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European Journal of Pharmaceutics and Biopharmaceutics 63 (2006) 356–359
European Journal of Pharmaceutics and Biopharmaceutics
www.elsevier.com/locate/ejpb

Note

Investigation of the glidant properties of compacted colloidal silicon dioxide by angle of repose and X-ray photoelectron spectroscopy

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Received 21 April 2005; accepted in revised form 16 November 2005
Available online 3 March 2006

Abstract

The optimal flow-enhancing effect of a new compacted, hydrophilic colloidal silicon dioxide (AEROSIL® 200 VV Pharma) on microcrystalline cellulose (Avicel® PH 101) and pregelatinized starch (Starch 1500®) was found to be 0.25% under gentle and 0.125% under strong mixing conditions, as measured by the angle of repose. The effect could be explained by X-ray photoelectron spectroscopy (XPS) investigations. The Si 2p signals of the silicon dioxide indicated that the coverage of the excipient surface with AEROSIL® was greater for all mixtures produced under strong mixing conditions and corresponded to a higher degree of de-agglomeration of the AEROSIL® aggregates. The more extensive surface coverage of Avicel® PH 101 as compared to Starch 1500 could be explained by the particle morphology on the one hand and by the XPS C 1s signals on the other. Due to the different conformation of the two excipients, Avicel® PH 101 offers a higher density of hydroxyl groups on its surface which are available for hydrogen bonding with the surface hydroxyl groups of hydrophilic colloidal silicon dioxide.

Keywords: Colloidal silicon dioxide; Angle of repose; X-ray photoelectron spectroscopy; Mixing process; Excipient

1. Introduction

Colloidal silicon dioxide (trade name AEROSIL®) is widely used as a glidant in the manufacture of powders, capsules, and tablets. AEROSIL® 200 VV Pharma is a new compacted hydrophilic colloidal silicon dioxide, designed for the pharmaceutical industry having improved handling compared to conventional AEROSIL® types. In a previous paper, its flow-enhancement properties were compared to those of a non-compacted hydrophilic standard type and a compacted hydrophobic colloidal silicon dioxide. Flowability studies using the angle of repose and a conveyor belt method have shown that the new compacted types are efficient glidants and even superior to the traditional non-compacted product [1]. The mechanism of the glidant action was later investigated on the particle level by secondary electron and atomic force microscopy [2].

X-ray photoelectron spectroscopy (XPS), also known as electron spectroscopy for chemical analysis (ESCA), is a surface analysis technique used to obtain chemical information about the surfaces of solid materials. The method utilizes an X-ray beam to excite a solid sample resulting in the emission of photoelectrons. An energy analysis of these photoelectrons provides both elemental and chemical bonding information about the material's surface. The applications of XPS in the field of materials science and engineering are numerous. Analysis of thin contamination of films, measurement of elemental composition of insulating materials, and identification of the chemical state are just some examples. However, only few investigations were reported in the pharmaceutical field to date.

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doi:10.1016/j.ejpb.2005.11.005

The aim of the present investigation was to use X-ray photoelectron spectroscopy to characterize the surface coverage of two common tablet filler/binders by colloidal silicon dioxide as well as to determine the influence of the mixing conditions.

2. Materials and methods

2.1. Materials

AEROSIL® 200 VV Pharma, a hydrophilic and compacted colloidal silicon dioxide, was used as received from Degussa AG (Düsseldorf, Germany). Microcrystalline cellulose (Avicel® PH 101, FMC Biopolymer, Cork, Ireland), pregelatinized starch (Starch 1500®, Colorcon, Kent, England), and starch (extra white maize starch, Roquette GmbH, Frankfurt, Germany) were used as supplied.

2.2. Preparation of the mixtures

The concentrations of AEROSIL® 200 VV Pharma were set at 0.0625%, 0.125%, 0.25%, 0.5%, and 1% by weight based on the total formulation. AEROSIL® 200 VV Pharma was pre-screened through a 315 μm sieve onto a portion of the filler/binder. The remaining portion of the filler/binder was added and initially mixed by hand. The mixture was sieved through an 800 μm sieve before and after 10 min of mixing in a free-fall mixer (Turbula T2C, W.A. Bachofen, Basel, Switzerland) using a 2 L vessel, a maximum filling degree of 75%, and a rotational speed of 42 rpm. The resulting mixture was named M1. A portion of the batch of mixture M1 was additionally mixed for 20 min in a high-speed mixer based on the plowshare principle (SW 1/S, Erweka GmbH, Heusenstamm, Germany) to produce mixture M2.

2.3. Characterization of the mixtures

2.3.1. Angle of repose

The angle of repose of the mixtures was measured using a sieve-cone-method according to DIN ISO 4324 [3]. The mean, the standard deviation, and the 95% confidence interval of six samples were calculated.

2.3.2. Specific surface area

The specific surface area of the mixtures was determined using nitrogen gas adsorption at a temperature of 77 K based on the method of Brunauer, Emmett, and Teller (BET) according to the European Pharmacopoeia [4]. A quantity of test powder having a surface area of at least 1 m^2 was accurately weighed (model AT 261 Delta range, Mettler Toledo GmbH, Gießen, Germany). Samples of Avicel® PH 101 and Starch 1500® were degassed in vacuo for 3 h at 90 °C and for 1 h at 90 °C, respectively. The analysis was then performed using the volumetric method (model SA 3100, Coulter, Beckmann Coulter GmbH, Krefeld, Germany) and the specific surface area was calculated using the Coulter software (Version 2.12, Beckmann Coulter GmbH). The measurements were repeated six times with different sample quantities.

2.3.3. XPS measurements

The samples were measured as loose powders without any pretreatment. They were supported by a tantalum sample container and were transferred into the XPS instrument by means of a differential pumping stage. After evacuation, a sample was transferred into the main spectrometer chamber and was measured at about 5×10^{-8} mbar. Broad area XPS conditions were adjusted to obtain information on the surface properties of about 0.5 cm^2 of the material in a single spectrum. The XPS measurements were performed using MgK_α radiation at a power of 150 W. The electron energy analyzer (model EA11A, Leybold, Cologne, Germany) was operated at a pass-energy of 75 eV in the fixed analyzer transmission mode. Additional details are given by Albers et al. [5].

3. Results and discussion

Fig. 1 depicts the influence of the AEROSIL® 200 VV Pharma concentration on the angle of repose of Starch 1500® under two different mixing conditions. Under mixing conditions 1, the angle of repose continuously decreased with increasing AEROSIL® 200 VV Pharma concentration, reaching a minimum value of 33.8° at 0.25% AEROSIL® 200 VV Pharma, before increasing to 38.8° at 1%. Under mixing conditions 2, the course of the angle of repose was almost parallel to the values obtained with mixing conditions 1 resulting in an optimum between 0.125% and 0.25%. Nevertheless, the values were overall lower, indicating better flowability due to additional mixing.

In order to elucidate these differences, X-ray photoelectron spectrometry was performed to determine the degree of AEROSIL® particle coverage and distribution on the Starch 1500® surface. The Si 2p photoelectron signals allowed a quantitative comparison of the substrate

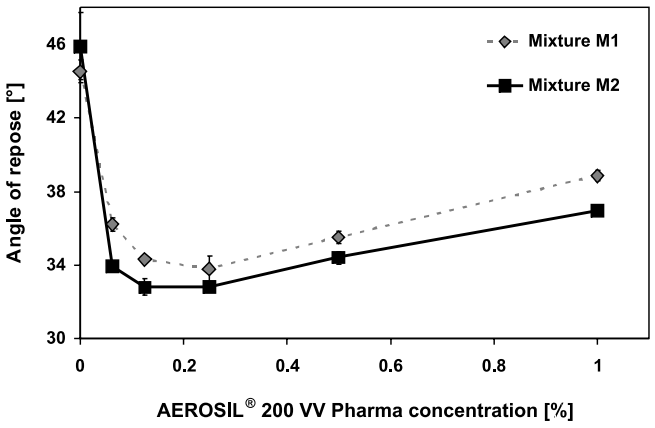

Fig. 1. Angle of repose of Starch 1500® mixtures in dependence of the AEROSIL® concentration and mixing process. Error bars indicate the 95% confidence interval of six measurements.

coverage by AEROSIL® particles. With increasing AEROSIL® 200 VV Pharma concentration, the Si 2p signal increased, i.e., the degree of coverage of Starch 1500® surface by AEROSIL® particles increased (Fig. 2). Furthermore, for a given AEROSIL® concentration, samples prepared under mixing conditions 2 showed a higher silicon concentration on the surface as compared to samples obtained with mixing conditions 1. This observation can be explained by the structure of AEROSIL®. The primary particles of colloidal silicon dioxide are fused together in relatively stable chain-like aggregates, which in turn form larger agglomerates in the micrometer range. Mixing breaks up and influences the size and the distribution of the agglomerates [1,2,6]. Additional mixing in the plowshare mixer led to a further reduction in size of the AEROSIL® agglomerates. Consequently, a greater number of smaller agglomerates and aggregates of AEROSIL® 200 VV Pharma were available to cover the surface of Starch 1500® and to act as glidant. This better coverage reduced the interparticle adhesion force between the Starch 1500® particles, leading to a reduction of the angle of repose under mixing conditions 2.

Fig. 3 shows the angle of repose as a function of the surface coverage represented by the Si 2p signals. The Si 2p signals revealed that higher AEROSIL® concentrations resulting in greater coverage of the excipient surface by AEROSIL® did not automatically lead to a lower angle of repose. Mixture M1 containing 1% AEROSIL® and mixture M2 containing 0.5% AEROSIL® showed approximately the same Si 2p values (8.63% for M1/1% and 9.1% for M2/0.5%) but a huge difference in the angle of repose (38.8° for M1/1% and 34.4° for M2/0.5%). The mixture containing the lowest AEROSIL® concentration showed the best flowability, indicating that the size of the agglomerates played a key role in the flow enhancement. In order to reach the same degree of coverage with half of the amount, the AEROSIL® agglomerates of the M2-mixture containing 0.5% AEROSIL® were smaller as the M1-mixture containing 1% AEROSIL®. The smaller size was due to additional breaking up in the plowshare mixer. So when the extent of coverage is identical, smaller agglomerates are more effective in enhancing flowability. As described by Rumpf [7], the smaller the particles adsorbed on the surface, the stronger the reduction of the van der Waals forces. Consequently, the lower the van der Waals forces, the better the flow enhancement [2,6]. These findings are supported by comparing mixture M1 containing 0.5% AEROSIL® and mixture M2 containing 0.25% AEROSIL®.

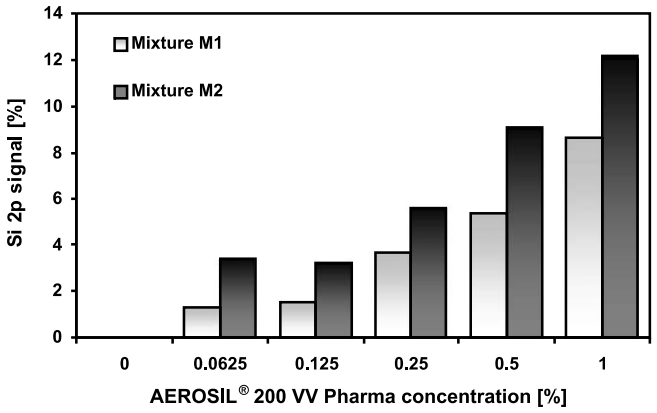

Fig. 2. Si 2p signals of Starch 1500® mixtures in dependence of the AEROSIL® concentration and mixing process.

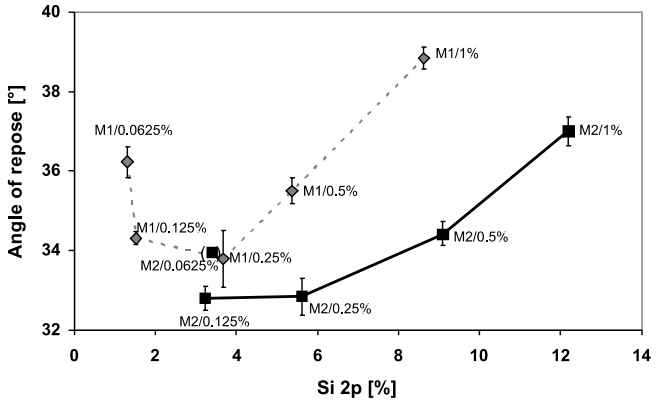

Fig. 3. Angle of repose of Starch 1500®/AEROSIL® 200 VV Pharma mixtures as a function of Si 2p signals. (M1 and M2 represent the mixing conditions, the percent values the AEROSIL® concentration by weight.)

Assuming that surface coverage of an excipient by a glidant is the dominating factor in the flow enhancement of powders, there should be a correlation between the surface of the excipient and the required amount of colloidal silicon dioxide to achieve a certain degree of flowability under defined mixing conditions. An Avicel® PH 101/AEROSIL®- and a Starch 1500®/AEROSIL® mixture containing the same amount of colloidal silicon dioxide based on the surface area of the excipient were compared. The BET surface area of Avicel® PH 101 (1.238 m^2/g) is four times higher than that of Starch 1500® (0.307 m^2/g). Therefore, mixtures M1 and M2 of Starch 1500® and Avicel® PH 101 containing 0.125% and 0.5% AEROSIL® 200 VV Pharma, respectively, were investigated. XPS measurements did not provide the expected identical AEROSIL® coverage (Table 1). The Si 2p signal of Avicel® PH 101/AEROSIL® mixtures was higher compared to those of Starch 1500®/AEROSIL®, indicating a better coverage and dispersion of AEROSIL® 200 VV Pharma on the Avicel® PH 101 surface. This difference could be explained on the one hand by the surface area measurements and on the other by the affinity of colloidal silicon dioxide for the excipient surface.

Table 1
Si 2p signals in % for Avicel® PH 101 containing 0.5% AEROSIL® 200 VV Pharma and Starch 1500® containing 0.125% AEROSIL® 200 VV Pharma under mixing conditions 1 and 2

	Avicel® PH 101	Starch 1500®
Si 2p signal mixture M1	2.76	1.52
Si 2p signal mixture M2	8.25	3.24

Table 2
Results of the Gaussian/Lorentzian line shape analysis of the C 1s signal for Avicel® PH 101, Starch 1500®, and two native starches as bulk material

	Avicel® PH 101		Starch 1500®		Native starch (commercial sample)		Extra white maize starch	
	eV	%	eV	%	eV	%	eV	%
C 1s peak 1	285.3	7	285.6	39	285.1	45	285.5	47
C 1s peak 2	286.8	83	287.2	44	286.8	38	287.1	37
C 1s peak 3	288.8	10	289.9	17	288.4	17	288.7	16

Scanning electron micrographs have shown that Avicel® PH 101 has a matchstick-like or rod-like structure composed of fibrils with a radius of 10–15 nm [8]. Due to this structure, the surfaces of cavities not reachable by AEROSIL® agglomerates were included in the BET surface measurement. Therefore, the 1.238 m^2/g of Avicel® PH 101 was an overestimation of the surface reachable by AEROSIL® agglomerates. Furthermore, XPS as a short range method is able to detect the signal of SiO_2 on planes and edges, the cavities and pores free of AEROSIL® agglomerates were not detected, leading to higher Si 2p signals than expected. In contrast, Starch 1500® consists of nearly round particles and aggregates thereof bonded by hydrolyzed starch showing a smooth surface. Therefore, the 0.307 m^2/g surface area of starch is almost entirely a realistic attainable surface area for the AEROSIL® agglomerates and detectable by XPS measurement.

Besides the Si 2p signals, XPS offers the possibility to characterize the chemical environment of each element through its binding energy and to differentiate between different carbon entities of the substrate.

With respect to high resolution XPS data reported by Beamson and Briggs [9], it follows that the signal at about 285/286 eV is due to CH_X-type functions in side chains, the signal at about 286/287 eV corresponds to the C atoms in the glucose ring which are directly connected to the OH-groups, and the signal at about 288/289 eV shows the C atoms bridging oxygen atoms in and between the glucose rings. Table 2 shows the binding energy values for Starch 1500® and Avicel® PH 101. Although the two substrates are based on glucose monomers, XPS measurements revealed that for Avicel® PH 101, the Gaussian/Lorentzian line shape analysis of the C 1s signal was dominated by the peak at about 286/287 eV (83%), while for Starch 1500®, this signal was only 44%. The Starch 1500® signal at 285/286 eV was with 39% in the same order of magnitude, while the corresponding Avicel® PH 101 signal was only 7%. The differences were due to the stereochemical configuration between the monomer units. In Avicel® PH 101, the glucose units are linked by – β-1,4-glucosidic bonds, forming a long straight-chain structure. Starch 1500® is comprised of amylose, consisting of glucose units linked by α-1,4-glucosidic bonds to form a helix of six glucose units, and amylopectin, consisting of glucose units linked by α-1,4-glucosidic bonds in the linear part and branched by α-1,6-glucosidic bonds [10]. The outer envelope of Starch 1500® consists mainly of amylopectin [11], leading to a branched-chain molecular structure detectable by XPS and attainable for the adhesion of AEROSIL® agglomerates.

The C 1s signal of Avicel® PH 101 was dominated by the peak around 286/287 eV corresponding to the carbon atoms in the ring which are directly connected to the OH-groups. Through the straight-chain structure, a large number of OH-groups are present on the surface of Avicel® PH 101 attracting agglomerates of colloidal silicon dioxide by hydrogen bonds. For Starch 1500®, the C 1s signal around 286/287 eV was lower. Due to its branched-chain molecular structure, the number of OH-groups, present at the surface of Starch 1500® and attainable for AEROSIL® agglomerates, was lower. The results of Gaussian/Lorentzian line shape analyses of the C 1s signal of Starch 1500®were supported by the analysis of two other starches. The difference in the outer molecular structure resulted in better anchor possibilities on the Avicel® PH 101 surface compared to Starch 1500®, leading to a better degree of coverage of AEROSIL® 200 VV Pharma and hence improved powder flow.

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