Current Research in Pharmaceutical Sciences
Available online at www.crpsonline.com

ISSN: 2250 – 2688

Received: 11/03/2023
Revised: 19/03/2023
Accepted: 26/03/2023
Published: 08/04/2023

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DOI: 10.24092/CRPS.2023.130102

Website: www.crpsonline.com

Quick Response Code:

A Concise Review on Spansules: A New Method of Drug Delivery

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ABSTRACT

Spansules are considered as an Advanced Drug Delivery System because they allow for controlled and sustained release of medication over an extended period of time. This type of delivery system can provide a constant plasma drug concentration over a wide range of time, which can improve treatment outcomes and reduce the risk of side effects. In addition to providing sustained release, Spansules can also be used to deliver multiple drugs in a single dosage form. The multi-drug regimen capability of Spansules is also beneficial, as it allows for the delivery of multiple drugs in a single dosage form. This can improve patient compliance with their medication regimen, simplify dosing, and reduce the risk of drug interactions. This can be particularly useful in cases where a patient requires treatment with multiple medications to manage a complex medical condition. Spansules can act as biphasic release drug delivery system that can be used to provide both immediate and sustained release of medication. These systems can be useful in cases where a patient requires rapid relief of symptoms followed by ongoing management over a longer period of time. Overall, Spansules are a versatile and effective drug delivery system that can provide several benefits to patients and healthcare providers.

Key words: Spansules, Biphasic, Controlled release, Sustained release, Drug.

1. INTRODUCTION

Spansules are a type of advanced drug delivery system that involve packing an active ingredient inside a capsule shell in the form of granules or micro particles of varying sizes. This type of capsule protects the granules or active ingredient from its surrounding environment and releases the medication at a required time.[1] Spansules present a new challenge in the design and manufacture of dosage forms, requiring various skills, experience, advanced technologies, and specialized equipment. Spansules were first introduced by Smith Kline & French in 1952 as a timed-release formulation, which sparked a widespread search for other applications in the design of dosage forms.[1] Today, Spansules have several potential advantages over conventional dosage forms, such as their ability to optimize drug delivery over a prolonged period of time, and their potential for delivering various medicaments with minimal side effects.

Spansules are a type of drug delivery system in which the medication is released slowly over an extended period of time. Spansules are made up of small beads or pellets that are coated with a special polymer that dissolves slowly, allowing the drug to be released gradually into the body. Spansules are often used to treat conditions that require long-term medication, such as hypertension, diabetes, and psychiatric disorders.[2] The slow release of medication from Spansules can help to maintain a constant therapeutic level of the drug in the body, which can improve treatment outcomes and reduce the risk of side effects. Spansules are available in a variety of formulations, including capsules, tablets, and pellets. They are typically prescribed by a healthcare provider and should be taken exactly as directed to ensure optimal treatment outcomes.[3]

Spansules are designed to release one or more drugs over a specified period of time. They are typically made up of granules or pellets that contain one or more active pharmaceutical ingredients (APIs), and are coated with a slow-dissolving polymer that controls the release of the medication. The coating of the Spansules determines the release pattern of the drug, and can be designed to release the medication at different and predetermined times. This allows for a controlled and sustained release of the medication over an extended period of time[2], which can improve treatment outcomes and reduce the risk of side effects. Spansules are available in various dosage forms, such as capsules, tablets, and pellets, and are commonly used to treat conditions that require long-term medication, such as hypertension, diabetes, and psychiatric disorders.

1.1 Advantages of Spanules

Spansules offer several advantages over other dosage forms, including.

- Controlled and sustained release: Spansules provide controlled and sustained release of medication, which can help maintain a therapeutic level of the drug in the body and reduce the need for repeated dosing.[4]
- Improved patient compliance: By reducing dosing frequency and providing a more convenient dosing schedule, Spansules can improve patient compliance with their medication regimen.
- Reduced side effects: Spansules can reduce the risk of side effects by controlling the release of the medication and maintaining a consistent therapeutic level in the body.
- Modified delivery profile: The delivery profile of Spansules can be modified to release the medication at specific times, which can improve treatment outcomes.
- Enhanced bioavailability: The controlled release of medication from Spansules can enhance drug degradation in the gastrointestinal tract (GIT) and improve bioavailability.
- Taste masking: Spansules can be formulated to mask the taste of medications, which can be particularly beneficial for patients who have difficulty swallowing tablets or capsules.

1.2 Limitation of Spanules

Spansules have some limitations, including.

- Limited in vitro-in vivo correlation data: There is limited data available to correlate in vitro release characteristics of Spansules with their in vivo performance.
- Risk of dose dumping: If the Spansules are damaged or otherwise compromised, there is a risk of "dose dumping" where the medication is released too quickly and can cause adverse effects.
- Low systemic availability: Spansules may have lower systemic availability compared to other dosage forms, as the medication is released slowly over an extended period of time.[4]
- Complex formulation: The formulation of Spansules can be complex and requires skilled labor to produce, which can increase the cost.
- Higher cost: Spansules can be more expensive than other dosage forms due to the complex formulation process and specialized equipment required for production.

2. DRUG RELEASE FROM SPANSULES

Various polymers are used to create a coating that is selectively permeable to water and other solvents, allowing the drug to be released at a controlled rate. The coating is designed to be sensitive to pH changes or enzymes in the gastrointestinal tract, which can cause it to dissolve or break down. However, this can also be a limitation if the coating is not designed properly, as it may lead to dose dumping or incomplete release of the drug. Additionally, Spanules may not be suitable for all types of drugs or formulations, as certain drugs may require immediate release or specific delivery systems.[5]

2.1 Methods of Preparation of Granules for Spansules

Spansules can be prepared by the following methods.

2.1.1 Coacervation-Phase Separation

Coacervation-phase separation is a process used in the formulation of microencapsulated drug delivery systems. It involves three main steps.

- Polymer selection and dissolution: The first step involves selecting a suitable polymer and dissolving it in a solvent to form a polymer solution. The polymer should have the ability to form a coacervate phase when mixed with a suitable coacervating agent.
- Coacervation: The polymer solution is then mixed with a coacervating agent, which is a substance that induces phase separation of the polymer solution into two phases: a dense polymer-rich coacervate phase and a dilute supernatant phase. This phase separation occurs due to changes in the solvent conditions, such as pH, temperature, or ionic strength.
- Encapsulation: The coacervate phase is then used to encapsulate the drug or active ingredient. This can be done by adding the drug to the coacervate phase or by dissolving the drug in the supernatant phase before mixing with the coacervate

phase. The drug is then surrounded by the coacervate phase, which forms a protective coating around it.

The resulting microcapsules have a core-shell structure, with the drug or active ingredient in the core surrounded by the coacervate phase as the shell. This process can be used to control the release of drugs over an extended period of time and protect them from degradation in the body.[6]

2.1.2 Spray Drying

Spray drying is a commonly used method for coating drug particles or granules. In this method, the drug is first dissolved or suspended in a coating material, which is then sprayed as a fine mist into a heated chamber. As the droplets of the mist move through the chamber, the solvent evaporates, leaving behind a dry, coated particle or granule. The coating solidifies upon contact with the hot air, forming a thin film around the drug.[6]

Spray drying is a rapid, single-stage process that can be used for thermolabile substances that might be damaged by exposure to high temperatures for long periods of time. It is also relatively easy to scale up, making it a popular choice for large-scale manufacturing of coated drug particles or granules.

2.1.3 Spray Congealing

In spray congealing, the substance being atomized is melted at high temperature and then sprayed through a nozzle to form droplets which are then solidified by passing through a cool air stream. The coating solidification takes place by thermally congealing a molten coating material, not by evaporation of a solvent like in spray drying. This method is particularly useful for heat-sensitive substances that cannot be exposed to high temperatures during the coating process.

2.1.4 Pan Coating

Pan coating is a commonly used method for coating small particles or pellets. The solid particles with a size greater than 600 microns are considered necessary for effective coating. In this method, the particles are tumbled in a coating pan while the coating material is slowly applied. The active ingredient is usually coated onto various spherical-shaped particles. The coating solution is applied by atomizing spray onto the solid core material. To remove the coating solvent, a blast of warm air is passed over the coated materials. This process is repeated several times until the desired coating thickness is achieved. Pan coating is a relatively simple and cost-effective method of coating particles and is widely used in the pharmaceutical industry.[6]

2.1.5 Solvent Evaporation

Solvent evaporation is a common method used in the preparation of microcapsules. In this process, the coating material is dissolved in a volatile solvent that is immiscible with the liquid vehicle phase. A core material is then dispersed in the coating solution with stirring to obtain uniform-sized particles. The granules size can be controlled by varying the stirring rate, the concentration of the coating material, and the type of solvent used. A variety of film-forming polymers can be used as coating materials in the solvent evaporation method. Examples include polyvinylpyrrolidone, polyethylene, polyvinyl alcohol, and polyacrylic acid. The choice of coating material depends on the desired properties of the microcapsules, such as stability, release rate, and compatibility with the core material. Solvent evaporation is a versatile and scalable method for the preparation of coated granules and is widely used in various fields, such as drug delivery, food and beverage, and personal care products.[6]

2.1.6 Fluidized Bed Technology

Fluidized bed technology is a method used for coating particles with a liquid coating material. In this process, the particles are suspended in a chamber containing a stream of air or gas that is rapidly flowing upward. As the gas flows through the particles, it causes them to become fluidized, behaving like a liquid, which creates a homogeneous mixing of particles. Liquid coating material is then sprayed onto the fluidized particles, forming a uniform coating on the particle surfaces. The rapid evaporation of the liquid coating material due to the high temperature and airflow helps in the formation of an outer rigid layer on the particles with the required thickness. The particles are constantly agitated during the process to ensure a uniform coating.

The fluidized bed technology can be used to coat various types of particles, including powders, granules, and pellets, with different materials, such as polymers, waxes, sugars, and other coating agents. The method offers several advantages, including uniform coating thickness, high coating efficiency, and controlled release of the active ingredients. Fluidized bed technology is widely used in various industries, including pharmaceuticals, food processing, agriculture, and cosmetics, for the production of coated particles. The method is also scalable and can be easily integrated into a manufacturing process.[4]

3. EVALUATION OF SPANSULES

3.1 Particle Size

Particle size is an important parameter in the production and characterization of granules, as it affects various properties such as flowability, compressibility, and dissolution rate. There are

various techniques available to determine the particle size distribution of granules. Sieve analysis is a simple and widely used method for particle size determination. It involves the separation of particles based on size using a set of mesh sieves with different pore sizes. The granules are passed through the sieves, and the weight of particles retained on each sieve is measured. The particle size distribution can be calculated from the weight percentages of particles retained on each sieve.

Static laser light scattering analysis and dynamic light scattering are other techniques used for particle size determination. These methods involve the measurement of the light scattering intensity by particles in a sample. The scattered light provides information on the size and shape of the particles. These techniques are particularly useful for determining the size of small particles, ranging from a few nanometers to a few micrometers. The particle size of granules in Spanules can be easily analyzed with the help of simple sieve analysis. As Spanules contains typically larger particles, sieve analysis can provide accurate results and is a cost-effective method for particle size determination. However, for smaller particle sizes, other techniques such as static laser light scattering analysis and dynamic light scattering may be more suitable.[7]

3.2 Moisture Content

Moisture content can be determined by measuring the weight loss of a sample after heating under specific conditions. The weight loss corresponds to the amount of moisture present in the sample.

The formula to calculate the moisture content is as follows:

Moisture content = (Wet weight - Dry weight)/Dry weight x 100%

Where,

Wet weight = weight of the sample before heating

Dry weight = weight of the sample after heating

The sample is first weighed in its wet state, and then heated under specific conditions to remove the moisture. After heating, the sample is weighed again in its dry state. The weight loss is then calculated using the above formula, which gives the percentage of moisture present in the sample. The specific conditions for heating depend on the type of sample and the method being used. For example, in the Karl Fischer titration method, the sample is heated to a specific temperature and mixed with a reagent to determine the moisture content. In the oven-drying method, the sample is dried in an oven at a specific temperature and time to remove the moisture. The specific conditions for each method should be carefully followed to obtain accurate results.[7]

3.3 Friability Testing

Friability testing is an important test to determine the physical integrity and stability of solid dosage forms, such as tablets, capsules, and granules. The test measures the susceptibility of the dosage form to damage during handling and transportation. In the case of Spansules, the friability can be calculated as follows.

- Weigh 10 grams of Spansules and place them in the friabilator.
- Set the friabilator to rotate the Spansules at 25 rpm for 4 minutes or for 100 revolutions.
- After 4 minutes or 100 revolutions, remove the Spansules from the friabilator and reweigh them.
- Calculate the percentage weight loss using the following formula:

Friability (%) = ((Initial weight - Final weight) / Initial weight) x 100

Where:

Initial weight = Weight of Spansules before the test

Final weight = Weight of Spansules after the test

A friability value of less than 1% is generally considered acceptable for most dosage forms, including Spansules. If the friability value is greater than 1%, it indicates that the Spansules are more susceptible to damage during handling and transportation, which can lead to reduced efficacy and quality.[8]

3.4 *In vitro* Release Studies from Spansules

In vitro release studies are important to evaluate the drug release characteristics of a dosage form in a controlled laboratory setting. Dissolution studies are a commonly used technique to perform in vitro release studies. Dissolution studies are performed using a calibrated dissolution apparatus, such as the USP apparatus I (basket), apparatus II (paddle), or apparatus IV (flow-through cell). In dissolution studies, the drug-containing spansules are placed in a dissolution medium, which typically consists of a buffer solution or simulated biological fluids. The dissolution medium is maintained at a specific temperature and agitated at a constant speed. The drug release is monitored by withdrawing samples of the dissolution medium at regular intervals and analyzing them for drug content.[9]

The UV spectrophotometer is a commonly used instrument for drug analysis in dissolution studies. UV spectrophotometry is a non-destructive technique that allows for the analysis of the drug in the dissolution medium without the need for complex sample preparation. The drug concentration in the dissolution medium can be determined by measuring the absorbance of the sample at a specific wavelength using the UV spectrophotometer. The drug release profile can be predicted by plotting the percentage of drug released versus time.[10]

4. FUTURE PROSPECTS

Spanules have shown promising results in the field of advanced drug delivery systems, and their future prospects are quite bright. The main advantages of Spanules are their ability to deliver multiple drugs in a single dosage form and their ability to enhance patient compliance while minimizing side effects. The following are some of the future prospects of Spanules.

- Development of targeted drug delivery: With the help of Spanules, targeted drug delivery can be achieved by coating the particles with a layer that can specifically target the site of action in the body. This will help in reducing the dose required and minimizing side effects.
- Development of site-specific drug delivery: Spanules can also be used to deliver drugs to specific sites in the body, such as the colon or the lungs. This will help in reducing the dose required and minimizing side effects.
- Combination therapy: Spanules can be used to deliver multiple drugs simultaneously, which can be helpful in treating complex diseases that require a combination of drugs.
- Improved bioavailability: Spanules can improve the bioavailability of drugs by controlling their release rate and protecting them from degradation in the gastrointestinal tract.
- Novel drug delivery systems: The concept of Spanules can be applied to various other drug delivery systems, such as liposomes, nanoparticles, and microspheres.

5. CONCLUSION

Spanules are a type of dosage form in which one or more active ingredients are kept inside a capsule shell in the form of particles or granules. The thick coating surrounding the granules prevents the active pharmaceutical ingredient from being exposed to its surroundings, and drug release takes place at a predetermined rate. Spanules represent a new area to explore in the field of advanced drug delivery systems, and their formulation requires skilled professionals, advanced technologies, and specialized equipment. Despite these requirements, Spanules are considered to be relatively easy to manufacture and offer potential benefits over conventional dosage forms. Overall, Spanules represent a promising area of research and development in the field of advanced drug delivery systems. In conclusion, Spanules have a bright future in the field of drug delivery systems, and their potential for targeted and site-specific drug delivery, combination therapy, and improved bioavailability makes them a promising candidate for future drug delivery applications.

ACKNOWLEDGEMENT

The authors would like to acknowledge Institute of Pharmacy, SAGE university, Indore for providing the facilities and support to conduct the review work.

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