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RESEARCH PAPER

Formulation of Activated Charcoal for Per Os Administration to Addicted Subjects

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ABSTRACT

The objective of this work was to develop a galenic form of activated charcoal appropriate for the needs of clinical toxicology. To preserve the adsorption capacity of charcoal, we developed an extemporaneous preparation of activated charcoal intended for clinical toxicology. To improve the wettability of activated charcoal, we used densification by wet granulation. The presence of a viscosity agent is necessary to ensure the homogeneity of the suspension and its adhesiveness on gastric mucous membrane. Five formulations with different viscosity agents were prepared, and their adsorption capacity, wettability, viscosity, and adhesiveness were studied.
Key Words: *Activated charcoal; Adhesiveness; Adsorption capacity; Formulation; Viscosity; Wettability.*

INTRODUCTION

In its monograph on activated charcoal, the third edition of the European Pharmacopeia defines it as a black powder that is light, odorless, free from granular particles, and practically insoluble in all usual solvents (1). Obtained through pyrolysis of organic substrates, charcoal is activated by different processes that bring it to high temperatures; pores formed in this way increase the surface and adsorbing power.

The therapeutic property of activated charcoal is essentially the adsorption of surface toxic substances. This property explains its use in the treatment of food poisoning or medicine overdoses (2–5).

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Table 1

Adsorption Percentage of Suspensions of Activated Charcoal over a Period of Time

	Adsorbing Power (%)	
Preparations	Day 1	3 Months
Nonformulated activated charcoal	62.74	62.62
Ready-for-use suspension	53.2	47.8
Dry suspension	53.06	53.13

The aim of this work was the development of a galenic form of activated charcoal appropriate for the needs of clinical toxicology.

CHOICE OF THE GALENIC DOSAGE FORM

Activated charcoal exists on the pharmaceutical market in several galenic dosage forms (tablets, sugar-coated tablets, granules). All these make the ingestion of activated charcoal easier, but their major drawback is a decrease in effectiveness due to compaction operations and the necessary addition of excipients (6–8). The lack of a formulation for activated charcoal suitable for hospital use has often limited its utility in intensive care units.

To preserve the adsorption capacity of charcoal, we developed an extemporaneous preparation of activated charcoal intended for clinical toxicology. First, we studied the adsorption capacity of two suspensions of activated charcoal over a certain period of time, a ready-for-use suspension and a dry suspension to be reconstituted at the time of use. Measurements of the adsorbing power of the preparations made on the first day of manufacture and 3 months later are given in Table 1.

It appears from these results that the two preparations possessed the same effectiveness on the first day of manufacturing. This effectiveness decreased with time in the ready-for-use suspension of activated charcoal.

The extemporaneous preparation will have to comply with several requirements:

It must contain a sufficient dose of activated charcoal (20%) to ensure correct effectiveness.
It must be immediately available.
It must be easy to use by hospital staff.

A dry suspension of activated charcoal that complies with these criteria has to possess certain inherent qualities:

The dry suspension must be wettable and have good dispersibility, ensuring homogeneity of the preparation after reconstitution.
The suspension, once reconstituted, must have (*a*) rheological behavior suitable for use; (*b*) a certain adhesiveness, enabling it to remain in contact with poisons on the digestive mucosa; (*c*) an adsorption capacity at the moment of use comparable with that of charcoal alone.

CHOICE OF ACTIVATED CHARCOAL

Preliminary work made it possible to choose the best charcoal for formulation from among several varieties of activated charcoal. The method used is the one recommended by the 3rd edition of the European Pharmacopoeia on how to evaluate adsorption capacity using phenazone (molecular weight 188.2) as the molecule to be adsorbed.

The quantity of the molecule to be adsorbed is determined by volumetric dosage with a titrant of potassium bromate. This quantity is expressed in the ''Phenazone index'' (%) and must be greater than 40%.

Because of their hygroscopic nature, charcoals were dried in a drying oven at 150°C for 5 hr before each assay. A comparison of adsorption capacity results enabled us to retain the Norit A Supra (Norit Farma, Amersfoort, Holland) (9) as a charcoal suitable for formulation.

Table 2

Characteristics of the Charcoal Chosen

Activated Charcoal	Source	Specific Surface (BET)	Median Diameter Microscope	Phenazone Index (%)
Norit A Supra	Vegetable	2000 m^2/g	7.5 μm	62.74

Table 2 shows the characteristics of the charcoal chosen.

IMPROVEMENT IN THE DISPERSIBILITY OF CHARCOAL PARTICLES

Activated charcoal is a very hydrophobic substance. To improve the wettability of its particles and in this way to ensure the homogeneity of the suspension in water, we used densification by the classic technique of wet granulation. To preserve the adsorption capacity of activated charcoal, we deliberately chose as binding agents two very hydrophilic excipients that can be easily wetted in solution and that have adsorbing properties. The selected excipients were Aerosil 200, a colloidal silica dioxide (Degussa AG GAC, Frankfurt, Germany), and Kollidon 30, a polyvinylpyrrolidone (PVP) (BASF, Ludwigshafen, Germany).

Granules were obtained with Aerosil 200 at a concentration of 0.5% and with Kollidon 30 at a concentration of 2%. Assays of wettabilitty and determination of adsorption capacity were then carried out on 1 kg of the granules obtained.

Measurement of Wettability

The assays were carried out according to Bever's technique as demonstrated by Nogami et al. (10); the technique is a measurement of the kinetics of water absorption through a powder bed. For the assays, 1 g of granules is placed on the sintered glass of an Allin tube in contact with water. The tube is connected to a horizontal graduated pipette on the level of the sintered glass. The movement of the meniscus in the graduated tube corresponds to the absorption of water by the powder bed. This movement takes place as a function of time and makes it possible to plot the kinetics of water absorption.

Figure 1 shows the curves that correspond to the wettability of activated charcoal granules. These assays showed a marked improvement in the wettability of activated charcoal particles after wet granulation. Penetration of water in nongranulated charcoal was very slow.

Adsorbing Power

The adsorbing power of granules was studied by the previously described method 1 day after manufacturing and is presented in Table 3. The granulation and excipient addition had no influence on the effectiveness of Norit A Supra. The adsorption percentages of the granules obtained are very near to those of nongranulated charcoal.

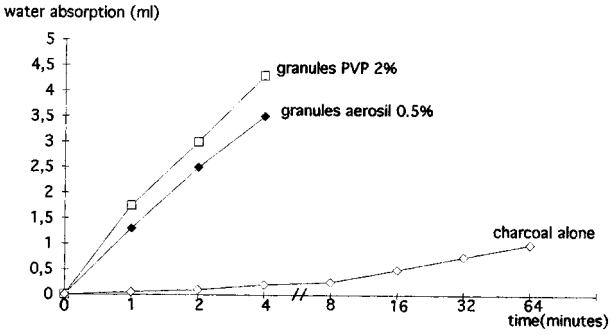

Figure 1. Water absorption kinetics of different granules of activated charcoal.

CHOICE OF THE VISCOSITY AGENT

The presence of a viscosity agent is necessary to ensure the homogeneity of the suspension. The aim is the formulation of an extemporaneous preparation, so the choice of the thickener agent depends on two essential parameters: (*a*) a homogeneous suspension is to be obtained at ambient temperature by simple dispersion of the viscosity agent; (*b*) rheological behavior is required in relation to its clinical use.

Preliminary assays to determine the viscosity agent to be used were carried out with different polymers: Aerosil 200, Avicel Rc 581, tragacanth gum, xanthan gum, and sodium alginate.

With Avicel Rc 581, xanthan gum, and sodium alginate, the addition of water followed by low agitation did not result in a homogeneous preparation. Tragacanth gum (Tragathan ORX 10259 is highly dispersible [Iranex-SA, Neuilly sur Seine, France]) at a concentration of 0.1% and Aerosil 200 at a concentration of 1% along with 20% activated charcoal offer better dispersibility and good flowability.

Table 3

Influence of Granulation on Adsorption Capacity

Charcoal Granules	Adsorbing Power (%)
Granules with Kollidon 30 (2%)	59.8
Granules with Aerosil 200 (0.5%)	60.2
Nonformulated charcoal	62.74

FORMULATIONS AND MANUFACTURING METHOD

Five preparations based on activated charcoal were manufactured using the wet granulation technique and by adding a viscosity agent. Viscosity agents were incorporated into the preparation in the external phase after granulation. The lack of gelling agents in the first two formulations had the advantage of underlining the influence of these excipients on viscosity and on the adsorption capacity of the different preparations.

The following five preparations were obtained by mixing each formulation with a sufficient quantity of demineralized water and 20 g Norit A Supra: formulation 1 had 2 g Kollidon 30; formulation 2 had 0.5 g Aerosil 200; formulation 3 had 2 g Kollidon 30 and 1 g Aerosil 200; formulation 4 had 0.5 g Aerosil 200 and 0.1 g tragacanth gum; formulation 5 had 2 g Kollidon 30 and 0.1 g tragacanth gum.

CONTROL OF THE FINISHED PRODUCT

Residual Humidity

Determination of the residual humidity of the preparations was carried out by placing 10 g of granules on Sauter infrared thermoscales (Mettler, Viroflay, France) at 100°C–105°C for 30 min. The residual humidity ranged from 1.6% to 2.1%. It varied very little from one preparation to another.

Determination of the Adsorption Capacity of Preparations

Evaluation of the effectiveness of the preparations was by the same method as for adsorbing power. The adsorption percentages of Phenazone (%)in Table 4 are those obtained on the first day of manufacturing and 3 months later. The adsorption percentages of different preparations did not vary in the presence of viscosity agents or over a period of time.

Table 4

Adsorption Percentage of Different Preparations of Activated Charcoal as a Function of Time

	Adsorbing Power (%)	
Preparations	Day 1	3 Months
1	59.8	59.9
2	60.02	60.3
3	59.3	59.33
4	58.2	58.2
5	58.1	58.01
Activated charcoal	62.74	

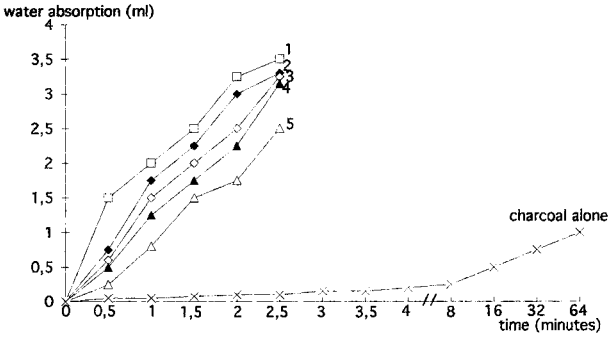

Figure 2. Kinetics of water adsorption for different formulations.

Wettability of Preparations

Wettability was measured using Bever's water absorption method, described above. Results are illustrated in Fig. 2. It appears on examination of Fig. 2 that activated charcoal preparations absorbed water more rapidly than activated charcoal alone. Granulation operations and the presence of hydrophilic excipients improved the wettability of activated charcoal particles.

Rheological Behavior of These Preparations

Rheological behavior was studied with a rotational viscosimeter, Rheomat 30 (Sté. Jean Lamy, Caluire, France). The measuring system used is the double ''entrefer.'' The assays were made on 20-ml samples 30 min

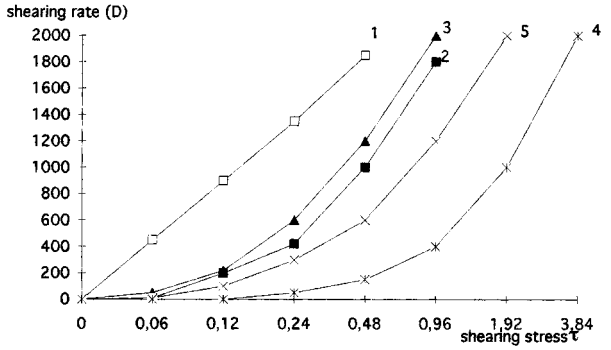

Figure 3. Rheological behavior of the different formulations.

Table 5

Influence of pH on the Viscosity of Different Preparations at a Shearing Rate of 43.95 sec^{-1}

	Viscosities in Pa.s for Different pH at 37°C			
Preparations	pH 1.35	pH 3.5	pH 5.5	pH 7.5
1	0.0054	0.0058	0.0059	0.0054
2	0.2494	0.4196	0.5265	0.1480
3	0.063	0.0336	0.0633	0.065
4	0.2204	0.1577	0.3440	0.2294
5	0.0888	0.0546	0.0660	0.0546

after reconstitution of the preparations. The measuring recipient containing the preparation to be studied was introduced into the water bath at 20°C and then allowed to stand for 10 min so that its temperature stabilized. Another study was made at the same time to illustrate the influence of pH and temperature on the different preparations.

With these samples, pH of 1.35, 3.5, 5.5, and 7.5 were obtained; evaluations were made at 37°C. The registering of rheograms was made by increasing and decreasing rotational speed. The obtained rheograms (Fig. 3) reveal the pseudoplastic behavior of the preparations, except for formulation 1, which showed Newtonian behavior.

To study viscosity as a function of the pH of different preparations, we chose a point on the rheogram that corresponded to a shearing rate of 43.95 sec^{-1}. Table 5 shows the influence of pH on the viscosity of different preparations at a shearing rate of 43.95 sec^{-1}. Variations of viscosity with pH were low.

Adhesiveness of the Preparations

Adhesiveness of the preparations was estimated by measuring the wrenching force of a platinum strip suspended from a balance according to Wilhelmy's technique (11,12). The wrenching system used was initially intended to evaluate surface tension. In the first stage, assays were made with initial preparations and then at different pH and at 37°C.

We used two measurement apparatus based on the same principle: a Wilhelmy balance with a graduated scale corresponding to different wrenching forces, with a platinum strip connected to the balance and a measuring buckle; and a dynamometer in which the strip was replaced by a platinum ring.

Table 6 shows the adhesiveness of preparations in relation to the pH studied; it is expressed as the wrenching force on the strip (mN) after its introduction in the sample to be measured. Values of wrenching force obtained were nearly the same from one suspension to another, and the influence of pH on adhesiveness of these preparations was not marked. These results are comparable to those obtained during studies of viscosity in relation to pH.

CONCLUSION

Using a classical technique, this work enabled the preparation of dry suspensions of activated charcoal that

Table 6

Influence of pH on Adhesiveness of Different Preparations of Activated Charcoal

	Adhesiveness Expressed as the Wrenching Force (mN) in Relation to pH			
Preparations	pH 1.35	pH 3.5	pH 5.5	pH 7.5
1	30.0	27.3	28.1	27.8
2	33.2	34.0	34.0	31.0
3	32.0	31.0	31.0	30.0
4	30.4	29.7	29.04	30.3
5	30.0	29.8	30.0	30.5

were easy to reconstitute and that had an adsorption capacity that did not vary over a period of time. A clinical study of these preparations in the intensive care unit of Calmette Hospital (Lille, France) is in progress as part of the two-step study. The first step was an estimation of the use conditions of the suspensions. The second is estimation of the effectiveness of the preparations on toxic products. The first results obtained are very satisfactory. They will enable us to chose the best preparation of activated charcoal.

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