A Review on Nanotechnology – Based drug delivery system

Shraddha Hajare, Akshada Falle, Bhavana Shelke,Sneha Ghodke, Mayuri Bhadalekar, Nilesh Chougule
Students, Ashokrao Mane Institute Of Pharmacy, Ambap
Assistant Professor, Ashokrao Mane Institute Of Pharmacy,Ambap
Principal, Ashokrao Mane Institute Of Pharmacy,Ambap

Abstract: Herbal medicines have been used since ancient times for their therapeutic value and fewer adverse effects. Nanotechnology can be used to design novel drug delivery systems (NDDS) for herbal constituents, reducing repeated administration and increasing therapeutic value. Integrating nanocarriers as NDDS in traditional medicine systems is essential for combating chronic diseases like asthma, diabetes, and cancer. Herbal medicines are popular for treating diseases with minimal side effects. However, delivery is problematic due to low digestion, poor availability, and early metabolism. Nano-sized drug delivery systems (NDDS) can enhance efficacy by targeting individual organs, improving selectivity, effectiveness, and safety. Combining herbal medicine with nanotechnology can reduce dose, side effects, and increase therapeutic value by reducing toxicity and bioavailability.

Key words: Nanotechnology, Novel drug delivery system, Herbal medicine

INTRODUCTION

Herbal remedies, a natural treatment method with thousands of constituents, have been used since ancient times to treat diseases, unlike the widely used allopathic system. Nanotechnology is a applied science aiming to develop devices and dosage forms in the 1 to 100 nm range, used in nanomedicine for treatment, diagnosis, monitoring, and control of biological systems. Nanocarriers are made of safe materials like biodegradable polymers, lipids, and polysaccharides. Phyto-formulation research aims to improve solubility, bioavailability, and protection of herbal medicines by developing nano dosage forms, which synergize their therapeutic value.[1] The National Nanotechnology Initiative established nanotechnology for manipulating matter with a minimum dimension of 1 to 100 nanometers. Nanotized herbal drugs with active ingredients are effective in various diseases, with polymeric nanoparticles increasing oral bioavailability. Nanotechnology is being used to tailor herbal constituents for potential benefits, with researchers focusing on nanotizing herbal proportions. Nanophytomedicines, prepared from active phytoconstituents or standardized extracts, are crucial for 80% of developing countries' basic health needs. [2]

HISTORY AND DEVELOPMENT

Natural products, including plants, have been used for treating human diseases since ancient times, and the foundation of modern medicine development is rooted in traditional therapies.[3,4] Plants have been used for medicinal purposes in ancient China, Egypt, Africa, America, and India, with chemical analysis enabling the extraction and modification of herbal ingredients in the early 19th century. [5] Modern phytopharmaceutical research addresses scientific needs for herbal medicines, leading to the development of novel formulations like nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, SLNs, nanomicellar systems[6], nanotubes[7], and colloidal nanogels for curcumin use alone or in combination with chemotherapeutic agents.

THE REQUIREMENT FOR A NANO-SIZED HERBAL MEDICINE DELIVERY SYSTEM

The following factors led to the selection of a nano-sized herbal delivery system as a means of overcoming the shortcomings of the conventional herbal medicine delivery systems:

1. By using nanoparticles to target specific organs, herbal medicines can be administered more

selectively, safely, effectively, and effectively reducing dosage and improving patient compliance in the process.

2. Better efficacy can be achieved by using nanoparticles to help localize the herbicide in a specific location and boost its solubility [8]
3. Their distinct size and large loading capacity seem to enable them to transport medications at high concentrations to disease locations.

NDDS improves herbal drug system's effectiveness by targeting individual organs, improving selectivity, solubility, and delivery. Nanoparticles enhance drug surface area, reducing toxicity and maintaining therapeutic effects, and can cross the Blood Brain Barrier.

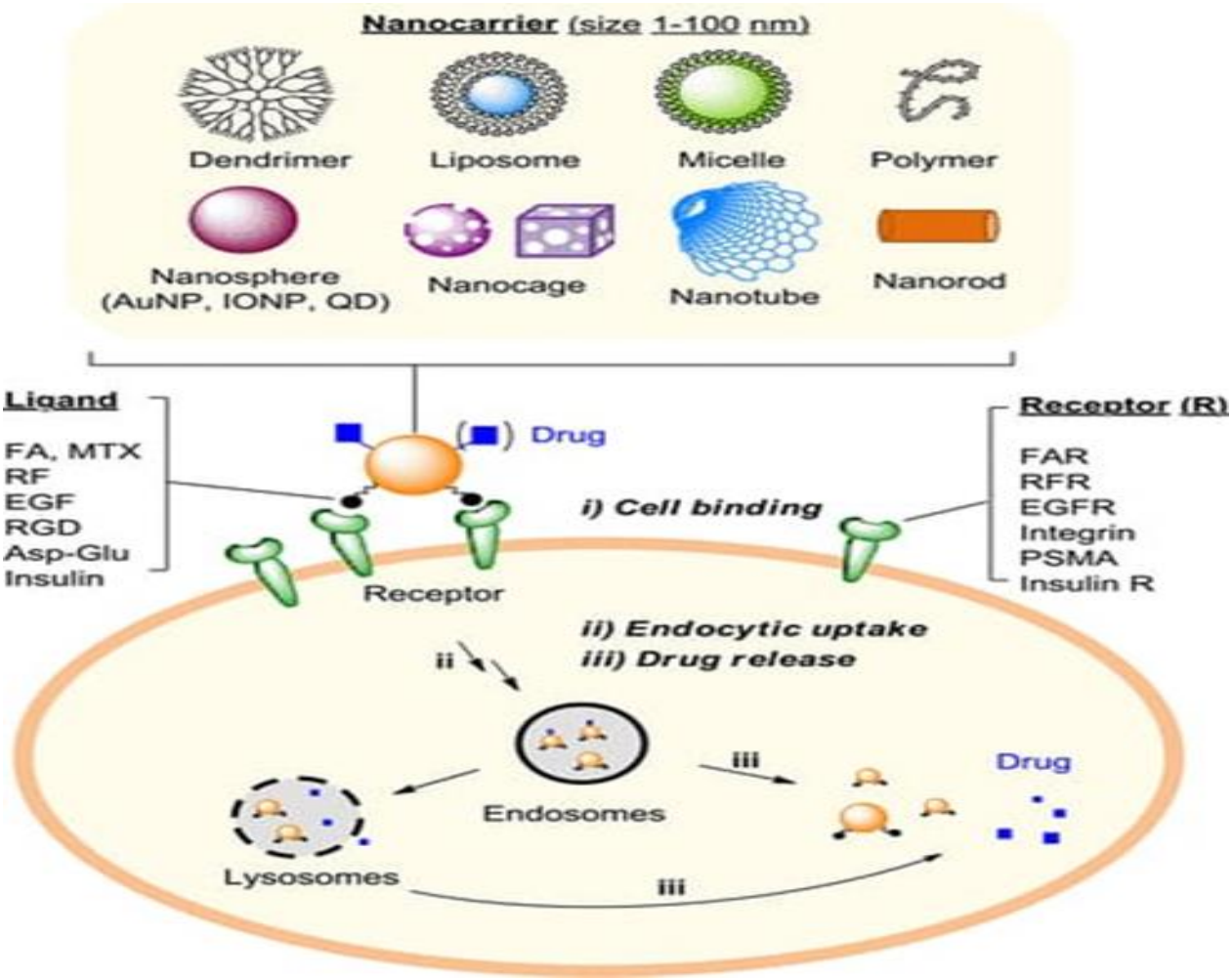

Fig 1: Release of drug molecules to the targeted site

REQUIREMENT FOR A NEW DRUG DELIVERY SYSTEM FOR "HERBAL REMEDIES": "NANO CARRIERS"

Many of the herbal drug's ingredients will be broken down in the stomach's extremely acidic pH before entering the blood, while other ingredients may be processed by the liver. As a result, the blood may not receive the ideal amount of the herbal medications. There won't be any way to demonstrate the medication's therapeutic impact if it doesn't reach the affected area in the ideal quantity at the "minimum effective level." When used to herbal medicines, nanocarriers will deliver the maximum amount of the medication to the site of action, avoiding all obstacles including the stomach's acidic pH and the liver's metabolism. This will also prolong the drug's circulation into blood.[9]

- The following characteristics of herbal treatments made them a viable drug candidate for distribution using a nano delivery system:

1. There are effective extracts in methanolic, petrol, acetone, and chloroform that might not be appropriate for distribution as such.

2. Since these are bulk medications, a dose reduction is planned.

3. Target specificity for a variety of chronic illnesses is Nano-sized delivery system was selected because of the following currently available formulations.

4. There are a few more adverse effects connected to the commercially available formulations.

5. Noncompliance from patients as a result of high dosages and inadequate efficacy with the current formulations.

NANOTECHNOLOGICAL STRATEGIES AS A NEW DRUG DELIVERY SYSTEM

Drug delivery system yielded an NDDS, a cutting-edge solution to the problems of conventional drug delivery systems.

The following factors led to the selection of a nanoscale delivery method :

• Because of their distinct size and large loading capabilities, they seem to be able to transport high concentrations of medications to illness locations.

• The concentration appears to stay at the sites for longer periods of time;

• The drug is delivered in small particle size that increases the drug's whole surface area and allocates faster breakdown in the circulation.

METHODS:

The following methods are frequently employed in the formulation:

1.Method of high-pressure homogenization:

Through a very high shear stress and high pressure (100–2000 bar), the lipid is pushed in this process, causing disruption of particles down to the submicrometer or nanometer range. A highly dependable and effective method for producing lipid drug conjugates, parenteral emulsions, nanostructured lipid carriers, and SLNs on a large scale is the high-pressure homogenization process. [10,11]

(A)Hot homogenization technique: This procedure will occur at a temperature higher than the lipid's melting point. When the medicine is loaded with melted lipids and heated surfactant aqueous solution is present, the pre-emulsion will form. The nanoparticles will eventually develop.

(B)Cold homogenization technique: Hot homogenization technique: This procedure will occur at a temperature higher than the lipid's melting point. When the medicine is loaded with melted lipids and heated surfactant aqueous solution is present, the pre-emulsion will form. The nanoparticles will eventually develop.[12]

2.Intricate coacervation technique:

This is the spontaneous phase separation of two liquid phases in colloidal systems caused by the interaction of two polyelectrolytes that have opposing charges when mixed together in an aqueous solution.

3.Method of co-precipitation:

The complicated coacervation method for the creation of nanoscale core-shell particles has been modified to create this technique. It has been found that using this approach gives weakly water-soluble medicines good dispersion stability.

4.Self-assembling techniques:

The physical process known as self-assembly occurs when previously disorganized atoms, molecules, or components arrange themselves into controlled nanoscale structures by chemical or physical processes on their own, without assistance from outside sources.

5.Solvent displacement method or nanoprecipitation method

The basis of this technique is the interfacial deposition of a polymer. Following the displacement of a semipolar solvent miscible with water from a lipophilic solution, the interfacial tension between the two phases decreases, increasing the surface area and causing the formation of tiny organic solvent droplets even in the absence of mechanical stirring.[13]

6. Polymerization technique:

This technique is based on the polymerization of monomers in an aqueous solutions. There are two methods utilized for the aqueous solution preparation.

a) Emulsion polymerization: In this process, monomer is emulsified in a nonsolvent phase.

b) Dispersion polymerization: In this technique, the monomer is dispersed in a non-solvent phase [14]

7. combined precipitation and homogenization [15,16] Precipitation and homogenization have the same fundamental ideas as nanoedge. In less time, a combination of these methods produces improved stability and smaller particle sizes. The nanoedge technology can address the primary shortcomings of the precipitation approach, including crystal development and long-term stability. By further homogenizing the precipitated suspension, this approach prevents crystal formation and reduces particle size.

CATEGORIES OR TYPES OF NANOMEDICINES

1. Nano crystals
2 .Nanocapsule
3. Polymeric nanoparticles
4. Dendrimers
5. Quantum dots
6. Metal and inorganic nanoparticles
7. Phospholipid micelles
8. Nanosphere
9. Magnetic nanoparticles
10. Colloidal nano- liposomes

CHARACTERIZATION OF NANOPARTICLES

A.In-vitro Evaluation :

a.Crystal structure and particle shape :

A combination of DSC and powder X-ray diffractometry (PXRD) is used to measure the particle dispersion's degree of crystallinity. By comparing the melting enthalpy/g of the bulk material with the dispersion's melting enthalpy/g, the rate of crystallinity using DSC is calculated. For such investigations, differential scanning calorimetry, or DSC, is most frequently employed. The extent of the drug's amorphous form and changes in crystallinity are frequently assessed using X-Ray Diffraction (XRD). The evaluation of both the crystalline state and the morphology of the particles aids in determining any polymorphism or morphological changes that a medication may experience during the nanosizing process.

b.Partical size or zeta potential :[17,18]

Zeta potential measurement is crucial for determining the physical stability of nanosuspensions, governed by the stabilizer and drug itself. Suspensions with a zeta potential above 30 mv are stable, while those below 20 mv have limited stability. Positively charged electrostatic stabilizers like chitosan can increase nanocrystal adhesion to the negatively charged GIT wall, enhancing oral bioavailability.

c. Paricle size and their distribution :

The mean particle size and distribution directly affect formulation solubility, dissolution rate, and physical stability. Particle size and polydispersity index (PI) govern solubility, dissolution velocity, and biological performance. Photon Correlation Spectroscopy (PCS), laser diffraction, and coulter current multisizer can determine particle size in the 3nm to 3μm size range.

d.Stability study:

The mean particle size and distribution directly affect formulation solubility, dissolution rate, and physical stability. Particle size and polydispersity index (PI) govern solubility, dissolution velocity, and biological performance. Photon Correlation Spectroscopy (PCS), laser diffraction, and coulter current multisizer can determine particle size in the 3nm to 3μm size range.[19]

e. The solubility and dissolution velocity at saturation:

Determining the saturation solubility and dissolution velocity is crucial since these two factors work together to predict changes in the drug's in-vivo performance, including blood profiles, plasma peaks, and bioavailability. The benefits that can be obtained over conventional formulations are reflected in the research of the saturation solubility and dissolution velocity of nanosuspensions, particularly when developing sustained-release dosage forms based on nanoparticulate medications. These are investigated at various pH levels in various physiological fluids. The Ostwald-Freundlich equations and the Kelvin equation can explain the rise in saturation solubility.

B. In –Vivo Evaluation :[20]

The in vivo assessment is unique to the medication and delivery method. The most often assessed parameters in vivo are:

- HPLC-UV Visible Spectrophotometry was used to quantify plasma drug levels.
  - Adhesion attributes

- Surface hydrophilicity/ hydrophobicity (determines contact with cells prior to phagocytosis)
- The relationship with bodily proteins

NANOTECHNOLOGICAL APPROACHES:

Polymeric Nanoparticles:

Colloidal systems with particle sizes ranging from 10 to 1000 nm are referred to as nanoparticles. In comparison to conventional herbal dosage forms, nanoparticles offer a number of benefits, such as increased absorption, dose reduction, bioavailability, efficacy, and solubility enhancement. [21]To get around triptolide toxicity and poor solubility, Liu et al. created triptolide-loaded poly (DL-lactic acid) nanoparticles.[22] In order to deliver curcumin to cancer cells, Sahu et al. created micellar nanocarriers using methoxy poly (ethylene glycol) - palmitate, a novel biodegradable and self-assembling polymer. The system was composed of hydrophilic methoxy poly (ethylene glycol), hydrophobic palmitic acid, and curcumin within controlled release of catechin.[23]

Microemulsion and Nanoemulsion:

A microemulsion is a liquid solution that is optically isotropic and thermodynamically stable, consisting of oil, water, and amphiphile. Microemulsion is regarded as the best substitute among medication delivery methods for the oral administration of poorly water-soluble substances. its ease of preparation, low viscosity, thermodynamic stability, improved bioavailability, and improved lipophilic drug solubility are just a few of its many benefits. Additionally, they can be given by a variety of methods, including pulmonary, ocular, parenteral, and transdermal. Docetaxel microemulsion was created by Yin et al. [24] in order to increase oral bioavailability. Similar to this, Wang et al. tried to increase curcumin's anti-inflammatory activity by combining it with an emulsion. [25]. Megha and colleagues developed a poly-herbal ointment with nanocapsules as an anti-inflammatory [26]. Zhang et al. created a medication that self-nanoemulsifies.

Quantum dots:

Semiconductor materials with luminous characteristics are used to create these nanoparticles. For biological applications, it is essential that the quantum dots be coated with another substance to facilitate the dispersion and stop the hazardous heavy metals from leaking. When exposed to ultraviolet light, quantum dots sparkle incredibly brightly. They can be covered in a substance that causes the dots to adhere only to the target molecule. Tumors practically glow when quantum dots attach themselves to proteins specific to cancer cells [27]

LIPOSOMES:

Liposomes are nanoparticles with lipid bilayer membranes surrounding an aqueous interior, used to improve drug efficacy and safety. They are classified into three categories based on size and lamellarity. Recently,'stealth liposomes' have been developed, allowing them to evade immune system interception and have longer half-life. Examples include Paclitaxel entrapped liposomes, Elastic Liposomes containing colchicine, and Liposomes entrapping essential oil.[28,29,30]

CERAMIC NANOPARTICLES:

These inorganic, porous structures have made a comeback as medication delivery technologies in recent years. Cancer treatment can make use of biocompatible ceramic nanoparticles as silica[31], titania, and alumina. The fact that these particles are non-biodegradable and can build up in the body to have negative effects is one of the main worries, though.

PROLIPOSOMES:

Although liposomes have several benefits for drug delivery, their physicochemical instability (aggregation, sedimentation, fusion, hydrolysis of phospholipids, oxidation, and sterilizing in large-scale manufacture) still presents certain challenges. Proliposomes, a revolutionary liposome synthesis technique, have been reported as a solution to these issues. When proliposomes come into touch with water, they instantly form liposomal suspension. Proliposomes are dry, freely flowing particles. Liposomes' solid characteristics aid in resolving their stability issues. A study on the oral bioavailability of proliposome-encapsulated dehydrosilymarin was carried out by researchers. When compared to its pure form, dehydrosilymarin proliposomes demonstrated an enhanced bioavailability and an encapsulation efficiency of over 90% [32].

NANOCARRIERS:

Nanocarriers encapsulating herbal drugs efficiently transport the drug through stomach acidity and liver metabolism, enhancing its prolonged circulation into the blood due to their small size.[33] Nanocarriers, including micelles, polymers, carbon-based materials, and liposomes, are used as transport modules for drugs, with their unique characteristics demonstrating potential in chemotherapy. Lipid-based carriers like liposomes and micelles, like gold nanoparticles, enable the effective delivery of hydrophobic and hydrophilic drugs throughout the human body, providing significant therapeutic benefits.[34]

CARBON NANOMATERIALS

Carbon nanomaterials like Fullerenes and Nanotubes, composed of 60 carbon atoms, offer numerous attachment points and functional tissue binding surfaces, while Nanotubes are widely used due to their high electrical conductivity and strength. Carbon nanotubes, categorized as single-walled (SWCNT) and multi-walled (MWCNT), are being utilized as functionalized components in nanoformulations for the delivery of therapeutic molecules.[35]

CONCLUSION

Herbal drugs have gained attention due to their potential to treat various diseases. However, issues like poor solubility, bioavailability, low absorption, instability, and unpredictable toxicity limit their use. Nanoparticles can help overcome these issues by delivering herbal medicines with better therapy. Nano-coating herbal drugs using methods like homogenization, sequentinoal simplex optimization, solvent evaporation, and precipitation techniques improve pharmacokinetic and bio-distribution of therapeutic agents, bypass blood barriers, and increase hydrophobic compound solubility and stability. Research combining traditional herbal remedies and nanotechnology has developed effective treatments for pharmaceuticals, potentially enhancing the significance of existing drug delivery systems.

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