Method and Apparatus for Forming Nanodroplets

This technique can create functionalized particles for targeted drug delivery.

Lyndon B. Johnson Space Center, Houston, Texas

This innovation uses partially miscible fluids to form nano- and microdroplets in a microfluidic droplet generator system.

Droplet generators fabricated in PDMS (polydimethylsiloxane) are currently being used to fabricate engineered nanoparticles and microparticles. These droplet generators were first demonstrated in a T-junction configuration, followed by a cross-flow configuration. All of these generating devices have used immiscible fluids, such as oil and water. This immiscible fluid system can produce mono-dispersed distributions of droplets and articles with sizes ranging from a few hundred nanometers to a few hundred microns. For applications such as drug delivery, the ability to encapsulate aqueous solutions of drugs within particles formed from the droplets is desirable.

Of particular interest are non-polar solvents that can dissolve lipids for the formation of liposomes in the droplet generators. Such fluids include ether, cyclohexane, butanol, and ethyl acetate. Ethyl acetate is of particular interest for two reasons. It is relatively nontoxic and it is formed from ether and acetic acid, and maybe broken down into its constituents at relatively low concentrations.

Further investigation of the liposome properties reveals that optimal liposome-forming mixtures have sufficient density and viscosity to form droplets, but also have the potential to be exchanged from aqueous solutions. Overall, ethyl acetate was found to be about 8 percent miscible in water, which suggests that it could eventually be exchanged into a buffer solution. Based on this solubility for ethyl acetate in water, it was hypothesized that this mixture of reagents was sufficiently immiscible to form droplets on the device. Also, the PDMS droplet generator devices were sufficiently resistant to the solvent effects of ethyl acetate and remained stable during the liposome-forming process.

The fluidic system looks very much like other solvent/water systems. Droplets in the range of 100 to 5,000 nm in diameter may be formed by adjusting the flow rates. Liposomes were successfully fabricated in the ethyl acetate/water system using various lipid mixtures. The liposomes were formed by dissolving a lipid mixture in ethyl acetate, and producing droplets, in the droplet generator. After droplet formation, the droplets flowed from an outlet and were dried down in a collection tube. This demonstrated the advantage of the droplet fluid system when the solvent phase has a high vapor pressure. After dry-down, the liposomes could then be rehydrated into an aqueous (buffer) solution for further use.

By way of contrast, a major limitation to the immiscible fluid system is the fact that the nanodroplets form an oil/water emulsion when aqueous droplets are formed in oil. In the case of nano- and micro-particle formation from the droplets, it is very difficult to separate out the target particles from the oil in the emulsion. Thus, it was desirable to demonstrate an alternative solvent system from which the particles can be more readily separated.

This work was done by Donald Ackley and Anita Forster of Nanotrope Inc. for Johnson Space Center. For further information, contact the JSC Innovation Partnerships Office at (281) 483-3809.

In accordance with Public Law 96-517, the contractor has elected to retain title to this invention. Inquiries concerning rights for its commercial use should be addressed to:

Nanotrope Inc.
2033 Cambridge Ave.
Cardiff, CA 92007
Phone No.: (760) 942-0301

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Rapid Detection of the *Varicella Zoster Virus* in Saliva

This kit provides a rapid, sensitive, specific, and inexpensive method for early virus detection.

Lyndon B. Johnson Space Center, Houston, Texas

Varicella zoster virus (VZV) causes chicken pox on first exposure (usually in children), and reactivates from latency causing shingles (usually in adults). Shingles can be extremely painful, causing nerve damage, organ damage, and blindness in some cases. The virus can be life-threatening in immune-compromised individuals. The virus is very difficult to culture for diagnosis, requiring a week or longer.

This invention is a rapid test for VZV from a saliva sample and can be performed in a doctor's office. The kit is small, compact, and lightweight. Detection is sensitive, specific, and noninvasive (no needles); only a saliva sample is required. The test provides results in minutes. The entire test is performed in a closed system, with no exposure to infectious materials. The components are made mostly of inexpensive plastic injection molded parts, many of which can be purchased off the shelf and merely assembled. All biological waste is contained for fast, efficient disposal.

This innovation was made possible because of discovery of a NASA scientists' flight experiment showing the presence of VZV in saliva during high stress periods and disease. This finding enables clinicians to quickly screen patients for