JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

NOVEL POLYMER FOR MICROSPONGE DRUG DELIVERY

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Abstract

Many researches were done on Microsponge drug delivery system (MDDS). This is possible due to easy method of preparation, rapid action, controlled released and ease of delivery. Mainly this system is delivered by topical and oral route. The success of formulation is depends on the selection of polymer and method of preparation which is used for preparation of Microsponge. Now a day's Microsponge drug delivery system is being used in cosmetics, over-the-counter (OTC) skin care, sunscreens and prescription products. This article covers the different polymers used in Microsponge preparation, method of preparation, release mechanism, characterization and evaluation.

Key words- MDDS, polymers, release mechanism, controlled release.

Introduction

The main aim of any drug delivery system is to get fast and desired therapeutic effect of drug. It is possible by Microsponge drug delivery system. Moreover, microsponge is the good carrier for drug delivery due to its spongy and porous surface (Roh et al., 2016; Vikrant and Jessy, 2007; Zhang et al., 2016). Porous nature of Microsponge helps in the controlled release of active ingredients. In polymeric microsponge, drug is suspended or incorporated in to different formulation products like gel, cream, liquid or powder. Scientist

given more emphasis on controlled release, drug targeting, product stability, desired therapeutic action, predictability and reproducible effects.

Polymer plays an important role in release of active ingredients from the microsponge. Here we report the best polymers used in microsponge formulation.

Mechanism of Microsponge

Microsponge having the open structure and not the continues membrane therefore active ingredients can easily move in and out. Active drug present in vehicle will adsorbed from skin. Then microsponge will retained on the surface skin or membrane and releases the drug for prolonged interval of time. Vehicle play a important in mechanism of action, if the active ingradient is soluble in vehicle, then finished product will not able to produce the therapeutic effect in controlled manner. So microsponge with entrapped drug should have minimum solubility in vehicle for excellent therapeutic effect.(Shelke, P.K., et, 2013, Wadhwa, G., 2019)

Release mechanism of microsponge (Rajeshree, M., 2013)

Release of active ingredients from microsponge is depends on following factors -

i. Pressure – for topical preparation of microsponges rubbing or pressure applied can release the drug on the skin.

ii. Solubility- water soluble ingredient, microsponges releases the drug in presence of water.

iii. Change in temperature – if drug incorporated in microsponge is too viscous to flow on the skin, then increase in temperature of the skin increases flow and release rate. for drug release study Franz – diffusion cell is used.

iv. pH dependant systems : by coating of microsponges pH triggered release can be obtained.

Polymers used in preparation of microsponge

Afrasim M et al. (2016) successfully developed Fluconazole topical microsponge formulation which was made up of Eudragit S-100 and showed the extended drug release (85.38% at 8 h) with respect to conventional marketed one.

Mohan K et al (2013), Mupirocin microsponges were prepared using an emulsion solvent diffusion method. FT-IR and SEM was used to study the shape and morphology of microsponges. Mupirocin microsponges were then incorporated into a vanishing cream base for release studies. It was shown that the drug: polymer ratio, stirring rate, volume of external and internal phase influenced the particle size and drug release behavior of microsponges. Cumulative release from microsponge after 8h ranged from 62-95%.

Barde P. (2015), concluded that Eudragit RSPO showed the excellent release of Terbinafine HCl which was dispersed in carbopol 934 gel base and showed extended release up to 12h. formulation showed good stability over the period of three month.

Yadav P. et al (2014) and Ravi R. (2013), prepared Microsponge loaded controlled release formulations using ethyl cellulose. Quasi emulsion solvent diffusion method is used for preparation of microsponge. In- vitro release studies using diffusion cell revealed that the drug release showed excellent release.

Sabyasachi M et al (2011), were prepared xanthan gum-facilitated ethyl cellulose microsponges by the double emulsification technique and further dispersed in a carbopol gel base for controlled delivery of diclofenac

sodium to the skin. The microsponges prepared at the lowest drug/polymer ratio exhibited a comparatively slower drug permeation profile and were hence considered most suitable for controlled drug delivery application. The lowest drug/polymer ratio showed useful for controlled release of diclofenac sodium to the skin.

Netal A et al (2009), developed and evaluated microsponge-based topical delivery system of mupirocin for sustained release and enhanced drug deposition in the skin.. Microsponges was prepared with ethyl cellulose. Mupirocin microsponge in emulgel was able to show a sustained release up to period of 24 h.

Jain and Singh (2009), had concluded that paracetamol loaded eudragit based microsponges were prepared using quasi-emulsion solvent diffusion method. The colon specific formulations were prepared by compression coating of microsponges with pectin: hydroxyl propylmethyl cellulose (HPMC) mixture followed by tableting. The In-vitro dissolution studies were done on all formulations and the results were evaluated kinetically and statically. Mine O et al (2006) concluded that to design novel colon specific drug delivery system containing flurbiprofen (FLB) microsponges. Microsponges containing FLB and Eudragit RS100 were prepared by quasi-emulsion solvent diffusion method. In-vitro studies exhibited that compression coated colon specific tablet formulations started to release the drug at the 8th hour. This study presents a new approach based on microsponges for colon specific drug delivery.

A biodegradable graft material containing collagen microsponge 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 pre-cellularization. Poly (lactic-coglycolic acid) as a biodegradable was used with collagen microsponge to form a vascular patch material. The results showed the formation of an endothelial cell monolayer, a parallel alignment of smooth muscle cells, and reconstructed vessel wall with elastin and collagen fibres. 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. (Emanuele AD, 1995)

The most widely used polymers for the preparation are Eudragit RS-100, Eudragit RS PO, Eudragit S-100, polyactide –co-glycolic acid, polyhydroxyl butyrate, polylactic acid and polydivinyl benzene.

Characterization of Microsponge (Aldawsari H. 2013, Dhanapal R. 2012**)**

1. Physicochemical properties

a) Particle size distribution: Optical microscope or electron microscope can be used for particle size and size distribution. The particle size affects the texture and stability of formulation. Particle size analysis of loaded or unloaded microsponge can be done by using diffractometry or other suitable methods. Effect of particle size on drug release can be obtained by plotting graph particle size against time.

b) Determination of pH: Microsponge containing gel or other topical formulation Ph can be determined by sophisticated Ph meter.

c) Determination of true density: It is measured by using ultra pyanometer under helium gas.

2. Surface Topography of Microsponges: Various techniques can b used such as photon correlation spectroscopy (PCS), SEM, TEM for study of surface topography of microsponges.

3. Determination of Loading Efficiency and Production Yield: The percentage loading efficiency of microsponges is calculated by following formula,

$$\frac{\text{Actual drug content of microsponges}}{\text{Theoretical Drug Content}} \times 100$$

4. Production yield: The production yield of microsponges can be determined by following equation.

$$\text{Production Yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass}} \times 100$$

5. Characterization of Pore Structure: The pore volume and diameter plays important role in releasing amount of active drug. It is also responsible for movement of drug from microsponge to vehicle. Pore surface area, average pore diameter, shape, morphology, bulk, density can b measured by intrusion porosimetry. The pore diameter of microsponge can be measured by Washburn equation,

$$\text{Production Yield } D = \frac{-4\gamma \cos\theta}{P}$$

Where, D is the pore diameter (μm);

γ the surface tension of mercury (485 dyn cm−1);

θ the contact angle (130o);

and P is the pressure (psi).

Total pore area (Atot) is calculated by using equation,

Pore morphology can be characterized from the intrusion–extrusion profiles of mercury in the microsponges.

6. Compatibility studies: The compatibility of active ingredient i.e. drug can be checked by TLC and FT-IR. Polymerization effect on crystallinity is examined by Powder X-ray diffraction (XRD) & DSC.

7. Polymer/monomer composition: Polymer composition study is necessary for calculating the release rate of microsponges. Polymer composition may affect partition coefficient between entrapped drug vehicle and microsponge system, hence influences release rate. It can be studied by plotting cumulative % of drug release against time.

8. Viscoelastic properties: Viscoelastic properties can be altered according to need of final product. As cross linking increases the rate of release decreases.

9. Dissolution tests: For dissolution study of microsponge dissolution test apparatus USP XXIII is used along with modified basket. The dissolution medium is selected according to solubility of active ingredient. The samples withdrawn at suitable intervals where analyzed by suitable analytical techniques.

10. Kinetics of release: For study of drug release mechanism the different mathematical models were used to analyze release data.

FUTURE SCENARIO

MDDS is novel and unique technology to deliver the drug for prolongs action. There is promising scope in various pharmaceutical applications due to their unique properties like elegancy in appearance, performance and pattern of release profile. Also they have good kind of physical, chemical and thermal stability which allows flexibility in manufacturing dosage form. The real future challenge is to prepare safe drug delivery system of drug by using various polymers.

Acknowledgment-

The authors would like to acknowledge Principal of Institute of Pharmaceutical Science and Research, Sardar Patel University, Balaghat (M.P.) for providing necessary research facilities.

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