hygroscopic substances. In such cases, absorbents, such as oxides and carbonates of magnesium and calcium and kaolin are added to the powered drug. These inert material acts as a protective absorbent.

3. *Glidants:* To ensure a regular flow of power into the automatic capsule machine glidants are mixed with the medicaments. The various glidants used for the purpose are talc, magnesium stearate and calcium stearate.
4. *Antidusting compounds:* During the filling of capsules by an automatic filling machine, a lot of dust comes out of the machines. The dust is inhaled by the operator of the machine. It can pose a serious health hazard especially when the dust of the potent drugs is inhaled by the workers. To avoid this, some antidusting components, like edible oils, are added to the formulation.
5. *Wetting agents:* Which improve water penetration for poorly soluble drugs, e.g. sodium lauryl sulfate.
6. *Disintegrants:* Which produce disruption of the powder mass, e.g. crospovidone, sodium starch glycolate.

Capsule Shell Filling

Hand operated hard gelatin capsule filling machines: Hand operated and electrically operated machines are in practice for filling the capsules but for small and quick dispensing hand operated machines are quite economical.

A hand operated gelatin capsule filling machine consists of the following parts and is shown in Fig. 1.3.

1. A bed with 200–300 holes.
2. A capsule loading tray.
3. A powder tray.
4. A pin plate having 200 or 300 pins corresponding to the number of holes in the bed and capsule loading tray.
5. A lever.
6. A handle.
7. A plate fitted with rubber top.

All parts of the machine are made up of stainless steel. The machines are generally supplied with additional loading trays, beds, and pin plates with various diameters of holes so as to

Optional ingredients for solution fills are mentioned below:

- *Water or alcohol:* Up to 10% w/w (if needed for solubility).
- *Glycerin:* 1 to 4% w/w (to retard the migration of the glycerin out of the shell into the fill).
- *Polyvinylpyrrolidone:* Up to 10% w/w used in combination with PEG (can increase drug solubility, and also improve stability by inhibiting drug recrystallization).

3 *Suspension fills:* Active dispersed in a carrier.

- Suspensions can accommodate about 30% solids before viscosity and filling become a problem.
- Suspensions can be heated up to 35°C to decrease viscosity during the filling process.
- Suspended solids must be smaller than 80 mesh–mill or homogenize before filling to prevent needles from clogging during filling.

Materials to be Filled

As stated earlier, it is possible to fill liquids, semi-solids as well as solids into soft gelatin capsules. The liquids that are packaged are generally of the following kinds:

1. Vegetable or aromatic oils, hydrocarbons, ethers, esters, alcoholos and organic acids which are water immiscible.
2. Polyethylene glycols and non-ionic surfactants which are water miscible.
3. Water miscible and relatively non-volatile compounds such as glycerin, propylene glycol (up to 5–10% of total liquid), isopropyl glycol, etc.

The liquid combinations for encapsulation in soft-gelatin capsules must be able to flow by gravity at about 35°C or less. In general, liquids ranging in viscosity from 0.2 to 3000 CPS. at 25°C, can be encapsulated without any difficulty, except in few cases like glycerin, where due to lack of tack, the blinding of slide valves and pumps may be caused. The liquids to be filled in soft capsules generally call for no formulation and can be right away filled. Liquids which cannot be capsulated are water (more than 5%), alcohols, ketones, acids, amines, esters, etc. which can leak through the capsule shell. Liquids with pH below 2.5 or above 7.5 should also be avoided since acidic liquids cause hydrolysis of the shell and alkaline ones cause tanning affecting solubility characteristics of the shells.

Record results

Capsule number	*Weight of intact capsules (A)*	*Weight of empty shell (B)*	*Weight of contents = A – B*
1			
2			
–			
–			
-up to 20			
Total weight			X

Average weight = X/20

Upper limit = average weight + (Average weight × error)

Lower limit = average weight – (Average weight × error.

4. Content Uniformity

Hard capsules containing below or less than 25 mg of the drug contents should meet content uniformity requirements. Assay 10 capsules individually and calculate the acceptance value.

The requirement is met if the acceptance value of 10 capsules is less than or equal to 15%. If acceptance value is greater than 15% or is about 25% then, test the next 20 units and calculate the acceptance value. The 30 capsules if less than or equal to 15% and no individual unit is 1–25×0.01 nor more than 1 + 25×0.01.

Calculation of Acceptance Value

(Reference value-mean of individual contents) + acceptability constant × sample standard deviation.

5. Disintegration

Disintegration is the state in which no residue except fragments of capsule shell, remains on the screen of the test apparatus or adheres to the lower surface of the disc. The disintegration test determines whether tablets or capsules disintegrate within a prescribed time when placed in a liquid medium under the prescribed experimental conditions.

materials are time:erosion-dependent rather than acid: base-dependent, i.e. they erode over time on exposure to gastrointestinal contents rather than over a pH gradient. There are, in addition, a number of newer materials with predictable pH solubility profiles.

Enteric-coated capsules: Enteric-coated capsules resist disintegration in the stomach but break up in the intestine. They have largely been superseded by enteric-coated tablets. Types of coating used commercially include cellulose acetate phthalate and mixtures of waxes and fatty acids and/or their esters. Enteric coating may be given to following categories of drugs.

- For substances that irritate the gastric mucosa or are destroyed by the gastric juice, and for medicaments, such as amoebicides and anthelmintics that are intended to act in the intestine.
- Which interfere with digestion, e.g. tannins, silver nitrate and other salts of heavy metals.
- Which are required to produce delayed action of the drug.

In general, the application of a coating requires skill and additional equipment. A general coating can be applied but should probably only be used in medications that would not be of a critical nature. In many cases, experience must be developed for specific formulations depending upon the requests of the physicians and the needs of the individual patients. Several coating methods may be used and are described as follows:

1. *Beaker-flask coating:* Place a very small quantity of the coating material in the flask and gently heat until it has melted. Add a few capsules, remove from the heat and rotate the flask to start application of the coating. Periodically add a few more drops of melted coating material with continued rotation. The addition of very small quantities is all that is required to keep the capsules from sticking together and clumping.
2. *Dipping:* Heat the coating material in a beaker at the lowest feasible temperature. Individual capsules can be dipped using tweezers, allowing the coating to cool and repeating the process until a sufficient layer has been developed.
3. *Spraying:* An alcoholic or ethereal solution of the coating material is prepared and placed in a small sprayer