**PREFORMULATION STUDIES OF GRANULES**

**AIM**

To perform the Pre-Formulation studies of given granules.

**REQUIREMENTS**

Paracetamol, Mannitol, Avicel pH 101, SSG, Talc, Magnesium stearate.

**PRINCIPLE**

The study prior to formulation of a dosage form is called as Pre-formulation study. The Pre-formulation of a solid dosage forms include study of Flow properties of the granules that were to be compressed or to be filled into capsules. In the preparation of solid dosage forms the Flow properties of granules plays a vital role as the flow properties like Angle of Repose, Carr’s Index, Hausner’s ratio and Density characteristics are having effect on the different desired characteristics of dosage forms like Content uniformity, Uniformity of Weight, Hardness etc.

**PROCEDURE**

Weighed quantities of Ofloxacin, Mannitol, Avicel PH-101, and SSG were added in geometric proportion and uniformly blended. This uniformly blended mixture was passed through a sieve. To this mixture Glidant and Mg. Stearate were added and gently mixed for 5-10 minutes in a polyethylene bag. The hardness was adjusted in between 2-3 kg and then the tablets were compressed by direct compression method.

The working formula for one tablet is

Paracetamol : 30 mg

Mannitol : 144.75 mg

Avicel pH 101 : 162.75 mg

SSG : 18 mg

Talc : 3 mg

**EVALUATION OF BLEND**

1. **Angle of Repose**

The angle of repose was determined by funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the blend. The drug excipient blend was allowed to flow freely on to the surface. The angle of repose was calculated by using following equation.

Tan ø = h/r

Where h = height of the powder pile.

r = radius of the powder pile.

|  |  |
| --- | --- |
| **ANGLE OF REPOSE(θ) DEGREES** | **FLOW** |
| <25 | Excellent |
| 25-30 | Good |
| 30-40 | Passable |
| >40 | Very poor |

1. **Carr’s consolidation index**

It is defined as

This property is also known as compressibility. It is indirectly related to the relative flow rate, cohesiveness and particle size. It is simple, fast and popular method of predicting powder flow characteristics.

Fluff density is the ratio of mass of powder to the fluff volume. Fluff volume is the volume occupied by a certain mass, when gently poured into a measuring cylinder.

Tapped density is the ratio of mass of powder to the tapped volume. Tapped volume is the volume occupied by the same mass of powder after a standard tapping of a measure.

Compressibility index can be measure of the potential strength that a powder could build up in its arch in a hopper and also the ease with which such an arch could be broken.

**Method:** Using a suitable adhesive, the base of a 10 ml tarred measuring cylinder is fixed to the standard rubber bung at the top of the 250 ml cylinder. A powder sample (about 5.0 g) is transferred into the tarred 10 ml cylinder with the help of a funnel. The 250 ml measuring cylinder is placed on the tapping apparatus. The initial volume occupied by the powder is denoted as V0.

The contents are tapped in the following order, 2, 4, 6, 8, 10, 20, 30 and 50 taps. After completing the tappings, the volume is denoted as V2, V4 .................V50.

The powder is carefully collected from the cylinder and weighed (W).

Fluff density (ρb, minimum) = w/vog/cc

Tapped sensity (ρb, maximum) = w/v50 g/cc

Consolidation index can be calculated using the equation

The nature of flow is inferred by comparing the data with the index given in the below table

|  |  |
| --- | --- |
| **Consolidation index** | **Flow** |
| 5-15 | Excellent |
| 12-16 | Good |
| 18-21 | Fair to passable |
| 23-35 | Poor |
| 33-38 | Very poor |
| >40 | Very very poor |

1. **Hausner ratio**

It is defined as the ratio of the tapped density to bulk density it can also be calculated by using the formula by using carr’s consolidation index

Where C is Carr’s consolidation index value

The relationship of Hausner ratio to that of flow property is as follows

| **Flow Character** | **Hausner’s Ratio** |
| --- | --- |
| Excellent | 1.00 – 1.11 |
| Good | 1.12 – 1.18 |
| Fair | 1.19 – 1.25 |
| Passable | 1.26 – 1.34 |
| Poor | 1.35 – 1.45 |
| Very poor | 1.46 – 1.59 |
| Very, very poor | >1.60 |

1. **Bulk density**

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is of great importance when considers the size of high dose capsule product or homogeneity of allow dose formulation in which these are large differences in drug and excipient densities

Bulk density is determined by graduated cylinder containing a known mass of powder whose initial volume is noted. Cylinder is fixed on the mechanical tapper apparatus. Then the final volume is noted, and this bulk volume. Then bulk density is calculated is using

1. **Tapped density**

It was determined by placing a graduated cylinder, containing known mass of drug excipients blend. The cylinder was allowed to fall under its own weight on to a hard surface from the height of 10cm at 2 second intervals. The tapping is continued until no further change in volume was noted.

**REPORT**

The different preformulation parameters of the granules were found to be as follows:

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Value** | **Inference** |
| Angle of repose |  |  |
| Carr’s consolidation index |  |  |
| Hausner ratio |  |  |
| Bulk density (gm/cc) |  |  |
| Tapped density (gm/cc) |  |  |