Reference Number: RSRM-PA-2017-08

Patent Application

Summary

A new and unique method for the production of nano/micro sized particles, in the form of solid arbitrary particles and spheres (and hollow spheres, also known as liposomes). The improved and novel ultrasound based method (based on Multifrequency, Multimode, Modulated Sonic & Ultrasonic Vibrations, also known as MMM) enables a resolution of the typically known and current production disadvantages, especially for liposome production, in both laboratory and commercial batch and continuous modes. The improved method enables a much narrower size distribution of resulting particles (typically 5nm to 100nm) along with a much shorter production time (which lies between factor 10 and 100 shorter of typical and known production times) along with a completely non-contamination of the end product.

Description

Due to the ever-increasing applications of liposomes in biophysics, physiology and medicine, many techniques have been developed over recent years to manufacture them. Micro and nano sized liposomes can be utilized as carriers of encapsulated drugs. All existing methods for the production of these Liposomes have serious drawbacks, namely rate of production, high production costs, low efficiency, low quality, end product contamination with metal particles during production, short operating life of used ultrasonic processors and difficult scale-up procedures. Specifically, for human drug delivery, liposomes (in the order of micro/nano size) are of growing interest as carriers of drugs. For medical applications, these micro/nano spherical shaped liposome carriers are of such a size so as to be able to travel freely throughout the human body and through the body tissue. The liposomes may also be addressed by means of specific coatings such as sugars and proteins so as to guide/target them only to specific tissues within the body. Through this new and innovative system of liposome production (high efficiency, selective sizing, batch/continuous methods for commercial production) for the production of the required liposomes, a highly effective liposomal drug delivery can be achieved.

Today chemotherapy is still the most common form of medication for the treatment of cancer patients. Through the application of the above mentioned liposomal drug delivery, high overall body dosages (which tend to cause severe side effects) are lowered and significantly higher cancer cell “drug concentration” can be achieved so as to enhance the therapeutic effects.

The application describes a new and unique method for the production of nano/micro sized particles, in the form of solid arbitrary particles and spheres (and hollow spheres, also known as liposomes). The improved and novel ultrasound based method enables a resolution of the typically known and current production disadvantages, especially for liposome production, in both laboratory and commercial batch and continuous modes. The improved method enables a much narrower size distribution of resulting particles (typically 5nm to 100nm) along with a much shorter production time (which lies between factor 10 and 100 shorter of typical and known production times) along with a completely non-contamination of the end product.

Turbulence is created in a mixture of small single particles and/or molecules within a carrier liquid. The turbulence can be created via various methods however this method utilizes

special and unique ultrasonic means. Turbulence, in the form of numerous small vortices within the bulk liquid mixture, are created so enabling the agglomerate and sticking together of individual particles/molecules in a highly concentrated and fast twisting/cyclonic manner.

The turbulence/vortices described above are created through the use of a special submerged bar or rod like resonating element which is activated via a special external power supply or electro-acoustic (or ultrasonic) generator. The resonating bar/rod has axial and perpendicular holes and channels, designed in a way that all of them are synchronously resonating, producing different wave motions, vortices and shear waves in both axial and radial directions, when submersed. Subsequently, the uniquely designed resonating bar is able to produce and propagate the required liquid vortices via a combination of low frequency oscillations, ultrasonic frequency oscillations, including forced and frequency-sweeping oscillating regimes with different signal modulations.

Claims

1. The creation of micro/nano sized particles through:
   the accumulation of numerous smaller particles or molecules

2. The building of a particle according to claim 1. is characterised in that: the action of turbulence and the sticking together (accumulation) of numerous single smaller particles or molecules which are present in a fluid carrier.

3. The building of a particle according to claim 1. is characterised in that: depending on the specifics of the liquid mixture (of which particles may be biomolecule, ferromagnetic, ions or other particles) various physical methods are employed so as to create a turbulence (such as acoustic, mechanical, optical, electromagnetic or electric field).

4. The building of a particle according to claim 1. is characterised in that: for the micro/nano sized particles, specifically for a biomolecule in liquid suspension, an acoustic method is employed for creating the turbulence in the form of numerous small vortices.

5. The building of a turbulence according to claim 2. & 3. is characterised in that: a resonating element is used to create numerous small vortices. Acoustic energy is transferred from an external ultrasonic power supply or generator through a resonating element and subsequently into the liquid.

6. The resonating element according to Claim 5. is characterised in that: the form of the resonating element is a bar or rod structure.

7. The specially designed bar or rod element according to claim 6. is characterised in that: the structure is able to produce and propagate the required liquid vortices via a combination of low frequency oscillations, ultrasonic frequency oscillations, including forced and frequency-sweeping oscillating regimes with different signal modulations.

8. The design of this resonating bar or rod structure according to claim 6. & 7. is characterised in that: within this bar or rod structure, axial and perpendicular holes and channels have been placed in a way that all of them are synchronously resonating, producing different wave motions, vortices and shear waves in both axial and radial directions, when submersed in a liquid.

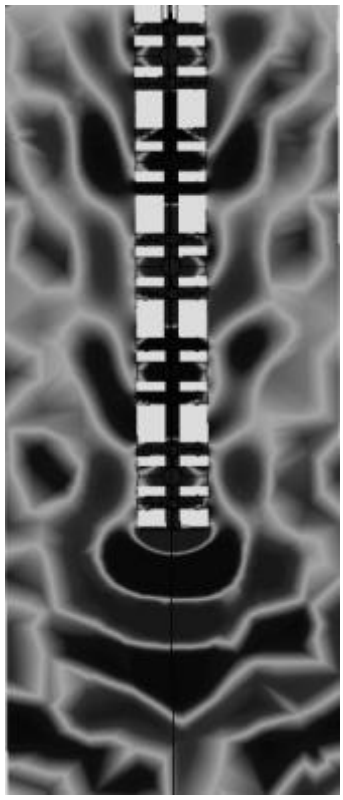
9. The design of this resonating bar or rod structure according to claim 6. - 8. is characterised in that: the resonating bar produces a very large spectrum of cavitation bubbles of varying diameter unlike traditional ultrasonic methods.

10. The design of this resonating rod structure according to claim 6. - 9. is characterised in that: the resonating bar is creating progressive ultrasonic waves (defined as directional, pushing waves).

Sketches

Fig. 1

Fig. 2



1. = Typical resonating element configuration. (also known as MMM-Sonorod)
2. = Example of unique acoustic field produced in liquid by resonating element (also known as MMM-Sonorod)