Patent Background

**Japanese Patent (US 20030143267 A1)**

<http://www.freepatentsonline.com/y2003/0143267.html>

Abstract:

The present invention provides a sugar-modified liposome having a sugar chain bonded to its membrane surface, preferably through a linker protein, and having excellent absorption qualities, particularly in the intestine. The molecular structure and quantity of the sugar chain is selectively varied to allow the liposome to be delivered in a targeted manner to selected cells and tissues. The liposome is applicable to medicinal drugs, cosmetics and other various products in the medical/pharmaceutical fields, and it is especially useful in a therapeutic drug delivery system that recognizes target cells and tissues, such as cancer cells, and in the delivery of drugs or genes locally to a selected region, or in a diagnostic cell/tissue sensing probe.

THERE IS REFERENCE ON HOW TO MODIFY AND UTILIZE THE LIPOSOME FOR DRUG DELIVERY. THERE IS NO REFERENCE AS TO HOW TO CREATE (MANUFACTURE) THE LIPOSOME

**Potential Competition**

[**http://sonomechanics.com/applications/pharmaceutical/drug-carrier\_liposomes\_and\_nanoemulsions/**](http://sonomechanics.com/applications/pharmaceutical/drug-carrier_liposomes_and_nanoemulsions/)

[**https://www.hielscher.com/ultrasonic-liposome-preparation.htm**](https://www.hielscher.com/ultrasonic-liposome-preparation.htm)

WAIT FOR RUSSIAN RESPONSE!

INTERNET SEARCH

**Patent Draft**

**Abstract**

Particles and droplets within the micro-meter scale are present in many industrial products and processes. It is often the case that they need to be separated in order to be further utilized for product formulations (e.g. starch particles of specific size or oil from enhanced recovery emulsions) or that they have to be discarded as waste (such as cleaning liquids that contain small oil droplets or other particulates). In large scale operation, attention is still primarily directed toward the overall throughput (and efficiency) of a system, and dimensions of production lines / equipment are generally many orders of magnitude different from that of the particles or droplets. Whereas the overall flow behaviour in large scale operation is well-understood, that of particles/droplets on micro/nano-meter scale is just coming of age, with many new developments in microfluidics and membrane separation adding to the knowledge base.

**Claims:**

What is claimed is:

1. The present invention provides for a new innovative method for the extremely fast and efficient production of micro and/or nano sized beads, particles or hollow sphere.
2. The production method, as defined in claim 1, can be run in both batch and continuous modes.
3. Liposomes (formed from lipids in non-organic suspensions) are a good example of a “hollow sphere” produced by the method described in claim 1.
4. The novel production method described in claim 1. utilizes proprietary Ultrasonic Technology developed by the companies MP-Interconsulting and Ultrasonic World Limited.
5. The Ultrasonic Technology described in claim 4. consists of an ultrasonic generator based on proprietary Multi-frequency, Multimode, Modulated Sonic & Ultrasonic Vibrations” (also known as MMM) in combination with innovative mechanical resonator designs.
6. The innovative mechanical resonator designs, as referred to in claim 5, relate to a cylindrical or rectangular bar shaped ultrasonic resonator, or solid-state body that has (at the same time mutually coupled and synchronized) combined axial, radial and different lateral modes resonances, produced by specific geometry of the same resonant body with axial and perpendicular resonating holes and channels.

**Description:**

1. Field of Invention:

The present invention relates to a novel and highly efficient separation of micro/nano sized particles or droplets from a liquid emulsion via Ultrasonic Processing. Compared to all other methods, including other known state of art ultrasonics, the production time is many factors faster than standard processes such as extrusion, high-pressure homogenization / ultrasonication, and microfluidic chambers. This method of separation is in parallel capable of forming the said particles or droplets into micro or nano sized beads or hollow spheres.

1. Background of Invention
2. Summary of Invention
3. Brief Description of Drawings
4. Detailed Description of the Invention
5. Examples of application fields

- **Human Drug Delivery**

<https://www.ncbi.nlm.nih.gov/pubmed/7600589>

During the last three decades, the value of liposomes as a drug delivery system has been examined. The interest in liposomes as carriers of active substances is based on their potential to enclose various types of biological materials and to deliver them to diverse cell types. Whereas experiments with systemically applied liposome-entrapped drugs often proved disappointing, recent work suggests that liposomes as vehicles for topical drug delivery may be superior to conventional preparations. The use of liposomes in ophthalmology for the diagnosis and treatment of different ocular diseases has been postulated recently. Dermatics based on liposomes as drug carrier systems have been tested for different types of ingredients, e.g., corticosteroids and local anesthetics. To understand more about the pharmacological potential of liposomes, it is important to investigate the interaction between liposomes and the epidermis. Analysis in this field suggests that only a compromised epidermal barrier enables intact liposomes to penetrate the skin. This is in accordance with clinical findings. A liposomal preparation of betamethasone dipropionate seems superior to a conventional commercial preparation in eczema but not in psoriasis vulgaris. However, one cannot rule out the follicular pathway as an alternate route. Many questions must be resolved before a complete understanding of liposomes as a drug carrier system in dermatology can be reached. However, examinations performed so far indicate that liposomes might be useful as vehicles for topical drug delivery in various diseases of the skin.

<https://www.ncbi.nlm.nih.gov/pubmed/10332745>

Intracellular delivery of novel macromolecular drugs against human immunodeficiency virus type-1 (HIV-1), including antisense oligodeoxynucleotides, ribozymes and therapeutic genes, may be achieved by encapsulation in or association with certain types of liposomes. Liposomes may also protect these drugs against nucleases. Low-molecular-weight, charged antiviral drugs may also be delivered more efficiently via liposomes. Liposomes were targeted to HIV-1-infected cells via covalently coupled soluble CD4. An HIV-1 protease inhibitor encapsulated in conventional negatively charged multilamellar liposomes was about 10-fold more effective and had a lower EC90 than the free drug in inhibiting HIV-1 production in human monocyte-derived macrophages. The drug encapsulated in sterically stabilized liposomes was as effective as the free drug. The EC50 of the reverse transcriptase inhibitor 9-(2-phosphonylmethoxyethyl)adenine (PMEA) was reduced by an order of magnitude when delivered to HIV-1-infected macrophages in pH-sensitive liposomes. A 15-mer antisense oligodeoxynucleotide against the Rev response element was ineffective in free form against HIV-1 replication in macrophages, while delivery of the oligonucleotide in pH-sensitive liposomes inhibited virus replication. The oligodeoxynucleotide encapsulated in sterically stabilized pH-sensitive liposomes with prolonged circulation in vivo, which were recently developed in the laboratories of the authors, was also highly effective. A ribozyme complementary to HIV-1 5'-LTR delivered in pH-sensitive liposomes inhibited virus production by 90%, while the free ribozyme caused only a slight inhibition. Cationic liposome-mediated co-transfection of the HIV-regulated diphtheria toxin A fragment gene and a proviral HIV clone into HeLa cells completely inhibited virus production, while the frame-shifted mutant gene was ineffective. Co-transfection of the proviral genome and a gene encoding a Rev-binding aptamer into HeLa cells via transferrin-associated cationic liposomes inhibited virus production. These studies indicate that liposomes can be used to facilitate the intracellular delivery of certain anti-HIV agents and to enhance their therapeutic effects. These properties may be particularly advantageous in the development of novel macromolecular drugs, which may be necessary because of the emergence of virus strains resistant to the currently available drugs.

- **Animal Drug Delivery**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3809611/>

Recent advances in nanomedicine have been studied in the veterinary field and have found a wide variety of applications. The past decade has witnessed a massive surge of research interest in liposomes for delivery of therapeutic substances in animals. Liposomes are nanosized phospholipid vesicles that can serve as delivery platforms for a wide range of substances. Liposomes are easily formulated, highly modifiable, and easily administered delivery platforms. They are biodegradable and nontoxic and have long *in vivo*circulation time. This review focuses on recent and ongoing research that may have relevance for veterinary medicine. By examining the recent developments in liposome-based therapeutics in animal cancers, vaccines, and analgesia, this review depicts the current significance and future directions of liposome-based delivery in veterinary medicine.

- **Cosmetics (active ingredient encapsulation)**

<https://www.hielscher.com/ultrasonic-liposome-preparation.htm>

Liposomes are minute vesicles with membranes comprised of a double layer of molecules called phospholipids. These phospholipids possess a spherical hydrophilic (water soluble) component and a tail-shaped lipophilic (fat soluble) component. At Dr. Baumann SkinIdent these natural phospholipids are extracted from soya. Under certain inputs they group themselves together in a watery medium into spherical structures, the liposomes. This is achieved as the lipophilic ends of the phospholipids fit together to form a double membrane, the outer layer of which is hydrophilic and the inner layer lipophilic. Therefore the inside and the outside of a liposome are hydrophilic and the inside of the liposome membrane is lipophilic. Consequently, liposomes can absorb both water soluble active ingredients (E. g. water soluble vitamins, chemical preservatives) within the liposome, and fat soluble substances (E. g. fat soluble vitamins, perfume) in the liposome membrane, and transport these into the skin. For substances which have a positive effect on the skin, this transport function is desired and welcomed. But for substances which commonly trigger allergies (perfume, chemical preservatives) and are foreign substances which cause a defensive reaction in the immune system, this is considered extremely risky. Therefore, the use of liposomes demands from the manufacturer as well as cosmeticians a particular sense of responsibility and knowledge of the physiological factors involved, otherwise damage could be inflicted on the user.

- **Food Industry** (vitamin and trace elements encapsulation)

<https://www.absorbyourhealth.com/what-are-liposomal-supplements/>

What Are Liposomal Supplements?

Liposomal supplements are a class of health supplements with an added liposomal shell around their major molecules, such allows for increased absorption in the body, helps higher doses be absorbed into one’s system faster, and have far less side effects than the normal supplement itself (if not in liposomal form.)



- **Agricultural** Herbicides / pesticides (encapsulation)

http://www.creative-biostructure.com/mempro™-liposome-in-agricultural-industry-493.htm

Creative Biostructure has established a novel Mempro™ Liposome platform in recent years. While the liposomes in medical and pharmaceutical studies have been used as model membrane systems to develop several drug and reagent delivery systems. In addition to the various medical and pharmaceutical applications, the use of liposomes in agriculture systems is another major application of liposomes. Liposomes also have been used to investigate the solutes transportation mechanism across the cellular membranes, to explicate the activity dynamics of toxin and antimicrobial, to study the actions of pesticides, and to transport therapeutics substances to farm animals.





- Industrial wastes (trace oils and contaminant separation)