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APPLICATIONS OF NANOTECHNOLOGY IN ENHANCING THE BIOAVAILABILITY OF HERBAL MEDICINES

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- **Abstract**

The advancement of modern medicine has been pivotal in the fight against infectious diseases. However, due to the numerous side effects associated with conventional treatments, there has been a resurgence of interest in natural remedies, valued for their gentler impact on the body. Herbal medicines, rooted in centuries-old practices, have emerged as promising alternatives. Yet, their widespread adoption is impeded by challenges such as low bioavailability and solubility. Plant-based nanoparticles offer a potentially superior solution. Combining plant extracts with nanoparticles has shown to enhance bioavailability and solubility, thereby amplifying the effectiveness of herbal medicines. This review aims to highlight the pivotal role of nanotechnology as an innovative drug delivery system for herbal medicines, augmenting their therapeutic effects and bioavailability. It also explores the methodologies for formulating herbal nanoparticles and the rationale behind integrating herbs with nanoparticles. These insights are expected to steer future biomedical research and open up new avenues in this field. Recent advancements in nanotechnology have ushered in new opportunities for ongoing research, serving as a pivotal force in enhancing the therapeutic potential of phytomedicine and herbal remedies. Methodically crafted nanoparticles have significantly propelled the development of innovative herbal-nanomedicine (HNM). These nano formulations adeptly address challenges encountered by traditional herbal remedies. Extensive analysis of nanomaterial-herbal interactions has deepened our understanding of the HNM interface, facilitating the enhancement of phytochemicals and herbal remedies in terms of bioavailability, biocompatibility, pharmacokinetics, pharmacodynamics, and therapeutic index. A comprehensive HNM formulation seamlessly integrates all essential active ingredients into nano dosage forms, showcasing superior therapeutic indices compared to conventional phytochemicals and herbal remedies. This assessment underscores nanoscale herbal-nanomedicine as a promising avenue for therapy and drug delivery. The utilization of state-of-the-art techniques and current knowledge is imperative for HNM progression, potentially leading to the development of novel formulations and overcoming challenges in clinical pharmacokinetics and pharmacodynamics. The discussion emphasizes the therapeutic profile of HNM, encompassing critical pharmacokinetic and pharmacodynamic parameters such as absorption,

distribution, metabolism, and excretion, crucial for the formulation of safe and effective herbal-nanomedicine products.

- **Keywords:** Nanoparticles , Bioavailability , Nanotechnology , ,phytoconstituents

- **Introduction**

Traditional herbal remedies, though steeped in historical usage, often lack empirical backing. The rising belief in the safety of natural medicines over synthetics has driven increased use of phytopharmaceuticals. Yet, globally, uniform regulatory systems ensuring safety and efficacy are not firmly in place. Evaluating therapeutic and toxic activity of herbal medicinal products has made recent strides, but analytical advancements bring forth new active constituents, making it challenging to establish the pharmacological basis for efficacy. To design rational dosage regimens in phytopharmaceuticals, understanding bioavailability, metabolic pathways, and interactions with synthetic drugs is crucial.

The effectiveness of any drug, whether obtained from plant, animal, sea, or synthetic sources, relies on the capacity of the dosage form to transport the medication to its designated site of action at a rate and quantity adequate to trigger the desired pharmacological response. This property of the dosage form is commonly referred to as physiologic availability, biological availability, or simply bioavailability. For most drugs, the pharmacological response can be directly correlated with plasma levels. Hence, bioavailability is defined as the rate and extent of absorption of the unchanged drug from its dosage form. In specific instances, a rapid absorption is pursued when a quick onset of action is necessary for the treatment of acute conditions.

The optimization of bioavailability and therapeutic outcomes in the field of herbal-nanomedicine holds promise as nanotechnology advances, allowing for fine-tuning properties through the versatility of multifunctional nanoparticles and enhancing efficacy through the composition of herbal medicines.

Recognizing their historical importance and frequently resorting to them for accessibility and cultural reasons, herbal remedies continue to endure in numerous developing nations, illustrating a varied approach to healthcare influenced by historical, cultural, and economic factors.

Nanotechnology provides promising possibilities for creating herbal nanomedicine, improving features such as biocompatibility and biodegradability. Utilizing multifunctional nanoparticles enables customization of hydrophobic and hydrophilic traits, fostering the creation of advanced and potent herbal remedies with enhanced therapeutic potential.

Nanomedicine employs nanotechnology to produce tablets with a diameter smaller than 100 nm, especially in the realm of Chinese medicine and its compound preparations. This method shows promise for accurate drug delivery and improved therapeutic outcomes. Nanotechnology entails manipulating materials and systems at a molecular scale, and in the field of medicine, particularly nanomedicine, it has enabled the development of drug-delivery vehicles on a nanoparticle scale. These breakthroughs enable more precise and targeted drug delivery, ultimately amplifying treatment effectiveness.

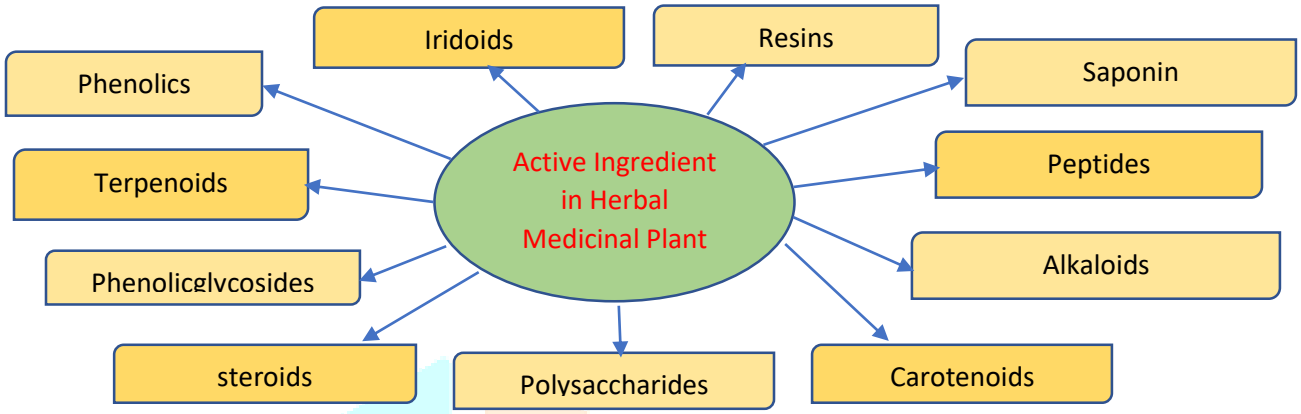
Phytochemicals, or secondary metabolites, are compounds synthesized by plants, showcasing varied biological activities and serving as the scientific basis for their use in traditional medicine. Promising drug delivery systems enhance the effectiveness of herbal drug delivery, ensuring the delivery of sufficient active compounds is crucial for the efficacy of any herbal product or medication.

Nanotechnology boosts herbal formulations, providing advantages such as enhanced bioavailability, stability, and solubility. Nano dosage forms play a role in controlled delivery, diminished toxicity, improved biological activity, and precise drug targeting, presenting a hopeful avenue for herbal drug research.

The increasing interest in the use of herbal medicines among the general population is fueled by the perception of them being gentler and safer, alongside growing clinical evidence demonstrating their therapeutic potential for various conditions.

The incorporation of carrier systems or structural modifications, integrating synthetic and natural drugs, shows significant potential in regulating distribution. Consequently, it improves efficacy and extends the duration of action in the body via innovative drug delivery systems.

Utilizing Nanoparticles in Innovative Drug Delivery Systems for herbal remedies provides a versatile benefit, refining therapeutic results via accurate targeting, improved absorption, and minimized side effects, ultimately enhancing the safety and efficacy of these treatments.

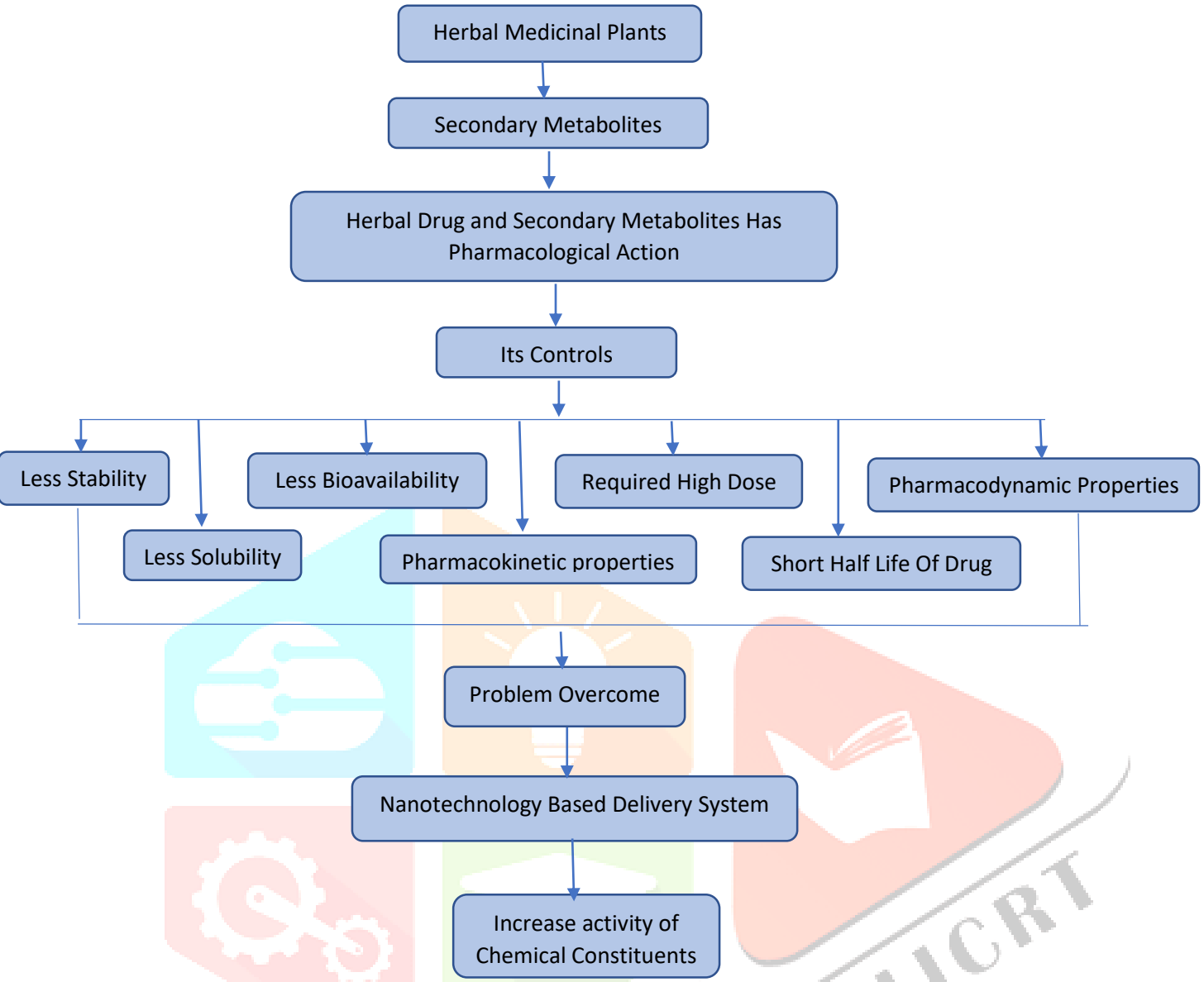


- **Nanotechnology**

Nanomedicine is transforming healthcare through the use of nanoscale materials for precise drug delivery and diagnostics. Nano-delivery systems allow targeted medication administration, reducing side effects and enhancing treatment outcomes. The field is advancing, promising personalized medicine and improved therapeutic interventions. Integrating nanotechnology with herbal medicine is a research focus, offering potential for increased activity, reduced dosages, and minimized side effects. This synergy contributes to widespread study and development in various fields, with nanotechnology playing a crucial role in novel drug delivery.

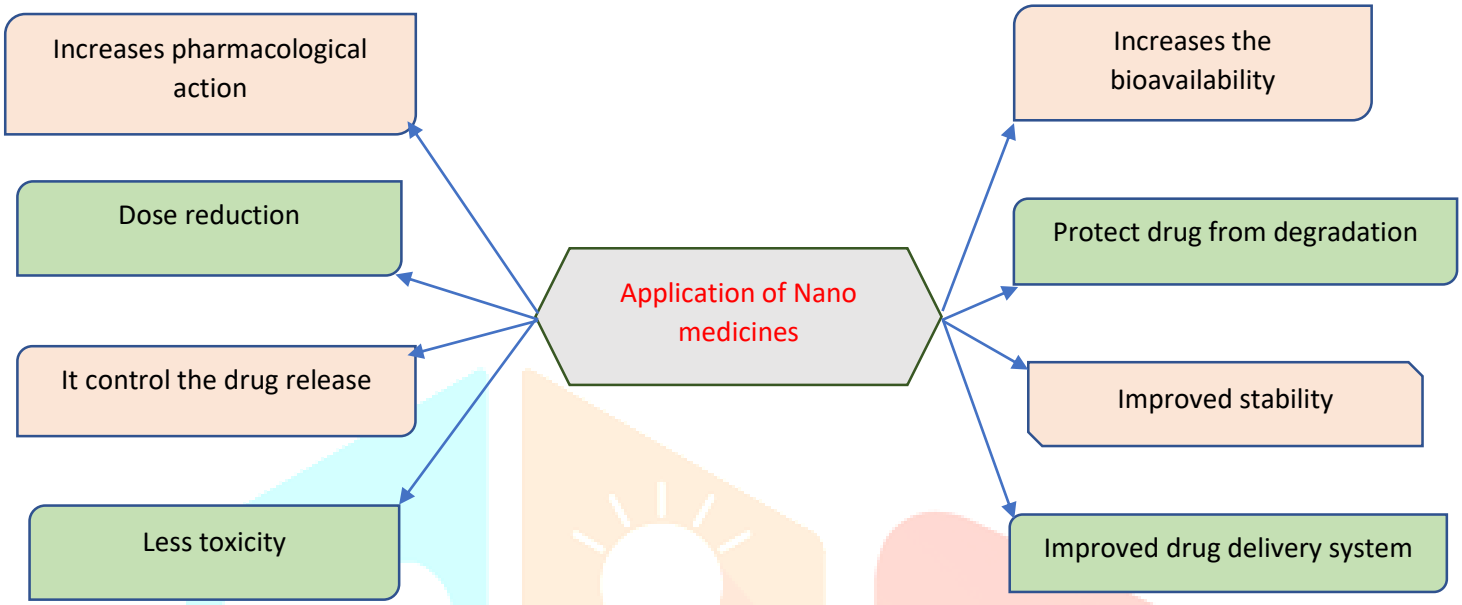
Nanotechnology is on the cusp of introducing a variety of innovative materials and approaches, transforming the medical and pharmaceutical field. Several areas of medical care are already experiencing the benefits provided by nanotechnology.

Nano formulations provide advantages such as enhanced permeability, solubility, bioavailability, therapeutic activity, stability, improved tissue distribution, and sustained delivery compared to conventional plant constituent preparations.


Herbal Medicinal Plants
Secondary Metabolites
Herbal Drug and Secondary Metabolites Has Pharmacological Action
Its Controls
Less Stability
Less Bioavailability
Required High Dose
Pharmacodynamic Properties
Less Solubility
Pharmacokinetic properties
Short Half Life Of Drug
Problem Overcome
Nanotechnology Based Delivery System
Increase activity of Chemical Constituents

- **Applications of Nanotechnology based medicines**

The incorporation of nanotechnology into herbal formulation research, termed nano phytomedicine, shows great potential. It tackles challenges in phytomedicine like solubility, bioavailability, toxicity, stability, and delivery, leading to improved efficacy and better herbal drug management. Benefits encompass enhanced tissue macrophages distribution, sustained delivery, and protection from degradation, indicating a promising future for advancing the effectiveness of herbal treatments.



- **Nanocarrier**

Nanocarrier technology employs nanomaterials to transport drugs, utilizing techniques like solid dispersion, inclusion technology, polymer nanoparticles carrier technology, and super emulsify nanometer dispersion technology, with each method playing a role in the overall impact. Nanocarriers are vital in drug delivery systems, providing the capability to encapsulate substances and improve drug administration through various routes. In topical formulations, they aid in achieving localized effects, targeting deeper tissues, and facilitating systemic effects via skin transportation.

- **Nanotechnology Based upon Chinese Herbal Medicine**

The ultra-fine crushing of particles in Chinese herbal medicine does, indeed, result in an augmented surface area, fostering the activation of atoms. This amplification enhances both physicochemical properties and biological activity not observable under typical conditions. As a result, the decoction time diminishes, solubility and dissolution rate advance, and overall effectiveness is heightened. This methodology is especially practical for medicines containing single ingredients, such as mineral medicine, or those with distinctive activities, providing a substitute for traditional crushing techniques.

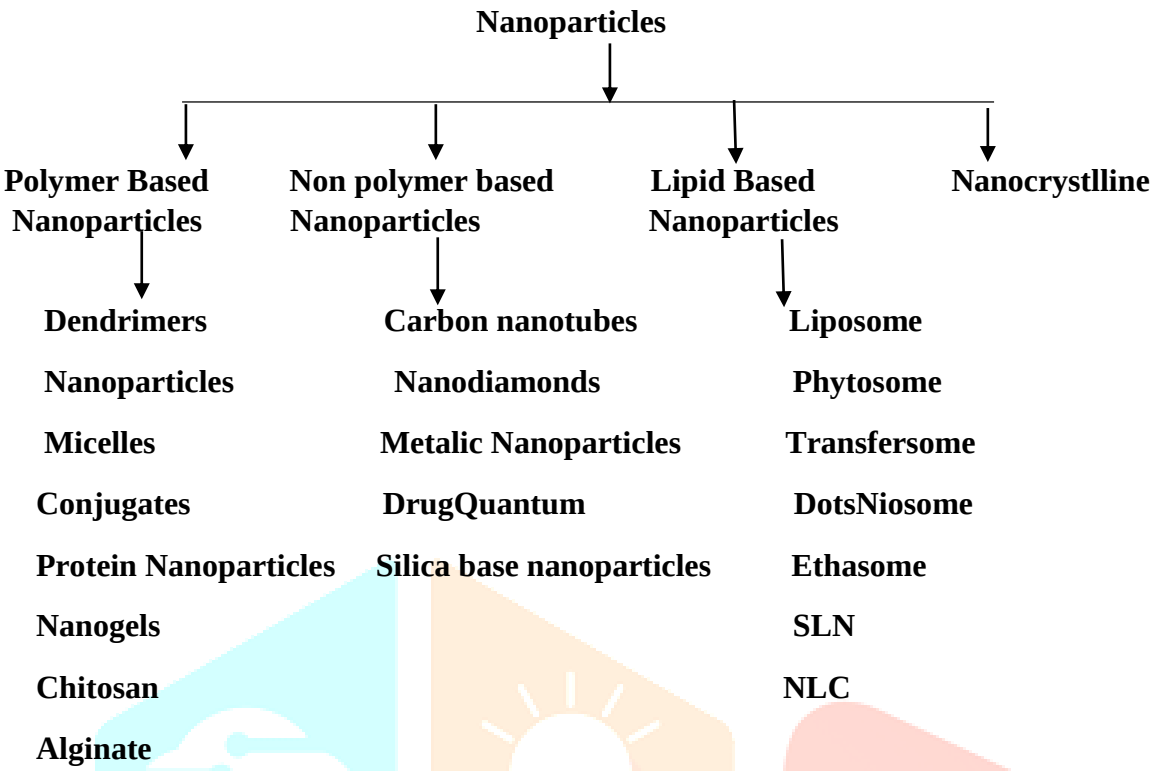
- **Bioavailability of the Herbal Drug**

Undoubtedly, integrating nanotechnology into phytomedicine involves employing strategies like reducing particle size, modifying surfaces, and incorporating micro or nano materials such as polymers. These approaches are designed to boost bioavailability and bioactivity by enhancing the delivery and absorption of phytomedicinal components.

Concerning Nano-Chinese medicine, the goal appears to be improving absorption by breaking down cell walls, increasing surface area, facilitating better dissolution, and extending the drug's residence time in the body. This has the potential to elevate the absorption levels of active ingredients.

The bioavailability of a drug or metabolite is a pivotal determinant of its effectiveness, governing how efficiently and swiftly the active component is absorbed into the bloodstream. This enables it to reach its designated site of action within the body.

- **Types of Nanoparticles**



- **Preparation of drugs in nanoparticles**

Methods like co-precipitation or sol-gel processes are frequently employed for nanoparticle synthesis, offering control over size, shape, and composition by adjusting reaction conditions in a solution. The subsequent steps you highlighted aid in depositing and stabilizing the nanoparticles on a substrate.

- **Properties of Nanoparticles**

1) They act as a link connecting bulk materials to atomic or molecular structures.
2) The high surface area to volume ratio in nanoparticles enhances diffusion, making sintering occur more efficiently at lower temperatures and in shorter durations than with larger particles.
3) The robust interaction between nanoparticle surfaces and the solvent enables suspensions, preventing materials from sinking or floating in a liquid despite the usual density differences.
4) Nanoparticles often reveal unexpected optical characteristics because of electron confinement and quantum effects arising from their small size. A case in point is the deep red to black color exhibited by gold nanoparticles in a solution.
5) Particles with both hydrophilic and hydrophobic characteristics, known as Janus particles, demonstrate significant effectiveness in stabilizing emulsions. They have the ability to self-assemble at water/oil interfaces, serving as solid surfactants.
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- **Nanoparticles Compress With the following materials**

1) Biodegradable Polymers
2) Inorganic Materials
3) Lipids
4) Organic materials

5) Polysaccharides
6) Good Compatibility Polymers

- **Role of nanoparticles**

1) Rich the drug at the site of action
2) Combination of treatment of two different drugs
3) Administering the drug in a small particle size is crucial, as it increases the overall surface area of the drug, promoting quicker dissolution in the bloodstream.
4) The drug delivery system is tailored to target in a specific manner.
5) The penetration of drugs through epithelial and endothelial barriers.

- **Method of Preparations of Nanoparticles**

1) Ionic Gelation

The versatility of ionotropic gelation makes it a valuable tool in pharmaceutical and biomedical applications. The ability to control drug release, co-encapsulate molecules, achieve site-specific functionalization, and extend the bioactivity of drugs enhances its significance in various therapeutic formulations and drug delivery systems. The versatility of ionotropic gelation makes it a valuable tool in pharmaceutical and biomedical applications. The ability to control drug release, co-encapsulate molecules, achieve site-specific functionalization, and extend the bioactivity of drugs enhances its significance in various therapeutic formulations and drug delivery systems.

2) Emulsion Diffusion

The emulsion-diffusion method is a technique used in polymer chemistry for nanoparticle synthesis. The first step involves creating an emulsion by mixing a partially-miscible solvent in water with a polymer-containing solution, along with an aqueous phase containing a stabilizer. This emulsion sets the foundation for the subsequent steps in the process.

3) Film Dispersion

It enhancing biopolymer films with nanoparticles, specifically montmorillonite, to improve their properties. Various dispersion techniques like mechanical homogenization, colloidal milling, and ultrasonic processing were employed. The dispersion quality was assessed by analyzing particle size and zeta potential. Films were then produced with different nanoparticle concentrations using spreading techniques, followed by characterization of physical and functional properties.

4) Solvent Evaporation

The factors collectively influence the size, morphology, and stability of the nanoparticles produced through the emulsification solvent evaporation method.

5) Antisolvent Precipitation

The Anti-solvent precipitation is a widely employed method for controlling the crystallization of substances in pharmaceutical and chemical manufacturing, providing a way to obtain desired particle sizes and forms for the drug.

6) High Pressure Homogenization

Using a mechanical approach, high-pressure homogenization achieves cell disruption by propelling cellular jets at high velocity against solid surfaces. The cell suspension is then pumped to a high pressure in a compression chamber.

7) Thin Film hydration method

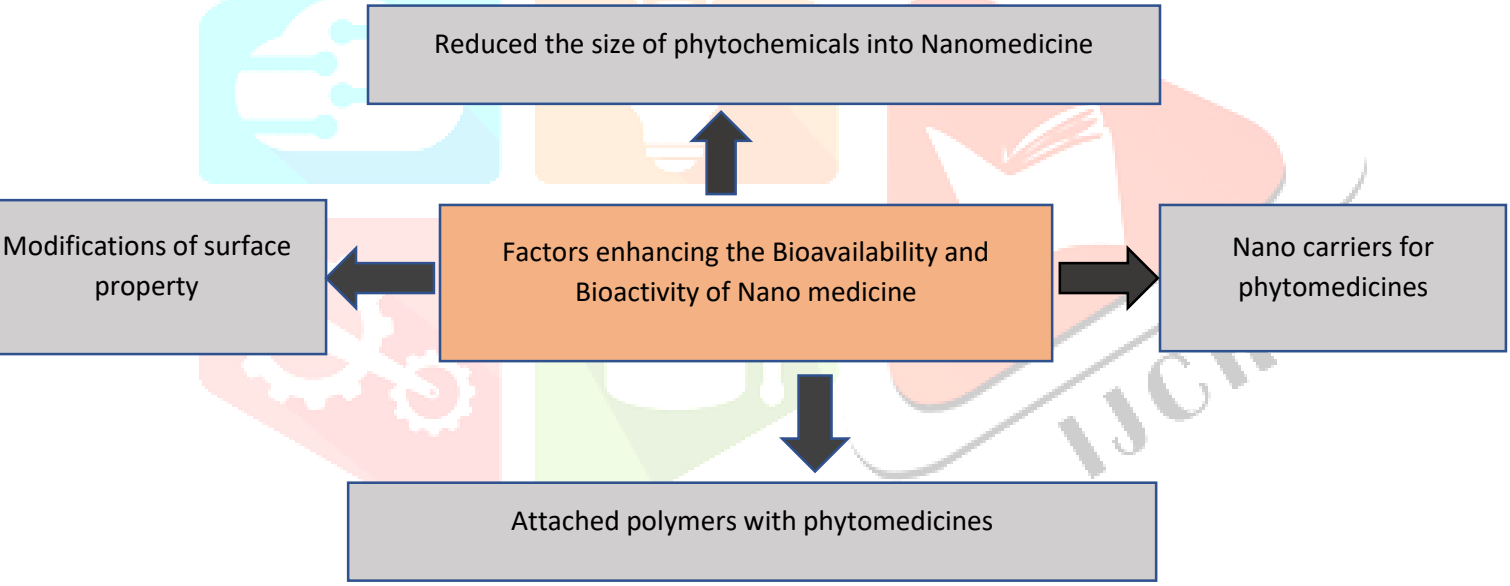
This procedure involves forming a thin lipid film in a round-bottom flask by removing the organic solvent. Upon introducing and agitating the dispersion medium, it results in the generation of heterogeneous liposomes. Finally, homogeneous small liposomes are obtained through extrusion using polycarbonate membranes.

- **The Use Of Bioavailability Enhancer Used in Nanotechnology**

Bioavailability enhancers, also referred to as bioenhancers, play a vital role in enhancing the effectiveness of drugs by improving their absorption, interaction, and receptivity at the cellular level, all without demonstrating significant pharmacological activity on their own.

Strategies focused on enhancing the dissolution rates and solubility of BCS Group II compounds in gastrointestinal fluids are pivotal for boosting bioavailability. This optimization effectively addresses challenges related to insufficient absorption, ultimately improving the compounds' effectiveness.

The collective modulation of plasma membrane fluidity, tight junctions, and active efflux processes by bioenhancers works collaboratively to enhance the bioavailability of drug molecules. This, in turn, leads to improved absorption and overall effectiveness in the bloodstream.



- **Formulation of Nanoparticles Its pharmacological action and also Its uses**

- **Medicinal uses of nanotechnology and Nano medicine**

SL No.	Nanoparticles Name	Active Ingredient	Method Of Synthesis	Biological Activity	Applications Of Nanoparticles Formulations
1)	Colchicine	Rutin Colchicine	Complex Coecervation Method	Antigout	Highskin Penetration

			Rotary evaporation sonification method		
2)	Curcumine	Curuminoid	Micro-emultion technique Curcumin phospholipid Complexation Encapsulation with sonication Solvent emulsion evaporation Hot homogenization Desolvation Method Wet milling technique	Anticancer Anti-inflammatory Anti-malarial Antinociceptive Antioxidant Antimicrobial Antitumor Antipsoriatic	Improved the biological activity on targeted site More bioavailability increased permeation High skin penetration
3)	Aloevera	Aloe -emodin Aloesin Acemannan	Anti solvent precipitation method	Antioxidant Protection of skin	Increased Bioavailability Improved skin penetration
4)	Taxus baccata	Paclitaxel	Nanoprecipitation Thin film hydration method	Antineoplastic Anticancer	It use against tumours, ovarian cancer and also breast cancer It is Ph sensitive
5)	Quercetin	Flavonide	Ethanol injection sonication method Nanoprecipitation technique High speed homogenization	Anti- liver toxicity Antioxidant Anticancer	Improved antioxidant activity Improved skin uptake High skin penetration

			Phase reversal technique Reversed evaporation technique Oil in water evaporation method		Protect skin from UV radiation It is use in the harmons therapy It contains less dose Easy to cross blood brain barrier It contains low dose
6)	Chitosan	Rutin	Complex coacervation method	Blood cloting	It use to treat cardiovascular disorder It act against cerebrovascular disorder It decreases the cholesterol level in the body
7)	Radix salvia	R.SalviaMiltirrhiza	Phospholipid complex method Spray drying technique	Hepatoprotective Antioxidant effect Coronary heart diseases Anti-hyperlipidaemia Antianginal	Improve the bioavailability Enhanced blood stasis It act against cerebrovascular diseases
8)	Genistein	Proteins Genistin	Spontaneous emulsification Nano emulsion method Chitosan Microsphere method	Anti-inflammatory Antioxidant Anticancer	Improve skin penetration It act against cardiovascular disorder It use to treat osteoporosis It act against breast cancer and also uterine cancer
9)	Garlic	Organosulfur Compounds	Reversible phase evaporation	Anti-hepatic	Impro the bioavailability

10)	ArtemissiaAnnua	Artemisinin	Film method Sonication method Self assembly procedure	Anticancer	Sustained drug release
11)	Berberine	Berberin	Emulsion Ionic Gelation	Anticancer Anti-inflammatory	It release drug slowly Increase the bioavailability
12)	CentellaAsiatica	Triterpenoids Madecassic acid	Ionic Gelation	Anxiolytic Anti-anxiety Anticancer	It is use to treat leprosy It cures the allergic reaction
13)	Camptothecin	Alkaloid	Encapsulated with hydrophobically modified glycol	Anticancer	It inhibit the DNA topoisomerase
14)	Catechins	Epicatechin Epicatechin gallate Epigallocatechin	Reverse phase evaporation	Antioxidant Anti-obesity Anti-inflammatory	Improved the bioavailability
15)	Silymarins	Silymarins	Cold homogenization Reverse evaporation technique	Hepatoprotective Anticancer	It act against liver disorder It act against breast cancer Improved Bioavailability
16)	Ginkgo Biloba	Flavonoids	Combination of dry and wet process Phospholipid complexation	Alzheimer dementia Antioxidant Anti -cardio vascular diisorder	Improved the satability
17)	Triptolide	Triptolide	Nano encapsulation Emulsification Ultrasound	Anti-inflammatory Anti-arthritis	Improve the penetration of drug Increase water solubility Improved the hydration
18)	Glycyrrhizic Acid	Glycyrrhizic acid	Phase inversion temperature method	Anti-inflammatory Antihypertensive	Increase the bioavailability of drug

				Antiviral Anti-ulcer Anti-tumor	Improved stability High penetration in transdermal layer
19)	Naringenin	Naringenin Flavonoids	Nano precipitation	Hepatoprotective Antioxidant Anti-inflammatory	Enhance the solubility Increase release of NAR
20)	Taxol	Taxol	Ionic gelation method	Anti-cancer Antianginal	Increase bioavailability and sustained released of drug
21)	Annualmugwort	Terpenes Phenols	Hydrophilic encapsulation	Anti -malerial Anti-asthmatic	
22)	Cynara scolymus	Cynara	Spray drying technique	Nutritional supplement	It controls the release of nutrition
23)	Garlicin	Garlicin	Reverse phase evaporation	Anti-Hepatic	Improved efficiency It increase bioavailability
24)	CuscutaChinensis	Flavonoid Lignans	Nano suspension method	Antioxidant Anti -Hepatic	It increase water solubility
25)	Tulsi	Eugenol	Hydro thermal synthesis Micro emulsion Solgel process	Anti-viral Anti-inflammatory	It use to prevent the food It used as a mouth washes It has wound healing property

Certainly, nanomedicine harnesses the power of nanotechnology to engage with biological molecules at a nano scale, unlocking novel physical properties and extending the scope of research and applications, both externally and within human cells. The distinct volume/surface ratio at the nano scale presents innovative opportunities for medical progress.

- **Advantages of nanotechnology**

1) Enhanced drug solubility for a highly lipophilic compound
2) Adjustable physical and chemical characteristics
3) Focused drug delivery
4) Controlled and sustained release of the drug
5) Reduced drug toxicity or side effects
6) It is used for diagnostic tool
7) It used in the cell therapy

8) Used as a biomaterials
9) Used for signaling molecules
10) Improved tissue engineering

- **Disadvantages of Nanotechnology**

1) Insufficient understanding of how nanoparticles impact biochemical pathway and processes within the human body
2) Insufficient toxicological assessment studies lead to unpredictable genotoxicity
3) Carcinogenesis
4) Metabolism and elimination differ depending on the material utilized in nanopartical synthesis
5) Limited self life

- **Conclusion**

Leveraging nanotechnology in herbal medicine can revolutionize pharmacy by efficiently processing data, recognizing patterns, and predicting, providing a transformative opportunity to predict ASR and reduce medication errors. This application allows healthcare professionals to boost patient safety, optimize treatment plans, and enhance medication management processes, preventing errors in pharmacy.

- **Acknowledgement**

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