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REVIEW ARTICLE

A Review on Microspheres Loaded Topical Emul Gel

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ABSTRACT

Topical gels are becoming more popular due to ease of application and better precutaneous absorption. Topical gels are intended for skin application orto certain mucosal surfaces for local action or percutaneous penetration of medicament or for their emollient or protective action. Trans dermal drug delivery systems are a constant source of interest because of the benefits that they afford in overcoming many drawbacks associated with other modes of drug delivery (i.e. oral, intravenous).Microsphere denotes that micrometre in size but the main motto is to deliver the drug and it depends on the routes of administration. Topical delivery of microsphere is one of the most important to deliver the drug into the body. Microsphere can work as a transporter for the drugs in a sustained control release manner. As a result, it clears the potential of the effectiveness of active pharmaceutical ingredients through the barrier of skin by the help of penetration property and vehicle technology of microsphere. In this review, some basic and primitive features of microspheres in the form of topical delivery has been discussed.

Keywords: Topicalgels, Microsphere, surfactant, co-surfactants, penetration.

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1. Introduction

Micro particles, microspheres, and microcapsules are common constituents of multiparticulate drug delivery systems offering numerous advantages based on their structural and functional abilities , and their application is suitable for convenient and tolerable drug administration viaseveralroutes.Dependingontheformulation,theycanbeincorporatedintodifferentpharmaceutical dosage forms such as solids (capsules, tablets, sachets), semisolids (gels, creams, pastes), or liquids (solutions, suspensions, and even parenterals). An advantage of microcarriers over nanoparticles is that they do not traverse into the interstitium over the sizeof 100 nm transported by the lymph, and thus act locally. Possibly toxic substances can becarried encapsulated and liquids can be handled as solids in the form of dried microparticles. In the case of multiparticulates, the dose is distributed in many small separate particles, which carry and liberate a part of the dose, hence the malfunction of an individual subunit does not cause the failure of the whole dosage. Multiparticulate drug delivery systems of ferout standing advantages to experts and patients, such as:

- Choice of dosage form for the desired drug delivery route (peroral tablets, parenteralinjections);
- Modified and targeted (evensite-specific) drug release and delivery;
- moreexpectablepharmacokineticswithreducedintra-orinter-subjectvariability;
- more homogenous distribution in the physiological environment;
- stable fixed-dose combinations of drugs;
- dose titration and less dose-dumping;
- patientcentricitythroughbettercompliance(e.g.,patientswithdysphagia)andadherence;
- individual therapy(e.g., for pediatricorgeriatric population);
- improving stability of the medicinal preparations;
- Isolating the constituents to ensure better compatibility
- Innovativeproductswithaprolongedlifecyclethroughpatentprotection.

Fromtheviewpointoftechnology,microencapsulationprovidesseveraladvantages:microparticles are formulated in order to protect the core from the environment; masking an unpleasant taste; preserving volatiles or the viability of the cells; separating incompatible substances; protecting the body from the side effects; and optimizing, prolonging, or targeting the effect of a drug. The polymerexcipient protects the active pharmaceutical ingredient

(API) from the environment (oxidation, temperature, pH) or the body from the irritative, ormucosa-damaging effect of the drugs ubstance. The lesion (e.g., bisectioning) of the multiparticulate solid dosage form (i.e., micropellets in spansuleorcompressed) affects only a small number of units, thus does not result in a significant change of the blood level. Microspheres can be characterized as matrix systems in which the drug is homogeneously dispersed, either dissolved or homogenously suspended. Microcapsules are heterogenous particles where amembraneshellissurroundingthecoreformingareservoir.1

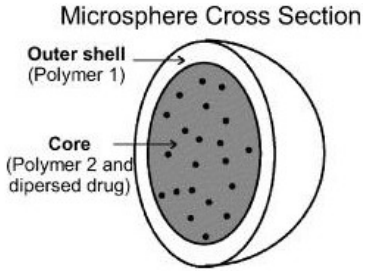

Fig1: Microsphere cross section Materials Used

Micro spheres used usually are polymers. They are classified into two types.

- Synthetic Polymers
- Natural polymers

Synthetic polymers are divided into two types.

- Non-biodegradablepolymers
- Polymethylmethacrylate(PMMA)
- Acrolein
- Glycidylmethacrylate
- Epoxypolymers

Bio degradable polymers

- Lactides, Glycolides & theircopolymers
- Poly alkylcyano Acrylates
- Poly anhydrides

Natural polymers obtained from different sources likeproteins, carbohydrates and chemically modified carbohydrates.

Proteins:

- Albumin
- Gelatin
- Collagen

Carbohydrates:

- Agarose
- Carrageenan
- Chitosan
- Starch

Chemically modified carbohydrates:

- Polydextran
- Polystarch

2. Types of Microsphere

Bioadhesive Microspheres

Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water soluble polymers. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc can be termed as bioadhesion. These kinds of microspheres exhibita prolonged residence time at the siteof application and causes intimate contact with the absorption site and produces better therapeutic action.

Magnetic Microspheres

This kind of delivery system is very much important which localizes the drug to the disease site. In this larger amount of freely circulating drug can be replaced by smaller

amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to amagnetic field from incorporatedmaterialsthatareusedformagneticmicrospheres are chitosan, dextran etc. The different types are therapeutic magnetic microspheres and diagnostic microspheres.

Therapeutic Magnetic Microspheres:

It is used to deliver chemotherapeutic agent to liver tumor. Drugs like proteins and peptides can also be targeted through this system.

Diagnostic Microspheres:

It can be used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominal structures by forming nano size particles supramagnetic iron oxides.

Floating microspheres

In floating types the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gastric content and increases gastric residence and increases fluctuation in plasma concentration. Moreover it also reduces chances of striking and dose dumping. One another way it produces prolonged therapeutic effect and therefore reduces dosing frequencies.

Polymeric Microspheres

The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and synthetic polymericmicrospheres.

Biodegradable Polymeric Microspheres:

Natural polymers such as starch are used with the conceptthatthey are biodegradable, biocompatible, and also bioadhesive in nature. Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is controlled by concentration of polymer and the release pattern in a sustained manner. The main drawback is in clinical use drug loading efficiency of biodegradable microspheres is complex and is difficult to control the drug release.

Synthetic Polymeric Microspheres:

The interest of synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulk in gagent, fillers, embolic particles drug delivery vehicles etc and proved to be safe and biocompatible. But the main disadvantage of these kinds of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism and furtherorgandamage.2

Advantages of microspheres:

- Particle size reduction for enhancing solubility of the poorly soluble drug.
- Provide constant and prolonged therapeutic effect.
- Provide constant drug concentration in blood thereby increasing patent compliance,
- Decrease dose and toxicity.
- Protect the drug from enzymatic and photolytic cleavage hence found to be best for drug delivery of protein.
- Reduce the dosing frequency and thereby improve the patient compliance
- Betterdrugutilizationwillimprovethebioavailability andreducetheincidenceorintensityofadverseeffects.
- Microspheremorphologyallowsacontrollablevariability indegradationanddrugrelease.
- Convert liquid to solid form & to mask the bitter taste.
- Protects the GIT from irritant effects of the drug.

Biodegradable microspheres have the advantage over large polymer implants in that they do notrequire surgical procedures for implantationandremoval.

Controlled release delivery biodegradable microspheres are used to control drug release rates thereby decreasing toxic side effects, and eliminating the inconvenience of repeatedinjections.

Limitation:

- Someofthedisadvantageswerefound to beasfollows
- Thecostsofthematerialsandprocessingofthecontrolledreleasepreparation,aresubstantiallyhigherthanthoseofstandardformulations.
- Thefateofpolymermatrixanditseffectontheenvironment.
- Thefateofpolymeradditivessuchasplasticizers,stabilizers, antioxidants and fillers.
- Reproducibility is less.
- Processconditionslikechangeintemperature,pH,solventaddition, and evaporation/agitation mayinfluencethe stabilityofcore particlestobe encapsulated.

Theenvironmentalimpactofthedegradationproductsofthepolymermatrixproducedinresponsetoheat,hydrolysis,oxidation,solarradiationorbiologicalagents.3MethodsofPreparation:Differenttechniqueshavebeentriedfortheformulationofmicrospheresusing different polymers. Some of these are discussed below:

Single Emulsion Solvent Evaporation Technique:

This method involves the dissolution of polymers in an organic solvent followed by emulsification in an aqueous phase containing emulsifying agent. The o/w emulsion thus formed is stirred for several hours under ambient conditions to allow evaporation of solvent, which is then filtered, rinsed and dried in desiccators.

Double Emulsification Technique:

Double emulsion technique involves the preparation of double emulsion either w/o/wor o/w/o. The aqueous drug solution is dispersed in a lipophilic organic continuous phase. The continuous phase that consists of polymer solution eventually encapsulates drug contained in dispersed aqueous phase to form primary emulsion. The pre-formed emulsion is subjected to homogenization or sonication before addition to aqueous solution of poly vinyl alcohol (PVA) to form primary emulsion.

Spray Drying Method:

Both drug and polymers are dissolved in suitable solvent to form solution which is subjected to spray through nozzle in a spray drierunder different experimental conditions.

Spray Congealing:
Drug is dissolved into melt of lipophilic polymer material to form hot mixture and allowed to atomize with pneumatic nozzle into a vessel that is stored in a carbondioxideicebath.Fabricatedmicroparticlesaredriedunde rvacuumatroomtemperature form anyhours.

Melt Dispersion Technique:
Hot mixture of drug and polymer is emulsified in to an aqueous surfactant solution that has been heated above polymer melting point to form emulsion which is finally allowed to cool in an ice bath.

Coacervation Phase Separation Method:
Coacervation is the separation of macromolecular solution into two immiscible liquid phases out of which one is dense coacervate phase while another is dilute equilibrium phase.

Chemical and Thermal Cross–linking Method:
Aqueous solution of natural polymer containing drug to be incorporated is dispersed in organic phase to form w/o emulsion followed by solidification either by thermalcrosslinkingoradditionofchemicalcrosslinkingagents uchasglutaraldehyde.

Ionic Gelation Method:
In this method, a hydrophilic polymer is complexed with a multivalent cationic (e.g. calcium chloride) orpolyanionic (e.g. sodium tripolyphosphate) to formhighlyviscous gel particles. An opalescent suspension is obtained. Then the suspension is centrifuged to obtain microspheres. Microspheres are freezed ried followed by lyophilization for 24 hours. The resulting microspheres are formed due to electrostaticinteractionsbetweenpositivelychargedgroupand negativelychargedanion.4

3. Topical drug delivery system

Topical drug delivery system is the dosage form which is administered on the skin and other routes of drug delivery get failed or for skin disorders. The topical drug delivery system hasthe advantage of negotiating the first pass metabolism. It also helps to avoid the risk and inconvenience of i.v route therapy. Topical formulations are prepared in different consistency such as solid, semisolid, and liquid. The topical delivery system is failed in the administration of hydrophobic drug. In each formulation with the active ingredients many excipients are used. Sometimes more than one formulation can be combined to enhance the drug delivery; emulgel is such type of combination. It is the combination of emulsion and gel. Emulgel is prepared both in oil- in- water and water- in oil type emulsion mixed with gel. Oil- in- watertypeis used for lipophilic drugs and water- in- oil type is used for hydrophobicdrugs' delivery. The emulgel have many advantages likethixotropic, greaseless, easilyspreadable, easily removable, emollient, non-staining, bio-friendly, pleasing appearance, transparent and cosmetically acceptable, which also have a good skin penetration and long shelf- life .The emulsion and gel preparations have their own properties. But the gels show some limitations as hydrophobic drug delivery. This limitation is overcoming by emulgel. By the use of gellingagent classical emulsion can be converted into emulgel.

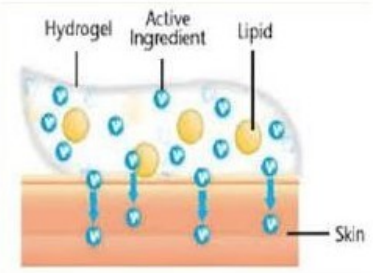

Fig 2: Emulgelstructure Advantages of emulgel

- Incorporationofhydrophobicdrugs
- Betterloadingcapacity
- Betterstability
- Controlledrelease
- No intensivesonication
- Avoidingfirstpassmetabolism
- Avoidinggastrointestinalincompatibility
- Moreselectiveforaspecificsite
- Improvedpatientcompliance
- Convenientandeasytoapply

Disadvantages of emulgel
- Skinirritationoncontactdermatitis
- Thepossibilityofallergenicreactions
- The poorpermeabilityofsome drugs throughtheskin
- Drugsoflargeparticlesizearenoteasyto absorbthroughtheskin
- Theoccurrenceofthebubbleduringformulationofem ulgel

Formulation of Emulgel
Forthepreparationofemulgelsomeconstituentsareusedincludi ngdrug, which are:

Vehicle
- Vehicle should follow the ideal characters given in the Pharmacopeias
- Aqueousmaterial
- The aqueous phases used are water, alcohol, etc.

Oil
- Oilsareusedforpreparationofemulsion.Mineraloilsa ndparaffinareusedeitheralone orincombination.
- Emulsifiers
- Emulsifiersusedforpreparationofemulsion.Someex amplesarespan80, tween 80, stearic acid, sodium stearate.

Gelling agents
- Gellingagentsare used for preparegels, which enhanceconsistency of preparation.
- Penetration enhancers
- Penetrationenhancershelptoabsorbdrugto theskin
- pHadjustingagent5

Microspherebasedgel
Microspheres are small spherical particles, with diameters in the micrometer range (typically1μmto1000μm). Microspheresaresometimesreferredtoasmicroparticles.Them icrospheres is free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature. There are two types of microspheres;
- Microcapsules

- Micromatrices

In microcapsules entrapped substance is distinctly surrounded by distinct capsule wall andinmicromatricesentrappedsubstanceisdispersingthrough outthemicrospheresmatrix.Solidbiodegradable microspheres incorporating a drug dispersed or dissolved through particlematrixhavethepotentialforthecontrolledreleaseofdrug Theyaremadefrompolymeric, waxy, or other protective materials (i.e.Biodegradable synthetic polymers and modified natural products).

Advantages

- Microspheresprovideconstantandprolongedtherapeuticeffect
- Reducesthedosingfrequencyandtherebyimprovethepatientcompliance.
- Theycouldbeinjected intothebodydueto the sphericalshapeandsmallersize.
- Betterdrugutilizationwillimprovethebioavailability andreducetheincidenceorintensityofadverseeffects.
- Microspheremorphologyallowsacontrollablevariability indegradationanddrugrelease.
- **Disadvantages**
- Themodifiedreleasefromtheformulations.
- Thereleaserateofthecontrolledreleasedosageformmayvaryfromavarietyoffactorslikefoodandtherateoftransitthoughgut.
- Differencesinthereleaseratefromonedosetoanother.
- Controlled release formulations generally contain a higher drug load and thus any lossof integrity of the release characteristics of the dosage form may lead to potentialtoxicity.
- Dosageformsofthiskindshouldnotbecrushedorchewed.

Evaluation parameters

- Particlesizeandshape
- Entrapmentefficiency
- Densitydetermination
- Isoelectricpoint
- SwellingIndex
- Angle ofcontact
- Invitrostudy6

Encapsulation of microsphere

Microencapsulationisaprocessbywhichverythincoatingsofinertnaturalorsynthetic poly mericmaterials are deposited around micronized particles of solids or droplets of liquids. Products thus formed are known as micro particles, coveringtwotypesofforms: microcapsules, micrometric reservoir systems, microspheres, and micrometric matrix systems (Figure 1). These systems consist of two major parts. The inner part is the core material containing one or more active ingredients. These active ingredients may be solids, liquids, orgases. The outer partisthecoatingmaterialthatisusually of ahighmolecular weight polymer or a combination of such polymers. The coating material can be chosen from a variety of natural and synthetic polymers and must be nonreactive to the corematerial, preferably biodegradable, and nontoxic. Other components, such as plasticizers and surfactants, may also be added.

4. Conclusion

Topicaldeliveryofmicrosphereshowsanimpactfulfutureinvariouspharmaceuticalapplicationsinthecomingyearsas they have unique properties like enhanced product performance and elegancy, extended-release, reduced irritation, improved thermal,physical, and chemical stability so flexible to develop novel product forms. Not only it isusing in facial moisturizer, sunscreen type cosmetic products but also it is using in anti-inflammatory,anti-fungal,anti-dandruff,etc.Thevarioustypesofworksaregoingonabout it in the research area and they're having lots of hope to overcome various challengesandwewillgotowards thelight.7

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