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Evaluation of Different Pre-Processed Directly Compressible Paracetamol

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1. Introduction

In this study, the behavior as well as compaction characteristics of different types of Paracetamol DC powder were investigated using compaction simulator. Paracetamol as API itself has poor flowability and compressibility and wet granulation is the common method for tableting. Atabay Fine Chemical company is the only European manufacturer of paracetamol and have directly compressible paracetamol alternatives for direct tableting process.

DC grade Paracetamol is a pre-processed formulation and there are several steps for increasing the powder flow properties during manufacturing. Importance of this study is to simplify the materials elasticity, plasticity and brittleness in order to understand the process and formulation composition on compaction behavior. Compaction Simulator was used to investigate the powder consolidation properties of pre-processed paracetamol under pressure.

2. Materials And Methods

Materials

Four different types of pre-processed directly compressible Paracetamol (Atabay Fine Chemicals) (B26, B29, B32, and B35 were evaluated in the study.

Table1 *Different types of pre-processed Paracetamol DC.*

ParacetamolTypes	Code
Paracetamol 90% DC (APC-230-PGS)	**B26**
Paracetamol 90% DC (APC-230-PGS-A)	**B29**
Paracetamol 90% DC/C (APC-230-CP)	**B32**
Paracetamol 90% DC (APC-230-C)	**B35**

Particle Size Distribution

Different formulation and processed Paracetamol DC grade samples particle size was determined using dry sieving method with Sieves (EP).

Scanning Electron Microscope (SEM)

Figure 3 a, b, c, and d shows morphology of powders by Zeiss EVO/LS 10 Scanning Electron Microscope (SEM) with 40x magnification.

Powder Properties

Compressibility of powders, were calculated using bulk and tapped density values. True density was measured using helium pycnometer.

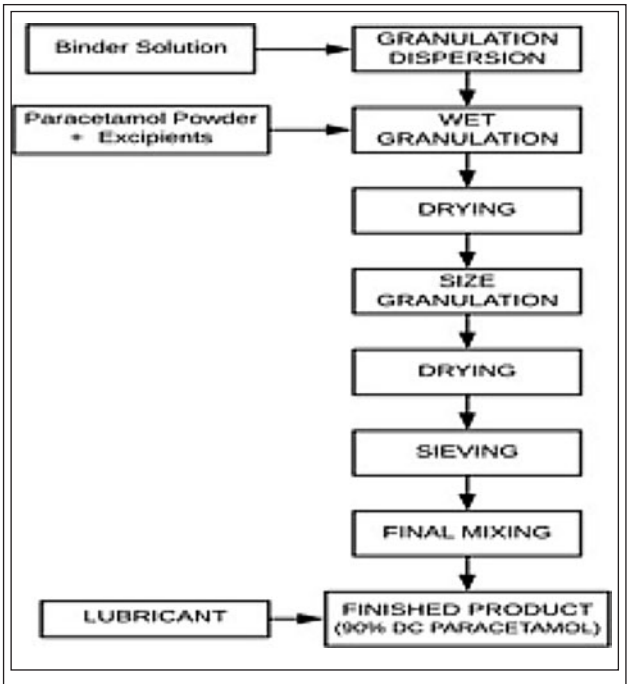

Figure 1 *Granulation steps of DC Paracetamol*

Pre-process steps

See *Figure 1.*

Tabletting

Tablets were produced with different types of DC Paracetamol at compaction pressures 50, 100, 200, and480MPa using Compaction Simulator, Stylcam R200 with an 11.28mm round, flat faced Euro B punch.

Tablet Controls

Tablets were controlled for weight variation, thicknessand hardness.

Tensile strength is calculated from tablet hardness (F),tablet diameter (D) and tablet thickness (t) as shown inthe equation below [1].

$$\textbf{\textit{Eq}}: Tensile\ strength\ (MPa) = \frac{2F}{\pi Dt}$$

Compaction properties of powders as well as quantify the materials elasticity, plasticity and brittleness using Yield pressure value (Py) was produced by compaction simulator Analis Software program.

3. Results

Particle Size Distribution

Particle size distribution graph shows the different types of Paracetamol DC structure. From the graph (***Figure 2***), it is seen that B32 has more fine particles. B26, B29, and B35 allhave similar structure, having similar percentage of retained particles between 60-325 mesh. Which is concurrent with the SEM images (***Figure 3***).

Pre-formulation Studies

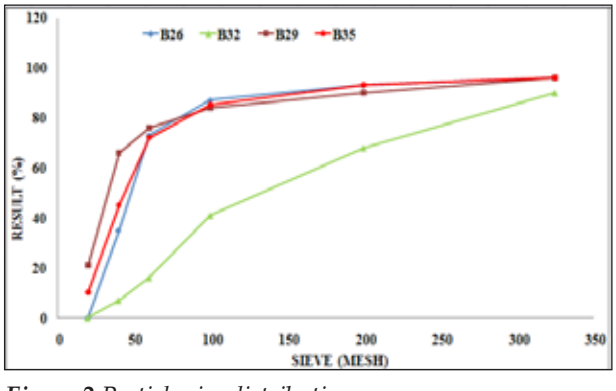

Figure 2 *Particle size distribution*

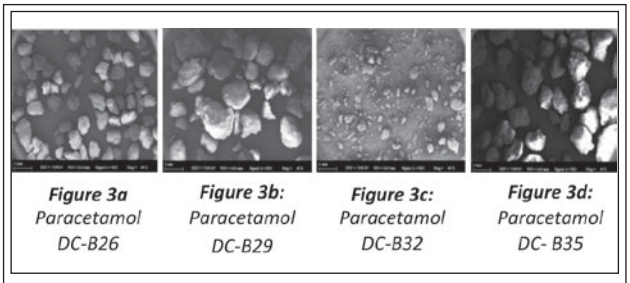

Figure 3

Using two densities data (tapped and bulk density), Carr's Index and Hausner's Ratio were calculated. The measurement results helped in understanding the flow property and compaction behavior of the different powder types. Carr's index and Hausner's Ratio resultswere given as: B29 and B35 (between 0-10% and 1.00-1.11respectively), as excellent, B26 (between 10%-15% and 1.12-1.18 respectively), as good, and B32 (between 16%-20% and 1.19-1.25 respectively), as fair. Smaller particle size as seen in ***Figure 3*** correlates to decrease in powder flow. [2].

Effect of Compression Pressure on Tensile Strength

Pressure between 50MPa and 480MPa was applied to 4 types of DC Paracetamol. Figure 4 shows the relationship between tensile strength and compaction pressure for DC Paracetamol tablets. All DC Paracetamol types between 200MPa and 480MPa showed significant increase, with exception to B35 which showed little response in tensile strength with increased compaction pressure. As compression pressure increased (above 250MPa), differences in tensile strength are more apparent for different types ofDC Paracetamol. An increase in surface area causes a concomitant increase in compact strength, due to increased bonding area. Tensile strength results showed B26

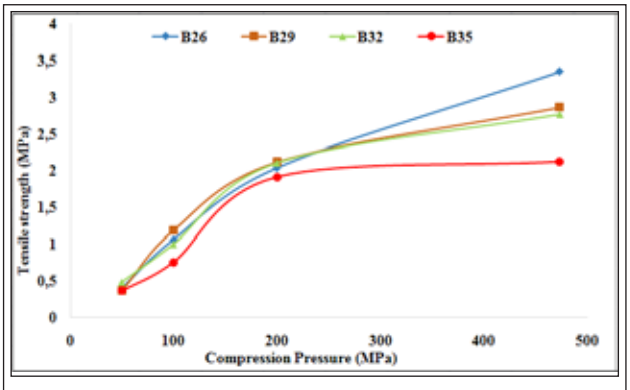

Figure 4 *Compactability plot: tensile strength as a function of compression pressure (n=6*

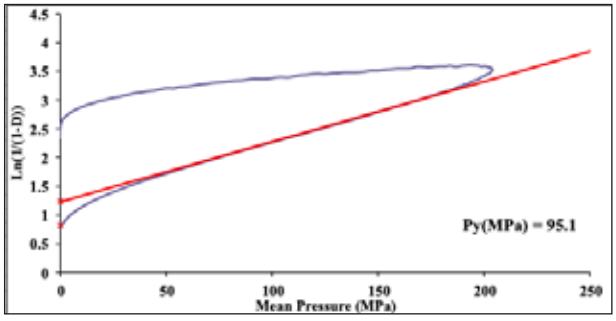

Figure 5 *Heckel Plot for B32 at 200MPa compaction pressure*

responded more positively to pressurewith a consistent linear increase. This is due to B26 having a surface area of 2.54 m^2/g.

As seen in figure 5, the mean yield pressure (Py), produced by Heckel plot, is directly related to the ability of a material to show brittle fragmentation under pressure. Py describes the tendency of the material to deform either by plastic flow or brittle fragmentation [3].

Generally, a higher Py value reflects high resistance to pressure and brittle fragmentation [4]. A Py value of 80 MPa reflects brittle fragmentation of a powder. Py values obtained for B26, B29, B32 and B35 are 81.3, 90.9, 95.1, and 81.6 MPa respectively. Results are fairly similar however, the highest Py value is seen to be B32.

Based on this, the order of brittle fragmentation is B32 B29 B35 B26.

4. Conclusion

The results from Carr's index and Hausner ratio for allDC Paracetamol types showed good powder compressibility. Differences in the particle shapes and size for all types of DC Paracetamol showed differences in tablet compactibility. With B26 having highest tensile strength above 250(MPa).

Differences in compressibility deformation mechanism was primarily dependent on pre-processed composition of DC Paracetamol. Further study can be done to investigate the effect of each component on final tabletproperties.

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