

Review

Microsponges as promising vehicle for drug delivery and targeting: Preparation, characterization and applications

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Accepted 18 April, 2013

Development of novel drug delivery systems for optimization of drugs' efficacy and cost-effectiveness has become highly competitive and rapidly evolving area of interest. Controlling the delivery rate of drugs to a predetermined site has been one of the biggest challenges faced by formulators. Amongst the novel drug delivery systems that proved their efficacy in achieving controlled drug release are microsponges. They are used mostly for topical use and have recently been used for oral administration. Microsponges are sponge-like polymeric microspheres with a large porous surface that can entrap a wide variety of active ingredients. They can then be further incorporated into a formulated product such as a gel, cream, liquid or even tablets. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability and reduce drugs side effects. This review introduces the potential features of microsponges along with their advantages. Moreover, it highlights the methods of preparation and characterization of microsponges and also covers their topical and oral applications.

Key words: Microsponges, drug delivery, preparation, characterization, topical, oral.

INTRODUCTION

Conventional topical formulations are designed to work on the outer layers of the skin. When the active ingredients of these formulations are released upon application, a highly concentrated layer of active ingredient is produced that is rapidly absorbed. Thus, there is a genuine need for delivery systems to prolong the time that active ingredients can be retained on the surface of the skin or within the epidermis while decreasing its transdermal penetration. Moreover, as a result of the high concentration of active agents employed in the conventional topical dosage forms, several side effects are recorded in significant users such as irritation and allergic reactions (Pradhan, 2011).

Recently, there has been considerable interest in the development of novel microsphere based drug delivery systems to achieve targeted and sustained release of drugs (Kaity et al., 2010). Microsponges are polymeric delivery systems consisting of porous microspheres that are mostly used for extended topical administration of a variety of active ingredients such as emollients, fragrances, essential oils, sunscreens, and anti-infective, anti-fungal, and anti-inflammatory agents. Microsponges offer many advantages such as delivering the active ingredients at minimum dose, enhanced stability, reduced side effects, and the ability to modify drug release profiles (Nacht and Kantz, 1992). Just like a real sponge, each

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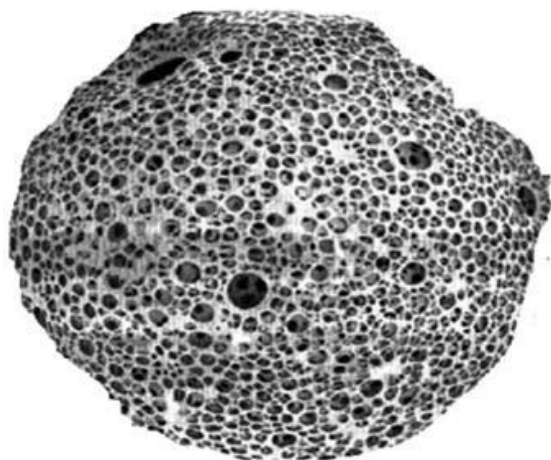


Figure 1. Highly porous nature of a microsphere. Source: Pradhan (2011).

microsphere consists of a myriad of interconnecting voids within a non-collapsible structure and a large porous surface. The resultant microsphere spheres are uniform, with a particle size range of 5 to 300 μg (Figure 1) (Pradhan, 2011).

Microsphere surrounded by the vehicle acts like microscopic sponges, storing the active ingredient until its release is triggered by skin application. Micropores within the spheres are employed for extensive drug retention. Microspheres consisting of non-collapsible structures with porous surface through active ingredients are released in a controlled manner. Release of drug into the skin is triggered by a variety of stimuli, including rubbing and higher skin temperature than ambient one. Their high degree of cross-linking results in particles that are insoluble, inert and of sufficiently strong strength to withstand the high shear commonly used in manufacturing of creams, lotions, and powders. Their characteristic feature is the capacity to load a high amount of active materials into the particle and on to its surface. Its large capacity for entrapment of drugs, up to three times its weight, differentiates microsphere products from other types of dermatological products. The active payload is protected in the formulation by the microsphere particle; it is delivered to skin via controlled diffusion. The sustained release of activities to skin over time is an effective tool to extend the efficacy and reduce the irritation commonly associated (Pradhan, 2011).

The microsphere technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer Systems, Inc. (Won, 1987). This company developed a large number of variations of the technique and applied it to the cosmetic as well as over the counter (OTC) and prescription pharmaceutical products (Pradhan, 2011). Nowadays, there are several

Food and Drug Administration (FDA)-approved products such as Retin-A Micro® (0.1 or 0.04% tretinoin) and Carac (0.5% 5-fluorouracil) that are used for acne treatment and actinic keratoses, respectively (Amrutiya et al., 2009).

Potential features of microsphere drug delivery systems

The potential features are as listed (Aritomi et al., 1996; Jain et al., 2011; Vyas and Khar, 2002):

1. Microspheres show acceptable stability over pH ranging from 1 to 11 and at high temperatures (up to 130 °C).
2. Microspheres exhibit good compatibility with various vehicles and ingredients.
3. Microspheres have high entrapment efficiency up to 50 to 60%.
4. Microspheres are characterized by free flowing properties.
5. The average pore size of microspheres is small (0.25 μm) in a way to prevent the penetration of bacteria, thus they do not need sterilization or addition of preservatives.
6. Microspheres are non-allergenic, non-irritating, non-mutagenic and non-toxic.
7. Microspheres can absorb oil up to 6 times their weight without drying.

Advantages of microspheres over other technologies and delivery systems

The advantages include (Kaity et al., 2010; Pradhan, 2011):

1. Microspheres offer better control of drug release than microcapsules. Microcapsules cannot usually control the release rate of the active pharmaceutical ingredients (API). Once the wall is ruptured, the API contained within the microcapsules will be released.
2. Microspheres show better chemical stability, higher payload and easier formulation compared with liposomes.
3. In contrast to ointments, microspheres have the ability to absorb skin secretions, therefore, reducing greasiness and shine from the skin. Ointments are often aesthetically unappealing, greasy and sticky, resulting in lack of patient compliance.

Characters of drugs to be entrapped in the microspheres

There are certain requirements that should be fulfilled (or

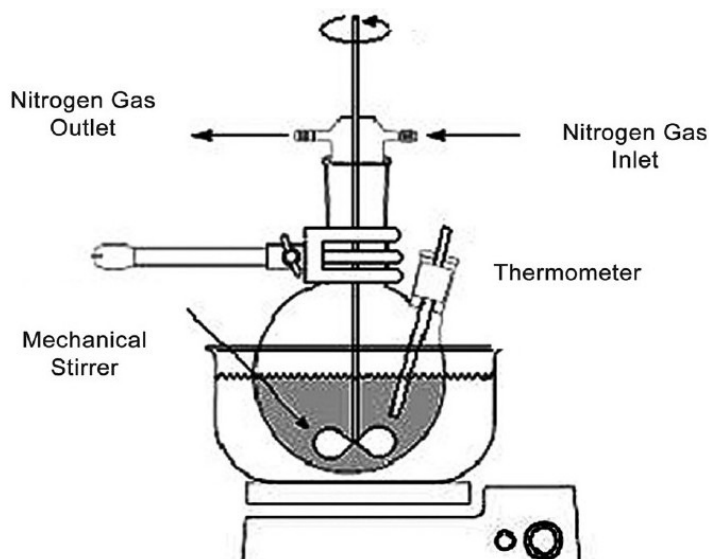


Figure 2. Reaction vessel for microsphere preparation by liquid-liquid suspension polymerization. Source: Kaity et al. (2010).

considered) when active ingredients are entrapped into microsphere (Jain et al., 2011; Pradhan, 2011):

1. It Should exhibit complete miscibility in monomer or have the ability to be miscible using the least amount of a water immiscible solvent.
2. Must be inert to monomers and do not increase the viscosity of the preparation during formulation.
3. It should be water immiscible or almost slightly soluble.
4. The solubility of active ingredients in the vehicle should be minimum; otherwise the microsphere will be diminished by the vehicle before application.
5. It should maintain (preserve) the spherical structure of microsphere.
6. It should be stable in polymerization conditions.
7. Only 10 to 12% w/w microsphere can be incorporated into the vehicle to eliminate cosmetic delinquent.
8. Payload and polymer design of the microspheres for the active must be adjusted to obtain the desired release rate of a given period of time.

Techniques of microspheres preparation

Preparation of microsphere can take place in a one-step or two-step process based on the physicochemical properties of drug to be loaded. If the drug is porogen, (that is an inert non-polar substance which will generate the porous structure), it will not deter the polymerization process or become activated by it and also is stable to free radicals. A porogen drug can be entrapped with one-step process (liquid-liquid suspension polymerization)

(Pradhan, 2011). Microspheres are prepared by the following methods:

Liquid-liquid suspension polymerization

Suspension polymerization process in liquid-liquid systems is utilized for the preparation of microspheres in a one step process (Figure 2). At first, the monomers are dissolved with the active ingredients (non-polar drug) in a proper solvent. The prepared solution is then dispersed in the aqueous phase containing surfactants and dispersants to facilitate the formation of suspension. Once the suspension is formed with droplets of the required size, then polymerization is initiated by the addition of catalyst, increasing temperature, or irradiation. As the polymerization process continues, a spherical structure is produced containing thousands of microspheres bunched together. During the polymerization process, an inert water-immiscible liquid but completely miscible with monomer is used to form the pore network in some cases, which is then removed once the process is complete. The particles are then washed and processed until they are substantially ready for use (Kaity et al., 2010; Pradhan, 2011).

Quasi-emulsion solvent diffusion

Microspheres can be prepared by quasi-emulsion solvent diffusion method. In this method, an internal phase is used containing polymer such as eudragit RS

100 or ethyl cellulose dissolved in organic solvent. The drug is then dissolved into the polymer solution under ultrasonication. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water with continuous stirring for adequate period of time (Shah et al., 1989). Microsponges are then separated by filtration. Finally, the microsponges are washed and dried in an air heated oven at 40°C for 12 h (Comoglu et al., 2003).

Characterization of microsponges

Measurement of particle size

Various formulation and process variables can greatly affect the particle size of microsphere formulations. Measurement of particle size of loaded and unloaded microsponges can be performed using laser light diffractometry or any other suitable method. Results can be expressed in terms of mean size range. Cumulative (%) drug release from microsponges of different particle sizes should be plotted against time to study the effect of particle size on drug release.

Particles larger than 30 µm can impart grittiness and hence particles of sizes between 10 and 25 µm are preferred to be used in topical formulations (Chadawar and Shaji, 2007).

Morphology and Surface topography

The surface structure of microsponges can be examined using scanning electron microscopy (SEM) technique. The prepared microsponges are coated with gold-palladium under an argon atmosphere at room temperature, and then SEM images are recorded at the required magnification. SEM images may also be recorded for a fractured microsphere to study its ultra-structure (Emanuele and Dinarvard, 1995; Nokhodchi et al., 2007).

Production yield and entrapment efficiency

Percentage yield can be calculated using the equation (Kilicarslan and Baykara, 2003; Sensoy et al., 2009):
 Percentage yield (PY) = (Final obtained mass of microsponges / initial mass of polymer and drug) × 100

The entrapment efficiency of the microsponges can be computed using the equation:

Entrapment Efficiency (EE%) = (Actual drug content / Theoretical drug content) × 100

Determination of true density

True density can be measured by an ultra-pycnometer using helium gas, and calculated as a mean of repeated determinations (Bertrand et al., 2007).

Pore structure

Porosity parameters of microsponges are essential in monitoring the intensity and the duration of active ingredient effect. Average pore diameters, shape and morphology of the pores can be determined by using mercury intrusion porosimetry technique. The effect of pore diameter and volume on the rate of drug release from microsponges can also be studied using the same technique (D'souza, 2008).

Viscoelastic properties

Microsponges with varying viscoelastic properties can be produced according to the needs of the final formulation. The degree of cross-linking affects the drug release from the prepared microsponges, where increased cross-linking tends to decrease the release rate. Hence, viscosity measurements should be done so that the viscoelastic properties of microsponges can be modified and adjusted to obtain the desired release properties (Jelvehari et al., 2006; D'souza, 2008).

Physicochemical characterization

Thermoanalytical methods: Thermal analysis using differential scanning calorimetry (DSC) is carried out for the pure drug, polymer and the drug-polymer physical mixture to confirm compatibility. DSC is also performed for the microsphere formulations to ensure that the formulation process does not change the nature of the drug. Samples (approximately 2 mg) are placed in aluminum pans, sealed and operated at a heating rate of 20°C/min over a temperature range 40 to 430°C. The thermograms obtained by DSC for the physical mixtures, as well as microsponges, should be observed for broadening, shifting and appearance of new peaks or disappearance of certain peaks. The peak corresponding to the melting of the drug should be preserved in all thermograms (Ceschel et al., 2003; Mishra et al., 2011).

Fourier transform infrared spectroscopy (FTIR): Fourier transform infrared spectroscopy (FTIR) is carried out for the pure drug, polymer and the drug-polymer physical mixture and microsphere formulations.

The samples are incorporated in potassium bromide discs and evaluated using FTIR spectrometer. The peaks corresponding to the characteristics bands of the drug should be preserved in the spectra of the microsponges to indicate that no chemical interaction or changes took place during the preparation of the formulations (Jain and Singh, 2010a, 2011).

Powder X-ray diffraction (XRD): Powder X-ray diffraction (XRD) can be performed for both pure drug, polymer and microsphere formulation to investigate the effect of polymerization on crystallinity of the drug. The disappearance of the characteristic peaks of the drug in the formulation could indicate that the drug is dispersed at a molecular level in the polymer matrix (Bodmeier and Chen, 1989; Singla et al., 2001).

***In vitro* release studies, release kinetics and mechanism**

In vitro release studies can be performed using United States Pharmacopeial (USP) dissolution apparatus equipped with a modified basket consisted of 5 μ m stainless steel mesh at 37°C. The release medium is selected according to the type of formulation that is, topical or oral, while considering solubility of active ingredients to ensure sink conditions. Sample aliquots are withdrawn from the medium and analyzed by suitable analytical method at regular intervals of time. The drug release from topical preparations (for example, creams, lotions and emulgels) containing microsponges can be carried out using Franz diffusion cells. Dialysis membrane is fitted into place between the two chambers of the cell. A predetermined amount of formulation is mounted on the donor side of Franz cell. The receptor medium is continuously stirred at and thermostated with a circulating jacket. Samples are withdrawn at different time intervals and analyzed using suitable method of assay (Embil and Nacht, 1996; Jelvehgari et al., 2006). To determine the drug release kinetics and investigate its mechanism from microsponges, the release data are fitted to different kinetic models. The kinetic models used are; first order, zero order, Higuchi and Korsmeyer-Peppas models (Higuchi, 1963; Wagner, 1969; Korsmeyer et al., 1983; Peppas, 1985). The goodness of fit was evaluated using the determination coefficient (R^2) values.

Applications of microsponges

Topical drug delivery

Topical formulations aim to deliver drugs to the outer

layers of the skin. Conventional topical formulations release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. However, microsphere systems are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose. They consist of non-collapsible structures with porous surface through which active ingredients are released in a controlled manner. Therefore, such systems can prevent excessive accumulation of active ingredients within the epidermis and the dermis, thus they can significantly reduce the irritation and side effects caused by drugs without reducing their efficacy. In addition to modification of drug release and reduction of side effects, microsponges are also capable of enhancing the stability of many drugs. The drug loaded porous microsponges can further be incorporated into creams, lotions or powders (Patel and Patel, 2006). Microsponges are applied for the topical delivery of several drugs and cosmetic agents as shown in Table 1 (Kaity et al., 2010).

Several studies have been performed for the development of microsponges loaded with topically applied drugs. A formulation of hydroquinone (HQ) 4%, with retinol 0.15%, entrapped in microsphere reservoirs, was developed by Grimes (2004) for the treatment of melasma and postinflammatory hyperpigmentation. The formulation was intended to release HQ gradually in order to prolong exposure to drug and to decrease skin irritation. The safety and efficacy of this product were evaluated in a 12-week, open-label study. In this open-label study, the microentrapped HQ 4% with retinol 0.15% was proved to be safe and effective. A microsphere system for retinoic acid was also developed and tested for drug release and anti-acne efficacy. The greater reductions in inflammatory and non-inflammatory lesions obtained with tretinoin entrapped in the microsphere was found to be statistically significant (James et al., 2005).

Topical application of benzoyl peroxide (BPO), a drug that is mainly used in the treatment of mild to moderate acne and athlete's foot, is commonly associated with skin irritation. It has been shown that controlled release of BPO from a delivery system to the skin could reduce irritation due to reduction of drug release rate from formulation (Wester et al., 1991; D'souza, 2001). Jelvehgari et al. (2006) developed a microspongy delivery system of BPO using an emulsion solvent diffusion technique, by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose, and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol. BPO microparticles were then incorporated into standard vehicles for release studies. It was found that the presence of emulsifier was essential for microsphere formation and that the drug to polymer ratio, stirring rate and volume of dispersed phase influen-

Table 1. Topical applications of microsponges.

Active agent	Application
Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization
Anti-acne for example, benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization
Anti-inflammatory for example, hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses
Antifungals	Sustained release of actives
Antidandruffs for example, zinc pyrithione	Reduced unpleasant odor with lowered irritation with extended safety and efficacy
Antipruritics	Extended and improved activity
Skin depigmenting agents for example, hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal
Rubefacients	Prolonged activity with reduced irritancy greasiness and odor

Source: Kaity et al. (2010).

ced the particle size and drug release behavior of the formed microsponges. Generally, an increase in the ratio drug to polymer resulted in a reduction in the release rate of BPO from microsponges which was attributed to a decreased internal porosity of the microsponges. Further studies showed that the morphology and particle size of BPO microsponges were also affected by drug to polymer ratio, stirring rate and the amount of emulsifier used (Nokhodchi et al., 2007).

Fluocinolone acetonide (FA) is a corticosteroid used in dermatological preparations to lessen skin inflammation and relieve itching, however, the percutaneous absorption increases risk related with systemic absorption of the drug from topically applied formulation. D'souza and Harinath (2008) developed topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsphere delivery system. The fluocinolone acetonide loaded microsponges were prepared using the quasi-emulsion solvent diffusion method aiming to control the release of drug to the skin which in turn reduces the drug percutaneous absorption and thus lessens its side effects. The prepared microsponges were evaluated for several parameters including particle size analysis, loading efficiency, production yield and surface morphology. Microsponges were then incorporated into carbopol 934, and comparative anti-inflammatory studies were performed with gels containing the free drug.

A microsphere based topical delivery system of mupirocin, a topical antibiotic used for skin infections, was developed by Amrutiya et al. (2009), aiming to achieve sustained drug release and enhanced deposition in the skin. Microsponges containing mupirocin were prepared by emulsion solvent diffusion method. A 3² factorial design was applied to examine and optimize the

effect of formulation and process variables, namely; internal phase volume and stirring speed, on the physical characteristics of microsponges. The optimized microsponges were incorporated into an emulgel base. The mupirocin-loaded formulations were evaluated for *in vitro* drug release, *ex vivo* drug deposition, and *in vivo* antibacterial activity. Drug release studies showed diffusion-controlled release pattern, and drug deposition studies using abdominal rat skin demonstrated significant retention of the drug in skin from microsphere-based formulations. The optimized formulations were stable and nonirritant to skin according to Draize patch test.

In addition, microsponges-based emulgel formulations exhibited prolonged efficacy in mouse surgical wound model infected with *Staphylococcus aureus*. The enhanced retention of mupirocin in the skin from the microsphere based formulations suggests the formulation to be an efficient delivery system for treatment of primary and secondary skin infections as compared with marketed mupirocin ointment and conventional mupirocin emulgel.

Saboji et al. (2011) developed microsponges containing ketoconazole drug with six different proportions of Eudragit RS 100 as polymer using quasi-emulsion solvent diffusion method. The microsphere formulations were evaluated for particle size, loading efficiency and production yield. The microsphere formulations showing the best properties were then incorporated into 0.35% w/w carbopol gel. The ketoconazole microsponges incorporated into gel formulations showed acceptable physical parameters, appropriate drug release profile and marked *in vivo* antifungal activity on guinea pig skin.

Administration of hydroxyzine HCl, an antihistaminic drug used in oral formulations for the treatment of urticaria and atopic dermatitis, is usually associated with

dizziness, blurred vision, and anticholinergic responses. Therefore, Zaki et al. (2011) investigated the formulation of eudragit RS-100 microsponges of hydroxyzine HCl with the objective of producing an effective drug-loaded dosage form that is able to control the release of the drug into the skin.

The oil in an oil emulsion solvent diffusion method was applied for the production of eudragit RS-100 microsponges of the drug using acetone as dispersing solvent and liquid paraffin as the continuous medium. Sucrose and pregelatinized starch were used as pore inducers to enhance the rate of drug release. The produced microsponges showed nearly 98% encapsulation efficiency and 60 to 70% porosity. The pharmacodynamic effect of the chosen preparation was tested on the shaved back of histamine-sensitized rabbits. Histopathological studies were also driven for the detection of the healing of inflamed tissues. The prepared systems proved their efficacy for relieving histamine-induced inflammation.

A xanthan gum-facilitated ethyl cellulose microsponges loaded with diclofenac were prepared by Maiti et al. (2011) using the double emulsification technique. The prepared microsponges were subsequently dispersed in a carbopol gel base for controlled delivery of the active to the skin. Scanning electron microscopy revealed the porous, spherical nature of the microsponges. Increasing the drug to polymer ratio positively influenced the production yield, drug entrapment efficiency and mean particle diameter. However, compared to the microsponges with high drug to polymer ratio, the permeation of entrapped drug through excised rat skin was reduced significantly for the microsponges prepared at low and intermediate drug to polymer ratios. In addition, the microsponges prepared at the lowest drug to polymer ratio exhibited a comparatively slower drug permeation and thus, were considered most suitable for controlled delivery of diclofenac sodium to the skin. The gel containing these optimized microsponges was comparable to that of a commercial gel formulation and did not show serious dermal reactions.

Deshmukh and Poddar (2012) have recently developed a glabridin microsphere-loaded gel for treating various hyperpigmentation disorders.

The microsponges were prepared using the emulsion solvent evaporation method and characterized for drug loading and morphology. SEM and porosity studies confirmed spherical and porous nature. *In vitro* diffusion studies of gel formulation depicted highest correlation with Higuchi treatment.

Animal studies carried out using brownish guinea pigs with ultra violet (UV)-induced pigmentation model supported the better depigmenting activity of the microsponges incorporated gels as compared to plain gel.

Oral drug delivery

A microsphere system offers several advantages for oral drug delivery, such as:

1. Preserve the active ingredients within a protected environment and offer oral controlled delivery to the lower part of the gastrointestinal tract (GIT).
2. Microsphere systems improve the solubility of poorly soluble drugs by entrapping these drugs in their porous structure.
3. As the porous structure of the microsphere is very small in size, the drugs entrapped will be reduced to microscopic particles with higher surface area, and consequently improved rate of solubilisation.
4. Maximize the amount of drugs to be absorbed, as the time it takes the microsphere system to pass through the intestine is considerably increased.

Several studies have been investigated for the development of microspheres loaded with topically applied drugs. Jain and Singh (2010b) prepared colon specific formulations by loading paracetamol in eudragit RS 100 based microspheres using quasi-emulsion solvent diffusion method. Compression coating of microspheres with pectin: hydroxypropyl methylcellulose (HPMC) mixture followed by tableting was used. The *in vitro* drug release studies were done on all the formulations and the results were evaluated kinetically and statistically. The study concluded that the release data followed Higuchi matrix but diffusion was the main mechanism of drug release from microspheres. *In vitro* studies showed that compression coated colon specific tablet formulations started the release of drug at the 6th h resultant to the arrival time to proximal colon.

In another study, Gonul et al. (2002) studied the effects of pressure and direct compression on tableting of microspheres using ketoprofen as a model drug. ketoprofen microspheres were prepared by two methods: quasi-emulsion solvent diffusion method with eudragit RS 100 and direct compression method. Different pressure values were investigated with the tablet powder mass to determine the optimum pressure value for the compression of the tablets. Results of the study indicated that microsphere compressibility was superior compared to the physical mixture of the drug and polymer. It was concluded that microspheres can produce mechanically strong tablets due to the plastic deformation of sponge like structure.

Jain and Singh (2010a) studied the potential of formulating dicyclomine loaded eudragit based microsphere by means of a quasi-emulsion solvent diffusion method for colonic delivery. The compatibility of the drug with various formulation components was studied. Surface morphology and shape of the microspheres were demonstrated using SEM.

The compatibility studies showed that there was no chemical interaction throughout the preparation of the formulations and that the drug remains stable in all the formulations. The release rate of the drug from the microsponges was decreased with increasing the drug: polymer ratio. Kinetic studies showed that the main mechanism of drug release followed Higuchi matrix controlled diffusion. An initial burst effect showed that the drug release was bi-phasic with 16 to 30% of the drug released in the 1st h. Cumulative release for the microsponges over 8 h ranged from 59 to 86 %. The authors concluded an approach for the alteration of microsponges of dicyclomine for prolonged drug release. The distinctive compressibility of microsponges can be applied to get efficient local action, as microsponges may be taken up by macrophages which are present in colon.

Colon specific drug delivery system containing flurbiprofen (FLB) microsponges was investigated by Orlu et al. (2006). The authors formulated microsponges containing FLB and eudragit RS 100 using quasi-emulsion solvent diffusion method. Also, FLB was loaded into a commercial Microsponge® 5640 system by means of entrapment method. Compression coating and pore plugging of microsponges with pectin: HPMC mixture followed by tableting was used to prepare colon specific formulations. The prepared microsponges were spherical in shape and found to be 30.7 to 94.5 µm in diameter and showed high porosity values (that is, 61 to 72%). The pore shapes of microsponges prepared by quasi-emulsion solvent diffusion method were found as spherical whereas by entrapment method it was found as cylindrical holes.

Due to the plastic deformation of sponge-like structure of microsponges, mechanically strong tablets were produced for colon specific drug delivery. *In vitro* studies revealed that colon specific tablet formulations prepared by compression coating started to release the drug at the 8th h resultant to the proximal colon arrival time due to the addition of enzyme which could follow a modified release pattern, whereas the drug release from the colon specific formulations prepared by pore plugging the microsponges showed an increase at the 8th h which was the time where the enzyme was added.

Conclusion

Microsponge has become a rapidly evolving technology that can be widely applied in the pharmaceutical field. Owing to their microporous structure and their ability to release their active ingredients in a controlled manner, microsponges can effectively target drugs to their desired sites of action. The most prominent advantages of this delivery system is the diminished side effects and improved stability. Thus, microsponge delivery systems

are regarded as a promising vehicle for the controlled and targeted release of various topical and oral active agents. More recently, researches are focused on merging the attractive characteristics of microsponges with the revolutionized nanotechnology trend to enhance their performance.

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