CHAPTER 4: INTRODUCTION TO SOLID DOSAGE FORMS NUTRACEUTICALS

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The objectives of this unit are to:

- Understand the solid dosage form nutraceutical
- Understand the characteristic, advantage and disadvantage of each solid dosage form nutraceutical.
LEARNING OUTCOMES

After completing this unit, student should be able to:

Â Explain the characteristic of the solid dosage form delivery system

Â Explain the characteristic of powders and granules nutraceutical.

Â Explain the characteristic of capsules and tablets nutraceutical.
CHAPTER 4: INTRODUCTION TO SOLID DOSAGE FORMS NUTRACEUTICALS
INTRODUCTION

Â Oral route has been one of the most popular routes of drug delivery due to its ease of administration, patience compliance, least sterility constraints and flexible design of dosage forms.

Â Tablets are defined as unit dose, temper evident solid preparations containing one or more active ingredients.

Â Conventional drug delivery systems like tablets and capsules often dissolve rapidly in the gastrointestinal tract for absorption into the bloodstream give rise to inordinately high drug concentrations in plasma.

1. The concept of making utility of food as health promoting factor beyond its nutritional value is gaining acceptance with in public arena and among scientific community. Nutraceuticals contain health-supporting ingredients or natural components that have an ability health benefit for the body.

2. A nutraceutical is a product isolated or purified from foods that is generally sold in medicinal forms not usually connected with food. A nutraceutical is bearing to have a physiological benefit or give protection against chronic disease.

Term coined by Dr. Stephen L De Felice, Founder and Chairman of the Foundation for Innovation in Medicine, New Jersey, USA. Nutraceuticals sometimes referred as functional foods have caused heated debate because they change the traditional dividing line between food, and medicine.
INTRODUCTION

3. A nutraceutical is "any non-toxic food component that has scientifically proven health benefits, including disease treatment or prevention." The functional component of the food must be standardized in the nutraceutical product and generate under good manufacturing practices (GMPs).

4. Increased public demand, trends in demography, socio-economic scenario. More researches and studies, nearly two thirds of the world's 6.1 billion people rely on the healing power of plant based materials for many reasons-availability, affordability, safety or their belief in traditional affordability, safety or their belief in traditional cures Medical benefits of food have been investigated for thousands of years.

Modern nutraceutical industry began to develop in Japan during the 1980s. Various benefits of nutraceuticals are may help us live longer, may increase the health asses of our diet, help us to abstain particular medical condition, it have a psychological advantage from doing something for oneself, and may be sensed to be more "natural" than traditional medicine and less likely to produce unpleasant side-effects.
5. The nutraceuticals normally contains required amount of lipids, protein, carbohydrates, vitamins, minerals and other necessary nutrients depending upon their emphases. Nutraceuticals in the market contains both traditional foods and non-traditional. When a supplement tablet is ingested, the body must digest and absorb the nutrients. Nutraceutical may include a whole area of products like isolated nutrients, dietary supplements, herbal products and other processed foods.

The growing disapproval among the patients about the synthetic therapeutic agents and affect about their toxicological profile gave birth to the Dietary Supplements Health and Education Act (DSHEA) in USA in 1994.

6. The concept behind the mode of action of nutraceutical dosage form is to provide functional benefits by enhancing the supply of natural building blocks. It works in to two ways that is to minimize diseases sign or to improve body performance.
CHAPTER 4: INTRODUCTION TO SOLID DOSAGE FORMS NUTRACEUTICALS

4.1: DELIVERY SYSTEMS
ROUTE OF ADMINISTRATION

ORAL

RECTAL

TOPICAL

PARENTERAL

RESPIRATORY
Absorption after oral administration can be quite variable. Dosage form design may also be used to modify the rate of absorption.

### Advantages:
- **Convenient** - portable, safe, no pain, easy to take.
- **Cheap** - no need to sterilize (but must be hygienic of course), compact, multi-dose bottles, automated machines produce tablets in large quantities.
- **Variety of dosage forms available** - fast release tablets, capsules, enteric coated, layered tablets, slow release, suspensions, mixtures.

### Disadvantages:
- **Sometimes inefficient** - high dose or low solubility drugs may suffer poor availability, only part of the dose may be absorbed.
- **First-pass effect** - drugs absorbed orally are transported to the general circulation via the liver. Thus drugs which are extensively metabolized will be metabolized in the liver during absorption.
- **Food** - Food and G-I motility can effect drug absorption. Often patient instructions include a direction to take with food or take on an empty stomach.
- **Local effect** - Antibiotics may kill normal gut flora and allow overgrowth of fungal varieties. Thus, antifungal agent may be included with an antibiotic.
### Advantages:
- Some irritant and unpleasant drugs can be introduced into rectum as suppositories.
- Generally less drug degradation via this route of administration.
- When a drug is ingested normally it is absorbed by the intestine.
- The dose can be retrieved if necessary.

### Disadvantages:
- This is rather inconvenient and embarrassing.
- Absorption is slower, irregular and unpredictable.
- Rectal inflammation can result from irritant drugs.
- Rectal mucous membranes are very sensitive when the introduction of drugs may irritate the rectum.
THE RATIONALE OF EXTENDED-RELEASE PHARMACEUTICALS

- Less fluctuation in drug blood levels
- Frequency reduction in dosing
- Enhanced convenience and compliance
- Reduction in adverse side effects
- Reduction in overall health care costs
TYPES OF EXTENDED-RELEASE IN PHARMACEUTICALS

- Modified release
- Targeted release
- Extended release
- Repeat action
- Delayed release
<table>
<thead>
<tr>
<th>Types of Extended-Release in Pharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modified release</strong></td>
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<tr>
<td><strong>Extended release</strong></td>
</tr>
<tr>
<td><strong>Delayed release</strong></td>
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<tr>
<td><strong>Repeat action</strong></td>
</tr>
<tr>
<td><strong>Targeted release</strong></td>
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</table>
CHAPTER 4: INTRODUCTION TO SOLID DOSAGE FORMS NUTRACEUTICALS

4.2: POWDER & GRANULES
INTRODUCTION

Definition:

Powder is a mixture of finely divided drugs and / or chemicals in dry form.

- Powders are intimate mixtures of dry, finely divided drugs and/or chemicals that may be intended for internal (Oral Powders) or external (Topical Powders) use. Because of their greater specific surface area, powders disperse and dissolve more readily than compacted dosage forms.

- Children and those adults who experience difficulty in swallowing tablets or capsules may find powders more acceptable. Drugs that are too bulky to be formed into tablets or capsules of convenient size may be administered as powders. Immediately prior to use, oral powders are mixed in a beverage or apple sauce.

- Often, stability problems encountered in liquid dosage forms are avoided in powdered dosage forms. Drugs that are unstable in aqueous suspensions or solutions may be prepared in the form of granules or powders. These are intended to be constituted by the pharmacist by the addition of a specified quantity of water just prior to dispensing. Because these constituted products have limited stability, they are required to have a specified expiration date after constitution and may require storage in a refrigerator.
INTRODUCTION

• Oral powders may be dispensed in doses premeasured by the pharmacist, i.e., divided powders, or in bulk. Traditionally, divided powders have been wrapped in materials such as bond paper and parchment. However, the pharmacist may provide greater protection from the environment by sealing individual doses in small cellophane or polyethylene envelopes.

Granules for veterinary use may be administered by sprinkling the dry powder on animal feed or by mixing it with animal food.

• Bulk oral powders are limited to relatively nonpotent drugs such as laxatives, antacids, dietary supplements, and certain analgesics that the patient may safely measure by the teaspoonful or capful. Other bulky powders include douche powders, tooth powders, and dusting powders.

• Bulk powders are best dispensed in tight, wide-mouth glass containers to afford maximum protection from the atmosphere and to prevent the loss of volatile constituents.

• Dusting powders are impalpable powders intended for topical application. They may be dispensed in sifter-top containers to facilitate dusting onto the skin. In general, dusting powders should be passed through at least a 100-mesh sieve to assure freedom from grit that could irritate traumatized areas.
POWDER & GRANULES

Powder

Granules
Particle size of powders is standardized according to the USP descriptive terms:

<table>
<thead>
<tr>
<th>Very fine</th>
<th>Fine</th>
<th>Moderately course</th>
<th>Course</th>
<th>Very course</th>
</tr>
</thead>
</table>
FACTOR AFFECTED BY PARTICLE SIZE

The dissolution rate of particles is dependent on the particle size.

In suspension preparation, it is important to have a good suspendability (i.e., ability to maintain uniform dispersion in liquid vehicle) of particles.

Intrarespiratory applications- size range is 1–5 µm

In dermal (ointment / cream)- use fine particle 50–100 µm
PARTICLE SIZE ANALYSIS

Seiving
Microscopy
Sedimentation Rate
Coulter counter

Light scattering
Gas absorption
DISADVANTAGES POWDER FORM

1. Misunderstand the correct method
2. Difficult to protect powders containing hygroscopic from decomposition.
3. Powder must be a homogeneous blend
4. High cost of production to make uniform powder
5. Undesirable to take bitter tasting drugs
GRANULES

Granules are agglomerates of powdered materials prepared into larger, free flowing particles.

They typically fall within the range of 850 µm (No. 20 sieve) to 4.75 mm (No. 4 sieve) size.

The shape of granules is generally irregular.
ADVANTAGES OF GRANULES

Granules flow better than powders.

Granules increase compressibility.

Granules have smaller surface area than a comparable volume of powders.

Granules are more easily wetted by a solvent than are certain powders, so that granules are also preferred in making solutions.

Granules produce particle-size uniformity, thus content uniformity.
**GRANULATION METHODS**

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet granulation</td>
<td>Liquid binder or an adhesive that added to the powder mixture</td>
</tr>
<tr>
<td>Dry granulation</td>
<td>Formed by compacting large masses of the powder mixture and subsequently crushing into pieces.</td>
</tr>
<tr>
<td>Fluid bed granulation</td>
<td>Sprayed onto the suspended particles that are then dried rapidly in the suspending air.</td>
</tr>
</tbody>
</table>
CHAPTER 4: INTRODUCTION TO SOLID DOSAGE FORMS NUTRACEUTICALS

4.3: CAPSULES & TABLETS
INTRODUCTION

DEFINITION:

CAPSULES:

Capsules are solid dosage forms in which the drug is enclosed within either a hard or soft soluble container or “shell.” The shells are usually formed from gelatin; however, they also may be made from starch or other suitable substances.

TABLETS:

Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They may be classed, according to the method of manufacture, as compressed tablets or molded tablets.
INTRODUCTION

CAPSULES:

- Hard-shell capsule sizes range from No. 5, the smallest, to No. 000, which is the largest, except for veterinary sizes. However, size No. 00 generally is the largest size acceptable to patients.

- Size 0 hard gelatin capsules having an elongated body (known as size OE) also are available, which provide greater fill capacity without an increase in diameter. Hard gelatin capsules consist of two, telescoping cap and body pieces.

- Generally, there are unique grooves or indentations molded into the cap and body portions to provide a positive closure when fully engaged, which helps prevent the accidental separation of the filled capsules during shipping and handling. Positive closure also may be affected by spot fusion (welding) of the cap and body pieces together through direct thermal means or by application of ultrasonic energy.

- Factory-filled hard gelatin capsules may be completely sealed by banding, a process in which one or more layers of gelatin are applied over the seam of the cap and body, or by a liquid fusion process wherein the filled capsules are wetted with a hydroalcoholic solution that penetrates into the space where the cap overlaps the body, and then dried. Hard-shell capsules made from starch consist of two, fitted cap and body pieces. Since the two pieces do not telescope or interlock positively, they are sealed together at the time of filling to prevent their separation. Starch capsules are sealed by the application of a hydroalcoholic solution to the recessed section of the cap immediately prior to its being placed onto the body.
The banding of hard-shell gelatin capsules or the liquid sealing of hard-shell starch capsules enhances consumer safety by making the capsules difficult to open without causing visible, obvious damage, and may improve the stability of contents by limiting O2 penetration. Industrially filled hard-shell capsules also are often of distinctive color and shape or are otherwise marked to identify them with the manufacturer. Additionally, such capsules may be printed axially or radially with strengths, product codes, etc. Pharmaceutical-grade printing inks are usually based on shellac and employ FDA-approved pigments and lake dyes.

In extemporaneous prescription practice, hard-shell capsules may be hand-filled; this permits the prescriber a latitude of choice in selecting either a single drug or a combination of drugs at the exact dosage level considered best for the individual patient. This flexibility gives hard-shell capsules an advantage over compressed tablets and soft-shell capsules as a dosage form.

Hard-shell capsules are usually formed from gelatins having relatively high gel strength. Either type may be used, but blends of pork skin and bone gelatin are often used to optimize shell clarity and toughness. Hard-shell capsules also may be formed from starch or other suitable substances. Hard-shell capsules may also contain colorants, such as D&C and FD&C dyes or the various iron oxides, opaquing agents such as titanium dioxide, dispersing agents, hardening agents such as sucrose, and preservatives. They normally contain between 10% and 15% water.
INTRODUCTION

Hard gelatin capsules are made by a process that involves dipping shaped pins into gelatin solutions, after which the gelatin films are dried, trimmed, and removed from the pins, and the body and cap pieces are joined. Starch capsules are made by injection molding a mixture of starch and water, after which the capsules are dried. A separate mold is used for caps and bodies, and the two parts are supplied separately. The empty capsules should be stored in tight containers until they are filled. Since gelatin is of animal origin and starch is of vegetable origin, capsules made with these materials should be protected from potential sources of microbial contamination.

Hard-shell capsules typically are filled with powder, beads, or granules. Inert sugar beads (nonpareils) may be coated with active ingredients and coating compositions that provide extended-release profiles or enteric properties. Alternatively, larger-dose active ingredients themselves may be suitably formed into pellets and then coated. Semisolids or liquids also may be filled into hard-shell capsules; however, when the latter are encapsulated, one of the sealing techniques must be employed to prevent leakage.

In hard gelatin capsule filling operations, the body and cap of the shell are separated prior to dosing. In hard starch shell filling operations, the bodies and caps are supplied separately and are fed into separate hoppers of the filling machine.
CAPSULES

- **Tapered rim** of the body engages easily with the cap for problem-free closure.
- **Six elongated dimples** maintain precise round capsule diameter, improving filling machine performance.
- **Two aerodynamic air vents** allow air to escape from the cap; critical when operating high-speed filling machines.
- **Closely-matched locking rings** provide full-circumference leak-free closure.
- **Rounded, hemispherical ends** are mechanically stronger and more resistant to deformation.
CAPSULES

**STAGE 1 Spraying**
Sealing fluid is sprayed onto joint between cap and body.
Capillary action draws fluid up between the cap and the body. Suction removes excess fluid.

**STAGE 2 Warming**
A gentle heat application completes melting and fusion.
Gentle heat melts the two layers, which fuse together to form an impervious seal.

**STAGE 3 Setting**
Capsules set and harden at room temperature.
CAPSULES SIZE
TYPE OF CAPSULES

Hard gelatin capsules

Soft gelatin capsules
GELATIN USE IN CAPSULES

Å Gelatin is heterogeneous product derived by hydrolytic extraction of animal collagen

Å The sources of gelatins including animal bones, hide portions and frozen pork skin

Å **Type of gelatin**

😊 **Type A** It is manufactured mainly from animal (pork skin).

😊 **Type B** It is manufactured mainly from starch or other suitable substances.
1. Developing and preparing formulation
2. Filling the capsule shell
3. Capsule sealing
4. Cleaning and polishing the filled capsules
INGREDIENT USE IN CAPSULES

1. **Diluents and fillers**: lactose, cellulose, starch
2. **Disintegrants**: sodium starch glicolate, pregelatinised starchgan
3. **Gligants & lubricants**: silicon dioxide, magnesium stearate, calcium stearate
4. **Wetting agents**: SLS / Lithium carbonate
FILLING OF CAPSULES
## COMPARISON

<table>
<thead>
<tr>
<th>HARD GELATIN CAPSULES</th>
<th>SOFT GELATIN CAPSULES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two piece (large body &amp; short cap)</td>
<td>One piece &amp; hermetically sealed</td>
</tr>
<tr>
<td>Cylindrical shape</td>
<td>Available in round, oval &amp; tube like shapes</td>
</tr>
<tr>
<td>Powder drug or pallets coated with drug are encapsulated</td>
<td>Liquid &amp; semi liquid fill &amp; unstable substances are encapsulated</td>
</tr>
<tr>
<td>Gelatin in Hard form is used</td>
<td>Molten gelatin are used</td>
</tr>
<tr>
<td>Capsules are sealed after they are filled to ensure that the medicaments may not come out of the capsule due to rough handling</td>
<td>Filling &amp; sealing of soft gelatin capsules are done in a combined operation on machine</td>
</tr>
<tr>
<td>8 different type of sizes are available</td>
<td>No specific sizes are available</td>
</tr>
</tbody>
</table>
## DISADVANTAGES & ADVANTAGES

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsules are tasteless, odourless &amp; can easily be administered</td>
<td>Hydroscopic for filling drug are not suitable into capsules, because they absorb water present in capsules shell makes shell very brittle and ultimately lead to crumble into pieces.</td>
</tr>
<tr>
<td>Combination of powders we can use</td>
<td>The concentrated solutions which require previous dilution are unstable for capsules.</td>
</tr>
<tr>
<td>There are attractive in appearance</td>
<td></td>
</tr>
<tr>
<td>They are economical</td>
<td></td>
</tr>
<tr>
<td>They are easy to handle &amp; carry</td>
<td></td>
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</tbody>
</table>
Definition

A Tablet defined as a compressed solid dosage form containing medicaments with or without excipients. Tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents.
## DISADVANTAGES & ADVANTAGES

<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.</td>
<td>Lighter and compact</td>
</tr>
<tr>
<td>Bitter testing drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen may require encapsulation or coating</td>
<td>Easiest and cheapest to package and strip</td>
</tr>
<tr>
<td>Difficult to swallow in case of children and unconscious patients</td>
<td>Suitable for large scale production</td>
</tr>
</tbody>
</table>
# TYPES OF TABLET

<table>
<thead>
<tr>
<th>Tablets ingested orally</th>
<th>Paracetamol tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Á Compressed tablet</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tablets used in oral cavity</th>
<th>Vitamin-c tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Á Buccal tablet</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tablets administered by other route</th>
<th>Clotrimazole tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Á Vaginal tablet</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tablets used to prepare solution</th>
<th>Dispirin tablet (Aspirin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Á Effervescent tablet</td>
<td></td>
</tr>
</tbody>
</table>
INGREDIENT

1. Active ingredient

2. Excipients / additives: >>>>

- Diluent
- Binder and Adhesive
- Disintegrants
- Lubricants
- Glidants
- Colouring agents
- Flavoring agents
- Sweetening agents
FUNCTION EVERY ADDITIVES:

**Diluent:**
- Improve cohesion
- **Ex:** Lactose-anhydrous and spray dried lactose

**Binder and Adhesive:**
- To form granules
- **Ex:** Acacia and Starch paste-10-20% solution

**Disintegrants:**
- To facilitate breaking or disintegration when it contact in water
- **Ex:** sodium carboxy methyl cellulose

**Lubricants:**
- Improve the rate of flow of the tablet granulation
- **Ex:** Stearic acid
FUNCTION EVERY ADDITIVES:

| Glidants:                | To promote flow of granules or powder material by reducing the friction between the particles  
|                        | Ex: Corn Starch in 5-10% conc. |
| Colouring agents:       | To masking of off color drugs and for product identification. Ex: FD & C blue 1 - Brilliant Blue |
| Flavoring agents:       | Flavor oil are used (chewable) |
| Sweetening agents:      | Sugar, mannitol (chewable) |
TABLETING METHOD / PROCESS

**Direct Compression**
- Drug
- Diluent
- Glidant
- Disintegrant
- Lubricant
- Mixing

**Dry Granulation**
- Drug
- Diluent
- Lubricant
- Mixing
- Compression
- Communion
- Screening
- Disintegrant
- Glidant
- Lubricant
- Mixing

**Wet Granulation**
- Drug
- Diluent
- Binder
- Solvent
- Wetting
- Granulation
- Drying
- Screening
- Disintegrant
- Glidant
- Lubricant
- Mixing

**Compression Mix**
- Fill Die, Compress Tablet, Eject Tablet
- Metal check, Dedusting, Coating, Packaging etc.