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Microsponges: A novel drug delivery system

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ABSTRACT

Microsponges are polymer based drug delivery system consisting of porous microspheres having a size range from 5 to 300 micron. The present review introduces microsponge technology along with its preparation, characterization and applications. Microsponges are preferred to develop drug and cosmetics products because of its safety and efficacy.

INTRODUCTION :

Microsponges are cross-linked, porous, non-collapsible, polymeric microspheres that can entrap wide range of drugs and release them in sustained manner. Due to sponge like texture of microsponges, it has unique dissolution and compression properties. They are highly effective, non-toxic, non-mutagenic and also improve patients compliance. Various biocompatible polymers such as Eudragit, polystyrene, ethyl cellulose can be used to prepare microsponge. Furthermore, these drug loaded microsponges can be incorporated into suitable dosage forms, such as capsules, gel and powders. Othman et al. ; Ahmed et al. ; Jain et al. have demonstrated potential use of microsponges for delivery of therapeutics. Thus current mini-review highlights preparation and potential applications of microsponges.

METHODS OF PREPARATION OF MICROSPONGE

Drug loaded microsponge can be prepared in two ways: one step process or two step process that is liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques, respectively. The selection of method for preparation of microsponge is based on physicochemical properties of drug candidate.

LIQUID-LIQUID SUSPENSION POLYMERIZATION

In liquid-liquid systems, the porous microsponges are prepared by suspension polymerization method. In this method the two immiscible monomers are dissolved along with active ingredient in a suitable solvent. In next step, the prepared monomer solution is dispersed in the aqueous phase containing surfactants or suspending agent to facilitate formation of suspension. The polymerization is then activated by increasing temperature or by addition of catalyst. The polymerization process results in formation of polymeric microsponges, the formed microsponges then separated from liquid medium using suitable technique.

QUASI EMULSION SOLVENT DIFFUSION

The porous microsponges are also prepared by two step process using quasi emulsion solvent diffusion technique. In this technique, a polymer and drug is dissolve in suitable volatile solvent. Most of the authors have reported to add plasticizers in volatile solvent to improve plasticity. The solvent is then poured into aqueous phase containing suitable stabilizer with continues stirring for at least 2 hrs. After complete evaporation of volatile solvent, the formed microsponges separated by suitable technique. The product was washed and dried using suitable technique.

Applications

According to recent research on microsponge, the system is suitable for topical, oral as well as ophthalmic administration of therapeutics. Several filed patents have reported use of microsponges as excipient due to its high drug loading capacity and sustained drug release behavior. Microsponges are designed to deliver therapeutics efficiently at minimum dose and to enhance stability and to modify drug release.

Microsponge for Topical drug delivery

Many topical formulations are based on microsponges. Drug loaded microsponges can be effectively incorporated into topical dosage forms such as a gel, cream or powder. Microsponges can possibly improve drug residence time in the dermis and epidermis area of skin. Thus it is possible to reduce frequency of application and side effects by using microsponges as drug carrier. Another way to reduce side effects is use of biocompatible, inert, non-mutagenic and non-toxic polymer. Table 1 highlights various applications of microsponges for dermatological purpose.

Table 1: Overview of microsponge based topical drug delivery

Drug	Method of preparation	Dosage form	Reference
glabridin	quasi-emulsion solvent diffusion	Carbopol gel	Deshmukh et al., 2012
acyclovir sodium	quasi-emulsion solvent diffusion	Carbopol 934 gel	Chandramouli et al., 2012
sertaconazole nitrate	quasi-emulsion solvent diffusion	Carbopol 934 gel	Pandey et al., 2015
oxybenzone	quasi-emulsion solvent diffusion	HPMC hydrogel	Pawar et al., 2015
fluconazole	quasi-emulsion solvent diffusion	Carbopol 940 gel	Moin et al., 2016
miconazole nitrate	quasi-emulsion solvent diffusion	Carbopol 934 gel	Gulati et al., 2016
mafenamic acid	quasi-emulsion solvent diffusion	Emulgel	Shuhaib B. et al., 2018

Deshmukh et al. have successfully formulated glabridin microsponge for effective management of hyperpigmentation disorder. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using ethyl cellulose as polymer. The SEM (Scanning electron microscopy) photographs showed porous, spherical, micron sized particles with uniform outline. The prepared microsponges were evaluated with respect to particle size, drug content, thermal stability and FTIR spectroscopy. Porosity parameters of microsponges were determined using mercury intrusion porosimetry. For ease of topical application, the prepared microsponges were incorporated into Carbopol gel. Skin whitening effect of glabridin microsponge based gel was assessed in guinea pigs. UV B radiation was used to induce hyperpigmentation in guinea pigs. After completion of therapy, the animal skin was subjected to histopathological evaluation. The effective reduction in melanin density was reported in animal treated with microsponge based gel. Finally authors proved role of microsponge effective treatment of hyperpigmentation disorder.

Chandramouli et al. have prepared microsponges based gel

for topical delivery of anti-viral therapeutic. Acyclovir sodium loaded microsponge was obtained from different concentrations of ethyl cellulose as polymer and polyvinyl alcohol as stabilizer using quasi-emulsion solvent diffusion technique. Surface morphology of prepared microsponge was assessed using SEM which revealed porous, spherical particles. The optimized microsponges were incorporated in Carbopol 934 gel for ease of topical application. The formulated gel was evaluated with respect to pH, spreadability, drug content, viscosity and drug diffusion profile. Reported pH of microsponge based gel was 6.7-6.8. Viscosity and spreadability were 205-210 ps. and 11.17-12.5 gm cm/sec respectively. In-vitro drug diffusion profile of microsponge based gel across egg membrane was assessed using modified Franz diffusion cell. The diffusion profile was suggested to follow zero order kinetics.

Pandey et al. have successfully entrapped sertaconazole nitrate in polymeric microsponge for effective management of tineapedis. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using different proportions of Eudragit RS 100. The SEM photographs showed porous, spherical, micron sized particles with uniform outline. The prepared microsponges were evaluated with respect to particle size, drug content, thermal stability and FTIR spectroscopy. Porosity parameters of microsponges were determined using mercury intrusion porosimetry. For ease of topical application, the prepared microsponges were incorporated into Carbopol 934 gel and characterized for pH, spreadability, drug content, texture, in-vitro release and viscosity. Viscosity and pH were reported to be suitable for topical application of microsponge based gel. In-vitro drug diffusion profile of microsponge based gel across cellophane membrane was assessed using Franz diffusion cell. The diffusion profile was suggested to follow Higuchi model. Authors reported sustained release of drug over the period of 10 hours. Finally authors concluded potential use of microsponge based drug delivery system for management of tineapedis with minimum side effects.

Pawar et al. have formulated oxybenzone microsponges for enhance topical sun protection with reduced toxicity. Drug loaded microsponge was obtained from different concentrations of ethyl cellulose as polymer and polyvinyl alcohol as stabilizer using quasi-emulsion solvent diffusion technique. Polymer concentration and volume of solvent were successfully optimized using 32 factorial design. The particle size, entrapment efficiency and drug release were selected as response variables. Surface morphology of prepared microsponge was assessed using scanning electron microscopy. The SEM photographs revealed porous, spherical, micron sized particles. The optimized microsponges were incorporated in hydroxy propyl methyl cellulose (HPMC) hydrogel for topical application. Skin irritation potential and minimal erythemal dose of microsponge based gel was assessed using Wistar rat. The prepared formulation showed negligible irritancy and skin protection as compared to conventional gel. Finally authors concluded usefulness of microsponge based topical drug delivery for skin protection against ultraviolet radiation.

Moin et al. have formulated fluconazole microsponges for facilitated topical fungal therapy. Drug loaded microsponge was obtained from different concentrations of Eudragit S100 as polymer and polyvinyl alcohol as stabilizer using quasi-emulsion solvent diffusion technique. The SEM photographs revealed porous, spherical, micron sized particles. X-Ray diffractogram of microsponge and pure drug reveled identical peaks pattern, indicated absence of polymorphic transition of entrapped drug in polymeric microsponge. The optimized microsponges were incorporated in Carbopol 940 gel for ease of topical application. Extrudability and pH of microsponge based gel were 96.72% and 6.3-6.9 respectively. Viscosity and spreadability were 2.25 Pa.s. and 4.25 gm cm/sec respectively. In-vitro release profile of microsponge based gel was reported to decline within range of 85.38-42.37% with respect to rise in drug: polymer ratio from 1:1 to 1:6. In-vitro anti-fungal activity against C. albicans revealed promising activity of microsponge based gel.

Gulati et al., have successfully entrapped miconazole nitrate in polymeric microsponge for effective management of diaper dermatitis. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using Eudragit RS 100. The SEM photographs showed porous, spherical, micron sized particles with uniform outline. The In-vitro drug release study showed sustained release of drug over the period of 12 hrs. The prepared microsponges were incorporated into Carbopol 934 gel. Viscosity and pH were reported to be suitable for topical application of microsponge based gel. The spreadability of prepared gel was reported to be 2.54 mg cm/sec. The diffusion across cellophane membrane was suggested to follow Higuchi model. In-vitro anti-fungal activity against C. albicans revealed superior anti-fungal activity of microsponge based gel over marketed gel. Authors reported sustained release of drug over the period of 10 hours. Finally authors concluded potential use of microsponge based drug delivery system for management of diaper dermatitis.

Shuhaib B. et al. 2018 have formulated mafenamic acid loaded microsponge for topical delivery in treatment of rheumatoid arthritis. Drug loaded microsponge was obtained from ethyl cellulose as polymer and polyvinyl alcohol as stabilizer using quasi-emulsion solvent diffusion technique. FTIR spectrum revealed no interaction between drug and excipients. The formulated microsponges were evaluated for production yield, drug content, entrapment efficiency and mean particle size. The prepared microsponge incorporated in HPMC and light liquid paraffin emulgel. The In-vitro diffusion of drug across egg membrane was assessed using modified Keshary-Chein (K-C) cell. The results revealed sustained diffusion of drug over the period of 8 hours. Finally authors concluded the suitability of microsponge based topical drug delivery system over conventional delivery of mafenamic acid.

Microsponges based oral drug delivery

The oral route is considered the most common route of administration due to its simplicity, high capacity to dissolve many drugs and low toxicity. However oral route is not suitable for drugs having short half-life and drugs that degrade by acidity of the stomach or bile juice or drugs which preferably absorb through colon. This gave rise to development of controlled release drug delivery system. Many drugs were loaded in microsponges for controlled drug delivery. Because of porous structure, microsponges show longer lag time, which can protects the drug against acidic environment of stomach. Table 2 highlights research on microsponge based oral drug delivery.

Table 2: Overview of microsponge based topical drug delivery

Drug	Method of preparation	Dosage form	Reference
Flurbiprofen	quasi-emulsion solvent diffusion	Colon targeted tablet	Orlu et al., 2006
Famotidine	quasi-emulsion solvent diffusion	Gastro-retentive	Charagonda et al., 2016
Curcumin	quasi-emulsion solvent diffusion	Carbopol 934P gel and Capsule	Bhatia et al., 2018
Diclofenac sodium.	quasi-emulsion solvent diffusion	Colon targeted tablet	Janakidevi et al., 2018

Orlu et al., 2006 have formulated flurbiprofen microsponges for effective colon targeted drug delivery. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using different proportions of Eudragit RS100 as polymer and polyvinyl alcohol as stabilizer. The effect of drug: polymer ratio, volume of volatile solvent and volume of outer aqueous phase on response variables were analyzed. The prepared microsponges were evaluated with respect to particle size, drug content, thermal stability, surface morphology, porosity parameters and FTIR spectroscopy. The ease of oral administration, microsponges was subjected to compression coating. The microsponge equivalent to 100 mg of drug was mixed with sodium carboxy methyl cellulose, magnesium stearate and compressed. The compressed core tablets were coated with mixture of pectin and HPMC. In-vitro drug release behavior microsponge based compression coated tablet was assessed by dissolution apparatus using simulated gastric fluid, simulated intestinal fluid and simulated colonic fluid. In order to simulate colonic microflora, probiotic culture was added in simulated colonic fluid. The formulation showed negligible drug release in simulated gastric fluid and maximum drug release in simulated colonic fluid.

Charagonda et al., 2016 have successfully prepared famotidine loaded gastro-retentive microsponges for treatment of gastric ulcer. The floating microsponges were prepared by a quasi-emulsion solvent diffusion technique using different proportions of Eudragit RS100 as polymer and polyvinyl alcohol as stabilizer. The prepared microsponges were evaluated with respect to particle size, drug content, thermal stability, surface morphology, powder characteristics and in-vitro drug release study. In-vitro drug release behavior was assessed in acidic medium (0.1N HCl) using USP Type II apparatus. The microsponges were reported to release drug sustained manner for the period of 12 hrs. and reported to follow zero order kinetics.

Bhatia et al., 2018 have formulated curcumin based microsponge formulation for oral as well as topical delivery. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using different proportions of ethyl cellulose. The optimized microsponges were incorporated into Carbopol 934P gel and characterized for pH, spreadability, mechanical characteristics, Ex-vivo skin deposition study and viscosity. The prepared microsponge based gel showed high adhesiveness with acceptable spreadability. Ex-vivo skin deposition study was performed on excised rat abdominal skin using Franz diffusion cell. The results showed improved drug residence time in skin. For oral drug delivery, microsponges were filled in hard gelatin capsules and characterized with respect to organoleptic properties. Finally authors concluded usefulness of microsponges for both oral and topical drug delivery over conventional drug delivery systems.

Janakidevi et al., 2018 have successfully formulated polymeric microsponge for colon targeted drug delivery of diclofenac sodium. Microsponges were prepared by a quasi-emulsion solvent diffusion technique using Eudragit RS 100, Eudragit S100 and Eudragit L100. The prepared microsponges were evaluated with respect to particle size, drug content, encapsulation efficiency and FTIR spectroscopy. The simulated gastric fluid, simulated intestinal fluid and simulated colonic fluid were used to assess In-vitro drug release behavior of colon targeted microsponges. The drug release was suggested to follow zero order kinetic. FTIR spectrum revealed negligible interaction between drug and polymer. Authors concluded efficiency of microsponge based drug delivery for local delivery of drug in colon as well as to improve bioavailability of drug in colon.

CONCLUSION

Microsponges based drug delivery offers several advantages over the conventional drug delivery systems and also consider as novel avenue of drug delivery in various pharmaceutical applications.

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