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Review on preparation, characterization, and pharmaceutical application of nanosuspension

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ABSTRACT

Nanotechnology is the science that deals with the process that occurs at molecular level and of nano length scale size. Nano refers to the particle size range of 1-1000 nm. Nanosuspension is an attractive and promising technology to improve poor solubility and bioavailability of the drugs. he following work deals with the special features of nanosuspensions, the preparation methods, advantages of such methods, characterization of nanosuspensions, evaluation parameters and applications of nanosuspension.

KEYWORDS

Nanosuspension, particle size, nanotechnology, solubility. ect

NANOSUSPENSION

Nanotechnology is an emerging field in all areas of science, engineering and technology. It is a novel interdisciplinary area of comprehensive research that combines medicine and other life sciences. In recent era, oral drug delivery is most prominent route amongst all other routes of drug administration. Oral pharmaceutical suspension has been one of the most preferable dosage forms for pediatric patients or patients incapable to tolerate solid dosage forms.

A Pharmaceutical suspension is a coarse dispersion in which internal phase is dispersed uniformly throughtout the external phase. Suspension is thermodynamically unstable, so it is necessary to add suspending agent which reduces the rate of settling and permits easy redispersion of any settled particulate matter both by protective colloidal action and by increasing the consistency.

Nano-suspensions will improve the potency of drugs which are insoluble and less drug membrane permeability which delivered at a size of less than 50 nm. During formulation of I.V. suspension, particle size should be less than 50 nm, the suspension particles circulate for long period by avoiding the normal reticuloendothelial system filtration mechanisms. In the case of oral delivery system, the nanometer size molecules are may be allowed to deliver the active pharmaceutical ingredient through gastrointestinal tract into the blood, at minimum degradation in GIT and with high desirable rate. To cross the barriers, insoluble particles of this size are designed. Nanoparticulate degradable polymer structures is one of another strategy that involve encapsulation of active drug.

ADVANTAGES OF NANOSUSPENSION DRUG DELIVERY SYSTEM

- It can be applied for poorly water soluble drugs.
- Physically more stable than liposomes.
- Most cost effective.
- Reduction in tissue irritation.
- Improved dose proportionality
- Its general applicability to most drugs and its simplicity.
- Can be given by any route.
- Reduced tissue irritation in case of subcutaneous/intramuscular administration. Rapid dissolution and tissue targeting can be achieved by IV route of administration.

CRITERIA FOR SELECTION OF DRUG FOR NANOSUSPENSIONS

Nanosuspension can be prepared for the API that is having either of the following characteristics:

1) Water insoluble but which are soluble in oil (high logP) or API are insoluble in both water and oils.
2) Drugs with reduced tendency of the crystal to dissolve, regardless of the solvent.
3) API with very large dose.

TECHNIQUES FOR PREPARATION OF NANOSUSPENSIONS

Technically preparations of nanosuspensions are simpler alternative than liposomes and other conventional colloidal drug carriers but reported to be more cost effective. It is particularly for poorly soluble drugs and to yield a physically more stable product. For manufacturing nanosuspensions there are two converse methods,

1) Top-down process technology
2) Bottom-up process technology

1) Top-down process technology

Top-down approaches are based on the size-reduction and breaking down of large materials into particles with nanometer dimensions via milling, high pressure homogenization and pulsed laser fragmentation.

I. High pressure homogenization

a. Nanoedge
b. Dissocubes
c. Nanopure

II. Media milling

2) Bottom up process technology

The term “Bottom-up technology” means that one starts from the molecular level, and goes via molecular association to the formation of a solid particle. That means that we are discussing classical precipitation techniques by reducing the solvent quality, for example, by pouring the solvent into a nonsolvent or changing the temperature or a combination of both. Precipitation is a classical technique in pharmaceutical chemistry and technology.

a. Solvent-Antisolvent method
b. Super critical fluid process
c. Emulsification Solvent evaporation technique
d. Lipid emulsion/Micro-emulsion template

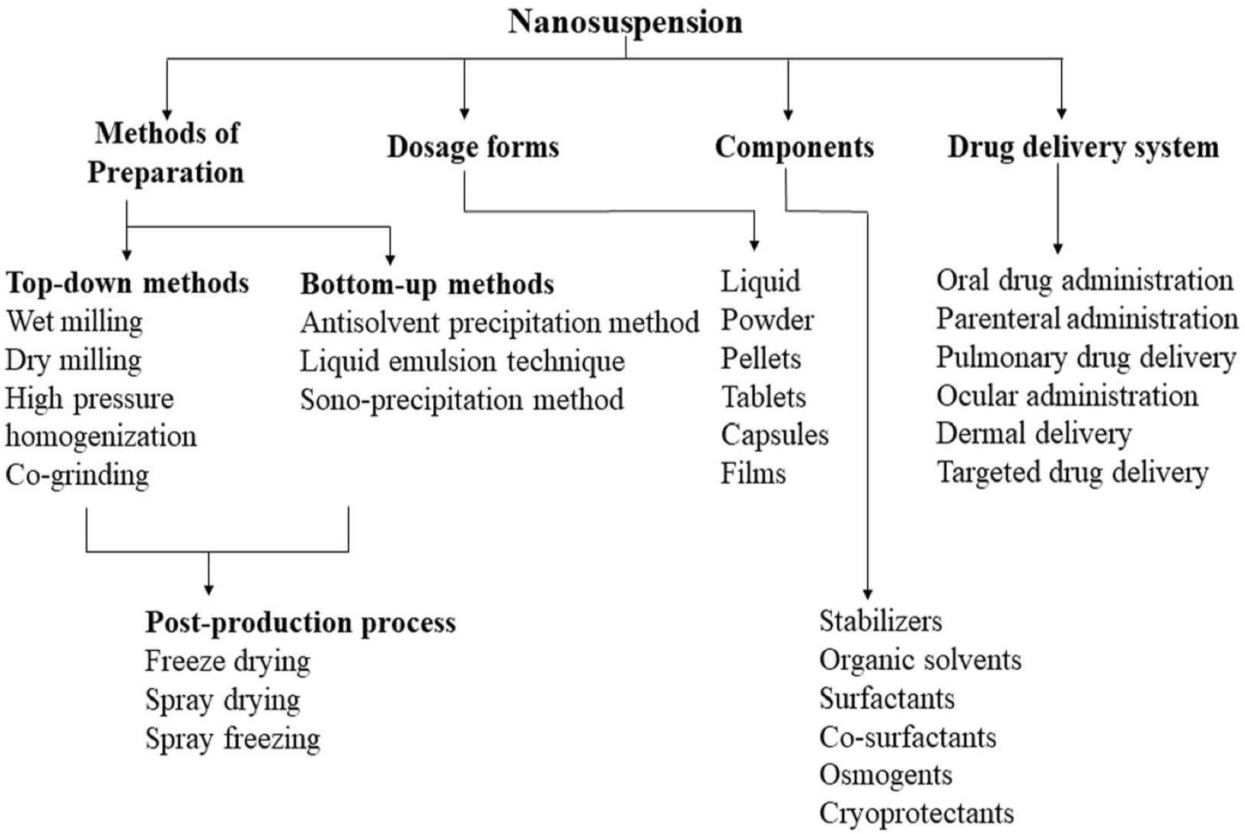

Fig. 1. Emerging role of nanosuspension in drug delivery system

FORMULATION OF NANOSUSPENSION

1. Stabilizers

Wet the drug particles thoroughly; prevent Ostwald's ripening and agglomeration of nanosuspensions, providing steric or ionic barriers. eg: Lecithins, Poloxamers, Polysorbate, Cellulosics, Povidones.

2. Cosurfactants

Influence phase behavior when micro emulsions are used to formulate nanosuspensions. eg: Bile salts, Dipotassium Glycerrhizinate, Transcutol, Glycofurol, Ethanol, Isopropanol.

3. Organic solvent

Pharmaceutically acceptable less hazardous solvent for preparation of formulation.eg: Methanol, Ethanol, Chloroform, Isopropanol, Ethyl acetate, Ethyl formate, Butyl lactate, Triacetin, Propylene carbonate, Benzyl alcohol.

4. Other additives

According to the requirement of the route of administration or the properties of the drug moiety. eg: Buffers, Salts, Polyols, Osmogens, Cryoprotectan.

EVALUATION PARAMETERS OF NANOSUSPENSION

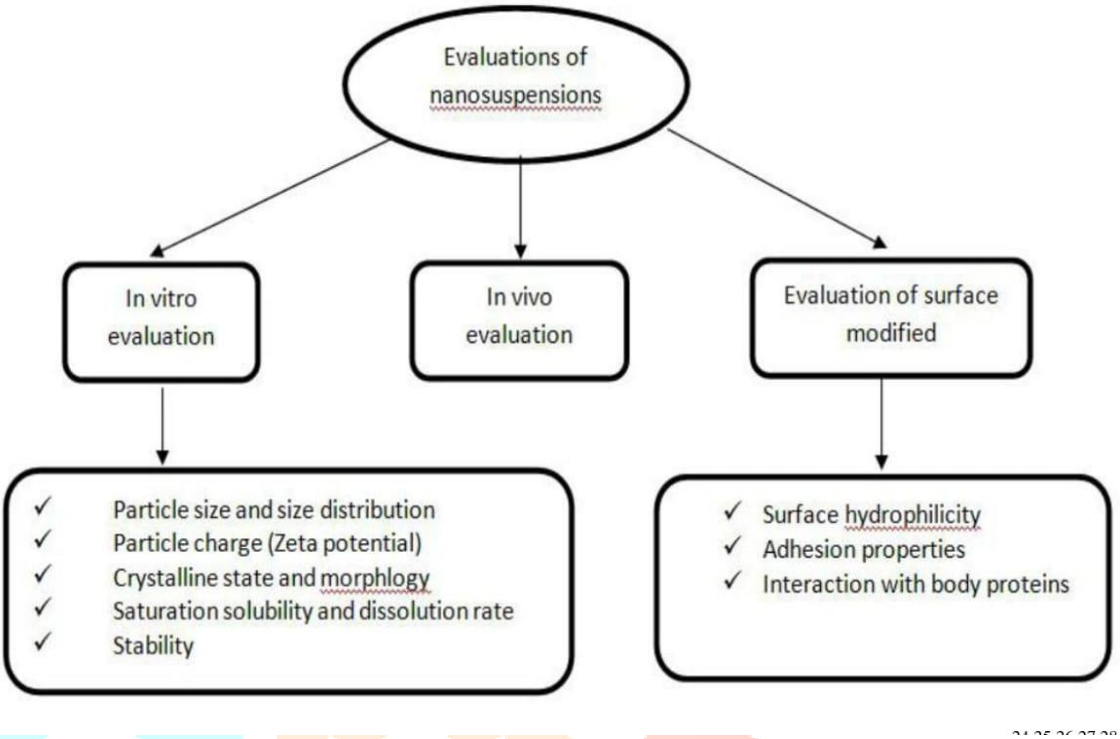

Fig.2 Evaluation of nanosuspension

APPLICATIONS OF NANOSUSPENSION

1. **Nanosuspension through oral route**

The main issue with oral drug administration is poor solubility, inadequate dissolution, and insufficient effectiveness. Oral nanosuspensions are specifically utilized to boost the absorption rate and bioavailability of poorly soluble medicines due to their smaller particle size and significantly higher surface to volume ratio.

2. **Bioavailability Enhancement**

The drug's poor oral bioavailability could be brought about by the digestive tract's poor solubility, permeability, or stability in the gastrointestinal tract (GIT). By addressing both the issues of poor solubility and poor permeability across the membrane, nanosuspensions are able to address the issue of poor bioavailability.

3. **Spray drying and lyophilization of Nanosuspension**

The solidified form is preferable over aqueous nanosuspensions due to the large reduction in aggregation and other instability issues. As a result, solidifying prepared nanosuspensions is a typical process. The powder is subsequently transformed into alternative dosage forms, such as sterile powder for injection, nebulized for pulmonary delivery, tablets, and capsules for oral administration.

4. **Oral Drug Delivery**

Poor solubility, incomplete dissolution, and insufficient efficacy are the major problem of oral drug administration. Due to smaller particle size and much larger surface to volume ratio, oral nanosuspensions are specially used to increase the absorption rate and bioavailability of poorly soluble drugs. The nanosuspension have advantages like improved oral absorption, dose proportionality, and low intersubject variability. By using standard manufacturing techniques, drug nanosuspensions can be simply incorporated into various dosage forms like tablets, capsules, and fast melts.

5. Parenteral Drug Delivery

The drug clofazimine is given as IV, the concentration in the liver, spleen and lungs reached a high level i.e. greater than minimum inhibitory concentration, for most of the mycobacterium avium strains. Tarazepide is formulated as nanosuspension in order to overcome the use of surfactants and cyclodextrins to improve the bioavailability.

6. Pulmonary Drug Delivery

For pulmonary delivery, nanosuspensions can be nebulized through mechanical or ultrasonic nebulizers. Due to the presence of many small particles, all aerosol droplets contain drug nanoparticles. Budesonide corticosteroid has been successfully prepared in the form of nanosuspension for pulmonary delivery. Aqueous suspensions of the drug can be easily nebulized and given by pulmonary route as the particle size is very small. Different types of nebulizers are available for the administration of liquid formulations. Some of the drugs successfully tried with pulmonary route are budesonide, ketotifen, ibuprofen, indomethacin, nifedipine, itraconazole, interleukin-2, p53 gene, leuprolide, doxorubicin, etc.

7. Ocular Drug Delivery

Nanosuspensions are used in ocular delivery of the drugs for sustained release. Liang and coworkers prepared cloricromene nanosuspension for ocular delivery using Eudragit. Experiment showed higher availability of drug in aqueous humor of rabbit eye. Thus, nanosuspension formulation offers a promising way of improving the shelf-life and bioavailability of drug after ophthalmic application.

8. Targeted Drug Delivery

Nanosuspensions are suitable for targeting particular organs because of their surface properties. Along with this, it is easy to alter in vivo behavior by changing the stabilizer. The drug will be taken up by the mononuclear phagocytic system which allows region-specific delivery. This can be used for targeting antifungal, antimycobacterial, or antileishmanial drugs to macrophages if the pathogens persist intracellularly.

CONCLUSION

Nanosuspension formulation have been largely solved the solubility as well as dissolution problems to improve drug absorption. It has therapeutic advantages, such as simple method of preparation, less requirement of excipients, increased saturation solubility and dissolution velocity of drug. Production techniques such as media milling and high-pressure homogenization have been successfully employed for large-scale production of nanosuspensions. Applications of nanosuspensions in parentral, oral routes, pulmonary and ocular delivery have been realized.

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