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Research Article

A Review on Recent Application of Novel Approach Microspounge

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Abstract:

In the field of drug delivery system, there are numerous new formulation techniques. Microsponge are one of the most recent novel technique which are gaining popularity now days due to their use of controlled release and targeted drug delivery system. Microsponge technology offers entrapment of ingredient and is believed to contribute towards reduced side effect, improved stability, increase elegance and enhanced formulation flexibility. In addition, microsponges are non-irritating, non-mutagenic, non-allergenic and non-toxic. One of the best features of microsponge is its self-sterilizing ability. Microsponges are porous, polymeric microspheres that are used mostly for topical use and have recently been used for oral administration. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose. This review is focused on compilation of all recent application of novel approach microsponge.

Introduction:

Microsponge Delivery System (MDS) is a unique technology for controlled[1] delivery of drug. MDS technology has been introduced in topical drug products to facilitate the controlled release of active drug into the skin in order to reduce the systemic exposure and minimize local cutaneous reactions to active drugs. A Microsponge delivery system is patented, highly cross-linked, porous, polymeric microspheres polymeric system consisting of porous microspheres that can entrap wide range of actives and then release them onto the skin over a time and in response to trigger. To control the delivery rate of active agents to a predetermined site in human body has been one of the biggest challenges faced by drug industry.Several predictable and reliable systems were developed for systemic drugs under the heading of transdermal delivery system (TDS) using the skin as portal of entry. It has improved the efficacy and safety of many drugs that may be better administered through skin. But TDS is not practical for delivery of materials whose final target is skin itself.

Characteristics of microsponge[2]:

- Microsponge formulations are stable over range of PH.
- Microsponge formulations are stable at the temperature up to 1300^0C.
- Microsponge formulations are compatible with most vehicles and ingredients.
- Microsponge formulations are self-sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate.
- Microsponge formulations have higher payload (50 to 60%), still free flowing and can be cost effective.

Advantages over conventional formulation[3-4]:

Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. When compared to the Microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs without reducing their efficacy. For example, by delivering the active ingredient gradually to the skin like MDS Benzoyl peroxide formulations have excellent efficacy with minimal irritation.

Microencapsulation and liposomes: The MDS has potential features over other technologies like microencapsulation and liposomes. The rate of release of actives usually cannot be controlled in microcapsules. The actives contained within microcapsules will be released once the wall is ruptured. Liposomes have limited capacity, difficult formulation, restricted chemical stability and microbial instability.

Ointments: Patient compliance with ointment is reduced due to its aesthetically unattractive, viscous and greasy nature. Ointments have low efficiency as drug delivery systems, thus they cause irritation and sensitization because these compounds need high concentration so fictive ingredients for effective treatment. Another drawback of topical formulations is the bad odour, uncontrolled evaporation of active ingredient and potential incompatibility of drugs with vehicles. The microsponge system, however, increases time during which an active resides either within epidermis or on skin surface.

Applications of Microsponge Systems[5]:

Microsponge delivery systems are used to enhance the safety, effectiveness and aesthetic quality of topical prescription, over-the-counter and personal care products. Products under development or in the market place utilize the Topical Microsponge systems in three primary ways:

1. As reservoirs releasing active ingredients over an extended period of time,
2. As receptacles for absorbing undesirable substances, such as excess skin oils.
3. As closed containers holding ingredients away from the skin for superficial action.

Microsponge technology is designed to allow a prolonged rate of release of the active ingredients, thereby offering potential reduction in the side effects while maintaining the therapeutic efficacy. Microsponges are porous, polymeric microspheres that are used mostly for topical and recently for oral administration. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release.

Topical drug delivery using microsponge technology:

- Benzoyl peroxide (BPO) is commonly used in topical formulations for the treatment of acne and athletes foot. Skin irritation is a common side effect, and it has been shown that controlled release of BPO from a delivery system to the skin could reduce the side effect while reducing per.
- Cutaneous absorption. Benzoyl peroxide micro particles were prepared using an emulsion solvent diffusion method by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol.
- Disorders of hyper pigmentation such as melasma and post inflammatory hyperpigmentation (PIH) are common, particularly among people with darker skin types. Hydroquinone (HQ) bleaching creams are considered the gold standard for treating hyper pigmentation. Recently, a new formulation of HQ 4% with retinol 0.15% entrapped in Microsponge reservoirs was developed for the treatment of melasma and PIH. Microsponges were used to release HQ gradually to prolong exposure to treatment and to minimize skin irritation[6].
- 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[7].
- Fluconazole is an active agent against yeasts, yeast-like fungi and dimorphic fungi, with possible drawback of itching in topical therapy. Microspongic drug delivery system using fluconazole with an appropriate drug release profile and to bring remarkable decrease in frequently appearing irritation. Microsponges were prepared by liquid-liquid suspension polymerization of styrene and methyl methacrylate Carac cream is the newest topical treatment for multiple actinic or solar keratoses. Carac provides sufferers with options for shorter duration of therapy (1, 2 or 4 weeks), once-a-day dosing, and more rapid recovery time from irritation[8]. An MDS system for retinoic acid was developed and tested for drug release and anti-acne efficacy. Statistically significant greater reductions in inflammatory and non-inflammatory lesions were obtained with entrapped tretinoin in the MDS.

Oral drug delivery using microsponge technology

In oral drug delivery the Microsponge system increase the rate of solubilization of poorly water soluble drugs by entrapping them in the Microsponge system's pores. A Microsponge system offers the potential to hold active ingredients in a protected environment and provide controlled delivery of oral medication to the lower gastrointestinal (GI) tract, where it will be released upon exposure to specific enzymes in the colon. This approach opens up entirely new opportunities for MDS by colon specific targeting of drugs. Paracetamol loaded eudragit based Microsponges were prepared using quasiemulsion solvent diffusion method, then the colon specific tablets were prepared by compressing the Microsponges followed by coating with pectin: hydroxypropyl methyl cellulose (HPMC) mixture.

- microsponge based[9] colon specific drug delivery system containing paracetamol. Eudragit S-100 based microsponges containing drug in varying amounts were prepared using quasi-emulsion solvent diffusion method. The microsponges were prepared by optimizing various process parameters.The colon specific tablets were prepared by compressing the microsponges followed by coating with pectin: hydroxypropylmethyl cellulose (HPMC) mixture. *In vitro* release studies exhibited that compression coated colon specific tablet formulations started releasing the drug at 6th hour corresponding to the arrival time at proximal colon. The study presents a new approach for colon specific drug delivery.

Bone tissue engineering using Microsponge technology:

3D biodegradable porous scaffold plays a very important role in articular cartilage tissue engineering. The hybrid structure of 3D scaffolds was developed that combined the advantages of natural type I collagen and synthetic PLGA knitted mesh. The mechanically strong PLGA mesh served as a skeleton while the collagen microsponges facilitated cell seeding and tissue formation. The scaffolds were divided into 2 groups:

(1) Thin:

collagen Microsponge formed in interstices of PLGA mesh;

(2) Semi:

collagen Microsponge formed on one side of PLGA mesh; (3) SANDWICH: collagen sponge formed on both sides of PLGA mesh. Bovine chondrocytes were cultured in these scaffolds and transplanted subcutaneously into nude mice for 2, 4, and 8 weeks. All three groups of transplants showed homogeneous cell distribution, natural chondrocyte morphology, and abundant cartilaginous ECM deposition. Production of GAGs per DNA and the expression of type II collagen and agger can mRNA were much higher in the SEMI and SANDWICH groups than in the THIN group. When compared to native articular cartilage, the mechanical strength of the engineered cartilage reached 54.8%, 49.3% in Young's modulus and 68.8%, 62.7% in stiffness, respectively, in SEMI and SANDWICH. These scaffolds could be used for the tissue engineering of articular cartilage with adjustable thickness. The design of the hybrid structures provides a strategy for the preparation of 3D porous scaffolds [10].

Cardiovascular engineering using microsponge technology:

Biodegradable materials with autologous cell seeding requires a complicated and invasive procedure that carries the risk of infection. To avoid these problems, a biodegradable graft material containing collagen Microssponge that would permit the regeneration of autologous vessel tissue has developed. The ability of this material to accelerate in situ cellularization with autologous endothelial and smooth muscle cells was tested with and without precellularization. Poly (lactic-co-glycolic acid) as a biodegradable scaffold was compounded with collagen microsponge to form a vascular patch material. Histologic and biochemical assessments were performed 2 and 6 months after the implantation. There was no thrombus formation in either group, and the poly (lactic-co-glycolic acid) scaffold was almost completely absorbed in both groups. Histologic results showed the formation of an endothelial cell monolayer, a parallel alignment of smooth muscle cells, and reconstructed vessel wall with elastin and collagen fibers. The cellular and extracellular components in the patch had increased to levels similar to those in native tissue at 6 months. This patch shows promise as a bioengineered material for promoting in situ cellularization and the regeneration of autologous tissue in cardiovascular surgery[11].

Reconstruction of vascular wall using microsponge technology[12]:

The tissue-engineered patch was fabricated by compounding a collagen-Microsponge with a biodegradable polymeric scaffold composed of polyglycolic acid knitted mesh, reinforced on the outside with woven polylactic acid. Tissue-engineered patches without precellularization were grafted. Histologic and biochemical assessments were performed 1, 2, and 6 months after the implantation. There was no thrombus formation in any animal. Two months after grafting, all the grafts showed good in situ cellularization by hematoxylin/eosin and immunostaining. The quantification of the cell population by polymerase chain reaction showed a large number of endothelial and smooth muscle cells 2 months after implantation. In the large graft model, the architecture of the patch was similar to that of native tissue 6 months after implantation and this patch can be used as a novel surgical material for the repair of the cardiovascular system[13].

Gastro-retention drug delivery system (GRDDS):

Microsponge hold certification as one of the potential approaches for gastric retention. Microsponge are porous spherical empty particles without core and can remain in the gastric region for delayed periods. They significantly increase the gastric residence time of medication, thereby enhance bioavailability, improves patient compliance by reducing dosing frequency, lessen the medication waste, enhance retention of medication which solubilize only in stomach, enhance solubility for medications that are less soluble at a higher pH environment[14].

Anti-Ulcer:

Microsponges as a means to target enteric cells with anti-ulcer drugs in peptic ulcers. microsponges as floating gastro retentive systems was affirmed by successful development of H_2 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:** 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. Topical 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:** 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. Azadira chtaindica, commonly known as the neemplant, and its extracts have shown to have antibacterial effects against various oral pathogens. Oligonucleotide therapy has proven to be an emerging focus area for drug delivery in chronic inflammatory lung diseases.
- **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[15].
- **Antiarthritis medication:** Diclofenac sodium targeted for Rheumatoid arthritis in joints. 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.Diclofenac sodium targeted for Rheumatoid arthritis in joints, Antihypertensive medication :Atenolol entrapped microsponges.
- **Antiepileptic Medication:** Carbamazepine (CBZ) is an anti-epileptic agent which is used in the therapy of trigeminal neuralgia, epilepsy and bipolar disorders. CBZ microsponges were prepared using quasi emulsion solvent diffusion technique with varying composition of ethyl cellulose and polyvinyl alcohol (PVA). Microsponges were evaluated using Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and X-ray diffraction[16].
- **Microsponges:** a pioneering tool for biomedical applications:

solid-phase porous microspheres having numerous interconnected voids, which serve as non-collapsible residence for bioactive compounds. A Micsys particle ranges from 5 to 300 μm in size and shows a wide range of entrapment efficiency with desired release rates.This topical drug delivery system bestows a controlled release of bioactive compounds into the skin with reduced systemic side effects. Currently, the application area of this promising system include oral, ocular, pulmonary, and parenteral delivery of bioactive compounds[17].

- **Self-assembled DNA hollow spheres from microsponge:**

This synthetic process was conducted in a water-based system without organic solvents, enabling the synthesis of biologically and environmentally friendly products. Based on the benefits of hollow shell structures, which include their high surface-to-volume ratio and ability to encapsulate small molecules, we envision that this simple approach for synthesizing DNA HSs will provide a new platform for maximizing their potential use in drug delivery and bio-imaging[18].

List of application of microsponge explained in tables:

Compilation of application of microsponge[19]:

Table-1: Application of microsponge according to advantage

S.no.	Application	Advantage
	Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization
1	Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization.
2	Anti-inflammatory e.g. hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses.
3	Anti-dandruffs e.g. zinc parathion, selenium sulphide	Reduced unpleasant odour with lowered irritation with extended safety and efficacy.
4	Antipruritic	Extended and improved activity.
5	Skin depigmenting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.

Examples of microsponge drug delivery with their formulations[21-23]

Table 2: Examples of microsponge drug delivery with their formulations

Microsponge Delivery Systems	Drug Disease	Drug Disease
Gels	Benzoyl peroxide	Anti-Acne Treatment
	Fluconazole	Inflammation
	Mupirocin	Antibacterial activity
	Diclofenac sodium	Inflammation
	Acyclovir	Viral infections
	Hydroxyzine HCl	Urticaria and atopic dermatitis
	Terbinafine HCl	Anti-fungal
Lotions	Benzoyl peroxide	Anti-Acne Treatment
Creams	Hydroquinone and Retinol	Melanoma
Tablets	Indomethacin	Inflammation
	Paracetamol	Anti-pyretic
	Chlorpheniramine	maleate Hay Fever
	Ketoprofen	Musculoskeletal pain
	Fenofibrate	Gout
	Flurbiprofen	Metabolic ratio
	Dicyclomine	Anticholinergic
	Meloxicam	Arthritis
	Paracetamol	Colon targeting
Implants	Poly (DL-lactic-co-glycolic acid)	Skin tissue engineering
Grafts	Poly (lactic-co glycolic acid)	Cardiovascular surgery
Injection	Basic fibroblast growth	Growth factor
Others	Benzoyl peroxide	Anti-Acne Treatment
	Mefenamic acid	Rheumatoid arthritis
	NSAID	Ibuprofen

List of Marketed Products based on Microsponges[23-25]

Table 3: List of Marketed Products based on Microsponge:

Product Name	Name Pharmaceutical Uses	Manufacturer
Glycolic Acid Moisturizer w/SPF 15	Anti-Wrinkles, soothing	AMCOL Health & Beauty Solution
Retin A Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc.
Carac Cream, 0.5%	Actinic keratoses	Dermik Laboratories, Inc.
Line Eliminator Dual Retinol Facial Treatment	Anti-wrinkle	Ortho-McNeil Pharmaceutical, Inc.
Line Eliminator Dual Retinol Facial Treatment	Anti-wrinkle	Avon
Retinol 15 Night cream	Anti-wrinkles	Sothys
Retinol cream	Helps maintain healthy skin	Biomedic
EpiQuin Micro	Hyper pigmentation	SkinMedicaInc
Sports cream RS and XS	Anti-inflammatory	Embil Pharmaceutical Co. Lt
Salicylic Peel 20	Excellent exfoliation	Biophora
Oil free matte block SPF 20	Sunscreen	Dermalogica
Lactrex™ 12% Moisturizing Cream	Moisturizer	SDR Pharmaceuticals, Inc
Dermalogica Oil Control Lotion	Skin protectant	John and Ginger Dermalogica Skin Care Products
Ultra Guard	Protects baby's skin	Scott Paper Company

Conclusion:

Microsponge drug delivery system has become extremely competitive and rapidly developing technology and most research are carrying out to optimize the effectiveness of cost and therapy efficacy. Microsponge delivery system holds a promising future in different pharmaceutical applications in the upcoming years as they have excellent properties like elegancy and superior performance of product. In the topical delivery system, the microsponges can be successfully incorporated for dosage form retention on the skin and it is also benefit for oral drug delivery using polymers which are biodegradable. Microsponge releases its actives on a time mode and also in response to other stimuli. The microsponge delivery system has a high potential and is very

emerging field which is needed to be explored in the coming years with more research study.

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