(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 August 2014 (07.08.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/121211 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/US2014/014480

(22) International Filing Date:
3 February 2014 (03.02.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/759,914 1 February 2013 (01.02.2013) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: REMOTE LOADING OF SPARINGLY WATER-SOLUBLE DRUGS INTO LIPOSOMES

(57) Abstract: The present invention provides liposome compositions containing sparingly soluble drugs that are used to treat life-threatening diseases. A preferred method of encapsulating a drug inside a liposome is by remote or active loading. Remote loading of a drug into liposomes containing a transmembrane electrochemical gradient is initiated by co-mixing a liposome suspension with a solution of drug, whereby the neutral form of the compound freely enters the liposome and becomes electrostatically charged thereby preventing the reverse transfer out of the liposome. There is a continuous build-up of compound within the liposome interior until the electrochemical gradient is dissipated or all the drug is encapsulated in the liposome. However, this process as described in the literature has been limited to drugs that are freely soluble in aqueous solution or solubilized as a water-soluble complex. This invention describes compositions and methods for remote loading drugs with low water solubility (< 2 mg/mL). In the preferred embodiment the drug in the solubilizing agent is mixed with the liposomes in aqueous suspension so that the concentration of solubilizing agent is lowered to below its capacity to completely solubilize the drug. This results in the drug precipitating but remote loading capability is retained. The process is scalable and, in liposomes in which the lipid composition and remote loading agent are optimized, the resulting drug-loaded liposomes are characterized by a high drug-to-lipid ratios and prolonged drug retention when the liposome encapsulated drug is administered to a subject.

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