Methods of Tablet Production

There are three main methods of tablet production, namely, direct compression, dry granulation and wet granulation.

I. *Direct compression (D.C.):* whenever it is applicable, D.C. is the most preferred method because of its simplicity. In fact, D.C. method composes only of three steps which are weighing, mixing and compression.

Advantages:

1. Low labor input.
2. Dry process (useful for water sensitive drugs).
3. Fewest processing steps.
4. Less time consuming.
5. Less cost than other methods.

Disadvantages:

1. The difference in particle size and density between the drug and the diluent may result in poor content uniformity.
2. Because of the dry nature of D.C., static charges may build up which may prevent uniform drug mixing.
3. Not suitable for large and small-dose drugs and is best applied for moderate-dose drugs. Large-dose drugs require large amount of diluents thus, large tablets are produced which cannot be swallowed. On the other hand, small-dose drugs are not preferred to be compressed directly because a uniform blend of the drug with the diluent cannot be achieved.

Note: it is worth to mention that not every diluent can be used for D.C. In addition to the general requirements that will be stated later, diluents that used for D.C. must be characterized by the followings:

1. They must have good flowability.
2. They must have good compressibility and good pressure-hardness profile.

Example: suppose there are three diluents A, B and C to be used in the preparation of tablets by D.C. technique:

Diluent A requires 1 ton to produce tablets with hardness of 5 Kg.

Diluent B requires 2 ton to produce tablets with hardness of 5 Kg.

Diluent C requires 3 ton to produce tablets with hardness of 5 Kg

Hence, diluent A is the best.

3. They must have high capacity.

Example:

Diluent A: 200 mg of the diluent can carry up to 100 mg of active ingredient. The total tablet weight is 300 mg and percentage of active ingredient is 33%.

Diluent B: 200 mg of the diluent can carry up to 50 mg of active ingredient. The total tablet weight is 250 mg and percentage of active ingredient is 25%.

Therefore, diluent A is more preferred.

4. Reworkable without loss of flowability or compressibility.

5. They must have high bulk density. Bulk density can be measured easily by measuring the *volume* of certain *weight* of that diluent.

Example: if 50 gm of diluent A and B were taken. Their volumes were measured in graduated cylinder and were found to be 40 and 50 ml, respectively. Thus:

Bulk density for A = weight/volume = 50/40 = 1.25

Bulk density for B = 50/50 = 1

Therefore, diluent A is more preferred.

Examples of diluents used commonly in D.C. technique are microcrystalline cellulose and dicalcium phosphate dihydrate.

II. *Dry granulation:* this method is used when D.C. is not applicable (e.g., large-dose or poor compressibility drugs) and when wet granulation cannot be used (e.g., drugs sensitive to heat or moisture). Vitamins and effervescent tablets are examples of products prepared by dry granulation.

Dry granulation involves the following steps:

1. Initial compression: this step is called *slugging*. After mixing of the formula, the powder is compressed into large tablets usually 25 mm in diameter called slugs. The pressure used to produce the slugs is usually less than that used in the final compression. This step may be repeated more than one time. In fact, the two or more times that the formula is subjected to compaction pressure will strength the bonds that hold the tablet together.

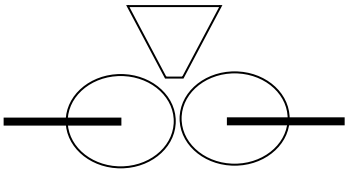
2. Milling: this step involves the breaking of slugs into smaller pieces by using a suitable mill.

3. Homogenization: to produce granules with uniform particle size. It is done by certain machine called homogenizer.

4. Final compression: to produce the final tablet.

Note: In slugging, the active ingredient is mixed with some of the excipients (not all of excipients) and compressed using the ordinary tablet machine but with large die.

On large scale production, another machine called roller compactor or chilsonator is used. Chilsonator is capable of producing as much as 500 kg/hr or more of ribbon-like material which is milled prior to the final compression.



Chilsonator

Advantages of dry granulation

1. Useful for heat or moisture sensitive materials.

2. Less equipments and space than that required by wet granulation.

3. Improve tablet disintegration since it does not involve the use of water so it increases water-uptake ability of the disintegrant.

4. This method is of value in the production of certain dosage forms as effervescent tablets.

Disadvantages

1. Required high duty machine if compared with D.C.

2. Since it is dry process, more dust is produced which may contaminate other drug.

III. *Wet granulation*: it resembles the dry granulation method in most of its steps except that in wet granulation the granules are formed by binding the powder together with an adhesive instead of compaction. This technique employs a binder as solution, suspension or paste. Sometimes, the binder is added as non aqueous solution or even as dry powder if the drug is negatively affected by the moisture.

Wet granulation technique can be summarized by the following steps:

Step1: weighing and mixing of active ingredients, diluents and disintegrant.

Step 2: preparation of the wet mass. The binder in a liquid form is added stepwise with continuous mixing to prepare the wet mass. The liquid plays a key role in the granulation process. Liquid bridges (bonds) are developed between particles and tensile strength of these bonds increased as the amount of the added liquid is increased.

The binding capacity of the binder in liquid form is more than that in dry form. e.g., starch can be used as a binder both as a dry powder and paste, but the latter is more effective.

Step 3: screening of the *wet* mass to form the granules. The wet mass is passed through a screen (usually 6-8 mesh) to prepare the granules. This can be done by the hand or suitable machine, e.g. oscillating granulator.

Step 4: drying. The wet granules are spread evenly on a piece of paper in the try oven to remove the solvent that used in the preparation of granules. Over drying is not preferred since it produces friable granules and water content of the granules should be between 2-4%.

Step 5: screening of the *dry* granules. The granules are passed through a screen of smaller size than that used to prepare the original granules. Screens of 12-20 mesh are usually used for this purpose.

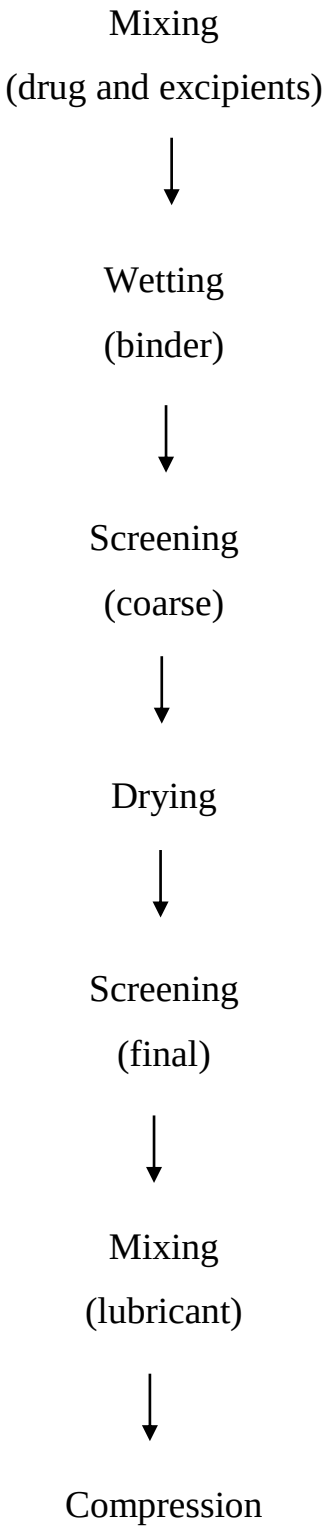
This step is necessary so that the die cavities are filled completely by the resulted free-flowing granules. Otherwise, air spaces left by the too large granules result in the production of uneven tablets. In addition, this step is useful in the separation of granules that have been aggregated during the drying process (step 4).

Step 6: addition of the lubricant and mixing with the granules.

It is worth to mention that the disintegrant may be added in step 1 (intragranular) or in step 6 (extragranular) and sometimes in both steps. The intragranular addition results in slow disintegration whereas the extragranular addition results in fast disintegration. If it is added in both steps, this results in faster disintegration.

Step 7: compression.

The following scheme summarizes the wet granulation.



Advantages of wet granulation

1. More homogeneous color is obtained since the color is dissolved in the binder solution.
2. Less dust and contamination.
3. No static charges due to the presence of water. Therefore, more uniform mixing.

Disadvantages

1. Requires more steps and machines.
2. Time consuming.
3. High labor input.
4. Costly.
5. Not suitable for water and/or heat sensitive drugs.

Advantages of granulation in general

Regardless of being wet or dry granulation, the process of converting a powder to granules involves the following benefits:

1. To increase the bulk density and flowability of the formula. This in turn will ensure proper die filling and minimize weight variation in the produced tablets.
2. To improve mixing homogeneity and prevent segregation.
3. To improve the compressibility either by the binder (in wet granulation) or by the more than one compression (in dry granulation).