Modified Cellulose II Powder: Preparation, Characterization, and Tableting Properties

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ABSTRACT: The reaction of UICEL-A/102, a cellulose II powder recently prepared from Avicel® PH-102 by treatment with an aqueous sodium hydroxide solution, with glutaraldehyde in 0.01 N HCl has been investigated to improve its binder properties, without adversely affecting the rapid disintegration characteristic. The results showed that UICEL-A/102 and glutaraldehyde when reacted in a 1:0.6 weight ratio at 100°C for 8.5 h produces a product, (hereinafter referred to as UICEL-XL), that, compared to UICEL-A/102, had a lower degree of polymerization, higher crystallinity, lower bulk density, lower tapped density, and higher porosity. Further, it showed lower yield pressure and higher crushing strength, and tensile strength values, indicating that UICEL-XL is more compressible and compactable than the starting material, UICEL-A/102. A comparison of "in-die" and "out-of-die" Heckel data indicated UICEL-XL to be less elastic than UICEL-A/102. Both UICEL-XL and UICEL-A/102 showed similar moisture sorption isotherms, and their compacts disintegrated rapidly in water. In conclusion, the glutaraldehyde-treated cellulose II powder not only serves as good a disintegrant as the untreated cellulose powder but also possesses superior binder properties.
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Keywords: cellulose II; direct compression excipient; modified cellulose; tablet; binder; disintegrant

INTRODUCTION

Tablets are widely used because they are convenient, easy to use, portable, and less expensive than other oral dosage forms.[1] The ideal tableting excipient should possess all of the following characteristics: excellent compressibility, adequate powder flow, good disintegration, physiologically safe, inert and acceptable to regulatory agencies, physically and chemically stable, compatible with other excipients and active excipients, high diluent potential, and inexpensive.[1,2] Currently, there is not a single excipient that fulfills all the optimum tableting requirements.

Cellulose, the most abundant natural polymer, is a linear homopolymer consisting of 1,4-linked β-D-glucose repeat units. It is widely used as a raw material to prepare a number of excipients. There exist four polymorphs of cellulose, namely cellulose I, II, III, and IV. Of these, cellulose I is the most prevalent.[3] In native cellulose, it exists as a mixture of I_α and I_β forms.[4] Cellulose II is typically prepared by mercerization and it is the most stable allomorph of cellulose.[5]

Microcrystalline cellulose (MCC), cellulose I powder, is perhaps the best filler-binder available today. It was first introduced in the market in 1964 under the brand name Avicel® PH by FMC Corporation (Philadelphia, PA). Since 1992, Avicel® PH is available in seven grades (Avicel® PH-101, Avicel® PH-102, Avicel® PH-

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105, Avicel® PH-112, Avicel® PH-113, Avicel® PH-301, and Avicel® PH-302). They differ in particle size and moisture content. Currently, MCC is available from different vendors under different trade names. MCC is prepared by hydrolysis of native α-cellulose, a fibrous, semicrystalline material, with dilute mineral acids.[6] During hydrolysis, the accessible amorphous regions are removed and a level-off degree of polymerization product is obtained. MCC serves as an excellent binder and possesses high dilution potential.[6]

Recently, a new cellulose II-based pharmaceutical aid, referred to as UICEL, that serves as a binder as well as a disintegrant, has been prepared.[7,8] Tablets prepared using this material, irrespective of the compression pressure employed to prepare them, disintegrate rapidly (less than 30 s) in water. However, this material displays a lower compactability than Avicel® PH-102, the commercial microcrystalline cellulose I powder.

The use of covalent bonding between the cellulose chains is the most important route to modify the polymer skeleton of cellulose, and it is widely employed on an industrial scale to improve the performance of cellulose textiles and in the paper industry.[9] Although cellulose is characterized by a self-crosslinking via intermolecular hydrogen bonds, these interactions are, however, reversible in the presence of water. Therefore, covalent crosslinking between cellulose chains avoids undesirable changes of cellulosic structure in the wet state.[9] There are two methods used to crosslink cellulose: wet- and dry-crosslinking. In the wet-crosslinking method, the cellulose fibers are treated in the swollen state with the crosslinking agent. The dry-crosslinking method, in contrast, involves collapsed fibers at the time of cross-linking.[10] Chebli and Cartilier[11] reacted cellulose I powder with epichlorohydrin in a strongly basic medium and found that the resulting cross-linked product shows improved binder/disintegrant properties.

In this research, the reaction of the cellulose II powder[7,8] with glutaraldehyde, a cross-linking agent, was investigated. The goal of the study was to improve the binder properties of the cellulose II powder while maintaining its rapidly disintegration characteristic. Glutaraldehyde has been shown to be an effective crosslinking agent for cotton, imparting improvement in wrinkle recovery angle and degree of polymerization (DP) rating of the treated fabrics[12] and to improve paper wet strength.[13] Since the hydroxyl groups on cellulose are weak nucleophile, the cross-linking reaction was carried out in an aqueous acidic solution. Under acidic conditions, the carbonyl groups of the glutaraldehyde are more reactive, facilitating nucleophilic attack by cellulose to produce the cross-linked product.

MATERIALS AND METHODS

Materials

UICEL-A/102 was prepared using Avicel® PH-102 as the starting material. The method of preparation has been discussed in detail in the previous publications.[7,8] Glutaraldehyde and concentrated hydrochloric acid were purchased from Fisher Scientific (Fair Lawn, NJ) and Spectrum Quality Products, Inc., (New Brunswick, NJ), respectively. Avicel® PH-102 was from FMC Corporation (Philadelphia, PA).

Preparation of UICEL-XL

UICEL-A/102 powder (50 g) was put in a three-neck round bottom flask, equipped with a condenser, a stirrer, and a stopper. Distilled water (300 ml) was added to the powder and the mixture was allowed to stand at room temperature for 12 h. To the hydrated UICEL-A/102 suspension, an appropriate amount of 1 N hydrochloric acid, equivalent to give a final acid concentration of 0.01 N, was added. This was followed by addition of glutaraldehyde solution (50% w/w), equivalent to a weight-by-weight ratio of cellulose to glutaraldehyde of 1:0.3 or 1:0.6. The mixture was heated at 70, 100, or 120°C, with constant stirring, for 4, 6, or 8.5 h. The reaction mixture was cooled to room temperature, filtered and then washed first with water until the pH of the washing was around 7 and then with acetone (cellulose powder:acetone = 1:0.5 w/v). The product was finally collected on a Bückner funnel and air dried at 60°C in a convection oven (Thelco Model 4, GCA/Precision Scientific) until the moisture content of the powder was <7%.

Powder X-Ray Diffractometry

The powder X-ray diffraction (XRD) measurements were conducted over a 5–40° 2θ range on a Siemens Model D5000 diffractometer, equipped with monochromatic CuK_α ($\alpha_1 = 1.54060$ Å, $\alpha_2 = 1.54438$ Å) X-rays. The step width was 0.020° 2θ/min with a time constant of 0.5 s. The