**PCT 302**

**TABLETS AND TABLETING, POWDERS AND PILLS**

**TABLET**

Tablets may be defined as the solid unit dosage form of medicament or medicaments with suitable excipients and prepared either by molding or by compression. It comprises a mixture of active substances and excipients, usually in [powder](https://en.wikipedia.org/wiki/Powder_(substance)) form, pressed or compacted from a powder into a solid dose. The excipients can include [diluents](https://en.wikipedia.org/wiki/Diluent), [binders](https://en.wikipedia.org/wiki/Binder_(material)) or granulating agents, glidants (flow aids) and lubricants to ensure efficient tableting, disintegrants to promote tablet break-up in the digestive tract; [sweeteners](https://en.wikipedia.org/wiki/Sweetener) or flavours to enhance taste; and pigments to make the tablets visually attractive or aid in visual identification of an unknown tablet. A polymer coating is often applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment (extending its shelf life), or to enhance the tablet's appearance.

The compressed tablet is the most popular [dosage form](https://en.wikipedia.org/wiki/Dosage_form) in use today. About two-thirds of all prescriptions are dispensed as solid dosage forms, and half of these are compressed tablets. A tablet can be formulated to deliver an accurate dosage to a specific site; it is usually taken orally, but can be administered sublingually, buccally, [rectally](https://en.wikipedia.org/wiki/Rectum) or intravaginally. The tablet is just one of the many forms that an oral drug can take such as [syrups](https://en.wikipedia.org/wiki/Syrup), [elixirs](https://en.wikipedia.org/wiki/Elixir), [suspensions](https://en.wikipedia.org/wiki/Suspension_(chemistry)), and [emulsions](https://en.wikipedia.org/wiki/Emulsion). Medicinal tablets were originally made in the shape of a disk of whatever color their components determined, but are now made in many shapes and colors to help distinguish different medicines. Tablets are often stamped with symbols, letters, and numbers, which enable them to be identified. Sizes of tablets to be swallowed range from a few millimeters to about a centimeter.

**Pill**

[Combined oral contraceptive pills](https://en.wikipedia.org/wiki/Combined_oral_contraceptive_pill) were nicknamed "the pill" in the 1960. A pill was originally defined as a small, round, solid pharmaceutical [oral](https://en.wikipedia.org/wiki/Oral_administration) dosage form of medication. Today, pills include tablets, capsules, and variants thereof like caplets — essentially, any solid form of medication colloquially falls into the pill category.

**Caplet**

Variations on a common tablet design, which can be distinguished by both color and shape. A caplet is a smooth, coated, oval-shaped medicinal tablet in the general shape of a [capsule](https://en.wikipedia.org/wiki/Capsule_(pharmacy)). Many caplets have an indentation running down the middle so they may be split in half more easily. Since their inception, capsules have been viewed by consumers as the most efficient method of taking medication. For this reason, producers of drugs such as [OTC](https://en.wikipedia.org/wiki/Over-the-counter_drugs) analgesics wanting to emphasize the strength of their product developed the “caplet” because it’s an easier-to-swallow shape than the usual disk-shaped tablet.

**Orally disintegrating tablet (ODT)**

An orally disintegrating tablet or orodispersible tablet (ODT), is a drug [dosage form](https://en.wikipedia.org/wiki/Dosage_form) available for a limited range of [over-the-counter](https://en.wikipedia.org/wiki/Over-the-counter_drug) (OTC) and [prescription](https://en.wikipedia.org/wiki/Prescription_drug) medications.

**Tableting formulations**

In the tablet-pressing process, it is important that all ingredients be fairly dry, powdered or granular, somewhat uniform in particle size, and freely flowing. Mixed particle sized powders segregate during manufacturing operations due to different densities, which can result in tablets with poor drug or active pharmaceutical ingredient (API) content uniformity, but [granulation](https://en.wikipedia.org/wiki/Granulation_(making_of_granules)) should prevent this. Content uniformity ensures that the same API dose is delivered with each tablet.

Some APIs may be tableted as pure substances, but this is rarely the case; most formulations include [excipients](https://en.wikipedia.org/wiki/Excipient). Normally, a pharmacologically inactive ingredient (excipient) termed a *binder* is added to help hold the tablet together and give it strength. A wide variety of binders may be used, some common ones including [lactose](https://en.wikipedia.org/wiki/Lactose), dibasic calcium phosphate, [sucrose](https://en.wikipedia.org/wiki/Sucrose), corn (maize) starch, microcrystalline [cellulose](https://en.wikipedia.org/wiki/Cellulose), povidone [polyvinylpyrrolidone](https://en.wikipedia.org/wiki/Polyvinylpyrrolidone) and modified cellulose (for example hydroxypropyl methylcellulose and hydroxyethylcellulose).

Often, an ingredient is also needed to act as a *disintegrant* to aid tablet dispersion once swallowed, releasing the API for absorption. Some binders, such as starch and cellulose, are also excellent disintegrants.

**Advantages and disadvantages**

1. Tablets are simple and convenient to use.
2. They provide an accurately measured dosage of the active ingredient in a convenient portable package.
3. Tablets can be designed to protect unstable medications or disguise unpalatable ingredients.
4. Colored coatings, embossed markings and printing can be used to aid tablet recognition.
5. Manufacturing processes and techniques can provide tablets with special properties, for example, [sustained release or fast dissolving formulations](https://en.wikipedia.org/wiki/Controlled_release).
6. Drugs which can be taken [sublingually](https://en.wikipedia.org/wiki/Sublingual_administration) are absorbed through the [oral mucosa](https://en.wikipedia.org/wiki/Oral_mucosa), so that they bypass the liver and are less susceptible to the first pass effect.

**Disadvantages**

1. Some drugs may be unsuitable for administration by the oral route. For example, protein drugs such as [insulin](https://en.wikipedia.org/wiki/Insulin) may be denatured by stomach acids. Such drugs cannot be made into tablets.
2. Some drugs may be deactivated by the [liver](https://en.wikipedia.org/wiki/Liver) when they are carried there from the [gastrointestinal tract](https://en.wikipedia.org/wiki/Human_gastrointestinal_tract) by the [hepatic portal vein](https://en.wikipedia.org/wiki/Hepatic_portal_vein) (the "[first pass effect](https://en.wikipedia.org/wiki/First_pass_effect)"), making them unsuitable for oral use.
3. The oral [bioavailability](https://en.wikipedia.org/wiki/Bioavailability) of some drugs may be low due to poor [absorption](https://en.wikipedia.org/wiki/Absorption_(pharmacokinetics)) from the gastrointestinal tract. Such drugs may need to be given in very high doses or by [injection](https://en.wikipedia.org/wiki/Injection_(medicine)).
4. For drugs that need to have rapid onset, or that have severe [side effects](https://en.wikipedia.org/wiki/Side_effect), the oral route may not be suitable. For example, [salbutamol](https://en.wikipedia.org/wiki/Salbutamol), used to treat problems in the [respiratory system](https://en.wikipedia.org/wiki/Respiratory_system), can have effects on the [heart](https://en.wikipedia.org/wiki/Heart) and [circulation](https://en.wikipedia.org/wiki/Circulatory_system) if taken orally; these effects are greatly reduced by inhaling smaller doses direct to the required site of action.
5. A proportion of the population have difficulties swallowing tablets either because they just don't like taking them or because their medical condition makes it difficult for them ([dysphagia](https://en.wikipedia.org/wiki/Dysphagia), [vomiting](https://en.wikipedia.org/wiki/Vomiting)). In such instances it may be better to consider alternative dosage form or administration route.

**Tablet properties**

Tablets can be made in virtually any shape, although requirements of patients and tableting machines mean that most are round, oval or capsule shaped. More unusual shapes have been manufactured but patients find these harder to swallow, and they are more vulnerable to chipping or manufacturing problems.

Tablet diameter and shape are determined by the machine tooling used to produce them - a die plus an upper and a lower punch are required. This is called a station of tooling. The thickness is determined by the amount of tablet material and the position of the punches in relation to each other during compression. Once this is done, we can measure the corresponding pressure applied during compression. The shorter the distance between the punches, thickness, the greater the pressure applied during compression, and sometimes the harder the tablet. Tablets need to be hard enough that they don't break up in the bottle, yet friable enough that they disintegrate in the gastric tract.

Tablets need to be strong enough to resist the stresses of packaging, shipping and handling by the pharmacist and patient. The mechanical strength of tablets is assessed using a combination of (i) simple failure and erosion tests, and (ii) more sophisticated engineering tests. The simpler tests are often used for quality control purposes, whereas the more complex tests are used during the design of the formulation and manufacturing process in the research and development phase. Standards for tablet properties are published in the various international pharmacopeias (USP/NF, EP, JP, etc.). The hardness of tablets is the principle measure of mechanical strength. Hardness is tested using a [tablet hardness tester](https://en.wikipedia.org/wiki/Tablet_hardness_testing). The units for hardness have evolved since the 1930s, but are commonly measured in kilograms per square centimeter.

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall, as well as between granules, which helps in uniform filling of the die.

Common minerals like talc or silica, and fats, e.g. magnesium stearate or stearic acid are the most frequently used lubricants in tablets or hard gelatin capsules.

**Manufacture of the tableting blend**

In the tablet pressing process, the appropriate amount of active ingredient must be in each tablet. Hence, all the ingredients should be well-mixed. If a sufficiently homogenous mix of the components cannot be obtained with simple blending processes, the ingredients must be granulated prior to compression to assure an even distribution of the active compound in the final tablet. Two basic techniques are used to granulate powders for compression into a tablet: wet granulation and dry granulation. Powders that can be mixed well do not require granulation and can be compressed into tablets through direct compression.

**Wet granulation**

Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with than solvent-based systems but may not be suitable for drugs which are degraded by hydrolysis.

Procedure

1. The active ingredient and excipients are weighed and mixed.
2. The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, cellulose derivatives such as methyl cellulose, [gelatin](https://en.wikipedia.org/wiki/Gelatin), and povidone.
3. Screening the damp mass through a mesh to form pellets or granules.
4. Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.
5. After the granules are dried, they are passed through a screen of smaller size than the one used for the wet mass to create granules of uniform size.

Low shear wet granulation processes use very simple mixing equipment, and can take a considerable time to achieve a uniformly mixed state. High shear wet granulation processes use equipment that mixes the powder and liquid at a very fast rate, and thus speeds up the manufacturing process. Fluid bed granulation is a multiple-step wet granulation process performed in the same vessel to pre-heat, granulate, and dry the powders. It is used because it allows close control of the granulation process.

**Dry granulation**

Dry granulation processes create granules by light compaction of the powder blend under low pressures. The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation equipment offers a wide range of pressures to attain proper densification and granule formation. Dry granulation is simpler than wet granulation, therefore the cost is reduced. However, dry granulation often produces a higher percentage of fine granules, which can compromise the quality or create yield problems for the tablet. Dry granulation requires drugs or excipients with cohesive properties, and a 'dry binder' may need to be added to the formulation to facilitate the formation of granules.

**Hot melt extrusion**

Hot melt extrusion is utilized in pharmaceutical solid oral dose processing to enable delivery of drugs with poor solubility and bioavailability. Hot melt extrusion has been shown to molecularly disperse poorly soluble drugs in a polymer carrier increasing dissolution rates and bioavailability. The process involves the application of heat, pressure and agitation to mix materials together and ‘extrude’ them through a die. Twin-screw high shear extruders blend materials and simultaneously break up particles. The extruded particles can then be blended and compressed into tablets or filled into capsules.

**Granule lubrication**

After granulation, a final lubrication step is used to ensure that the tableting blend does not stick to the equipment during the tableting process. This usually involves low shear blending of the granules with a powdered lubricant, such as [magnesium stearate](https://en.wikipedia.org/wiki/Magnesium_stearate) or [stearic acid](https://en.wikipedia.org/wiki/Stearic_acid).

**Manufacture of the tablets**

Whatever process is used to make the tableting blend, the process of making a tablet by powder compaction is very similar. First, the powder is filled into the die from above. The mass of powder is determined by the position of the lower punch in the die, the cross-sectional area of the die, and the powder density. At this stage, adjustments to the tablet weight are normally made by repositioning the lower punch. After die filling, the upper punch is lowered into the die and the powder is uniaxial compressed to a porosity of between 5 and 20%. The compression can take place in one or two stages (main compression, and, sometimes, pre-compression or tamping) and for commercial production occurs very fast. Finally, the upper punch is pulled up and out of the die (decompression), and the tablet is ejected from the die by lifting the lower punch until its upper surface is flush with the top face of the die. This process is repeated for each tablet.

Common problems encountered during tablet manufacturing operations include:

* Fluctuations in tablet weight, usually caused by uneven powder flow into the die due to poor powder flow properties.
* Fluctuations in dosage of the Active Pharmaceutical Ingredient, caused by uneven distribution of the API in the tableting blend (either due to poor mixing or separation in process).
* Sticking of the powder blend to the tablet tooling, due to inadequate lubrication, worn or dirty tooling, or a sticky powder formulation
* Capping, lamination or chipping. This is caused by air being compressed with the tablet formulation and then expanding when the punch is released: if this breaks the tablet apart, it can be due to incorrect machine settings, or due to incorrect formulation: either because the tablet formulation is too brittle or not adhesive enough, or because the powder being fed to the tablet press contains too much air (has too low bulk density).
* Capping can also occur due to high moisture content.

**Tablet presses**

Tablet presses, also called tableting machines, range from small, inexpensive bench-top models that make one tablet at a time (single-station presses), with only around a half-ton pressure, to large, computerized, industrial models (multi-station rotary presses) that can make hundreds of thousands to millions of tablets an hour with much greater pressure. The tablet press is an essential piece of machinery for any pharmaceutical and nutraceutical manufacturer. Common manufacturers of tablet presses include Natoli, Stokes, Fette Compacting, Korsch, Kikusui, Bosch-Manesty, B&D, PTK, Sejong, IMA and Courtoy. Tablet presses must allow the operator to adjust the position of the lower and upper punches accurately, so that the tablet weight, thickness and density/hardness can each be controlled. This is achieved using a series of cams, rollers, and/or tracks that act on the tablet tooling (punches). Mechanical systems are also incorporated for die filling, and for ejecting and removing the tablets from the press after compression. Pharmaceutical tablet presses are required to be easy to clean and quick to reconfigure with different tooling, because they are usually used to manufacture many different products. There are 2 main standards of tablet tooling used in pharmaceutical industry: American standard ‘TSM’ and European standard ‘EU’. TSM and EU configurations are similar to each other but cannot be interchanged.

Modern tablet presses reach output volumes of up to 1'700'000 tablets per hour. These huge volumes require frequent in-process quality control for the tablet weight, thickness and hardness. Due to reduce rejects rates and machine down-time, automated tablet testing devices are used on-line with the tablet press or off-line in the IPC-labs.

**Tablet coating**

Many tablets today are coated after being pressed. Although sugar-coating was popular in the past, the process has many drawbacks. Modern tablet coatings are [polymer](https://en.wikipedia.org/wiki/Polymer) and [polysaccharide](https://en.wikipedia.org/wiki/Polysaccharide) based, with [plasticizers](https://en.wikipedia.org/wiki/Plasticizer) and [pigments](https://en.wikipedia.org/wiki/Pigment) included. Tablet coatings must be stable and strong enough to survive the handling of the tablet, must not make tablets stick together during the coating process, and must follow the fine contours of embossed characters or logos on tablets. Coatings are necessary for tablets that have an unpleasant taste, and a smoother finish makes large tablets easier to swallow. Tablet coatings are also useful to extend the shelf-life of components that are sensitive to moisture or oxidation. Special coatings (for example with pearlescent effects) can enhance brand recognition.

If the active ingredient of a tablet is sensitive to acid, or is irritant to the stomach lining, an [enteric coating](https://en.wikipedia.org/wiki/Enteric_coating) can be used, which is resistant to [stomach](https://en.wikipedia.org/wiki/Stomach) acid, and dissolves in the less acidic area of the intestines. Enteric coatings are also used for medicines that can be negatively affected by taking a long time to reach the [small intestine](https://en.wikipedia.org/wiki/Small_intestine), where they are absorbed. Coatings are often chosen to [control the rate of dissolution](https://en.wikipedia.org/wiki/Controlled_release) of the drug in the gastrointestinal tract. Some drugs are absorbed better in certain parts of the digestive system. If this part is the stomach, a coating is selected that dissolves quickly and easily in acid. If the rate of absorption is best in the large intestine or colon, a coating is used that is acid resistant and dissolves slowly to ensure that the tablet reaches that point before dispersing. To measure the disintegration time of the tablet coating and the tablet core, automatic disintegration testers are used which are able to determine the complete disintegration process of a tablet by measuring the rest height of the thickness with every upward stroke of the disintegration tester basket.

There are two types of coating machines used in the pharmaceutical industry: coating pans and automatic coaters. Coating pans are used mostly to sugar coat pellets. Automatic coaters are used for all kinds of coatings; they can be equipped with a remote control panel, a dehumidifier, and dust collectors. An explosion-proof design is required for applying coatings that contain alcohol.

**Pill-splitters**

It is sometimes necessary to split tablets into halves or quarters. Tablets are easier to break accurately if scored, but there are devices called [pill-splitters](https://en.wikipedia.org/wiki/Pill_splitting) which cut unscored and scored tablets. Tablets with special coatings (for example enteric coatings or [controlled-release](https://en.wikipedia.org/wiki/Controlled_release) coatings) should not be broken before use, as this will expose the tablet core to the digestive juices, circumventing the intended delayed-release effect.

## Types of tablets

## a. Compressed tablets

Compressed tablets represent a significant proportion of tablets that are clinically used to provide systemic administration of therapeutic agents either in an uncoated state (i.e., in their simplest form) or in a coated state. These tablets are designed to provide rapid disintegration in the gastric fluid following ingestion hence, allowing rapid release of the drug and, ultimately, systemic absorption of the dosage form.  
Compressed tablets are formed by compression of powdered, crystalline, or granular materials into the required geometry by the application of high pressures, utilizing steel punches and die. In addition to the Active Pharmaceutical Ingredient(s) (APIs), compressed tablets usually contain a number of pharmaceutical excipients e.g., bulking agents, disintegrants, binders, lubricants, controlled-release polymers and other miscellaneous adjuncts such as colourants and flavourants which serve different and specialized purpose during tablet manufacture, storage, and use. Examples of compressed tablets include tablets for oral, buccal, sublingual, or vaginal administration.

### b. Sugar-coated Tablets

These are compressed tablets that have been coated with concentrated sugar solution to improve patient’s compliance, increase aesthetic appeal, mask objectionable tastes or odors, increase stability and/or modify the release of therapeutic agent(s). Sugar coating was once quite common but lost commercial appeal due to the time and expertise required in the coating process, the increase in size and weight of coated tablets, high cost of process validation and shipping. The advent of film-coated tablets has also greatly decreased use of sugar coatings due to the improved mechanical properties of the technique. Examples of sugar-coated tablets include dried ferrous sulphate BP 200mg (Reagan Remedies Ltd.), Advil – Ibuprofen tablet BP 200mg (Pfizer Consumer Healthcare), Ebu-200 – Ibuprofen tablet BP 200mg (Me cure Industries Ltd) etc.

### c. Film-Coated Tablets

Film-coated tablets are conventional tablets coated with a thin layer of polymer (e.g., hydroxypropyl methylcellulose, hydroxypropyl cellulose) or a mixture of polymers (e.g., Eudragit E100) capable of forming a skin-like film. The film is usually coloured and also impacts the same general characteristics as sugar coating with the added advantage of being more durable, less bulky, and less time-consuming to apply. By its composition, the coating is designed to break and expose the core tablet at the desired location in the gastrointestinal tract. Advances in material science and polymer chemistry have made these coatings the first choice for formulation scientists. [Examples of Film-coated tablets](https://www.pharmapproach.com/tablet-coating-process-film-coating-2/) include Curefenac 100 – Diclofenac potassium USP 100mg (Unicure Pharmaceutical Ltd), Valsartan 320mg Film-coated Tablets (Actavis UK Ltd), etc.

### d. Effervescent Tablets

Effervescent tablets are uncoated tablets that generally contain organic acids (such as tartaric or citric acid) and sodium bicarbonate in addition to the medicinal substance or API.  They react rapidly in the presence of water by releasing carbon dioxide which acts as a disintegrator to produce either a drug suspension or an aqueous solution. These tablets are prepared by compressing granular effervescent salts (organic acid and bicarbonate) with the medicinal substances. A typical example of this tablet type is Ca C1000 Sandoz effervescent tablet (Novartis).

### e. Enteric-coated Tablets

Enteric-coated tablets are compressed tablets that have delayed-release properties. They are coated with polymeric substances (such as cellulose acetate phthalate/cellulose acetate butyrate; hydroxypropylmethylcellulose succinate; and methacrylic acid copolymers) that resist solution in gastric fluid but disintegrate and allow drug dissolution and absorption in the intestine.  
Enteric coatings are primarily employed when the drug substance is inactivated or destroyed by gastric acid (e.g., erythromycin) or is particularly irritating to the gastric mucosa (e.g., non-steroidal anti-inflammatory drugs) or when bypass of the stomach substantially enhances drug absorption. Example of enteric-coated tablets includes Lofnac 100 – Diclofenac sodium delayed-release tablet USP 100mg (bliss GVS Pharma Ltd), Ecotrin tablets and caplets (GlaxoSmithKline Beecham).

### f. Chewable Tablets

Chewable tablets are big sized tablets which are difficult to swallow and thus, are chewed within the buccal cavity prior to swallowing. They are especially useful for administration of large tablets to children and adults who have difficulty swallowing conventional tablets or antacid formulations in which the size of the tablet is normally large and the neutralisation efficacy of the tablet is related to particle size within the stomach. These tablets are not conventionally used if the drug has issues regarding taste acceptability. Examples of chewable tablets include Danacid – compound magnesium trisilicate tablet B.P. (Dana Pharmaceuticals Limited), Gestid – tasty chewable antacid (Ranbaxy) etc.

### g. Buccal and Sublingual Tablets

Buccal and sublingual tablets are small, flat, oval tablets that are intended to be dissolved in the buccal pouch (buccal tablets) or beneath the tongue (sublingual tablets) for absorption through the oral mucosa to produce a systemic effect. These tablets are employed to achieve either rapid absorption into the systemic circulation e.g. glyceryl trinitrate sublingual tablets or, alternatively, to enable oral absorption of drugs that are destroyed by the gastric juice and/or are poorly absorbed from the gastrointestinal tract.

### h. Lozenges or Troches

These are disc-shaped solid preparations containing medicinal agents and generally a flavoring substance in a hard candy or sugar base. They are intended to be slowly dissolved in the oral cavity, usually for local effects. Examples include Strepsils Dry Cough Lozenges

### i. Tablet Triturates

Tablet triturates are small, usually cylindrical, moulded, or compressed tablets containing small amounts of usually potent drugs mixed with a combination of sucrose and lactose or any suitable diluent. They are prepared from moist material, using a triturate mould that gives them the shape of cut sections of a cylinder. Since tablet triturates must completely and rapidly dissolve in water, only a minimal amount of pressure is applied during their manufacture. One of the problems encountered during the manufacture of this tablet type is the failure to find a lubricant that is completely water-soluble. A typical example of tablet triturate is NTG tablets (Nitroglycerin).

### j. Hypodermic Tablets

Hypodermic tablets are soft, readily soluble tablets that were originally used by physicians in extemporaneous preparation of parenteral solutions. These tablets are dissolved in a suitable vehicle (water for injections) and administered by parenteral route. Hypodermic tablets are no longer used in most countries due to the difficulty in achieving sterility. Also, the availability of stable parenteral solutions and prefabricated injectable products, some in disposable syringes have also discouraged their use in recent times. e.g., Dilaudid – Dihydromorphinone HCl (Bilhuber Knoll Corp.).

### k. Dispensing Tablets

Dispensing tablets also referred to as compounding tablets are tablets supplied primarily as a convenience for extemporaneous compounding. These tablets contain large amounts of highly potent APIs, and thus are used by a pharmacist to compound prescriptions that can be incorporated readily into powders and liquids, thus, circumventing the necessity to weigh small quantities of these potent drug substances. Dispensing tablets are no longer in use and had the dangerous potential of being inadvertently dispensed as such to patients. Examples include silver potentiate, bichloride of mercury merbromin and quarternary ammonium compounds.

### l. Gelatin-Coated Tablets

Gelatin-coated tablets are compressed tablets coated with either a one or a two-toned colour gelatin. The gelatin coating impacts the same general characteristics as sugar coating and film coating with the added advantage of improving the stability of photosensitive APIs. The gelatin coating also facilitates swallowing, enables custom branding,  and prevents counterfeit since they are more tamper evident than unsealed capsules. Gelatin-coated tablets are also ideal for double-blind clinical studies, or for drug substances that can irritate the oesophagal mucosa when they are incorporated in an immediate-release tablet such as bisphosphonates. Example of gelatin-coated tablets includes gelatin coated hydrochlorothiazide tablet (Qualitest Pharmaceuticals), Tylenol Cold Multi-Symptom Daytime (McNeil Consumer) etc.

### m. Multiple Compressed Tablets/ Multi-compressed Tablets

Multiple compressed tablets, also called multi-compressed tablets are tablets that are composed of two or more layers. These tablets are prepared by subjecting the fill material to more than one compression cycle.  The result may be a multiple-layer tablet or a tablet within a tablet, the inner tablet being the core and the outer portion being the shell. This process is best used when separation of active ingredients is needed for stability purposes or if the mixing process is inadequate to guarantee uniform distribution of two or more active pharmaceutical ingredients. Multiple compressed tablets can also be used when there is a need to mask the bitter taste of a drug substance or where the drug substance in question is irritant to the stomach. There are three subclasses of multiple compressed tablets and they include:

#### i. Compression Coated Tablets

Compression coated tablets also referred to as dry-coated tablets or press-coated tablets, are tablets with two parts; internal core and surrounding coat. These tablets are prepared by feeding previously compressed tablets into a special [tablet press](http://pharmapproach.com/tablet-press/) and compressing another granulation layer around a preformed tablet core. Compression coated tablets have all the advantages of compressed tablets (i.e., slotting, monogramming, speed of disintegration) while retaining the attributes of sugarcoated tablets in masking the taste of the drug substance in the core tablets. These tablets can also be used to separate incompatible drug substances (one in the core and the other in the coat); in addition, they can provide a means of giving an enteric coating to the core tablets.

#### ii. Layered Tablets

They are tablets composed of two or more layers of ingredients. Layered tablets are prepared by compressing additional tablet granulation on a previously compressed granulation to form two-layered or three-layered tablets, depending on the number of separate fills. Each layer may contain a different medicinal agent, separated for reasons of physical or chemical incompatibility, staged drug release, or simply the unique appearance of the layered tablet. Unlike conventional tablets where we have a single piece of substance moulded to shape, layered tablets have the appearance of a sandwich because the edges of each layer are exposed.

#### iii. Inlay Tablets

Inlay tablets also referred to as dot, or bull’s-eye tablet is a variation of compressed tablet with a partially surrounded core. Instead of the tablet core being completely surrounded by the coating, its top surface is completely exposed. Inlay tablets are prepared by feeding previously compressed tablets into a prefilled die cavity of Stokes, Colton, or Kilian machines. When compressed, some of the coating material is displaced to form the sides.  With a yellow core and a white coating, Inlay tablets resemble a fried egg. Inlay tablets can be useful in sustained release preparations to reduce the size and weight of the tablet. A typical example is a European preparation containing 25 mg of hydrochlorothiazide in the bull’s-eye and 600 mg of potassium chloride in the outside portion.

### n. Immediate-Release Tablets

Immediate-release tablets are tablets designed to disintegrate and release their medication with no special rate-controlling features, such as special coatings and other techniques. This is the most common type of tablet and examples include, chewable, effervescent, sublingual and buccal tablets.

### o. Rapid-release Tablets

Rapid-release tablets, also called rapidly dissolving tablets, rapidly disintegrating tablets, orally-dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid-dissolving tablets, or porous tablets are characterized by disintegrating or dissolving in the mouth within 1 minute, some within 10 seconds, leaving an easy-to-swallow residue. Tablets of this type are prepared using very water-soluble excipients designed to wick water into the tablet for rapid disintegration or dissolution without chewing. Rapid-release tablets offer increased convenience and ease of administration with the potential to improve compliance, especially when swallowing conventional solid oral-dosage forms presents difficulties for the patient. Notwithstanding these advantages, there are a number of disadvantages and difficulties associated with formulating rapid-release tablets, including drug loading, taste masking, friability, manufacturing costs, and stability of the product. Examples of rapid-release tablets include Clarinex Reditabs [desloratadine], Schering.

### p. Extended-Release Tablets

Extended-release tablets sometimes called controlled-release tablets, prolonged-release, delayed release or sustained release tablets are tablets designed to release their medication in a predetermined manner over a prolonged period of time. These tablet types are categorized into

* Those that respond to some physiological condition to release the drug, such as enteric coatings;
* Those that release the drug in a relatively steady, controlled manner; and
* Those that combine combinations of mechanisms to release pulses of drug, such as repeat action tablets.

A typical example of this tablet type is e.g Nifecard tablets.

### q. Vaginal Tablets/ Vaginal Inserts

Vaginal tablets are uncoated, bullet-shaped, or ovoid tablets designed for vaginal administration. They are prepared by compression and are shaped to fit tightly on plastic inserter devices that accompany the product. Following insertion, retention and slow dissolution of the tablet occur, releasing the medicaments to provide the local pharmacological effect (e.g. for the treatment of bacterial or fungal infection). Vaginal tablets may also be used to provide systemic absorption of therapeutic agents. Examples include Gyno-Tiocosid (Neimeth), Gynesatum- Clotrimazole vaginal Tablet (Chazmax Pharmaceutical Industries Limited).

### r. Implantation Tablets/ Implants

### Implanon, etonogestrel

These are long-acting sterile tablets designed to provide continuous release of drugs, often over a period of months or a year. They are placed subcutaneously for systemic or local delivery. Implants are mainly used for the administration of hormones such as testosterone steroids for contraception. They usually contain rate-controlling excipients in addition to the active ingredient(s).  Several types of implants are available including pellets, resorbable microparticles, polymer implants, in situ–forming gel/solid implants, metal/plastic implants, and drug-eluting stents. Examples of implantation tablets include Implanon – etonogestrel (Organon), Disulfiram Tablet for Implantation etc.

## Tablet Excipients/ Ingredients

In tablet formulation, many materials are usually combined at various quantities to produce a tablet that is of good standard. These materials serve different and specialized functions in the tablet. The type and quantity of each raw material used is dependent on the intended tablet type and formulation technique. Examples of tablet excipients include:

* **Binders /granulating fluid** –e.g., include acacia gum, tragacanth, corn starch, methyl cellulose, gelatin, mucilage of isapol husks, carboxymethylcellulose, methylcellulose, polyvinylpyrrolidone and sugars, such as sucrose, glucose, dextrose, molasses, and lactose etc.
* **Bulking agents/ diluents/fillers –**anhydrous lactose, spray dry lactose, microcrystalline cellulose, corn starch, dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, mannitol, sodium chloride, etc.
* **Disintegrating agents –** e.g., starch, clays, celluloses, algins, gums, and cross-linked polymers (croscarmellose, crospovidone, and sodium starch glycolate) etc.
* **Lubricants –** metallic stearate (0.1-0.2 % w/w) e.g., magnesium stearate, calcium stearate, stearic acid (0.25-1 %), hydrogenated vegetable oil, corn starch, boric acids, sodium chloride, sodium lauryl sulphate etc.
* **Glidants** – e.g., colloidal silicon dioxide Cab-o-sil (Cabot), Talc (asbestos-free) etc.
* **Colouring agents/ Colourants –** e.g., FD&C Blue No. 1, (triarylmethane dye) FD&C Blue No. 2, FD&C Green No. 3,
* **Flavoring agents/ Flavorants** – e.g., Aspartame (Pfzer)
* **Adsorbent** – e.g., silicon dioxide, magnesium oxide, starch, magnesium silicate etc.

**PHARMACEUTICAL POWDERS**

Historically, powders represent one of the oldest dosage forms. A pharmaceutical powder is solid dosage form which contains mixture of finely divided drugs or chemicals in a dry form meant for internal or external use. It is a preparation in which drug is blended with other powdered substances and used for internal or external purpose. Powder as a dosage form permits drugs to be reduced to a very fine state of division, which often enhances their therapeutic activity or efficacy by an increase of dissolution rate and/or absorption. Divided powders are also found to be convenient for administering drugs that are excessively bitter, nauseous, or otherwise offensive to the taste.

A good powder formulation has a uniform particle size distribution. If the particle size distribution is not uniform, the powder can segregate as per to particle size which may result in inaccurate dosing or inconsistent performance. A uniform particle size distribution ensures a uniform dissolution rate if the powder is to dissolve, a uniform sedimentation rate if the powder is used to remain in a suspension, and minimizes stratification when powders are stored or transported. Reduction in particle size of a powder results in-a uniform distribution of particle size. The process of reducing the particle size is called comminution.

In extemporaneous compounding, there are three methods of comminution:

Trituration: - Trituration is the continuous rubbing or grinding of the powder in a mortar with a pestle. This method is used when working with hard, fracturable powders.

Pulverization: - method is used with hard crystalline powders that do not crush or triturate easily, or gummy-type substances. The first step is to use an "intervening" solvent (such as alcohol or acetone) that will dissolve the compound. The dissolved powder is then mixed in a mortar or spread on an ointment slab to enhance the evaporation of the solvent. As the solvent evaporates, the powder will recrystallize out of solution as fine particles.

Levigation: - Levigation reduces the particle size by triturating it in a mortar or spatulating it on an ointment slab or pad with a small amount of a liquid in which the solid is not soluble. The solvent should be somewhat viscous such as mineral oil or glycerin. This method is also used to reduce the particle size of insoluble materials when compounding ointments and suspensions.

**Advantages:-**

(i) Drugs that have to be given in bulk can be best administered in powder form by mixing them with food or drinks.

(ii) Useful for bulky drugs with large dose.

(iii) Powders are more stable than liquid dosage form; hence many antibiotics and injections are manufactured as powder for reconstitution in respective vehicle.

(iv) More convenient to swallow than tablet or capsules.

(v) Powder possesses good chemical stability.

(vi) Since powders are in the form of small particles; they offer a large surface area and are rapidly dissolved in the gastrointestinal tract minimizing the problems of local irritation.

(vii) Rapid dissolution powder facilitates rapid absorption.

(viii) Highly compatible compared to liquid dosage tom.

(ix) Manufacturing of powder is economic hence product coat is quite low as compared to other dosage forms.

Disadvantages:-

(i) Bulk powders are not suitable for administering potent drug with low dose.

(ii) Not suitable for drugs which are unstable in normal atmospheric condition.

(iii) Powder form is not suitable for drugs that are inactivated in. or cause damage to stomach: these should he presented as enteric-coated tablets.

(iv) Not suitable for bitter. nauseating and corrosive drugs, if are meant tor oral administration.

(V) The masking unpleasant tastes may be a problem with this type of preparation a method of attempting this is by formulating the powder into a pleasantly tasting or taste- masked effervescent product. whereas tablets and capsules are a more common alternative for low-dose products

(vi) Inaccuracy of dose in case of bulk powder.

(vii) inconvenient to carry.

(viii) They are susceptible to physical instability

**CLASSIFICATION OF POWDERS**

1.Powders for internal use (a) Divided powders (i) Simple powders (ii) Compound powders (iii) Powders enclosed in cachet (iv) Tablet triturates (b) Bulk powders (i) Antacid (ii) Laxative

2. Powders for external use (a) Dusting powders (i) Medicated dusting powders (ii) Surgical dusting powders (b) insufflations (c) Douche powder (d) Dentifrices

3. Special powders (a) Eutectic mixtures (b) Effervescent powders

**Bulk Powders**

Bulk powders are nonpotent and can be dosed with acceptable accuracy and safety using measuring devices such as the teaspoon, cup, or insufflator. This practically limits the use of orally administered bulk powders to antacids, dietary supplements, laxatives, and a few analgesics. Many bulk powders are used topically.

**Dusting Powders**

Dusting powders are fine medicinal (bulk) powders intended to be dusted on the skin by means of sifter-top containers. A single medicinal agent may be used as a dusting powder; however, a base is frequently used to apply a medicinal agent and to protect the skin from irritation and friction. Bentonite, kaolin, kieselguhr, magnesium carbonate, starch, and talc are used as inert bases for dusting powders. Powder bases absorb secretions and exert a drying effect, which relieves congestion and imparts a cooling sensation. All extemporaneous dusting powders should be passed through a 100-200 mesh sieve to ensure that they are grit free and will not further mechanically irritate traumatized areas.

**Douche Powders**

Douche powders are used to prepare solutions that cleanse the vagina. Most douche powders are used for their hygienic effects, but a few contain antibiotics.

Douche powders are prescribed as a matter of convenience for the patient, since a powder is more portable than a bulky solution. The formula is developed so that a teaspoonful or tablespoonful of powder dissolved in a specified volume of water provides the desired concentration. The pH usually ranges from 3.5 to 5 when the solution is prepared. Feminine bulb syringes or fountain syringes are used for vaginal irrigation. Since many of the ingredients are volatile (e.g., menthol, thymol, and volatile oils), douche powders should be packaged in glass jars with a wide mouth. Some commercial douche powders are available in metal foil packets, which contain the proper amount of powder for a single douche. Many douches are also available as prepared unit of use solutions in disposable applicators.

**Insufflations**

Insufflations are extremely fine powders to be introduced into body cavities. To administer an insufflation, the powder is placed in the insufflator, and when the bulb is squeezed, the air current carries the fine particles through the nozzle to the region for which the medication is intended. All extemporaneously compounded insufflations must be passed through a 100 mesh sieve. Pressurized packages provide an elegant approach to the administration of insufflations.

**Powder Sprays**

In contrast to dusting powders, powders dispensed under pressure will deliver targeted and uniform application at the desired site. Also, in an aerosol container medicated powders may be maintained in a sterile condition. The powder particles must be a definite size range to prevent clogging of the valve orifice and to provide uniformity of application. In general, powders that are to be packaged as powder sprays must not contain particles greater than 50 microns if they are to be sprayed successfully.

**Divided Powders**

Divided powders or charts are single doses of powdered medicinals individually wrapped in cellophane, metallic foil, or paper. The divided powder is a more accurate dosage form than bulk powder because the patient is not involved in measurement of the dose. Cellophane and foil-enclosed powders are better protected from the external environment until the time of administration than paper-enclosed powders. Divided powders are commercially available in foil, cellophane or paper packs.