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Herbal Nanogel Formulation: A Novel Approch

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Abstract:*Increasing research interest has been focused on controlled as well as sustained drug delivery using natural and biocompatible constituents in recent years. Many of them herbal constituents are avoided due to pharmacokinetic and pharmacodynamic issues of herbal constituents. There are many new technological ways and comparisons have been studied to upgrade the herbal discoveries in pharmaceutical market. This review will focus on the nanogel for herbal medicines with high delivery rate, patient compliance and efficiency. A nanoparticles contained hydrogel with cross linked polymer networks called as 'Nanogel'. Nanogel preferred for herbal medicines due to stability and for the ease. Nanogels in terms of herbal drugs are promising and novel approach which also can be called as future generation drug delivery systems owing to high drug encapsulation capacity, uniformity, minimum toxicity, greater stability.*

Keywords*: Herbal medicines, nanogel, bioavailability, drug delivery*

I. Introduction

Herbal medicine is often defined as "the therapeutic practices that are alive for many years, before the event and spread of recent medicines". This branch of other medicines that exploits medicinal plants for therapy is applied as herbal medicine which exploits medicinal plants for therapy is applied as herbal medicine which is mostly researched by many researchers.[1]
Herbal medicines from traditional herbs or natural herbs are logically considered as alternative medicines during this era to treat and cure most communicable diseases also as non-communicable diseases like cancer and diabetes[2]. Herbal medicines have played an important role in fixing the inspiration for current pharmacopoeia which is within the pharmaceutical market. Herbal medicines get preferences over modern medicines due to minimum side effects and also healthier option for the patients. Mostly 85% of Worlds population used herbal drugs to treat skin related diseases like viral, fungal, diabetic related issues, hypersensitive reactions etc. But in reality despite their appropriate pharmacological activity, they are less used in medicinal practices due to many reasons like solubility issues, bioavailability problems, high dose requirement etc[3]. They can be used in day to day medicinal practices by using them in a novel way. And it results to reduces the dose of the herbs as a drug which is used for pharmacological activity, however easy accessibility and also cost effectiveness of these traditional medicines by making them more desirable as a alternative option for modern medicines[6].
Nanotechnology, a novel technique which having the broad scope for the drug delivery. Development of novel drug delivery system has a impact on disease prevention, diagnosis, and treatments. This novel way have overcome the issues by improving absorption of drugs, sustained release of drug, controlled release of drugs, by reducing toxicity of drugs etc. the application of nanotechnology to medicines has the development of nanoparticles which act as carriers can be loaded with drugs or genetic material which released in controlled or sustainable manner to specific target site. Many nanotechnological techniques available nowadays for drug delivery like nanoemulsions, nanosuspensions, nanotubes, and nanogels but despite other techniques nanogels are mostly available in market due to its advantages over other formulations. A nanoparticle which contains hydrogel with cross linked polymer network called as "Nanogel"[2]. A nanogel which is nanosized hydrogels which is cross-linked, small swollen particles which is made up from amphiphillic or hydrophilic polymer

networks, these networks might be anionic or ionic. They acts as carrier for drug molecules and designed in the way that can absorb active compounds by the formation of bimolecular interactions like hydrogen bonding, salt bonds etc[2].

The main biological compound can be loaded into nanogels by allowing the interaction between matrix and active agent and these results more dispersed hydrophilic particles. This structure provides physical protection to active loaded molecule from degradation. And for that nanogels become the more flexible structure for controlled and sustained drug release to the target site.

II. Advantages

1. Less amount of drug is required.
2. Provide protection from biodegradation of drug molecule inside the body system.
3. Size of nanogel can be adjustable according to delivery molecule
4. Enhance the bioavailability of drug molecule
5. Reduces the toxicity of drugs.
6. Nanogels are able to cross physiological barrier of skin also the blood brain barrier.
7. Nanogels with loaded drug can be delivered inside the body without any side effects and also can be applied topically.
8. Easy for scale up and biofriendly formulation route.
9. Appropriate for many of bioactive compounds like proteins, antibodies, peptides etc.

III. Disadvantages

1. Sometimes particles of surfactant can cause toxicity.
2. It requires expensive techniques.

. IV. Herbal Medicines Nanoformulations

For pharmaceutical companies, the development of a complete herbal medicine is very annoying, because many factors affect the biological efficacy of the plant herbal medicine and the reproducibility of its therapeutic potential. In some cases, due to certain complications, such as asthma, pain, fever, etc., drugs need to act quickly, while in controversial cases, chronic treatments such as hypertension, cancer, and diabetes also need to extend the duration of action. Due to its physical and chemical properties, herbal medicines are strictly restricted in both stages. These factors have undoubtedly reduced their dominance in modern medical practice. In recent years , many research investment have been made to bring effective deliverables in herbal medicines. However, in order to obtain the desired efficacy, nanotechnology strategies are needed to control the efficacy of the active plant ingredients in the system[11].

Attempt to use nanomaterials (such as polymer nanoparticles, solid lipid nanoparticle, lipid crystal systems, liposomes and nanoemulsions) as carriers to protect the herbal medicines from external degradation and improve their biological utilization. Facts have proved that nanotechnology increases the chances of implementing herbal-based medicines by increasing the potential of drug action, promoting the sustained release of active ingredients, reducing the required dosage and improving biological activity[15,16].

Due to its inherent site-targeting ability and response to external stimuli, the research on polymer nanoparticles has been greatly developed in the last decade. When designing polymer nanoparticles for herbal preparations, the biotoxicity and stability of the polymer should be considered. Therefore, through biodegradable and biocompatible polymers, such as PLA (polylactic acid), PLGA (polylactic-glycolic acid), chitosan, etc., the delivery mechanism of such herbal compounds can be very effectively practiced[13,14].

Certain polymers such as chitosan provide a series of advantages for transdermal delivery applications by enhancing functions such as sustained, targeted drug release, high biocompatibility and biodegradability[24].

Due to its good physical and chemical properties (controllable drug delivery and affinity for aqueous solutions), excellent colloidal stability, high cell internalization properties, and tendency to remain inert in the blood, nanogels are modern pharmaceuticals that need special consideration. In addition, nanogels can easily meet current challenges in herbal formulations.

V. Techniques Of Drug Loading In Nanogels

Nanomaterials and nanogel composites have the ability to interact with many inorganic and organic components. The interaction between these components is mainly through hydrogen bonds, covalent bonds, electrostatic forces and van der Waals forces . These interactions determine the effectiveness of nanogels for embedding drugs. Biomolecules are released from the nanogel through various mechanisms, such as diffusion, degradation, pH and environmental stimuli[19]. The various methods are as follows:

1. Covalent conjugation
2. Self assembly

1. Covalent Conjugation

Nanosystems provide a convenient platform for drug delivery. This is the result of its inherent functional groups participating in determining the structure and properties of nanoparticles. The covalent conjugation of the drug to the cross-linked nanogel provides additional stability to the encapsulated drug[20]. Polysaccharides contain hydroxyl groups that are easy to interact with hydroxyl groups, which are formed by forming ester bonds with the carboxyl groups in the drug . In this case, due to the cleavage of functional groups by enzymes such as esterases, the drug will be released prematurely.

2. Self Assembly

When the autonomous organization of components is gathered to a good structure-the definition is called self-assembly. Many molecules are self-assembled, which is characterized by diffusion, and then through non-covalent interactions, hydrophobic associations or including electrostatic, specific binding of molecules occurs. Because it involves a lot of interaction, it has weaknesses and dominates the structure and conformational behavior of the assembly. Polyelectrolyte-based nanogels have a tendency to self-assemble in the presence of oppositely charged solutes (such as surfactants, polynucleotides, proteins and synthetic polyions). Amphoteric molecules instantly form self-assembled nanoparticles in an aqueous environment, which facilitates better drug interaction and release from the nanogel. The orientation of the drug molecule should expose the hydrophilic part to polar or aqueous media, while the hydrophobic area should be fixed in the core of the component. From a physical and chemical point of view, the important feature is that the hydrophobic part accumulates in the inner core and hydrophilic region in to polar region[23]. The concentration of polymer above which chains are aggregates is called critical micelle concentration or critical aggregate concentration.

VI. Mechanism Of Drug Release From Nanogels

a) pH stimulus
b) Degradation of nanogels
c) Ionic exchange with environment
d) Simple diffusion
e) From external energy sources

The release by stimulation of pH from the gel is the result of side group ionization. Nanogel polymers are composed of anionic or cationic side groups. In an aqueous environment, these groups will ionize at the appropriate pH and ionic strength. This creates a fixed charge on the polymer, causing electrostatic repulsion, which enlarges the pores of the gel. As a result, the flow of water into the gel increases, leading to swelling of the nanogel and drug release. The degradable nature of the nanogel ensures low toxicity and prevents unnecessary accumulation after repeated administration. Easily cleavable bonds can be introduced into the polymer backbone. Degradation is for specific reducing compounds, pH or even enzymatic activity. The lowest critical solution temperature (LCST) of the thermosensitive nanogel poly(N-isopropylacrylamide) in an aqueous medium is 32°C. At a temperature lower than the LCST, the amide group of the polymer interacts with the hydrogen of water, so the polymer is hydrated[25]. When the temperature increases, the hydrophobic-hydrophobic interaction of the polymer becomes obvious. The hydrogen bond with water is broken, the water phase separates and nanogel aggregation occurs; thereby releasing the captured drug into the environment. The diffusion release of the drug from the gel is the result of the difference in environmental concentration. The drug moves from the higher concentration area (inside the gel) to the lower concentration area (around). Another method is displacement by ions which is present in environment. A lot of research work is developing nanogels that can release biological agents in response to environmental cues at specific sites of action[26]. When a cationic nanogel containing a negatively charged drug interacts with negatively charged particles in the environment/cell surface, the drug will be exchanged for negatively charged particles.

VII. Drift of Nanogels

As mentioned earlier, compared with other delivery systems, nanogels can meet almost all the basic requirements of adaptive nanocarrier delivery media. Nanogels have the characteristics of hydrogels and nanomaterials, and their diameter ranges from 1 nm to 1000 nm. Nanogels are mainly used in nanomedicine applications as a new drug carrier for response-based treatments. Nanogels are ionic or non-ionic nanoparticles composed of physically or chemically cross-linked polymers, which can be hydrophilic, hydrophobic or amphiphilic. The new drug carrier should have two main features, namely, delivering the drug at the required rate and effectively delivering the drug to the site of action. Therefore, nanogels have many advanced functions, which can be equivalent to the demand for modern drugs. Nanogels are used for local drug action and systemic drug action due to their inherent swelling properties, which are attributed to their chemical modification to help release the drug in the desired dosage form. Nanogels have important functions, such as enhancing drug absorption across physiological barriers and sustained drug release. Nanogels are easy to formulate skin patches, biosensors and ionic drug delivery. Nanogels can be prepared using a variety of polymers, such as chitosan, alginate, polyvinyl alcohol, polyethylene oxide, polyethyleneimine, polyvinylpyrrolidone and Carbomer. The nanogel is composed of a polyethylene glycol shell, a polyphosphate core containing a drug, and a lipase-sensitive poly(ε-caprolactone) cross-linked between the two layers. Nanogels are widely used as carriers of therapeutic agents in biomedicine. Compared with other nanocarriers (such as polymer micelles, liposomes or nanoparticles), they have extraordinary swelling ability in water environment, which determines higher drug carrying capacity.

VIII. Challenges and Opportunity

According to the World Health Organization (WHO) report, 80% of the world's population will be highly dependent on herbal medicines to meet their health needs. A Nanogels formulated with herbs have opened a multi-billion dollar market for the growing pharmaceutical industry. As people's social, political and economic values have undergone major changes, the therapeutic application of herbal medicine has been greatly reduced. Nanogels can greatly help herbal medicine enter many applicable clinical practices through effective research programs. The fascinating properties of nanogels (such as biocompatibility and degradability, swelling properties in aqueous media, higher drug loading, permeability and particle size, non-immune reaction and colloidal stability) are always, There are new opportunities[27]. Nanogels are useful for designing delivery systems that respond to external stimuli that control the rate of drug release at the site of action. This can make the herbs play a multifunctional role by improving their efficacy[28].

IX. Conclusions

Nano gel formulation is a versatile platform for enhancing herbal properties. Herbal nanogels transform natural products into the most suitable drugs for the treatment of various diseases, such as cancer, skin diseases, diabetes, etc. Chitin, chitosan, PLGA, PEG and other polymers are widely used in the synthesis of cross-linked herbal nanogels. These cross-linked nanogels have excellent potential in delivering drugs through the transdermal route. Compared with oral drugs, this has less side effects on patients' compliance with herbal medicines. Although many natural medicinal products have been developed, not all of these products are safe. Some are highly toxic, can interact with conventional drugs and have adverse side effects. For herbal products to be accepted in modern medical systems, the quality of herbal products needs to be evaluated. Herbal nanogel formulations are currently expected in the pharmaceutical industry and can provide the required synergistic effects at low drug concentrations and almost no side effects. In general, herbal nanogel products can be a practical new drug carrier system.

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