

# A REVIEW ON CONTROLLED DRUG RELEASE FORMULATION: SPANSULES

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**Abstract:** Spansules are a dosage form which was considered as one of the Advanced Drug Delivery System. Multidrug preparations can be delivered easily by spansules or granules in capsule technology. This type of delivery system designed to release a drug or a medicament at two or more different rates or in different span of time. A quick/slow release system provides an initial release of drug followed by a constant rate of drug release over an extended period or a defined period of time and in slow/quick release system provides release vice versa [1]. This will overall provide constant plasma drug concentration over a wide range of time. The drug release is followed by zero order kinetics so that constant release of drug is maintained.

Biphasic release system is generally used when maximum relief is to be achieved suddenly followed by sustained release phase over a prolonged period of time to avoid repeated administration [2].

**Keywords:** Controlled release, sustained release, granules formation and microencapsulation.

## **Introduction:**

Controlled release drug delivery system, Sustained drug delivery system both terms are used to achieve a prolonged drug delivery system over an extended period of time. Spansules are considered as one of the controlled release capsules which release a medicament over a different span of time.

The oral route is considered as more acceptable and convenient route for controlled delivery of drugs because of the following reasons-

1. Greater flexibility in dosage form design.
2. Ease of production.
3. Ease of administration.

The controlled release system for oral use are mostly solids and quite a few are liquids such as suspensions containing controlled release coated or complexed drug particles, granules, pellets or microcapsules. We are mainly considering controlled release form of capsules namely spansules. These are mainly formed by encapsulation techniques hence known as Encapsulation / Coating Dissolution Controlled System (Reservoir Devices).

In this formulation the drug particles are coated or encapsulated by one of the several microencapsulation techniques with slowly dissolving materials like waxes, polyethylene glycol PEGs cellulose etc. The resulting pellets or coated granules are filled in hard gelatine capsules popularly called as Spansules. These are mainly transparent in appearance we can see easily colour granules in it. This system can produce a rapid increase in plasma concentration of drugs such as analgesic, anti-inflammatory, anti-hypertensive, etc. That are requested promptly exercise the therapeutic effect followed by a prolonged release phase to avoid repeated administration [3]. The dissolution rate of coat depends upon the solubility and thickness of coating (1-200 microns) [4]. The thickness of coating allows the slowly dissolving of a medicament over a long period of time.

A spansule contains hundreds of coloured pellets or granules divided into 3 to 4 groups which differ in their thickness of time-delay coating. These pellets or granules provide loading dose and release drugs at 2 or 3 hours, 4 or 6 hours, and 6 or 9 hours. The drug release depends on permeation of moisture to the coated particles (core) resulting in the swelling, ruptures the coating, thus followed by releasing drug [5].

**Definition:** - Spansules are defined as capsules containing medicines (in form of granules), coated with materials having slow dissolving rates so that the medicament is delivered at different specific time.

In other words, it is combination of two words i.e. span and capsule, hence it is a capsule that slowly gives off medication over a different span of time.

**Classification of oral CDDS:**

1. Continuous Release System
  - a) Dissolution controlled release systems
  - b) Diffusion controlled release systems
  - c) Dissolution and diffusion controlled release systems
  - d) Ion exchange resin drug complexes
  - e) pH dependent formulations
  - f) Osmotic pressure controlled system
  - g) Hydrodynamic pressure controlled systems
  - h) Slow dissolving salts and complexes
2. Delayed Transit and continuous release system
  - a. Altered density system
  - b. Mucoadhesive system
  - c. Size-based system
3. Delayed Release System
  - a. Intestinal release system
  - b. Colonic release system

Spansules comes under dissolution controlled release systems, reservoir type. Generally, hydrophilic polymers or hydrophobic polymer either single or combinations are used for the coating of granules. Examples include gelatine, cellulose derivatives (ethyl cellulose, methyl cellulose, HPMC, etc.), polyvinyl alcohol, cellulose acetate phthalate.

**Methods of preparation of granules for spansules: [6, 7]**

1. Coaservation-phase separation: - It mainly contains three steps.
  - a. Formation of three immiscible chemical phases- the three immiscible phases are liquid manufacturing vehicle phase, core material phase and coating material phase. The coating material phase, an immiscible polymer in a liquid phase is formed by using one of the methods of phase separation coaservation i.e. by changing the temperature of polymer solution, by adding salt to the polymer solution, by adding non solvent to the polymer solution, by inducing a polymer interaction.
  - b. Deposition of the coating material:- this step consist of deposition of liquid polymer coating material upon the core material by incorporating adsorption of the polymer at the interface formed between the core material and liquid vehicle phase. The continued deposition of the coating material is then promoted by reduction in surface tension of the system.
  - c. Rigidization of the coating:- it is carried out usually by thermal cross-linking or desolvation technique.
2. Spray drying: - in this method the active ingredient dissolved or suspended in coating material and then dried off using dry and hot air. The coating solidification is effected by rapid evaporation of a solvent in which coating material is dissolved. It is rapid, single stage operation and can be used for thermo labile substances.
3. Spray congealing: - the substance which has property of melting at high temperature are used in this technique. The substance being atomised and congealing when the droplet formed passed through the cool air on spray dryer. In this the coating solidification takes place by thermally congealing a molten coating material.
4. Pan coating: - it is widely used for formation of small coated particles or pellets. The solid particles having size greater than 600 microns are considered essential for effecting coating. The particles are tumbled in a coating pan while coating material is applied slowly, an active ingredient are usually coated onto various spherical shaped particles. The coating solution is applied by atomizing spray to the solid core material. To remove coating solvent a blast of warm air is passed over the coated materials.
5. Solvent evaporation: - in this process the coating material is dissolved in volatile solvent, which is immiscible with the liquid vehicle phase. A core material is dispersed in coating solution with stirring to obtain uniform size microcapsules. This mixture is then heated to evaporate the solvent with constant agitation. A variety of film forming polymers can be used as coating materials such as polyvinylpyrrolidone, polyethylene, poly vinyl alcohol, poly acrylic acid, etc.
6. Fluidised bed technology:- in this method liquid coating material is sprayed onto the particles and the rapid evaporation helps in the formulation of an outer rigid layer on particle as per the required thickness. There are mainly three different type of fluid bed coaters :-
  - a. Top spray

- b. Bottom spray
- c. Tangential spray

**Advantages of Spansules:**

1. Provide both controlled and sustained release for single or multiple prescription and over the counter medicine[8]
2. Improved patient compliance and reduce side effects [9].
3. It reduces the dosing frequency
4. It increases the safety margin of high potency drugs and reduces the incidence of both systemic and local side effects in sensitive patient [10].
5. It also reduces the rate of rise of drug concentration in blood and enhanced bioavailability.
6. Customised delivery profiles.
7. The drug release can be controlled by adjusting the thickness and rate of dissolution of granules. Thus drug will be released at different predetermined time [11].
8. It increases stability by protecting the drug from degradation in gastro-intestinal tract [12].
9. The necessity of administration of drug several times is eliminated and it also guards against missing a dose by a patient [13].
10. Mask the taste of powders or granules.

**Disadvantages of Spansules:**

1. Lack of *in vitro- in vivo* correlation [14].
2. Sometimes dose dumping may occur.
3. The systemic availability is decreased as compared to immediate- release conventional capsules.
4. Poor *in vitro- in vivo* correlation as compared to conventional one.
5. The fluctuation in plasma drug levels may lead to precipitation of side effects especially drug with small Therapeutic index (TI) when over medication occur[15].
6. Complicated process and requires skill labour to prepare this type of formulations.
7. Toxicity caused due to long acting preparations is difficult to treat.
8. Economic limitation.

**Marketed Preparation**

| <b>Encapsulated dissolution product of spansules</b> |  |
|--|--|
| <b>Product Name</b>                                  | <b>Active Intergradient</b>                                  |
| Benzedrine   | Amphetamine Sulphate   |
| Combid   | Prochlorperazine Maleate, Isopropamide Iodide                |
| Hispril  | Biphenyl Pyraline Hydrochloride                              |
| Ornade   | Phenyl propanolamine hydrochloride, chlorpheniramine maleate |
| Thorazine  | Chlorpheniramine hydrochloride                               |
| Balkapofen   | Ibuprofen  |
| Dexedrine  | Dextromethorphan   |
| Fefol  | Ferrous sulphate, folic acid                                 |
| Prilosec   | Omeprazole   |
| Fesovit -Z   | Ferrous sulphate, zinc supplements and vitamins              |
| Fenbid   | Ibuprofen  |
| Thorazine  | Chlorpromazine   |
| Feospan  | Dried ferrous sulphate                                       |

**Future consideration:**

Spansules are one of the most advanced and modified form of drug delivery system. Since the granules have different coating thickness, they release drug at different manner, those with thinnest layer will provide initial dose. This will give one of the best methods to deliver multiple drugs at one time. This is main principal of Spansules capsules [16]. It can also maximise the patient compliance by increasing the efficiency of the dose and its dosage forms with less side effects.

**Conclusion:**

Spansules means packing an active ingredient inside a capsule shell in a form of granules or micro particles ranging in its size from one micron to several millimetres. This type of capsule protects the granules or active ingredient from its surrounding environment and releases the medicament at a required time. This formulation provides an fresh challenge in a new application. It include various skills, experience and well trained personnel's , advanced technologies and specialised equipment for its manufacture. In 1952, Smith Kline & French introduced this Spansule, a timed- release formulation that had launched a wide spread search for other applications in design of dosage forms [17].

From above discussion it can be concluded that this dosage form is easy to optimise and helpful to delivering various medicaments over a prolong period of time and have potential advantages over conventional dosage forms.

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