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Carriers for therapeutic delivery for coronary and cardiovascular disease and stroke

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Ischemic stroke is the most common acute neurologic illness and, in 2008, accounted for more than $65 billion in costs. In the U.S., atherosclerosis continues to be the number one underlying cause of disability and death with annual estimated costsexceeding $431.8 billion. New methods of diagnosing and treating heart disease, stroke and their complications are needed.

We have been developing "intrinsically echogenic liposomes" (ELIP) as a platform technology for visualization and directed, controlled treatment of a wide variety of disorders. Intellectual property covers a broad technology using the ELIP platform with targeting for tissue highlighting and therapeutic delivery. Our proprietary production procedure causes very small air pockets to become entrapped inside the ELIP and in the ELIP membrane bilayer. Our ELIPs reflect ultrasound and are "intrinsically" echogenic; 99% of ELIP are between 40 and 100 nm in size, making them truly a nanotechnology. With targeting, we have demonstrated ELIP highlighting of thrombi and various stages of atherosclerotic plaques in vitro and in vivo in preclinical studies, using five different molecular markers. Highlighting was demonstrated with conventional ultrasound techniques.

We have developed the ELIP technology into a highly versatile therapeutic platform, featuring targeted, controlled release of agents with clinical Doppler ultrasound, with greater efficacy and less toxicity than conventional formulations of the same agents. Stealth transport of therapeutic agents and targeted delivery of these agents, triggered by application of ultrasound energy, is an advantage. These advantages fall into four major categories:

1. Drugs- We are exploring the clinical applicability of ELIP formulations of thiazolidinediones and bevacizumab for inhibiting atherosclerosis progression. A bevacizumab formulation also has obvious cancer applications.For liposomal-tPa formulation, see separate Fresh Air submission
2. Bioactive Gases- We have developed formulations that encapsulate bioactive gases and release them. These include ELIP-encapsulated nitric oxide (NO-ELIP) to increase therapeutic penetration into tissue beds; and noble gas encapsulation (Xenon) for tissue stabilization and protection ofneurons following acute stroke or myocardial cells following heart attack
3. Genes- For gene therapy of atherosclerosis
4. Stem Cells- See separate fresh air submission

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Biophysical techniques to determine skin permeation mechanism of nanovesicles

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The use of nanovesicles for enhanced topical/transdermal delivery of therapeutic agents has been extensively explored in recent years. However, the exact mechanism of better skin permeation and deposition of drugs from nanovesicles is not yet fully understood. Therefore, the investigation was aimed to understand the mechanisms for better inter and intracellular drug delivery from nanovesicles by quantitative estimation of skin lipids and microscopic evaluation of nanovesicles treated skin for lipid perturbation effects. Results of the biochemical estimation showed that nanovesicles gel formulation produced maximum perturbation of skin lipids as evidenced by highest quantity of cholesterol and triglycerides extracted after 24 h from excised rat skin. In comparison, percentage of cholesterol and triglyceride extracted with conventional cream formulation was found to be significantly less than the nanovesicles gel formulation treatment. Microscopic study revealed that nanovesicles gel formulation influenced the ultra structure of the skin. Distinct regions with lamellar stacks derived from vesicles were observed in the intracellular region of deeper skin layers. The results of the present study demonstrated that the nanovesicles can forge paths in the disordered stratum corneum, change its biochemical constituents and finally release the drug in the deeper layers of the skin. So the nanovesicles based topical drug delivery systems seems to be a good approach for delivery of drugs for the treatment of skin cancer, acne and other skin related diseases.

Biography

Subheet Kumar Jain is Associate Professor of Pharmaceutics in the Department of Pharmaceutical Sciences, Guru Nanak Dev University, Amritsar, India. At the age of 26 he has earned his Ph.D. in Pharmaceutics from Dr. H.S. Gour University, Sagar, India. He has more than 12 years of teaching and research experience. His research areas of interest include nanocarrier for topical site specific delivery and oral controlled drug delivery system. He has more than 70 research publications of international repute in his credit. Recently he has been honored with Prestigious Bhart Jyoti award for the year 2012 in the field of academics.

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