AN OVERVIEW ON MICROSPONGE DELIVERY SYSTEM

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Abstract
Microsponge were prepared by liquid-liquid suspension polymerization of styrene and methyl methacrylate. Microsponges were dispersed in gel prepared by using carbopol 940 and evaluated for drug release using Franz diffusion cell. Free flowing powder with size distribution 30 to 107 µm was obtained. The average drug release from the gels containing microsponge flucnazole was 67.81% in 12 h. drug release from the gels containing microsponge loaded flucnazole and marketed formulation has followed zero order kinetics. Microsponge system for topical delivery of flucnazole was observed potential in extending the release. A microsponge system for retinoic acid was developed and tested for drug release and anti-acne efficiency. Statistically significant greater reductions in inflammatory and non-inflammatory lesions were obtained with entrapped tretinoin in the microsponge system. A new formulation of Hydroquinone (HQ) 4% with retinol 0.15% entrapped in microsponge reservoirs was developed to release HQ gradually to prolong exposure to treatment and to reduce skin irritation.

Introduction
There has been an ever-increasing interest by the consumer, primarily the female in skin treatment products. This interest has been fostered by the widespread use of ingredients like α-hydroxy acids and vitamins in topical products that can induce perceivable and demonstrable benefits especially in aging or photo-damaged skin. In many instances, these ingredients may produce irritation. Such irritation can be perceived as redness, burning or stinging and particularly occurs in individuals with sensitive skin. These approaches in many cases also reduce the beneficial effects of the final product. Drug delivery systems can precisely control the release rates or target drugs to specific body site have had an enormous impact on the health care system. Several predictable systems were developed for systemic drugs under the title of transdermal delivery system (TDS) using the skin as portal of entry. Controlled release of drug onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is an area of research. No efficient vehicles have been developed for controlled and localized delivery of drugs into the stratum corneum and not beyond the epidermis. The application of topical drugs suffers many problem such as ointment, which are often aesthetically unappealing, stickiness and greasiness that results into lack of patient compliance. The drawbacks are unpleasant odour, uncontrolled evaporation of active ingredient and potential incompatibility of drugs with the vehicles. The microsponge delivery system have resulted in a new generation of very well tolerated, and highly efficacious, novel products.

Microsponge
The microsponge technology was developed by Won in 1987 and the original patents were assigned to Advanced Polymer Systems, Inc. Presently, this technology has been licensed to Cardinal Health, Inc., for use in topical products. The size of the microsponge varied from 5-300 µm in diameter. Although the microsponge size may vary, a typical 25 µm sphere can have up to 250000 pores and an internal pore structure equivalent to 10 ft in length providing a total pore volume of about 1 ml/g. The microsponge particles are too large to be absorbed into the skin and this adds a measure of safety to these microsponge materials. Bacterial contamination of the materials entrapped in the microsponge, because the size of pore diameter is smaller than bacteria, ranging from 0.007 to 0.2 μm. Microsponges are polymeric delivery systems consisting of porous microspheres that can entrap active ingredients such as fragrances, sunscreen, essential oil, emollients, anti-fungal, anti-infective and anti-inflammatory agents. Like a true sponge, each microspheres consists of myriad of interconnecting voids within a non-collapsible structure with a large porous surface.

Microsponge Preparation
Microsponges are prepared by two methods

• Quasi-Emulsion Solvent Diffusion
To prepare the inner organic phase, Eudragit RS 100 is dissolved in ethyl alcohol. The drug is added to solution and dissolved under ultrasonication at 35º C, the inner phase is poured into the polyvinyl alcohol solution in water. Following stirring for 60 min, then mixture is filtered to separate the microsponge. The microsponges are dried in an air-heated oven at 40º C for 12 h. Ingredients can be entrapped in microsponge polymers
at the time of synthesis. They can be post-loaded after the microsphere structure has been pre-formed. The letter process is the preferred mode since many pharmaceuticals and cosmetic ingredients, would decompose at the temperatures used for polymerization.

- Liquid-Liquid Suspension Polymerization:
  In general, a solution is made comprising the monomers and the functional or the active ingredients which is immiscible with water. Then suspended with agitation in an aqueous phase, usually containing additives such as surfactants, and dispersants to promote suspension. Once the suspension is established with discrete droplets of the desired size, polymerization is effected by activating the monomers either by catalysis, increased temperature or irradiation. As the polymerization process continues, a spherical structure is produced containing thousands of microsphere bunched together like grapes. When the polymerization is complete the solid particles that results from the suspension. The microsphere product can be made using styrene and methylmethacrylate and ethylene glycol dimethacrylate as starting materials.

**Mechanism of action**

The finished product is applied to the skin, the active ingredients that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore disturbing the equilibrium. This will start a flow of the active ingredients from the microsponge particle into the vehicle and, from it to the skin until the vehicle either absorbed or dried. Even microsphere particles retained on the surface of the stratum corneum will continue to release the active ingredients to the skin providing prolonged release over time. If the active ingredients is too soluble in the desired vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release. For the conventional system it is normally recommended to maximize the solubility of the active ingredients in the vehicle.

To avoid undesirable premature leaching of the active ingredients from the microsphere polymer is to formulate the product with some free and some entrapped active ingredients so the vehicle is pre-saturated. The rate of active ingredients release will depend not only on the partition coefficient of the active ingredients between the polymer and the vehicle but also on some parameters that characterize the beads. Examples of these are surface area and primarily, mean pore diameter. Release can be controlled through diffusion or other triggers such as friction, moisture, temperature or pH.

**Marketed products using Microsponge Delivery System**

**Carac cream:**

Carac cream contains 0.5% fluorouracil. With 0.35% being incorporated into a patented porous microsphere methyl methacrylate/glycol dimethacrylate cross-polymer and dimethicone. Carac is a once a day topical prescription product for the treatment of actinic keratoses (AK). Dermik Laboratories, Inc., USA is the manufacturer of this product.

**Lactrex™ 12% Moisturizing Cream:**

Lactrex™ 12% Moisturizing Cream contains 12% lactic acid as the neutral ammonium salt, ammonium lactate. Lactrex™ also contains water and glycerin, a neutral humectant, to soften and help moisturize dry, flaky, cracked skin. SDR Pharmaceuticals, USA is the manufacturer of this product.

**EpiQuin Micro:**

The microsponge system uses microscopic reservoirs that entrap hydroquinone and retinol. The microsponges release these ingredients into the skin throughout the day. This provides the skin with continuous exposure to hydroquinone and retinol over time, which minimize skin irritation. (SkinMedica, Inc.)

**Retin-A Micro:**

Tretinoin (0.1% and 0.04%) has been entrapped in methyl methacrylate/glycol dimethacrylate cross-polymer porous microspheres for topical treatment of acne vulgaris as an aqueous gel. This product is marketed by Ortho-McNeil pharmaceutical, Inc.

**Sportscream RS and XS:**

Topical analgesic, anti-inflammatory and counterirritant actives in a microsponge Delivery System for the treatment of musculoskeletal conditions. Embil Pharmaceutical Co. Ltd. Is the manufacturer of this product.

**Conclusion**

The microsponge delivery system is unique and has brought much useful tool to the skin care field. Microsponge technology was developed in 1980s to fill the void. They are very simple and practical to use because they can be incorporated into conventional dosage form such as creams, gels, and lotions. These products are normally employed by the users to cover wide areas of the skin. By providing a gradual release of the active ingredients to the skin, this technology offers to reducing the possible side effects such as irritation, erythema and over drying. It facilitates the development of novel product forms.

**References**

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