CHAPTER I

GENERAL INTRODUCTION

Direct compression technique is a method of tablet production by which the processing steps are composed of mixing all ingredients such as active ingredient(s), diluent, disintegrant, glidant, lubricant and then compressing the mixed powders without subjection to the granulation step. The important ingredient in this process is a directly compressible diluent (DC diluent) which have two main important properties : flowability and compressibility. A number of materials from various sources have been developed to be used as DC diluents such as lactose, starch, cellulose, inorganic material, sucrose, and so on.

Starch is the excipient that has been used in tablet formulations to act as a binder, filler, or disintegrant depending on the type used and the quantity. The first directly compressible starch is Starch®1500 that is partially pregelatinized corn starch. This modified starch is more compressible, has better flowability, and disintegration properties than those of starch USP (Manudhane et al., 1969). Although the compression property is improved, the hardness of the compact and dilution potential are still low and powder is very sensitive to alkaline stearate. Bos et al. (1987) examined the tabletting properties of various starches without modification and found that rice starch gave the best compressibility with less sensitive to alkaline stearate compared to the other starches. However, the flowabililty of rice starch is very poor due to small starch grains of 2 – 8 μm (Schoch, 1967). To improve the flow property, rice starch is subjected to spray drying technique to produce agglomerated starch (Bos et al., 1992; Hsu et al., 1997; Mitrevej et al., 1990, 1996). In Thailand this agglomerated rice starch is marketed under the trade name of Eratab®. Mitrevej et al.(1990, 1996) studied and compared the physical and compression properties of Eratab® to various DC diluents. They found that Eratab® gave the best flowability while lactose and microcrystalline cellulose (MCC) exhibited poor flowability. Although the hardness was reduced when magnesium stearate was incorporated, the binding property of spray dried rice starch was still sufficient to form a required tablet strength. When this material was used to produce drug tablets, its tablets

gave good disintegration time and dissolution. To improve the compressibility properties of rice starch, it was subjected to chemical modification by crosslinking reaction before spray drying (Timaroon, 1993; Timaroon and Kulvanich, 1992; Weechanrangsan, 1995). They found that modified rice starch has higher compressibility than other DC diluents, e.g., Eratab®, Starch® 1500, and Emcompress® while its compressibility is less than that of Avicel®.

In addition to the improvement of the physical and compressibility properties of each diluent using physical and/or chemical modification, coprocessing of various diluents or excipients were also performed. Coprocessing is the process of producing new excipient from combined various excipients via one of this process such as coprecipitation, spray drying, and slugging (Bolhuis and Chowhan, 1996). The resultant product could be called coprocessed excipient or composite particles which was found to give better properties than single excipient or physical mixture of those excipients. The commercially available coprocessed excipients are Ludipress® (lactose, PVP, and crosprovidone), Cellactose® (lactose and cellulose), Cel-O-Cal®(cellulose and calcium sulfate) and Prosolv®(cellulose and silicon dioxide). The coprocessed excipients of starch have been reported. An example is Bavitz and Schwartz (1974, 1976) who evaluated the physical properties and compressibility of physical mixtures of microcrystalline cellulose (MCC) and other diluents in the ratio of 1 : 1 in comparison with coprocessed starch USP and MCC at the ratio of 84 : 16 (according to USP XVIII, starch referred in this report implied starch that derived from corn). They found that the physical mixture of starch and MCC could not produce tablets due to its poor flowability while the coprocessed excipient produced tablets that had acceptable hardness and good disintegration. When drug ingredient was incorporated in the formulation, this coprocessed excipient could not provide tablets with an acceptable hardness although the highest compression force was used. This might be due to the type of starch used, the modification of starch, or the insufficient quantity of MCC. Ohno and Ikeda (1986, 1991) prepared DC diluent by using cellulose powder or MCC and hydroxypropyl starch in the ratio from 9 : 1 to 4 : 6 and subsequently spray dried. They found that this invented product gave well in molding characteristics and resulted in good disintegration

time with higher hardness than physical mixture of hydroxypropyl starch and cellulose when compressed with rotary tabletting machine. Cellulose or hydroxypropyl starch alone could not be compressed into tablets because of its poor flowability and their physical mixture only gave 25 % yield.

From the above mentions, coprocessed excipient is of interest as it not only possesses the better properties than single material and physical mixture of the materials but also combines the good properties of each material. As far as the literature search has been done, there is no report on the coprocessing of rice starch and cellulose to be introduced as DC diluent. From the preliminary study, there is the possibility to develop this coprocessed excipient to be used as a new DC diluent. Rice starch was chosen because of its best compressibility. Moreover, it has the low price and also readily available in Thailand. MCC was chosen due to the high compressibility. However, it has some disadvantages, e.g., poor flowability and more expensive price. Therefore in tabletting process, it is usually formulated by the addition of other excipients with better flowability and/or lower cost. The coprocessing technique used was spray drying because it could transform the powder into aggregated form which more spherical and rather of uniform particle size than other techniques. Moreover, it could be done in single step. Combining these two materials, rice starch and MCC, would lead to a new DC diluent with improved compressibility, good flowability, and combined beneficial properties of two materials. Furthermore, this development would be not only to obtain the new excipient with reasonable price but also to increase the value of the starch that is the local agriculture product. The objectives of this study are listed as follows.

Objectives of This Study

1. To develop composite particles of rice grains and MCC by spray drying technique for using as directly compressible diluent
2. To evaluate and compare the physical and tabletting properties of composite particles between rice flour / MCC and rice starch / MCC with respect to the ratio of rice flour or rice starch and MCC, and particle size of MCC used

3. To study the effect of process variables of spray drying on the physical and tabletting properties of the coprocessed excipient and scale up to examine the reproducibility of the production
4. To investigate and compare the compression characteristics of prepared composite particles with other commercial available DC diluents

The Significance of This Study

1. There is no report on the preparation of composite particles of rice starch and cellulose to be used as a directly compressible diluent.
2. The coprocessed excipient can be introduced as a new directly compressible diluent.
3. The main raw material used in this experiment was rice starch which is local agricultural product, cheap, and also available in our country.
4. This coprocessed excipient has a high potential to be produced for commercial purpose.