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Microsponges- A Novel DrugDelivery System- A Review

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Abstract: Microsponges are a novel drug delivery system that has been developed for targeted drug delivery . They are polymeric spherical particles with small diameter and large surface area. They are hollow inside and entrap active ingredients and release them in a slow, sustained manner.It is one of the most versatile drug delivery systems that are used currently.Microsponges have various properties with enhanced drug stability and decreased side effects. One of the delivery system's advantages is its versatility, meaning it can be prepared in various forms such as powder, gel, solutions and lotions. The particle is nanometer sized and there are currently two methods of preparation of Microsponges. The polymer material is a patented product that is commercially available. Recently, pharmaceutical companies have marketed microsponges as an oral and topical product. They are most commonly used for dermatological products, like sunscreen, topical antifungal and antibiotic drugs etc. The main disadvantage of oral and most of the parenteral delivery systems is the side effects that arise due to the specific drug delivery mechanism. Thereare so many discrepancies between the viability of the product in-vivo in clinical studies when compared to the actual usage in patients. Microsponges seem to offer comparatively effective drug action and fewer side effects.Most recent researches have focused primarily on the use of microsponges in specific fields such as anti-ulcer drugs, antibacterial and antifungal, anticancer drugs . Some researchers have explored the possibility of targeted drug delivery for arthritis and hypertension using microsponges. This review highlights the newer drug delivery strategies using microsponges.

Keywords: controlled release, Drug delivery systems,, microcapsules, Microsponges, polymeric drug delivery

1. INTRODUCTION

In recent years, enough emphasis has been placed on the side effects arising from various

enteral and parenteral drug delivery systems throughout the Pharmacological research world. So a general question arises which was aimed at developing and formulating a better drug delivery system.Microsponges wasone of the outcomes. Microsponges are in essentiality, a sponge at a micro level (Kaity*et al.*, 2010). It's a polymeric structure composed of porous microspheres which are able to entrap active ingredients. It is a patented polymeric delivery system, capable of entrapping a wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens, and anti-infective, anti-fungal, and anti-inflammatory agents (Saxena and Nacht, 2005). Like a normal sponge, it consists of a myriad of interconnecting voids within a non-collapsible structure, with a large porous surface. The size of the microsponges vary, from 5
– 300 μm in diameter, depending upon the degree of smoothness or after-feel required for the end formula.
A typical 25 μm sphere can have up to 250000 pores, providing a total pore volume of about 1 ml/g. This creates a large reservoir within each microsponge, which can be loaded with up to its own weight of active agent (Saxena and Nacht, 2005). The microsponge particles are too large to be absorbed into the skin, hence offering a non-invasive approach. As the size of the pore diameter is smaller,most of the bacteria of the average size range cannot penetrate into the tunnel structure of the microsponges.

Microsponges are capable of absorbing skin secretions, thereby reducing oiliness and shine from the skin (Wilson *et al.*, 2018). Microsponge particles do not pass through the skin. Instead, they tend to collect in the tiny nooks and crannies of the skin to slowly release the entrapped drug. This prevents the excessive accumulation of ingredients. Potentially, the microsponge delivery system can significantly reduce effective drug irritation without reducing their efficacy (Osmani*et al.*, 2015). The empty spheres are then washed away normally. The microsponge products are typically presented in conventional forms like creams, gels or lotions. The microsponges currently being used are in cosmetics, over-the-counter skin care, sunscreen and prescription products. Numerous studies have confirmed that the Microsponge drug delivery systems are non-toxic, non-allergenic, non-irritating and non-mutagenic. (Mathew *et al.*, 2009; Osmani*et al.*, 2015)

METHODS OF PREPARATION

Liquid- Liquid suspension Polymerization
A solution consisting of monomers and the functional or active ingredients is made. The Active ingredients are immiscible in water. This solution is suspended with agitation in an aqueous phase, usually containing additives, such as surfactants and dispersants (Kumar and Ghosh, 2017). Once the suspension isestablished, polymerization is initiated by activating the monomers either by catalysis, increased temperature or irradiation. As the polymerization process continues, a spherical structure is produced. This structure contains thousands of microsponges bunched together like grapes, forming interconnecting reservoirs (Li *et al.*, 2013). Once the polymerization is complete the solid particles are recovered from the suspension. The particles are then washed and processed, ready for use. The microsponge starting materials can be made using styrene and divinylbenzene or methyl methacrylate and

ethylene glycol dimethacrylate.

Quasi-emulsion solvent diffusion

Eudragit RS 100 is dissolved in ethyl alcohol to prepare the inner organic phase. Next, the drug is added to the solution and dissolved under ultrasonication at 35°C (Deshmukh and Poddar, 2012). The inner phase is poured into the polyvinyl alcohol solution in water (outer phase). Following 60 minutes of stirring, the mixture is filtered, to separate the microsponges. The microsponges are dried in an air-heated oven at 40°C for 12 hours. Ingredients are entrapped in microsponge polymers either at the time of synthesis, or if too labile to withstand polymerization conditions, they can be post-loaded after the microsphere structure has been formed.

Hypothetical mechanism of action

As the microsponge particles have an open structure, the active ingredient is free to move in and out from the particles and into the vehicle until saturation is reached. Once the finished product is applied to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore disturbing the equilibrium (Salah, Awad and Makhlouf, 2018). This will start a flow of the active from the microsponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed. The rate of active release will ultimately depend not only on the partition coefficient of the active ingredient between the polymer and the vehicle (or the skin), but also on some of the parameters that characterize the beads. Examples of these include surface area and primarily, mean pore diameter. Release can also be controlled through diffusion or other triggers such as moisture,pH, friction or temperature (Rençber*et al.*, 2017).

DRUGS DELIVERY USING MICROSPONGES

Many Anti-ulcer, Antimicrobial, Anti-cancer, anti-hypertensive, anti-inflammatory drugs are developed using Microsponges and are described below.

Anti-Ulcer Drugs

Khatab et al were among the few researchers who delved into the application of microsponges as a means to target enteric cells with anti ulcer drugs in peptic ulcers (Khattab and Zaki, 2017). This research was focusing on Gastroretentive microcapsules. This paved the way for Jafar et al to formulate Ranitidine hydrochloride encapsulated microsponges(A and Abarnadevika, 2017) and Resveratrol encapsulated in ethyl cellulose microsponges by Gandhi et al. (Gandhi *et al.*, 2020)Newer antiulcer drugs embedded microsponges have been developed like Cimetidine encrusted floating microsponges, Pirenzepine embedded microballoons, Omeprazole embedded Microsponges in the treatment of GERD.

The expediency of microsponges as floating gastro retentive systems was affirmed by successful development of H2 blockers loaded gastro retentive microsponges to provide sustained release of drug at the site of action. The high drug loading capacity of microsponges offered a convenient approach for fabricating into a conventional capsular

system to heal gastric ulcers. For scientific as well as economic reasons, such delivery systems have potential advantages which include enhanced therapeutic response, predictable rate of release, extent of absorption and improved patient acceptance.

Antifungal Drugs

The purpose of microsponges is to facilitate the absorption of many hydrophobic substances. Most of the topical antifungal drugs are found to be quite hydrophobic. Moin et al formulated fluconazole entrapped microsponges gel with enhanced drug delivery (Moin*et al.*, 2016), while Mahaparale studied the antifungaltherapy of terbinafinemicrosponges(Mahaparale*et al*, 2018). Salwa et al did the same with Miconazole(Salah *et al*, 2018). Itraconazole hollow microsponges are used in the treatment of Dermatological infections.

Most antifungal agents are prepared as a gel or a cream that promises to aid in faster absorption. Microsponges loaded gel showed controlled and sustained release and a good drug yield and drug loading capacity. Tropical treatment with fluconazole for severe life threatening skiing fungal infections has shown to be an efficient therapy occupying a high flying position among the alternatives of treatment. As compared to conventional formulation, these microsponge gel are expected to remain on the skin for a longer time, gradually releasing their contents over the time. Hence, oxiconazole nitrate microsponges and microsponge gel prepared in this study are promising as being more useful than conventional formulation therapy.

Antibacterial drugs:

Some of the many advancements made in microsponges in regard to antibacterial drugs include Mupirocinmicrosponges (Bhatia and Saini, 2018), Dicyclomine loaded microsponges(Rajurkar and Gosavi, 2018), and Benzoyl Peroxide gel by Jelvahgiri et al (Jelvehgari*et al.*, 2006). Microsponges-based emulgel formulations showed prolonged efficacy in mouse surgical wound models infected with S. aureus. Mupirocin was stable in topical emulgel formulations and showed enhanced retention in the skin indicating better potential of the delivery system for treatment of primary and secondary skin infections, such as impetigo, eczema, and atopic dermatitis. Antibiotic drugs have a very wide use in the medical field. The requirement changes every year owing to bacterial resistance and ineffectiveness of the preparation. It is hence vital that there's an arsenal of drug delivery systems at our disposal for the ever changing world. Looking at the more natural ingredients and products, there has been considerable development in the organic antibacterial drugs development.*Azadirachtaindica*, commonly known as the neemplant, and its extracts have shown to have antibacterial effects against various oral pathogens (Lakshmi *et al.*, 2015). Oligonucleotide therapy has proven to be an emerging focus area for drug delivery in chronic inflammatory lung diseases. (Mehta *et al.*, 2019)

Anticancer drugs:

Nowadays, chemotherapy, radiation, and surgery are classical treatment methods for cancer, but they have stark mental and biochemical side effects which predominantly destroy the healthy cells of patients. Chemotherapeutic drugs have a broader spectrum of activity against

several types of cancer such as skin cancer, breast cancer, pancreatic cancer, stomach cancer and colorectal cancer. The anticancer drug delivery is a developing field and many delivery systems have been formulated for specific types of cancer.

Curcuminmicrosponges by Bhatia et al (Bhatia and Saini, 2018) and Curcuminbetacyclodextrin have been formulated for skin cancer and 5-Fluorouracil for colon cancer. Enteric coated HPMC capsules plugged with 5- fluorouracil loaded microsponges are promising to be a good dosage form for colon targeting.

Some natural products have shown good potential as anticancer agents. *Carallumafimbriata*has shown good cytotoxic effect against human colon cancer cells (Ashwini*et al*, 2017), many emerging trends in novel drug delivery approaches for the treatment of lung cancer have been discovered (Sharma *et al.*, 2019), *Acacia catechu*ethanolic bark extract can induce apoptosis in human oral squamous carcinoma cells (Lakshmi, *et al.*, 2017), *Acacia catechu*ethanolic seed extracts against SCC cells (Ezhilarasan, *et al.*, 2017), Coumarin derivatives have shown anticancer effects against stomach cancer (Perumalsamy*et al.*, 2018), Syringic acid mediates cytotoxicity in Hepatic cells (Gheena and Ezhilarasan, 2019), Selenium nanoparticles as a chemotherapeutic agent (Menon*et al.*, 2018), Antihyperglycemic activity of*Carallumafimbriata*(Anitha and Ashwini, 2017), oxidative stress in chronic liver disease (Ezhilarasan, 2018) and targeted drugs for hepatic fibrosis (Ezhilarasan, *et al* 2018).

Zinc oxide synthesis using *Mangiferaindica*for lung cancer (Rajeshkumar, *et al.*, 2018), and so on. Nanotechnology is an ever growing field with loads of opportunities. Each and every year, there has been a breakthrough using nanoparticles. Some of the more prominent antibacterial nanoparticles include Larvicidal activity of Antimicrobial silver nanoparticles synthesised using *Garciniamangostana* bark extract (Karthiga, *et al*, 2018) and zinc oxide nanoparticles synthesised using *Brassica oleracea* which shows bacteriotoxic activity against many common pathogens (Rajeshkumar, Agarwal, *et al.*, 2018).All these recent researches give hope for more plant-based microsponges in future for various diseases.

Miscellaneous drugs:
Anti Arthritis medication: Diclofenac sodium targeted for Rheumatoid arthritis in joints by Osmani et al (Osmani*et al.*, 2015) .Anti hypertensivemedication :Atenolol entrapped microsponges by Biswas et al (Kapoor*et al.*, 2014). Nebivolol by Pandit et al (Pandit*et al.*, 2017) and Topical antibiotics Tretinoin, Erythromycin and Voriconazole(Mahant*et al.*, 2019).The human skin is an important target site for drug application in dermatological disorders. For its treatment, topical drug delivery is preferred to limit the therapeutic effect.

CONCLUSION

The microsponge drug delivery system is a unique technology for a controlled and sustained release of drugs. It offers a potential reduction in side effects while maintaining their therapeutic efficacy. This also gives a huge scope of uses as a drug delivery system; however

it should be further studied to improve drug delivery and drug efficacy to use it as a regular drug formulation in the future .

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Samyuktha P S contributed to data collection and drafting the article. Critical revision of the manuscript was done by Dr. Anitha Roy and Dr. Jayalakshmi S.

CONFLICT OF INTEREST
The authors declare no potential conflict of interest

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