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Novel Herbal Drug Delivery System

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Abstract: *Herbal formulation means a dosage form consisting of one or more herbs or processed herbs in specified quantities to provide specific nutritional, cosmetic benefits, and/or other benefits. Herbal preparations are obtained by subjecting whole plant, fragmented or cut plants, plants parts to treatments such as distillation, extraction, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates. Herbal drug itself is complex structure of many active constituents; As all of them provide synergistic action and enhance the therapeutic value. Herbal drugs have lesser side effects..*

Keywords: NDDS in herbal drugs, Approaches, Herbal excipient, Analytical aspect and applications of novel herbal drug formulations

I. INTRODUCTION

1.1 Definition of NDDS

Nanosized drug delivery systems (NDDs) are widely gaining attraction among scientific community as promising and innovative approach in combination therapy to increase the effect of co-delivered chemotherapeutic drugs because of their enhanced retention, permeability, extended blood circulation time, controlled release of drug, prevention of drug from degradation, maximum accumulation rate at targeted site, and minimum side effects on normal cell.

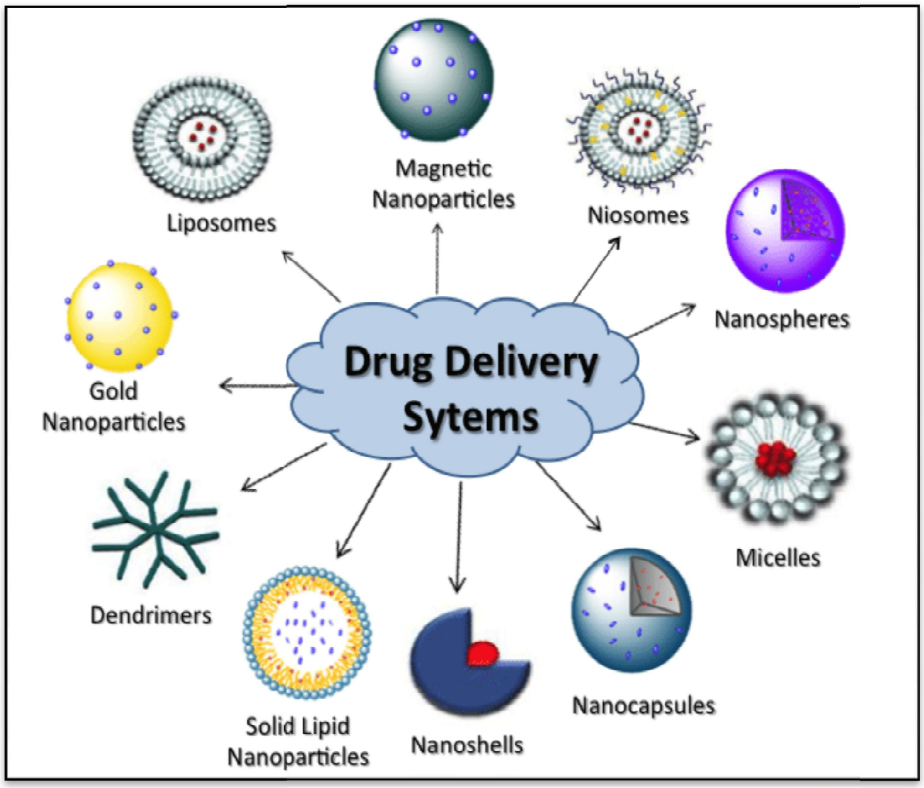

Figure 1: : Drug Delivery System

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Novel drug delivery systems can include those based on physical mechanisms and those based on biochemical mechanisms. Physical mechanisms also referred as controlled drug delivery systems include osmosis, diffusion, erosion, dissolution and electro transport. Biochemical mechanisms include monoclonal antibodies, gene therapy, and vector systems, polymer drug addicts and liposomes. Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms c Therapeutic benefits of some new drug delivery systems include optimization of duration of action of drug, decreasing dosage frequency, controlling the site of release and maintaining constant drug Level. The distinguished of addressing the desired sites for drug release: (i) Passive and (ii) Active targeting. Therapeutic benefits of some new drug delivery systems include optimization of duration of action of drug, decreasing dosage frequency, controlling the site of release and maintaining constant drug Levels.

1.2 Physicochemical and biological properties of herbal drugs: -

1. Physicochemical properties: -

- Solubility
- Partition co-efficient
- Hydrogen bonding
- Complexation
- Ionization of drug
- Redox potential
- Surface activity
- Protein binding

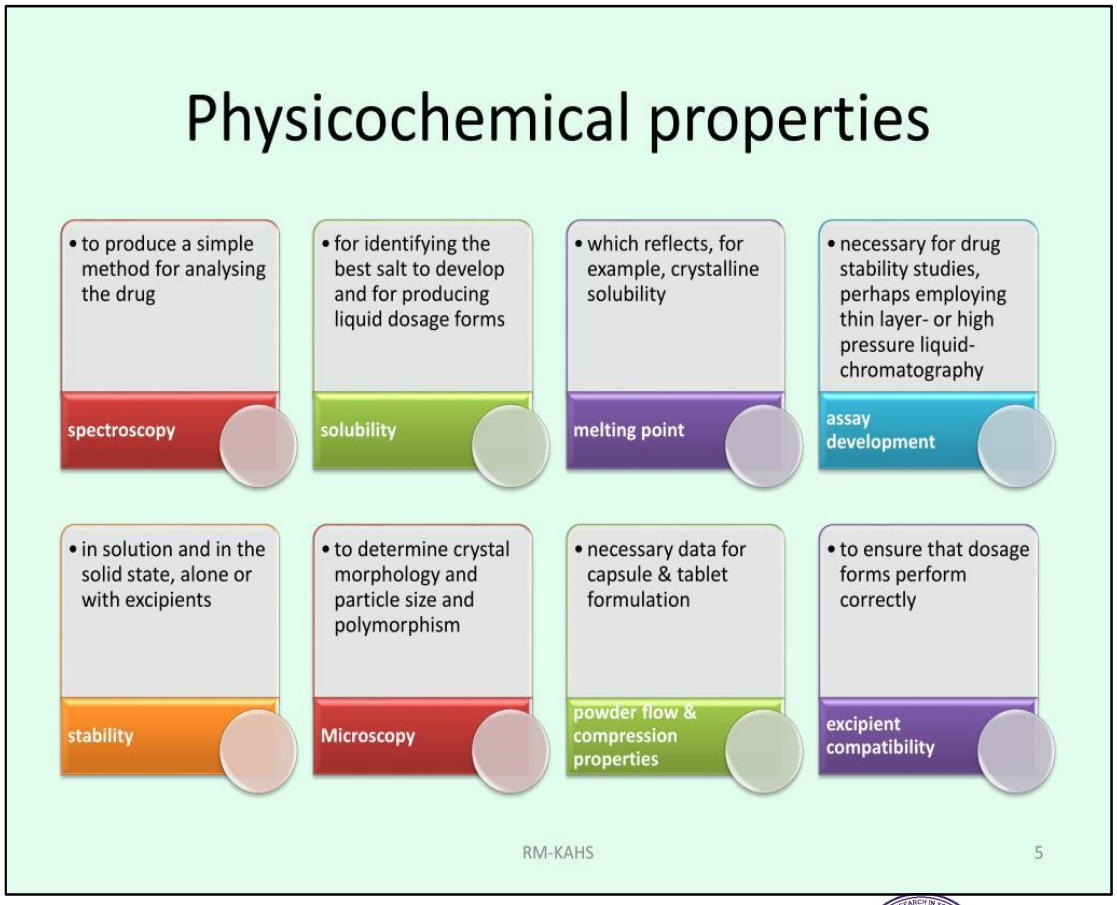

Figure 2 : physiochemical properties

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2. Biological properties

- Antimicrobial
- Anti-inflammatory
- Anti-oxidant
- Antiviral
- Antitumor

1.3 Selection of herbal drug and novel drug delivery system: -

Herbal formulations are defined as products that contain one or more herbs, processed herbs and other phyto-constituents in certain quantities and proportions to offer a range of benefits, including those related to nutrition, health, and beauty. Herbal preparations can be synthesized using a variety of processes, including extraction, distillation, fractionation, purification, fermentation, and concentration, on the entire plant, plant parts, or plant fragments. They consist of herbal compounds that have been pulverised or powdered as well as tinctures, extracts, essential oils, expressed juices, and processed exudates. The herbal remedy as a whole has a complexstructure with numerous active ingredients, all of which work together constructively to increase its therapeutic efficacy. Herbal medications can be recommended to minimize the adverse effects. The use of herbal medicines and phyto-constituents has emerged as a new approach to treating various health conditions. In recent times, people across the globe now tend to rely on herbal treatments.

New formulations and methods have been developed over time, furthering the science of medication administration. The delivery of effective medication is frequently challenged by the physiochemical properties of the drug and biological barriers like the skin and membrane linings of various human organs. Depending on the size, chemical structure, hydrophilicity, and ability to bind a specific receptor, drug qualities might vary greatly even when used to treat identical symptoms. Due to their insolubility in physiological fluids and restricted organ permeability, many medications have insufficient bioavailability. Additionally, some medications only have a therapeutic effect when they are present at a particular concentration; above and below that concentration, they have toxic side effects or have no therapeutic effect at all. The novel drug delivery system is a technique that facilitates the delivery of the drug to the site of action and significantly affects the medicine's efficacy. Hence, therapeutic effectiveness is based not only solely on the drug's activity when applied but also on its bioavailability at the target site.

Forever and a day, patients acquire medications through a range of conventional dosage forms like tablets, capsules, pills, creams, ointments, liquids, aerosols, injectables, and suppositories that are used as carriers to treat serious diseases or chronic illnesses. However, the fundamental challenge with this kind of drug administration was keeping the plasma drug concentration within the therapeutic range for a long time without fluctuation.

Conventional drug delivery is associated with systemic adverse effects that can be related to inconsistent drug release properties and non-specific biodistribution. Thus, a new delivery system is designed to facilitate the controlled release of payloads at the specified can reduce dosing frequency while keeping the drug concentration in the targeted organs and tissues for a prolonged period of time. Novel drug delivery system, the drug is either incorporated into a carrier system or the molecular structure is altered to modulate the dispersion of the drug. The novel drug delivery assists in increased bioavailability, stability, enhanced solubility, protection from toxicity, sustained delivery, and safeguarding from chemical and physical degradation.

1. Nano- particles
2. Microspheres
3. Dendrimers
4. Micelles
5. Phytosomes
6. Liposomes
7. Implantation
8. Microcapsules

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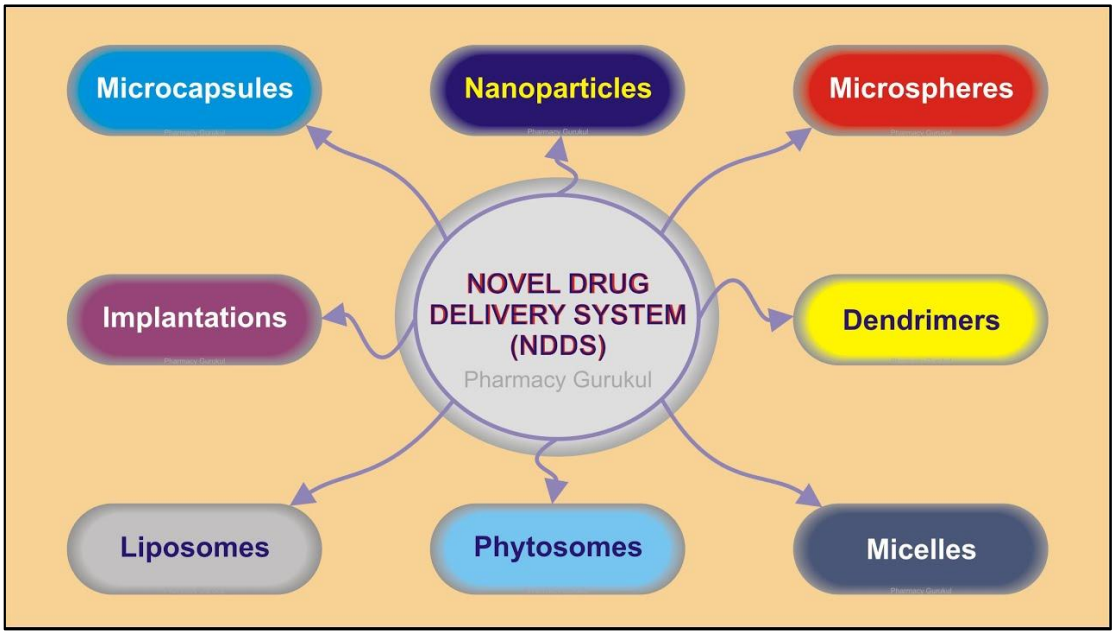

Figure 3: : Types of NDDS

1.4 Advantages and Disadvantages of in NDDS in herbal drugs

1. Advantages

- Increased solubility and bioavailability.
- Protection from toxicity.
- Increased pharmacological activity.
- Increased stability.
- Improved tissue macrophage distribution.
- Sustained delivery.
- Protection from physical and chemical degradation.

2. Disadvantages

- Their rapid clearance from circulation due to uptake.
- Leakage of encapsulation drug delivery during storage.
- Difficult in large scale manufacture and sterilization.
- Physical /chemical stability Very high production cost.
- Possibility of dumping due to faulty administer

1.5 Current challenges in upgrading and modernization of herbal formulation

a) Standardization Safety and efficacy assessment
b) Evaluating "drug" interactions
c) Communication of uncertainty
d) Pharmacological, toxicological, and clinical documentation
e) Pharmaco-vigilance
f) Constraints with clinical trials and people available.

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II. APPROACHES IN NOVEL HERBAL DRUG DELIVERY SYSTEM

Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Our country has a vast knowledge base of Ayurveda whose potential is only being realized in the recent years. However, the drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. If the novel drug delivery technology is applied in herbal medicine, it may help in increasing the efficacy and reducing the side effects of various herbal compounds and herbs. However, modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on.

Herbs are staging a comeback, herbal 'renaissance' is happening all over the globe and more and more people are taking note of herbal therapies to treat various kinds of ailments in place of mainstream medicine.The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio-recognition and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry and molecular biology.

As herbal novel drug delivery systems have lots of potential, several researches are working towards developing novel drug delivery systems like mouth dissolving tablets sustained and extended-release release formulations, mucoadhesive systems, transdermal dosage forms, microparticles, microcapsules, nanoparticles, implants etc. of herbs. If the novel drug delivery technology is applied in herbal medicine, it may help in increasing the efficacy and reducing the side effects of various herbal compounds and herbs. This is the basic idea behind incorporating novel method of drug delivery in herbal medicines. Thus, it is important to integrate novel drug delivery system and Indian Ayurvedic medicines to combat more serious diseases.

The future of medicine is rooted in the past, before chemists undertook to synthesize synthetic silver bullets for all those ailments, and before pharmaceutical companies hitched our collective health to what has become for them a multibillion-dollar wagon. Modern medicine cures a particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area.

Different types of Novel herbal formulations currently used in market

Over the past several years great advances have been made on development of novel drug delivery system (NDDS) for plant active & extracts the variety of novel herbal formulations likely polymeric nanoparticles, nano capsules, liposomes, phytosome, nanoemulsion, microspheres, transferors, and ethosomes has been reported using bioactive and plant extracts.

- Polymeric nanoparticles
- Nanocapsules
- Liposomes
- Phytosomes
- Nanoemulsion
- Microspheres
- Transferons
- Ethosomes

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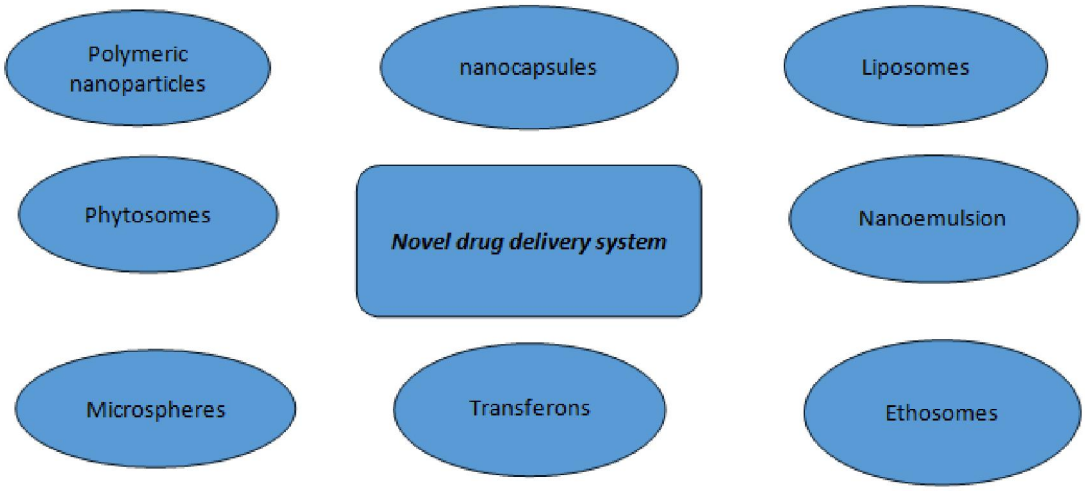

Figure 2.1: Types of NDDS

Method of preparation:

Nanotechnology

Current research into the role of engineered nanoparticles in drug delivery systems (DDSs) for medical purposes has developed numerous fascinating nanocarriers.

The methods by which the polymeric nanoparticles can be formulated from preformed polymers include solvent displacement/nanoprecipitation, solvent evaporation, dialysis, salting-out, emulsification/solvent diffusion, and supercritical fluid extraction of emulsions

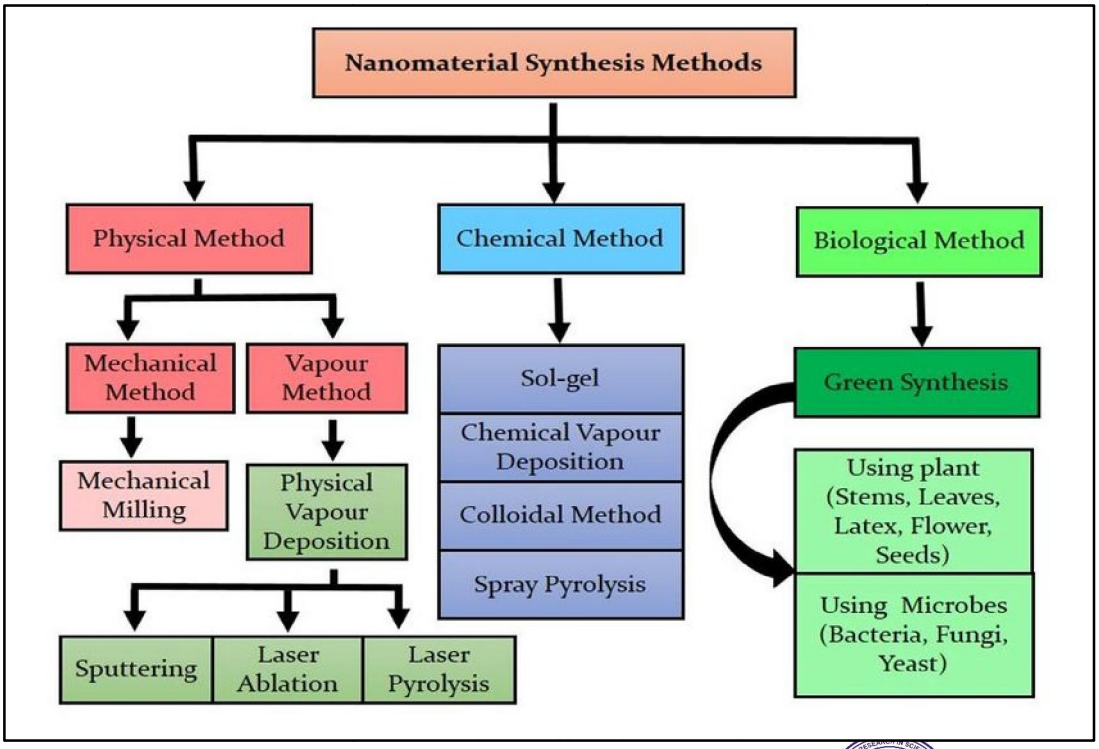

Figure 2.2: Method of Preparation

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The techniques commonly used for the formulation are:

1. High-pressure homogenization method
2. Complex coacervation method
3. Co-precipitation method
4. Salting-out method
5. Nanoprecipitation method or solvent displacement method
6. Solvent emulsification–diffusion method
7. Supercritical fluid methods.

Preparation of liposomes:

To prepare herbal liposomes, follow these steps:

1. Select Herbal Extract: Choose and prepare the herbal extract or essential oil you want to encapsulate.
2. Prepare Lipid Solution: Dissolve lipids (such as phosphatidylcholine) in an organic solvent like chloroform or ethanol.
3. Mix Herbal Extract: Incorporate the herbal extract into the lipid solution.
4. Evaporate Solvent: Remove the solvent using a rotary evaporator to form a lipid film.
5. Hydrate Lipid Film: Hydrate the lipid film with an aqueous phase (e.g., buffer or water) and sonicate or vortex to form liposomes.
6. Size Reduction: Optionally, use techniques like extrusion or high-pressure homogenization to achieve the desired liposome size.

Lipid Selection:

- Phospholipids: Common choices include phosphatidylcholine (PC), phosphatidylethanolamine (PE), and phosphatidylserine (PS). They help form the bilayer of the liposome.
- Cholesterol: Often added to stabilize the lipid bilayer and control membrane fluidity.

Dissolution:

Lipids are dissolved in an organic solvent like chloroform or methanol. The choice of solvent affects the efficiency of lipid dissolution and subsequent film formation.

Film Formation:

The solvent is evaporated under reduced pressure (using a rotary evaporator) to form a thin lipid film on the walls of the flask.

Hydration:

The lipid film is hydrated with an aqueous solution containing the drug or active ingredient. This can be done using a buffer or another aqueous medium, depending on the requirements of the drug.

Size Reduction and Homogenization:

Sonication:

Uses ultrasonic waves to disrupt the lipid bilayer and form smaller liposomes.

Extrusion:

Forces the liposome suspension through filters to achieve uniform size.

High-Pressure Homogenization: Applies high pressure to reduce liposome size and improve uniformity.

Characterization:

Evaluate liposome size, size distribution, morphology, and drug encapsulation efficiency. Techniques like dynamic light scattering (DLS), transmission electron microscopy (TEM), and drug concentration assays are commonly used.

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Stabilization and Storage:

Liposomes may be stabilized with cryoprotectants if freeze-dried (lyophilized) for storage. Stability is assessed over time to ensure liposome integrity and drug release.

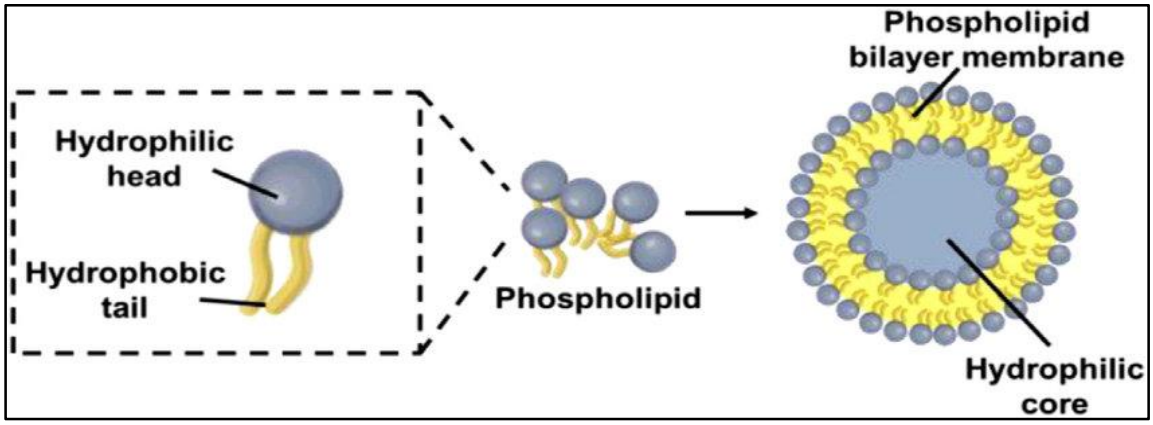

Figure 2.3: Liposome

ADVANTAGES:

- Very long-term stability.
- Good control over release kinetics of encapsulated compound.
- Nanoparticles can enhance the bioavailability of entrapped bioactive.
- Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
- Both hydrophobic and hydrophilic drug can be incorporated.
- Nanoparticles have longer clearance time.
- Different routes of administration can be Lyophilization is also possible.
- Dose accuracy and thus decreased toxicity.
- Suitable for combination therapy with two or more drugs.

DISADVANTAGES:

- Nanoparticles have low encapsulation efficiency.
- It may involve use of harsh toxic solvents in the preparation process.
- Small particles size and large surface area readily result in limited drug loading and burst release.
- Their small size and large surface area can lead to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms.
- They may cause immune response and allergic reactions in body.
- Loss of drug during storage.
- Water- soluble drugs can be rapidly leaked out in the presence of blood components.
- If any damage occurs at the molecular level then it is not possible to revert it.
- High water content of the dispersions (70-99.9%).
- The high manufacturing costs of nanoparticle leads in overall product cost.

III. HERBAL EXCIPIENTS

Herbal excipient are non-active ingredients that are mixed with therapeutically active compounds to make medicine they can have practical application and should be compatible with the active ingredients in the preparation

The use of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials. However advantages offered by these natural excipients are their being non-toxic, less expensive and freely available. The

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performance of the excipients partly determines the quality of the medicines. The traditional concept of the excipients as any component other than the active substance has undergone a substantial evolution from an inert and cheap vehicle to an essential constituent of the formulation. Excipients are any component other than the active substance(s) intentionally added to formulation of a dosage form.

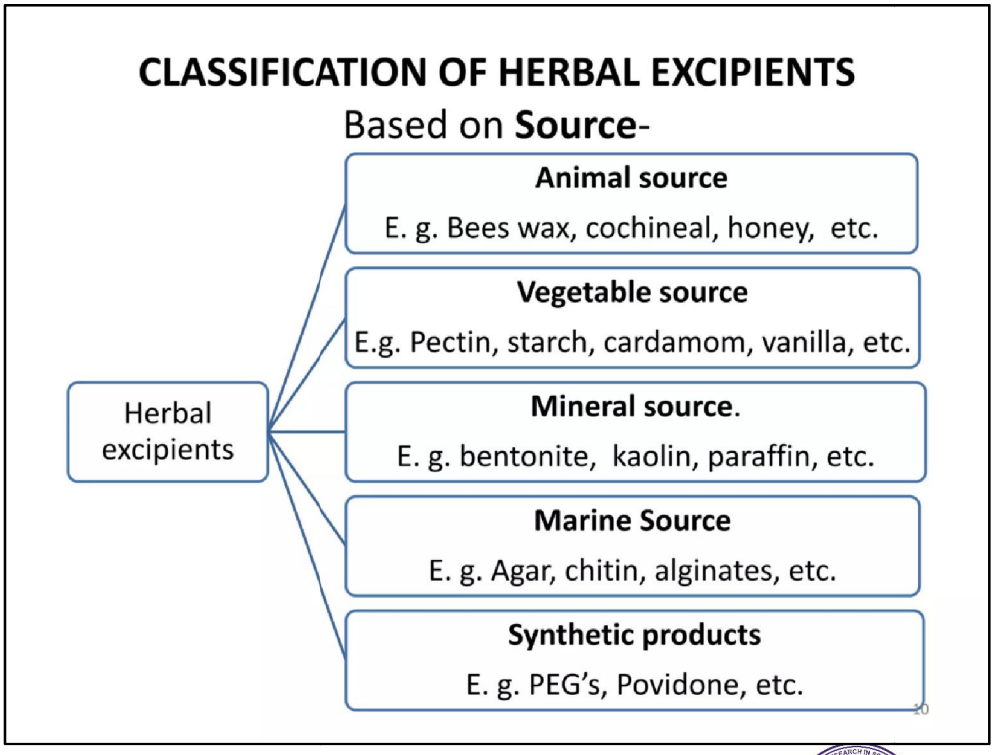
Excipients are primarily used as diluents, binders, disintegrants, adhesives, glidants and sweeteners in conventional dosage forms like tablets and capsules[1]. As the establishment of toxicity and approval from regulatory authorities poses a problem with synthetic excipients, of late more interest is being shown by researchers in herbal excipients. The drawback posed by heavy metal contamination often associated with herbal excipients is superseded by their lack of toxicity, easy availability, and economic considerations in pharmaceutical industry as compared to their synthetic counterparts. Present day consumers look for natural ingredients in food, drugs, and cosmetics as they believe that anything natural will be more safe and devoid of side effects.

The traditional view that excipients are inert and do not exert any therapeutic or biological action or modify the biological action of the drug substance has changed and it is now recognized that excipients can potentially influence the rate and/or extent of absorption of a drug. As herbal excipients are non-toxic and compatible, they have a major role to play in pharmaceutical formulation.

In the past, excipient was mainly employed to make up the bulk of the formulation since it included a strong medication that could not be taken on its own and to ensure that the medication was uniformly distributed in the dosage form. A large variety of excipients are employed in dosage forms, and they are attached in various concentrations and correspond to various administration routes, formulation states, and excipient strengths. Excipients are used as a stabilising agent for API in the formulation, which conforms the active compound are active & stable significantly till the self-life of the product to challenge with other similarities by masking unpleasant task and authorise to guarantee, that the required amount of the active ingredient reached the right place to the body at the estimated time

CLASSIFICATIONOF HERBAL EXCIPIENT :

Based on source:



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Sr no	Chemical nature	Role	Examples
1	Alcohols	For patient compliance	Volatile oils, poly phenolic compounds, lanoline
2	Ether/ester/aldehyde/carboxylic acid	For dose precision and accuracy	Fixed oil, citric acid
3	Glycerides and waxes	To enhance stability	Bees wax and lanolin
4	Carbohydrates	Assist in manufacturing process	Gum and mucilage
5	Hydrocarbon and halogen derivative	Dug tolerance	Paraffin and poly phenolic compounds
6	Polymers (natural and synthetic)	Ti avoid drug disaggregation	Cellulose, pectin
7	Minerals	Help in drug dissolution	Bentonite, talc
8	Protein	To prepare control release formulation	Gelatin and soyabean
9	Preservative , dyes, sweetener	To enhance absorption, to preserve, to make bitter taste and colour	Stevia, honey, henna, cochineal, polysorbates

Difference between herbal excipient & synthetic excipient :

Herbal excipient	Synthetic excipient
1.Source Derived from natural plant materials, such as roots, leaves, seeds, or flowers (e.g., gum acacia, starch from corn).	Man-made substances produced through chemical processes (e.g., polyethylene glycol, synthetic polymers).
2 composition Generally contain a complex mixture of natural compounds, including polysaccharides, proteins, and phytochemicals, which may have additional therapeutic benefits.	Typically consist of specific, well-defined chemical compounds that are designed for consistent performance.
3 functionality Often offer multifunctional benefits, such as acting as binders, stabilizers, and bioavailability enhancers while potentially providing health benefits.	Primarily designed for specific roles in formulations, such as enhancing stability, controlling release, or acting as emulsifiers
4 Biocompatibility Generally regarded as more biocompatible and are often perceived as safer due to their natural origins, although they can still provoke allergic reactions in some individuals.	While many are well-studied for safety and efficacy, some synthetic materials may cause sensitivity or adverse reactions in certain populations.
5 Cost & Availability Availability can vary based on environmental factors, cultivation, and harvesting practices, which can influence cost and supply stability.	Generally produced at scale and may be more readily available and consistent in quality.

Advantages herbal excipient :

1. Biodegradable- Naturally occurring polymer produced by all living organisms. They show no adverse effects on the environment or human being.
2. Biocompatible and Nontoxic- Chemically nearly all of these plant materials are carbohydrates in nature and composed of repeating monosaccharide units. Hence they are non-toxic.
3. Economic- They are cheaper and their production cost is less than synthetic material.

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4. Safe and devoid of side effect-They are from a natural source and hence, safe and without side effects.
5. Easy availability-In many countries they are produced due to their application in man.

Disadvantages of excipient

1. Microbial contamination– During production, they are exposed to external environment and hence, there are chances of microbial contamination.
2. Variation– Synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on environment and various physical factors.
3. The uncontrolled rate of hydration—Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary.
4. Slow Process– As the production rate is depends upon the environment and many other factors, it can't be changed. So natural polymers have a slow rate of production.
5. Heavy metal contamination– There are chances of Heavy metal contamination often associated with herbal excipients

Application of herbal excipient

- Stabilizers and Binders: Herbal excipients can enhance the stability of active ingredients and improve the cohesion of powder blends in tablet formulations.
- Flavouring Agents: Many herbal excipients possess pleasant aromas and flavours, making them useful in improving the palatability of oral dosage forms.
- Controlled Release: Some herbal materials can be formulated to provide controlled release of active compounds, prolonging their therapeutic effects.
- Thickeners and Gelling Agents: Herbal excipients can be used in topical formulations to create gels or creams, enhancing texture and application.
- Dilution Agents: They can serve as fillers or diluents in formulations, especially in the preparation of capsules and tablets.
- Bioavailability Enhancers: Certain herbal excipients can improve the absorption and bioavailability of active compounds.
- Sustainability: Utilizing herbal excipients can align with natural product trends and sustainability in pharmaceuticals.
- Safety and Compatibility: Herbal excipients are often perceived as safer alternatives compared to synthetic counterparts, making them attractive for natural and holistic formulations.

IV. ANALYTICAL ASPECTS OF NOVEL HERBAL FORMULATION

Preparation of rubusosidenanomicelle

Natural RUB encapsulated short-chain C6-Cer so as to form Cer–RUB nanomicelles (32 nm in diameter) that substantially enhanced Cer solubility and its levels in tissues and tumors of mice dosed intraperitoneally. Intriguingly, Cer–RUB nanomicelle treatments restored p53-dependent tumor suppression and sensitivity to cisplatin in OVCAR-3 ovarian cancer cells and xenograft tumors carrying p53 R248Q mutation. Moreover, Cer– RUB nanomicelles showed no signs of significant nonspecific toxicity to noncancerous cells or normal tissues, including bone marrow. Furthermore, Cer–RUB nanomicelles restored p53 phosphorylated protein and downstream function to wild-type levels in p53 R172H/þ transgenic mice. Altogether, this study, for the first time, indicates that natural Cer–RUB nanomicelles offer a feasible approach for efficaciously and safely targeting cancers carrying p53 missense mutations.

Materials and methods:

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Cer-RUB preparation and characterization

The nanomicelles were prepared via a solvent evaporation method, as described previously (32, 33). Briefly, C6-Cer (or NBD C6-Cer) and RUB (2:100 ratios in weight) were added and mixed in ethanol (at 1,000-fold w/v dilution) for optimal solubility. After filtration, the resulting ethanoic solution was allowed to stand at room temperature (22C) for 30 minutes, followed by evaporation under reduced pressure at 50C with agitation in a RAPIDVAP evaporation system until dry powder was obtained (Labconco). This Cer–RUB complex powder was stored at 20C until needed.

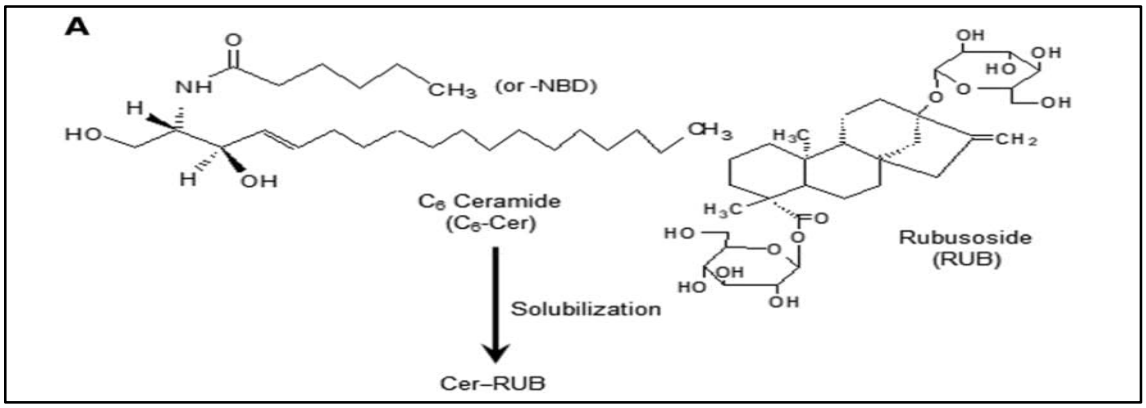

Figure 1.1: Characterization of Nanomicelle

Visualization:

C6-Cer was encapsulated in RUB, forming Cer–RUB complex (Cer/RUB, 1:20 w/w).

Particle size:

Transmission electron microscopy of Cer–RUB nanomicelles (70,000 magnification). TEM images revealed the average diameter of the nanomicelles is 32 4 nm in water.

Chromatography:

HPLC chromatograms of cellular NBD C6-Cer. Lipids were extracted from OVCAR-3 cells incubated with NBD Cer–BSA or NBD Cer–RUB (1 mmol/L; 30, 240 min) and analysed using HPLC. Cer, NBD C6-ceramide; GlcCer, NBD C6-glucosylceramide. NBD Cer levels in A2780 cells.

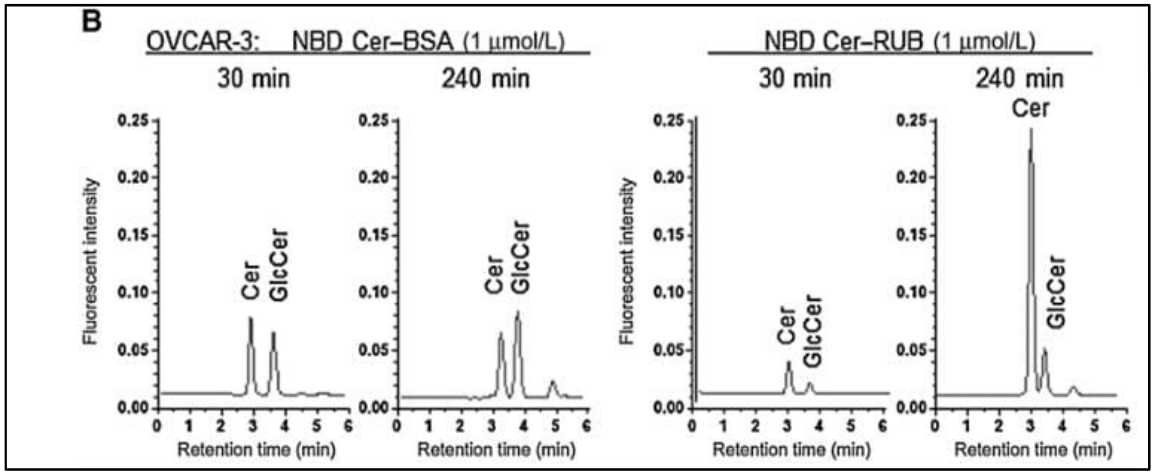

Figure 4.2: HPLC Chromatograms of cellular nanomicelle

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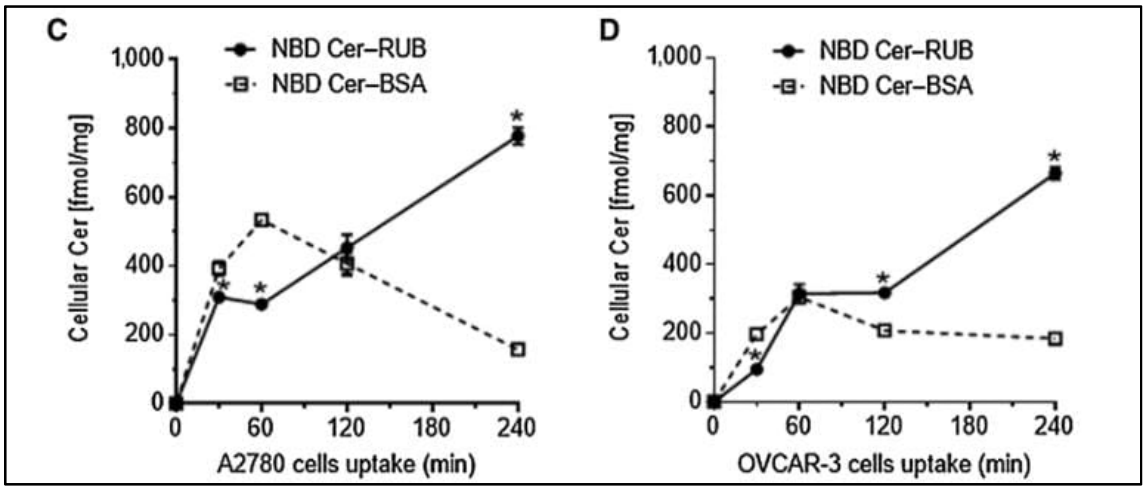

Figure 4.3: Nanomicelle at cellular level

In-vitro drug release study:

Cer levels in tissues of mice bearing A2780 tumors or OVCAR-3 tumors 3 hours following administrations.

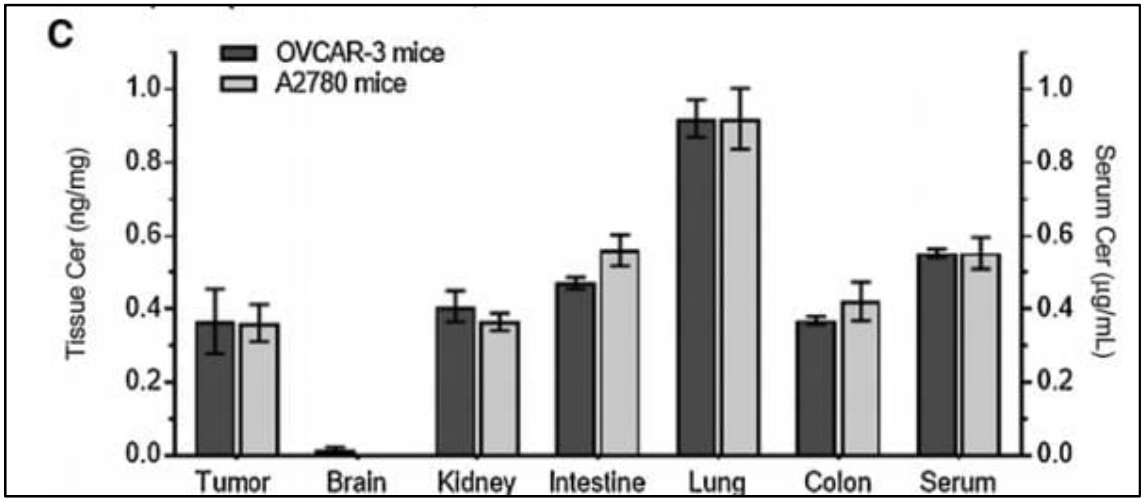

Figure 4.4: in vitro dug release

V. APPLICATIONS OF NOVEL HERBAL DRUG DELIVERY SYSTEM

5.1 Application of novel herbal drugs delivery system of Diabetes

- NDDS include enhancement of solubility, bioavailability, protection against toxicity, enhancement of pharmacological activity and stability, improve tissue macrophage distribution and protection against chemical degradation.
- To address the challenges related to bioavailability, novel nano-formulations have been devised for diabetes treatment.
- These formulations offer site-specific targeting, sustained release properties, enhanced bioavailability and improved therapeutic outcome.

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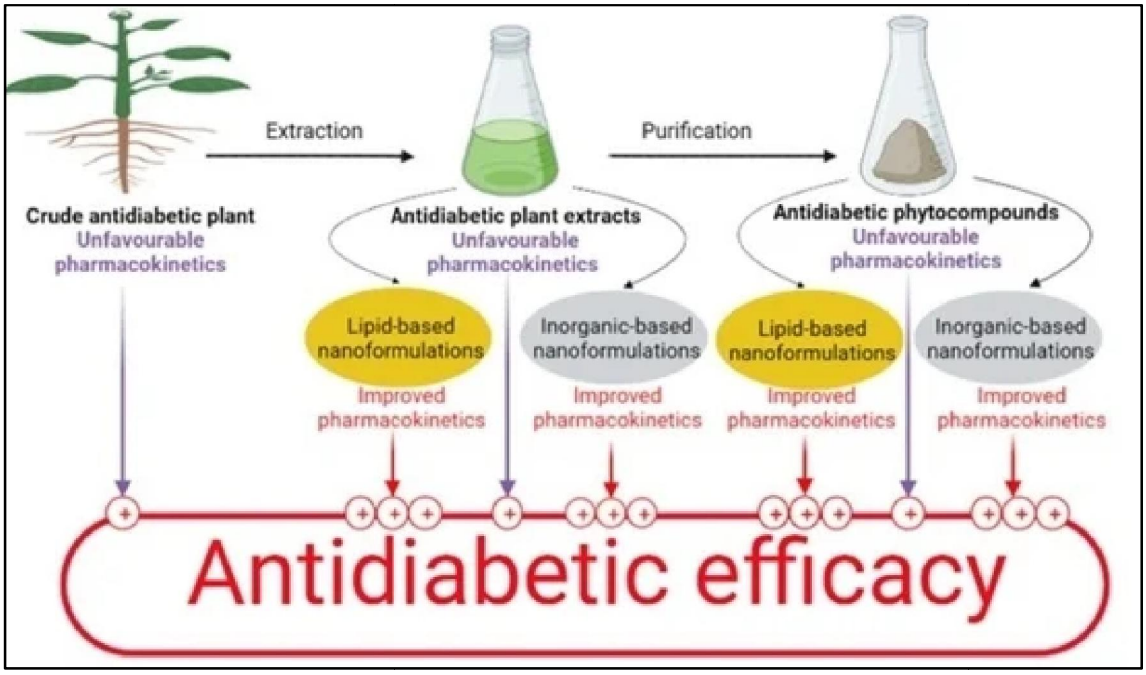

Figure 2.1: Application of NDDS

5.2 Application of novel herbal drugs delivery system in Hepatoprotective:

1. Liver-specific drug delivery platforms: These platforms can be used to improve the efficacy of drugs that act in the liver, while reducing systemic side effects. They can be made from lipid vesicles, inorganic nanoparticles, or biological systems.
2. Nanocarriers: Nanocarriers can be used to load natural plant extracts and enhance their efficacy. The size, shape, constituents, and surface properties of nanocarriers can be altered to tune their physiochemical properties.
3. Galactosylated ligand: This ligand can be used to target the liver by interacting with the asialoglycoprotein receptors on the surface of hepatocytes.
4. Other novel drug delivery systems include: polymeric nanoparticles, nanocapsules, liposomes, nanoemulsion, phytosomes, microsphere, and ethosomes. -The goal of NDDS is to increase the efficiency and safety of drug delivery, while also making it more convenient for patients.

5.3 Application of novel drug delivery system in antioxidants: -

- Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Antioxidants interact with and stabilize free radicals and may prevent some of the damage free radicals might otherwise cause. Free radical damage may lead to cancer.
- Several of the antioxidant molecules are labile to degradation in the presence of oxygen, water and light, hence it becomes all the more appropriate to use a delivery system which will augment their stability and hence enhance the performance.

5.4 Application of novel herbal drugs delivery system in cardiovascular disorders:-

Novel drug delivery systems (NDDSs) have many applications in the treatment of cardiovascular diseases (CVDs), including.

1. Drug-eluting stents and balloons : These devices ensure that drugs are delivered effectively and in sufficient quantities.

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2. Nanoencapsulation : This technique uses nanocarriers to deliver therapeutics in the cardiovascular space. Nanoencapsulation can use liposomes, nanogels, and layer-by-layer coating.
3. Nanoliposomes : These nano-sized vesicles are made of phospholipid membranes and are a promising drug-delivery system for CVDs.
4. Iron oxide nanoparticles (IONPs): These nanoparticles can improve the therapeutic potential of mesenchymal stem cells (MSCs) for myocardial infarction repair.
5. Nano-coating technology: This technology can be used to conceal nanomaterials and control the rate of administration of the coating agent.
6. Extrinsic stimuli: These drug delivery systems can be activated by an externally-triggered process. - NDDSs can help solve problems with conventional CVD treatments, such as poor water solubility, low biological efficacy, and drug resistance. However, there are some challenges with NDDSs, such as cytotoxicity.

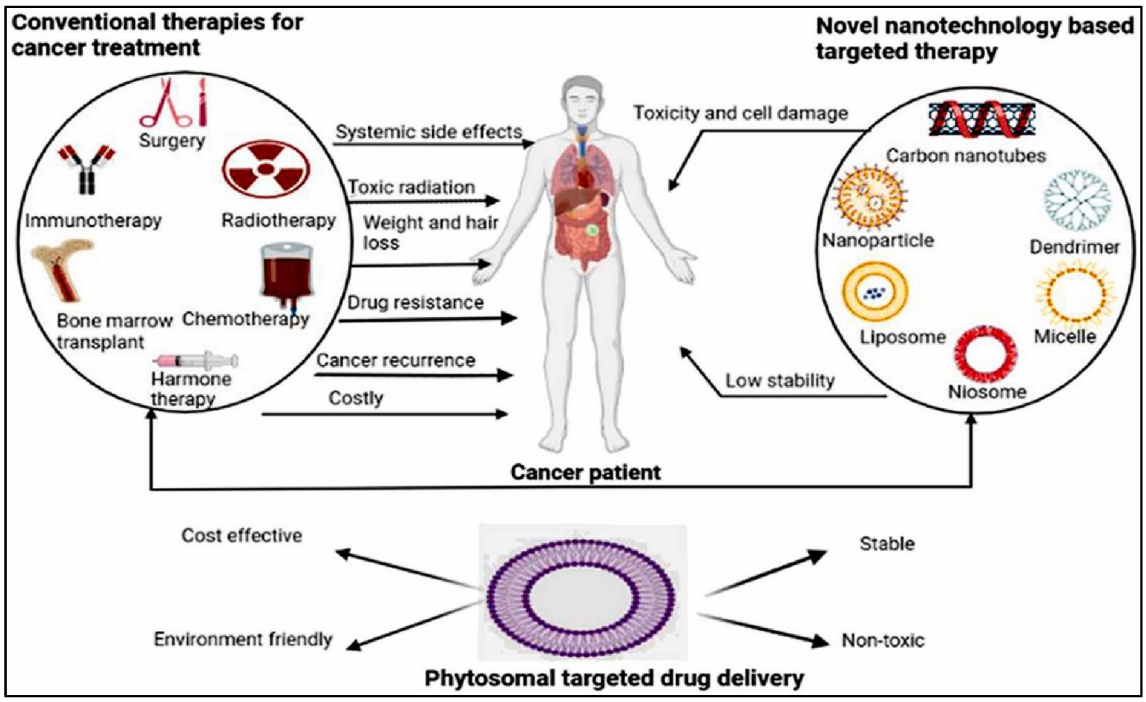

Figure 5.2: Applications of NDDS

5.5 Application of novel herbal drugs delivery system in any other major disorders of mankind

- Incorporation of novel drug delivery technology to herbal or plant actives minimizes the drug degradation or presystolic metabolism and serious side effects by accumulation of drugs to the nontargeted areas and improves the ease of administration in the paediatric and geriatric patients.
- Novel drug delivery approaches for improving therapeutic applications of berberine and berberine-rich herbal preparations.

VI. TARGETED HERBAL DRUG DELIVERY SYSTEM

Targeted drug delivery systems in cancer therapy aim to improve the efficacy and reduce the side effects of treatment by delivering drugs specifically to cancer cells. Here's a detailed overview of importers (molecules or mechanisms involved in drug uptake) and various approaches used in these systems.

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Importers in Targeted Drug Delivery

Receptor-Mediated Endocytosis:

Many cancer cells overexpress specific receptors that can be exploited for targeted drug delivery. For example, folate receptors (FR) are often overexpressed in certain cancers. Folate-conjugated nanoparticles can bind to these receptors, facilitating endocytosis and delivering the drug directly into the cancer cells.

Transport Proteins:

Membrane transport proteins, such as the glucose transporter (GLUT), can also be targeted. Many tumors exhibit increased glucose uptake due to their high metabolic rates, allowing glucose-conjugated drugs or nanoparticles to preferentially enter cancer cells.

Antibody-Drug Conjugates (ADCs):

ADCs utilize monoclonal antibodies that specifically bind to antigens expressed on cancer cells. Upon binding, the ADC is internalized, releasing the cytotoxic drug inside the cell. This approach has been successfully used in treatments like trastuzumab-emtansine (Kadcyla) for HER2-positive breast cancer.

Approaches in Targeted Drug Delivery Systems

Nanoparticle Systems:

Liposomes: Liposomal formulations can encapsulate hydrophobic drugs and target cancer cells through passive or active targeting. For example, Doxil, a liposomal formulation of doxorubicin, enhances drug delivery to tumors and reduces systemic toxicity.

Polymeric Nanoparticles: These can be engineered to respond to the tumor microenvironment (e.g., pH-sensitive or temperature-sensitive polymers) for controlled drug release.

Metallic Nanoparticles: Gold and silver nanoparticles can be modified to carry drugs or genes, enhancing their uptake by cancer cells.

Smart Delivery Systems:

pH-Sensitive Systems: These release drugs in the acidic environment of tumors. For instance, the use of polyacrylic acid-coated nanoparticles can facilitate drug release in the tumor's microenvironment.

Enzyme-Responsive Systems: These utilize specific enzymes that are overexpressed in tumors to trigger drug release. For example, matrix metalloproteinases (MMPs) can be targeted to release therapeutics in the tumor area.

Gene Delivery Systems:

Viral Vectors: Engineered viruses can deliver therapeutic genes specifically to cancer cells. This approach can be particularly useful in gene therapy, such as using adenoviral vectors to express tumor suppressor genes.

Non-Viral Vectors: Lipid-based or polymer-based systems can also deliver RNAi or plasmid DNA directly to cancer cells, facilitating targeted gene silencing.

Immunotherapy Approaches:

Checkpoint Inhibitors: Targeting immune checkpoints such as PD-1/PD-L1 enhances the body's immune response against cancer cells. These therapies often rely on targeted delivery to avoid systemic immune activation.

CAR-T Cell Therapy: Chimeric antigen receptor T-cell therapy modifies a patient's T cells to target specific cancer antigens, providing a tailored approach to treatment.

Combination Therapies:

Combining targeted drug delivery with other modalities, such as radiation or chemotherapy, can enhance therapeutic efficacy. For instance, delivering chemotherapeutic agents along with radiotherapy can optimize treatment outcomes.

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VII. CONCLUSION

Targeted drug delivery systems in cancer therapy represent a significant advancement in improving treatment specificity and reducing side effects. By utilizing importers and sophisticated delivery mechanisms, these approaches aim to enhance the therapeutic index of anticancer agents.

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