A REVIEW ON OVERALL STUDY OF NANOPARTICLE AS DRUG DELIVERY SYSTEM

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Abstract

There's a growing interest in using nanoparticles for drug delivery systems. These tiny materials have special properties, like their very small size, large surface area, and ability to be easily modified. These features help improve how drugs behave in the body, making it possible to deliver medications more effectively.

Nanoparticles can help target cancer treatments specifically to tumors making them more efficient. They can also help with early detection of cancer through non-invasive imaging techniques. By using these nanostructured materials, we can protect drugs while they travel in the bloodstream, ensure they only reach the intended site, and release them in a controlled manner. This not only reduces unwanted side effects but also allows for a more effective use of the drugs, overcoming some of the limitations of traditional treatments.

This review focuses on the key features of nanoparticles used for targeted drug delivery. It covers how these nanoparticles can deliver drugs not just to specific cells but also to particular organelles within those cells. Additionally, it discusses some of the well

Known ways nanoparticles behave in the body (their pharmacokinetics) and the common modifications made to enhance their effectiveness in delivering therapies.

Recently, nanoparticles have emerged as a valuable method for improving how drugs work in the body. These tiny particles help protect drugs as they travel through the bloodstream, ensure that the drugs reach specific areas, and release them in a controlled way at the target site. Research in drug delivery is increasingly shifting from using larger particles to focusing on these much smaller, nanosized systems.

***Key word**: Drug targeting drug, Delivery, Nanotechnology, Nanodelivery, Particulate system, Nanomaterials, Drug delivery.*

Introduction:

Drug delivery methods primarily involve oral intake or injections. When a drug is administered, it travels throughout the body, impacting both unhealthy cells and healthy ones, which can lead to serious side effects. A key challenge is that only a small portion of the drug actually reaches the intended target site; much of it disperses to other areas, limiting its effectiveness.

To improve this situation, researchers are exploring advanced drug delivery systems. These systems aim to enhance the drug's action while minimizing side effects. One promising approach involves the use of nanoparticles—tiny particles ranging from 1 to 1000 angstroms in size. These nanoparticles can be engineered to deliver drugs more precisely, ensuring that a larger amount reaches the desired area in the body while reducing exposure to healthy tissues. This targeted approach holds great potential for improving treatment outcomes and reducing adverse effects.

Nanotechnology is a rapidly growing field focused on creating materials that are between 5 and 200 nanometer in size. To

put that in perspective, this size range is much smaller than standard organic molecules, but it's close to the size of many proteins and other biological structures.

The first real-world uses of nanotechnology have emerged from advances in various areas, including communication, engineering, physics, chemistry, biology, robotics, and medicine. In the medical field, nanotechnology is particularly promising for things like targeted drug delivery and developing new treatments for various diseases and disorders. As we continue to create and refine nanomaterials, we're seeing exciting progress across these disciplines.

Nanotechnology is a fascinating field that combines ideas from physics, chemistry, biology, materials science, health sciences, and engineering. It has a wide range of applications in many areas of science and everyday life.

At its core, nanotechnology deals with nanoparticles, which are tiny particles that measure between 10 and 1,000 nanometer in size. To give you a sense of scale, a nanometer is one-billionth of a meter! These tiny particles can have unique properties that make them useful for everything from medicine and electronics to environmental solutions.

Magnetic micro- and nanoparticles have indeed revolutionized various biomedical applications over the last two decades. Their unique properties allow for enhanced imaging and targeted therapies.

In magnetic resonance imaging (MRI), these particles serve as contrast agents, improving the clarity and detail of images by altering local magnetic fields. This helps clinicians better diagnose and monitor diseases.

In magnetic cell sorting these particles can be functionalized with antibodies that bind specifically to target cells. When subjected to a magnetic field, the targeted cells can be separated from a mixture, facilitating more efficient sample preparation for research and clinical applications.

To enhance treatment effectiveness, it's crucial to deliver drugs precisely to specific targets in the body. This is where nanoparticles come in. Their tiny size allows them to pass through tiny blood vessels and into individual cells, making it easier to concentrate the medication exactly where it's needed. This could lead to more effective treatments and fewer side effects for patients.

Importance of nanoparticle in drug delivery:

1. Improved Solubility: Nanoparticles can help drugs dissolve better in the bloodstream.
2. Longer Circulation Time: They can stay in the body longer, which may enhance their effectiveness.
3. Controlled Release: Nanoparticles can release drugs slowly and steadily, rather than all at once.
4. Targeted Delivery: They can be designed to deliver drugs specifically to certain tissues or cells, increasing the chances of success.
5. Combination Therapy: Nanoparticles can carry multiple drugs at the same time, which is useful for treating complex conditions.

Characteristics:

1. Importance of Circulation Time: For effective drug delivery, nanoparticles (NPs) need to stay in the bloodstream longer to reach target cells and provide a consistent release of the drug. Conventional drugs can

be quickly cleared from the body, making nanoparticle design crucial.

2. Role of Particle Size: Significance: The size of NPs influences their distribution, bioavailability, and ability to penetrate target tissues.

3. Particle Surface Characteristics: Surface Properties: The surface of NPs affects their stability and how long they remain in circulation. Hydrophobic surfaces lead to rapid clearance by immune cells (opsonization).

4. Particle Shape: Shape Influence: The shape of NPs significantly impacts in the body, including circulation time and targeting efficiency. While many NPs are spherical, non-spherical shapes (like filaments) have shown improved properties in certain studies.

Nanoparticale Types:

1.Inorganic Nanoparticles

Inorganic nanoparticles are tiny particles made from non-organic materials, like metals or metal oxides. They can be designed to avoid the body's immune system by changing their size and surface features. Many have a hollow structure that can protect drugs from breaking down.

For example, hollow silica nanoparticles can store drugs in their center and release them in a controlled way. Researchers have experimented with these nanoparticles to find the best ways to deliver medications, like ibuprofen, by adjusting their pore sizes. Some teams have even created caps made of cadmium sulfide that can release drugs when stimulated, showing that it's possible to control when and how much medicine is released.

Inorganic nanoparticles are stable but may raise safety concerns since they don't break down easily in the body.

2.Polymeric Nanoparticles:

Polymeric nanoparticles are made from biodegradable and biocompatible materials, making them a popular choice for drug delivery. They can carry a wide variety of drugs and are easier to modify for specific uses.

Common materials include gelatin and various polymers. One useful polymer, polyethylene glycol (PEG), can be attached to nanoparticles to help them avoid being cleared by the immune system, increasing the drug's effectiveness.

These nanoparticles have been approved for human use and can help deliver drugs in various medical applications, including cancer treatment. Their surfaces can be tailored to improve how they are taken up by cells, making them versatile for different therapies.

3. Solid Lipid Nanoparticles

Solid lipid nanoparticles are tiny carriers made of lipids (fats) that are solid at room temperature. They are more stable than other types of lipid carriers,

like liposomes, and can be designed to release drugs in response to temperature changes.

These nanoparticles can be used to deliver medications in several ways, such as orally or through inhalation, and are considered less toxic than some other nanoparticle types.

4. Liposomes

Liposomes are spherical structures made of phospholipids, which can carry both hydrophilic (water-loving) and hydrophobic (water-repelling) substances. They are great for protecting drugs in the body but have struggled to achieve significant medical use due to stability issues.

PEG can enhance their stability, allowing for longer circulation in the body, which is beneficial for drug delivery.

5. Nanocrystals

Nanocrystals are tiny crystalline forms of drugs coated with surfactants to improve their solubility and bioavailability. They can enhance the delivery of poorly soluble medications but have limited stability and can be tricky to produce.

6. Nanotubes

Nanotubes are cylindrical structures made of carbon or other materials. They can hold a lot of substances inside and have surfaces that can be modified. While promising for drug delivery, concerns about their safety and potential toxicity need to be addressed.

7. Dendrimers

Dendrimers are branched, tree-like molecules that can encapsulate drugs within their structure. Their unique design allows for easy modification, which can enhance their ability to deliver medications.

Method of preparation of nanoparticle of chitosan:

1.Emulsion cross-linking:

1. Emulsion Preparation: An aqueous solution of chitosan is emulsified in an oil phase, creating tiny droplets stabilized by a surfactant.

2. Cross-Linking: These stable droplets are then hardened using a cross-linking agent. Afterward, the resulting microspheres are filtered, washed with solvents like n-hexane and alcohol, and dried.

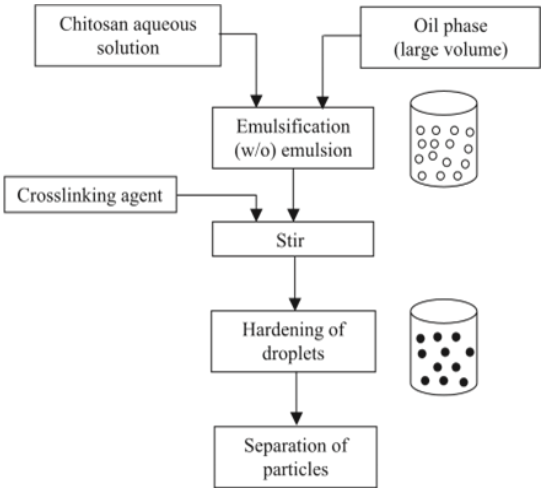

Fig. Schematic representation of preparation of chitosan particulate systems by emulsion cross-linking method.

2.Coacervation/precipitation:

This method takes advantage of chitosan's (CS) unique property: it becomes insoluble in alkaline solutions but can precipitate when in contact with them. To create particles, a chitosan solution is sprayed into an alkaline solution like sodium hydroxide mixed with methanol or ethane diamine using a compressed air nozzle. This process forms coacervate droplets. After that, the particles are separated and purified through filtration or centrifugation followed by rinsing with hot and cold water.

The size of the particles can be controlled by adjusting the air pressure or the diameter of the spray nozzle. Additionally, a cross-linking agent can be used to harden the particles which also influences how the drug is released.

In another approach, sodium sulfate solution is added slowly to an acidic chitosan solution that contains a surfactant, while stirring and using ultrasonication for 30 minutes. The resulting microspheres are purified by centrifugation and then re-suspended in demineralized water, where they are cross-linked with glutaraldehyde.

This method results in particles with better stability in acidic conditions compared to other techniques.

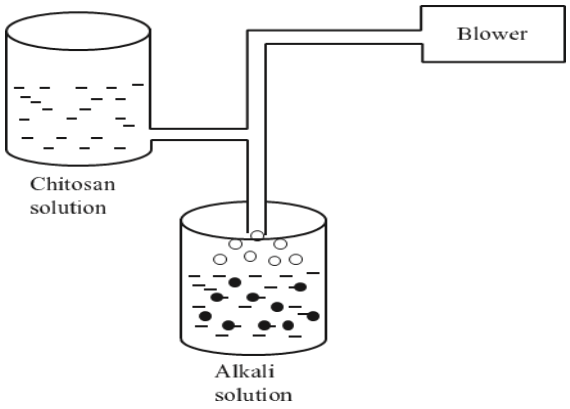

Fig. Schematic representation of preparation of chitosan particulate systems by coacervation/precipitation method.

3.Spray-drying:

Spray-drying is a popular method used to create powders, granules, or agglomerates from mixtures of drug and excipient solutions or suspensions. This process involves drying tiny droplets formed from these mixtures in a stream of hot air.

To start, chitosan (CS) is dissolved in an aqueous acetic acid solution, and the drug is either dissolved or dispersed in this solution. A cross-linking agent is then added, and the mixture is atomized into small droplets in a hot air stream. As these droplets dry quickly, they turn into free-flowing particles.

The size of the resulting particles can be controlled by adjusting various process parameters, including the size of the nozzle, spray flow rate, atomization pressure, inlet air temperature, and the level of cross-linking.

Research has shown that both un-cross-linked and cross-linked CS microparticles can be prepared using this spray-drying method to deliver medications like cimetidine, famotidine, and nizatidine. The resulting microspheres are spherical and can vary in size: un-cross-linked microspheres measure between 4 and 5 micrometers, while cross-linked ones range from 2 to 10 micrometers. These particles are all positively charged, and their size and zeta potential (a measure of surface charge) are affected by how much cross-linking is done. Notably, less cross-linking leads to larger particle sizes and higher zeta potential. Additionally, increasing the spray flow rate with a larger nozzle increases particle size, whereas higher airflow rates produce smaller particles. Inlet air temperature has a lesser effect on particle size in the range of 140 to 180 °C.

Explored how spray-dried particles could be treated with cross-linking agent vapors, while incorporating cetylpyridinium chloride into CS microspheres. The level of cross-linking was controlled by adjusting the exposure time to the cross-linking agent.

Ganza-Gonzalez et al. confirmed that the spray-drying technique is efficient and straightforward for creating microspheres. They produced CS microspheres containing metoclopramide hydrochloride using varying amounts of formaldehyde as a cross-linker, achieving drug release for over 8 hours, regardless of the medium's pH.

Another study highlighted the effective encapsulation of vitamin D2 (ergocalciferol) in CS microspheres via spray-drying, with the resulting product being coated with ethyl cellulose for sustained release, aimed at treating prostatic diseases. The method was also utilized to create ampicillin-loaded CS microspheres with distinct shapes and sizes.

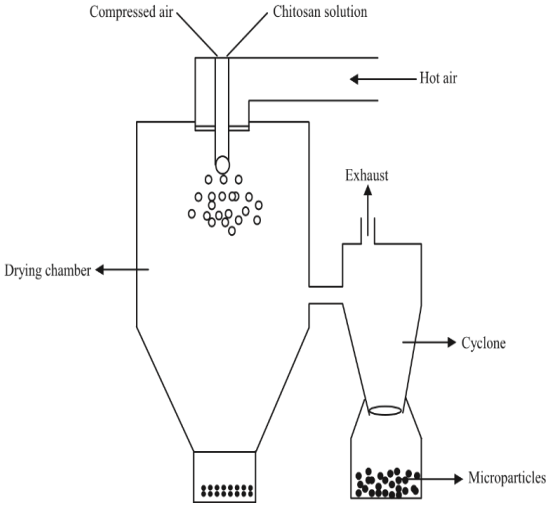

Fig. Schematic representation of preparation of chitosan particulate systems by spray drying method.

4. Emulsion-droplet coalescence method:

The emulsion-droplet coalescence method, developed by Tokumitsu and colleagues, combines ideas from both emulsion cross-linking and precipitation techniques. Instead of linking stable droplets together, this method promotes the merging of chitosan (CS) droplets with sodium hydroxide (NaOH) droplets to create solid particles.

Here's how it works: First, a stable emulsion containing an aqueous solution of chitosan and a drug is created in liquid paraffin oil. Next, another emulsion is prepared with an aqueous solution of chitosan and NaOH. When these two emulsions are mixed together while being stirred rapidly, the droplets collide and merge, which causes the chitosan to precipitate and form small particles.

For example, gadopentetic acid-loaded chitosan nanoparticles were created using this method for a specific type of therapy. The size of the nanoparticles varied depending on the chitosan used; as the degree of deacetylation (the process that affects chitosan's properties) decreased, the particle size increased, while the amount of drug it could hold decreased. Using fully deacetylated chitosan resulted in nanoparticles with an average size of 452 nanometers and a drug loading of 45%. Interestingly, the size of the nanoparticles didn't directly correspond to the size of the original droplets.

Because gadopentetic acid is a negatively charged compound, it can interact with the positively charged amino groups in chitosan. This interaction wouldn't happen if a cross-linking agent were used, as it would block these amino groups. As a result, the emulsion-droplet coalescence method allowed for higher loading of gadopentetic acid compared to traditional cross-linking methods.

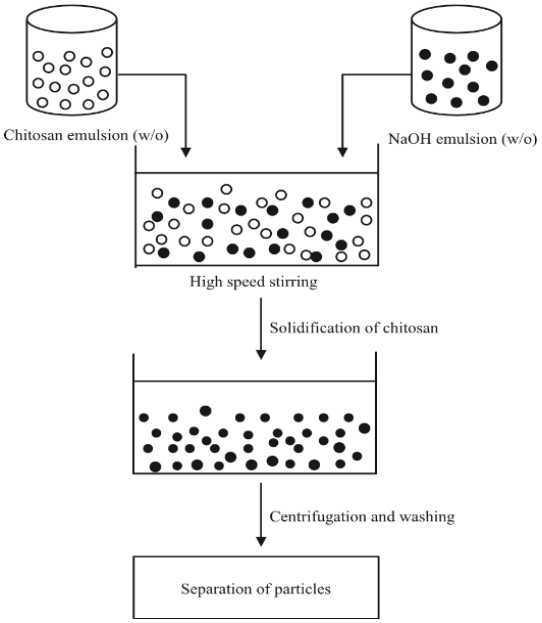

Fig. Schematic representation of preparation of chitosan particulate systems by emulsion-droplet coalescence method.

5. Ionic gelation:

The method of creating chitosan (CS) microspheres by complexing oppositely charged macromolecules has gained interest due to its simplicity and mild conditions. This approach uses reversible physical cross-linking via electrostatic

interactions, avoiding the potential toxicity associated with chemical cross-linkers. Tripolyphosphate (TPP), a negatively charged polymer, interacts with the positively charged chitosan through these electrostatic forces.

Researchers have explored the pharmaceutical applications of TPP-CS complexes, particularly after a method was developed where CS droplets are added to a TPP solution, leading to the formation of spherical particles through ionic gelation. However, one drawback of these TPP-CS microspheres is their poor mechanical strength, which limits their effectiveness in drug delivery.

In one study, insulin was loaded into CS nanoparticles by mixing it with a TPP solution and then combining this with a CS solution. Different types of chitosan were used, each with varying molecular weights and degrees of deacetylation. The resulting nanoparticles were about 300–400 nm in size and had a positive charge. The method allowed for insulin loading of up to 55%, which was influenced by the deacetylation level of the chitosan.

Further research demonstrated that CS nanoparticles could enhance the oral bioavailability of insulin. In an experiment, diabetic rats showed improved insulin absorption when given insulin-loaded CS nanoparticles compared to a standard insulin solution. The nanoparticles were stable, with sizes ranging from 250 to 400 nm, and achieved an insulin association rate of up to 80%. Release tests showed a quick initial release followed by a sustained, pH-sensitive release.

Other studies have examined various formulations of CS nanoparticles, revealing that their size ranged from 20 to 200 nm. Factors affecting the delivery of proteins, like bovine serum albumin (BSA), included the molecular weight of chitosan and the concentration of both chitosan and BSA. Increasing chitosan's molecular weight improved BSA encapsulation
efficiency while reducing its release rate. Interestingly, adding polyethylene glycol (PEG) hindered encapsulation efficiency and increased the release rate.

In another approach, CS microparticles were produced using TPP, with sizes between 500 and 710 micrometers and over 90% drug encapsulation efficiency. The shape and surface smoothness of the particles improved with lower pH in the TPP solution and higher chitosan molecular weights. Drug release rates varied depending on the preparation conditions, with slower releases observed at lower pH levels or with higher TPP concentrations. In contrast, decreasing chitosan concentration or molecular weight led to faster drug release. Overall, the ionic gelation method offers a promising route for developing effective drug delivery systems using chitosan and TPP.

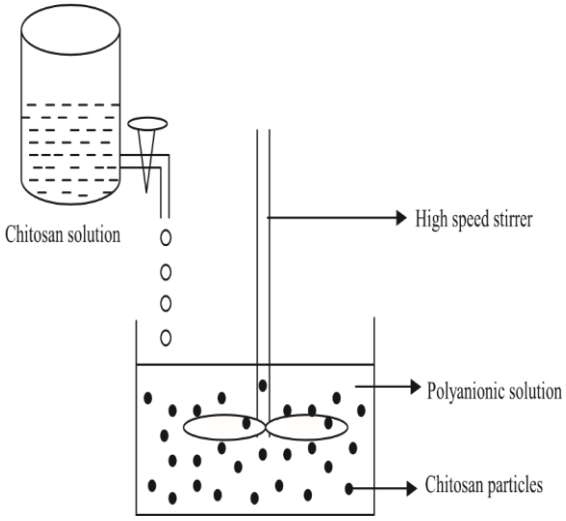

Fig. Schematic representation of preparation of chitosan particulate systems by ionic gelation method.

6. Reverse micellar method:

Reverse micelles are stable mixtures of water, oil, and surfactants. While they look homogeneous and isotropic on a larger scale, they actually have a complex structure at the microscopic level, with separate aqueous and oil domains surrounded by surfactant layers. One key feature of these systems is their dynamic behavior.

Using reverse micelles to create nanoparticles allows for the production of ultrafine polymeric particles that are much smaller than those made by traditional methods, which often result in larger particles (around 200 nm) with a wide size range. The aqueous core of the reverse micelles serves as a tiny reactor, enabling the formation of very fine nanoparticles with a narrow size distribution. The size of the micelles is typically between 1 and 10 nm, and they maintain a stable and uniform size due to continuous movement and coalescence on a fast timescale (milliseconds to microseconds).

Preparation Process:

1. Dissolving Surfactant: Start by dissolving a surfactant in an organic solvent to create reverse micelles.
2. Adding Aqueous Solutions: Gradually add aqueous solutions of chitosan (CS) and the drug while stirring to maintain clarity and avoid turbidity. You can control the amount of water added to achieve the desired nanoparticle size.
3. Cross-Linking: Introduce a cross-linking agent while stirring continuously, allowing the mixture to stir overnight for effective cross-linking.
4. Determining Drug Solubility: The maximum amount of drug that can be incorporated varies by drug. You need to find this threshold by slowly increasing the drug concentration until the solution becomes translucent.
5. Evaporating the Solvent: Remove the organic solvent to get a dry, transparent mass.
6. Dispersing in Water: Disperse the dry mass in water and add a suitable salt to precipitate the surfactant out of the solution.
7. Centrifugation: Centrifuge the mixture, decant the supernatant to collect the drug-loaded nanoparticles, and dialyze for about an hour to purify the product. Finally, lyophilize to obtain a dry powder.

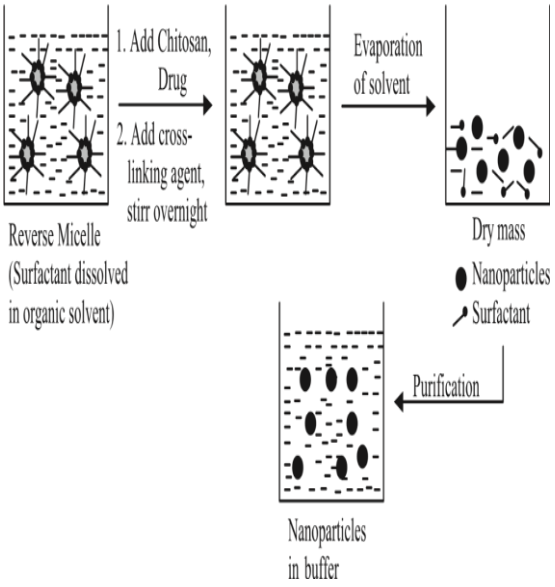

Fig. Schematic representation of preparation of chitosan particulate systems by reverse micellar method.

7.Sieving method:

Agnihotri and Aminabhavi recently developed a straightforward and innovative method for producing chitosan (CS) microparticles. Here's how it works:

First, they dissolved chitosan in a 4% acetic acid solution to create a thick gel. They then added glutaraldehyde to this mixture, which caused it to cross-link and become a non-sticky hydrogel. Next, they passed this gel through a sieve to create microparticles of uniform size.

To ensure purity, the microparticles were washed with a 0.1 N sodium hydroxide solution to remove any unreacted glutaraldehyde and were then dried overnight in an oven at 40°C. Notably, clozapine was mixed into the chitosan before the cross-linking process, achieving an impressive entrapment efficiency of up to 98.9%.

This method is simple and can be scaled up easily for larger production. The resulting microparticles had irregular shapes, with sizes ranging from 543 to 698 micrometers. In laboratory tests, the microparticles released clozapine gradually over 12 hours, and animal studies showed a slow release of the drug in vivo.

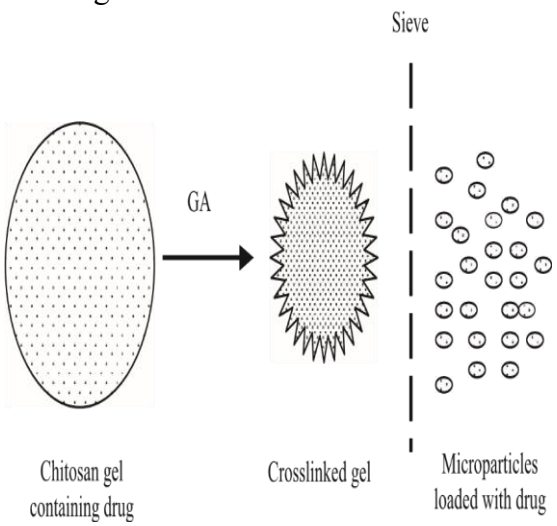

Fig. Schematic representation of preparation of chitosan particulate systems by sieving method

Nanoparticle synthesis and conjugation methodologies:

1.Gold nanoparticles:

Gold nanoparticles are typically made by chemically reducing gold salts in various solvents. However, the gold surface can be very reactive, leading to the aggregation of particles. To prevent this, stabilizers are often added during the reduction process. These stabilizers bind to the surface of the gold nanoparticles, helping to prevent aggregation through charge and structural properties.

There are several types of stabilizers used, including citrate, thiol-containing organic groups, and polymer coatings. Notably, gold nanoparticles can also be coated with biomolecules, which opens up exciting possibilities for applications in biological sensing and imaging.

These coated gold nanoparticles have significant biological applications, such as detecting polynucleotides through hybridization with oligonucleotides attached to their surface.

2.Carbon nanotubes:

Carbon nanotubes were first discovered in 1991 when researchers found them in deposits from graphite during an arc evaporation process. Soon after, scientists figured out how to isolate carbon nanotubes by heating hydrocarbons like ethylene or acetylene in the presence of metal nanoparticles, such as iron or cobalt. These metals play a key role in determining the size and type of the resulting nanotube.

Interestingly, the outcome varies based on the conditions: heating nickelocene with benzene at 1100°C mainly produces MWNT, while using acetylene leads to mostly SWNT. This difference likely arises because acetylene has fewer carbon atoms per molecule, influencing the formation of the nanotubes.

3. Layered double hydroxide nanoparticles:

Layered double hydroxide nanoparticles are gaining attention in the fields of drug delivery, gene therapy, and controlled release because they have low toxicity and high compatibility with biological systems. Traditional methods for making these nanoparticles involve mixing salts in

hydroxide solutions at various pH levels and then heating them. However, these techniques often lead to particle aggregation, which can be problematic.

To improve size and reduce aggregation, researchers like Zhao et al. have developed methods that separate the processes of nucleation and curing, resulting in nanoparticles ranging from 1 to 10 micrometers. While this size range is interesting, it may not be ideal for drug delivery applications.

To create smaller nanoparticles that are more suitable for delivering drugs, precise control during the hydrothermal treatment stage is crucial. Recent research by Xu et al. has successfully produced monodisperse nanoparticles with sizes between 40 and 300 nanometers, which is much closer to the size range that is considered biologically compatible for effective drug delivery.

4. Iron oxide nanoparticles:

There are various methods to create ferromagnetic iron oxide nanoparticles. One popular approach involves using a water-in-oil microemulsion system, which employs reverse micelles. This technique is particularly effective for producing maghemite (γ-Fe2O3) and magnetite (Fe3O4) nanoparticles. It involves mixing a metal salt solution with a base to raise the pH, followed by hydrolysis within the microemulsion.

Another method takes advantage of certain bacteria that naturally produce magnetic nanoparticles, which typically measure between 50 and 100 nanometers in diameter.

Additionally, iron oxide nanoparticles can be synthesized through other techniques, such as the sonochemical decomposition of iron pentacarbonyl, thermal decomposition of various iron compounds, or first decomposing iron pentacarbonyl and then oxidizing the resulting material.

5. Calcium phosphate nanoparticles:

Calcium phosphates, primarily found as hydroxyapatite, make up most of the inorganic components in human bones and teeth. This gives calcium phosphate nanoparticles excellent compatibility with the body. These nanoparticles can be created using various methods, including wet chemical processes, solid-state reactions, hydrothermal techniques at high temperatures, biosynthetic approaches, and microemulsions.

Among these methods, microemulsion is particularly attractive because it allows for precise control over the size and shape of the nanoparticles, producing uniform particles with minimal clumping. In a microemulsion, surfactant molecules create protective structures

that help manage the formation and growth of nanoparticles in a water-in-oil mixture. The success of this synthesis depends on factors like the concentrations of calcium and phosphate ions, pH levels, ionic strength, temperature, and the type and amount of surfactant used.

6. Silica nanoparticles:

Silica nanoparticles can be made using sol-gel methods, as previously discussed. Notably, Stöber and colleagues developed a co-condensation process that produces uniform silica nanoparticles. This research has been expanded to modify the silica surface chemically, allowing for the addition of various functional groups. Some of these include 3-aminopropylethoxysilane, N-(2-aminoethyl)-3-aminopropyltrimethoxysilane, and several others that enhance the silica's properties.

Another approach involves using microemulsions, like the organic-aqueous systems studied by the Tan group. In these systems, tiny "solvent cages" help control the size and behavior of the silica nanoparticles as they form. MCM-41 is an example of a type of mesoporous silica nanoparticle created through these methods.

8.Fullerenes:

1. Curvature Induction: They first induce curvature in the polyarenes through a method called flash-vacuum pyrolysis.
2. Radical Coupling: They then design reactions that help connect the curved structures while preventing them from adopting distorted shapes.
3. Hydrogen Shifts: They utilize 1,2-hydrogen shifts to simplify complex reactions.
4. Cascades: Finally, they use cyclodehydrogenation to link the structures together after curvature is introduced.

8.Quantum dots:

Quantum dots are tiny particles that can emit light, and they're often used for imaging in biological research. These particles have three main parts: the core, the shell, and the coating, each of which affects how they behave when it comes to light. Quantum dots can be made in sizes ranging from just a few nanometers up to micrometers, and they can be produced with consistent sizes through methods that often require high heat.

Bare quantum dot cores are unstable because they have a high surface area relative to their volume, which can lead to uneven light emission due to imperfections on their surfaces. To improve their stability and brightness, these cores are often coated with zinc sulfide (ZnS), which enhances their light-emitting properties. However, ZnS alone doesn't provide enough stability for the core, especially when used in biological environments.

Evaluation of nanoparticles:

Zeta potential:

Zeta potential is a way to measure the surface charge of nanoparticles, which helps us understand how they behave in a liquid. This charge is affected by both the particles themselves and the surrounding fluid. When nanoparticles have a zeta potential greater than ±30 mV, they tend to stay well-dispersed and don't clump together. This stability is important for various applications.

Particle shape:

Before evaluating the nanosuspension, we use Scanning Electron Microscopy (SEM) to examine its characteristics. Then, we lyophilize the nanosuspension to create solid particles. These solid particles are coated with a platinum alloy using a sputter coater.

Particle shape:

Particle size and size distribution are key factors in how nanoparticle systems behave in the body. They affect how these particles are distributed, their biological impact, and their potential toxicity and ability to target specific areas. These characteristics also play a role in how well drugs can be loaded into the nanoparticles, how they release the drugs, and how stable they are over time.

Delivery and targeting:

1. Passive Targeting:

Passive targeting relies on the natural properties of drug carriers, such as their size and surface charge, to accumulate at target sites. This strategy often capitalizes on differences between healthy and diseased tissues.

Key Mechanism: Enhanced Permeation and Retention (EPR)

The EPR effect describes how nanoparticles (NPs) can enter tumor tissue through leaky blood vessels and accumulate due to the lack of a functional lymphatic system. This effect was first noted by Matsumura and Maeda.

2. Active Targeting:

Active targeting enhances drug delivery by modifying nanoparticles with ligands that specifically bind to receptors on target cells, tissues, or organs.

Mechanisms of Active Targeting

Active targeting can be achieved by attaching various molecules to NPs, including:

- Receptor ligands: Targeting receptors overexpressed in cancer cells (e.g., folate and transferrin receptors).
- Antibodies: Targeting specific proteins.
- Nucleic acids: For precision targeting at the molecular level.
- Small molecules: Such as peptides or carbohydrates.

Conclusion

Both passive and active targeting strategies are crucial in developing effective drug delivery systems, allowing for improved therapeutic outcomes while minimizing side effects. Understanding the mechanisms and factors that influence these strategies can lead to more targeted and efficient therapies in treating diseases, particularly cancer.

Advantages of nanoparticle:

a) Customizable Size and Surface: The size and surface properties of nanoparticles can be adjusted to enhance both passive and active targeting of drugs after they are injected.

b) Controlled Drug Release: Nanoparticles can control and sustain the release of drugs, improving how the drug spreads in the body and how quickly it's cleared, which helps boost effectiveness and minimize side effects.

c) Targeted Delivery: By attaching specific targeting molecules to their surface or using magnetic guidance, nanoparticles can be directed to specific areas in the body.

d) Versatile Composition: The materials used to make nanoparticles can be selected to control how they release drugs and degrade over time. Drugs can be loaded into these systems without altering their chemical structure, which helps maintain their effectiveness.

e) Multiple Administration Routes: This system is versatile and can be used for various ways of delivering drugs, including orally, through the nose, via injections, or even in the eyes.

Limitation of nanoparticle:

a) The tiny size and large surface area of nanoparticles can cause them to clump together, making them hard to handle, whether they're in liquid or powder form.

b) Additionally, their small size and large surface area can make it difficult to load enough drugs onto them and can lead to quick release of the drug. These challenges need to be addressed before nanoparticles can be used in hospitals or sold commercially.

Application of nanoparticles:

1.Colon targeted drug delivery:

Chitosan is a promising polymer for delivering drugs to the colon because it can be broken down by bacteria found there and has good adhesive properties. Researchers developed a special system where chitosan microcores are surrounded by enteric acrylic microspheres. In this system, sodium diclofenac is effectively trapped in the chitosan cores and then encapsulated in two types of enteric coatings, Eudragit L-

100 and Eudragit S-100, to create a multi-reservoir delivery system.

2. Mucosal delivery:

Recent research has highlighted mucosal surfaces—like the nasal, oral, and pulmonary areas—as promising routes for delivering medications systemically. Chitosan, a natural polymer with mucoadhesive properties, is particularly valuable for creating bioadhesive drug formulations for these applications (including ocular, nasal, buccal, and vaginal therapies).

One of the key benefits of nasal mucosa is its high permeability, which allows drugs to be absorbed easily. Chitosan helps enhance drug absorption through mucosal surfaces by temporarily widening the tight junctions between epithelial cells without harming the tissue.

3. Cancer therapy:

Gadopentetic acid-loaded chitosan (CS) nanoparticles have shown promise for gadolinium neutron-capture therapy (Gd-NCT) in cancer treatment. These nanoparticles effectively retain gadopentetic acid in tumors, making them suitable for direct tumor injections. In laboratory studies, Gd accumulation in various cancer cell lines, like B16F10 melanoma and SCC-VII squamous cell carcinoma, was significantly higher with the nanoparticles compared to traditional gadolinium solutions. This higher accumulation correlates with better tumor growth suppression in animal models.

4. Gene delivery:

1. Targeting: The delivery system must reach the specific cells that need treatment.
2. Membrane Transport: The DNA must cross the cell membrane.
3. Endolysosomal Uptake: Once inside, the DNA can be trapped and degraded in cellular structures called endolysosomes.
4. Nuclear Transport: Finally, the DNA must travel to the nucleus, where it can be used.

5. Topical delivery:

Chitosan (CS) is effective for topical drug delivery because it sticks well to tissues and can release active ingredients over time. Researchers have created bioadhesive CS microspheres
to deliver cetyl pyridinium chloride and found that these microspheres improve the antibacterial activity of the treatment.

6. Ocular delivery:

De Campos and colleagues conducted research on using chitosan (CS) nanoparticles to improve how drugs are delivered to the eyes. They used cyclosporin A (CyA) as a test drug. To create the CyA-loaded nanoparticles, they employed a modified ionic gelation method. The resulting nanoparticles were about 293 nm in size and had a positive charge (+37 mV), with a high efficiency for carrying CyA—loading 73% of the drug.

8. Chitosan as a coating material:

Chitosan is a great material for creating coatings, making it useful in drug delivery systems. When microparticles are coated with chitosan, they offer several benefits, including improved drug loading, better adhesion to tissues, and a slower release of the drug compared to uncoated particles. For instance, researchers have made chitosan-coated microspheres using a blend of poly(lactic acid) and poly(caprolactone), which show promise for delivering drugs that can help treat restenosis (the re-narrowing of blood vessels).

9. Improved bioavailablity:

Researchers have found that incorporating poorly soluble drugs into solid lipid nanoparticles (SLNs) can significantly improve their oral bioavailability. For example, a study by Demirel et al. involved preparing SLNs of piribidil, which, when given to rabbits, resulted in more than a two-fold increase in bioavailability compared to the pure drug.

10.Controlled release:

Controlled release of certain drugs, like CA from stearic acid solid lipid nanoparticles (SLNs), can last up to 154 hours in a phosphate buffer at pH 7.4. For prednisolone, it can be incorporated into SLNs made with cholesterol at concentrations up to 3.6% and with compritol at 1.67%, showing prolonged release over five weeks. Interestingly, the release rates differ between the cholesterol and compritol SLNs.

Future opportunities and challenges:

Nanoparticles are really promising in medicine because they can help deliver drugs more effectively and even combine diagnosis with treatment. Their main advantages include improving how stable they are in the body, how well they distribute medication, and how they target and release drugs where they're needed.

However, a big challenge is that some nanoparticles can be toxic to cells or break down into harmful substances. Therefore, making sure these nanoparticles are safe and compatible with the body is a key focus for future research

Conclusion:

Nanoparticle-mediated drug delivery could significantly change healthcare for the better. It has the potential to enhance patients' quality of life by enabling earlier detection of diseases, reducing the severity of illnesses, and leading to better overall treatment outcomes. Nanotechnology is set to play a crucial role in how we deliver drugs and treat illnesses. There are many types of nanoparticles already available, and scientists have developed various methods to create them. The way these nanoparticles behave in the body can change based on their size, shape, and the modifications made to their surfaces.

By carefully designing these nanoparticle delivery systems, we can improve how drugs are targeted to specific areas in the body while avoiding detection by the immune system. This can lead to more efficient drug delivery.

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