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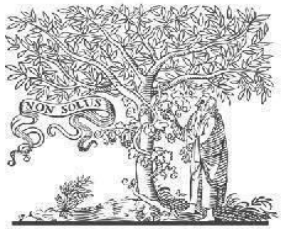

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INNOVATIVE DRUG DELIVERY APPROACHES: EXPLORING NANOSUSPENSIONS AS PHYTOSOMES

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ABSTRACT:
Background: Phytosome technology represents a significant advancement in herbal drug delivery, enhancing the bioavailability and efficacy of phytochemicals. This review examines the structure, biosynthesis, and regulation of polyphenols in plants and their practical applications. It also explores the therapeutic potential of phytoconstituents as immunomodulators and their broader health benefits.
Body: The review highlights the role of phytosomes as biocompatible nanocarriers for active pharmaceutical ingredients, particularly in improving the solubility and permeability of hydrophilic bioactive compounds with low bioavailability. Various nanotechnologies, such as nanosuspensions and phyto-phospholipid complexes, are discussed as methods to enhance the absorption and bioavailability of active ingredients. Phyto-phospholipid complexes, in particular, significantly increase membrane permeability and the oil-water partition coefficient, leading to improved absorption and bioavailability compared to free active components.
Conclusion: Phytosome technology offers a promising solution to the challenges of poor absorption of active components in medicinal formulations. By employing nanosuspensions of phytosomes, researchers can enhance the dissolution rate and bioavailability of phytopharmaceuticals. This review underscores the potential of phytosomes and nanosuspensions as innovative delivery systems for improving the therapeutic efficacy of phytochemicals across various applications.

KEYWORDS: Phytosome, Nanosuspension, Nanotechnology, Dissolution rate, Bioavailability.

INTRODUCTION:

Phytosomes (herbosomes) are structures created by the stoichiometric reaction of phospholipids in a non-polar solvent with standardized extracts or polyphenolic components. Phytosomes offer numerous advantages: they protect active components in crude extracts from destruction by gut bacteria and gastrointestinal secretions, and their production is straightforward, requiring minimal equipment, space, and relatively inexpensive materials. These characteristics facilitate scalability. Composed of biodegradable lipids generally regarded as harmless, phytosomes enhance the bioavailability of active phytochemical components by easily permeating and traversing lipid-rich biological membranes.

The use of nanocrystalline active pharmaceutical ingredients (APIs) has increased the dissolution rate of orally delivered medicinal formulations. Nanosuspension, an emerging nanotechnology, involves dispersing nanocrystalline medicines in a colloidal solution with stabilizers such as poloxamer, tween, polyvinyl alcohol, and lecithin. Phytosomes are also recognized as biocompatible nanocarriers that can improve the solubility and permeability of phytopharmaceuticals. They are particularly beneficial for hydrophilic bioactive chemicals with low bioavailability and absorption, either due to larger molecular sizes or very low solubility, which inhibits their diffusion through lipid biomembranes.

Phytosomes are self-assembled nanocarriers based on the phospholipid complexation technique, involving hydrogen bonding complexation between phospholipids and phyto compounds. This hydrogen bonding complexation increases physical stability, thereby enhancing the absorption and bioavailability of phytoconstituents.

Modification Techniques for Enhanced Bioavailability:

To address the challenge of poor absorption, several techniques have been proposed, including the creation of emulsions, liposomes, nanoparticles, and the alteration of chemical structures and administration as prodrugs. Among these, phyto-phospholipid complexes, also known as phytosomes, have shown significant promise in enhancing the bioavailability of active ingredients. Phytosomes are formed by complexing active components with phospholipids at specific molar ratios and conditions. Amphipathic phospholipids act as "ushers," helping active substances pass through the gastrointestinal cell membranes and eventually reach the bloodstream. The formation of phospholipid complexes gradually increases the membrane permeability and oil-water partition coefficient of the components, making them more easily absorbed and bioavailable compared to free active components. This approach has successfully improved the bioavailability of several active components.

Nanosuspensions, with particle sizes ranging from 50 to 200 nm, have a significantly higher dissolving rate than traditional suspensions (0.5 to 10 µm). A new formulation of complex-loaded nanosuspensions has been developed, which enhances the in vivo dissolution and absorption rate of phytosomes. This strategy leverages the reduced particle size to increase the solubility and bioavailability of active ingredients.

The study of antimicrobial activity is essential in the search for new methods to combat microbial resistance. Researchers are exploring both natural and synthetic sources to find effective antimicrobial agents. Various testing methods, such as disk diffusion and dilution techniques, are employed to evaluate the efficacy of these agents. Understanding antimicrobial properties is crucial for developing treatments against resistant pathogens and addressing global health concerns.

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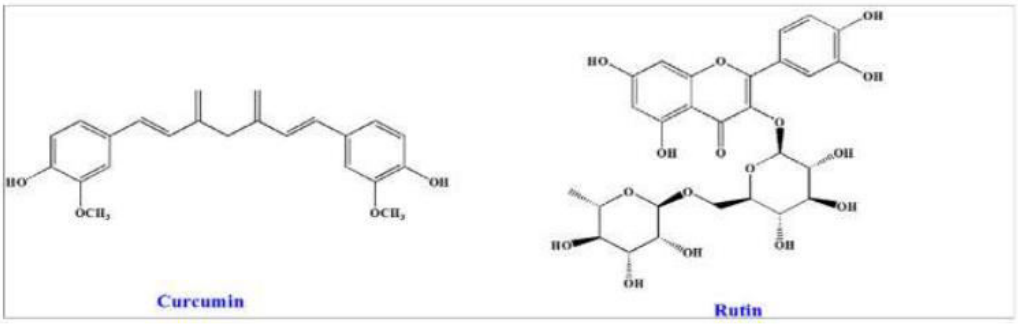
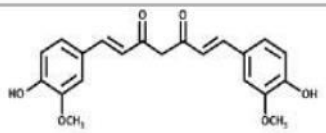
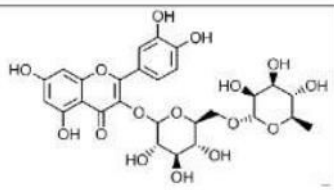


Fig. 1 – Polyphenols structure: (a) Curcumin, and (b) Rutin

Table 1: Properties of Curcumin and Rutin

Sl no.	Polyphenol	Structure	Uses	References
1.	Curcumin		1. Used in the management of oxidative and inflammatory conditions, metabolic syndrome, and anxiety. 2. It is used in cosmetics in Thailand. 3. Also used colorant in China.	(15)(16)
2.	Rutin		1. Its potent antioxidant and anti-inflammatory activities. 2. Also Prevent neurodegenerative disorders, cardiovascular diseases, and skin cancer	(17)

FACTORS AFFECTING NANOSUSPENSIONS

1. **Stabilizers:** Stabilizers are crucial in nanosuspensions to ensure effective wetting of drug particles, preventing Ostwald ripening and agglomeration. Stabilizers such as lecithins, povidones, and polysorbates enhance physical stability by impeding these phenomena. Lecithin is particularly favored for developing autoclavable nanosuspensions suitable for parenteral administration.
2. **Organic Solvents:** For creating nanosuspensions with emulsions or microemulsions, it is essential to use pharmaceutical-approved, less hazardous solvents like isopropanol, methanol, ethanol, or chloroform. Safer, somewhat water-miscible solvents such as benzyl alcohol, ethyl acetate, or ethyl formate are preferred over riskier alternatives like dichloromethane to meet strict safety and pharmaceutical compliance standards.
3. **Co-Surfactants:** The choice of co-surfactant in nanosuspension development using microemulsions significantly affects internal phase uptake and drug loading, impacting phase behavior. While bile salts and dipotassium glycyrrhizinate are commonly used, other solubilizers like transcutol, glycofurol, ethanol, and isopropanol are also suitable for microemulsion formulation without introducing undue risks.

APPLICATIONS OF NANOSUSPENSIONS

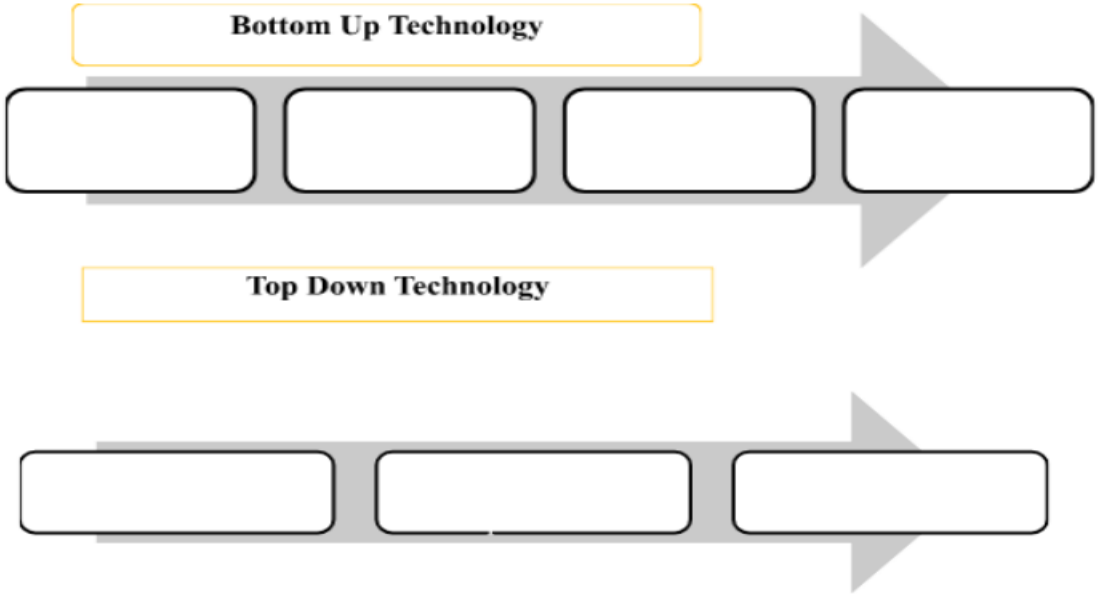
1. **Ocular Application:** Topical ocular medication delivery is widely used for treating both external and internal ocular conditions. Depending on the target site (e.g., cornea or conjunctiva for conjunctivitis, blepharitis, or keratitis sicca; or inner eye tissues for glaucoma

or uveitis), the delivery approach is tailored. Drug bioavailability in the eyes is limited to around 5% due to factors like blink reflex, fluid drainage, and enzymatic breakdown. After application, drug molecules are temporarily retained in the precorneal area, and they must pass through tissues like the cornea and conjunctiva to reach the inner eye. The choice of technique for ocular drug administration depends on the medication's properties, desired release profile, and safety considerations, requiring a balance between effective delivery and potential side effects.

2. **Topical Application:** Inhalers and nebulizers are used to deliver aerosols directly into the lungs, offering local and systemic therapeutic options for lung diseases. Local application benefits include higher medication concentrations and selectivity, while the pulmonary route is increasingly explored for systemic distribution due to its avoidance of first-pass metabolism and large alveolar surface area. Effective delivery depends on various parameters, including aerosol characteristics and respiratory system clearance. Optimizing aerodynamic parameters is crucial, considering the needs of the patient and the medication properties, necessitating customized delivery systems.

PREPARATION OF NANOSUSPENSIONS

Nanosuspensions are generally prepared using two main techniques: "Bottom-up technology" and "Top-down technology.



CONCLUSION:

The integration of nanosuspension technology with phytosome delivery systems marks a significant advancement in drug delivery. Encapsulating active ingredients within nanoscale particles, nano-suspended phytosomes enhance solubility, bioavailability, stability, and targeted delivery of poorly soluble drugs. This innovative approach offers numerous advantages over traditional phytosome complexes, including increased surface area for better absorption, improved stability, targeted delivery to specific sites, and faster onset of action. The synergistic combination of nanotechnology and phytosome technology holds great promise in revolutionizing drug delivery systems, ultimately leading to improved therapeutic efficacy and patient outcomes.

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