Int. J. Sci. R. Tech., 2025 2(10)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

A Review Article on Spansule Technology

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ABSTRACT

Spansule technology is a significant advancement in oral drug delivery systems, particularly in terms of controlled, sustained, and targeted release of active medicinal ingredients.Spansules are hard gelatin capsules that contain tiny coated granules or pellets, each with its own unique releasing characteristics. The fundamental concept is based on multiphasic drug delivery, in which pellets covered with different polymer thicknesses disintegrate at staggered intervals, allowing for biphasic or triphasic drug release profiles. This ensures both fast therapeutic action and prolonged drug availability in systemic circulation, resulting in constant plasma drug concentrations throughout time.The history of spansule technology dates back to the 1950s, when Dexedrine Spansules and Contac 600 were first introduced. Since then, the technology has expanded to include advanced coating materials including carnauba wax, cellulose derivatives, ethyl cellulose, Eudragit, and polyvinyl alcohol, which provide greater control over dissolving rates and release kinetics. Drug release from spansules normally follows zero-order kinetics, which reduces variations in drug levels and improves treatment effectiveness. Spansules are particularly beneficial in the treatment of chronic ailments such as attentiondeficit hyperactivity disorder (ADHD), hypertension, pain disorders, and respiratory diseases, where stable therapeutic levels are essential. These systems also reduce dose frequency, increase patient compliance, reduce adverse effects, and safeguard sensitive medications from harsh gastrointestinal conditions.

Keywords: Spansule Technology Controlled Drug Release Sustained Release Multiphasic

INTRODUCTION

Spansule technology is a significant innovation in pharmaceutical drug delivery methods, designed to overcome the constraints of traditional dosage forms. This technology, first introduced in the early 1950s by Smith, Kline & French with products such as Dexedrine Spansules, was designed to deliver medications in a regulated and sustained manner, allowing for consistent therapeutic levels in the bloodstream over extended periods. [1,3] The term "spansule" is a combination of "span" and "capsule," signifying the capacity to release medications gradually over time. Spansules are gelatin capsules that contain hundreds of coated pellets or granules. Each pellet is designed with distinct coating thicknesses and compositions that disintegrate at varying rates once inside the gastrointestinal tract. These coatings are often composed of hydrophilic and hydrophobic polymers, including ethyl cellulose, hydroxypropyl methylcellulose (HPMC), cellulose acetate phthalate, Eudragit, and carnauba wax. [2,4] By changing the coating materials, spansules can be designed to offer rapid, delayed, or sustained release, or a mix of the three—making them ideal for biphasic or triphasic drug delivery. [5] The primary purpose of spansule technology is to maintain consistent plasma medication concentrations, reduce dose frequency, reduce peak-to-trough fluctuations, and improve patient compliance. This is especially useful in chronic diseases such as hypertension, diabetes, ADHD, and psychiatric disorders, where consistent medication levels are critical for optimal therapy. [6] Several innovative manufacturing techniques are used to manufacture spansules, including extrusion-spheronization, coacervation-phase separation, fluidized bed coating, spray drying, and pan coating. Each approach contributes to the production of homogenous, stable pellets with consistent drug release characteristics. [1,4] Despite their many advantages, spansules have significant drawbacks, including difficult production methods, greater prices, and the possibility of dose dumping if the coating's integrity is compromised. [3] Nonetheless, the

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

capacity to tailor drug delivery patterns and improve therapeutic outcomes makes capsule technology a promising platform in modern pharmaceutics.

Definition: - Spansules are capsules carrying medicines (in the form of granules) coated with materials that have slow dissolving rates, allowing the medicament to be supplied at different times. In other terms, it is a mix of two words, span and capsule, resulting in a capsule that slowly releases medication over a variable period of time.

Fig 1

❖ **Drug Release Types in Spansules**

Spansules are a type of controlled-release dosing method that releases the active pharmaceutical ingredient (API) in a precise manner. This is accomplished by utilizing several tiny coated pellets or granules, each with a unique polymer coating that dissolves at a variable rate. This enables spansules to distribute pharmaceuticals using one or more of the following release profiles: [4,6]

1. Immediate Release (IR) Purpose:

Delivers a portion of the medication dose immediately following intake. Uncoated or thinly coated grains dissolve rapidly in stomach juices. Advantage: Provides a rapid onset of therapeutic effect, making it useful for immediate alleviation (for example, pain or allergy problems). Application: Loading dose for biphasic/triphasic spansules [5].

2. Sustained release (SR).

The purpose is to slowly and continuously release the medicine over a lengthy period of time.

Mechanism: Hydrophobic polymers (such as ethyl cellulose and cellulose acetate) cover graules, slowing disintegration.

Advantage: Maintains a consistent plasma concentration, lowering the frequency of dose and enhancing patient adherence.

Application: Commonly used to treat chronic illnesses such as hypertension and ADHD. [2,4]

3. Delay Release (DR)

Purpose: Delays drug release to a later stage of the gastrointestinal tract, typically to avoid stomach degradation or irritation.

Mechanism: pH-sensitive coatings (such as Eudragit L or cellulose acetate phthalate)

breakdown only at higher pH values. Advantage: Protects acid-sensitive medications while ensuring site-specific delivery (e.g., to the gut).

Application: Effective for NSAIDs, enzymes, and probiotics. [1,6]

4. Biphasic Release.

Purpose: Combines quick and sustained release in a single capsule.

Mechanism: some granules dissolve fast, while others are coated to provide continuous release. Advantage: Advantage: Provides a fast-therapeutic response followed by long-term control, making it appropriate for pain management or psychiatric drugs. [3,5]

5. Triphasic Release

Purpose: The medicine is delivered in three phases: immediate, intermediate, and extended.

Mechanism: Uses numerous layers of coating of varied thickness and solubility.

Advantage: Combines numerous dosages in a single administration, giving sustained therapeutic coverage.

Application: Frequently used in once-day formulations to replace 2-3 daily doses. [2,6]

❖ **Summary Table**

Release Type	Time of release	Purpose	Common Polymers
Immediate Release (IR)	Rapid (0–30 min)	Quick onset of action	No coating or thin hydrophilic
Sustained Release	6–12 hours	Maintain steady drug level	Hydrophobic (e.g., ethyl cellulose)
Delayed Release	2–4 hours	Bypass stomach, release in intestine	pH-sensitive (e.g., Eudragit)
Biphasic	Dual Immediate + Slow	Fast relief + extended effect	Mixed polymer coatings
Triphasic	Immediate + Intermediate + Extende	Simulates multiple doses	Multi-layered polymer coatings

❖ **Release Control Factors in Spansules.**

Drug release from spansules is finely controlled by manipulating various formulation and physiological parameters. These factors influence how quickly or slowly the drug is released from the coated pellets or granules inside the capsule [8,12]

1. Coating Thickness

The thickness of the polymer coating surrounding the drug-loaded pellets directly affects the release rate. Thicker coatings create a longer diffusion path and stronger resistance to fluid penetration, resulting in delayed drug release [11]. Conversely, thinner coatings dissolve more rapidly, leading to faster release.

2. Polymer Type: Hydrophilicvs.Hydrophobic

Hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) allow faster diffusion of gastrointestinal fluids and drug molecules, thus promoting faster release [12] Hydrophobic polymers like ethyl cellulose and cellulose acetate form more water-resistant barriers, significantly slowing down drug release [7]

3. Environmental pH Sensitivity

Certain enteric coatings, such as Eudragit L/S, are pH-sensitive and designed to dissolve only at higher pH levels found in the intestine (typically pH >5.5). This is useful for drugs that are either acid-labile or irritating to the stomach lining (10]

4. Enzymatic Sensitivity

Some coatings or matrix systems incorporate components that degrade in the presence of specific gastrointestinal enzymes, such as amylases or proteases, triggering drug release [9]. This enzymatic-triggered mechanism can provide targeted or time-dependent release in specific parts of the gut.

❖ **Advantage of spansules**

1. Controlled and sustained drug release.

Maintains a stable plasma concentration of the medication over time. Avoids peaks and troughs in drug levels, which reduces unwanted effects. [16]

2. Improved patient compliance.

Reduces the frequency of dose (for example, once or twice per day). Simplified complex drug regimes, particularly for chronic illnesses. [18]

3. Reduced Side Effects.

Gradual release helps to reduce unpleasant responses caused by medication buildup or overdose. [19]

4. Enhanced bioavailability.

Protects the medication against breakdown in the GI tract. Improves absorption through prolonged exposure. [14]

5. Customized Drug Release Profiles.

Enables biphasic, triphasic, or timed-release formulations. Can have both rapid and delayed release in a single dose. [15]

6. Masking an unpleasant taste.

The coated pellets successfully conceal the harsh or metallic taste of medications. [20]

7. Reduced risk of dose omission.

A single dose delivers therapeutic action for several hours, mitigating the effects of missed doses. [17]

8. Improved stability.

The protective coatings improve the chemical and physical stability of the medication. [13]

9. Flexibility in formulation

Allows the mixing of various medications in a single capsule with distinct release times. [15]

10. Avoiding nighttime dosing.

The delayed release action eliminates the requirement for midnight dosing. [19]

❖ **Limitations of Spanules**

1. Fixed Dose with Release Kinetics:

Once created, a spansule's medication release profile cannot be changed. This reduces the flexibility for dose modifications in patients who require personalized therapy. [19]

2. Complicated Manufacturing Process:

The creation of spansules requires complicated coating processes and multiple technologies, which raises costs and necessitates precision equipment and experienced labour. [15]

3. Risks of Dose Dumping:

If the coating is destroyed (for example, due to incorrect storage, mechanical breaking, or gastrointestinal pH fluctuation), the entire drug dose may be released rapidly, resulting in toxicity. [22]

4. Delayed beginning of action:

Because of the sustained-release method, therapeutic effects may be delayed compared to instant-release formulations, which is a concern in situations requiring immediate relief. [21]

5. Not suitable for all drugs.

Drugs with extremely short half-lives, low GI tract stability, or quick onset are not appropriate for spansule formulation. [13]

6. Higher cost:

Spansules are more expensive to produce than traditional tablets or capsules, influencing patient affordability and accessibility in resource-limited environments. [18]

7. Problem with Patient Compliance:

Some patients may not comprehend the objective of sustained-release formulations and may misuse the medicine (for example, crushing spansules), which might result in altered pharmacokinetics or unwanted effects. [20]

8. GI Transit Time Variability:

Individual differences in stomach emptying and intestinal transit periods can have an impact on drug absorption and treatment response. [14]

❖ **Methods for Spansule Preparation**

Spansules are made up of drug-loaded granules or pellets covered in polymers that control drug release. Granule production and coating are carried out using the following methods:

1. Separation of Coacervation Phase Steps:

1. Three immiscible phases emerge: drug core, polymer coating phase, and liquid vehicle.
2. Coating deposition: the polymer phase deposits on the drug's core.
3. Coat rigidification via chilling, cross-linking, or desolvation.
   Use: To create microcapsules with specific release. [22,15]

2. Spray Drying

The process involves atomizing a drug solution with a coating polymer into hot air, followed by rapid drying and particle formation.

Advantage: Quick, appropriate for heat-sensitive medicines (if optimized). limitation is that the particle size may vary. [21]

3. Spraying Congealing

Melted drug-polymer mixture is sprayed in a cold air chamber, resulting in hardened pellets.

Advantage: No solvents are employed, making it suitable for heat-stable materials. [14]

4. Pan Coating.

Drug cores (>600 µm) are tossed in a pan, then coated and dried with heated air. Batch processing is a common practice. [17]

5. The Method of Solvent Evaporation.

The coating polymer is dissolved in a volatile solvent, then the drug core is dispersed, the solvent is evaporated, and film-coated grains are created. [22] The polymers employed were PVP, PEG, polyacrylates, and polyvinyl alcohol.

6. Fluidized Bed Coating (Wurster Process).

Types include top spray, bottom spray, and tangential spray. The process involves suspending drug cores in air and spraying them with a homogenous, scalable coating solution.

Ideal for: Controlled, enteric coating of tiny particles. [15]

7. Extrusion and Spheronization Steps:

1. Dry combining the components.
2. Wet massing.
3. Extrusion produces rod-shaped particles.
4. Spheronization involves transforming rods into homogeneous pellets. Used to create robust, homogenous pellets for coating. [21]

8. Freeze Pelletization:

Droplets of molten carrier and drug are dropped into a cold immiscible liquid, resulting in pellets that solidify upon cooling. Use temperatures table formulas. [14]

❖ **Evaluation of Spansules**

To verify the quality, safety, and efficacy of spansule formulations, different preformulation and post-formulation evaluation studies are carried out:

1. Physical appearance.

Objective: Assess the colour, shape, size, and consistency of spansules. Tools for visual inspection include magnification.

Importance: Ensures batch uniformity and aesthetic acceptability [23]

2. Particle Dimensions and Size Distribution

Objective: Determine the homogeneity of granules or pellets. Methods include sieve analysis, laser diffraction, and optical microscopy.

Importance: The uniform size provides consistent coating and medication release. [24]

3. Flow Properties.

Test: Angle of repose.
Bulk Density
Tapped Density
Carr's Index

The goal is to determine the compressibility and flow behaviour during encapsulation. [25]

4. Uniformity in Drug Content

Method: Sample is crushed and dissolved in a suitable solvent before being examined using UV spectrophotometry or HPLC.

Requirement: Drug content within pharmacopeial limits (usually ±5%). [26]

5. In-vitro Drug Release Research

The apparatus is USP Type I (basket) or Type II (paddle).

Typically, the media consists of 0.1 N HCl (pH 1.2) and phosphate buffer.

Analysis: A dissolution profile was created by plotting the percentage of drug release at different time intervals. [27]

6. Coating Thickness: Measured via microscopy gravimetric analysis.

Purpose: Verifies the coating layer to ensure optimum release rates. [28]

7. Encapsulation Efficiency:

The percentage of drugs successfully encapsulated in the capsules. [24]

8. Surface morphology

Scanning Electron Microscope (SEM)

The purpose is to examine the smoothness of the pellet surface and the homogeneity of the coating. [30]

9. Stability Studies.

Conditions: Follow ICH recommendations (e.g., 40°C/75% RH for 6 months). The following parameters were monitored: Appearance, drug content, and release profile. [29]

Moisture Content Method: Karl Fischer titration or loss on drying (LOD).

Importance: Prevents pellet deterioration and agglomeration. [25]

❖ **Spansules act in the following manner**

A material with a slow dissolving effect coats each medication granule or particle used in spanules. When these coated tablets are compressed into tablet shape, they are called SPACETABS; when they are compressed into capsule form, they are called SPANSUSLE. Through microencapsulation, drug dissolution in spanules can be regulated. The drug granules' covering dissolves, releasing the medication and preparing it for dissolution. It is possible to predict drug release with minor adjustments to the mixture and coating thickness. Chewing or breaking spanules could damage the coating, therefore avoid doing so. The coating thickness of many of the granules within a spanule varies from one another. Before releasing the medication at a predetermined pace over a variety of time intervals, these granules give a loading dosage. Every two to three hours, every four to six hours, and every six to nine hours, these coated grains release their medication. Moisture soaking into the particle coating, which causes the thickness material to swell and eventually burst, is the mechanism by which medication is released. A spanule is the best example of a dissolution release technique. [31, 32]

Spansule Coating Technology Principles

The capsule is among the most sophisticated, specialized, and innovative drug delivery methods on the market. The initial dose will be administered by the granules with the thinnest covering since each granule has a different coating thickness exit, allowing for different drug releases. Using capsules is one of the most effective ways to deliver multiple drugs at once. Additionally, it can optimize patient compliance by decreasing side effects and increasing the efficacy of the dose and its administration forms. Encapsulated pelleted items have the largest advantage in that the start of absorption is less susceptible to stomach emptying. [33]

FUTURE ASPECTS:

This is a novel approach to drug production that, by encapsulating the medicinal elements inside a capsule

shell, produces efficient drug delivery. Numerous dosage formulations are accessible. By altering the granules' thickness and rate of disintegration, the amount of medication delivered can be managed. The release of the medication will so occur at various prearranged times.

CONCLUSION:

Spansules are specialized capsules that contain medication in the form of granules, which are coated with substances that dissolve slowly to ensure controlled drug release throughout the day. This mechanism enhances the safety profile of potent drugs. They are formulated by encapsulating the active ingredient as granules or microparticles, typically ranging from one micron to several millimetres in size. Such capsules provide a sustained and timely release of the drug while shielding the granules or active compound from environmental factors.

Marketed Preparations of Spansules Brand

Brand Name	Active Ingredient
Dexedrine spansule	Dextroamphetamine sulfate
Rynatan spansule	Chlorpheniramine +Phenylephrine
Thorazine spansule	Chlorpromazine hydrochloride
Lomotil spansule	Diphenoxylate +Atropine
Oranade spansule	Phenylpropanolamine + Chlorpheniramine
Fefol	Ferrous sulphate, folic acid
Prilosec	Omeprazole
Fesovit-Z	Ferrous sulphate

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HOW TO CITE: Aditya Shinde, Sayali Pagire*, Gaurav Zalte, Dnyaneshwar Shinde, Divya Shinde, Varsha Nyaharkar, A Review Article on Spansule Technology, Int. J. Sci. R. Tech., 2025, 2 (10), 94-101. https://doi.org/10.5281/zenodo.17294601