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A Review on Herbal Nanosuspension from Herbal Extract

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ABSTRACT: Herbal nanosuspensions have emerged as a promising strategy to overcome the challenges associated with the poor solubility and bioavailability of many herbal extracts. This review explores the advancements in herbal nanosuspension research, highlighting their preparation methods, characterization, and potential applications

Nanosuspension, which consists of nanosized herbal drug particles dispersed in a liquid medium, offer increased surface area, enhanced dissolution rates and improved drug delivery. Various techniques including high pressure homogenization, media milling and antisolvent precipitation have been employed to formulate stable nanosuspension from a wide range of herbal extract.

Nanosuspensions, which consist of nanosized herbal drug particles dispersed in a liquid medium, offer increased surface area, enhanced dissolution rates, and improved drug delivery. Various techniques, including high-pressure homogenization, media milling, and antisolvent precipitation, have been employed to formulate stable nanosuspensions from a wide range of herbal extracts.

The resulting nanosuspensions have demonstrated improved therapeutic efficacy in various in vitro and in vivo studies. This review also discusses the challenges and future directions in the development of herbal nanosuspensions, emphasizing the need for standardized protocols, stability studies, and clinical trials to fully realize their potential in herbal drug delivery.

1. Introduction

Nanosuspension

The 21st century has seen the rise of nanotechnology as a significant and promising field of research, particularly in the creation of nanoparticles with diverse sizes and shapes, offering notable potential benefits for clinical applications. Nanotechnology introduces numerous tools and strategies for advancement of therapeutics and pharmaceuticals. In the current time it plays a significant role in development of biological medicines and improving the bioavailability of plant derived drugs. The nanosizing of herbal drugs is new era of discovery in this field.[1] Nanosuspension is a type of colloidal dispersion, characterized by submicron drug particles within the nm size range and maintained in a stable state through the use of suitable surfactant or polymeric stabilizers.[4] Nanoparticle drug formulations typically feature particle size below 1 mm with a common average size between 200 and 600 nm. These formulations are characterized by low manufacturing expenses. The capacity for high drug loading and minimal excipient-related side effects. To enhance the dissolution rate and bioavailability of synthetic drugs and phytochemicals can be effectively achieved through formulation of nanosuspension, primarily due to increase in surface area provided by the nanoparticles.[2] The application of nanosuspension is for herbal medicines, primarily because it allows for lower drug doses compared to conventional methods, potentially reducing side effects

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and improving the physical and chemical stability of the therapeutic compounds.[3]

Herbal Extract

For centuries, herbal medicines have been utilized worldwide. The efficacy of many therapeutic plants depends on the release of biologically active compounds. A common challenge is that most of these active components exhibit either high molecular weight or poor water solubility, hindering their ability to pass through the cell membranes and thus leading to limited absorption and bioavailability.[5] Due to poor absorption phytomedicines exhibit less or no in-vivo activity despite of in- vitro capacity. Due to these obstacles some herbal plant extracts are not used clinically.[2] The use of herbal(medicinal) plants has increased due to health efficacy and safety.[1] The formulation of herbal extracts for oral administration presents several hurdles. The highly acidic environment of the stomach can lead to the breakdown of numerous constituents. Furthermore, hepatic first-pass metabolism may limit the systemic availability of other compounds. Beyond these biological barriers, the inherent physicochemical properties of many herbal extracts, such as poor compressibility, high hygroscopicity, and inadequate powder flow, pose significant challenges in manufacturing consistent dosage forms.[6]

2. Methods of preparation of Herbal Nanosuspension

Ionic Gelation Method: Prepared a guava leaf extract solution (0.01% concentration) using 1% acetic acid as a solvent. To this 0.25% chitosan solution in 1% acetic acid was added. Combined solutions were subjected to magnetic stirring for 10 minutes. A solution of 0.1% sodium tripolyphosphate solution was introduced drop by drop into mixture while stirring at 500 rpm for 1 hour. Methylparaben was added in a beaker containing hot water with continuous stirring and dissolved methylparaben, mint flavouring agent, simple syrup and guava leaf extract nanoparticle was added and volume was made up. [3]

Antisolvent Precipitation Method: Plant extract was thoroughly diluted in ethanol. In another beaker HPMC (hydroxypropyl methylcellulose) in aqueous medium was diluted. The organic solution was slowly injected (ml/min) with the help of syringe into aqueous phase with continuous stirring at 6000 rpm for 6hr at room temperature. [2]

Nanoprecipitation Approach: Prepared a plant extract which was dissolved in ethanol. The resultant solution acts as an organic phase and it is filtered. In another beaker water and 2% v/v polysorbate -80 was mixed with the help of stirrer. The organic phase was slowly injected (ml/min) into aqueous phase with continuous mechanical stirring at 6000 rpm for about 6hr at room temperature. [4]

Nanoprecipitation Method: Prepare plant extract in solution containing acetone and ethanol (in a ratio of 3:1) was dissolved by sonication for 60 seconds. In another beaker PVA 1.5% w/v was added to water. The extract solution was gradually injected with the help of syringe (at a rate of ml/min) to aqueous solution with continuous stirring at 500 rpm for 6hr at room temperature. [1]

Media Milling Method: suspension of rutin was prepared in water, followed by the addition of excipients (SLS and HPMC K4M) according to the specific quantities outlined in the Design of Experiments (DoE) batches. This mixture was then homogenized using a Magnetic stirrer mixer at 500 rpm to achieve a uniform dispersion. The initial particle size of rutin, d (90), was 7 µm. Subsequently, the dispersion was processed in the milling chamber with 0.2 mm zirconium beads. The suspension was fed at a rate of 100 mL/min and milled in recirculation mode. Milling duration and speed were adjusted for each DoE batch as required. [14]

3. Evaluation of Herbal Nanosuspension

Nanosuspension particle size and shape were examined using SEM at various magnifications. The powder was sputter-coated before imaging, and the SEM scale bar was accurately calibrated for measurements.[1]

The evaluation of guava leaf extract nanosuspensions typically involves several analyses, including organoleptic assessment, determination of specific gravity, pH measurement, sedimentation volume analysis, and viscosity testing.[3]

The mean particle size (Z-average, expressed in nm), polydispersity index (PDI), and zeta potential of the formulated nanosuspension were determined using the dynamic light scattering technique. A Nano (Malvern Instruments, UK) was utilized for this analysis.[4]

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The nanosuspension with the optimal entrapment efficiency was subsequently characterized for particle size, PDI, zeta potential, pH, and particle morphology.[8]

Mean particle size and zeta potential were determined using a dynamic light scattering (DLS). To minimize multi-scattering effects, samples were diluted with deionized water prior to analysis. All measurements were performed in triplicate at 25 °C using a 633 nm laser and reported values represent the average of these readings. To examine the shape of nanoparticles within the optimized HPMC-based nanosuspension, scanning electron microscopy (SEM) (S-4800, Hitachi Technologies Corporation, Tokyo, Japan) was employed. The SEM was operated at an excitation potential of 15 kV.[10]

(R Sumathi et al., 2017) evaluated the herbal nanosuspension by examining its Particle size distribution, Zeta potential analysis, Differential scanning calorimetry, SEM (Scanning electron microscope) and Powdered X ray diffraction pattern.[11]

The pH of nano suspension formulations was measured in triplicate using a calibrated digital pH meter with 10 ml samples, and the average was reported. Viscosity was determined using a Brookfield LV DV-1 Prime viscometer (S64 spindle, 10 rpm) after a 5-minute immersion. Accelerated stability studies, following ICH guidelines, were performed by storing samples for 3 months in a Remi (India) stability chamber. Drug content, physical appearance, and chemical stability were assessed at 0, 1, 2, and 3 months to evaluate changes during storage.[12]

4. Research done on Herbal Nanosuspension

Table: Past researches done on Herbal Nanosuspension

S.no	Herbal drug used	Method used for preparation	Uses	Reference
1	Thistle, Elaichi, Coriander	Nanoprecipitation	Anti-oxidant	[1]
2	Wormwood	Antisolvent precipitation	Hepatoprotective	[2]
3	Guava leaf	Ionic gelation	Diarrhea	[3]
4	Arjuna bark	Nanoprecipitation	Anti-diabetic, cardioprotective	[4]
5	*Rauvolfia serpentina*	Antisolvent precipitation	Hypertension	[10]
6	*Scoparia dulcis*	Ionic gelation	Analgesic, antipyretic	[12]
7	*Kaempferia parviflora*	Antisolvent precipitation	improve fitness of male	[13]
8	*Cosmos caudatus*	Ionic gelation	Anti-cancer	[7]
9	*Ginkgo biloba*	Antisolvent precipitation	increase oral bioavailability of drug	[8]

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5. Future Prospects

The future holds significant promise for nanosuspension technology utilizing herbal extracts across the pharmaceutical, nutraceutical, and cosmetic sectors. These nanosuspensions, which are essentially stable mixtures of nm-sized drug particles maintained by surface-active agents or polymers, offer a compelling strategy to improve how well poorly water-soluble plant-derived compounds are absorbed by the body. Numerous bioactive plant components, including curcumin, quercetin, and resveratrol, possess strong medicinal effects but face limitations in their practical use due to their poor solubility, instability, or limited uptake. Reducing the particle size of these compounds into nanosuspensions substantially increases their rate of dissolution, stability, and ability to pass through biological barriers, leading to a quicker therapeutic effect and improved overall outcomes. Furthermore, formulating nanosuspensions avoids the use of aggressive chemical solvents. Novel applications are emerging in areas such as cancer therapy, where nanosuspensions can deliver cytotoxic herbal extracts directly to tumor sites, minimizing side effects. The development of "smart" nanosuspensions, capable of responding to specific physiological stimuli, will further enhance their therapeutic efficacy.

6. Conclusion

In conclusion, nanosuspensions of herbal extracts represent a frontier in modern medicine and natural health care. Their ability to significantly enhance the therapeutic potential of herbal compounds while aligning with consumer trends toward natural, safe, and effective treatments positions them as a cornerstone of next-generation drug delivery systems. As research continues to advance and regulatory pathways become clearer, herbal nanosuspensions are poised to make a profound impact on both preventive and therapeutic health strategies globally.

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