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REVIEW ARTICLE **OPEN ACCESS**

Suppository Formulations: Current Trends and Future Prospects

Kinnari Patel[1], Vivek Shrivastava[2*], Lalit Lata Jha[3], L D Patel[4]
[1]Department of Pharmaceutics, School of Pharmacy, Parul University, Vadodara-391760, India
***Corresponding Author**- Vivek Shrivastava
Email: vivek.shrivastava121147@paruluniversity.ac.in

ABSTRACT
Suppository formulations have long been an essential pharmaceutical delivery system, offering unique advantages such as bypassing hepatic first-pass metabolism and providing targeted drug delivery. The present review explores the current trends and future prospects of suppository formulations, highlighting recent advancements in formulation technologies and their potential applications. Emphasis is placed on various types of suppository bases, including lipid-based, water-soluble, and biodegradable polymers, discussing their advantages and limitations. Additionally, the review examines novel approaches such as nanostructured suppositories and 3D printing techniques, which show promise in enhancing drug solubility, bioavailability, and patient compliance. The future of suppository formulations lies in personalized medicine, with tailored suppositories designed to meet specific patient needs and preferences. Overall, The present review provides a comprehensive overview of the evolving landscape of suppository formulations, offering insights into their current status and the exciting prospects that lie ahead.
Keywords: *Suppository Formulations, Rectal administration, pharmaceutical applications, Three-dimensional printing, Therapeutic outcomes.*

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INTRODUCTION

Suppository formulations have stood the test of time as a versatile and effective method of drug delivery. With their ability to bypass the gastrointestinal system and provide targeted release, suppositories offer a valuable alternative for patients unable to take medications orally. The review delve into, the current trends and future prospects of suppository formulations, exploring the latest advancements in formulation technologies, types of suppository bases, novel approaches, and the evolving landscape of personalized medicine [1].

ADVANCEMENTS IN FORMULATION TECHNOLOGIES

Recent years have witnessed significant advancements in suppository formulation technologies. One notable area of progress is in the development of lipid-based suppositories. Lipid-based formulations offer several advantages, including improved drug solubility, enhanced bioavailability, and prolonged release profiles [2]. Lipid matrices such as fatty acids, triglycerides, and waxes are commonly used due to their biocompatibility and stability. These matrices not only provide a suitable vehicle for drug delivery but also allow for controlled release, making them ideal for medications requiring sustained action [3]. Water-soluble suppository bases have also gained traction in pharmaceutical development. These bases, such as polyethylene glycols (PEGs) and glycerinated gelatin, offer advantages regarding ease of formulation and rapid drug release. Water-soluble bases are particularly useful for drugs with high water solubility, ensuring efficient absorption and onset of action. However, their quick dissolution may limit their use for sustained-release formulations [4]. Biodegradable polymers represent another exciting avenue in suppository formulation. Polymers like polylactic acid (PLA) and poly (lactic-co-glycolic acid) (PLGA) offer the advantage of sustained drug release combined with biocompatibility and biodegradability. These polymers can be tailored to achieve specific release profiles, allowing for precise control over drug delivery kinetics. Biodegradable suppositories are especially promising for long-term treatments, as they minimize the need for frequent dosing while reducing the risk of systemic side effects [5].

Types of Suppository Bases

The choice of suppository base plays a crucial role in the effectiveness of drug delivery. Among the various types available, cocoa butter remains a popular choice due to its melting point close to body temperature, facilitating easy insertion and drug release. Cocoa butter suppositories are well tolerated by patients and

exhibit good compatibility with a wide range of drugs. However, its susceptibility to oxidation and rancidity may limit its shelf life [7]. In contrast, polyethylene glycol (PEG) bases offer advantages in terms of water solubility and rapid drug release. PEG suppositories are easy to prepare and handle, making them suitable for a variety of drugs, especially those with high water solubility. Glycerinated gelatin suppositories, on the other hand, provide a water-soluble alternative with good bioadhesive properties, ensuring prolonged contact with the mucosal surface for enhanced drug absorption [8].

Novel Approaches in Suppository Formulations

The field of suppository formulations continues to evolve with the introduction of novel approaches aimed at improving drug delivery efficacy and patient compliance. One such approach is the utilization of nanostructured suppositories. Nanostructured lipid carriers (NLCs) and solid lipid nanoparticles (SLNs) offer advantages such as increased drug loading capacity, improved stability, and controlled release. These nanocarriers can protect drugs from degradation, enhance their solubility, and facilitate targeted delivery to specific tissues or cells. Another innovative technique is the use of 3D printing for suppository manufacturing. 3D printing enables the precise fabrication of suppositories with customized shapes and sizes, allowing for personalized medicine. This technology not only enhances patient compliance but also offers the potential for on-demand production, reducing waste and improving cost-effectiveness. Furthermore, 3D-printed suppositories can incorporate multiple drugs or dosages in a single formulation, catering to individual patient needs [9].

Future Prospects: Personalized Medicine and Tailored Suppositories

The future of suppository formulations lies in the realm of personalized medicine. Advances in pharmacogenomics and patient-specific treatment approaches are paving the way for tailored suppositories designed to meet the unique needs of each individual. By considering factors such as genetic variations, disease characteristics, and patient preferences, suppositories can be optimized for maximum efficacy and minimal side effects. Personalized suppositories may involve customized drug combinations, dosages, and release profiles based on a patient's genetic profile and therapeutic requirements. This approach holds immense potential for improving treatment outcomes, reducing adverse reactions, and enhancing patient adherence. Moreover, the advent of digital health technologies, such as wearable devices and smart drug delivery systems, can further enhance the monitoring and effectiveness of personalized suppositories [10]

INNOVATIVE TECHNOLOGIES OR NOVEL APPROACHES OF SUPPOSITORY:

Bi-layered Suppositories:

Bi-layered suppositories represent a novel approach by integrating multiple active ingredients into a single dosage form. This innovative method helps prevent potential drug interactions and allows for the sequential release of medications. The controlled delivery system of bi-layered suppositories aims to enhance treatment effectiveness and patient adherence by targeting drugs to specific sites, reducing dosages, and ensuring consistent distribution. The advantages of bi-layered suppositories include eliminating the need for repetitive dosing, preventing drug interactions, and enabling controlled release of active components [11].

Double Layered Suppositories:

The development of double-layered suppositories is a recent advancement in the field. These suppositories are designed to enhance the absorption of medicine in the lower rectal vein. The innovative approach combines different medications with distinct qualities to create unique layers within the suppository. The upper layer is formulated to prevent drug diffusion and increase drug availability, while the lower layer provides immediate and sustained release effects. For example, suppositories containing aspirin aim to improve their bioavailability and prevent the diffusion of other medications, while those with bitter bean extracts target vaginal delivery for gynecological inflammation [12].

Homogeneous Plain Suppositories:

Suppositories are categorized based on their administration method, with torpedo-shaped ones being the most convenient for rectal insertion. Adult suppositories typically weigh 2 grams and measure 3 to 4 centimeters in length, while those for children weigh 1 gram, adjusted according to age. Vaginal suppositories come in various shapes such as spherical, ovoid, duckbill, or fusiform, with weights ranging from 2 to 5 grams and diameters between 1.5 to 2.5 centimeters. Additionally, there are urethral, nasal, and ear suppositories among other variations [13].

Effervescent Suppositories:

Effervescent suppositories are effective for treating gynecological conditions as they produce foam, improving drug contact and effectiveness. These suppositories utilize fatty acids, sodium bicarbonate, and citric acid to create foam, enhancing drug concentration in the tissue. For instance, Danazol is a key medication in these plugs. Povidone iodine plugs are created using povidone-iodine, sodium bicarbonate, citrate, and a specific molding technique, providing a simple, stable, and convenient approach for quality

control. These plugs have a long validity period and consistent iodine content when stored at low temperatures[14].

Sustained Release:

Sustained-release suppositories gradually release medication using a non-soluble polymeric substance. The matrix delays the drug release process, which is influenced by mucosal fluid. For example, indomethacin sustained-release suppositories have a unique profile with delayed time to peak, lower peak concentration, and prolonged efficacy. Metronidazole and miconazole nitrate sustained-release suppositories are prepared using hydroxypropyl methylcellulose, extending drug effectiveness, reducing administration frequency, and maintaining therapeutic concentrations[15].

EVALUATION OF SUPPOSITORIES

The evaluation of suppository formulations involves several key parameters to ensure their quality, efficacy, and stability.

Weight variation: It is a crucial aspect, where the weight of each suppository is measured and compared to an average weight. This helps identify deviations, with only two suppositories showing more than a 5% difference from the average[16].

Hardness: It is another vital parameter, assessed using a Monsanto hardness tester. This test determines the suppositories' ability to withstand handling and transportation challenges, providing insights into their tensile strength and fracture points [17].

Disintegration test: They are conducted to assess the breakdown of suppositories in different mediums. The USP pill disintegration test instrument is used with distilled water at 37°C. Understanding the disintegration time is essential for both water-soluble and oily-based suppositories [18].

Macro-melting range test: It involves observing the liquefaction of suppositories in capillary tubes immersed in water, gradually increasing the temperature. This helps identify the range within which the suppository melts [19].

Liquefaction time and temperature: are determined using a specialized apparatus with a pipette and glass rod, providing insights into the suppository's behaviour under specific conditions [20].

Solidification time: It is crucial to understand the relationship between melting and the solidification of suppositories. It influences the release of the active substance and the pharmacological effect [21].

Dissolution test: This test challenges researchers due to melting distortion, but various techniques, such as using natural membranes or dialysis tubing, have been employed to regulate mass or medium interface variation[22].

Stability study: They are conducted to assess the formulation's shelf life, with suppositories subjected to room temperature and refrigerated conditions for 6 weeks. These studies, using carefully packaged samples, provide insights into drug content and release properties over time[23].

Breaking test: It evaluates suppositories' fragility, helping to address issues of brittleness and determining how well they withstand handling forces[24].

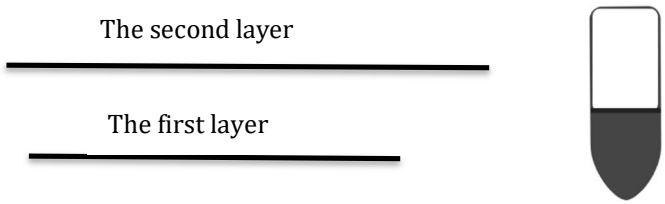

Figure 1: Schematic Illustration of Bi-layered Suppository

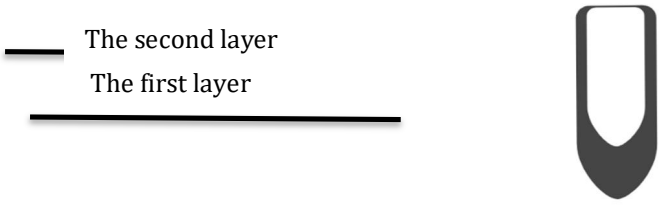

Figure 2: Schematic Illustration of Bi-layered Suppository with Outer and Inner Layers

Table 1. Ingredients in suppositories, their indication, and adverse effect [6].

Ingredients	Indication	Adverse effect
Local anesthetics (Lidocaine, Benzocaine, and Centbucridine)	Discomfort from hemorrhoids, fissures, or surgery in the anal region.	Inflammation accompanied by cryptitis or proctitis.
Steroids (Hydrocortisone, Prednisolone)	Swollen veins in the rectum.	Absorption into the bloodstream over time.
Astringents (Zinc oxide)	Inflammation of anal crypts, itching around the anus, and swollen rectal veins.	Local reaction.
Vasoconstrictors (Phenylephrine)	Swollen rectal veins with blood clot formation.	Head pain, skin redness, and rapid heart rate.
Protectants and Emollients (Aloe vera, Zinc oxide, Calamine)	Hemorrhoids, anal fissures, pruritus ani	No specific adversity
Antiseptics (Boric acid, Benzalkonium chloride)	Inflammation of the rectum, anal crypts, and tears in the anal lining.	Itching, discomfort, and a burning sensation

CONCLUSION

In conclusion, suppository formulations continue to be a vital and evolving aspect of pharmaceutical development. Advances in formulation technologies, including lipid-based, water-soluble, and biodegradable polymers, offer diverse options for drug delivery optimization. Novel approaches such as nanostructured suppositories and 3D printing hold promise in improving drug solubility, bioavailability, and patient compliance. The future of suppository formulations lies in personalized medicine, with tailored suppositories designed to meet the specific needs and preferences of individual patients. As we embrace these advancements, the potential for enhanced therapeutic outcomes and patient well-being in the field of suppository formulations is indeed promising.

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