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A REVIEW ON SPANSULES

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Abstract: One of the Advanced Drug Delivery Systems was formerly thought to be the dosage form known as spansules. The Granules or capsule technologies can distribute multidrug formulations with ease. The goal of this type of delivery system is to disperse a medicine or therapy at two or more different speeds, or at different time intervals. In a slow/quick release system, the medicine is released in the opposite direction from a quick/slowrelease system, which releases the medication initially and then steadily over time or for a predetermined amount of time. Overall, this will maintain a steady plasma medication concentration over a long period of time. The drug release follows zero order kinetics to ensure a consistent release of the medication.

Keywords: Spansules, controlled release, sustained release, drug release systems

INTRODUCTION

A controlled drug delivery happens when the medication is administered for a predetermined period of time at a predetermined pace, either locally or systemically. Continuous oral medication delivery over a set time period with predictable and repeatable kinetics during the GIT.

Once thought to be among the most advanced drug delivery techniques, spansules are a type of dosage form. A sort of drug delivery system called a spansule is intended to release a drug or medication over a range of times or at many varied rates[1].

A spansule comprises hundreds of colored pellets or granules that have been separated into 3 to 4 groups according to how thick the time-delay coating is on each group. These pellets or granules deliver a loading dosage and release the medication after two or three hours, four or six hours and six or nine hours[2]. The medicine is released when moisture penetrates the coated particles, causing the swelling and break the coating. Because it allows for the controlled and continuous release of medication over a prolonged period of time, this innovative drug delivery technique is revolutionary. This method of distribution can lessen the chance of unwanted effects while improving therapeutic results[3].

Furthermore, spansules can be used to provide many drugs in a single dosage form. As a biphasic drug delivery method, spansules can provide both an instantaneous and a prolonged release of medication[4].

Sustained drug delivery systems and controlled release drug delivery systems are two terms used to describe drug delivery methods that are intended to last for an extended period of time. Among the several forms of controlled release capsules that distribute a drug over time are spansules.

The oral route is thought to be more practicable and desirable for regulated medicine delivery due to the following reasons.

1. More design options for dose forms.

2. Production simplicity.

3. Administration is simple.

Released under supervision Drug delivery uses capsules to hold medications in place for controlled, long-term release at controlled rates. This can take days or months. Compared to more traditional delivery methods, these systems provide several advantages, including the capacity to regulate drug release rates, protect sensitive drugs, and enhance patient comfort and compliance[5].

Drug release types

- Sustained release: These are drug delivery techniques that, in order to extend the therapeutic effect of a drug after it has been administered once, release medication gradually over time.

- Controlled release dosage form: In a controlled release dosage form, the drug is released from the delivery mechanism over a longer period of time in a scheduled, predictable, and slower way than usual[6]. This type of medication is used to treat certain diseases or other biologically active products.
- Extended release: ER versions of medications are designed to remain in your body longer. Due to this, you may only need to take 1 to 2 doses of the drug per day rather than 3 to 4 as you would with the IR form.
- Delayed release: In delayed release systems, medications combining one or more immediate release units into a single dosage form are dosed periodically and frequently.
- Repeat action drug delivery system: This is a substitute sustained release method in which the dosage form comprises numerous drug doses, each of which is released at regular intervals.

- Time release drug delivery systems: The medicine is released after a lag time of roughly 4-5 hours using a time release drug method.
- Receptor release and site-specific: These are designed to direct the medication to a particular biological spot. Site-specific drug delivery targets a specific organ or tissue, whereas receptor-based drug delivery targets a specific receptor inside an organ or tissue[7][8].

Oral medication administration method:

The oral route is the most practical and beneficial way to administer medication, which provides a far larger active surface area than other methods of drug administration. The vitality and allure of these dosage forms stem from the understanding of the danger and significance of medications, which are typically taken orally inside capsules and tablet form.

Traditional oral dosages may be ineffectual and unintentionally hazardous, because the human body shows variations in medication concentration in bodily tissue and the bloodstream. Consequently, maintaining the medicine concentration in plasma within the therapeutic range is essential for an effective course of treatment. Oral drug administration is being hampered by these oral factors, such as frequent dosing and irregular absorption. Conversely, these two features are not present in the controlled release medication administration method.

Therefore, the controlled release drug delivery system employs the oral medication delivery approach. The number of mechanisms in the controlled release medication delivery system was excessive for controlling the drug's release rate. Creating medication that follow a controlled release drug delivery mechanism is a significant issue for all pharmaceutical scientists. Various formulation methodologies have been employed to predict drug release through matrix systems, including water penetration, polymer swelling, drug dissolution, drug diffusion, and matrix erosion[9][10].

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 fall under the reservoir type category of dissolution controlled release mechanisms. Granule coating typically involves the use of single or mix hydrophilic and hydrophobic polymers. Gelatine, polyvinyl alcohol, cellulose derivatives (ethyl, methyl, HPMC, etc.), and cellulose acetate phthalate are a few examples.

Factors influencing the design and act of controlled release products

1. Physiological properties
    - Aqueous Solubility's
    - Partition coefficient (P-value)
    - Drug pKa
    - Drug stability
    - Molecular size & molecular weight
    - Protein binding
2. Biological factors
    - Therapeutic window
    - Patient physiology
    - Biological half-life (t1/2)
    - Absorption

Spansules:

The term "Spansules" refers to capsules that contain medication (in the form of granules) and are coated with substances that dissolve slowly, enabling the medication to be administered at distinct times.

Mode of action of spansules

Spanules" behavior"

Every medicine granule or particle used in Spanules is coated with a substance that has a slow dissolving action. These coated tablets can be characterized as SPACETABS when they are pressed into tablet shape, or as SPANSUSLE when they are pressed into capsule form. Drug dissolution in Spanules may be controlled by microencapsulation. The medicine is liberated and prepared for dissolving when the coating on the drug granules dissolves. With slight modifications to the mixture and coating thickness, drug release can be anticipated. Spanules shouldn't be chewed or broken because doing so could harm the coating.

Many granules in a spanule differ from one another in terms of coating thickness. These granules provide a loading dosage before releasing the medicine over a range of time intervals at a specified rate. These coated granules

release medications every 2 to 3 hours, every 4 to 6 hours, and every 6 to 9 hours. The mechanism by which medication is released is dependent upon moisture seeping into the coating of the particles, which causes the thickness material to inflate and eventually burst.

The best illustration of a dissolution release method is a spanule. Typically, either alone or in combination, hydrophobic or hydrophilic polymers are utilized. Gelatin, polyvinyl alcohol, and cellulose acetate phthalate are a few examples[11][12].

Technology Principle for Coating Spansules

- The capsule is one of the most advanced, specialized, and cutting-edge drug delivery devices available.
- The granules with the thinnest covering will deliver the initial dose since each granule has a varied coating thickness outlet, which allows drugs to be released in various ways.
- One of the best ways to administer several medications at once is with capsules.
- It can also increase the effectiveness of the dose and its dosing forms while minimizing negative effects to maximize patient compliance.
- The fact that the beginning of absorption is less vulnerable to stomach emptying is the greatest advantage of encapsulated pelleted goods[13][14].

Method of preparation of spansules:

1. Coacervation- phase separation
    - Formation of three immiscible chemical phases
    - Deposition of the coating material
    - Rigidization of the coating
2. Spray drying
3. Spray congealing
4. Pan coating
5. Solvent evaporation
6. Fluidised bed technology
    - Top spray
    - Bottom spray
    - Tangential spray

1. Coaservation-phase separation: - It mainly contains three steps.
    a. Three immiscible chemical phases form: the liquid production vehicle phase, the core material phase, and the coating material phase. One of the methods of phase separation conservation, such as altering

the temperature of the polymer solution, adding salt, adding non-solvent, or inducing a polymer interaction, is used to form the coating material phase, which is an immiscible polymer in a liquid phase.

b. Coating material deposition: In this step, liquid polymer coating material is deposited on top of the core material by means of polymer adsorption at the interface that forms between the liquid vehicle phase and the core material. The system's decreased surface tension then encourages the coating material to continue to deposit.

c. The process of rigidizing the coating is often accomplished by the use of thermal cross-linking or desolvation techniques.

2. Spray drying: Using hot, dry air, the active ingredient is first suspended or dissolved in the coating substance. A solvent that dissolves the coating material quickly evaporates, causing the coating to solidify. It works quickly in a single step and is applicable to compounds that are thermolabile.

3. Spray congealing: This method makes use of a material with the ability to melt at high temperatures. When the droplet formed on the spray dryer and went through the chilly air, the substance began to atomize and solidify. This involves thermally congealing a liquid coating substance to cause the coating to solidify.

4. Pan coating: This method is frequently employed to create tiny coated pellets or particles. Solid particles larger than 600 microns in size are thought to be necessary for coating. An active ingredient is typically coated onto different spherical shaped particles, which are tumbling in a coating pan while coating material is applied slowly. The solid core material is coated using an atomizing spray application of the coating solution. Warm air is blasted over the coated materials in order to eliminate the coating solvent.
5. Solvent evaporation: In this procedure, a volatile solvent that is immiscible with the liquid vehicle phase is used to dissolve the coating material. To create microcapsules of a consistent size, a core material is mixed into the coating solution and distributed. After that, this mixture is heated while being stirred constantly to evaporate the solvent. As coating materials, a range of film-forming polymers, including polyvinylpyrrolidone, polyethylene, poly vinyl alcohol, polyacryl acid, etc., can be utilized.
6. Fluidized bed technology: A fast evaporation process helps build an outer, hard layer on the particle with the necessary thickness. Liquid coating material is sprayed over the particles in this manner[15][16][17].

Evaluation parameter of spansules:

1. Particle size: Several widely used techniques for ascertaining the particle size distribution include sieve analysis, dynamic light scattering, static laser light scattering analysis, and so on. Every technology listed above has the ability to measure particles ranging in size from 1 to 3 mm. The particle size of the granules in Spanules can be rapidly ascertained using a straightforward sieve analysis[18][19].

2. Friability test: The percentage weight loss of 10 g of spanules after 100 rotations in a friabilator can be used to determine the spanules' friability[20].
3. Loss on drying: This test technique is frequently used to ascertain a sample's moisture content[21].
4. Moisture content: Sample heating can be used to determine the moisture content under certain circumstances. The following formula can be used to calculate the weight loss.

   % moisture content is equal to w2-w1 × 100/ w2-w1.

Marketed preparation of spansules:

Product name	Active ingredient
Dexedrine	Dextromethorphan
Combid	Prochlorperazine Maleate
Ornade	Phenyl propanolamine
Fefol	Ferrous sulphate, folic acid
Benzedrine	Amphetamine sulphate
Thorazine	Chlorpheniramine hydrochloride
Feospan	Dried ferrous sulphate
Hispril	Biphenyl pyraline hydrochloride
Fenbid	Ibuprofen
Balkaprofen	Ibuprofen
Prilosec	Omeprazole
Fesovit-Z	Ferrous sulphate

Advantages of spansules:

1. Patient compliance has improved, and adverse effects have decreased[22].
2. Give single or several prescription and over-the-counter medications both controlled and supported delivery[23].
3. By preventing the medicine from degrading in the gastrointestinal tract, it improves stability[24].
4. It increases the safety margin for very strong drugs and reduces the chance of both local and systemic adverse effects in sensitive patients[25].
5. Customised delivery profiles.
6. It also protects against a patient skipping a dose because there is no longer a need to administer the medication many times[26].
7. It masks the taste.

Disadvantages of spansule:

1. Economic limitation.
2. When overmedication occurs, fluctuations in plasma drug levels can cause negative effects, particularly for drugs with low Therapeutic Index (TI)[27].
3. It is challenging to treat toxicity brought on by long-acting preparation.
4. Lack of *in vitro- in vivo* correlation[28].

Future aspects:

This is a new method of drug preparation that results in effective drug delivery since the therapeutic ingredients are microencapsulated and placed inside a capsule shell. There are numerous dose forms available. The amount of medicine released can be controlled by adjusting the thickness and rate of disintegration of the granules. The medication will therefore be released at different predetermined periods.

Conclusion:

Spansules are capsules that hold medication (granules) and are coated with materials that dissolve gradually, enabling the medication to be taken throughout the day. This increases the safety margin for really strong drugs. They are created by enclosing an active ingredient in a capsule shell in the form of granules or microparticles, which can vary in size from one micron to several millimeters. This specific type of capsule gives the medication when it's needed while protecting the granules or active component from the environment.

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