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Short Communication

Pharmaceutical Applications of Nanosuspension

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Abstract

Objective: The gut microbiome has evolved as a considerable factor in cerebral aneurysm formation through a complex and multifaceted relationship. This would uncover potential insights into how dysbiosis and inflammation may contribute to the development of an aneurysm and subsequent rupture. This article aims to shed new light on our understanding of this intricate biological interplay.

Results:

A link between the gut microbiome and cerebral aneurysms was observed. The dysbiosis in the gut microbial community can cause inflammation and metabolic disorders, elevating the risk of ruptured aneurysms. Inflammation triggers cerebral aneurysm formation and rupture. There appears to be a significant difference in the microbial flora between patients with stable and unstable unruptured intracranial aneurysms.

Conclusion:

The maintenance of overall health depends on the gut microbiome, which also may contribute to developing cerebral aneurysms. Any changes in microbial metabolite production or dysbiosis can lead to inflammation and metabolic disorders that increase susceptibility to aneurysm formation and rupture. By conducting further studies exploring the link between gut microbes and this condition, new preventive as well as therapeutic measures could be developed.

Keywords: gut microbiome; intra-cranial aneurysm; dysbiosis; gut-brain axis

Introduction

Nanosuspensions are colloidal dispersion of solid drug particles size. A pharmaceutical nanosuspension is defined as very finely colloidal, biphasic, dispersed solid drug particles in aqueous vehicle, size below 1µm without any matrix material, stabilized by the use of surfactants and polymers, prepared by suitable methods for drug delivery applications. A nanosuspension not only solves the problem of poor solubility and bioavailability but also alters the pharmacokinetics of the drug and improves safety and efficacy. These are simple to prepare and more advantageous than other approaches. Various techniques employed in the preparation of Nanosupsension are; wet milling, high pressure homogenization, emulsification-solvent evaporation and super critical fluid. It also has the advantage of delivery of the drugs by various routes, including oral, parentral, pulmonary and ocular routes

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 nanosuspension is specially used to increase the absorption rate and bioavailability of poorly soluble drugs. In case of azithromycin nanosupsension, more than 65% of drug was found to be dissolved in 5 hours as compared with 20% of micronized drugs. The nanosuspension has advantages like improved oral absorption, dose proportionality, and low intersubject variability. By using standard manufacturing techniques, drug Nanosupsension can be simply incorporated into various dosage forms like tablets, capsules, and fast melts. The nanosuspension of Ketoprofen was successfully incorporated into pellets for the sustained release of drug over the period of 24hours [1,2].

Parentral Drug Delivery: -The present approach for parentral delivery include micellar solutions, salt formation, solubilization using cosolvents, cyclodextrins complexation and more recently vesicular system such as liposomes and niosomes. But this method has limitations like solubilization capacity, parentral acceptability, high manufacturing cost, etc. to solve the above problems the nanosuspension are administered through parentral route such as intrarticular, intreperitoneal, intravenous, etc. additionally nanosuspension increase the efficacy of parenterally administered drugs. Paclitaxel nanosuspension resulted no death at maximum dose of 100mg/kg whereas taxol at dose 30mg/kg demonstrated a death rate of 22% in human lung xenograft murine tumor. Therapeutic effect of paclitaxel nanosuspension was enhanced in comparison to taxol employing transplantable mouse 16/c mammary adenocarcinoma [3,4].

Pulmonary Drug Delivery: -For pulmonary delivery, nanosuspension can be nebulized through mechanical or ultrasonic nebulizer. Aqueous suspension of the drug can be 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. Antioxidant coenzyme Q10 nanosuspension stabilized with PEG32 sterate demonstrated maximum respirable fraction (70.6%) having smallest mass median aerodynamic diameter (3.02µm) in comparison to nanosuspension stabilized with lecithin and vitamin E TPGS [5,6].

Ocular Drug Delivery: - Low ocular bioavailability of many drugs from conventional ophthalmic drug delivery system is largely due to the major anatomical, physiological and physicochemical barriers of the eye. Nanosuspension offers a means of administrating increased concentrations of poorly soluble drugs and extended residence time to targeted site of cul-de-sac. Investigation of poly (lactic-co-glycolic acid) based sparfloxacin ophthalmic nanosuspension demonstrated an improvement in pre corneal retention time and ocular permeation [7,8].

Nanosuspension is used in ocular delivery of the drugs for sustained release.

Targeted Drug Delivery: -Nanosuspension is suitable for targeting particular organ because of their surface properties. Their versatility and ease of scale up enables the development of commercially viable nanosuspension for targeted delivery [9,10]. Overall nanosuspensions have indicated a good potential in targeted drug delivery but thus has yet to be fulfilled. Kayser formulated an aphidicolin nanosuspension that improved the drug targeting to macrophages if the pathogens persist intracellularly. He stated that the drug in the form of nanosuspension had EC50 of 0.03µg/ml, whereas the conventional form had 0.16µg/ml. Scoler et al. described an enhanced drug targeting to brain in the treatment of toxoplasmic encephalitis using an atovaquone nanosuspension [11,12].

Bioavailability Enhancement: - The poor oral bioavailability of the drug may be due to poor solubility, poor permeability or poor stability in the GIT. Nanosuspension resolves the problem of poor bioavailability by solving the twin problems of poor solubility and poor permeability across the membrane. The oral administration of naproxen nanoparticles leads to an area under the curve (AUC)(0-24h) of 9.75mg-h/l compared with just 44.7mg-h/l for naproxen suspensions and 32.7 mg-h/l for naproxen tablets. Oral administration of the gonadotropin inhibitor Danazol as a nanosuspension leads to a absolute bioavailability of 82.3 and the conventional dispersion (Danocrine0 only to 5.2% [13,14].

Langutth et al. Showed a nearly 5.7-fold increase in the AUC for spiranolactone, a low solubility drug made as a solid lipid nanoparticle. They observed that the improvement in drug solubility in the intestine as well as in the dissolution rate of spiranolactone is the most likely mechanism for the increase in the AUC [15,16].

Intravenous Administration: - It is preferred route for drugs undergoing first-pass metabolism and those that are not absorbed in the GIT or degraded in the GIT. IV administration of poorly soluble drugs without using a higher concentration of toxic co-solvents, improving the therapeutic effect of the drug available as conventional oral formulations and targeting the drug to macrophages and the pathogenic microorganism residing in the macrophages. Peters et al. prepared Clofazimine nanosuspensions for IV use and showed that the drug concentration in the liver, spleen and lungs reached a comparably higher level, well in excess of the minimum inhibitory concentration for most mycobacterium avium strains. A stable intravenously Injectable formulation of omeprazole has been prepared to prevent the degradation of orally administered omeprazole [17,18].

Mucoadhesion of the Nanoparticles: - The particles are immobilized at the intestinal surface by an adhesion mechanism referred to a bioadhesion. From this moment on, the concentrated suspension acts a reservoir of particles and an adsorption process takes place very rapidly. The direct contact of the particles with the intestinal cells through a bioadhesive phase is ye first step before particle absorption. e.g., Cryptosporifium parvum, Bupravaquone nanosuspensions have been reported to demonstrate an advantage in TRC-alpha- deficient mice infected with Cryptosporidium parvum oocytes. The bioadhesion can also be improved by including a Mucoadhesion polymer in the formulation [19,20].

Transdermal Drug Delivery: - Transdermal delivery of methotrexeate coated with non-ionic surfactant and stabilized by l-arginine was tested by solid-in-oil technique. The Transdermal efficiency for the solid-in-oil nanosuspension was 2-3 folds than the control aqueous solution. On account of smaller particle size (<100nm), the oil-based nanosuspension is more efficient in permeating the stratum corneum. Diclofenac sodium a non-steroidal –inflammatory drug was successfully dispersed into isopropyl as a nanosized solid-in-liquid suspension via complex formation using surfactant, sucrose erucate. The resultant formulation enhanced the steady state flux of the drug upto 3.8-fold when compared with the control in Yucatan micropig skin model. The size of the nanosuspension was found to depend on the weight ratio of the surfactant and the average diameter of the nanoparticles was 14.4nm [21].

Conclusions

This article explains about the varios pharmaceutical applications of nanosuspension.The reduced particle size renders the possibility of intravenous administration of poorly soluble drugs without blockade of blood capillaries. More research is required for further improvements in the formulation of nanosuspension to reduce the cost of the formulation and to enhance the stability.

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