Review Article

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Revolutionary Microsponge Delivery System: Provides Efficient, Steady And Controlled Drug Release

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Abstract

The mechanism of drug delivery has develops more competing and developed swiftly. Cost effective with increased efficacy have been integrated by various drug delivery arrangements. In spite of these technologies, the drug delivery systems lack to accomplish the requisite systemic circulation in control manner like Peptides and proteins. Conventional topical formulations have also many problems, such as establishment of active ingredient intense layer resulting irritation and allergic reactions etc. So predetermined delivery charge of active compound to target site develops into drug industry's principal challenges. This review article focuses on the Novel approaches of product formulation like microsponge automation which entrap ingredient so, that to increase elegance and improved formulation elasticity and reduces its side effect. In extension, many studies share for microsponge systems as non- irritant, non-toxic prevents rapid and enormous growth of components inside the epidermis and the dermis. Thus Microsponges bear dynamic constituent having capably of least dose, with improved stability and modified drug discharge.

Keywords: Drug; Enhanced; Epidermis; Microsponge; Stability; Topical.

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Introduction

Microsponges are polymeric hovering of permeable microspheres. They are miniature sponge-like bulbous particle with a bulky leaky surface. They are porous, polymeric deliverance properties, composed of spongy microsphere which suspends or trap different variety of active ingredients i.e. cologne, essential oil, sunscreen, anti- infective, anti-fungal, and anti-inflammatory agents. This can be formulating as a gels, creams, liquids and powders [1]. They were widely used for topical application and had been freshly used for oral administration. A microsponge conveys pharmaceutical active ingredients proficiently at least dose and also enhances stability that reduces side effects and alters drug discharge [2]. Won proposed the Microsponge technology in 1987 and applied to cosmetic and OTC product. Microsponge consist of non collapsible structures with porous surface which active ingredients are released in a controlled manner. Depending upon the size, the total pore length may up to 10ft and pore volume up to 1 ml/g [3].

Currently, the technology was license to Cardinal Health, in topical products. The dimension of the Microsponge varies from 5-300 ìm in diameter having large pores as a reservoir within each microsponge [4]. Several formulations are examined for systemic drugs delivery like microcapsules, microsphere and liposome etc, but they have some limitation such as microcapsules cannot frequently command the active drug discharge rate when the wall is disrupter and liposome endure a minor pay load, chemical and

microbial volatility. Thus there is need to exploit the incidence time of active component both on to the skin surface or inside the epidermis with minimize transdermal infiltration hooked on the body [2].

Microsponges are steady over pH range of 1-11 and temperature must be between 130°C. Microsponge are microscopically spherical, free flowing, and better entrapment efficiency to reduced side effects, increased elegance, non-irritating etc. Currently microsponges are generally worn in cosmetics, over-the-counter (OTC), skin care and sunscreens preparations. The detailed applications of microsponges and list of marketed products are enumerated (Table 1) and (Table 2).

Table 1: Applications of Microsponge [26].

Active agents	Applications
Sunscreens e.g. Cornstarch and Vinyl Dimethicone	Improve efficacy & protection against harmful sunrays and U.V. rays.
Anti-acne e.g. Benzoyl peroxide	Uphold the effectiveness with weaken skin impatience and sensitization.
Anti-inflammatory e.g. hydrocortisone	Extended activity with decline of skin allergic reaction.
Anti-fungal	continuous discharge of activity
Anti-dandruffs e.g. zinc pyrithione, selenium sulfide	Reduces disagreeable odor with lower irritation, protracted safety and efficacy
Rubefacients	Extensive activity with compact irritancy
Skin depigmenting agents e.g. hydroquinone	Enhanced stabilization alongside oxidation with hydroquinone hydroquinone better efficiency

Table 2: List of marketed products [27]

Manufactured goods name	Producer's name	Advantages
Retin-A-Micro™	Ortho-McNeil Pharmaceutical, Inc.	0.1 and 0.04% Tretinoin entrap in MDS, for relevant application of acne vulgaris.
Carac cream 0.5%	Dermik Laboratories, Inc. Berwyn, PA19312 USA	Carac cream contain 0.5% Fluorouracil, with 0.35% included into a original porous microsponge poised of methyl methacrylate / glycol dimethacrylate cross-polymer and dimethicone.
Line eliminator dual retinol facial treatment	Avon	Frivolous cream with retinol (Vitamin A) in MDS produces mutually instant and time-released wrinkle- fighting action.
Retinol cream	Biomedic	The retinol particle is reserved in the microsponge system to guard the strength of vitamin A. This helps to widen the retinol quantity, while lessening the opportunity of irritation. Retinol is a topical vitamin A derivative, which helps to sustain healthy skin, hair, and mucous membranes.
Retinol15 night cream	Biomedic, sothys	A night time remedy emulsion with Microsponge system. The procedure contains pure retinol. constant use of Retinol 15 determination produce the noticeable fading of fine lines and wrinkles, and recover skin discolorations.
EpiQuin micro	Skin Medica Inc	The Microsponge® system entraps hydroquinone and retinol. The microsponge liberate these all ingredients interested in the skin regularly right through the day, which could lessen skin irritation.
Sports cream RS and XS	Embil Pharmaceutical.	Topical analgesic, anti-inflammatory and counter irritant activity intended for the management of musculoskeletal conditions.
Salicylic peel 20 and 30	Biophora	Deep BHA peeling agent: Tremendous exfoliation and stimulation of the skin for quicker results that get better fine lines, pigmentation, and acne concerns.
Micro peel plus	Biomedic	It precures cell turnover from side to side application of salicylic acid in the form of microcrystals by means of Microsponge technology and violently outperforms other chemical peels by acquittal the skin of all dead cells, while doing no harm to the skin.

Lactrex™ 12% moisturizing cream	SDR Pharmaceuticals, Inc., Andover, NJ, .S.A. 07821	It formulates by 12% lactic acid as the neutral ammonium salt and ammonium lactate. It also contains water and glycerin, as natural humectant, which reduce and moisturize dry, flaky, cracked skin.
Dermalogica oil control lotion	John and Ginger Dermalogical skin care products	It is a feather-light lotion, prepared with oil by this technology and hydrating botanicals, forming complex which helps soothe and purify the skin.
Ultra guard	Scott Paper	It contains dimethicone to protect baby's skin from diaper rash.

Advantage of Microsponge [3,5,6]

- Microsponges are capable of absorbing skin secretions so reducing the oiliness of the skin.
- It offer unique controlled release up to 12 hours and it is biologically safe and effective.
- Microsponges systems are stable over range of pH 1to 11and temperature up to 130°C.
- They are self-sterilizing as average pore size is 0.25 μm where bacteria cannot penetrate.
- Improves thermal, physical and chemical stability.
- Reduces irritation and have improved patient compliance.
- Microsponges flexible to develop novel product form.
- It can be improves product aesthetics.
- Its allows incorporation of immiscible product
- Improves materials processing eg. Liquid can be converted to powders
- Microsponges can improves bioavailability of same drug

Characeritistics of Drugs to Be Entrapped into Microsponges

- The material which to be entrapped should have fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should not increase the viscosity of the mixture during formulation process.
- It should be water immiscible or at most only slightly soluble.
- It should not collapse spherical structure of the microsponges.
- It should be stable in contact with polymerization catalyst and also in condition of polymerization.
- It should be inert to monomers
- Not more than 10-12% w/w microsponges must be incorporated into vehicle. Otherwise, vehicle will deplete microsponges before the application. So the solubility of actives in the vehicle must be limited.

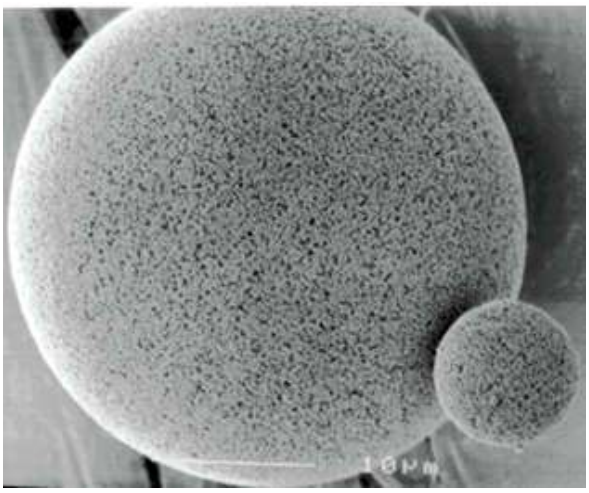

Fig. 1: Microsponges

Method of Preparation of Microsponge

The active material should be water immiscible or soluble to some extent, static to monomers (Table 3). It ought to stable when it was touch with the polymerization method and beneath situation of polymerization.

The globular arrangement of the microsponges is not crumple [7]. Drug loading in microsponge can take place in two ways, by one step or two-step process depending upon the physicochemical properties of drug to be loaded. In case if the drug is typically as inert non-polar materials, it will create the porous structure, which is called as porogen. A porogen drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid-liquid suspension polymerization) [3,5,6,7]. Microsponge are suitably prepared by the following method.

Table 3: Drugs used in microsponge delivery system

Drugs	Polymer	Offering Benefits
Mupirocin	Ethyl cellulose and dichloromethane as a solvent which contained PVA as emulsifying agent	Improved withholding in the skin indicates better probable of the delivery system intended for the management of principal and inferior skin infections [18].
Benzyl peroxide	Ethyl cellulose and dichloromethane used as a solvent. Suspension polymerization of styrene and methyl methacrylate	Decrease the side effect by diminishing percutaneous absorption and controlling the release BPO to the skin [19].
Fluconazole	liquid-liquid suspension polymerization of styrene and methyl methacrylate	Reduce the side effect and controlled the release [20].
Flurbiprofen	Eudragit RS 100 by minute opening plug of microsponges with pectin: HPMC mixture followed by tableting	Microsponge system contains flubiprofen prepared intended for the colonic delivery of the drug designed for specific targeted action [21].
Dicyclomine	Eudragit RS 100	System was based on microsponges which could decreases the GI side effects of the drug [22].
Paracetamol	Eudragit S 100 based microsponges	Colonic delivery of the drug for target action [23].
Hydroxyzine HCl	Eudragit RS 100 microsponges	Control discharge of the drug through the skin which reduces the side effects whereas to reduce the percutaneous absorption [24].
Ketoprofen	Eudragit RS 100	Microsponge based system which decreases the GI side effects of the drug [21].
Diclofenac sodium	Xanthan gum assists ethyl cellulose microsponges	At the smallest drug/polymer ratio that should be helpful for controlled release of diclofenac sodium to the skin [25].

Polymerization Technique

The permeable microsphere is equipped by suspension polymerization method i.e. liquid-liquid system. In this research, the monomers are primarily dissolving with dynamic ingredient in an appropriate solvent solution of monomer and the solution of monomers is isolated in the aqueous phase containing surfactant etc [8,9]. The polymerization is proposed by accumulated catalyst or by rising warmth or irradiation [10].

Various steps involved in the preparation of microsponge by polymerization are as follows:

1. Selection of monomer or combination of monomers.
2. Formation of chain monomers as polymerization begins.
3. Formation of ladders as a result of cross-linking between chain monomers.
4. Folding of monomers ladder to form special particles.
5. Agglomeration of microsponge leads to the production of bunches of microsphere.
6. Binding of bunches to form microsponges.

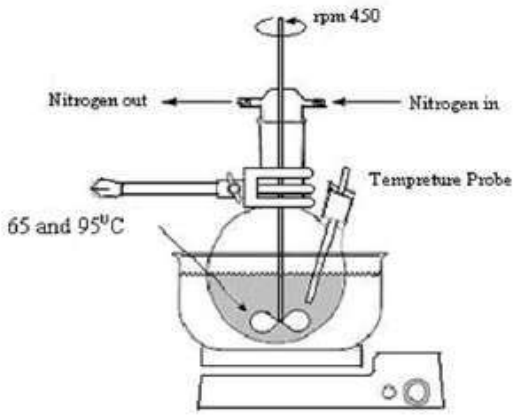

Fig. 2: Reaction Vessel for Liquid-liquid suspension polymerization technique [5]

Quasi-Emulsion Solvent Diffusion Method of Polymerization

Microsponges are formulated by a quasi-emulsion solvent diffusion method by means of an exterior segment which contain 200 ml distilled water and 40 mg Polyvinyl Alcohol (PVA) 72000. The inner segment contains drug, ethyl alcohol, polymer and triethyl citrate, which was added at an amount of 20%, of the polymer in order to facilitate the plasticity. Then the drug added to

solution and dissolved under ultrasonication at 35°C. At first, the interior segment was prepared at 60°C and was added to the exterior segment at room temperature. After emulsification, the combination was constantly mixed for at least 2 hours. Then the mixture was filtered and separate out the microsponges. The produced microsponge be then washed and dried by vacuum oven at 40°C for 24 hours [11].

Evaluation

Evaluations of microsponges are carried out by various methods which are given in Table 4.

Future Perspective

Microsponges are best way for the novel drug delivery systems, which were generally prepared for topical application of drugs. This can be used for tissue engineering and proscribed oral drug delivery by means of biodegradable polymers. It also incorporated by a wide range of formulating advantages. Liquids can be changed into open flowing powders. Preparations can be industrialize with contrarily unsuited ingredients, with extended stability, devoid use of preservatives. Therefore, microsponges are considered to be an ideal drug delivery system associated with other formulations like the transdermal delivery system. As we realize the nanosized particles have immense advantages like a large outside area to size ratio and a superior potential to transform the liberated of active ingredients as compare to micro-sized particles. While inorganic nanosponges contain different applications in electronics, the first pharmaceutical nanosponge based on cross linked cyclodextrins comprise been reported [28].

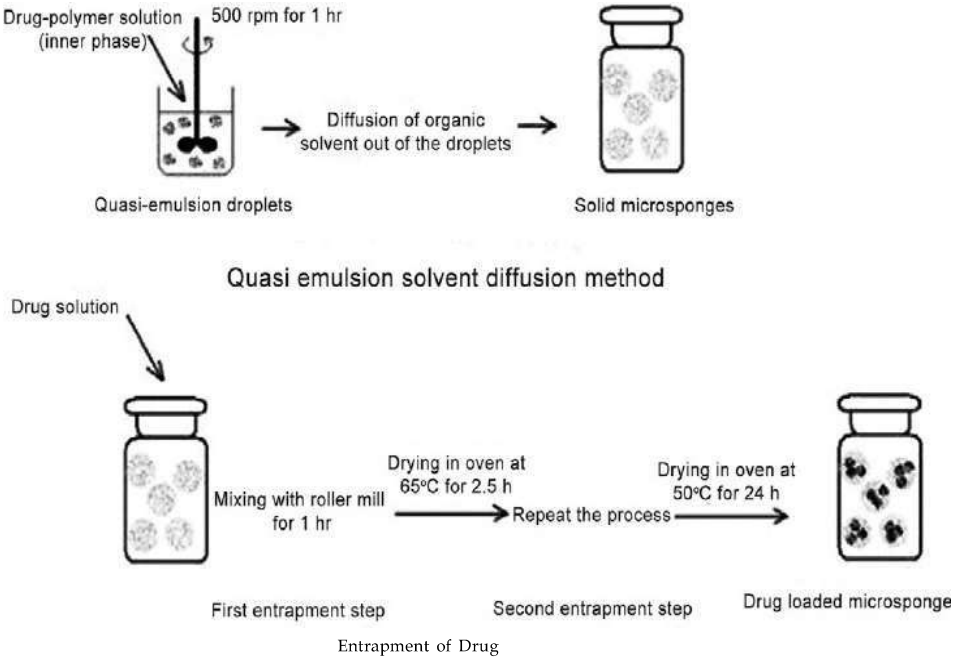

Fig. 3: Method of quasi-emulsion solvent diffusion [5]

Table 4: Evaluation of Microsponge

Parameters	Methods
Particle size (Microscopy), size distribution and polydispersity	Diffractometry, Optical Microscope [12]
Morphology & surface topography	Electron microscopy [!3]
Density	Displacement method[14]
Pore structure	Mercury intrusion porosimetry [14]
Drug polymer interaction	FTIR[15]
Crystallinity	XRD studies [16]
Drug release study from topical formulation	Franz diffusion cell [17]

A remarkable relevance of the microsponge technology might be in oral cosmetics, i.e. to uphold release of volatile ingredient by rising the time of the 'fresh feel'. Microsponges of such volatile ingredient may be simply integrated in tooth pastes or mouth washes and also colors incorporated in microsponges used in a various colored cosmetic products such as rouge or lipsticks to make them durable [29].

Conclusions

Microsponge delivery system is an ideal skill for the controlled release of macroporous beads, laden with active agent, presenting a possible decrease in side effects, while increasing their therapeutic efficacy. It also offers entrapment of its ingredients. In accumulation, various studies have established that this system of drug delivery is non-irritating, non-mutagenic, non-allergenic, and non-toxic.

This expertise is currently using in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This type of drug delivery system leads for a better perceptive of the healing of several diseases. Hence, the microsponge-based drug delivery tool is expected to develop a precious drug delivery system for various therapeutic applications in the future.

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