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Nanocomposite Hydrogel: A Novel Drug Delivery System for Topical Application

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ABSTRACT

Nanocomposite hydrogel as an onychomycosis treatment provides a barrier that effectively prevents the fungal infection of the nail as well as the nail bed and further progression of infection to deeper tissues and cuticles. The two different drugs encapsulated within the nanoparticle and also hydrogel increases the drug concentration locally and decreases systemic drug concentration and hydrogel combine the feature of moist onychomycosis with good fluid absorption. And act as a barrier against fungal cell growth, it is easy to handle, so it improves clinical efficacy and also justifies patient compliance. In addition, by nature of transparency, hydrogels promote monitoring of onychomycosis treatment. This review highlights the current status of nanocomposite hydrogels and will focus on novel strategies for the treatment of onychomycosis.

INTRODUCTION

Nanocomposite hydrogel have an advantage over other traditional formulations such as creams, ointment and gels. They increase the skin retention of the drug, at the same time a high concentration in the skin and cuticle slow down the systemic absorption of drugs. Nanocomposite hydrogel play various unique properties such as high, sustained and controlled release of drug loading capacity increase the duration of action for the targeted site. [1]

The structure and concentration of the lipid in the nanoparticle are playing an important role in the rheological properties of hydrogels involved in nanoparticle.

In the case of drugs used in hydrophilic formulation, drug release is not affected by the amount of lipid loaded into the hydrogel, but can be influenced by the amount of rigid membrane which is used in the nanoparticle. In the case of drug used in lipophilic formulation, the concentration of the lipid added to the nanoparticle in the hydrogel has a strong effect on drug release and membraneHardness is not significant. The release of drug is controlled by the degradation of the hydrogel matrix and the controlled release rate of the drug can be obtained by designing hydrogel degradation.[2]Nanoparticles and hydrogels are very effective for topical application. Formulating a new formulation of nanocomposite hydrogel is one of the most difficult tasks for the pharmaceutical sciences. In this article we are focus on nanoparticle and hydrogel for the effective use of topical application.

NANOPARTICLES APPROACH FOR DRUG DELIVERY SYSTEM

Nanoparticles are particles of substance with a size of 1-100nm. The drug is trapped, dissolved, or joined to the nanoparticle matrix. Different methods of preparation are used to obtain different nanomedicines.e. nanocapsules, nanospheres, nanoparticles, nanoshells, nanorobots, and nanosuspension.[3]The vesicles can be filled with natural components such that the vesicle membrane forms a bipyramidal structure that is similar to the lipid portion of natural cell membranes. The vesicles can be made entirely of artificial components, which have been selected for their superior chemical properties. In addition, the nanoparticle could entrap both hydrophilic and lipophilic.[4]

The physical properties of the nanoparticle, the type of polymer can be changed by changing the composition and the ratio of different proteins, polysaccharides and various synthetic

polymers in nanoparticle formulation, altering the temperature, size and pH sensitivity of vesicles in these nanoparticles characterizations can be performed as shown in Table 1.

Table 1. Various Parameters and characterization methods for Nanocomposite Hydrogel [5]

Parameter	Characterization methods
size distribution and Particle size	Scanning electron microscopy,
Charge determination	Zeta Potentiometer
Surface hydrophobicity	X-ray photoelectron spectroscopy
Carrier-drug interaction	Differential scanning calorimetry
Release Profile	In vitro release characteristics using suitable buffer solutions and sink condition using the dialysis bag technique.
Rheological analysis	Viscosity studies

Nanoparticles as Topical Drug Delivery Systems

Nanoparticle can produce various actions after topical application. They provide a localized effect to the skin, cuticle as well as targeted delivery and can improve drug deposition within the skin at the site of action, reduce systemic absorption and also reducing side effects. These function and mechanisms of release drug of the nanoparticle are briefly described.

Mechanism of Action of Nanoparticles as Skin Drug Delivery Systems

El Maghraby et al. 2008, de Leeuw et al. 2009, [6, 7] suggested various other mechanisms for skin drug delivery of nanoparticle.

These include:

(a) Intact vesicular skin transit

(b) Lateral proliferation of vesicles in the SC

(c) Transappendageal pathway

Lipid Nanoparticle are also known as SLN (solid lipid nanoparticles) and NLC (nanostructure lipid carriers). And these nanoparticles are widely used for cosmetic and dermatological use. Due to lipid vesicles, they project an easily encapsulated drug molecule. [8]

NOVEL DRUG DELIVERY STRATEGIES FOR ONYCHOMYCOSIS TREATMENT

This review will focus on such novel strategies for the treatment of onychomycosis. The probability of cases of onychomycosis is very high. An extremely long period of oral medical treatment causes hepatotoxicity and the risk of suffering drug-drug interactions and topical therapy. [9]

Nanocomposite hydrogel maintain site-specific drug release for long-term production of therapeutics drug concentration.[10]

ADVANTAGES OF NANOPARTICLES FOR TOPICAL APPLICATION[11-15]

- The drug encapsulated in nanoparticle lipid vesicles which enhances pharmacokinetic and pharmacodynamics properties.
- Antifungal drug were incorporated into the nanoparticle for better tolerability and enhanced therapeutic effect.
- Nanoparticle target are specific and enhanced efficacy.
- Antifungal drug loaded nanoparticles show low toxicity.

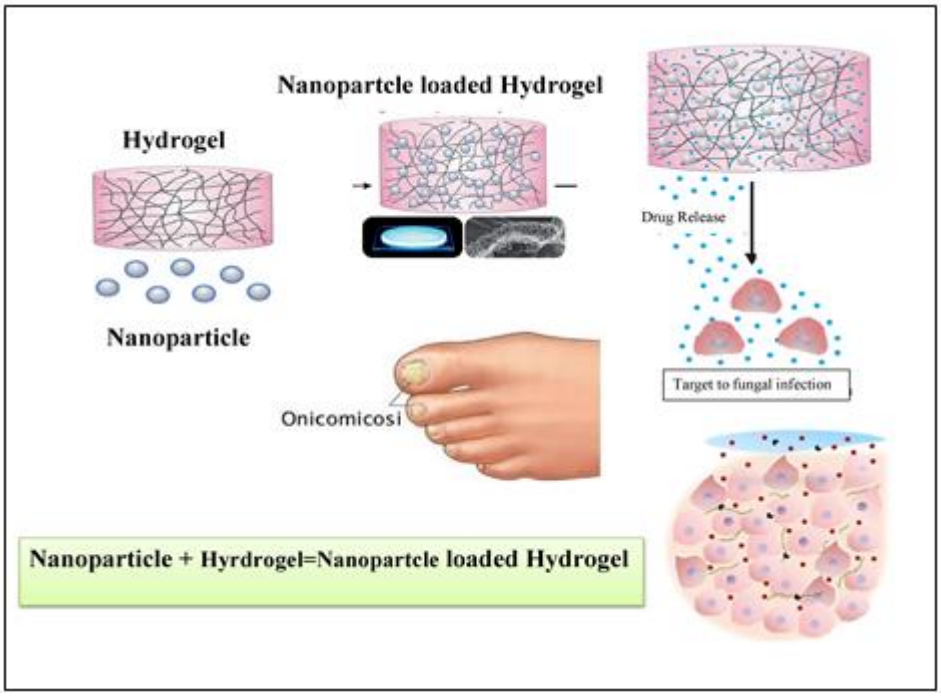

Fig. 1 Nanocomposite Hydrogel

HYDROGELS [16-17]

The hydrogel is a three-dimensional, cross-linked hydrophilic polymeric network. They are capable are assimilating large amount of water or biological fluids and tissues. Hydrogels prepared by both natural and synthetic polymers. Several techniques have been reported for the synthesis of crosslinking of hydrogel co-monomer like co-polymerization using multidimensional which act as crosslinking agents. [18]

CLASSIFICATION OF HYDROGELS

Chemically Cross-linked Hydrogels: They are termed as chemical gels. These hydrogels networks are covalent cross-linked type. When these hydrogelsare exposed to water, they begin to swell and disintegrate from their cross-linked structure. [19-20]

Physically Cross-linked Hydrogels: They are termed as reversible or physical gels;they have polymer chain entanglement i.e. transient junction, ionic interactions, hydrogen bonds or hydrophobic interactions. [21]

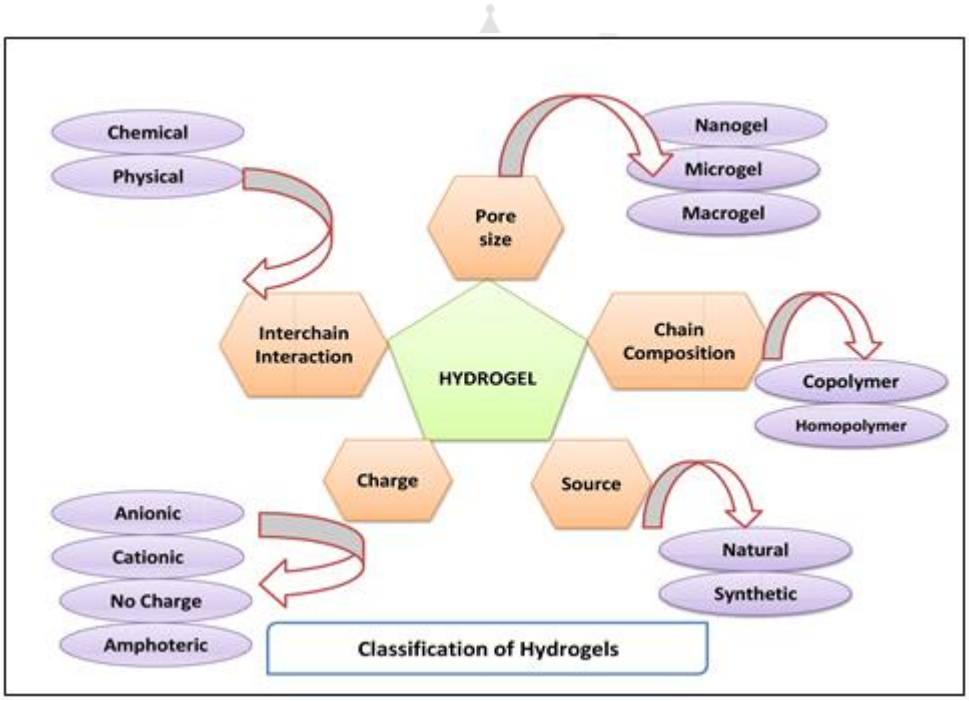

Fig. 2 Classification of Hydrogels

PREPARATION OF HYDROGELS

The hydrogels are the polymeric network. They can be prepared from natural polymers or synthetic polymers. Synthetic polymers are chemically stronger than natural polymers due to

being hydrophobic. The degradation rate is slow due to their mechanical strength. Their mechanical strength increases durability. Various preparation techniques adopted are cross-linking, Copolymerization, Radiation cross-linking, and nanocomposite hydrogels of polymers.

Cross-linking of polymers:

In this method chemically cross-linked gels are prepared by radical polymerization and monomer used, or branched homopolymers, or copolymers are used in the presence of crosslinking agent.

Copolymerization: Many hydrogels are produced by copolymerization reaction.For example,poly (hydroxyethyl methacrylate), (poly HEMA, PHEMA) is one of the most important hydrogel biomaterials.[22]

Radiation cross-linking: High energy crosslinking from radiation used for polymerization of unsaturated compounds, such as gamma and electron beam radiation. For example, vinyl groups can be converted into hydrogel using high energy radiation. [23]

Nanocomposite Hydrogels:NC gel is prepared using polymers such as synthetic polymers and natural polymers i.e.Poly (vinylpyrrolidone), alginate, chitosan, hyaluronic acid. These polymers are used to design nanocomposite network.[24]

ADVANTAGES OF HYDROGEL FOR TOPICAL APPLICATION

- Hydrogel is more elastic and stronger.
- Incompatibility in GIT will be avoided.
- Low doses also provide effectiveness and continuous drug input.
- Convenience in handling.
- Good tissue compatibility.

APPLICATIONS OF HYDROGELS IN TOPICAL APPLICATION

Hydrogel were used in the treatment of topical application. Hydrogel also promote tissue repair or regeneration and prevent infections. Various skin diseases, skin disinfection are treated for topical use of dermatological drugs.

Hydrogels have found wide applications in drug delivery systems, Perfume delivery, Cosmetics, dental applications, wound healing applications, Hydrogel Implants, Hydrogel Inserts, Contact Lenses, Rectal delivery, Ocular delivery, Transdermal delivery, Subcutaneous delivery.

THE FUTURE PERSPECTIVE OF NANOCOMPOSITE HYDROGELS

The Recent trend of the development of nanocomposite hydrogels applied to drug delivery has been focused on their characterization, immediate relive pain. Thetreatment provides a barrier that effectively prevents the fungal infection of the nail as well as nail bed and prevents the infection from moving into deeper tissues and thecuticle. Also improve the distribution of sensitive molecule such as proteins, nucleic acids, antibodies and hydrophobic molecule. Nanocomposite hydrogel topical formulation of active ingredient in skin enhancing penetration. Promising new methods in the drug delivery of candidiasis, antibacterial, osteoinduction, anti-inflammatory, Wound Dressing (as shown in Table 2).

Table 2: Various Therapeutic Applications of Nanocomposite Hydrogels

Application	Materials	Drug Candidate	Purpose
Topical delivery	Tristearin, Soya Lecithin,Tween80	Miconazole nitrate	Antifungal agent-Used in the treatment of candidiasis.[25]
Topical delivery	Polyvinyl alcohol, Chitosan, ZnO, MTT (3-[4,5-dimethylthiazol-2-yi]-2,5-diphenyltetrazolium bromide)	Heparin	Antibacterial properties-Used in the treatment of wounds dressings. [26]
Bone graft	Polyethylene glycol, methyl ether methacrylate, silver nitrate and citric acid, 2-dimethylamino ethyl Methacrylate	Methacrylate	Used in the treatment of osteoinduction.[27]

Topical delivery	soybean lecithin, tristearin glyceride, triethanolamine, poloxamer 188	Triptolide	Anti-Inflammatory [28]
Wound Dressing	Acrylamide, Poly (vinyl sulfonic acid) ammonium persulfate, silver nitrate	Curcumin	Wound Dressing and Antibacterial Application [29]

CONCLUSION:

Nanocomposite as topical drug delivery shows permeation and enhanced drug delivery. With the help of nanocomposite drug release in a controlled mode. This property of nanocomposite is useful for the treatment of topical fungal infection. By incorporating of nanocomposite into hydrogels, the versatility can also be interrupting. Carrier's hydrogel can be used for nanoparticle-containing antifungal drugs. Both of these formulations are widely used for controlled drug delivery. Drug molecules are also incorporated into the nanoparticle along the hydrogel network, and this network is released by the diffusion process by the swelling nature and as well as chemically mechanism.

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