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Compression & Compaction Behavior of Paracetamol Granules by Heckel Plot Analysis

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ABSTRACT: Heckel plots are based on the assumption that the porosity of a tablet decreases as the compression pressure increases. They are sensitive to variations in *.369measured density, so it's important to report the density values used and includes the standard error in the measurement. Paracetamol is a analgesic, and anti-pyretic agent used in the management of fever & pain. Most of drugs are marketed as tablets. The current aim of the study was to systematically investigate compression and compaction behavior of Paracetamol granules by Heckel Plot analysis. Before the development of any dosage form, it is essential to find some fundamental physical and chemical properties of the drug molecule and other divided properties of the drug powder are determined. It helps to decide many of the approaches in formation and development. Thus before selection of any API, excipients, the Heckel Plot analysis should be completed for any successful formulation. In this research article we focused on compression and compaction behavior of Paracetamol which were investigated and reported.

KEYWORDS: Heckel Plot analysis, Compression, Compaction, Paracetamol

I. INTRODUCTION:

A Heckel plot is a graph that shows the relationship between the negative natural logarithm of ε and the applied compression pressure. It has several significant uses, including:

- **Identifying deformation**

A Heckel plot can help identify the primary type of deformation in a sample.

- **Studying compaction**

A Heckel plot can be used to study how a sample compacts and compresses.

- **Determining tablet formation**

The point of intersection on a Heckel plot shows the lowest force needed to form a coherent tablet.

- **Correlating crushing strength**

The values of k on a Heckel plot can be correlated with the crushing strength of tablets.

- **Deriving material properties**

A Heckel analysis can be used to derive important material properties of powders, such as yield strength.

- **Quantifying powder plasticity**

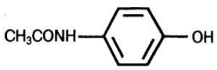
An in-die Heckel analysis can be used to quantify powder plasticity. It can also be used to evaluate the effects of factors such as lubrication efficiency, pressure, and tooling size.

Heckel plots are based on the assumption that the porosity of a tablet decreases as the compression pressure increases. They are sensitive to variations in measured density, so it's important to report the density values used and include the standard error in the measurement

PARACETAMOL(Acetaminophen) :

Synonyms:

- ynonyms: 4′-Hydroxy-acetanilide; para - acetaminophenol; acetophenum; para-acetylamidophenol; N-acetyl-para-aminophenol; para-acetylaminophenol; para-hydroxyacetanilide; N-para-hydroxyphenylacetamide



$C_8H_9NO_2$ Mol. wt: 151.16

Physical & Chemical Property:

- Description: White odourless crystalline powder; large monoclinic prisms from water
- Melting-point: 169–170.5 °C
- Solubility: Soluble in water (1:70, 1:20 at 100°C), ethanol (1:7), acetone (1:13), chloroform (1:50), glycerol (1:40), methanol (1:10), propylene glycol (1:9) and solutions of alkali hydroxides; insoluble in diethyl ether. A saturated aqueous solution has a pH of ~6.
- Spectroscopy data: Infrared, ultraviolet, nuclear magnetic resonance, fluorescence and mass spectra have been reported.
- Stability: Dry, pure Paracetamol is stable to 45°C. Contamination with traces of Para-aminophenol, and humid conditions that cause hydrolysis to Para-aminophenol, result in further degradation and discoloration. Slightly light-sensitive in solution, and degradation is catalyzed

by acids or bases.

- Dissociation constant: pKa = 9.0–9.5
- Partition coefficient: Pc = 6.237 (octanol: pH 7.2 buffer)

Use of Paracetamol:

Paracetamol is used as an analgesic and antipyretic drug. It is the preferred alternative analgesic-antipyretic to aspirin (acetylsalicylic acid), particularly in patients with coagulation disorders, individuals with a history of peptic ulcer or who cannot tolerate aspirin, as well as in children

Dose:

The conventional oral dose for adults is 500–1000 mg. Dosing may be repeated every 4 h as necessary, but the total daily dose should not exceed 4000 mg. For children, the recommended dose is 10–15 mg/kg bw; no more than five doses should be administered over 24 h. Prolonged use (for more than ten days) and use for young children is not recommended

II. MATERIALS AND METHODS:

The process of powder compression into a tablet can be generally divided into four predominant stages. Although they are defined as sequential, they can in reality occur simultaneously. These stages are; rearrangement of particles, plastic deformation and (or) fragmentation and elastic deformation and elastic shape recovery following unloading (figure 1)

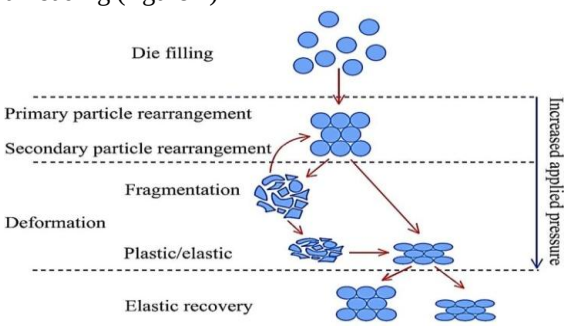


Figure 1: Schematic illustration of the powder compression cycle

After filling the powder into the die cavity, the consecutive action of the punch causes rearrangement of the particles. Soon thereafter, the system reaches a state where its capacity to rearrange is exhausted as the particles are constrained or locked into position by more structurally stable contact with their neighbors. This junction can be referred to as a constrained state. During this initial stage a degree of fragmentation can occur. Upon reaching the constrained state, any further reduction in the porosity of the powder bed can only occur as a result of a mechanical change in the structure of each of its composing particles. Such a change must take place in response to the increasing pressure on the powder. For simplicity two main ways of absorbing external loads can be considered; deformation and fragmentation of the particles. If the particles are plastic or elastic in nature they will deform to absorb the increasing applied load. If a particle is brittle in nature, it will break into small earpieces which then fill up the pores.

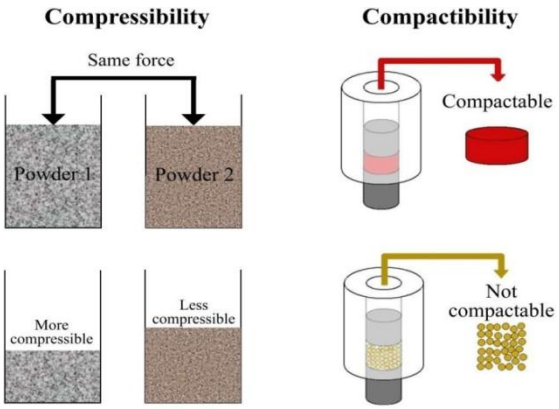


Figure 2.Examples of compressibility and compactibility

Assuming the applied force is large enough, the particles can undergo one or all of these structural changes. It is during this transitional phase that bonding between the contacting surfaces of the powder particles occurs, either as in the case of deformation, by an increased area of contact between the particles, or by an increase in the number of bonding sites, as in the case of breakage. Finally, at maximum applied pressure, when the porosity is reduced to 5 - 10 %, i.e. when almost all pores are eliminated, the powder will no longer be an autonomous system of particles, but rather a single solid unit. Further compression past this point will invariably be controlled by the elastic deformation of this solid unit, as there is no other possibility for permanent structural change. Consequently, when the pressure is removed, the tablet begins to relax into its final dimensions. The terms compressibility and compatibility are often used to describe a powder (Fig.2). A very compressible powder is one that significantly densifies upon compression. Powders with very small particle size are normally very compressible. However, this does not mean that they are able to form tablets. The compactibility of a powder determines whether or not it can form a tablet.

Compacting powders into a tablet form is a process of reducing porosity and of forming materials into a solid compact. The structure of powders changes during compression and densification takes place mainly due to the rearrangements of particles, their fragmentation and

plastic deformation. The compression of powders into a tablet form is a complex and irreversible dynamic process. Several relationships between stress- strain, pressure-volume, pressure-porosity or pressure-density have been proposed to define the compaction behavior of powders, since natural strain is proportional to changes in powder-bed height or volume under applied pressure. Compaction equations put into relation the state of compaction parameters such as porosity, volume or density with respect to the applied pressure. In the interpretation of the data of compaction it is important to know what compaction mechanisms operate at different levels of pressure.

Heckel Equation:

The Heckel equation is one of the most common equations describing the mechanism of reducing volume during compaction. It is based on the assumption that powder compression follows first-order kinetics with interparticulate voids as the reactant and the densification of the powder as the product. Then the degree of compaction with increasing compressing pressure is proportional to the porosity.

The Heckel equation is based upon analogous behavior to a first-order reaction, where the pores in the mass are the reactant, that is: where,

$$\mathrm{Log}\frac{1}{E} = K_y P + K_r$$

Ky is a material-dependent constant inversely proportional to its yield strength S (Ky = 1/3S), and Kr is related to the initial repacking stage, and hence E0. The above relationships may be established by simply measuring the applied compressional force F and the movements of the punches during a compression cycle and translating this data into values of P (applied pressure) and E (porosity). For a cylindrical tablet, P is given by

$$P = \frac{4F}{\pi \cdot D^2}$$

$$E = 100 \cdot \left[1 - \frac{4w}{\rho_t \cdot \pi \cdot D^2 \cdot H} \right]$$

where, D is the tablet diameter. Similarly, values of E can be calculated for any stage from:
where, w is the weight of the tabletting mass, ρt is its true density, and His the thickness of the tablet at that point (obtained from the relative punch displacement measurements). The particular value of Heckel plots arises from their ability to identify the predominant form of deformation in a given sample. Materials that are comparatively soft and that readily undergo plastic deformation retain different degrees of porosity, depending upon the initial packing in the die. This in turn is influenced by the size distribution, shape, etc. of the original particles. Heckel plots for such materials are shown by type ‘a’in Fig. 3; **sodium chloride** is a typical example. Conversely, harder materials with higher yield pressure values usually undergo compression by fragmentation first, to provide a denser packing. Label ‘b’ in Fig. 3 shows Heckel plots for different size fractions of the same material that are typical of this behavior. **Lactose** is one such material. Type ‘a’ Heckel plots usually exhibit a higher final slope (Ky) than type ‘b’, which implies that the former materials have a lower yield stress. Hard, brittle materials are, in general, more difficult to compress than soft, yielding ones because fragmentation with subsequent percolation of fragments is less efficient than void filling by plastic deformation. In fact, as the porosity approaches zero, plastic deformation may be the predominant mechanism for all materials.

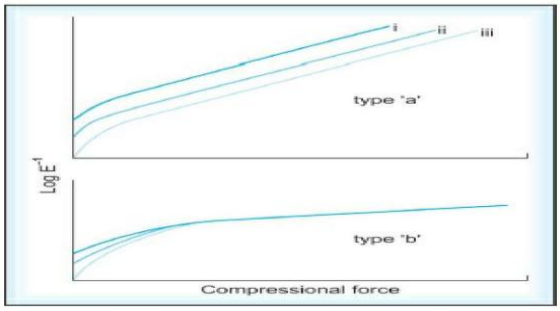


Fig. 3: Examples of Heckel plots. Curves i, ii and iii represent decreasing particle size fractions of the same material. Type ‘a’ curves are typical of plastically deforming materials, while those in which fragmentation occurs initially tend to show type ‘b’ behavior.

The two regions of the Heckel plot are thought to represent the initial repacking stage and the subsequent deformation process, the point of intersection corresponding to the lowest force at which a coherent tablet is formed. In addition, the crushing strength of tablets can be correlated with the value of Ky of the Heckel plot; larger values of Ky usually indicate harder tablets. Such information can be used as a means of binder selection when designing tablet formulations. Note that Heckel plots can be influenced by the overall time of compression, the degree of lubrication, and even the size of the die, so that the effect of these variables can also be studied. Another important factor in the use of all force-porosity relationships is that for many formulations, there is a relatively narrow optimum residual porosity range that provides adequate mechanical strength, rapid water uptake, and hence, good disintegration characteristics. It is to the formulators’ advantage to identify this

optimum range and be able to predict compressing conditions needed to reach it. In addition to the predictive capability, establishing behavioral patterns for a given formulation (so-called "fingerprinting") may provide valuable diagnostic information in the event that a particular batch of the product causes problems. Note also that the initial porosity can affect the course of the entire compressional sequence, and that in general, slow force application leads to a low porosity for a given applied load.

Procedural sequence:

1. Weigh 600mg of Paracetamol granules.
2. Compress the granules using KBR press for 30sec at pressure 0.5ton.
3. Repeatstepstep1 & 2, and prepare minimum10 tablets.
4. Similarly prepare 10 tablets of Paracetamol granules at pressure of 1, 1.5, 2 and 2.5 ton.
5. Take weight of tablets and record it in the table.
6. Determine thickness and diameter of tablets using Vernier caliper and record in the table.
7. Record hardness of tablet using Monsanto hardness tester and record in the table.
8. Place above data in the predesigned Excel and calculate density, relative density, porosity and tensile strength.
9. Finally Plot the graphs.

EQUIPMENT'S USED:

Paracetamol granules, KBR press, 13 mm die and punches, Vernier caliper, Monsanto hardness tester.

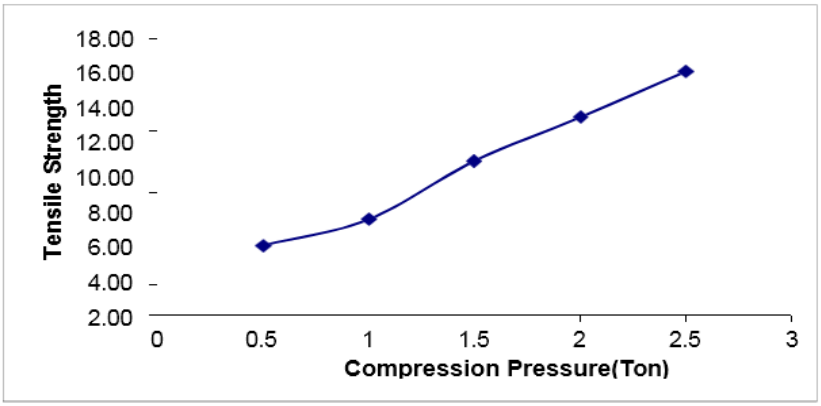
Observations

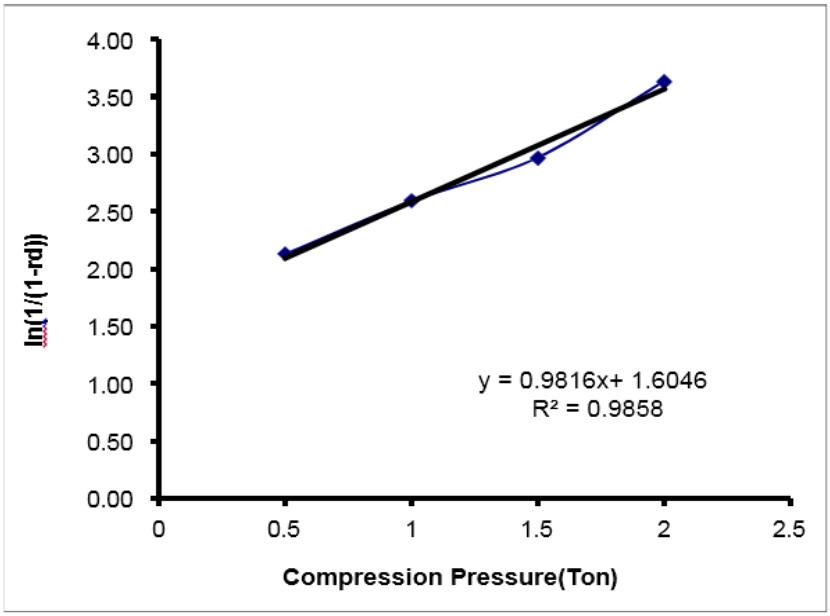
Compression pressure in ton	Weight of Tablet in gm	Thickness of Tablet in cm	Diameter of Tablet in cm	Radius of Tablet in cm	Hardness of Tablet in kg/cm^2
0.5	0.6	0.42	1.3	0.65	3.9
1	0.6	0.4	1.3	0.65	5.1
1.5	0.6	0.39	1.3	0.65	8
2	0.6	0.38	1.3	0.65	10
2.5	0.6	0.37	1.3	0.65	12

Calculations

Compression pressure ton	Density gm/mm^3	Relative density (rd)	1/(1-rd)	ln (1/(1-rd))	Porosity	Tensile strength
0.5	1.08	0.88	8.40	2.13	11.90	4.55
1	1.13	0.93	13.33	2.59	7.50	6.25
1.5	1.16	0.95	19.50	2.97	5.13	10.05
2	1.19	0.97	38.00	3.64	2.63	12.89
2.5	1.22	1.00				15.89

Graphs





III. RELSULT & DISCSION:

Heckel plot analysis of Paracetamol granules is as follows:

Slope(K)	Intercept(A)	Yield Strength	Mean Yield Pressure
0.98	1.60	2.94	1.02

Graph of tensile strength verses compression pressure indicated that increase in the tensile strength of tablet with increase in compression pressure. Graph of porosity verses compression pressure indicated that decrease in porosity of tablet with increase in compression pressure. Heckel plot analysis is important for tablet formulation because it can help identify the optimum residual porosity range for a formulation. This range provides adequate mechanical strength, rapid water uptake, and good disintegration characteristics

IV. CONCLUSION:

Compression and Compaction behavior of Paracetamol granules studied successfully by Heckel plot analysis. Higher value of K indicates more plastic material, Mean yield pressure is reciprocal of K, Yield strength (Y) is 3K.

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