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Effect of diluents on the swelling force of the tablet

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Abstract

The swelling force, especially the swelling force development rate, is a very important parameter in studying the effect of a disintegrant in a tablet. However, a tablet also contains diluents in most cases and the effect of diluents on the swelling force has not been studied. In this study two commonly used diluents, microcrystalline cellulose and calcium phosphate dihydrate, were investigated for their effect on the swelling force with or without a superdisintegrant, Polyplasdone XL. It was found that microcrystalline cellulose alone can develop swelling force depending on the compression force of the tablet. When combined with Polyplasdone XL, it can significantly change the swelling force of Polyplasdone XL. The effect of diluents on the swelling force is not consistent with the disintegration and dissolution studies of the tablet.

Key words: Swelling force; Disintegration; Diluent

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I、 Introduction

A tablet usually contains a diluent to increase its weight if the active ingredient has a low dosage (1). A tablet also usually contains a disintegrant to increase the dissolution of the active ingredient (1). Nowadays superdisintegrants, namely, sodium croscarmellose, sodium starch glycolate, and crospovidone are most commonly used (2). The swelling force, especially the swelling force development rate (SFDR) which is the rate of swelling force development when the tablet contacts water and swells, has been considered as a unifying factor to evaluate the efficiency of the disintegrant used (3-7). However, the effect of the diluents on the swelling force of a tablet has never been investigated so far as we know.

Therefore, the purpose of this study is to evaluate the effect of two commonly used diluents, namely microcrystalline cellulose (Avicel) and calcium phosphate dihydrate (Di-tab) in direct compression method on the swelling force. Tablets using Avicel, Di-tab, or their combinations with or without crospovidone were prepared and their swelling force were measured. At the same time the disintegration and the dissolution of the tablets were also evaluated to understand their mutual relationships.

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II、Materials and methods

1、Materials

Hydrochlorothiazide (Ipca, India), crospovidone (Polyplasdone XL, ISP, USA), microcrystalline cellulose(pH 102, Asahi Kasei, Japan), dicalcium phosphate dihydrate (Di-tab, Rhodia, USA), and the reagents including monobasic potassium phosphate (Merck, Germany), hydrochloric acid (Merck, Germany), potassium chloride (Merck, Germany) and sodium hydroxide (Katayama, Japan) and filter paper No. 41 (Whatman, England) were used as received.

2、Methods

i、Tablet preparation

A suitable amount of each ingredient was weighed according to the following tablet formulation. Formulation A contains 300 mg of Avicel or Di-Tab only. Avicel tablet was compressed at 1000, 2000 or 4000 lbs of force respectively. Formulation B contains hydrochlorothiazide 20 mg, Avicel and Di-tab in 1: 9, 2: 8, or 3: 7 ratios q.s. to make 300 mg. Formulation C contains hydrochlorothiazide 20 mg, crospovidone 6 mg, Avicel or Di-tab q.s. to make 300 mg. Each ingredient was passed through an 80-mesh screen and mixed well by a planetary mixer (YUYAMA YM-500, Japan) for 10 minutes. The mixture was accurately weighed and compressed by carver press at 2000 lbs for 30 seconds. The diameter of the tablet was 8.0 mm and the thickness was 3.3 mm. .

ii、Swelling force measurement

A vertical Franz diffusion apparatus was inserted with a piece of sintered glass filter (porosity grade G1). A piece of filter paper (Number 41, Whatman, England) was placed on the glass filter. The apparatus was filled with pH 1.2 HCl or pH 6.8 phosphate buffer at 37 °C all the way up to filter. One side of the tablet was adhered to the probe of the texture analyzer (Stable Micro Systems, UK) by a double-sided tape. The circumstance of the tablet was surrounded by an impermeable tape to prevent the dissipation of force in other directions (8-9). The probe was lowered at a speed of 0.2 cm/sec. As the bottom of the tablet touched the wetted filter paper on sintered glass filter, it began to uptake the liquid. The result is the mean of six determinations.

iii、Disintegration Study

The disintegration test was run according to USP 30th edition in the disintegration tester (Shin kwang CT-2, Taiwan). The pH 1.2 HCl or pH 6.8 phosphate buffer at 37°C was used as the medium.

iv、Dissolution Study

The dissolution test was run according to USP 30th edition by paddle method with a rotating speed of 100 rpm in the automatic dissolution tester (Venkel, VK7000, USA). The pH 1.2 HCl or pH 6.8 phosphate buffer at 37°C was used as the medium. Sampling times were set at 2, 4, 6, 8, 10, 15, 20, 25, 30 minutes and samples were assayed at 272 nm.

III、Results and Discussion

1、Swelling force studies

It was found that pure Di-tab tablet of Formulation A shows no swelling force at all (not shown) but pure Avicel tablet shows swelling force as shown in Fig. 1. Di-tab belongs to the fragile material but Avicel belongs to plastic material (10). As water contacts the Avicel tablet, the stretch of the deformed Avicel granules probably results in the force measured (11-12). The curve increased gradually while the Avicel tablet was slowly wetted by water.

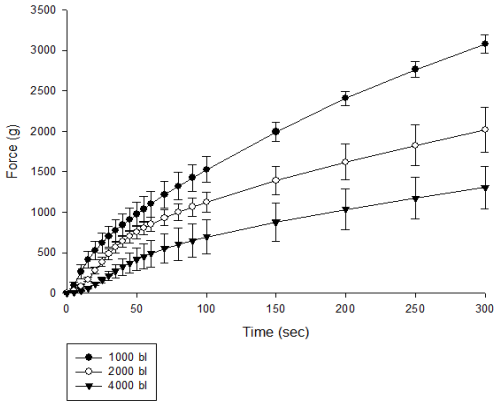

Fig. 1A Effect of compression force on the Avicel tablet in pH 1.2 buffer

The swelling force and SFDR decreases as the compression force increases as shown in Fig. 1A and 1B. As the compression force increases, the porosity decreases. According to the Washburn equation (13) the rate of water penetration inside the tablet decreases and results in decreased swelling force and SFDR.

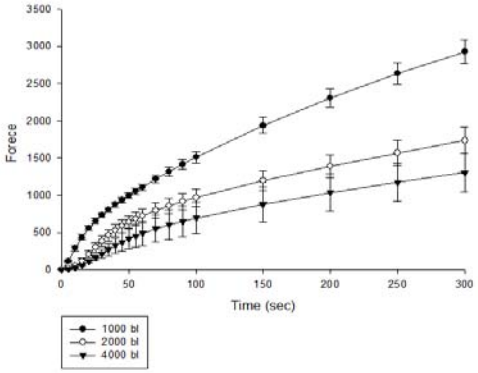

Fig. 1B Effect of compression force on the Avicel tablet in pH 6.8 buffer

Fig. 2A shows the swelling force of Formulation B tablets. The curve is different from that of Avicel tablets by increasing the force to a certain value and plateauing quickly. The higher the percentage of Avicel the tablet contains, the higher this value appears. The SFDR and the final swelling force increase as the ratio changes from 1 : 9 to 2 : 8 in pH 1.2 buffer. However, the SFDR doesn't further increase as the ratio changes from 2 : 8 to 3 : 7 and only the final swelling force increases. A similar behavior was obtained in pH 6.8 phosphate buffer as shown in Fig. 2 B.

Fig. 3A shows the swelling force of Formulation C tablet containing Di-tab and Polyplasdone XL. The force developed quickly and reached the plateau. The swelling force comes from the swelling of the Polyplasdone XL particles inside the tablet (14) since Di-tab itself doesn't have any swelling force.

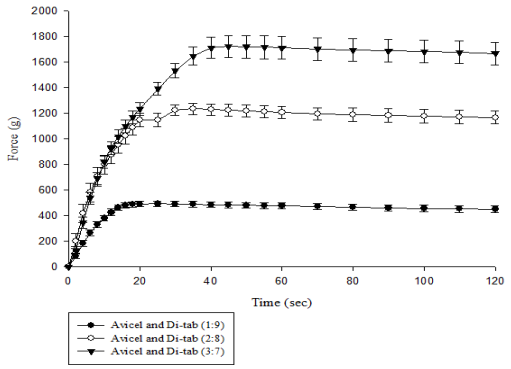

Fig. 2A Effect of ratio of Avicel and Di-tab on the swelling force of hydrochlorothiazide tablet in pH 1.2 buffer

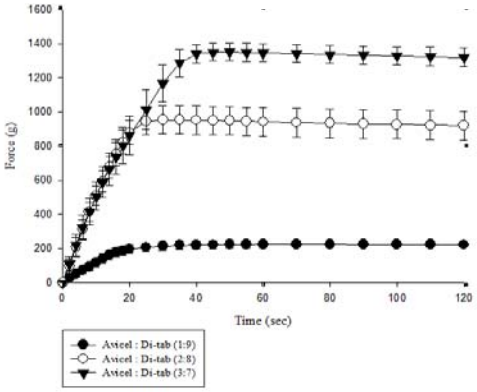

Fig. 2B Effect of ratio of Avicel and Di-tab on the swelling force of hydrochlorothiazide tablet in pH 6.8 buffer

Fig. 3B shows the swelling force of Formulation C tablet containing Avicel and Polyplasdone XL. The

curve shows a biphasic pattern with a fast-growing phase and a slow-growing phase. Polyplasdone XL is probably responsible for the fast-growing phase and Avicel for the slow-growing phase. Since the tablet contained Polyplasdone XL alone (that means polyplasdone XL with Di-tab), the force developed quickly and reached the plateau. For the tablets containing Avicel alone the swelling force developed slowly with very short or unclear fast-slowing phase.

The swelling force comes from the combinational effect of Polyplasdone XL plus Avicel. This combination changes the shape of the swelling force but the effect appears to be additive and the interactive effect is not significant.

The development of the swelling force by Polyplasdone XL is by the swelling of Polyplasdone XL particles, which is different from the force given by stretch of deformed Avicel particles. The two different mechanisms seem to be independent of each other and appear no significant interactive effect.

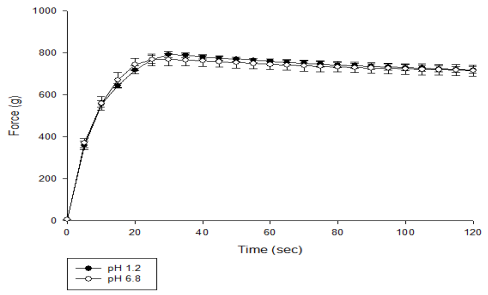

Fig. 3A The swelling force of Formulation C tablets containing Di-tab and Polyplasdone XL

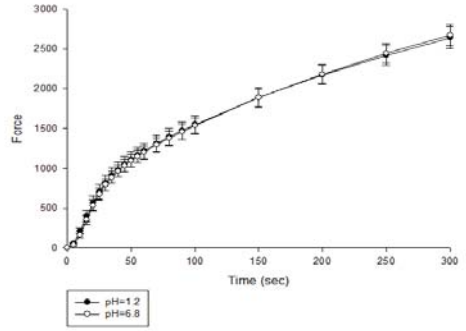

Fig. 3B The swelling force of Formulation C tablets containing Avicel and Polyplasdone XL

2、Disintegration and dissolution Studies

Di-tab and Avicel are both direct-compression excipient with the binding ability, and can be formed into a tablet under the compression force (15). The Avicel tablet of Formulation A forms the tablet with extremely great hardness (> 30 Kg) but the Di-tab tablet of Formulation A forms the tablet with much lower hardness of about 6 Kg.

The disintegration time increases when Avicel increases in Formulation B tablets as shown in Table 1. This is related with the higher binding ability of Avicel. Apparently this is not consistent with swelling force study. Therefore swelling force, especially the SFDR used as an indicator for disintegration efficiency, is not applicable when the tablet contains a diluent which displays the swelling force.

Disintegration time (sec)		
Ratio	pH 1.2 buffer	pH 6.8 buffer
1: 9	10 ± 1	23 ± 4
2: 8	21 ± 2	56 ± 8
3: 7	194 ± 25	868 ± 61

Table 1 Effect of ratio for Avicel and Di-tab on the disintegration of Formulation B tablets in pH 1.2 and pH 6.8 buffer

Fig. 4 shows the effect of ratio for Avicel and Di-tab on the dissolution of Formulation B tablets. The dissolution in pH 1.2 buffer becomes slower as the percentage of Avicel increases. The dissolution in pH 6.8 buffer for three kinds of ratio is all extremely slow. This is because Di-tab dissolves in acidic environment (16). Again the dissolution result is not consistent with swelling force study.

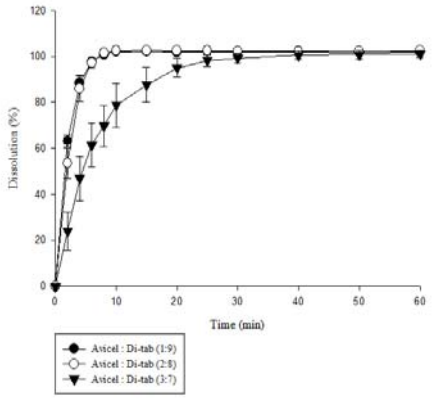

Fig. 4A Effect of ratio for Avicel and Di-tab on the dissolution of Formulation B tablets in pH 1.2 buffer

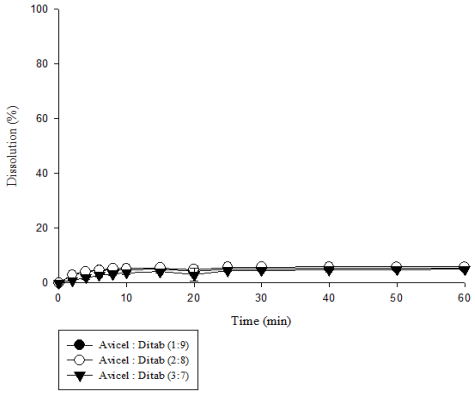

Fig. 4B Effect of ratio for Avicel and Di-tab on the dissolution of Formulation B tablets in pH 6.8 buffer

V. Conclusion

Depending on the nature, the diluent can display the swelling force or not. Di-tab doesn't show any swelling force but Avicel shows varied degrees of swelling force depending on the compression force. Avicel alone shows gradual force development. With Di-tab added a plateau appears quickly.

When the diluent is combined with a disintegrant the shape of the swelling force curve can be significantly changed. The curve shows a biphasic pattern with Avicel and disintegrant each responsible for the slow-growing phase and fast-growing phase respectively.

Disintegration and dissolution studies are not consistent with swelling force study. SFDR used as a unifying factor for disintegration should be used carefully when the tablet contains a diluent displaying swelling force too.

IV、Acknowledgement

The authors appreciate Chia Nan University of Pharmacy for the financial support.

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稀釋劑對於錠劑膨脹力之影響

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摘要

膨脹力，尤其是膨脹力發展速率，在崩散劑對錠劑的作用研究中，一直扮演著重要的角色。大部份錠劑皆含有稀釋劑，但稀釋劑的膨脹力卻一直未被研究。本研究用了兩種常見之稀釋劑 microcrystalline cellulose 及 calcium phosphate dihydrate，來探討這兩種稀釋劑單獨使用時及併用超級崩散劑 Polyplasdone XL 時的膨脹力。研究結果顯示 microcrystalline cellulose 單獨使用時，其膨脹力會受到錠劑打錠力量的影響。當 microcrystalline cellulose 與 Polyplasdone XL 併用時，它會改變 Polyplasdone XL 的膨脹力。但稀釋劑膨脹力的作用並未和錠劑的溶離及崩散試驗結果一致。

關鍵字：崩散、膨脹力

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