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Sachita Gavade
Research Scholar, Shri Ganpati Institute of Pharmaceutical Sciences and Research, Tembhurni, Solapur, Maharashtra, India

Snehal Salunke
Research Scholar, Shri Ganpati Institute of Pharmaceutical Sciences and Research, Tembhurni, Solapur, Maharashtra, India

Divya Waghmode
Research Scholar, Shri Ganpati Institute of Pharmaceutical Sciences and Research, Tembhurni, Solapur, Maharashtra, India

Namdeo Shinde
Associate Professor, Department of Pharmaceutics, Shri Ganpati Institute of Pharmaceutical Sciences and Research, Tembhurni, Solapur, Maharashtra, India

Corresponding Author:
Sachita Gavade
Research Scholar, Shri Ganpati Institute of Pharmaceutical Sciences and Research, Tembhurni, Solapur, Maharashtra, India

Beyond conventional dosage forms: Foam-based systems for dermatological, wound healing, and mucosal drug delivery

Sachita Gavade, Snehal Salunke, Divya Waghmode and Namdeo Shinde

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Abstract
Foam-based drug delivery systems represent a significant advancement beyond conventional dosage forms, offering unique physicochemical and therapeutic advantages for dermatological, wound healing, and mucosal drug administration. These systems utilize gas-liquid or gas-solid dispersions to create low-density, highly spreadable formulations that enhance drug penetration, patient comfort, and adherence, particularly in sensitive or inflamed skin conditions and hard-to-reach areas. In dermatology, foam formulations have demonstrated superior therapeutic efficacy, such as a 30% improvement in psoriasis treatment compared to traditional topicals, and are especially beneficial for disorders like eczema due to improved skin coverage and hydration For wound healing, foam dressings often composed of biocompatible polymers and sometimes loaded with antimicrobials or growth factors provide a moist environment, absorb exudate, and facilitate controlled drug release, accelerating tissue regeneration and reducing infection risk. Mucosal delivery benefits from foam's mucoadhesive properties and rapid drug release, as seen in multi-layered systems that improve peptide permeation and bioavailability. Recent innovations include propellant-free foams, nanotechnology integration, and tailored polymer compositions to optimize stability, drug release, and patient outcomes. Collectively, foam-based systems are poised to transform topical and mucosal therapies by enhancing bioavailability, safety, and patient quality of life.

Keywords: Dermatology, wound healing, mucosal delivery, foam drug delivery

Introduction

Foam drug delivery systems represent a sophisticated approach to administering medication, offering unique advantages over conventional methods like pills, ointments, and intravenous solutions (Langer, 1990) [21]. Traditional drug delivery often grapples with limitations such as poor bioavailability, erratic plasma drug levels, and the inability to sustain drug release, potentially compromising therapeutic efficacy and necessitating frequent dosing (Adepu & Ramakrishna, 2021; Nguyen *et. al.*, 2023) [1, 30]. These systems typically involve incorporating a drug into a foam matrix, which then allows for topical, or internal administration. The capacity of these systems to regulate drug release, target specific tissues, and diminish adverse effects underscores their pivotal function in enhancing medication's therapeutic effectiveness (Nguyen *et. al.*, 2023) [30]. The design of effective drug delivery systems is complex, involving careful consideration of factors such as drug absorption, diffusion limitations, and the need for site-specific or time-dependent controlled delivery (Ülker & Erkey, 2014) [42]. Advanced drug delivery technologies offer substantial advantages for drug administration (Coelho *et. al.*, 2013) [7]. Ideally, these systems enhance patient compliance by simplifying self-dosing (Sershen & West, 2002) [38]. The ultimate goal of these systems is to create personalized treatment for a broad range of highly prevalent diseases (Coelho *et. al.*, 2013) [7].

Foam-based formulations are thermodynamically unstable systems, characterized by a dispersion of gas bubbles within a continuous liquid phase, frequently stabilized by surfactants (Homayun *et. al.*, 2019) [15]. These systems are known to be beneficial for topical and local drug delivery due to their ease of application, prolonged contact time with the application site, and ability to deliver drugs to targeted areas (Garg & Jain, 2021) [10]. Foams possess inherent properties such as spreadability, and ease of application, rendering them particularly well-suited for dermatological applications, wound healing, and delivery to mucosal surfaces (Ramesh *et. al.*, 2020) [36]. Foam drug delivery systems are designed to optimize drug concentrations at the target site, prolong drug residence time, and enhance patient compliance. The oral route is frequently favored for drug delivery because it is easy, causes less discomfort, and can be self-administered (Li *et. al.*, 2019) [23]. However, some drugs may be broken down in the gastrointestinal tract or not absorbed well enough to be effective. Local drug delivery curtails the side effects and overdose risks linked to systemic administration, concurrently amplifying the medication's concentration at the intended site (Mouriño & Boccaccını, 2009) [26]. The development of these systems requires a comprehensive understanding of formulation science, material properties, and drug delivery principles to achieve optimal therapeutic outcomes.

Several types of foam drug delivery systems exist, each tailored to specific applications and drug characteristics. These include, but are not limited to, aqueous foams, oleaginous foams, and emulsion foams, each possessing distinct physicochemical properties that influence drug release and delivery kinetics. Aqueous foams, for instance, are typically composed of water, a surfactant, and a drug, offering a hydrophilic environment suitable for water-soluble drugs. Oleaginous foams, on the other hand, utilize an oil-based continuous phase, making them ideal for lipophilic drugs or applications requiring enhanced skin hydration. Emulsion foams combine the properties of both emulsions and foams, allowing for the delivery of both hydrophilic and lipophilic drugs in a stable formulation (LB *et. al.*, 2018) [22]. These are versatile, offering a range of applications spanning from dermatology and wound healing to oral and nasal drug delivery. The selection of the appropriate foam type depends on factors such as the drug's solubility, the desired release profile, and the target site of action.

Foam drug delivery systems offer numerous advantages over traditional drug delivery methods. These systems allow for direct application to localized areas of the body without affecting the entire system, reducing toxicity and side effects (Herbig *et. al.*, 2023) [14]. These advantages include enhanced drug bioavailability, improved patient compliance, and the ability to deliver drugs to specific target sites. The ability to deliver drugs in a controlled and sustained manner minimizes the need for frequent dosing, further enhancing patient convenience and adherence to treatment regimens (Keraliya *et. al.*, 2012) [19]. These systems can maintain drugs at the intended site for an extended period, facilitating sustained release and lowering the necessity for repeated administrations (Goudanavar *et. al.*, 2021) [12]. Furthermore, foam formulations can be easily applied to large or irregular surface areas, making them particularly useful for dermatological conditions, wound care, and other topical applications.

Despite their advantages, foam drug delivery systems also have certain limitations. These systems are not suitable for all drugs or patients, and careful consideration must be given to factors such as drug stability, foam structure, and patient sensitivity. The optimization of foam formulations requires meticulous selection of excipients, surfactants, and propellants to ensure foam stability, drug compatibility, and consistent drug release. Issues such as foam collapse, drug precipitation, and variations in foam density can affect the accuracy and reliability of drug delivery. Moreover, the production and scale-up of foam formulations can be challenging, requiring specialized equipment and expertise to ensure consistent product quality and performance.

Ideal candidates for foam drug delivery include patients with dermatological conditions, wound healing needs, or those requiring localized drug delivery to mucosal surfaces. These systems can also be used to deliver drugs to specific areas of the body, such as the lungs or nasal passages. Foam drug delivery is especially useful for individuals who may have difficulty swallowing pills or those who require targeted drug delivery to specific tissues or organs (Kefalides, 1998) [18]. Topical drug delivery systems have shown great preclinical results for skin problems (Raina *et. al.*, 2023) [35]. However, because the skin acts as a barrier, it can be challenging to deliver drugs effectively (Raina *et. al.*, 2023) [35]. Nanoformulations can help with this (Mousavi *et. al.*, 2023) [27]. They improve drug penetration, target specific skin layers, provide controlled release, and reduce side effects (Chacko *et. al.*, 2012) [6]. Microemulsions and nanoemulsions, which are nanosystems, offer significant potential for targeted drug delivery to and through the skin (Nastiti *et. al.*, 2017) [29].

Current trends in foam drug delivery involve the incorporation of nanotechnology, stimuli-responsive materials, and advanced imaging techniques to enhance drug targeting, controlled release, and real-time monitoring of drug delivery. Nanoparticles, liposomes, and microparticles can be integrated into foam formulations to improve drug encapsulation, stability, and penetration into target tissues (Mumtaz *et. al.*, 2023) [28]. Micelles composed of amphipathic copolymers have received wide attention owing to their attractive features, such as small and uniform size, tumor targeting ability via the enhanced permeability and retention effect, high stability in aqueous solution and excellent biocompatibility (Yang *et. al.*, 2019) [45]. Stimuli-responsive polymers that respond to changes in pH, temperature, or enzyme activity can be used to trigger drug release at the desired site of action. These methods improve the therapeutic efficacy of foam-based drug delivery systems and pave the way for customized medicine (Das *et. al.*, 2020) [8]. Microfluidics is being investigated for the fabrication, characterization, and evaluation of nanoparticle drug delivery (Ahn *et. al.*, 2018) [2].

Industry trends in foam drug delivery reflect a growing demand for innovative and patient-centric drug delivery solutions. Pharmaceutical companies are increasingly investing in research and development to create novel foam formulations with improved therapeutic efficacy, safety profiles, and patient acceptability (Sultana *et. al.*, 2020) [40]. The collaboration between academic institutions, pharmaceutical companies, and technology providers is accelerating the development and commercialization of foam-based drug products. Furthermore, regulatory agencies are providing clear guidelines and frameworks for the approval of foam drug products, fostering innovation and ensuring patient access to safe and effective therapies. Nanocrystals have emerged as a promising strategy to improve topical drug delivery. In the past two decades, nanocrystals of poorly soluble drugs have been extensively studied for the delivery of a wide range of drugs, including those for topical application.

Nanogels, with their ability to hold active molecules and respond to external stimuli, are emerging as promising drug delivery vehicles for a wide range of applications, including cancer, CNS disorders, cardiovascular diseases, and wound healing (Pinelli *et. al.*, 2020) [34]. These three-dimensional, nanoscale networks, formed by either physical or chemical cross-linking of polymers, possess advantageous properties such as biocompatibility, high stability, tunable particle size, and high drug loading capacity, making them ideal candidates for drug delivery systems (Hajebi *et. al.*, 2019; Kabanov & Vinogradov, 2009; Moscovici *et. al.*, 2017) [13, 17, 25]. Their surfaces can be easily modified for active targeting by attaching ligands that recognize specific receptors on target cells or tissues, enhancing their precision and effectiveness. Nanodrugs can easily pass through the fine capillary blood vessels and the lymphatic endothelium, and they might have longer circulation times in the blood and/or higher binding capability and accumulation at some target sites (Onoue *et. al.*, 2014) [32].

Foam-based drug delivery leverages the unique properties of foams, which are essentially dispersions of gas bubbles within a liquid or solid matrix, to optimize drug delivery (Langer, 1990) [21]. Foams can be tailored to possess a wide range of characteristics, including varying bubble sizes, structures, and rheological properties, enabling the design of drug delivery systems suited to specific applications (Liechty *et. al.*, 2010) [24]. These delivery mechanisms are crucial for the effective application of therapeutic methods and address numerous difficulties, including the limitations of conventional formulations. The versatility of foam-based systems allows for the incorporation of various drugs, including small molecules, proteins, and even cells, making them suitable for treating a broad spectrum of conditions (Wang, 2020) [43]. Moreover, foam formulations can be engineered to provide controlled drug release, ranging from rapid release for immediate effect to sustained release for prolonged therapy, further expanding their utility in clinical settings. The growing interest in developing novel formulations and delivery systems for existing therapeutics, rather than focusing solely on synthesizing new chemical entities, highlights the importance of enhancing clinical outcomes and drug bioavailability (Nsairat *et. al.*, 2025) [31].

Nanotechnology contributes significantly to the development of micro-scale drug delivery systems that administer medication in precise, therapeutically effective doses over extended periods (Park, 2007) [33]. Foam drug delivery systems are categorized based on their structure, composition, and administration route, with each type offering unique advantages tailored to specific therapeutic applications. These include aqueous foams, which are typically composed of a surfactant, water, and a gas, and are suitable for delivering hydrophilic drugs, and non-aqueous foams, which utilize oils or other non-polar solvents as the continuous phase, making them ideal for hydrophobic drugs. Polymer foams are often employed for their biocompatibility and biodegradability, allowing for controlled drug release as the polymer matrix degrades over time (Nguyen *et. al.*, 2023) [30]. Furthermore, the self-assembling properties of polymers and surfactants in drug delivery formulations facilitate the creation of colloidal structures that protect drugs from harsh environments and enhance their dissolution (Santos *et. al.*, 2013) [37].

The advantages of foam drug delivery systems are multifaceted, offering improvements over traditional drug formulations in several key areas. Foams can enhance drug solubility, thus boosting bioavailability and therapeutic efficacy, particularly for poorly soluble drugs (Garnero *et. al.*, 2020) [11]. Targeted drug delivery to tumors minimizes adverse effects on healthy cells (Wu *et. al.*, 2014) [44]. Foam formulations can improve patient compliance by reducing dosing frequency and simplifying administration, especially in topical applications. Foam formulations can be engineered to provide both immediate and sustained drug release, offering flexibility in tailoring the therapeutic effect to the patient's needs. However, several challenges must be addressed to fully realize the potential of foam drug delivery systems. These include the need for improved foam stability, particularly in the presence of biological fluids, and the optimization of foam rheology to ensure ease of application and retention at the target site.

The selection of ideal candidates for foam drug delivery hinges on a thorough evaluation of patient-specific factors, encompassing the nature of the condition, the site of action, and the desired therapeutic outcome. In general, patients with localized skin conditions such as dermatitis, psoriasis, and eczema are well-suited for topical foam formulations, as the foam can deliver medication directly to the affected area, minimizing systemic exposure and side effects. Foam formulations can also be used to deliver drugs to the nasal cavity, lungs, or gastrointestinal tract, offering a non-invasive alternative to injections or oral medications. Patients requiring long-term treatment with medications that have a narrow therapeutic window may also benefit from foam drug delivery systems, as the controlled release properties of the foam can help maintain stable drug levels in the body, reducing the risk of toxicity or subtherapeutic effects. Moreover, foam drug delivery systems can be particularly advantageous for pediatric and geriatric patients, who may have difficulty swallowing pills or adhering to complex dosing regimens.

Current Trends in Foam Drug Delivery

Current trends in foam drug delivery are centered on enhancing targeting capabilities, improving stability, and expanding the range of treatable conditions. Foam drug delivery systems are being explored for a wide range of applications, including wound healing, pain management, and even cancer therapy (Ezike *et. al.*, 2023) [9]. The development of stimuli-responsive foams that release drugs in response to specific triggers, such as pH, temperature, or enzymes, is gaining momentum. The industry trends in foam drug delivery reflect a growing emphasis on patient-centricity, with companies investing in the development of user-friendly foam formulations that are easy to apply and well-tolerated. Furthermore, there is an increasing focus on sustainable and environmentally friendly manufacturing processes, with companies seeking to develop foam formulations that utilize biodegradable and non-toxic excipients. The application of nanotechnology to drug delivery addresses the limitations of conventional methods by improving medication efficacy and safety (Sun & Davis, 2021) [41].

Future Perspectives

The future perspectives of foam drug delivery are promising, with ongoing research focused on overcoming existing limitations and exploring new applications. Nanoparticle drug delivery, despite its potential, encounters difficulties related to production quality control and batch-to-batch variation (Ahn *et. al.*, 2018) [2]. Foam formulations are being investigated as a means of delivering gene therapies, vaccines, and other biological therapeutics, offering the potential to treat a wide range of diseases that are currently difficult to manage. Moreover, the integration of foam drug delivery systems with diagnostic imaging techniques, such as ultrasound and MRI, is enabling the development of theranostic platforms that can simultaneously diagnose and treat disease. These models facilitate the simulation of diverse delivery scenarios, improve drug formulations, and predict drug behavior within the body (Akhtar *et. al.*, 2024) [3]. Furthermore, advancements in polymer chemistry and materials science are leading to the development of novel foam-forming materials with improved biocompatibility, biodegradability, and drug release properties (Krawczak, 2013; Liechty *et. al.*, 2010) [20, 24]. The ongoing developments in drug delivery systems are revolutionizing therapeutic approaches across various medical fields (Shirazi, 2013) [39].

The future perceptions of foam drug delivery include the development of smart foams that can adapt to changing physiological conditions, the use of 3D printing to create personalized foam formulations, and the integration of artificial intelligence to optimize drug delivery parameters. As our understanding of disease mechanisms and drug delivery principles advances, foam drug delivery systems will play an increasingly important role in improving patient outcomes and transforming healthcare. These polymers can be activated to release a medicinal agent *in vivo* or that can respond to changes in the environment to enhance the effectiveness of therapy. This includes using nanotechnology-based drug delivery systems, which have shown great promise in enhancing the effectiveness of existing drugs and enabling new therapies. Over a decade, investigators have appreciated the enrichment of potential uses of bionanotechnology in offering huge advancements in novel drug delivery and targeting.

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