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Research paper

Effect of the type of lubricant on the characteristics of orally disintegrating tablets manufactured using the phase transition of sugar alcohol

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Abstract

The aim of this study was to evaluate the effect of lubricants on the characteristics of orally disintegrating (OD) tablets manufactured using the phase transition of sugar alcohol. OD tablets were produced by directly compressing a mixture containing lactose–xylitol granules, disintegrant, glidant and lubricant, and subsequent heating. The effect of the type of lubricant on the tablet characteristics was evaluated using magnesium stearate (Mg-St), sodium stearyl fumarate (SSF), and talc as lubricants. The hardness of the tablets increased to ca. 6 kp as a result of heating, regardless of the kind of lubricant. The oral disintegration time of the tablets containing Mg-St or SSF increased with an increase in the hardness. In contrast, the oral disintegration time of the tablets containing talc was not changed despite of an increase in hardness. The water absorption rate of the tablets containing talc was much faster than that of the tablets containing other lubricants. The surface free energy measurement showed that the polarity of the tablet components containing talc was remarkably increased by heating. The water absorption rate of the tablets containing talc was also increased by heating. These results indicate that a more hydrophilic surface might be attained by heating the talc. Consequently, talc was demonstrated to be the most desirable lubricant for the preparation of OD tablets based on the principle of the phase transition of sugar alcohol.

Keywords: Orally disintegrating tablets; Phase transition; Sugar alcohol; Saccharide; Lubricant; Talc

1. Introduction

In accordance with the transition to an aging society and changes in the living environment, a demand has arisen for the development of drug dosage forms that can be readily handled and taken by the elderly, children, or patients whose intake of water is restricted. For example, a dosage form which can be taken without water is useful in the case of the acute onset of a symptom. Thus, attempts have been made to develop an orally disintegrating dosage form which, when taken in the oral cavity, rapidly disintegrates or dissolves merely in the saliva or a small amount of water [1–3]. For example, a solution or suspension containing a drug and excipients is charged into the pockets of a blister pack sheet which has been molded beforehand, and then the sheet is subjected to freeze-drying in order to make the OD product [4]. In another preparation method, OD tablets are produced by using wet powder containing a drug and subsequent drying in an oven [5]. However, these methods require special equipment, since it is impossible to freeze-dry an entire blister pack sheet with ordinary equipment or to compress wet powder using a conventional tabletting machine.

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On the other hand, attempts have been made to develop OD tablets with sufficient hardness by commonly used equipment. Mizumoto et al. reported that OD tablets could be manufactured using a combination of saccharides with low and high moldability [6]. In their method, the OD tablets were manufactured by compressing granules consisting of low and high moldability saccharides, and then conditioning them. The tablet hardness was increased by the crystal change from an amorphous to a crystal state by the conditioning process. Sugimoto et al. also reported preparing OD tablets by storing the tablets compressed with a mixture of mannitol and amorphous sucrose at low compression pressure [7,8]. In this method, the increase in the tablet hardness was due to the transition from amorphous to crystalline sucrose in the tablet.

To obtain OD tablets of sufficient hardness without any special equipment, we focused on the melting points of sugar alcohol (SA) and proposed a novel method to prepare OD tablets of sufficient hardness by utilizing the phase transition of SA [9]. In our preparation method, the tablets are produced by compressing powder or wet granules which are composed of two types of SAs or an SA and a saccharide with high and low melting points, and subsequently heating the obtained tablets. Before the heating process, the tablets do not have sufficient hardness because of low compactability. The tablet hardness is increased by the heating process. The increase in the tablet hardness resulting from heating did not depend on the crystal state of the lower melting point of SA. The tablet hardness was related to the increase of inter-particle bonds or the bonding surface area in tablets induced by the melting, diffusion, and solidification of the lower melting point SA. Therefore, in our preparation method a combination of two SAs or SA and a saccharide and the heating process was needed to prepare OD tablets with sufficient hardness.

We made OD tablets from only two types of SAs or an SA and a saccharide in order to investigate the characteristics and formation mechanism of OD tablets prepared by the phase transition of lower melting point SA. However, lubricants are required for the continuous tabletting of OD tablets because the lubricants prevent the tablets from sticking to the die wall and punch faces. However, it is well known that the lubricant influences the disintegration or dissolution properties of tablets [10,11]. In the case of OD tablets, it is important to maintain the rapid disintegration properties of tablets with a sufficient hardness. Therefore, the purpose of the present study was to evaluate the effect of the type and amount of lubricant on the tablet characteristics of OD tablets prepared based on the principle of the phase transition of SA. We prepared OD tablets containing various types and amounts of lubricants and evaluated the tablet characteristics before and after heating. Additionally, the surface free energy of the tablet components and the water absorption rate of the tablets were measured to evaluate the physicochemical properties related to the disintegration of OD tablets containing various lubricants.

2. Materials and methods

2.1. Materials

Lactose (m.p.: 201.6 °C, Pharmatose 200 M, DMV Japan) was used as the high melting point saccharide. Xylitol (m.p.: 93–95 °C, Towa Chemical Industry Co., Ltd.) was used as the low melting point SA. Crospovidone (Polyplasdone XL, ISP Japan, Ltd.) and light anhydrous silicic acid (Aerosil 200, Nippon Aerosil Co., Ltd.) were used as the disintegrant and glidant, respectively. Magnesium stearate (Nitto Chemical Industry Co., Ltd.), talc (Matsumura sangyo) and sodium stearyl fumarate (Pruv, Mendell) were used as the lubricants.

2.2. Preparation method of tablets

Xylitol was dissolved in purified water to make 26.7 w/w%. Lactose was granulated using the xylitol solution with a fluidized-bed granulator (Flow coater mini, Freund Corporation). The granulation conditions were set as follows: inlet temperature: 90 °C; outlet temperature: 45 °C; spray air pressure: 1.5–2.0 kg/cm^2; rate of spray: 0.9 g/min. According to the composition shown in Table 1, the granules were mixed with crospovidone and light anhydrous silicic acid with a turbula mixer for 10 min, and then mixed with lubricant for 3 min. The mixture was compressed using a single punch tabletting machine (KT-II, Okada-seikou Co., Ltd.) under the following conditions: weight: 300 mg; compression pressure: 500 kgf; punch: 9.5 mm in diameter with a flat surface. The obtained tablets were placed in a drying oven to heat at 95 °C for 15 min, and then allowed to cool at room temperature.

2.3. Measurement of tablet hardness

Tablet hardness, which is defined as the force required to break a tablet by radial compression, was measured with a tablet hardness tester (TBH 21, ERWEKA GmbH) ($n = 3$).

2.4. Determination of disintegration time

A tablet was put into the mouth of a healthy male adult volunteer without water and the oral disintegration time was recorded as the time until the volunteer felt that the tablet had disappeared in his mouth while moving his tongue ($n = 3$).

2.5. Determination of water absorption rate of tablets

The water absorption rate of the tablets was studied using the apparatus described by Nogami et al. [12]. A tablet containing 10% lubricant was put on the glass filter of the apparatus, as shown in Fig. 1. The water absorption rate of the tablet (mL/s) was calculated from the time until