

DEVICE AND METHOD FOR FORMATION OF VESICLES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/582,846, filed Jan. 4, 2012, and is incorporated herein by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This work is funded by the National Institute of Standards and Technology under the U.S. Department of Commerce.

FIELD OF THE INVENTION

[0003] This invention relates to a device and method for the formation of vesicles, and more particularly toward a device and method for creating an outer aqueous flowing stream sheathing an organic stream containing amphiphilic molecules for the formation of vesicles.

BACKGROUND

[0004] Traditionally, a vesicle is a small structure within a biological cell. This structure is enclosed by lipid bilayer. Currently, vesicles may be made naturally (in vivo) or artificially (in vitro), and in both cases they may be unilamellar—having only one phospholipid bilayer; or multilamellar—having more than one phospholipid bilayer. Artificially prepared vesicles are often called liposomes. Liposomes are formed when phospholipids and their derivatives are dispersed in water. Upon dispersion in water the phospholipids form closed vesicles or liposomes, which are characterized by lipid bilayer(s) substantially encapsulating an aqueous core. Various liposomes have been used as carriers for administration of nutrients and pharmaceutical drugs and enzymes, and in genetic sequencing.

[0005] Liposomes are composite structures made primarily of phospholipids and often small amounts of other molecules. Further liposomes may encapsulate other molecules in their aqueous core or in their lipid bilayer membrane. Though liposomes can vary in size from tens of nanometers to tens of micrometers, unilamellar liposomes, are typically in the lower size range and may have various targeting ligands attached to their surface allowing for their surface-attachment and accumulation in pathological areas for treatment of disease. Liposomes of different geometries, size and/or shape ranges, may be used for targeting delivery. For example, the in vivo bioavailability of liposomes may exhibit a strong dependence on size and geometry/shape of the liposomes. Thus, providing liposomes of selected size and/or geometry may better enable designing drug delivery carriers for targeting specific tissue or disease biomarkers.

[0006] Traditional liposome preparation methods may be based on mixing of bulk phases of fat-soluble and water-soluble constituents leading to inhomogeneous chemical and/or mechanical conditions during formation. Therefore, liposomes prepared by those traditional methods are often polydisperse in size and lamellarity. Controlled mixing of said phases may provide the ability to better control the liposome size and size distribution, or polydispersity; key elements to their potential use in various applications. Conventional modes of liposome preparation may require the mixing

of two or more phases, typically liquid-liquid or liquid-solid, resulting in the spontaneous self-assembly of the lipid mixture into a spherical membrane structures. These conventional modes of liposome formation in vivo may provide any one of many different sets of mechanical and chemical conditions during its self-assembly, which may lead to liposome preparations with large polydispersity with respect to size and lamellarity.

[0007] What is needed is a device and method for a more controlled formation of vesicles with a smaller polydispersity, with respect to size, shape, and/or lamellarity.

SUMMARY

[0008] In one aspect of the present disclosure, a device configured for the formation of vesicles comprises a fluid introduction zone and a vesicle formation zone. The fluid introduction zone comprises a first outlet and a second outlet configured and disposed to provide parallel flow of an outer flow stream, flowing from the first outlet, sheathing an inner flow stream, flowing from the second outlet. The vesicle formation zone is configured and disposed to receive a parallel flow of the outer flow stream, flowing from the first outlet, sheathing the inner flow stream, flowing from the second outlet, and configured for a controlled and substantially uniform dispersion of an organic material, flowing in the inner flow stream, at a plane perpendicular to the vesicle formation zone. The vesicle formation zone has an outlet.

[0009] In another aspect of the present disclosure, a process for the formation of vesicles comprises the steps of flowing an aqueous stream and flowing an organic stream centrally into and parallel with the flow of the aqueous stream. The aqueous stream completely sheaths the organic stream. The process further comprises dispersing a miscible organic material, flowing in the organic stream, with the aqueous stream that forms vesicles at the interface between the two streams.

[0010] In yet another aspect of the present disclosure, a device configured for the formation of vesicles comprises a longitudinally extending sheath configured and disposed for the flowthrough of an aqueous stream and a parallel flowing organic stream. The longitudinally extending sheath comprises an aqueous stream inlet configured and disposed to receive the aqueous stream into the sheath, an organic stream inlet configured and disposed to receive a parallel flowing organic stream centrally within the aqueous stream, and an outlet.

BRIEF DESCRIPTIONS OF THE DRAWINGS

[0011] The following figures, which are idealized, are not to scale and are intended to be merely illustrative and non-limiting;

[0012] FIG. 1 shows a parallel flow device configured for the formation of vesicles;

[0013] FIG. 2 shows an exploded view of a section of the parallel flow device for the formation of vesicles of FIG. 1;

[0014] FIG. 3A shows another aspect of a parallel flow device for the formation of vesicles;

[0015] FIG. 3B shows a further aspect of a parallel flow device for the formation of vesicles;

[0016] FIG. 4 is an illustration of a mechanism of action for liposome formation using the parallel flow device for the formation of vesicles of the present disclosure;