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Preliminary Approach to Application of Modified Smectite Clay to Form Tablets in Direct Compression Process

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Abstract

In this study, the modified smectite clay was used as a disintegrating agent and its suitability to form placebo tablets by the direct compression method was evaluated. The modification of the commercial purified smectite clay (Veegum®F, R.T. Vanderbilt Company, Inc.) was done in aqueous NaCl solution to provide relatively short disintegration time of tablets while maintaining their sufficient mechanical properties. To evaluate the influence of the new material on the quality of tablets obtained, the following parameters were investigated: disintegration time, hardness and friability. It was stated that the modified clay material may be used to form tablets by the direct compression method.
Keywords: Smectite clay, Disintegrating agent, Pharmaceutical application

WSTĘPNE BADANIA NAD ZASTOSOWANIEM MODYFIKOWANEGO IŁU SMEKTYTOWEGO DO FORMOWANIA TABLETEK W PROCESIE BEZPOŚREDNIEJ KOMPRESJI

W prezentowanych badaniach wykorzystano modyfikowany ił smektytowy jako czynnik dezintegrujący i oceniono jego przydatność do formowania tabletek placebo metodą bezpośredniej kompresji. Modyfikację komercyjnego, oczyszczonego iłu smektytowego (Veegum®F, R.T. Vanderbilt Company, Inc.) przeprowadzono w wodnym roztworze NaCl, aby zapewnić względnie krótki czas dezintegracji tabletek, zachowując jednocześnie ich wystarczające właściwości mechaniczne. Aby ocenić wpływ nowego materiału na otrzymane tabletki zbadano następujące parametry: czas dezintegracji, twardość i kruchość. Stwierdzono, że modyfikowany materiał ilasty można wykorzystywać do formowania tabletek metodą bezpośredniej kompresji.
Słowa kluczowe: ił smektytowy, czynnik dezintegrujący, zastosowanie farmaceutyczne

1. Introduction

Clay minerals, such as smectites, are successfully used in the drug delivery systems due to their hydrophilic and swelling properties [1-3]. Whether as active ingredients or as excipients, these minerals must comply with a number of textural and compositional requirements (concerning grain size, degree of mineral purity, water content, major and trace element contents or microbial contamination) and have specific technical properties. The most common solid single-unit dosage forms of drug delivery system are tablets, yet there are many patients having difficulty swallowing conventional tablets or capsules. Thus, the slid dosage forms, designed for rapid disintegration in the mouth, have recently received much attention [4]. Advantages of oral fast-disintegrating dosage forms include:

– the administration to patients who cannot easily swallow, such as the elderly, stroke victims, healthcare facility and bedridden patients and patients who refuse to swallow, such as pediatric, geriatric and psychiatric patients [5. 6],
– more rapid drug absorption [6],
– convenience and patient compliance [6],
– product differentiation, line extension and life-cycle management, exclusivity of product promotion and patient-life extension [7].

Commercially available rapidly disintegrating tablets (RDT) are prepared by various techniques [10], mainly lyophilisation [11, 12], moulding [13] and direct compression [14, 15]. The lyophilisation and moulding techniques produce RDT which disintegrate within about 30 s, but that have low physical resistance and high friability. On the other hand, the tablets obtained by direct compression are less friable but disintegrate in a longer time. Attempts were made in order to decrease the disintegration time of tablets that have sufficient hardness prepared by direct compression. Some researchers [16, 17] used microcrystalline cellulose and low-substituted hydroxypropyl cellulose (L-HPC) as disintegrants to prepare rapidly disintegrating tablets by direct compression.

In this study, the modified smectite clay was used as a disintegrating agent and its suitability to form placebo tablets by the direct compression method was evaluated. To obta-

in desirable disintegration time, the tablets were additionally treated by the cation exchange reaction method. The microstrutural changes were investigated as well as the major properties of tables made of the modified clay material, such as disintegration time, hardness and friability were studied.

2. Materials and methods

Veegum®F pharmaceutical smectite material was used as a substrate (Vanderbilt Company, Inc.) to produce tablets by direct compression method. The exchange reaction of the clay material was done by the use of 2M NaCl solution in order to exchange Ca^{2+} ions with Na^{+} in the structure. The solution was centrifuged and rinsed till the absence of Cl^{-} ions and then the obtained gel was subsequently lyophilized. The tablet matrix was composed of 25 % of the modified clay, 73 % of Ludiflash® filler (granular material used in pharmacy as an excipient in tablets mass production) and 2 % of stearate fumarate sodium which was used as a lubricant. Tablets containing 73 % of Ludiflash®, 25 % of Veegum®F and 2 % of the lubricant were formed as a reference. Tablets were compacted on a single-punch tablet press by using the flat-faced punches. The compression force ranged from 10 to 30 kN. To evaluate the influence of the new material on the quality of tablets obtained, disintegration time, hardness and friability were investigated. Disintegration time was determined by using the pharmacopoeial disintegration test apparatus ED-2 SAPO (India). Hardness was measured using the hardness tester Vanderkamp Benchsaver (Germany). A hardness tester was used to measure the crushing strength of tablets. Specific crushing strength (SCS) was calculated on the basis of crushing strength, diameter and height of the tablet. Friability was determined according to the pharmacopoeial method - friabilator Erweka (Germany). Microstructure of powders: Veegum®F and Veegum®F after cation exchange reaction was observed by scanning microscope NOVA NANO SEM 200.

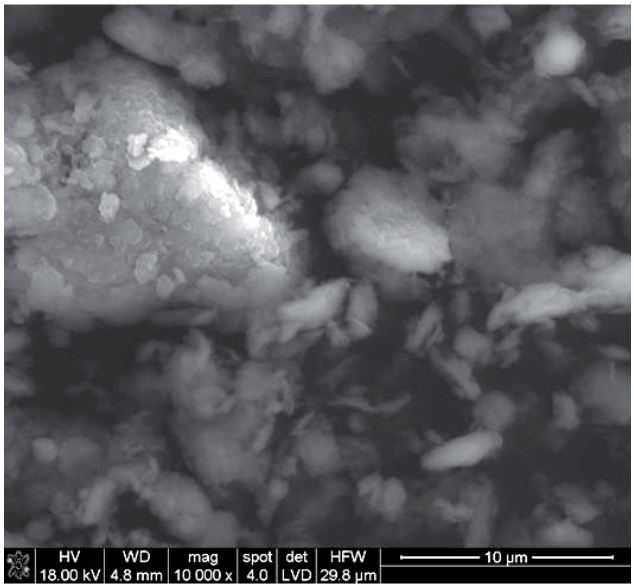

Fig. 1. SEM microphotograph of Veegum®F powder before ion exchange reaction.

3. Results and discussion

SEM microphotographs show changes in the microstructure of powder before and after the ionic exchange reaction process. In the case of substrate powder the structure is characterized by big aggregated particles, shown in Fig. 1.

After the cation exchange reaction and lyophilization, very characteristic 'chaotic' distribution of smectite packets (called: "house of cards") is visible (Fig. 2). Both figures demonstrate that the cation exchange process of powders influences microstructural properties of the clay material. Resulting from this, the changes reported in microstructure of powders influence the overall properties of tablets, such as disintegration time, hardness and friability.

The following pictures show the changes of mentioned parameters as a function of compression force. Fig. 3 illustrates the changes of the disintegration time for the tablets obtained by the direct compression method, where different compression forces in the range of 10 to 30 kN were used. It is shown that the disintegrating times increase as the compression force increases.

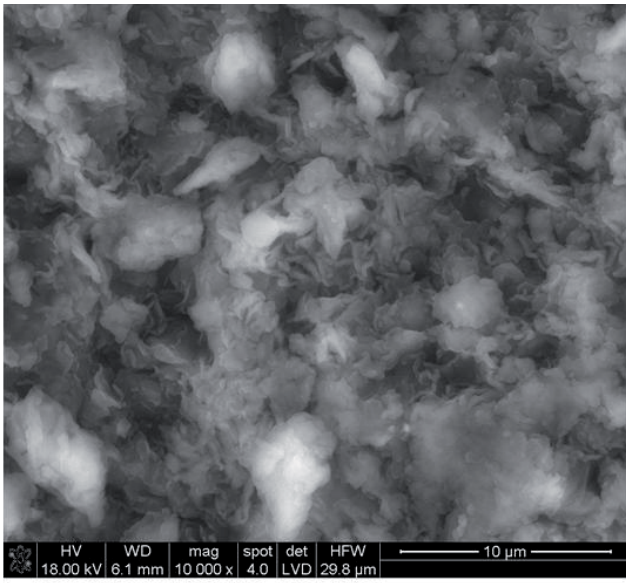

Fig. 2. SEM microphotograph of Veegum®F powder after ion exchange reaction.

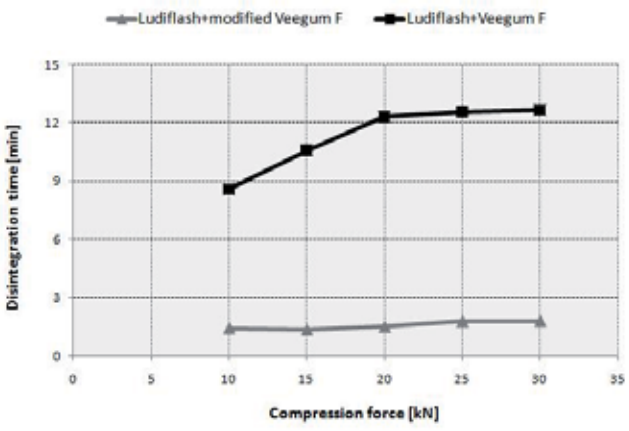

Fig. 3. Changes in the disintegration times as a function of compression force.

It is also clearly visible that the tablets, where the modified clay material was used, have disintegration times about eight times shorter than these reported for not modified clay materials. This confirms that this substrate material can be potentially used to form tablets with disintegrating times shorter than 3 minutes by the direct compression method.

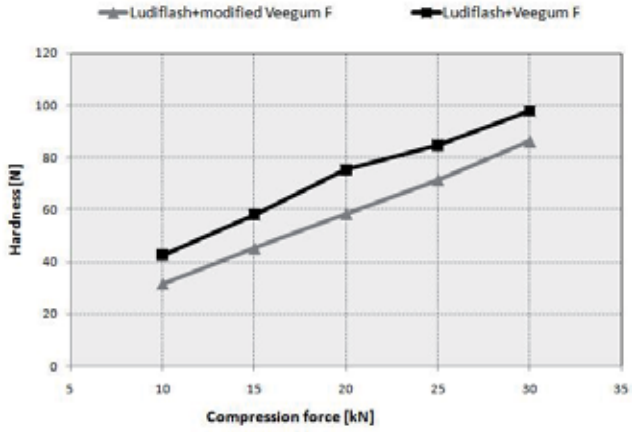

Fig. 4. Changes in the hardness of tablets as a function of compression force.

Fig. 4 shows changes in the hardness of tablets in the function of compression force. As one can expect, the hardness increases significantly as the compression force increases. It is important to note that to prepare the tablets made of modified clay material having hardness comparable to the hardness of tablets made of not-modified clay it was necessary to use 5 kN higher compression force.

The same tendency was observed during analysis of the changes of the friability of the tablets (Fig. 5). The friability below 1 % was possible to achieve when the compression force higher by 5 kN was used.

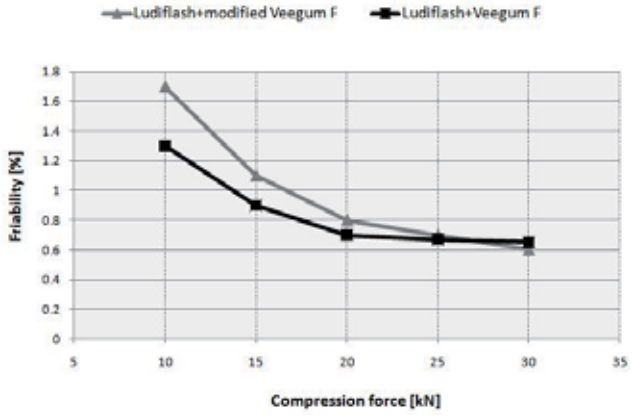

Fig. 5. Changes in the friability of tablets as a function of compression force.

4. Conclusions

It was found that the modified clay material may be the used to form tablets by direct compression method. The modification of Veegum®F had a beneficial effect on the disintegration time of tablets. The disintegration time of tablets containing modified Veegum®F ranged from 1'25 min to 1'48 min while the disintegration time of tablets made of non-modified Veegum®F was even eight times longer and its value was from 8'35 min to 12'39 min. However the mechanical resistance of the tablets prepared by using modified Veegum®F was lower than in the case of tablets containing the non-modified excipient. To prepare tablets of the friability below 1 % with the modified form of Veegum®F, it was necessary to apply the compression force 5 kN higher than in case of Veegum®F.

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