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Review Article

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A SCIENTIFIC REVIEW ON NANOGEL FOR THE TREATMENT OF INFLAMMATION

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ABSTRACT

Nanogels based materials have high drug loading capacity, biocompatibility, and biodegradability which are the key points to design a drug delivery system effectively. The pursuit of this review article is to concisely describe the recent development of Nanogel drug delivery system in terms of drug loading and swelling of drug from Nanogels. Nanogels have enabled enlargement of functionalized nanoparticles, which act as a drug carriers that can be loaded with drugs and other active material to be released in a controlled manner at specific site. Nanogel may be ready by many strategies just like the particle gelation, Inverse mini emulsion, Dispersion, Chemical cross linking, fabrication of biopolymers and so on. It can be characterized by SEM, DSC, FTIR, Drug content, Particle size, Zeta potential and drug efficiency. Further, it can be evaluated by in vitro drug release and in vivo study in suitable animal modelling. In this review article, we have focused on basic methodology of Nanogels, evaluation terms, their application in industries.

KEYWORDS: Nanogel, advantages, disadvantages, release mechanism, classification, methods, evaluations, applications.

INTRODUCTION

Nanogels are innovative drug delivery system that can play an integral part in pointing out many issues related to old and modern courses of treatment such as nonspecific effects and poor stability. Biomedical and pharmaceutical applications of Nanogels have been explored for tissue regeneration, wound healing, surgical device, implantation, and peroral, rectal, vaginal, ocular, and transdermal drug delivery.

Nanogels are proficiently internalized by the target cells, avoid accumulating in nontarget tissues thereby lower the therapeutic dosage and minimize harmful side effects. Nanogels may be defined as highly cross linked nano-sized hydrogels ranges from 20-200 nm. They can be administered through various routes, including oral, pulmonary, nasal, parenteral, intra-ocular etc. They have a high degree of drug loading capacity and it shows better permeation capabilities due to smaller size. Nanogels are the novel drug delivery systems for both hydrophilic and hydrophobic drugs.[1]

Nanogels may entrap drugs and biological molecules. Therefore, they can be vastly employed in protein and gene delivery. The particle size and surface properties can be manipulated to avoid rapid clearance by Phagocytic cells, allowing both passive and active drug targeting. Controlled and sustained drug release at the target site, improving the therapeutic efficacy and reducing side effects.[2]

The characteristics of Nanogels" is derived from their parent "hydrogels." The best options of Nanogels be their optimum size (ranging from ten to two hundred nm), tunable degradation, high practicality, bio-compatibility glorious drug loading capability, sensible unharness characteristics, high binary compound dispersion, prolonged blood circulation, and immunocompatibility.[3]

Features of Nanogel

1. **Size control:** Nanogel size and surface properties are frequently with chemicals obsessed to limit the rate of clearance by somatic cells furthermore to modify either passive or active cell targeting. Nanogels should be sufficiently small to traverse capillaries and penetrate tissues through either paracellular or Tran's cellular pathways.
2. **High encapsulation stability:** Drug molecules loaded into the Nanogel ought to be maintained and not to be transported out or leak untimely whereas current so as to supply most therapeutic effects and minimum toxicity or facet effects.
3. **Controlled and sustained drugged release**: Drug transport ought to occur at the target website, thereby providing each therapeutic effectively and reduced facet effects. Drug loading ought to be sufficiently high to attain therapeutic goals.
4. **Targeting:** Site specific delivery of Nanogels carriers are often achieved via either coupling to their surface affinity ligands binding to focus on

determinants of victimization responsiveness to native factors as on top of, or via "passive" targeting approaches together with extrapolation within the pathological sites and retention within the microvasculature.

5. **Low toxicity:** The Nanogels themselves ought to be extremely biocompatible and free from toxicity, and may be perishable with non-toxic degradation merchandise that area unit pronto cleared from the body.[4]

Ideal characteristics of drug for Nanogel

- The drug ought to be of low weight unit. Wt. (<500 da)
- The drug ought to be compatible with the polymers wont to prepare Nanogels
- The charge density on a drug ought to below
- Hydrophobic or hydrophilic drugs will be incorporated in Nanogel.

Advantages of Nanogel

- Nanogels have high bio-compatibility and biodegradability.
- Each deliquescent and hydrophobic medication will be developed in Nanogels formulation.[5]
- Macro molecular medical specialty like DNA, siRNA, amide & proteins will be incorporated into nanogel.[6]
- Good for specific target and transport characteristics.[7]
- Reticuloendothelial area unit invasion in nature which might be prevented by Nanogel.
- Target or site-specific delivery to be achieved.
- Helps in enhancing oral and brain bio-availability of low relative molecular mass medication and biomacromolecules.[8]

Disadvantages of Nanogel

- Surface-active agent & Monomers will impart toxicity to the tissues
- Polymerization reactions for the preparation of the Nanogels area unit terribly harsh.[9]

RELEASE MECHANISM OF DRUG FROM NANOGEL

The discharge of the drug from Nanogels within the site of the action happens by following ways that.[10]

- Easy diffusion of the drug from the Nanogel.
- Degradation of Nanogel.
- pH stimulant.
- Ionic exchange with the surroundings.
- External energy supply.

It has been shown in fig.5

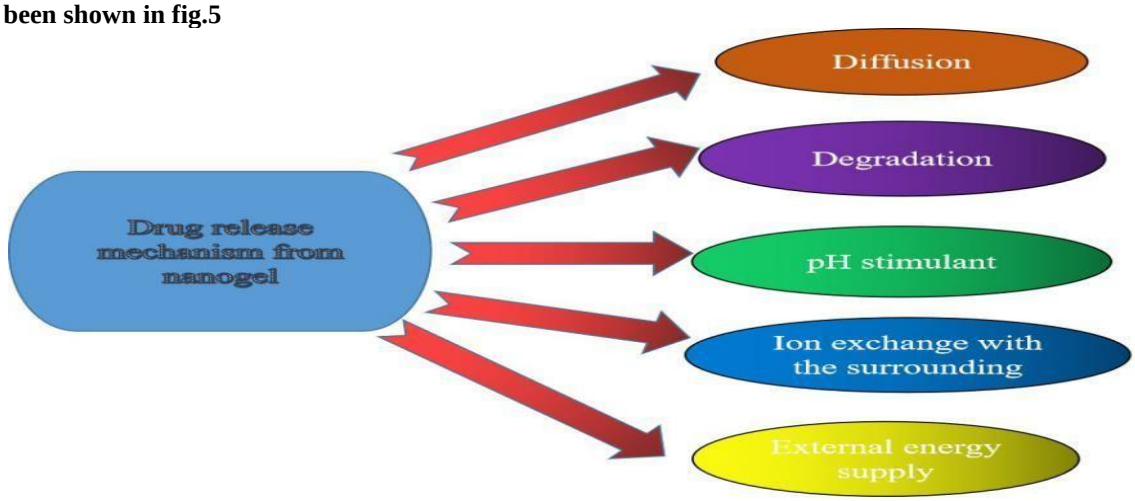

Figure 5: Drug release mechanism from Nanogel.

CLASSIFICATION OF NANOGEL

Basically, Nanogels are classified into three types (fig.6)

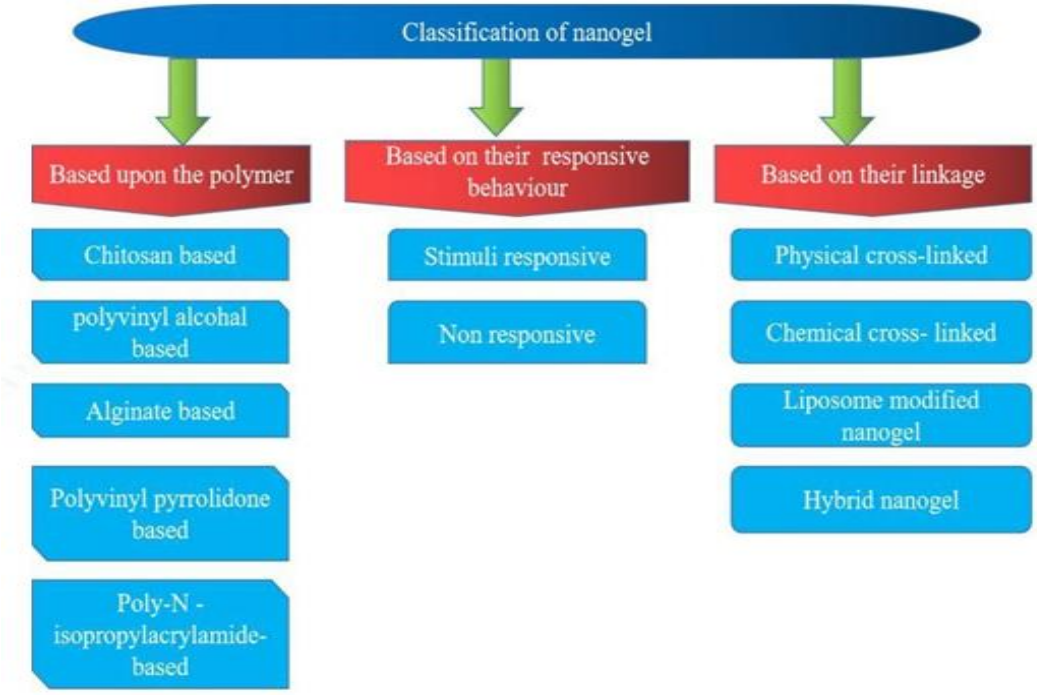

Figure 6: Classification of Nanogel.

Based upon the polymers

❖ **Chitosan-based Nanogel**

Chitosan, α (1-4)-2 amino-2-deoxy β-D-glucan, is a polyose which is a DE acetylated form of chitin and present in crustacean shells.[11] The polymer chitosan having a positive charge and easily hydro-soluble in the nature of these properties permit interacting with negatively charged polymers and have contact with polyanion in an aqueous state of affairs.[12]

❖ **Poly (vinyl alcohol) - based Nanogel**

PVA plays an essential role in Nanogel studies. It has the cross-linking characteristics that are administrated using physical and chemical ways. Physical ways like e.g.: (freezing/ thawing) ways and chemical ways like e.g.: cross- linking agents, ray, γ- irradiation). Even though the cross- linking method is challenging but it is helpful for various applications in medical and pharmaceuticals fields.[13] Biodegradable polymers having short polylactone chains grafted to PVA or amendment sulfobutyl- PVA was ready and used as a completely unique category of water- soluble comb-like polymers.[14]

❖ **Alginate - based Nanogel**

The prepared alginate nanoparticles {metal alginate drug carrier} with a wide range of particle sizes (250 – 850 nm), by using the sodium alginate and calcium chloride and resulted by polylysine. The anti-tubercular chemotherapy increases the bioavailability by using the alginate nanoparticles and of all drug encapsulated in alginate nanoparticles were significantly higher than those with free drug.[15]

❖ **Poly (vinyl pyrrolidine)-based Nanogel**

Polyvinyl based mostly colloidal gel nanoparticle with final length is a smaller amount than a hundred nm, using the aqueous centre was reverse micellar depicted by Baharali.[16] These reverse micellar are highly monodispersed, the droplet sizes can be well- controlled and size can be softened by controlling the size of the reverse micellar droplets.[17]

❖ **Poly-N-Isopropyl acrylamide-based Nanogel**

Dextran containing hydrogel has been developed by G. Huang.[18] In this study, covalent cross-linking is formed by the PNIPAM -co-allylamine nanoparticles network. Thermo responsive core-shell PNIPAM nanoparticles via seeding and feeding precipitation polymerization are described by Gan & Lyon.[19]

2. Based on their responsive behaviour

❖ **Stimuli-responsive**

In this form of Nanogel, it may be swelling or Deswell. It depends upon exposure to environmental changes like temperatures, PH, magnetic field and ionic strength. The Nanogels which have the multi-responsive character have more than one environmental stimulus.

❖ **Non-responsive**

These have a characteristic like absorbing water and swelling.[20]

3. Based on their linkages present in the network chains

Based on their linkage it has a capacity like to form a gel structure, polymeric gels (including Nanogel) and these divided as follows.

❖ **Physical Cross-linked Gels**

These types of gels are also known as pseudo gels. They are formed by weaker linkages through Vander-Waal forces, hydrogen bonding, hydrophobic or electron static interactions.

❖ **b) Chemically cross-linked Gels**

These types of gels are permanently linkages through the covalent bonds. It has properties like a cross-linked gel system and depends on the functional group present in the gel system. By the polymerization of vinyl monomers in the presence of multifunctional cross-linkers the deliquescent polymers and deliquescent-hydrophobic copolymers are obtained.

❖ **c) Liposome Modified Nanogels**

When liposomes are mixed with the succinylated poly (glycidol) s; these liposomes can be expeditiously delivered calcein to the cytoplasm by nuclear reaction to the chain below pH 5.5. Liposomes which area unit the Thermo and pH-responsive Nanogel like as poly (N isopropyl acrylamide) area unit being examine for Trans dermic drug delivery.

❖ **d) Hybrid Nanogels**

When the Nanogel particles dispersed in organic and inorganic matrices are thought of as hybrid Nanogels. These sorts of Nanogel formation take place in equal degree watery medium by self-assembly or accumulation of chemical compound amphiphiles, like pullullan-PNIPAM, hydrophobic polyoside, and hydrophobic pullan.[21] These forms of hybrid Nanogel are shaped physical cross-linking and capable to deliver the hypoglycaemic agent and anti-cancer medication additional efficaciously.[22]

METHODS FOR NANOGEL PREPARATION

By the employment of Isostatic ultra-high pressure (IUHP), cross, water, and important conditions of drying, nucleophilic substitution reaction, gelling agents and irradiation, and freeze-thawing, we will additionally prepare Nanogel.

❖ **Heterogeneous atom polymerization**

Various heterogeneous chemical action reactions of deliquescent or soluble monomers inside the presence of either dysfunctional or multifunctional cross linkers are chiefly in use to arrange the well-defined artificial micro gels. They embody precipitation, inverse (mini) emulsion, inverse small emulsion, associate degree dispersion chemical {process chemical change chemical action} utilizing an uncontrolled atom chemical action process.[23]

❖ **Inverse (mini) emulsion method**

A W/O emulsion is created from a combination consisting of binary compound biopolymer droplets and never-ending lipid portion exploitation either a homogenizer or a high- speed mechanical stirrer. Resulting binary compound droplets of biopolymers area unit then cross-linked with applicable cross-linking agents. Then cross-linked micro gel particles area unit primed as dispersion in organic solvents. Sublimate by precipitation, natural process, laundry with organic solvents like isopropyl alcohol, and dehydration.

❖ **W/O heterogeneous emulsion method**

W/O emulsion strategies involve typically two steps: emulsification of binary compound droplets of water-soluble biopolymers in continuous oil section with associate degree aid of oil-soluble surfactants and cross-linking of biopolymers with soluble cross linkers. The water-in-oil emulsion method has recently been custom-made to organize γ-cyclodextrin (γCD) or hydroxypropyl-β- cyclodextrin (HPβCD) Nanogels inside which the crosslinking takes place at the same time with an associate degree in emulsification/solvent evaporation method.[24]

Precipitation polymerization

Precipitation chemical process involves the formation of a uniform mixture at its initial stage, and therefore, the incidence of initiation and chemical process within the homogeneous solution. Because the designed polymers don't seem to be sellable however soluble within the medium, employment of a cross-linker is critical to cross-link chemical compound chains for the isolation of particles. As a result, the ensuing cross-linked particles typically have equal degree casual form with high polydispersity (PDI).[25]

The preparation of micro gels and Nanogels supported PNIPAM and its derivatives by precipitation chemical process in water has been extensively explored for medical speciality applications.

Inverse micro emulsion polymerization

While inverse (mini) emulsion chemical process forms kinetically stable macro emulsions at, below, or close to the essential micellar concentration (CMC), inverse micro emulsion chemical process produces thermo-dynamically stable micro emulsions upon any addition of surfactant higher than the essential threshold. Poly (vinylpyrrolidone)-based Nanogels incorporated with Dex as a soluble organic compound macromolecule drug were ready[26] cationic Nanogels of poly (HEA-co-AETMAC) were ready within the presence of olio(ethylene glycol) dimethacrylate (OEGDMA) as a cross-linker.

Heterogeneous controlled/ living radical polymerization

C-reactive protein has been explored as a tool for the preparation of well-controlled polymer– protein/peptide

bio conjugates. Varied ways for C-reactive protein are developed; but, the foremost successful techniques embrace atom transfer radical chemical process (ATRP), stable a tom chemical process (SFRP), and reversible addition- fragmentation chain transfer (RAFT) chemical process.

Atom transfer radical polymerization

ATRP is one of the foremost successful C-reactive protein techniques, sanctionative the preparation of a good spectrum of polymers with planned relative molecular mass and comparatively slender relative molecular mass distribution (Mw/Mn < 1.5)41-42. ATRP additionally permits for the preparation of copolymers with completely different chain architectures, like block, random, gradient, comb- shaped, brush, and multimedia star copolymers.[27]

Nanogel synthesis by RAFT chemical process in water

The primary example of nanogel synthesis by direct RAFT chemical process below precipitation/dispersion chemical process condition was reported by AN and co-workers in 2007[28]. Two sorts of poly (N, N′-dimethyl acrylamide) s (PDMAs) bearing a tri-thiocarbonate cluster were first synthesized by RAFT answer chemical process and were afterward used as an each stabilizer and RAFT agents for nanogel synthesis by RAFT precipitation/dispersion chemical process.

Dispersion polymerization

In the method, most ingredients as well as monomers, chemical compound stabilizers and initiators area unit soluble in an organic solvent as a continual section. At the onset, chemical process occur in an extremely jelled reaction mixture; but, the shaped polymers become insoluble within the continuous medium, ultimately resulting in the formation of stable dispersion of chemical compound particles with an aid of mixture stabilizers.

Evaluation and characterization of Nanogels

Total drug content (TDC)

0.5 g of the Nanogel is diluted with a suitable solvent and faltered using a 0.45-µm filter.

The total drug content is determined by UV spectrophotometry, using the formula

$$\text{TDC} = \frac{\text{Total amount of Nanogel} * \text{Amount of drug in 0.5g of Nanogel}}{\text{Amount of Nanogel in grams}}$$

Entrapment efficiency

A small portion of the nanodispersion is centrifuged at 10,000 rpm for 1 h using a micro centrifuge. The supernatant is removed, and the amount of unincorporated drug is measured from the absorbance of the solution using a UV spectrophotometer against a blank/control nanodispersion. The entrapment efficiency is calculated using the equation

$$\text{Entrapment efficiency (\%)} = \frac{\text{Initial weight of drug} - \text{final weight}}{\text{Initial weight}} \times 100$$

Measurement of viscosity

The viscosity of the Nanogel can be determined using a Brookfield DV-III remoter. A sample is placed in a sample holder, and the spindle (number 14) is rotated at 10 rpm for 10 s at 25 °C.

In vitro release of Nanogel

An in vitro release study is performed using a modified Franz diffusion cell. A suitable solvent is used as a release medium (acceptor compartment). A gel sample (1 g) is placed on a cellulose nitrate membrane (0.1 mm pore diameter), which acts as a diffusion barrier (donor compartment). The assembly is water-jacketed and maintained at 32±0.5 °C. Aliquots are withdrawn at different time intervals during a time period of 48 h and are analysed using HPLC.

Water uptake

The amount of aqueous solution in hydrogel particles is determined using a thermal gravimetric analyser (TGA). The weight of the dried hydrogels is determined by soaking them in distilled water and allowing the particles to swell for 3 h. The water uptake is calculated as the difference in weight between the fully hydrated hydrogel (Wh) particles and dried particles (Wd).

Compatibility

The compatibility of a drug and polymer can be determined using FTIR spectroscopy. Spectral analysis of the drug, different polymers, and combinations of the any changes in the chemical composition of the drug after it is combined with polymers.

Transmission electron microscopy and photon correlation spectroscopy

Transmission electron microscopy (TEM) may be used to determine the shape of a Nanogel, and photon correlation spectroscopy using a Malvern Nanosizer ZS may be used to determine the particle size and the distribution profile (polydispersity index, PI) of particles dispersed in a Nanogel.

Sol–gel transition behaviour of Nanogels

The thermo sensitive volume phase transitions of Nanogels can be evaluated by measuring the relative turbidity of aqueous dispersions of the Nanogels at various temperatures using a thermo-regulated UV/VIS spectrometer. The appropriate wavelength of the formulation is selected, and the formulation is maintained at the set temperature for 5 min before each measurement. An appropriate amount of a lyophilized powder of the formulation is weighed and pours into 5-ml plastic bottles along with water to prepare Nanogel dispersions of different concentrations. The formulations are stood overnight and swelling allowed. The ‘vial

inversion with visual inspection' method is used to study the sol–gel transition temperature.[29]

MECHANISM OF DRUG RELEASE FROM NANOGELS

Diffusion

The diffusional release of doxorubicin from stable hydrogel nanoparticles based on pluronic block copolymer (Missirlis et al., 2006). This release mechanism is simple and has been successfully employed in various Nanomedicine, such as polymeric micelles that have already reached a clinical stage.

Nanogel Degradation

The degradation of these Nanogels was shown to trigger the release of encapsulated molecules including Rhoda mine 6G, a fluorescent dye, and Doxorubicin, an anticancer drug, as well as facilitate the removal of empty vehicles. Example: The release of Doxorubicin was significantly increased due to glycol chitosan nanoparticles sensitivity to pH stimuli due to grafting of diethylaminopropyl group. Significant mesh size alteration has been seen in dietylaminoethylmethyacrylate cationic Nanogel for release of medium size molecules by virtue of pH sensitivity.

Displacement by Ions Present in the Environment

There is an increased interest in developing Nanogels that can release biological agents in response to environmental cues at the targeted site of action. For example: disulphide cross-linked POEOMA Nanogels biodegraded into water soluble polymers in the presence of a glutathione tripeptide, which is commonly found in cells. Cell membrane-triggered release of negatively charged drugs from complexes with cationic Nanogels was also proposed to explain cellular accumulation of an NTPs drug delivered with Nanogels.

OTHERS

Photochemical Internalization and Photo isomerisation

Excitation of photosensitizers loaded Nanogels leads to production of singlet oxygen and reactive oxygen species which cause oxidation of cellular compartment walls such as endosomal barrier walls which effects release of therapeutics into cytoplasm. Polyelectrolyte hydrogels that incorporate biological agents via electrostatic bonds allow for release of biological agents in response to environmental changes. For instance, hydrogels of crosslinked PEG and PAA were shown to release an oppositely charged protein upon 1) addition of calcium ions that reacted with carboxylate groups of PAA and displaced the protein or 2) acidification of the media by decreasing pH from 7.4 to 5.5.A similar mechanism was proposed for release of oligonucleotides from PEG-cl-PEI Nanogels. In this case, electrostatically bound oligonucleotides are believed to be displaced by negatively charged cellular components[1].

APPLICATIONS OF NANOGELS

Local Anaesthetics (LA)

The analgesic effect of local anaesthetics is due to the blockage of the nerve impulses in nerve cell membrane by shutting the voltage gated Na+ channels. The manner and the intensity of nerve stimulation as well as its resting membrane potential will determine the degree of numbness induced by a specific concentration of a local anaesthetic. Local anaesthetics are clinically classified into two classes, depending on their chemistry: amino esters and amino amide. Over dosage of local anaesthetics leads to their high toxicity, which has sparked the interest in formulating controlled release drug delivery systems of them. Incorporating local anaesthetics into drug delivery systems like Nanogels can improve their regional administration.

Cancer Treatment

Biodegradable Nanogel prepared by cross linking of polyethylene mine and PEG/pluronic used for 5'-triphosphorylated ribavirin reduced toxicity. Doxorubicin loaded self-organizing Nanogel formulated by acetylated chondroitin sulphate used for cancer treatment. PH responsive doxorubicin uptake accelerated Nanogel containing glycol chitosan, which was grafted with 3-diethylaminopropyl groups. Self-quenching polysaccharide based pullulan folate-pheophorbide used in minimal toxicity of pheophorbide. Cross linked branched network of polyethylene mine and PEG Polyplex Nanogel used for elevated activity and reduced toxicity of fludarabine. Self-assembled Nanogel composed of heparin pluronic used to deliver RNAasenzyme to internalize in cell.

Autoimmune Disease

The treatment of autoimmune disorders is based on the ability of the drug delivery system to selectively disable the immune cells that mediate the autoimmunity response. The incorporation of immunosuppressant drugs into Nanogel delivery systems have been extensively studied for this purpose since Nanogels can improve the immunosuppression effect by targeting the antigen presenting cells that contribute to disease and enabling systemic accumulations of the loaded drug. A Nanogel system of mycophenolic acid complexed with non-methylated β- cyclodextrin was formulated by loading of liposome's with a diacrylate terminated copolymer of poly (lactic acid-co-ethylene glycol) and tested for the treatment of systemic lupus erythematosus, an autoimmune disease. The cross linking between acrylated monomers and the gelation of the particles into a stable mix was achieved by exposing the Nanogel system to ultraviolet radiation.

Neurodegenerative Disease

Currently, neurodegenerative disorders like Alzheimer's & Parkinson's disease have no known cure, therefore, when oligonucleotides showed a potential to be used as a diagnostic or therapeutic tool for these diseases, they became the focus of many studies. So far, the application

of oligonucleotides in the treatment of neurodegenerative disease is significantly hindered by their instability against metabolism, their inability to penetrate the blood brain barrier, and their rapid clearance by renal excretion. To enhance the performance of oligonucleotides, they were incorporated into Nanogel delivery systems. The novel properties of Nanogels allow oligonucleotides to cross the blood brain barrier, thereby aiding their delivery into the central nervous system. A Nanogel of oligonucleotide, which was formulated by cross linking poly (ethylene glycol) and polyethylenimin, was found to have the ability to form a stable aqueous dispersion of polyelectrolyte complex by encapsulating negatively charged particles of the drug. Modifying the surface with insulin or transferrin, results in enhanced transport efficacy.

Anti-Inflammatory

Nanogels have found an application dermatology and cosmetology as topical delivery systems of non-steroidal anti-inflammatory drugs (NSAIDs) and for the treatment of allergic contact dermatitis and psoriatic plaque. Nanogels are ideal for this application since they can overcome the major limitation of topical delivery systems, which is the relatively short contact time between active drugs and the application site. This is done by retaining water into the gel matrix and forming a uniform a dispersion of the Nanogel. The simultaneous topical delivery of two anti-inflammatory drugs, Spantid II and ketoprofen was successfully achieved through a Nanogel of poly-(lactide-co-glycolic acid) and chitosan. Oleic acid was used for surface modification. A variety of inflammatory disorders can be treated using this Nanogel system as it can effectively permeate to deep layers of the skin.

Vaccine Delivery

Vaccination is based on the induction of an immune response that antigen-specific. In order to enhance the potency and the performance of vaccines, polymeric Nanogels are being utilized as novel, alternative means of vaccine delivery. The advantage of Nanogels over conventional vaccines lies in the ability of the Nanogel network to protect vaccine antigens from enzymatic Degradation. Target specificity of the vaccine delivery can be significantly enhanced by using surface modified Nanogels with attached antibodies and other ligands.

Transdermal Drug Delivery

Transdermal route of administration has advantages over other routes in that it bypasses first pass effect, improves the efficiency of drugs, provides steady state drug concentration in plasma and increases patient compliance. A variety of approaches were considered to enhance the penetration of drug into site of action. A promising approach is the use of Nanogels for topical delivery of active pharmaceutical ingredients to the stratum corneum. As the oral administration of aceclofenac causes a number of side effects like ulcers and gastric bleeding, Transdermal delivery of the drug, was studied as an alternative, and showed better stability and permeability. Through the emulsion solvent diffusion method, a dispersion of aceclofenac was formed and incorporated into a gel matrix to formulate a Nanogel for the transdermal delivery of the drug.

Bone Regeneration

For the successful regeneration of bones, biodegradable cell scaffolds should release lithium as well as other medicament slowly and locally. Bone growth can be increased by lithium, hence, lithium Nanogels, synthesized by micro-emulsion polymerization of polyacrylic acid and incorporated into the biodegradable polyhydroxybutyrate matrix, are formulated for the controlled release of lithium into bone tissue.

Antibacterial and Anti-Microbial Activity

Infections are becoming increasingly difficult to cure due to resistance to conventional delivery systems of antibiotics. In order to treat a microbial infection, a quick and localized action is required, which is possible in Nanogel delivery systems. Dextran cross linked polyacrylamide Nanogels (polysaccharide based Nanogels) loaded with zinc nitrate (zinc ions) as antibacterial agent were prepared by mini-emulsion method. The crosslinking agent used was methacrylate Hyaluronic acid. The purpose of this Nanogel was to target the methicillin-resistant strains of staphylococcus aureus.

Diabetics

As diabetes becomes more and more prevalent in the world's population, revolutionized approaches are being considered for its treatment. An injectable Nanogel network that is sensitive to changes of glucose levels in the blood and releases specific amounts of insulin accordingly has been formulated, containing a network of oppositely charged nanoparticles. These nanoparticles attract each other, forming a gel matrix that remains intact and responds to changes in pH. By utilizing dextran, the Nanogel network will carry insulin and other enzymes necessary for the conversion of glucose into gluconic acid. Under conditions of hyperglycaemia, glucose molecules, being easily diffusible through the Nanogel, pass the gel network and trigger the conversion process of glucose into gluconic acid, thereby decreasing the pH of the medium. This will, in turn, stimulate the release of insulin. Even though this approach is very promising for the treatment of diabetes, it is still new and needs some work to be done before this Nanogel is suitable for human trials.

Ophthalmology

Dexamethasone containing eye drop was prepared by solvent evaporation or emulsification method using 2-hydroxypropyl-γ-clclodextrin (HP γ CD) medium containing γ- CD Nanogel for sustain release. pHsensitive polyvinylpyrrolidone-poly [acrylic acid] (PVP/PAAc) Nanogels, formulated by γ radiation-induced polymerization of acrylic acid (AAc) in an

aqueous solution of polyvinylpyrrolidone (PVP) acting as a template, were used to encapsulate pilocarpine, thus enhancing the bioavailability as well as the stability of pilocarpine and maintaining an adequate concentration of the drug at the site of action for prolonged period of time[1].

Stopping bleeding

Protein molecules present in solutions have been used for the formation of Nanogels to stop bleeding, even in severe gashes. The proteins self-assemble on the nanoscale into biodegradable gels.

Vaginal drug delivery

Vaginal Nanogels containing antibacterial drugs can be used to prevent various vaginal infections.

Intracellular delivery of Nanogels

In this type of drug delivery, Nanogels facilitate intracellular distribution of drugs. The cellular take-up is by endocytosis and the enhanced permeation and retention (EPR) effect. In a recent study, drug-loaded Nanogels showed enhanced potency compared with the free drug after exposure to M21 cells. The EC50 values of cells exposed for 20 min and cells exposed to the free drug for 72 h are compared with those of drug-loaded Nanogels.[29]

CONCLUSION

Nanogel systems have been studied for both theoretical and practical aspects. They are widely used for controlled delivery system, targeted delivery system, coatings purpose, and for the cosmetics products. Nanogels show promising future developments, widening the prospects for drug delivery. Nanogel seems to be an excellent candidate for the solubility enhancement of poorly water-soluble drugs. Nanogels have versatile properties that make them capable of efficient delivery of biologically active molecules, particularly biopharmaceuticals. They can also be used as a carrier, or chaperone, to treat diabetes, cancer, neurodegenerative disease, etc. It is widely used in pharmaceutical field. One future goal of research in this area should be the improved design of Nanogels with specific targeting residues to enable highly selective uptake into particular cells. This will be especially important for the targeting of cancer cells, thereby reducing non-specific uptake into healthy cells. More and more in vivo and in vitro study should be needed to confirm the use of this delivery system on human being.

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