$  wt.% (histogram 1) and  $C_{PVP} = 0.3$  wt.% (histogram 2); (d)  $C_{PVP} = 0.48$  wt.% (1), 0.42 wt.% (2), 0.36 wt.% (3) (ZetaPlus apparatus).

![](_page_11_Picture_4.jpeg)

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![](_page_12_Figure_0.jpeg)

Fig. 7. Particle size distributions in respect to the light scattering (solid lines), particle volume (dashed lines) and particle number (dot-dashed lines) for the aqueous suspensions of fumed silica A-300/PVP sonicated for 5 min at  $C_{SiO2} = 0.25$  (a-d) and 1 (e,f) wt.% and  $C_{PVP}/C_{SiO2} = 0.04$ ; pH values are shown in the legends (Zetasizer 3000 apparatus).

![](_page_13_Figure_0.jpeg)

![](_page_13_Figure_1.jpeg)

![](_page_13_Figure_2.jpeg)

**Fig. 8.** (a) Turbidity of PVP/SiO<sub>2</sub> suspension versus  $C_{PVP}$  at constant  $C_{SiO2} =$ 6 wt.% (curve 1) and  $D_{min}$  (average diameter for the first peak in the particle size distribution) as a function of  $C_{PVP}$ (curve 2). Effective viscosity of PVP/SiO<sub>2</sub> suspension versus (b)  $C_{PVP}$  at constant  $C_{SiO2} =$ 6 wt.% for fresh (curve 1) and aged for 3 months (curve 2) dispersions; and sediment volume as a function of  $C_{PVP}$  for suspension aged during 10 days (curve 3); and (c)  $C_{SiO2}$ at  $C_{PVP}/C_{SiO2} = 0.1$ .

**Fig. 9.** (a)  $\Delta G$  on PVP adsorption on silica  $(C_{SiO2} = 6 \text{ wt.\%})$  calculated with Eq. (4) and corresponding derivative  $d(\Delta G)/dC_{PVP}$  (solid symbols); (b)  $\Delta G$  on PVP adsorption on silica  $(C_{SiO2} = 5 \text{ wt.\%})$  calculated with Eq. (4); and (c)  $\Delta G$  distribution computed with Eq. (2) as a kernel of Eq. (3) with the regularization procedure.

Changes in average charges of oxide particles upon agglomeration with PVP molecules can lead to reduction in the zeta potential in comparison with the pure aqueous suspensions of fumed silica (Fig. 10) due to enlargement of the shear layer thickness and shielding of the surface by PVP molecules. The zeta potential of the mixture is a nonlinear function of pH and its changes at pH > 6 are more complicated than those are at pH < 5 (Fig. 10). At pH  $\approx$  10, the  $\zeta$  potential of PVP/silica changes in opposite direction in comparison with that of pure silica. This effect can be explained from trapping cations (H<sup>+</sup> or metal cations) by PVP molecules bound to the silica surface that causes reduction in the average charge of these complex agglomerates. Consequently, adsorption of PVP on the silica surface at pH > pH(IEP) does not inhibit strong interaction of PVP with dissolved cations. Localization of cations between the side rings of PVP can promote a tighter adsorption of PVP onto the silica surface having increased negative charge density with pH > pH(IEP).

![](_page_14_Figure_1.jpeg)

**Fig. 10.** Zeta potential at different  $C_{SO2}$  and  $C_{PVP}$  values for the ball-milled suspensions of PVP/silica. The sample with the asterisk at  $C_{SiO2} = 3$  wt. % was prepared by dilution of 6 wt. % suspension (ZetaPlus apparatus).

Changes in the state of the interface of PVP/silica can correlate with alterations in the adsorbed water layer. For example, a strong interaction between peptides and silica particles causes a reduction in the amounts of unfrozen interfacial water in comparison with a pure protein solution or a pure silica suspension [5].

Two specific regions in the graph of  $\Delta G = G_o$ -G versus the relative amounts of the unfrozen interfacial water ( $C_{ufw}$ ) [14] can be found in Fig. 11 for the pure silica, PVP/silica, and ball-milled PVP/silica suspensions. The first corresponds to a significant decline in the amount of unfrozen water in a relatively narrow range of  $\Delta G$  at T near 273 K, and for another region, the amount of unfrozen water goes down slightly, but  $\Delta G$  changes more strongly. The interfacial water, responsible for the first region, corresponds to a relatively thick layer of water weakly bound to the surface and perturbed due to the long-range components of intermolecular interaction (mainly electrostatic and polar). Another water (strongly bound to the surface) responsible for the second region in the  $\Delta G$  graph is linked to a thin layer adjacent to the surface. Its characteristics are influenced by short-range components of the interaction (such as polar, Lifshitz-van der Waals, and electrostatic) [1] between the surface and adsorbate molecules. The amount of each type of water and maximal values of the corresponding changes in the free energy of the interfacial water layers ( $\Delta G_s$  and  $\Delta G_w$ ) can be estimated by extrapolation of the corresponding dependencies to the x and y axes on the graph  $\Delta G(C_{ufw})$ [14]. The  $\Delta G_{\Sigma}$  (overall reduction in the Gibbs free surface energy),  $\Delta G_s$ ,  $\Delta G_w$ ,  $C^s_{ufw}$ , and  $C^w_{ufw}$ values are given in Table 4 for the ball-milled suspension of pure silica and PVP/silica. The interaction between PVP and silica surface reduces  $\Delta G$  and  $C^{s}_{ufw}$  but  $C^{w}_{ufw}$  increases.

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![](_page_15_Figure_4.jpeg)

**Fig. 11.** The free energy changes of the interfacial water as a function of the amounts of unfrozen water (mg) per g of oxide for month-stored ball-milled suspensions of pure silica ( $C_{SiO2} = 6 \text{ wt. }\%$ ), pure solution of PVP ( $C_{PVP} = 1 \text{ wt. }\%$ ), ball-milled suspension of PVP/silica (storage period of 1 month) at  $C_{SiO2} = 6 \text{ wt. }\%$  and  $C_{PVP} = 0.3 \text{ wt. }\%$ , and silica suspension at  $C_{SiO2} = 6 \text{ wt. }\%$  of pure PVP.

This result is in agreement with reduction in the zeta potential of the PVP/silica

suspension (Fig. 11). An enhancement in  $C^{*}_{ufw}$  can be due to the nonuniform electrostatic field in a relatively thick interfacial layer. The amount of weakly bound water in this layer is larger than that around the pure silica particles (Table 4) as well as the thickness of the interfacial laver perturbed by PVP + dissolved ions and silica particles in comparison with that for the initial silica suspension, as polymer molecules set a significant portion (all PVP molecules are bound to the silica surface) in this layer, however, the sum  $C^{s}_{ufw} + C^{w}_{ufw}$  is the same. It should be noted that even a very long-period storage of the ball-milled suspension of silica has a weak effect on  $\Delta G$  [5], and the difference between the corresponding  $\Delta G_{\Sigma}$  values is only 12 mJ/m<sup>2</sup> that is in agreement with a high adsorptive ability of fumed silica in the aged ball-milled suspensions tested using protein adsorption. 0.3 wt. % of PVP impacts the strongly bound interfacial water close to 1 wt. % of pure PVP (Table 4,  $C_{ufw}$  and  $\Delta G_s$ ). The weakly bound water is perturbed by 0.3 wt. % of PVP in the physiological buffer solution weaker than by 1 wt. % of pure PVP; however, changes in the Gibbs free energy of this layer ( $\Delta G_w$ ) are similar An increase in  $C_{PVP}$  to 5 wt. % leads to growth of the thickness of the unfrozen water layer (Fig. 11),  $C^{s}_{ufw} + C^{w}_{ufw}$  and  $\Delta G_{\Sigma}$  (Table 4). Notice that the sum  $\Delta G_{s} + \Delta G_{w}$  (Table 4) is in agreement with the results based on the PVP adsorption data (Fig. 10). These changes in the interfacial water (i.e., EDL) suggest an increase in the bonding interaction between particles and polymer molecules in the PVP/silica system that gives enhancement in their agglomeration (flocculation) and corresponds to the large values of  $D_{min}$  and  $D_{ef}$  (Figs. 4-8).

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Interfacial Water Parameters for Silica and PVP/Silica Suspensions ( $C_{SiO2} = 6$ wt %)							
System	$\Delta G_s$	$\Delta G_w$	$C^{s}_{ufw}$	C <sup>w</sup> ufw	$\Delta G_{\Sigma}$		
	kJ/mol	kJ/mol	mg/g	mg/g	$mJ/m^2$		
SiO <sub>2</sub> (I)	3.2	1.3	700	700	253		
<sup>a</sup> SiO <sub>2</sub> (I)+0.3 wt.% PVP	2.5	1.0	500	900	186		
SiO <sub>2</sub> (II)	3.0	1.4	730	680	279		
1 wt.% PVP	1.6		300				
SiO <sub>2</sub> (II)+1 wt.% PVP	3.0	0.9	520	1600	220		
SiO <sub>2</sub> (II)+5 wt.% PVP	3.0	1.0	1100	1400	403		

Note.  $S_{BET} \approx 300$  and 190 m<sup>2</sup> g<sup>-1</sup> for SiO<sub>2</sub>(I) and SiO<sub>2</sub>(II), respectively. <sup>a</sup>In physiological buffer.

![](_page_16_Figure_0.jpeg)

**Fig. 12.** Distributions of the activation energy of TSD for pure water (curve 1), water (7 wt.%) adsorbed on silica in the gas phase (2); PVP/SiO<sub>2</sub> at  $C_{SiO2} = 3$  wt.% and  $C_{PVP} = 0.12$  wt.% (3); SiO<sub>2</sub> suspension at  $C_{SiO2} = 7$  wt.% (4); PVP/SiO<sub>2</sub> at  $C_{SiO2} = 7$  wt.% and  $C_{PVP} = 0.28$  wt.% (5); SiO<sub>2</sub> suspension at  $C_{SiO2} = 14$  wt.% (6); PVP/SiO<sub>2</sub> at  $C_{SiO2} = 14$  wt.% and  $C_{PVP} = 0.56$  wt.% (7); and pure PVP solution at  $C_{PVP} = 0.56$  wt.% (8).

TSD study shows changes in the state of water and polymer molecules with increasing  $C_{PVP}$  and  $C_{SiO2}$  (Fig. 12). Silica particles in the concentrated aqueous suspension ( $C_{SiO2} = 7$  wt.% (curve 4) or 14 wt.% (curve 6)) disrupt the hydrogen bond network in a significant portion, as the bulk free water ( $f(E_a)$  peak at 44 kJ/mol in curve 1) is practically absent at such a concentration of silica [1,5]. In the case of PVP/SiO<sub>2</sub> suspension at the same  $C_{SiO2}$  (curves 5 and 7) or at lower  $C_{SiO2}$  (curve 3), the amounts of the bulk water are larger than that for pure silica suspensions; however, the displacement of this peak towards lower energy with  $C_{SiO2}$  is observed (i.e., average number of hydrogen bonds per a molecule tends to diminish). Consequently, shielding of the silica surface by polymer molecules results in appearance of nearly free bulk water disappearing in the PVP/SiO<sub>2</sub> suspensions at large  $C_{SiO2} = 14$  wt.% (curve 7) or in pure silica suspension (curves 4 and 6) or pure PVP solution at  $C_{PVP} = 0.56$  wt.% (curve 8). Additionally, increase in the concentration of silica in PVP/SiO<sub>2</sub> dispersion results in appearance of water molecules with a low number of hydrogen bonds per a molecule corresponding to the  $f(E_a)$  peak at low  $E_a = 10-15$  kJ/mol, which shifts towards lower  $E_a$  with increasing  $C_{SiO2} + C_{PIP}$  (Fig. 12).

![](_page_16_Picture_3.jpeg)

Thus, at low  $C_{PVP}$ , polymer molecules adsorb strongly (large changes in the Gibbs free energy) and the number of free pyrrolidone groups can be relatively low; i.e., adsorbed PVP layer is relatively dense and interaction between water molecules and oxide particles or PVP molecules disturbs a minor portion of the water. At great  $C_{PVP}$ , a significant portion of PVP molecules has free tails (at  $\gamma \approx 0.2$ , the relative number of free C=O groups in PVP adsorbed on silica from solution and then dried at room temperature is approximately 2/3, according to IR spectra), which do not interact with the silica surface but effectively interact with water molecules, and a large portion of water is disturbed. Therefore, the  $\Delta G(C_{ufw})$  graph shifts towards larger  $C_{ufw}$  (Fig. 11) and  $f(E_a)$  shifts towards lower  $E_a$  (Fig. 12) due to reduction in the number of hydrogen bonds per a molecule. These features of the adsorbed PVP layer and reduction of the number of PVP molecules interacting with several oxide particle swarms simultaneously cause diminution in the viscosity with  $C_{PVP} > 0.3$  wt.% (Fig. 8).

Powders prepared by soft drying of the aqueous suspensions of fumed silica with drugs or polymers (e.g., PVP) can be of interest as possible medicines; therefore, such materials were studied using the adsorption and PCS methods. The structural characteristics of the solid residual of the suspension of fumed silica differ significantly from those of the pristine silica powder (Table 5, Fig. 13); for instance, the specific surface area SBET decreases, but the pore volume  $(V_p)$  increases and a marked peak of the pore size distribution  $f(R_p)$  appears at  $R_p > 10$ nm. The  $f(R_p)$  distributions were computed on the basis of the nitrogen adsorption-desorption isotherms using a computation technique described in details elsewhere [9]. Notice that the difference in the pristine powder parameters results in the difference in those for the solid residual of the dried suspensions (Table 5) and one can assume that smaller primary particles (larger  $S_{BET}$ ) in dried powders from the suspensions from more densely parked structures. Addition of 5 wt.% of PVP (in respect to  $C_{SiO2}$  corresponding to  $\Theta_{PVP} \le 0.5$ ) results in increase in  $V_p$  but decrease in  $S_{BET}$  and the  $f(R_p)$  peak slightly shifts toward larger  $R_p$ . Addition of 10 wt.% of PVP (at  $\Theta_{PVP}$  close to 1) leads to strong reduction in  $V_p$  and a small diminution in  $S_{BET}$ that is in agreement with the displacement of the main  $f(R_p)$  peak toward smaller  $R_p$ . In the case of the albumin or gelatin adsorbed on silica (Table 5), changes in the structural characteristics are smaller than those for PVP/silica (Fig. 13).

#### Table 5

Structural Parameters of Pristine Powders and Dried Suspensions of Fumed Silica, Silica/PVP, Silica/Egg Albumin and Silica/Gelatin

Powder	$C_X$ (wt.%)	S <sub>BET</sub>	Vp
	(X=PVP, Albumin)	m²/g	cm <sup>3</sup> /g
<sup>a</sup> A-300	-	342	0.566
<sup>b</sup> A-300	-	182	0.612
<sup>b</sup> A-300/PVP	5	170	0.923
<sup>b</sup> A-300/PVP	10	157	0.383
<sup>a</sup> A-300*	-	322	0.613
<sup>b</sup> A-300*	-	275	1.147
<sup>b</sup> A-300*/Albumin	17.2	175	0.903
<sup>b</sup> A-300*/Albumin	23.0	157	0.868
<sup>b</sup> A-300*/Albumin	27.6	138	0.724
<sup>b</sup> A-300*/Gelatin	21.1	143	0.745
<sup>b</sup> A-300*/Gelatin	31.3	123	0.701

Note. \*Pristine powder, <sup>b</sup>dried powders from solid residual of the suspensions.

water (7  $E_{PP} = 0.12$   $E_{PP} = 0.28$  $and C_{PVP} = 0.28$ 

with increasing  $C_{SiO2} = 7$   $C_{SiO2} = 14$  wt.%  $C_{FVP} = 0.56$   $C_{O2} = 14$  wt.%  $C_{SiO2} = 14$  wt.%  $C_{SiO2} = 0.56$   $C_{O2} = 0.56$  $C_{O2} =$  The PSDs for PVP/silica suspensions (Figs. 4-7) can be multi- or monomodal depending on the component concentrations and pH. However, small aggregates give the main contribution for all the samples due to decomposition of agglomerates and large aggregates of primary silica particles under action of polymer molecules. This result is in agreement with the  $f(R_p)$  distributions for PVP/silica powders (Fig. 13) showing decomposition of silica structures responsible for formation of large mesopores at  $R_p > 15$  nm. Small aggregates give the main contribution not only to the PSDs in respect to the particle number (PSD(N)) but also to the particle volume (PSD(V)).

![](_page_18_Figure_1.jpeg)

Fig. 13. Pore size distributions for pristine fumed silica A-300 and powders prepared by drying aqueous suspensions of silica, PVP/silica, egg albumin/silica, and gelatin/silica.

The peaks of the PSDs in respect to the light scattering (PSD(I)) shift toward larger  $d_{PCS}$  in comparison with PSD(N) and PSD(V). In the case of egg albumin/silica (suspended-dried-suspended), the PSDs depend on the albumin concentration (C<sub>alb</sub>) (Fig. 14) and the distributions become more complex with C<sub>alb</sub>. At a maximal C<sub>alb</sub> value, a large peak of PSD(V) appears at  $d_{PCS} > 1 \ \mu m$  (Fig. 14c) corresponding to agglomerates with the main contribution of protein molecules as PSD(I) has a low intensity in this region (clearly, the scattering capability of protein molecules is lower than that of silica particle swarms). Additionally, small particles at  $d_{PCS} > 30 \ nm$  can correspond to both albumin molecules and silica particles as PSD(I) has low intensity at  $d_{PCS}$  between 30 and 100 nm.

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![](_page_19_Figure_4.jpeg)

Fig. 14. Particle size distributions in respect to the light scattering (solid lines), particle volume (dashed lines) and particle number (dot-dashed lines) for the aqueous suspensions of fumed silica A-300/egg albumin (suspended-dried-suspended) at  $C_{SiO2} = 0.25$  wt.% and  $C_{alb}/C_{SiO2} = 0.172$  (a), 0.23 (b) and 0.276 (c).

For all the protein/silica samples, the PSD(V) peaks lie to the left from PSD(I) that corresponds to the availability of large agglomerates of protein molecules with smaller contribution of silica particles. Therefore one can assume that interaction of egg albumin with silica surface is weaker than intra-molecular interactions in protein molecules (i.e., globular structure of proteins does not decompose) in contrast to PVP molecules, which interact with the silica surfaces stronger than one molecule with another. This feature of protein-silica interactions results in a weak influence of protein molecules on the pore formation on drying of the protein/silica suspensions (Fig. 13), but opposite results is observed for PVP/silica.

#### Conclusion

Maximal adsorption (in mg/m<sup>2</sup>) of BSA was observed in treated aqueous suspension of alumina/titania/silica. For gelatin or egg albumin, adsorption is maximal for non-treated suspension SA23. A maximal adsorption of BSA (in mg/g) and drugs (in percent of the initial concentration) from solution was found for silica possessing the highest S value among all the studied oxides. However, adsorption of drugs in  $\mu g$  per m<sup>2</sup> of the oxide surface area is a maximal for ST20. Adsorption of Verapamil and HSA from mixed solution onto the silica surface shows a weak influence of the protein on the drug adsorption but the corresponding slope increases. For very small concentration of oxides in aqueous suspension, BSA adsorption (in mg/g) increases exponentially with decrease in oxide concentration, however, that is accompanied by decreasing the efficiency of albumin adsorption (in per cent of the initial concentration) from the solution.

Addition of poly(vinyl pyrrolidone) to the aqueous suspension of fumed silica and its mechanochemical activation or sonication enhance the effective diameter of the particles depending on pH. At pH close to pH(IEP), large particles observed can be formed due to agglomeration of silica particles with PVP molecules or oxide particles themselves, as the repulsive electrostatic forces between them are weak in comparison with the attractive polar and Lifshitz-van der Waals forces. By and large PVP irreversible adsorbed on the silica surface at the concentrations less than 10 % of the amount of oxide causes nonlinear changes in the characteristics of the PVP/fumed silica suspensions (versus CPVP), such as viscosity, effective diameter of particles, electrophoretic mobility, dielectric parameters, interfacial water layer state, etc. Intra-molecular interactions in globular protein molecules are stronger than that between these molecules and the silica surfaces in contrast to PVP/silica.

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![](_page_21_Picture_18.jpeg)