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# A comprehensive review on spanules: A novel drug delivery system

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## Abstract

Spanules are considered one of the most advantageous drug delivery systems. Multi-drug regimen is the key benefit of Spanules (capsules having granules.) Spanules are constructed for the release of API (Drug) at different rates and times. The first immediate /slow-release pattern gives an initial drug release which is followed by drug release at a constant rate for an extended time.This will result in constantdrugsbeing available for a long time of period. This doses form is useful to overcome repeated drug dosing.

**Keywords:** Spanules; Hard gelatin capsule; Immediate drug release; Novel drug delivery system

## 1. Introduction

Spanules are the doses form when administered show a drug release profile of one or more than one drug over a specified period of time. Spanules are the doses form having one API or more than one API in the form of granules, with a specific coating having a slow dissolving rate which alters the release pattern of the medicament in the Spanulesata different and predetermined time[1, 2]

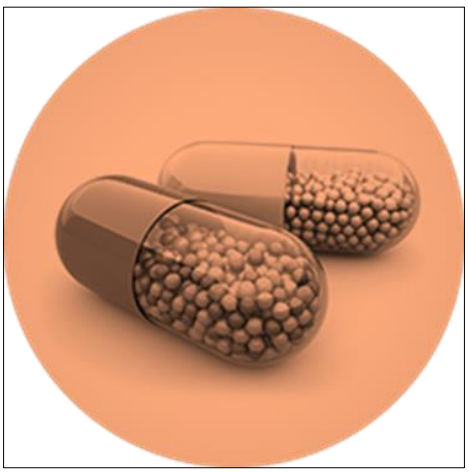

**Figure 1** Spansules

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The oral route for drug delivery is the most used route with the following benefits[3]

- Ease of administration
- Patient compliance
- Multidrug management
- Easy to plan drug delivery from doses form

### 1.1. Dosage form: spansusle

Spanules are the capsules that contain API or more than one APIS in granules form which is coated with slow dissolving rate materials resulting in delivery of drugs at different times. Spanules can be defined as combing both Span and capsule (Span capsule =Spanules). The dosages form which delivery medicine at different time span[4].

### 1.2. MOA of spanules

*1.2.1. How Spanules acts*

Every drug particle or granule which is incorporated in Spanulesiscoated with a material having slow dissolving activity. When these coated tablets are pressed into tablet form can be defined as SPACETABS or in form of capsules defined as SPANSUSLE. In Spanules, drug dissolution can be governed by microencapsulation.When the coating of the drug granules gets dissolved drug is released and now ready for dissolution. By changing the coating thickness, varying the composition, drug release can be predetermined. Spanules cannot be chewed or broken because it may lead to damage of coating material[5, 6].

A Spanules contains many granules which are different from each other on the basis of coating of thickness. These types of granules deliver a drug at a predetermined rate, first of all, the granules provide loading dose followed by drug release at different time span. These coated granules deliver drugs at 2 – 3 hours, 4-6 hours, and 6-9 hours. Drug release is dependent on moisture permeation into the coating of particles which causes swelling of thickness material followed by rapture resulting in the drug release[7-11].

Spanules are the best example of dissolution release systems. Principally hydrophobic or hydrophilic polymers are used in combination or in single. Some examples are cellulose acetate phthalate, gelatin, and polyvinyl alcohol[12].

### 1.3. Advantages of spanules[13-16]

- Spanules are the dosage form that provides controlled as well as sustained release for single or multiple drug regimens.
- Reduce side effects by improving patient compliance.
- Reduces dosing.
- Modified delivery profile.
- Controls drug concentration in systemic circulation resulting in enhanced bioavailability.
- Enhances drug degradation in GIT
- Taste masking is one more beneficial aspect.

### 1.4. Limitation of spanules[17, 18]

- Less data is available for in-vitro-in vivo correlation.
- Dose dumping may be a reason for system failure.
- Systemic availability of the drug is low.
- Complex to formulate, skilled labor is required.
- Expensive

### 1.5. How to prepare spanules[19, 20]

Spanules can be prepared by the following methods. Mentioned below

- Spray drying
- Coaservation –phase separation
- Pan coating
- Spray congealing
- Fluidized bed technology
- Solvent evaporation

*1.5.1. Spray drying*

In this method, APIs are suspended in the coating material followed by drying with hot air. The coating solidification may cause drying of solvent in which coating material is diffused. This method can be employed for thermolabile drugs[21].

*1.5.2. Coacervation –phase separation*

It includes 3 steps

- Formation of three immiscible chemical phases.
- Deposition of the coating.
- Solidification of the coating.

STEP (A) - Formation of three immiscible chemical phases.

In this method, a core material will be dispersed in the polymeric solution of coating material. The solvent used is the liquid phase for the polymer.

In the coating materials phase, an immiscible polymer in a liquid phase is shaped by utilizing one of the coacervation phase separation methods. That can be changed by temperature change or via salt addition[22].

STEP (B) - Deposition of the coating.

In this step liquid polymer coating deposits on the particles of active pharmaceutical ingredients and allow it for the further manufacturing process.

STEP (C)- Solidification of the coating

In this step solidification of coating material takes place using thermal energy.

*1.5.3. Pan coating*

This technique is widely used for the preparation of tiny coated particles or pellets/Spanules. In this solid particles/granules are shaken in a pan and coating material is poured upon the drug particles resulting in coated drug particles with different shapes and sizes. Automized mist is used to coat solid material[23].

*1.5.4. Spray congealing*

The spray congealing methodis useful for the substances having melting properties when the temperature rises. Cool air is used on the sides of the spray dryer to prevent the melting of the substance. In this method, solidification occurs using thermal congealing with a coating material in molten form[7].

*1.5.5. Fluidized bed technology-*

In this technique,the liquid polymeric solution is sprayed on Spanules. A pid fading is used to form a rigid layer on granules with different thicknesses[8].

Three types offluid bed coaters are used for fluidized bed technology

- Top spray
- Bottom spray

- Tangential spray

*1.5.6. Solvent evaporation*

In this method, a volatile solvent is mixed with the coating material which is not miscible with liquid medium. Drug particles will be dispersed in the polymeric coating with proper mixing to form uniform size Spanules.

After that volatile solvent is evaporated with heating with stirring. Few examples of coating materials that can be used coating material polyacrylic acid, polyvinyl alcohol, polyvinyl pyrrolidone, etc[9].

## 2. Evaluation parameters of spanules

### 2.1. Particle size

The most common techniques to determine the particle size distribution are sieve analysis, static laser light scattering analysis, dynamic light scattering, etc.Above mention, techniques determine particle size. All mentions methods can measure particle size ranging from 1µm to 3mm.The particles size of granules in Spanules can be easily analyzed with the help of simple sieve analysis[10,11].

### 2.2. Assay by Ultra Violet Spectroscopy

For UV analysis following steps to be followed:

Sample preparation

100mg of drug in 100 ml volumetric flask.

Addition of suitable solvent.

Sonification to liquefy

Addition of buffer solution of pH 1.2 and mix

Transfer 5ml solution to 50 ml volumetric flask and make the volume by means of buffer sol. Of pH 1.2[12].

### 2.3. Procedure

Check the absorbance at a specific wavelength with the filtered part of the test solution in comparison with a standard solution using a 1.2 pH buffer.

Calculate percentage purity with the following formula

% purity = actual amount of desired material × 100/ total amount of material

### 2.4. Friability test

Friability of Spansules can be calculated as percentage weight loss after 100 revolutions of 10 gm of Spanules in friabilator[13].

### 2.5. Moisture content

Moisture content can be calculated under specific conditions with sample heating. The weight loss can be calculated with the following formula[17].

% Moisture content = w2-w1 × 100/ w2-w1

Where,

W1= Weight of the container with lid

W2= Weight of the container with lid and sample before drying

W3= Weight of the container with lid and sample after drying

### 2.6. Loss on drying

In this method, an empty crucible was weighed and dehydrated for 30 minutes. 1 gm of drug sample is placed in this crucible and kept in a furnace for approximately one hour at 250-300°C. After 1-hour crucible is kept in a desiccator for cooling. After colling crucible is weighed again for weight loss[19].

LOD can be calculated with the following formula

% loss= W1-W2 × 100/W1

Where;

W1= Initial weight of the sample

W2= Final retained weight on sample container after 10 cycles

### 2.7. *In –vitro* release study: Dissolution studies

Dissolution studies are performed in calibrated dissolution apparatus.The drug release profile can be predicted through UV Spectrophotometer[23].

**Table 1**Marketed preparation of spanules

| S.NO | Product name | Active ingredient |
|---|---|---|
| 1 | Benzedrine | Amphetamine sulphate |
| 2 | Combid | Prochlorperazine maleate, isopropamide iodide |
| 3 | Balkaprofen | Ibuprofen |
| 4 | Biotin | B7 |
| 5 | Fefol | Ferrous sulphate, folic acid |
| 6 | Becosules | Vitamin B12, folic acid |

## 3. Future prospects

- Spanules are the doses form with an advanced drug delivery system.
- The main principle of Spanules works on different coating thickness layers, which can provide multiple drugs at one dosages form.
- Spanules can maximize patient compliance by enhancing the effectiveness of dose and dosage form having minimum side effects.
- Spanules would be the best dosage form for targeted drug delivery.
- Spanules would be the best choice for site-specific drug delivery[17].

## 4. Application of spanules[7, 11]

- Spanules could be used as a multi-dosage regimen because the granules have different thicknesses of coating material.
- Spanules can release drug at different and predetermine time span.
- Granules with the thinnest layer of coating material will release the initial or loading dose.
- Increases patient compliance by increasing the effectiveness of dose.

## 5. Conclusion

Spanules are the dosage form in which one or more active ingredient is kept inside the capsule shell in form of particles or granules. In Spanulesthick coating prevent active pharmaceutical ingredientfrom their surrounded environment and drug release take place at a predetermined rate. Spanules provides a new area to explore. Formulation of Spanulesskilled professional, advanced and specialized equipment isrequired. It can be concluded thatSpanules are the dosages from easy to manufacture with potential benefits over conventional dosage form.

## Compliance with ethical standards

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*Disclosure of conflict of interest*

No conflict is associated this work.

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