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SIMULATION OF THE RHEOLOGICAL BEHAVIOR OF ENTEROSORBENTS IN THE GASTROENTERIC TRACT *IN VITRO*

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The influence of the temperature, pH, and a polymer on the properties and stability of activated coal suspensions serving as nonspecific enterosorbents has been considered. The rheological properties of the small-intestine chyme in vitro and the influence of an enterosorbent on them have been investigated. The advantages of using a water-soluble cellulose polyelectrolyte, as compared to an amylum, for preparation of tableted or grained activated coal are demonstrated.

Introduction. Enterosorbents are effectively used for removal of poisonous, ballast, and potentially dangerous exo- and endogenous substances from an organism. The methods of treatment of diseases with the use of enterosorbents are, in essence, polar to the traditional methods involving the introduction of medicines into an organism [1]. The most abundant and widely used nonspecific enterosorbent is an activated coal that represents a material with a developed porous structure. It is introduced into the gastroenteric tract of a patient by the peroral or intubation method. The peroral method is used in the case of such diseases as exointoxication, uremia, food allergy etc., and the intubation method, involving the introduction of an enterosorbent into the intestine through a probe, is performed by a surgeon in the process of treatment of patients (operated on in connection with an acute ileus of different genesis) with an endointoxication [2].

The medicinal forms of an activated coal taken perorally are tablets or (more rarely) a powder, and activated coal suspensions, stabilized as a rule with amylum, glycerin, liquid petrolatum, or castor oil, are used in the process of nasointestinal intubation. In both cases, an enterosorbent enters the gastroenteric tract in the form of an aqueous suspension and inevitably makes contact with the substances contained in the intestine, i.e., with the chyme. The chyme represents, from the colloid-chemical standpoint, a complex disperse system, in which the disperse phase is formed by food particles of size 10^{-4} m (comminuted in the stomach), bile acid micelles, and other biochemical formations; the dispersive medium contains pancreas secretions, peptides, amino acids, and other substances [3].

Since the therapeutic effect of an activated coal depends on the stability and fluidity of the suspensions formed by it, we investigated the properties of activated coal suspensions in the gastroenteric tract *in vitro* by simulation of the corresponding conditions.

Experimental. We used a fibered coal based on a fine-grained activated carbon (FGAC) allowed for medical use (Provisional Pharmacotherapy Regulations of the Republic of Belarus 0289–2000). The medicinal FGAC was prepared in the form of tablets and granules. The binder was an amylum used for this purpose in the food industry and a new water-soluble cellulose derivative (WSCD) synthesized at the Scientific-Research Institute of Physicochemical Problems of the Belarusian State University. The polymer substances contained in the coal accounted for 0.08% of its mass. Coal suspensions were prepared in different media by mixing performed with equal rates and for equal times. The concentration of the disperse phase was 5–35 wt. %. As the dispersive medium, we used distilled water, a 0.1-n sodium hydroxide, and model systems corresponding to the stomach medium free of pepsin and the intestine medium free of pancreatin [4]. The small-intestine chyme was taken intraoperatively from patients with peritonitis and enteral insufficiency syndrome.*

*Chyme samples were given by Yu. N. Sokolov.

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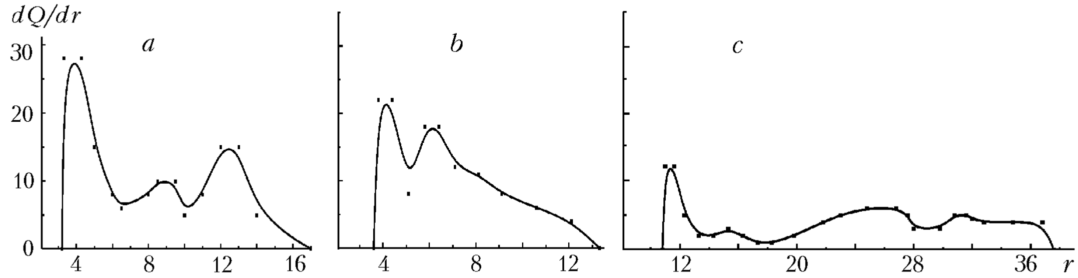


Fig. 1. Differential curves of the particle-size distributions of the nonmodified-coal suspensions in the aqueous (a), base (b), and acid (c) media at 20°C.

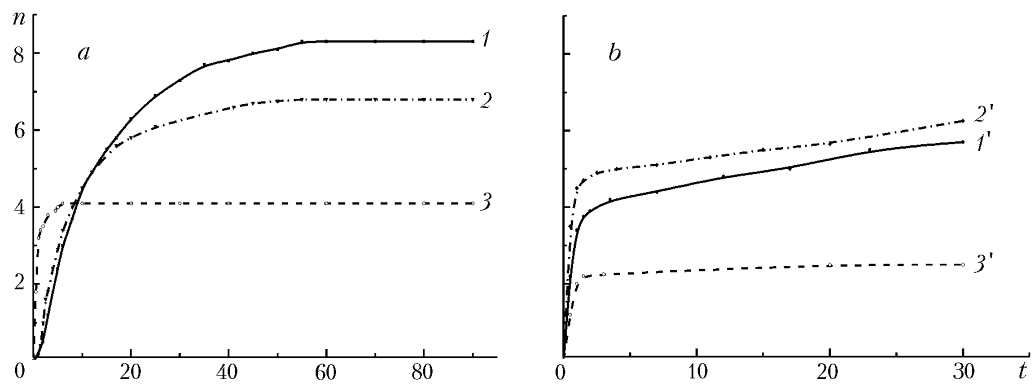


Fig. 2. Sedimentation curves of the nonmodified-coal suspensions at 20 (a) and 37°C (b) in aqueous (curves 1 and 1′), base (curves 2 and 2′), and acid (curves 3 and 3′) media.

Sedimentation analysis of 5% suspensions in various media was performed on a Figurovskii sedimentometer [5]. The mass of the fine-grained fraction was determined gravimetrically [6]. For determining the volume of the sedimentation residues, the 5% suspensions were held in narrow test tubes ($d = 1.4 \cdot 10^{-2}$ m) with divisions for 30 days. The suspension volume was $25 \cdot 10^{-4}$ m^3 and the suspension-column height was $25 \cdot 10^{-2}$ m. Rheological investigations were performed on a Rheotest-2 rheoviscosimeter with a working cylinder–cylinder unit in the range of shear stresses 1–200 Pa at 20 and 37°C.

Results and Their Discussion. It is known [7, 8] that the aggregation stability of suspensions substantially influences the character of their flow. Therefore, before the rheological investigations, we determined the influence of the pH level and the temperature of a medium and the modification of the activated-coal particle surface by water-soluble polymers on the aggregation stability and the rate of sedimentation of suspensions formed by the coal. It follows from Fig. 1 that the size distribution of coal particles in an acid medium is wider as compared with that in aqueous or base media. This points to the fact that the aggregation processes intensify in an acid medium. A consequence of these processes is an increase in the rate of precipitate accumulation, which leads to a decrease in the slope of the sedimentation curve (Fig. 2, curves 3 and 3′), and a decrease in the mass of precipitated particles to a level (remaining unchanged with time) lower than that in aqueous and base media, at which a plateau appears on the sedimentation curve. The decrease in the mass of the particles completely precipitated in the acid medium can be due to an intensive aggregation of particles. It was observed with the naked eye as the formation of flakes and resulted in a large part of the aggregates being precipitated for a time shorter than 30 sec, i.e., before the beginning of the sedimentation analysis. The change in the slope of the sedimentation curves with increase in the temperature (Fig. 2) indicates that the temperature exerts a destabilizing action, as a result of which the rate of sedimentation increases. The temperature influence manifests itself most pronouncedly in aqueous and base media.

Comparison of the differential particle-size distributions in suspensions modified by the polymers studied (Fig. 3) shows that the modification of the coal-particle surface leads, in the case of the amylum, to an additional aggregation of particles, while in the case of the WSCD it aids in the peptization of coal aggregates and the formation of a

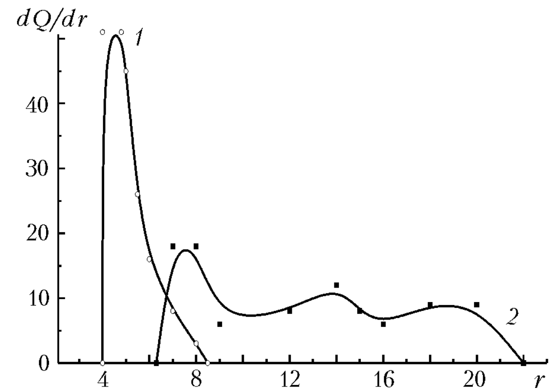


Fig. 3. Differential curves of the particle-size distributions of the coal suspensions modified with the WSCD (1) and the amylum (2) at 20°C in the aqueous medium.

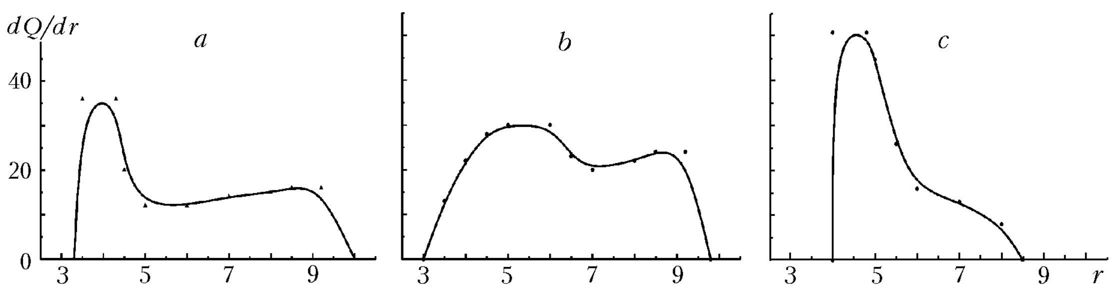
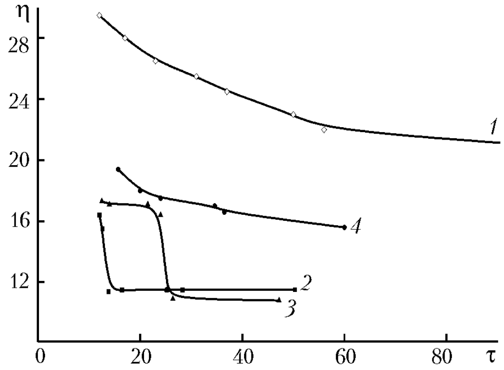


Fig. 4. Differential curves of the particle-size distributions of the coal suspensions modified with the WSCD in the aqueous medium (a), stomach (b), and intestine (c) at 37°C.

fine-grained fraction. The content of this fraction, including particles that did not sedimentate over 30 days or more, was 8 wt. %. This sedimentation stability is characteristic of particles with sizes of less than 1 μm. Such particles were absent in the nonmodified-coal suspension, and in the presence of the amylum their content exceeded 1%. The volumes of the sedimentation precipitates of the 5% suspensions also point to their different stability. The sedimentation volumes of the initial-coal suspension and the suspensions modified by the WSCD and the amylum were respectively 0.80, 0.54, and 1.6 ml/g. Note that the existence of a sedimentation precipitate, even one not large in volume, in a highly stable suspension of the coal with the WSCD can be explained by the fact that the WSCD, providing an aggregation stability of small particles, does not prevent the sedimentation of large particles ($r > 10$ μm) that can entrain smaller particles in the process of precipitation. The suspensions with the WSCD are distinguished by the fact that their aggregation stability depends more weakely on the pH level of the medium, as compared to the nonmodified-coal suspensions (see, respectively, Fig. 4 and Fig. 1).

It was established that, by analogy with the coal, the chyme in an aqueous medium *in vitro* forms a sedimentationally unstable suspension. The time of its decomposition at a chyme:water ratio of 75:25 (vol. %) is 3 h at 20°C. The addition of a nonmodified powderlike coal to such a chyme diluted with water leads to a rapid decomposition of the system and the separation of the coal. At the same time, a coal modified with the WSCD (such a coal in tablet form was introduced into the same chyme–water system) formed a suspension that was not decomposed for 5 h, i.e., for the time exceeding the time of existence of the chyme–water suspension.

It follows from the data presented in Fig. 5 that, under dynamic conditions, the chyme behaves as a weakly structurized system. Its viscosity decreases with increase in the shear stress fairly uniformly (curve 1). The solution of the chyme with water to the ratio 1:3 leads to the formation of a suspension whose viscosity sharply decreases with a small increase in the shear stress (curve 2). The introduction of one tablet of the coal with the WSCD (0.0037 g/ml of the chyme) into this system practically does not change its viscosity. In this case, on the rheogram there appears a portion corresponding to the situation where the structure reconstructs at small shear stresses after the decomposition.



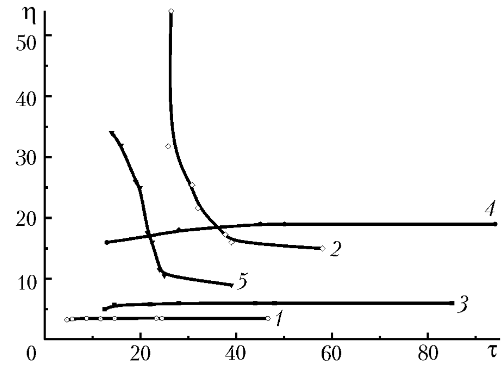


Fig. 5. Rheological curves of the chyme (a) and the chyme–water (75:25) system without addition (2) and with addition of a tablet of the coal with the WSCD (3) and a powderlike coal (4) at 37°C.

Fig. 6. Rheological curves of the 15 and 25% aqueous suspensions of the initial coal (1, 2) and the coal modified with the WSCD (3, 4) respectively and of the 15% suspension of the coal modified with the amylum.

Initially the viscosity of this structure does not change, and then it decreases to a value that does not further change, which points to the complete rupture of the bonds between the particles (curve 3). At the same time, the introduction of the nonmodified coal leads to an increase in the heterogeneity and viscosity of the system (curve 4).

Then we investigated the influence of polymers on the rheological properties of activated-coal suspensions free of chyme. It has been established that a flow of diluted suspensions is close to the Newton flow. An increase in the concentration of the disperse phase changes the character of the flow. Practically for all suspensions there exists a disperse-phase concentration, at which the structure formation begins in the system. It is equal to 21 wt. % for the nonmodified coal. At this concentration of the disperse phase, on the rheogram there appears a portion of sharp decrease in the viscosity, which points to a decomposition of the structure, and a constant-viscosity portion corresponding to a flow with a critically disrupted structure. When the deformation is performed by increasing and decreasing the shear stress, the experimental points are practically coincident, which allows the conclusion that the structure is coagulative-thixotropic in character.

For suspensions of the coal modified with the amylum, the concentration at which a structure was formed in the system was lower and equal to 15 wt. %. Under these conditions, the behavior of the suspensions of the coal modified with the WSCD seems to be entirely unusual. In them, we detected a practically Newton flow at a concentration as high as 35% that is maximum for the given experiment since the suspensions with higher concentrations do not possess fluidity under static conditions. The very small increase in the viscosity with increase in the shear stress may be due to the polyelectrolite nature of the WSCD. It is conceivable that the approach of particles, as a result of a shear, within distances providing the overlapping of absorption-solvate polymer layers creates the prerequisities for the appearance of repulsive forces and realization of "constrained" conditions of flow characteristic of dilatant systems. It is seem from Fig. 6 that the rheological curves of the suspensions of the initial coal and the coal modified with the amylums or the WSCD differ at disperse-phase concentrations of 15 and 25% respectively.

Conclusions. The results of our rheological investigations and the data obtained on the stability of coal suspensions allow one to select a polymer for the use as a binder in a medicinal enterosorbent prepared in the form of tablets or granules. It is apparent that the amylum should not be used for this purpose since this substance, even if it is present in a small amount in a suspension, gives rise to an aggregation of particles that is favorable for the structure formation at high concentrations of the disperse phase, which hampers the taking of large doses of the enterosorbent. At the same time, the WSCD transforms a coal suspension into a system that, under the dynamic conditions, practically has no a structure. The higher fluidity of the suspensions with the WSCD makes their movement in the intestine and the further evacuation of them easier, which is especially important when it is necessary to take a large amount of the preparation, e.g., by oncologic patients after chemotherapy. The high fluidity and aggregation stability of suspensions with the WSCD are also important for the intubation introduction of enterosorbents, since amylum suspensions block a probe, are difficult to evacuate from the intestine and, unlike the WSCD suspensions, do not provide the reclamation of the intestine motility, which gives no way of decreasing the time of treatment of young patients and preventing the fatal outcome of elderly patients. The peculiar behavior of the coal suspensions in the presence of the WSCD can be explained by the hydrophilization of the hydrophobic surface of the coal particles and, consequently, by the increase in the affinity of the interfacial layer with the dispersive medium. It should be also noted that the highly hydrophilic polyelectrolite WSCD provides not only high stability and fluidity of suspensions, but also a superrapid dispergation of the coal in the liquid phase and its high sorptive activity as compared to that of the nonmodified coal.

NOTATION

d, diameter, m; dQ/dr, probability density of the masses of different-radius particles; n, number of microscope divisions equivalent to the mass of the precipitated particles; Q, fraction of precipitated particles, %; r, radius of particles, μm; t, time, min; η, viscosity, Pa·sec; τ, shear stress, Pa.

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