Microporous Drug Delivery Systems: A Literature-Based Analysis of Formulation, Development, and In Vitro Evaluation

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Abstract: Traditional methods of delivering drugs are usually constrained by low solubility, absence of targeted delivery to specific sites, uncontrolled release of the drug, and largely varying plasma drug concentrations, in particular with Biopharmaceutics Classification System (BCS) Class II drugs. Such limitations contribute to the decrease in the therapeutic efficacy and the increase in the adverse effects. In this review, the discussed solution to these difficulties is a type of drug delivery system, known as microsponges, which are drug-loaded microporous systems. Microsponges are porous microspheres made of a polymer that can entrap hydrophilic and lipophilic drugs and allow controlled and sustained drug delivery. This is a systematic review of the literature on formulation methodologies, polymers employed, and ways of preparation and in vitro characterization of the polymers. The results of the significant findings are high solubility, stabilization, lower dosing, and decreased plasma variability. They are also flexible systems in terms of oral, topical, and controlled-release. Although the benefits are there, issues like scalability, reproducibility, and lack of in vivo validation still exist. The review covers recent achievements, outlines research gaps, and proposes further directions for the development of microporous drug delivery systems.

Keywords: Microsponges; Controlled release; Solubility enhancement; polydispersity index; particle size

Introduction

Drug delivery systems have greatly enhanced the efficacy of drugs, but still, traditional dosage forms continue suffering various setbacks, including low bioavailability, poor solubility, and rapid elimination of the drug in the body, and toxicity, particularly dose-related toxicity. Such limitations are especially pronounced with drugs that are not easily soluble in water, which form a significant percentage of new pharmaceutical compounds.

Microporous drug delivery systems (MPDS), also referred to as microsponges, are a new technology that will help in these challenges. These are systems that consist of porous microspheres of polymeric nature that have a sponge-like structure that can trap active pharmaceutical agents. As explained in the given document, microporous particles encompass a width of 5-300 lm in diameter, and a large interwoven network of pores, and each of them may have up to 250,000 in number [1-3].

Porous systems have a number of benefits, such as high drug loading capacity, controlled release of the drug, and enhanced stability. Also, microsponges may be used to entrap both lipophilic and hydrophilic drugs, and this enables them to be used as a universal carrier for many treatments.

This review is motivated by the main issues that have been identified in the traditional drug delivery systems, such as Low solubility and dissolution rate, Uncontrolled release of the drug, need to be dosed frequently, Side effects that are dose-related, and the absence of effective carriers to deliver various drug molecules.

The purpose of this review is to give an overall summary of the microporous drug delivery systems, their formulation strategies, characterization methods, as well as its use in enhancing therapeutic efficacy [1,2].

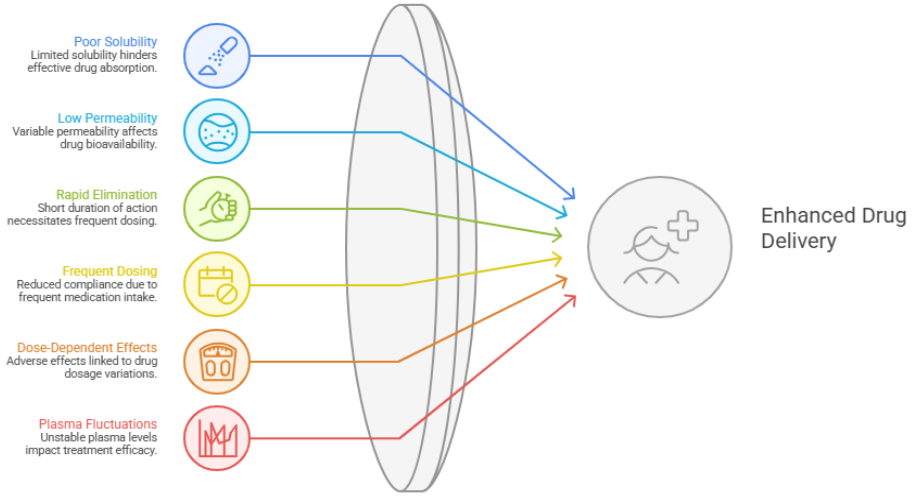

Figure 1. Challenges in Conventional Drug Delivery

Hydrochlorothiazide (HCTZ) is a widely prescribed thiazide diuretic, which is utilized in the management of hypertension and edema, but in spite of all its clinical relevance, it is linked to a number of pharmaceutical and therapeutic issues. The weak aqueous solubility of HCTZ is one of its greatest weakness because it is in the Biopharmaceutics Classification System (BCS) Class IV, and it severely limits its dissolution and absorption. Also, it has poor permeability, which causes inconsistent and insufficient bioavailability. The pharmaceutical is also eliminated by the body faster, which means that the action of the drug is not long-lasting, requiring frequent administration. This repeated use may result in a decreased patient compliance especially where the condition is chronic like in the case of hypertension. In addition, the HCTZ is linked to adverse events that are dose-dependent, such as electrolyte imbalance and dehydration, which may negatively affect patient safety. In the traditional dosage forms like tablets, the drug concentration in the plasma varies causing variation in the extent of therapy. In terms of pharmaceuticals, these traditional preparations are not able to offer controlled drug release, enhanced dissolution, and homogenous drug delivery, thus creating a necessity of the use of advanced systems of drug delivery to overcome these shortfalls [1,3,4].

Related work

The idea of microsponges was published in the early nineties by the use of suspension polymerization. The creation of porous microspheres with the help of such polymers as Eudragit was also shown by Kawashima et al., which has become the basis of modern technology of microsponges. Further research covered the utilization of alternative polymers, methods of preparation, and use. Topical delivery systems, especially dermatological delivery systems, were studied early, and subsequently oral and controlled release formulations were studied later. [5-7].

Table 1. Structure of the Literature Review

Sr. No.	Author (Year)	Drug	System Type	Polymer Used	Method	Key Findings	Relevance to HCTZ Microsponges

1	Patel et al. (2006)	HCTZ	Microspheres	Ethyl Cellulose	Solvent evaporation	Sustained release up to 12 hrs	Demonstrates polymer suitability
2	Rao et al. (2008)	HCTZ	Floating microspheres	EC + HPMC	Emulsion method	Improved gastric retention	Applicable for oral microsponges
3	Singh et al. (2009)	HCTZ	Solid dispersion	PEG 6000	Fusion method	Enhanced solubility	Addresses the solubility issue
4	Kulkarni et al. (2010)	HCTZ	Nanosuspension	PVP	Antisolvent precipitation	Improved dissolution	Highlights the BCS limitation
5	Sharma et al. (2011)	HCTZ	Microspheres	Eudragit RS100	Solvent evaporation	80% EE	Polymer feasibility
6	Kawashima et al. (1992)	Various	Microsponges	Eudragit	Suspension polymerization	Porous structure formation	Foundational MSPGs technology
7	Orlu et al. (2012)	Other	Oral microsponges	EC	Quasi-emulsion diffusion	Controlled release achieved	Oral applicability
8	Jain et al. (2013)	HCTZ	Matrix tablets	HPMC	Direct compression	24 hr release	Controlled release comparison
9	Deshmukh et al. (2014)	HCTZ	Microspheres	PCL	Solvent evaporation	Sustained release	Biodegradable polymer option
10	Vyas et al. (2014)	Other	Microsponges	EC	QESD method	High porosity	Process relevance
11	Patil et al. (2015)	HCTZ	SMEDDS	Oils + Surfactants	Self-emulsification	Enhanced bioavailability	Alternative NDDS
12	Patel et al. (2016)	Other	Microsponges	Eudragit RS	QESD	Controlled diffusion	Polymer optimization
13	Chaudhari et al. (2016)	HCTZ	Floating beads	Sodium alginate	Ionotropic gelation	10 hr release	Gastroretentive concept
14	Khandelwal et al. (2017)	Other	Microsponges	EC	Solvent diffusion	Particle size control	CPP relevance
15	Bansal et al. (2017)	HCTZ	Inclusion complex	β-CD	Kneading	Solubility ↑ 3 fold	Pre-formulation enhancement
16	Shaikh et al. (2018)	Other	Oral microsponges	Eudragit RS	QESD	Sustained release 12 hr	Oral feasibility
17	Patra et al. (2018)	HCTZ	Nanosponges	Crosslinked polymer	Solvent method	Enhanced dissolution	Porous nano approach
18	Pawar et al. (2019)	HCTZ	Microspheres	EC	Emulsion method	75–85% EE	Entrapment reference
19	Shinde et al. (2019)	Other	Microsponges	EC	QESD	High EE & stability	Method reliability
20	Kumar et al. (2020)	HCTZ	SLNs	Lipid matrix	Homogenization	Improved PK	Comparison

21	Thakur et al. (2021)	Other	Microsponges	Eudragit	Solvent evaporation	Controlled kinetics	Kinetic modeling
22	Verma et al. (2021)	HCTZ	GRDDS	HPMC	Swelling approach	Extended release	Comparative
23	More et al. (2022)	Other	Microsponges	EC	QESD	Optimized CPP	QbD potential
24	Khan et al. (2023)	HCTZ	Nanocarriers	Polymeric	Nanoprecipitation	Bioavailability ↑	Translational need
25	Recent review (2024)	HCTZ	NDDS review	Multiple	–	Highlights lack of microsponge data	Research gap evidence

Key Contribution

The review points to the possibility of microporous (microsponge) drug delivery systems to address the shortcomings of traditional formulations of hydrochlorothiazide regarding improving solubility, enabling controlled and sustained release, enhancing stability, and reducing dosing frequency, as well as ascertaining the gaps in the current research with regards to limited studies in vivo, and scale-up issues [1-3].

Method, Experiments and Results

The systematic literature review was carried out in major scientific databases including Scopus, PubMed, and science direct and included the works related to the microporous systems of drug delivery. The further inclusion criteria were relevant articles, i. e., peer-reviewed research and studies providing formulation and characterization data. They were different formulation techniques like quasi-emulsion solvent diffusion, solvent evaporation, and suspension polymerization. The gathered information about various studies was compared according to the type of polymers, preparation methods, and parameters of evaluation such as particle size, entrapment efficiency and in vitro drug release. The general results were in agreement to indicate that the microporous systems enhance drug solubility, controlled as well as sustained release, stability and better therapeutic performance in comparison to the traditional dosage forms [8-12].

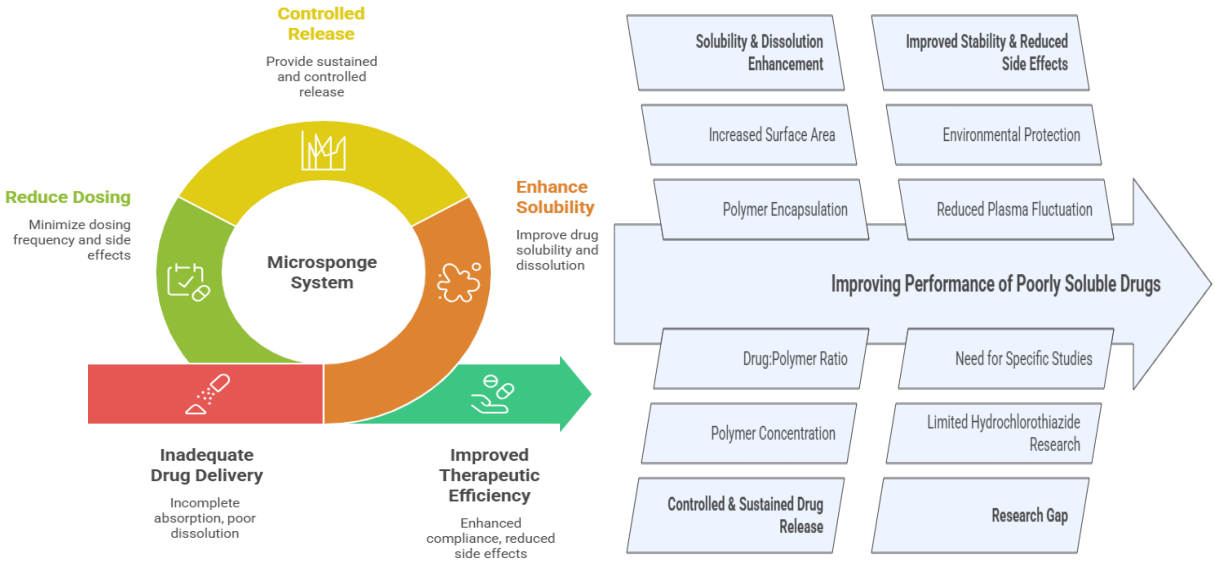

Figure 2. Microsponges drug delivery system and its traits and benefits.

Discussions

The resulting literature is very clear that the microporous drug delivery systems particularly the microsponges have offered an attractive alternative to surmount the limitations of the conventional dosage forms of poorly soluble drugs such as hydrochlorothiazide. The structure of these systems is highly porous and its surface area is large which is pertinent in the enhancement of the drug dissolution process and controlled release. The research results will never disagree on the fact that the choice of polymer, the drug to polymer ratio and the method of preparation will significantly influence the primary parameters, such as the size of particles, entrapment, and release rates.

Among the specific strategies of formulation, the quasi-emulsions solvet diffusion and solvent evaporation have been predominant due to their consistency and ability to make porous networks of the same uniformity. Ethyl cellulose and Eudragit derivatives are some of the polymers that have been successful in offering sustained drug delivery and also increasing the stability of the formulation [1-4].

In comparison and contrast to other innovative drug delivery systems like nanosuspension, solid lipid nanoparticles and SMEDDS, it has been argued that the microporous systems provides a moderate balance as regards to controlled release and high drug loading capacity. However, despite these strengths, some weaknesses still exist. These are the challenges of mass production, potential variations in batch production and absence of in vivo and clinical validation data. Formulation parameter optimization is also an essential requirement to uphold reliability. As much as Microporous systems have a lot of potential in terms of improving better therapeutic outcomes, further studies are required to ensure such systems are developed past laboratory-scale development to clinical and industrial uses [5-8].

Conclusions

Problem Statement Addressed / Motivation:

The review discusses the significant weaknesses of the existing drug delivery systems of hydrochlorothiazide, including low bioavailability, solubility, lack of control of drug release, and the necessity to administer the drug regularly, and all of them have an impact on the therapeutic effects and

self-adherence. These issues prompted the motivation to consider microporous drug delivery systems as the possible solution to the challenges.

Method Used:

The systematic literature review methodology was used, which included the gathering and evaluation of the pertinent literature on the existing scientific databases. It was about the techniques of formulations, the type of polymers, and in vitro methods of characterization of the microporous drug delivery systems.

Key Findings:

As the analysis shows, by using microporous systems, drug solubility and dissolution, controlled and sustained release, improved stability, and reduced changes in drug plasma levels are achieved. These systems are also versatile in both delivering hydrophilic and lipophilic drugs, which have resulted in a better therapeutic performance.

Limitations of the Work and Future Work:

Although it has promising results, it has issues like the absence of large in vivo research, scale-up challenges, and formulation variability. The future efforts in the field should be directed to optimization with the help of the innovative methods, consideration of new polymers, and thorough clinical trials to determine their feasibility and commercial use.

Further studies are expected to be dedicated to the elimination of these limitations with the help of further optimization methods, using the principles of quality-by-design and the development of innovative polymeric materials. Further in vivo studies and clinical verifications are also needed to determine the real life applicability and commercial viability of microporous drug delivery systems.

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