EFFECT OF THE APPLIED PRESSURE ON THE ESSENTIAL CHARACTERISTICS OF SODIUM STARCH GLYCOLATE TABLETS

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Abstract. Immediate onset of action in a lot of cases is extensively used than ordinary therapy, however; produce tablets with acceptable features as tensile strength, suitable with acceptable industrial limits, reduced ordered unit segregation tendency, and rapidly or appropriate disintegration time, is a classic problem. Use disintegrant is considered one of corner stone to achieve pharmaceutical tablets that meet requirements of recommended tablet formulation in the markets. Sodium Starch Glycolate as an elastic material (super disintegrant) is the component of compacted tablets by direct compression in current work. Uniaxial compaction process was implemented by utilizing a universal testing machine. The tablets were compacted under applied load ranging from 75 to 375 MPa. A 13 mm diameter cylindrical die was used to characterize the compression behaviour of the 1.0 ± 0.01 g of material. Number of the evidences from this study is, the tabletted powder characteristics and the volume-pressure measurements relationship were investigated. The recommended tablet formulations were evaluated by using elastic relaxation, indirect tensile strength, friability, and disintegration tests.

Applying load higher than 150 Mpa produces compacts with a longer disintegration time, low elastic relaxation, in addition to tensile strength and friability percentage identical to recommended tablets formulation in the markets.

Keywords: pharmaceutical tablets, SSG, tensile strength, disintegration, direct compression (DC)

Introduction

Due to its compactness and it doesn’t need many efforts during manufacturing, and convenience of self administration; tablet is the most popular among all the dosage forms existing nowadays to treat pathological conditions [1]. Various excipients are used in the pharmaceutical tablet industries to present desirable properties in the final product. To produce homogenous distribution of the pharmaceutical powders at the point of mixing, the excipients have to be hydrophilic as a disintegrant and have proper compactibility [2]. The principle of immediate release tablets initiated from the desire to supply patient with more routine or ordinary means of taking their medication when emergency treatment is required to overcome the drawbacks of extended release tablet[3]. The common manner of immediate
release tablets manufacturing, so that the tablet disintegrates rapidly, uses super disintegrant pharmaceutical powders [4]

Super disintegrant shows fast onset of action, cost effective and lead to better patient demands. So that, immediate release tablet is a best way for extending product life cycles, expanding active markets, and presenting opportunities for the products [5]

The utilizing of super disintegrating agent powders might be important to enhance the absorption, so that increasing the bioavailability of medicine [6]. To improve dosage form design, this research presents a detailed analysis of tablet formulations containing super disintegrant SSG as a single component to investigate its properties as a pure excipient without any effect from other active or inactive ingredient. These properties were examined from two different views, namely the effect of the most important process parameter which is the applied pressure during compaction cycle, and the effect of material properties on the tablet characteristics.

The most attractive option for using DC in tablet industry is due to it being affordable since it needs minimal processing actions, the produced tablets have faster dissolution, shows steadiness in the face of moisture and heat, exhibits less wear and tear on the used punches and facilitates validation to meet the needs of recent desired manufacturing practices [7, 8]. Direct compaction technique is used to form tablet containing a few milligrams of active ingredients which can be mixed with relatively coarse excipient particles so that the compaction properties of the components are controlled basically by the excipients [8, 9]

One of the knowledge gap in the previous literatures is most of these studies related to SSG tableting, have only been carried out by using wet granulation or mixtures of SSG with other ingredient by DC technique. In contrast, a key aspect of this study is use SSG as a single component by DC technique to address the properties of SSG tablets. Another significant to emerge from this study is the effect of applying different pressures on tablet specifications as the volume reduction during compression. Also the particle shape and morphology of SSG were visualized by SEM image and their effect on the ejected tablets specifications was stated. In addition, the impacts of these variables were investigated on the elastic relaxation, tensile strength, porosity, weight loss during the friability test, and the disintegration time of the formed compacts.

Materials and Methodology

A super disintegrant excipient, sodium starch glycolate (SSG), manufactured by Yung Zip Chemical Ind. Co. Ltd company, Malaysia. SSG is a form of modified starches that shows elastic properties with dramatic disintegrating properties[10] compacted by DC technique by the applied pressure ranged from 75,150,225,300, to 375 MPa. by using a universal testing instrument (Instron Universal Testing, Model 3382, Canton MA, USA) and A 13 mm diameter cylindrical-uniaxial-stainless steel die (Specac, UK).

Essential Tests to Check Tablet Characteristics and Quality

Brazilian Test

The radial tensile strength of tablets is determined by utilizing the maximum fracture force, tablet thickness, and tablet diameter by using Equation 1. In this study, the tensile force of the tablets was measured using a universal testing machine (Instron, Model 3356). Mathematical formula in the following equation [11].

\[
\sigma_t = \frac{2P}{\pi Dt}
\]  \hspace{1cm} (1)

Friability Test
The weight loss of each tablet was determined by placing 10 tablets of each formulation in a friabilator (Distek brand Model DF-3). The test was carried out by applying the standard method for friability by operating the drum for 4 min and 25 rpm[12]. Friability was determined using the following equation[13]:

\[
\text{Friability} = \left( \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \right) \times 100 \% \tag{2}
\]

Normally, a weight loss of less than 1 % during a friability test is acceptable. [14].

**Disintegration Test**

The disintegration time was measured by using a disintegration tester (Pharma Test D-63512, Germany). This test is beneficial to examine tablets or controlled-release formulations. For this reason, the test is used to determine the time required for disintegration compared to the duration of disintegration inside the GI tract [15].

**Elastic Relaxation Test**

To quantify the overall elastic relaxation that the tablet experiences during compaction and after ejection, the elastic relaxation or recovery was determined by comparing the minimum height of the tablet (\(T_{\text{min}}\)) during the loading stage and the height measured 24 hours after ejection (\(T_{\text{max}}\)) from the die. The percentage of the elastic relaxation (\(E\%\)) to characterize the ejected tablet elastic relaxation is given by the following equation[16-18].

\[
E\% = \left( \frac{T_{\text{max}} - T_{\text{min}}}{T_{\text{min}}} \right) \times 100 \% \tag{3}
\]

**Results and Discussion**

**Particle Shape and Morphology by SEM**

![SEM images for SSG](image)

The SEM images for SSG in Figure 1 shows that it has a perfectly spherical shape and sometimes an oval shape with a smooth surface without any meanders, ramifications or projections. This morphology for the SSG particle surface prevents the particles from deep or extreme overlap or interlocking with each other or with other powders during compression. In other words this shape and morphology helps the particles to slide past each other instead of interlocking during compression which make the particles deform elastically and absorb solvent rapidly.
Applied Pressure-Volume Relationship during Compression

Generally, when applying high pressures during tableting, low volume compacts may be obtained. As shown in Figure 2 for each tablet a dramatic volume change occurs when the compression stress increases from 75 MPa to 150 MPa, then further increases in the compression pressure give lesser corresponding volume reduction within the compact. The most acceptable explanation for this is the volume decrease reaches almost to a steady state level with a further increase in compression pressure due to the limited space for additional fragmentation and plastic deformation. This finding supports previous research into this subject area which links compression pressure and volume reduction [7, 19].

![Figure 2: applied pressure-volume relationship](image-url)

Essential Characteristics of a Compact

Elastic Relaxation Test

As shown in Figure 3, all ejected tablets show a decrease in elastic recovery with the compression pressure increasing till it reaches to almost near constant value after a 225 MPa compression pressure even as the compression pressure reaches the maximum value. As deduced by many researchers such as Kasa, Wu and others, this result may be explained by the fact that increasing the applied pressure may reach to the stage when there is almost no more room for particle rearrangement [19, 20]. At this stage the ejected tablets (tabletted under higher applied pressure) has less elastic relaxation than those compacted under low compression pressure. As a result, a high applied pressure may confer tablet volume and porosity size stability until the tablets reach the end user. there is almost no corresponding change in the elastic relaxation after 225 MPa.
Brazilian Test

Shang and others have interpreted this result as a higher compression pressure tends to give denser and more cohesive tablets which usually have higher strength [21]. This can result in permanently changing the shape of the particles, changing the relative positions of the particles, and decreasing the free space dimensions which leads to positively affecting the tensile strength of the tablets as shown in Figure 4. Tablets compacted under load equal to 225 Mpa and above, as stated in Figure 4 confer tensile strength to the tablets higher than 0.3 Mpa which consider desired conditions and fail product compacted under load less than 225 Mpa to keep desired shape as shown in Figure 5.
Friability

The results presented in Figure 6 show that the increase of compression pressure causes a reduction of friability percentage for all tablets. This is stated due to the high applied pressure resulting in good compactibility and high strength. As same as in the section 3.3.2, the tablets compacted under compression load less than 225 Mpa shows unacceptable products conditions in term of weight loss by friability. With a result lower than the dashed line (the 1 % control line) or achieved an acceptable limit for friability in Figure 6.

Disintegration Time

Tablet disintegration in this study has received considerable attention as an essential step in obtaining fast drug release. Figure 7 shows the disintegration time of tablets as a function of applied pressure during tableting. It is obvious that the disintegration time of the tablets increases quite linearly within the range of compression pressure used. There are several possible explanations for this result such as that stated by Riippi and others, where they interpreted this result as applying high pressures to a
powder bed then low porosities of the resulting compact can be achieved [22]. The porosity of tablets after production directly influences the activity of the tablets and makes liquid penetration easy via the tablets. As a result this leads to releasing the API immediately from the solid dosage form and improves the disintegration of the tablet [23]. Furthermore, in terms of the tensile strength-disintegration time relationship, porosity which is mainly decreased by increased applied pressure as shown in Figure 8, has a direct impact on the volume of the ejected tablets and affects their tensile strength [24]. This is further support for the findings in this section and demonstrates why the tablets compacted under a low pressure need a shorter time for disintegration than those compacted under a higher pressure.

Figure 7: Disintegration time for SSG tablets versus applied pressure

Figure 8: SSG Tablet porosity-applied pressure relationship
This finding is in agreement with the findings of Uddhav who showed that SSG powder is composed of granules that have the ability to quickly absorb and swell with water. The mechanism behind this action involves fast absorption of water leading to a huge increase in the volume of the SSG particles which results in uniform and rapid disintegration [25]. On the other hand, the small particle size, particle surface and morphology of SSG as shown in Figure 1 is another reason for the faster disintegration rate for this excipient as it can lead to faster water penetration and easier drug release in water.

**Recommended tablets formulation**

The recommended formulation have to achieve no less than 0.3 MPa tensile strength, no more than 1 % weight loss according to the friability test, and finally a moderate disintegration time[9, 12]. To validate the tested tablets in this research, the recommended tablet formulation is supported by previous studies and according to the current compacting parameter (13 mm die diameter) [9, 12]. The results of the percentage of tablets that passed successfully the tensile strength and friability tests are summarised in the following Figure 9a,b.

![Figure 9a: SSG tablets% passed tensile strength test](image)

![Figure 9b: SSG tablets% passed friability% test](image)

**Conclusion**

This study also illustrated a systematic analysis of the effect of changing applied load on the volume-applied pressure parameters during the compression process in addition to recommended formulation of the produced tablets. SSG powder has a free flowing characteristic due to it has spherical shape particles with smooth visualized by SEM images. And it attracts solvent fast to enlarge the tablets and disintegrate quickly as well as dissolve and accelerate the absorption of medicine from
gastrointestinal tract. Therefore, we have employ SSG in DC technique in this study. The tablets that can be considered as recommended formulations are those have good hardness can resist the marketing conditions, meet the needs of the patients in terms of the disintegration time, and protects the amount of API from interspersion or fragments by friability. These fragments are easy to lose, wear, and lead to a decrease in the weight of the tablets when exposed to any attrition and shocks.

All of these specifications are met in the SSG tablet compacted under 225, 300, 375 Mpa compression load so it can be considered as a recommended tablet formulation with regard to the industrial scale. Disintegration time in this study tolerance between 32 seconds for the tablets compacted under 75 Mpa, to 2.07 minutes for the tablets compacted under 375 Mpa. This can be considered as the most obvious finding to emerge from this study.

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