Table S1 – Articles on the encapsulation of antitumour agents in Nanostructured lipid carriers, from 2000-2021. Descriptions include AA, cancer type, NLC composition, preparation method, physicochemical properties - size, polydispersity (PDI), zeta potential (ZP) and encapsulation efficiency (%EE) - tests conducted and main achievements.

Antimetabolite agents

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the main text
5-fluorouracil (5-FU)	Hepatocellular carcinoma (**HepG2**) cell line	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA or Labrafac 5 Surfactant: Lecithin Tween 80 or Solutol HS15 Functionalization: Galactisilated-stearyl amine	Emulsification-solvent diffusion	DLS Microscopy (SEM) DSC FTIR NMR	Size 139.2 nm PDI 0.5 ZP –18 mV %EE 34.2% Stability: Not informed	Pharm. development *In vitro* tests	✓ Improved cytotoxicity ✓ Enhanced drug uptake to HepG2 tumour cells	[1]	[27]
5-FU	Not tested	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: Labrasol Surfactant P-188 Solutol HS15	High-pressure homogenization (HPH)	DLS Microscopy (TEM)	Size 211.2±4.9 nm PDI 0.412±0.065 ZP −21.6±0.7 mV %EE 82.42 ± 3.14%	Pharm. development *In vitro* tests *In vivo:* Skin permeation and irritation	✓ Increased 5-FU permeation ✓ Reduced skin irritation	[2]	-

					Stability: Not informed				
5-FU	Not tested	(Synthetic lipids) Solid lipid: Tripalmitin Tristearin Liquid lipid: Transcutol Surfactant: Lecithin Tween 80	High-pressure homogenization (HPH)	DLS Microscopy (TEM) DSC XRD	Size 205.8 nm PDI 0.279 ZP −30.20 mV %EE 48.17% Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* Skin permeation	✓ Increased 5-FU permeation	[3]	-
Cytarabine (CYT)	Meningeal leukemia (**EL-4**) cell line	(Synthetic lipids) Solid lipid: SA Liquid lipid: OA Surfactant: Polysorbate 80	Sonication or ultra-sonication	DLS Microscopy (TEM) DSC XRD	Size 90.7 nm PDI 0.16 ZP -24.2 mV %EE 49.5% Stability: 3 months	Pharm. development *In vitro* tests	✓ Improved cytotoxicity against EL-4 cells	[4]	[29]
Decitabine (DCB)	Human non-small cell lung cancer (**A549**) cell line	(Synthetic lipids) Solid lipid: Precirol ATO5 Liquid lipid:	High-pressure homogenization (HPH)	DLS Microscopy (AFM and TEM) DSC XRD	Size 116.66 nm PDI 0.194	Pharm. development *In vitro* tests *Ex vivo*:	✓ Improved cytotoxicity ✓ Improved bioavailability after oral administration than intravenously DCB administration ✓ Improved gut permeation	[5]	[14]

	Ehrlich Ascites Tumour (**EAT**) bearing mice Oral delivery	Transcutol Surfactants: Tween 80 P-188 Solutol HS 15			ZP −31.8 mV %EE 84.42 ± 5.38% Stability: 45 days	Gut permeation *In vivo:* Biodistribution			
Methotrexate (MTX)	Human prostate cancer (**DU-145)** and ovarian human cancer (**A2780)** cell lines	(Synthetic lipids) Solid lipid: Imwitor 812 Liquid lipid: Neobee Surfactant: Cremophor RH40 P-188	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 255.56±15.40 PDI 0.140±0.08 ZP −25.0±2.70 %EE 60% Stability: 90 days	Pharm. development *In vitro* tests	✓ Improved cytotoxicity in ovarian cancer cells	[6]	[33]
MTX	Not tested	(Synthetic lipids) Solid lipid: Witepsol E85 Liquid lipid: Miglyol 812 Surfactant: PVA	Sonication or ultra-sonication	DLS Microscopy (TEM) FTIR	Size 252 nm PDI 0.06 ZP −14 mV %EE 87% Stability: 4 weeks	Pharm. development *In vitro* tests	✓ No toxicity in fibroblasts ✓ Safe application	[7]	[34]

MTX	Human breast -cancer cell (**MDA-MB-231)**	(Synthetic lipids) Solid lipid: Witepsol E85 Liquid lipid: Miglyol 812 Surfactant: PVA Functionalization: SPIONs	Sonication or ultra-sonication	DLS	Size 214 ± 3 nm PDI 0.090 ± 0.017 ZP −12.6 ±1.6 mV %EE 75% Stability: 3 months	Pharm. development *In vitro* tests	✓ Improved cytotoxicity ✓ Hemo-compatibility ✓ Caveolae-mediated endocytosis	[8]	[35]
MTX	Tested in normal cells	(Synthetic lipids) Solid lipid: cetyl palmitate Liquid lipid: Miglyol 812 Surfactant Polysorbate 80	Sonication or ultra-sonication	DLS Microscopy (TEM / Cryo-SEM)	Size 458 nm PDI 0.260 ZP -24 mV %EE 83% Stability: 3 months	Pharm. development *In vitro* tests	✓ Low toxicity in fibroblasts and human keratinocytes	[9]	-

Antimitotic agents

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review

Cabazitaxel (CBZ)	Human breast adenocarcinoma (**MDA-MB-468** and **MCF-7**) cell lines	(Synthetic lipids) Solid lipid: Precirol ATO5 Liquid lipid: Labrafac PG Surfactant: Tween 80	Microemulsion technique	DLS Microscopy (SEM) DSC XRD FTIR	Size 102.90 nm PDI 0.140 ZP -23.00 mV %EE 84.12 ± 1.1% Stability: 60 days	Pharm. development *In vitro* tests	✓ High cellular uptake and apoptosis ✓ Improved cytotoxicity	[10]	[38]
Docetaxel (DTX)	Human ovarian carcinoma (**SKOV3**), human prostate cancer (LNCaP, **PC-3** and **DU145**) and **MCF-7** cell lines **SKOV3** cell xenograft mouse model Intratumourally	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: Labrafil M 1944 Surfactant: PVA Tween 20 Functionating: RIPL	Emulsification-solvent evaporation	DLS Microscopy (TEM) DSC	Size 240.83 ± 3.44 nm PDI 0.265 ZP 14.27 ± 0.78 mV %EE 97.59 ± 0.13% Stability: 2 weeks	Pharm. development *In vitro* tests *In vivo:* Tumour growth inhibition (TGI)	✓ Improved tumour inhibition ✓ No body weight loss	[11]	-
DTX	Fibrosarcoma (**HT1080**), **MCF-7, A549** and human mouth epidermoid carcinoma (**KB**) cell lines	(Synthetic lipids) Solid lipid: Crodamol SS Liquid lipid: Crodamol GTCC	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 35.57 ± 0.31 nm PDI 0.10 ±0.01 ZP -0.29 ± 0.17 mV	Pharm. development *In vitro* tests *In vivo:* TGI	✓ Increased cell uptake ✓ Improved cytotoxicity ✓ Increased tumour cell apoptosis. ✓ Greater antitumour efficacy	[12]	-

	KB tumour-bearing mice Intravenous	Surfactant: Soy lecithin and Solutol HS15			%EE 97.47 ±0.90% Stability: Not informed				
DTX	Human cells lines: **HepG2**, **SKOV3**, **A549** and murine malignant melanoma (**B16**) cell line Mice implanted with **B16** cells Intravenous	(Synthetic lipids) Solid lipid: GMS SA Liquid lipid: OA Surfactants: P-188 Soya lecithin	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 193.47 ± 5.69 nm PDI Not informed ZP -33.17 ± 1.20 mV %EE 89.72 ± 0.89% Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* TGI	✓ Superior antitumour activity ✓ Minor side effects compared to Duopafei	[13]	-
DTX	Not tested	(Synthetic lipids) Solid lipid: Precifac ATO 5 Liquid lipid: MCT Surfactant: Tween 80 Soybean lecithin Functionalization: Cysteine-PEG-MSA	Sonication or ultra-sonication	DLS Microscopy (TEM) DSC NMR FTIR XPS	Size 96.6 ± 8.0 nm PDI 0.196 ± 0.004 ZP −13.72 ± 0.07 mV %EE 99.27 ± 0.44% Stability: Not informed	Pharm. Development *In situ:* perfusion experiments *In vivo:* Rat biodistribution, and pharmacokinetics	✓ Cysteine increased mucoadhesion ✓ Increased bioavailability after oral administration ✓ Improved drug absorption	[14]	[43]
DTX	**MCF-7**, **DU 145**,	(Synthetic lipids)	Microemulsion technique	DLS Microscopy (SEM)	Size 170.7 ± 3.78 nm	Pharm. development	✓ Improved cytotoxicity	[15]	-

	Glioblastoma (**U-87 MG**) cell lines	Solid lipid: Molten M Liquid lipid: Capmul MCM Surfactant: Tween 80 Transcutol HP		DSC XRD FTIR	PDI 0.192 ± 0.027 ZP −3.87 ± 0.048 mV %EE 70.42 ± 3.68% Stability: 12 months	*In vitro* tests *In vivo:* Pharmacokinetic using a rat model administered by intravenous route	✓ Improved bioavailability ✓ The *in vivo* toxicological studies of did not show changes organs studied (heart, liver and lungs)		
DTX	**SKOV3** cells **SKOV3**-xenografted mouse model Intravenous	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: Labrafil M 1944 CS Surfactant: Polysorbate 20 PVA Functionalization: PEGylated -RIPL	Emulsification-evaporation	DLS Microscopy (TEM and CLSM)	Size 187.1 ± 6.6 nm PDI 0.328 ± 0.053 ZP −17.2 ± 0.2 mV %EE 94.8 ± 0.2% Stability: 4 weeks	Pharm. development *In vitro* tests *In vivo:* Antitumour effects	✓ Increased cell apoptosis. ✓ Improved antitumour effect	[16]	[45]
DTX	Not tested	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: MCT Surfactant:	Hot High-pressure homogenization	DLS Microscopy (TEM) DSC XRD	Size 245.3 ± 13.6 nm PDI Not informed ZP − 38.8 mV	Pharm. development *In vitro* test: release *In vivo:*	✓ Improved bioavailability ✓ High uptake in reticuloendothelial system organs ✓ Concentration of DTX in the lungs was higher	[17]	-

		Soybean lecithin Brij 78			%EE 97.8 ± 1.5% Stability: 6 months	Pharmacokinetic using a rat model administered by intravenous route			
DTX	Cervical cancer (**HeLa**) cell line **HeLa** tumour xenograft mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: PC Functionalization: SA-PEG-FA	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size ~ 30 nm PDI Not informed ZP Not informed %EE Not informed	Pharm. development *In vitro* tests *In vivo:* Tissue distribution and antitumour effects	✓ Increased tumour accumulation ✓ Higher antitumour efficacy	[18]	[44]
DTX	**HepG2**, **A549** and mouse **B16** cell lines Mice with **B16** cells Intravenous	(Synthetic lipids) Solid lipid: GMS SA Liquid lipid: MCT Surfactant: P-188 Functionalization: DSPE-PEG-NH_2	Solvent diffusion method	DLS Microscopy (TEM)	Size 168.70 ± 2.07 nm PDI 0.195 ± 0.01 ZP − 28.89 ± 1.3 mV %EE 98.43 ± 0.51% Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* Efficacy, pharmacokinetics and tissue distribution effects	✓ Superior antitumour efficacy against malignant melanoma *in vitro* and *in vivo*	[19]	[42]
DTX	Human lung cancer **(NCL-H460)** cell line	(Synthetic lipids) Solid lipid: Precirol ATO 5	High-pressure homogenization	DLS Microscopy (TEM) DSC XRD	Size 154.1 ± 3.13 nm PDI	Pharm. development *In vitro* tests	✓ Improved cytotoxicity	[20]	-

		Liquid lipid: GMO Surfactants: Polysorbate 80			0.376 ± 0.04 %EE 86.12 ± 3.48% Stability: 6 months				
DTX	**HeLa** and **B16** cell lines	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: P-188 Gel formulation: Pluronic F127	Sonication or ultra-sonication	DLS Microscopy (TEM) DSC	Size 123.5 nm PDI 0.218 ZP −33.44 ± 2.54 mV %EE 80 ± 2.64% Stability 30 days	Pharm. development *In vitro* tests *In vivo:* Tissue distribution studies in rats.	✓ Cytotoxicity was lower than free DTX on B16 and HeLa cells. ✓ Improved concentration on breast tissue	[21]	-
DTX	**Sarcoma-180** cells in mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: Miglyol 812N Surfactant/co-surfactant P-188 Soybean lecithin Functionalization:	High pressure hot homogenization	MS	Not informed	Pharm. development *In vivo* Pharmacokinetics and tissue distribution study using male pathogen-free Sprague–Dawley rats and male Kunming mice	✓ Improved pharmacokinetic profile and distribution in tissues. ✓ Successful targeting of DTX, for skin cancer treatment	[22]	-

		FA-PEG-PCHL							
DTX	Human glioblastoma **(U87 MG)** and human grade IV glioblastoma **(BTNW911)** cell lines	(Synthetic lipids) Solid lipid: Dynasan Phospholipon 90H Liquid lipid: Labrasol Lauroglycol 90 Capryol Surfactant: Lipoid S75	Hot homogenization method	DLS NTA Microscopy (TEM) DSC XRD TGA AF4 FTIR Raman	Size 123.300 ± 0.642 nm PDI 0.234 ± 0.016 ZP - 32.400 ± 0.967 mV %EE 99.130 ± 1.200% Stability: 6 months	Pharm. development *In vitro* tests	✓ Superior cell internalization ✓ Improved cytotoxicity ✓ Decreased mitochondrial reserve capacity Surpass of the blood-brain tumour barrier	[23]	[41]
DTX	Tested in normal skin	(Synthetic lipids) Solid lipid: GMS Liquid lipid: CT Surfactant: Egg lecithin Functionalization: Nicotinamide Gel: Carbomer 940	Emulsion evaporation-solidification	DLS Microscopy (CLSM and TEM) PXRD DSC TGA FTIR	Size 59.48 ± 4.29 nm PDI 0.24 ± 0.08 ZP −31.03± 5.30 mV %EE 79.48 ± 8.02% Stability: Not informed	Pharm. Development *In vitro*: *Permeation* in abdominal rat skins *In vivo:* skin permeation	✓ *In vitro,* greater skin permeation promoted by DN ✓ *In vivo,* DN-NLC gel remained mostly on the inner skin	[24]	-
Paclitaxel (PTX)	**SKOV3** cells	(Synthetic lipids) Solid lipid:	Sonication or ultra-sonication	DLS Microscopy	Size 115.20 ± 3.90 nm	Pharm. development	✓ Improved cytotoxicity	[25]	[54]

		GMS Liquid lipid: Capryol 90 Surfactant: P-188 Tween 80 Functionalization: Platelet membrane		(CLSM / TEM / STEM-EDS) DSC PXRD	PDI 0.284 ± 0.015 ZP -15.00 ± 0.93 mV %EE 99.88 ± 0.01% Stability: Not informed	*In vitro* tests			
PTX	**MCF-7** cells Mice bearing **MCF-7** tumours Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: Tween 20 Functionalization: 2-DG	Sonication or ultra-sonication	Microscopy (TEM / CLSM) DSC NIR XRD LPSA	Size 135.00 nm PDI ~0.270 ZP - 21.8 ± 1.60 mV %EE 95.50% Stability: 90 days	Pharm. development *In vitro* tests *In vivo:* Efficacy	✓ high anticancer potential ✓ lower systemic toxicity	[26]	[48]
PTX	Human colorectal adenocarcinoma (**HT-29**) cell line	(Synthetic lipids) Solid lipid: Chol Liquid lipid: OA Surfactant: P-188	Sonication or ultra-sonication	DLS Microscopy (AFM)	Size 181.6 ± 14.8 nm PDI ~0.10 ZP −12.9 ± 0.2 mV %EE	Pharm. development *In vitro* tests	✓ Improved cytotoxicity	[27]	-

					53 ± 4.2% Stability: Not informed				
PTX	**HepG2** cells	(Natural lipids) Solid lipid: GMS Liquid lipid: Soybean oil Chol Surfactant: Tween 80 P-188	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 153.82 ± 5.58 nm PDI 0.221 ± 0.02 ZP −22.12 ± 2.48 mV %EE 86.48 ± 6.46% Stability: Not informed	Pharm. development *In vitro* tests *Ex vivo:* Intestinal permeation *In vivo:* Pharmacokinetic study in Wistar rats administrated orally	✓ Improved cytotoxicity ✓ Improvement in oral bioavailability	[28]	-
PTX	Human epithelial colorectal adenocarcinoma cell line (**Caco 2**)	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: Tween 20	Sonication or ultra-sonication	DLS Microscopy	Size 283.4 ± 4.5 nm PDI 0.226 ± 0.94 ZP -25.12 mV %EE 85.60% Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* Organ distribution studies after pulmonary administration	✓ Maximum cell uptake by **Caco-2** cells ✓ Improved pulmonary bioavailability	[29]	[50]
PTX	Breast cancer (**MCF-7** and **MDA-MB-231)** cell lines	(Synthetic lipids) Solid lipid:	Hot melting homogenization	DLS Microscopy (PLM) DSC	Size 67 ± 15 nm	Pharm. development	✓ Improved cytotoxicity	[30]	-

		ATO Liquid lipid: Chol Glycerol Surfactant: Polysorbate 80			PDI 0.30 ± 0.12 ZP − 14.5 ± 1.4 mV %EE 90% Stability: 30 days	*In vitro* tests			
PTX	**A549** cells	(Synthetic lipids) Solid lipid: GMS Liquid lipid: MCT Surfactant: Kolliphor HS15 Gelucire 44/14 Functionalization: SA-R8	Fusion-emulsification method	DLS Microscopy (CLSM)	Size 42.34 ± 0.87 nm PDI 0.2 ± 0.01 ZP 16.84 ± 0.96 mV %EE 65.94% Stability: Not informed	Pharm. development *In vitro* tests	✓ Improved cytotoxicity	[31]	[52]
PTX	**MCF-7**, **A549** and **HeLa** cell lines	(Synthetic lipids) Solid lipid: SA Liquid lipid: OA Surfactant: P-188	Solvent diffusion method	DLS Microscopy (TEM)	Size 237.10 nm PDI 0.27 ZP -33.9 mV %EE 49%	Pharm. development *In vitro* tests *In vivo:* biodistribution in *Wistar* rats after intravenous injection	✓ higher cell uptake ✓ *in vivo* higher uptake in folate receptor-positive organs	[32]	[53]

		Functionalization: Fol-PEG-CHEMS			Stability: Not informed				
PTX	Murine melanoma (**B16**), mouse colon cancer (**CT26**) and human colon cancer (**HCT116**) cell lines **B16** in mice Intravenous	(Synthetic /Natural lipids) Solid lipid: GMS Liquid lipid: Soybean oil Surfactant: Soya lecithin Functionalization: HA	Hot emulsion method	DLS Microscopy (TEM)	Size 197.47 ± 8.24 nm PDI 0.26 ± 0.03 ZP -39.61 ± 0.69 mV %EE 90.25 ± 0.41% Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* Efficacy, pharmacokinetics and tissue distribution studies in rats.	✓ Improved cytotoxicity ✓ Greater antitumour efficacy ✓ Prolonged circulation time in the blood ✓ Increased accumulation	[33]	[49]
PTX	**HepG2** cells **H22** (murine liver cancer carcinoma cells) tumour xenograft mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: PEG-SA Functionalization: SA-polyethylene glycol-folate	Microemulsion technique	DLS Microscopy (TEM)	Size 25 ± 2.5 nm PDI 0.102 ZP Not informed %EE Not informed Stability: Not informed	Pharm. development *In vitro* tests *In vivo:* Tumour penetration and anti-tumour studies	✓ Improved cytotoxicity ✓ Improved *in vivo* effect ✓ Low systemic toxicity	[34]	-
PTX	Human lung cancer (**NCl-H1299**) and murine sarcoma	(Synthetic lipids) Solid lipid: ATO	Emulsification–evaporation	DLS Microscopy (TEM and CLSM)	Size 63.27 ± 1.14 nm PDI	Pharm. development *In vitro* tests	✓ Increased cell uptake by tumour cells and decreased recognition by macrophages	[35]	-

	cancer **(S180)** cell lines **S180** tumour-bearing mice Intravenous	GMS Liquid lipid: MCT Surfactant: Kolliphor ELP and HS15 Functionalization: RBCm			0.095 ± 0.021 ZP -29.56 ± 1.17 mV %EE 93.44 ± 0.17% Stability: 15 days	*In vivo:* Tumour-targeting effect and anti-tumour studies was performed in mice.	✓ prolonged PTX blood circulation ✓ Increased the antitumour effect ✓ extended the survival period ✓ lower collateral effects.		
PTX	**U-87** cells	(Synthetic lipids) Solid lipid: Chol Liquid lipid Triolein Soy lecithin Surfactant: P-188 Functionalization: Transferrin	Emulsification-solvent evaporation	PCS Microscopy (TEM) XRD	Size 205.4 ± 11 nm PDI Not informed ZP 25.7 ± 6.22mV %EE 91.8 ± 0.5% Stability: Not informed	Pharm. development *In vitro* tests	✓ Increased cytotoxicity ✓ Higher cellular uptake	[36]	[51]
Vincristine sulfate (VCR)	**MCF-7** cells	(Synthetic lipids) Solid lipid: GMS Liquid lipid: CT Surfactants: SDS Egg lecithin	Emulsion solvent evaporation method	DLS Microscopy (TEM / CLSM)	Size 192 ± 4.41 nm PDI 0.184 ± 0.05 ZP 26.3 ± 1.44 mV %EE 33.28 ± 2.31%	Pharm. development *In vitro* tests *In vivo:* Pharmacokinetic in rats with oral administration	✓ Improved cytotoxicity ✓ HA induced cell apoptosis. ✓ Superior cell uptake *in vitro* ✓ Improved oral bioavailability	[37]	[16]

		Tween 80 CTAB Functionalization: HA			Stability: Not informed				

Alkylating agents

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review
Cisplatin (CIS)	**HeLa** cells **HeLa** mice-bearing xenograft Intravenous	(Natural lipids) Solid lipid: SA Liquid lipid: Soybean oil Surfactant: Tween-80 Soya lecithin Functionalization: FA-PEG-DSPE	Emulsification method	DLS	Size 143.2 ± 5.3 nm PDI 0.15 ± 0.02 ZP 25.7 ± 2.3mV %EE: 87.5 ± 3.2% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Anti-tumour efficiency in mice	✓ Superior cytotoxicity and tumour inhibition	[38]	[60]
CIS	**SKOV3** cells **SKOV3** cells in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Precirol ATO 5 Liquid lipid: Miglyol 812 Surfactant:	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 132.4 ± 5.3nm PDI 0.158 ± 0.015 ZP −19.3 ± 1.9mV %EE:	Pharm. Development *In vitro* tests *In vivo:* Pharmacokinetics, biodistribution and antitumour efficiency	✓ Improved cytotoxicity and cellular uptake ✓ Sustained plasma retention until 48h ✓ Best tumour inhibition rate	[39]	-

		Tween 80 Lecithin			82.6 ± 3.9% Stability: Not informed				
Dacarbazine (DZ)	Not tested	(Synthetic lipids) Solid lipid: Glyceryl palmitostearate Isopropyl myristate Liquid lipid: TS Polyethylene glycol succinate Surfactant: P-188 Soybean lecithin	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size: 190 ± 10 nm PDI: 0.2 ± 0.01 ZP: Not informed %EE: 98.5% Stability: Not informed	Pharm. development	NLC with high encapsulation efficiency	[40]	[62]
Ifosfamide (IFOS)	Not tested	(Synthetic lipids) Solid lipid: GMO Liquid lipid: OA Surfactant: P-188 Functionalization: Chitosan and Sodium alginate	Sonication or ultra-sonication	DLS Microscopy (TEM) FTIR DSC XRD	Size 223 nm PDI 0.194 ± 0.025 ZP −25 mV %EE: 77% Stability: 6 months	Pharm. Development	✓ Enhanced NLC stability ✓ High entrapment efficiency ✓ Sustained release	[41]	[63]
IFOS	Dalton's ascitic lymphoma (**DAL**) cells in mice	(Synthetic lipids) Solid lipid:	Sonication or ultra-sonication	DLS	Size 223 nm	*In vivo:*	✓ Increased IFOS plasma concentrations	[42]	[18]

	Oral route	GMO Liquid lipid: OA Surfactant: P-188 Functionalization: Chitosan and Sodium alginate			PDI 0.194 ± 0.025 ZP −25 mV %EE: 77% Stability: 6 months	Pharmacokinetics study and Antitumour Activity	and bioavailability. ✓ Oral administration as efficient as intravenous administration of IFOS suspension, but with less side effects		
IFOS	Not tested	(Synthetic lipids) Solid lipid: GMO Liquid lipid: OA Surfactant: P-188 Functionalization: Chitosan and Sodium alginate	Sonication or ultra-sonication	DLS	Size 223 nm PDI 0.194 ± 0.025 ZP −25 mV %EE: 77% Stability: 6 months	*In vivo:* Toxicity after oral delivery in rat	✓ No mortality ✓ No signs of behavioural changes or toxicity after oral administration of IIFOS NLC ✓ Reduced severity of renal dysfunction induced by IFOS	[43]	[64]
Mechlorethamine (MCTN)	Myelogenous leukemia (**K562**) cell line	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Miglyol 812 Surfactant:	Sonication or ultra-sonication	DLS Microscopy (TEM) DSC	Size 105.92 ± 1.04 nm PDI 0.02 ZP - 30.1 ± 0.82 mV	Pharm. Development *In vitro* tests *In vivo:* Pharmacokinetics study in rat by oral route	✓ Improved cytotoxicity ✓ Increased MCT plasma concentration ✓ Greater absorption	[44]	[17]

		P-188			%EE: 91.7 ± 1.20% Stability: 180 days				
Temozolomide (TMZ)	Not tested	(Synthetic lipids) Solid lipid: Gelucire 44/14 Liquid lipid: Trascutol Surfactant: Tween 80 Functionalization: Vitamin E	High-pressure homogenization (HPH) followed by ultrasonication	PCS Microscopy (TEM) DSC	Size 131.58 nm PDI 0.177 ZP 15.21 ± 3.11 mV %EE: 81.64 ± 3.71% Stability: Not informed	Pharm. development *Ex Vivo*: Transport Study Across Nasal Mucosa *In vivo:* (Wistar rats) absorption and brain uptake/ Pharmacokinetic and Brain Distribution	✓ Greater permeation through the nasal mucosa ✓ increased nose-to-brain drug delivery ✓ Long lasting (24h) effect ✓ Tween 80 enhanced drug penetration	[45]	[66]
TMZ	**U87 MG** cells **U87 MG** in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Cremophor Surfactant: Tween-80 Soya lecithin	Emulsification-solvent diffusion	DLS Microscopy (TEM)	Size 121.4±5.6 nm PDI 0.21±0.06 ZP 29.1±2.4 mV %EE: 81.4 ± 3.7% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Anti-tumour efficacy	✓ Improved cytotoxicity ✓ High tumour regression rates	[46]	[67]
TMZ	Malignant glioma Intravenous	(Synthetic lipids) Solid lipid:	Emulsification-solvent diffusion	DLS	Size 178.9 ± 2.7 nm	Pharm. Development *In vitro* tests	✓ Higher cytotoxicity	[47]	[68]

		ATO Liquid lipid: Cremophor ELP Surfactant: DDAB Lecithin Tween-80			PDI 0.16 ± 0.05 ZP: 22.8 ± 2.8 mV %EE: 82.7 ± 2.5% Stability Not informed	*In vivo:* Gene transfection analysis Anti-tumour efficacy	✓ Higher tumour inhibition rates		
TMZ	**U87 MG** cells **U87 MG** solid tumours in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Cremophor Surfactant: Tween-80 Soya lecithin Functionalization: RGD	Emulsification-solvent diffusion	DLS	Size 118.3 ± 2.6 nm PDI 0.11 ± 0.02 ZP 28.9 ± 2.9 mV %EE: 84.7 ± 3.2% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Anti-tumour efficacy	✓ Significantly higher cytotoxicity ✓ Superior tumour growth inhibition	[48]	[69]
Oxaliplatin (OXA)	**HT-29** cells	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Miglyol 812 Surfactant: Poloxamer	Sonication or ultra-sonication	DLS Microscopy (SEM)	Size ~ 98nm PDI 0.2 ZP -11,4mV %EE: 87%	Pharm. Development *In vitro* tests	✓ Higher inhibition of cell proliferation, ✓ Increased cell death and apoptosis	[49]	-

		Functionalization: Naringenin			Stability: Not informed				

Antitumour antibiotics

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review
Doxorubicin (DOX)	**MCF-7** cells	(Synthetic lipids) Solid lipid: SA Liquid lipid: OA Surfactant Lecithin P-188	Emulsification-solvent evaporation	DLS Microscopy (SEM)	Size 134.0 ± 2.3nm PDI 0.265 ± 0.031nm ZP −15 ± 3.4 to −29.4 ± 7.3 mV %EE 75 Stability: 60 days	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity	[50]	-
DOX	Murine breast cancer cell line (**4T1**) **4T1** in mice Intravenous	(Natural lipids) Solid lipid: ATO Liquid lipid: Sesame oil Surfactant Tween 80	Sonication or ultra-sonication	DLS	Size 93.76 nm PDI 0.262 ZP -29.9 %EE 96.54%	Pharm. Development *In vitro* tests *In vivo:* Antitumour activity	✓ Improved cytotoxicity ✓ Improved antitumoral efficiency compared to other DDS.	[51]	[76]

					Stability: Not informed				
DOX	**MDA-MB-231** and **4T1** cells **4T1** in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: OA Surfactant Tween 80 Functionalization: DHA TS	Sonication or ultra-sonication	DLS	Size 72.5 ± 2.6nm PDI 0.139 ± 0.006 ZP - 21.7 ± 2.2 mV %EE 95.7 ± 3.3% Stability: Not informed	Pharm. Development *In vivo:* Antitumour Activity, Biodistribution, histology and toxicity	✓ Improved cytotoxicity ✓ Improved antitumoral efficiency with reduced toxicity.	[52]	[77]
DOX	**MDA-MB-231** and **4T1** cells **4T1** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: MCT Surfactant Tween 80 Functionalization: TS	Sonication or ultra-sonication	DLS NTA Microscopy (AFM)	Size 85.0 ± 4.1nm PDI 0.204 ± 0.02 ZP −41.0 ± 2.6 mV %EE 98.97 ± 0.33% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Pharmacokinetics, biodistribution and antitumour activity	✓ Improved cytotoxicity DOX/TS synergy) ✓ Improved bioavailability and antitumour activity	[53]	[78]
DOX	**A549** cells	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid:	High-pressure homogenization (HPH)	DLS Microscopy (SEM)	Size 86.2 nm PDI 0.28	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity ✓ Improved cellular internalization ✓ Induced cellular apoptosis	[54]	-

		Miglyol Surfactant Poloxamer 407 Functionalization: SiC RGD			ZP −18.5 mV %EE 56.04 ± 1.25% Stability: 8 weeks				
DOX	**A549** cells **A549** solid tumours in mice Intravenous	(Natural lipids) Solid lipid: Precirol ATO-5 Liquid lipid: Olive oil Lipoid S100 Surfactant Tween-80 Lecithin Functionalization: pEGFP-N1	Emulsification-solvent evaporation	DLS Microscopy (TEM)	Size 198.2 ± 3.1nm PDI 0.13 ± 0.02 ZP 18.9 ± 2.6 mV %EE 86.7 ± 2.7% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Gene transfection analysis and antitumour effect in mice	✓ Improve gene transfection efficiency of the vector ✓ Improved efficacy on solid cancer	[55]	[81]
DOX	**4T1** cells **4T1** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Docosahexaenoic triglyceride Surfactant: Tween 80 Functionalization:	Sonication or ultra-sonication	DLS NTA Microscopy (TEM) DSC SAXS	Size 85 ± 3 nm PDI 0.22 ± 0.01 ZP − 41 ± 1 mV %EE 81 ± 2% Stability:	Pharm. Development *In vitro* tests *In vivo:* Evaluation of antitumour activity and toxicity evaluation in mice	✓ DOX, DHA, and TS synergistic effects ✓ Increased cellular uptake ✓ Improved tumour inhibition and reduced mortality, metastasis and toxicity in liver and heart	[56]	[80]

		DHA TS			Not informed				
DOX	**4T1** cells **4T1** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: Cholesteryl ester Triolein Liquid lipid: OA Surfactant: CTAB Functionalization: ApoB-100	Emulsification-solvent evaporation	DLS Microscopy (CLSM and TEM)	Size 129.0 ± 2.4 nm PDI 0.19 ± 0.02 ZP - 21 ± 0.82 mV %EE 91.4 ± 1.9% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Bio-distribution, antitumour efficiency and toxicity	✓ Higher tumour cell uptake and tumour cell inhibition ✓ Improved in vivo efficacy with lower toxicity	[57]	[79]
DOX	**B16F10** cells	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Miglyol 812N Surfactant: Poloxamer Functionalization: Stattic	Sonication or ultra-sonication	DLS Microscopy (SEM	Size 67–115 nm PDI 0.24 ZP 30 mV %EE Not informed Stability: Not informed	Pharm. Development *In vitro* tests	✓ Synergistic activity ✓ Inhibition of STAT3 signalling/ downregulation of antiapoptotic Bcl-2 family genes	[58]	-
DOX	**MDA-MB-231** cells	(Synthetic lipids) Solid lipid: Gelucire Cetyl palmitate	Sonication or ultra-sonication	DLS and ELS Microscopy (TEM)	Size 281 ± 18 nm PDI 0.15 ± 0.04	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity and cellular uptake	[59]	-

		Liquid lipid: OA Miglyol Surfactant: Polysorbate 80 Functionalization: PEG-FA			ZP − 28.0 ± 0.9 mV %EE 66 ± 8% Stability: 42 days				
DOX	**MCF-7** and **MCF7/ADR** cells	(Synthetic lipids) Solid lipid: ATO Liquid lipid: OA Surfactant: Tween 80 Functionalization: DHA .	Sonication or ultra-sonication	DLS Microscopy (CLSM)	Size 76–86 nm PDI 0.22 ZP −23 and −36 mV %EE ~100 Stability: Not informed	*In vitro* tests Spheroids: Cytotoxicity Penetration	✓ Improved cytotoxicity and penetration in spheroids	[60]	[74]
DOX	**4T1** cells **4T1** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: OA DHA Surfactant Tween 80 Functionalization:	Sonication or ultra-sonication	DLS Microscopy (SEM / TEM)	Size 128 ± 1 nm PDI 0.098 ZP 5 ± 3 mV %EE Not informed Stability:	Pharm. Development *In vitro* tests *In vivo:* Tumour growth inhibition, toxicity and pharmacokinetic	✓ Improved pharmacokinetics (higher plasma concentration) ✓ lower accumulation in the liver and higher accumulation in tumour ✓ Enhanced effect (tumour growth inhibition)	[61]	[75]

		LbL-PEG			14 days				
DOX	**MCF-7** cells	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Miglyol 812N Surfactant: Poloxamer 407 Functionalization: Vitamin D	Sonication or ultra-sonication	DLS Microscopy (SEM) FTIR	Size 87.5 nm PDI 0.24 ZP -12 mV %EE Not informed Stability: Not informed	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity ✓ Increased percentage of MCF-7 cells in sub-G1 arrest	[62]	-
DOX	**PC-3** cells	(Natural lipids) Solid lipid: GMS Liquid lipid: Soybean oil Surfactant: Lecithin PEG-40-St DSPE-PEG	Emulsification-solvent evaporation	DLS Microscopy (TEM)	Size 170 nm PDI Not informed ZP −14.8 mV %EE 74.18 ± 0.3% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Oral bioavailability	✓ Improved cytotoxicity ✓ Improved DOX bioavailability	[63]	[19]
DOX	**HCT116** cells	(Synthetic lipids) Solid lipid: SA GMS	High-pressure homogenization (HPH)	DLS Microscopy (TEM) DSC SAXS	Size 168 − 173 nm PDI was less than 0.2 ZP	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity ✓ Higher cellular uptake	[64]	-

		Liquid lipid: OA MCT Surfactant P-188			30 mV %EE 97.80% Stability: 30 days				
Pirarubicin (THP)	**4T1** cell Mice bearing **4T1** Intravenous	(Synthetic lipids) Solid lipid: Structured triglyceride Liquid lipid: OA Surfactant: Solutol HS 15 Lecithin Functionalization: TS	High-pressure homogenization (HPH)	DLS Microscopy (TEM / CLSM)	Size 112 ± 2.8 nm PDI 0.18 ± 0.02 ZP −17.5 ± 1.3 mV %EE 90.01 ± 3.03% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Distribution and pharmacokinetic studies, flow cytometry (Analysis of Immune cells and cytokine Assay), histological and immunohistochemical analysis, antitumour efficacy in mice Co-administering iRGD	✓ Higher levels of tumour distribution, ✓ enhanced tumour cell death ✓ increased immune-mediated antitumour effect	[65]	[82]
Irinotecan (Ir)	**HT-29** and **Colo-320** cell lines Ehrlich's ascites tumour in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Capmul MCM	Emulsification-solvent evaporation	DLS Microscopy (CLSM / TEM) FTIR NMR	Size 386 ± 2.2 nm PDI Not informed ZP 19.7 ± 1.2 mV	Pharm. Development *In vitro* tests *In vivo:* biodistribution studies	✓ Low macrophage engulfment ✓ Enhanced uptake and prolonged accumulation in in vivo	[66] [67]	[84] [85]

		Surfactant P-188 Deoxycholate Lecithin Functionalization: HA			%EE 98.22 ± 2.06% Stability: Not informed	and antitumour efficiency	✓ Enhanced antitumoral activity ✓ Low (hematologic) side effects		
Etoposide (ETP)	Human gastric cancer (**SGC7901**) cell line Mice bearing **SGC7901** cells xenografts Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA SPC Surfactant: DOTAP Lecithin	Solvent injection (or solvent displacement)	DLS	Size 91.3 ± 2.8 nm PDI 0.12 ± 0.03 ZP 23.1 ± 3.3 mV %EE 78.4 ± 3.6% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* antitumour effects	✓ Improved cytotoxicity ✓ Improved anti-tumour efficacy	[68]	[87]
ETP	Acute myelogenous leukaemia (**K562**) cell line	(Synthetic lipids) Solid lipid: Cetyl palmitate Liquid lipid: Octyldodecanol Surfactant: P-188 Lecithin Functionalization: Tf	Emulsification-solvent diffusion	DLS FTIR	Size 171.0 ± 1.4 nm PDI 0.287 ± 0.043 ZP 23.3± 0.6 mV %EE 74.07 ± 0.78% Stability: Not informed	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity	[69]	-

ETP	Human Burkitt's lymphoma (**Raji**) cell line Lymphoma model in mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: Miglyol 812N Surfactant CTAB Functionalization: HA TAT TS	Solvent injection (or solvent displacement)	DLS Microscopy (TEM) FTIR NMR	Size 125.2 ± 7.1 nm PDI 0.27 ± 0.07 ZP 21.3 ± 3.4% %EE 90.74 ± 3.08% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Tissue biodistribution Antitumour efficacy	✓ Improved cytotoxicity and cellular uptake ✓ Improved antitumour efficacy with low side-effects	[70]	-
ETP	**A549** cells	(Natural lipids) Solid lipid: GMS Liquid lipid: Soybean oil Surfactant: Lecithin Functionalization: DSPE-PE or PEG-40-st	Emulsification-solvent evaporation	PCS Microscopy (TEM)	Size 125.9–91.2 nm PDI < 0.2 ZP 28.49 to 15.34 mV %EE 57.9 – 89.7% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Pharmacokinetic study in rats and Intestinal absorption	✓ Improved cytotoxicity ✓ Superior absorption by the guts ✓ Improved bioavailability in rats after oral administration	[71]	[86]
ETP	**CT26**, **SGC7901** and **NCI-H209** cells Gastric	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA	Solvent injection (or solvent displacement)	PCS Microscopy (TEM)	Size 120.91 ± 3.59 nm PDI 0.139 ± 0.026 ZP	Pharm. Development *In vitro* tests *In vivo:*	✓ Selective delivery to human gastric cancer cells ✓ Enhancement of the antitumour capacity	[72]	[88]

	tumour-bearing mice (**SGC7901** cells) Intravenous	Surfactant: DOTAP Lecithin Functionalization: FA-PEG-DSPE			21.3 mV %EE 83.86 ± 3.21% Stability: 24 h	Tissues distribution assay and antitumour effects	✓		
Topotecan (TPT)	**B16F10** cells	(Synthetic lipids) Solid lipid: SA Liquid lipid: OA Surfactant: Lecithin Taurodeoxycholate	Microemulsion technique	DLS NTA Microscopy (AFM)	Size 183.2 nm PDI 0.3 ZP 75.9 mV %EE Not informed Stability: Not informed	Pharm. Development *In vitro* tests Skin permeation	✓ Enhanced cytotoxicity	[73]	-

Codelivery of conventional AA by NLC

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review
DOX + PTX	**A549** cells Pulmonary carcinoma Nasal	(Synthetic lipids) Solid lipid: SA GMS Soya lecithin	Emulsification-solvent evaporation	DNPA Microscopy (SEM) DSC XRD	Size 394.1 ± 5.6 nm PDI 0.180 ± 0.02	Pharm. Development *In vitro* tests *In vivo:*	✓ Enhanced retention and drug accumulation in the lung without signs	[74]	[20]

		Liquid lipid: OA Surfactant Cremophor EL			ZP -18.17 ± 2.3 mV %EE 79.87 ± 3.32% Stability Not informed	Lung deposition, bio-distribution (lungs, liver, kidney, and spleen) and lungs histology	of tissue abnormality		
DOX + PTX	**NCL-H460** cells Mice models grafting **NCL-H460** cells Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: OA Surfactant DOTMA	Sonication or ultra-sonication	DLS	Size 129.3 ± 4.2 nm PDI 0.18 ± 0.05 ZP 26.6 ± 3.2 mV % EE_{DOX} 83.7 ± 4.1 % EE_{PTX} 81.9 ± 4.4 Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Antitumour efficiency	✓ Improved cytotoxicity ✓ Improved efficacy ✓ Synergistic DTX-PTX effects ✓ Lower systemic toxicity	[75]	[92]
DOX / PTX *	**MCF-7**, **SKOV3** cells and their multidrug resistant (**MCF-7/ADR** and **SKOV3-TR30**) cells	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: P-188	Emulsification-solvent diffusion	DLS	Size 306.3 ± 40.1 nm PDI 0.325 ± 0.022 ZP -32.1 ± 2.5 mV %EE 67.05 ± 2.60%	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity and cellular uptake	[76]	-

		Functionalization: FA–SA			Stability Not informed				
DOX + PTX	**MCF-7/ADR** cells	(Synthetic lipids) Solid lipid: SA Liquid lipid: SPC Surfactant: CTAB Functionalization: FA	Emulsification-solvent evaporation	DLS Microscopy (TEM) DSC FTIR	Size 196 ± 2.5 nm PDI 0.214 ± 0.04 ZP 23.4 ± 0.3 mV %EE_{DOX} 89.6 ± 0.5 %EE_{PTX} 88.3 ± 0.2 Stability Not informed	Pharm. Development *In vitro* tests	✓ Improved cytotoxicity and synergistic effect of drug combination	[77]	-
DOX + PTX	Glioma stem cells (CD133+) **U87** cells Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: OA SPC Surfactant: DOTMA Lecithin .	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 122.83 ± 1.97 nm PDI 0.31 ± 0.04 ZP 18.64 ± 1.46 mV %EE_{DOX} 66.45 ± 4.02 %EE_{PTX} 62.96 ± 3.38	Pharm. Development *In vitro* tests *In vivo:* tumour progression; Immunohistochemistry; Biochemical analysis.	✓ Inhibitory effect on colony formation ✓ Suppression of proliferation and induced apoptosis by blocking the PI3K/Akt/mTOR signalling	[78]	[93]

					Stability Not informed				
DOX + CIS	**MCF-7** and **MCF-7/ADR cells** MCF-7/ADR tumour-bearing mice models Intravenous	(Synthetic lipids) Solid lipid: SA Liquid lipid SPC Surfactant: DDAB	Emulsification-solvent evaporation	PCS	Size 108.3 ± 2.3 nm PDI Not informed ZP 16.4 ± 1.6 mV $\%EE_{DOX}$ 89.5 ± 3.7% $\%EE_{CIS}$ 86.7 ± 2.8% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Anti-tumour efficacy	✓ Improved cytotoxicity ✓ Efficient on DOX-resistant MCF-7 cells ✓ Improved tumour concentration than in the heart and kidney ✓ Higher tumour inhibition	[79]	[94]
DOX + VCR	Diffuse large B-cell lymphoma (DLBCL) Cell lines (**LY1**) **LY1** cells in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Cremophor ELP Surfactant: DDBA	Microemulsion technique	DLS	Size 95.8 ± 2.1 nm PDI Not informed ZP 21.3 ± 2.8 mV $\%EE_{DOX}$ 87.9 ± 2.4 $\%EE_{VCR}$ 83.3 ± 2.1 Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* *Animal* Antitumour efficacy	✓ High anti-tumour activity against lymphoma cells ✓ DOX-VCR synergistic effect	[80]	[95]

DOX + GEM + VCR	**Raji** cells **Raji** cells in mouse Intravenous	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: PVA Surfactant: Lecithin	Solvent injection (or solvent displacement)	DLS Microscopy (TEM)	Size 112 ± 5.7 nm PDI 0.187 ± 0.051 ZP −39.7 ± 4.1 mV %EE_{DOX} 86.1 ± 2.7% %EE_{GEM} 86.8 ± 3.1% %EE_{VCR} 89.2 ± 2.9% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Efficacy, biodistribution	✓ Enhanced cytotoxicity ✓ Low drug concentration to heart and kidney ✓ Better antitumour therapeutic efficiency	[81]	[96]
DOX + Baicalein (BCL)	**MCF-7/ADR** cell **MCF-7/ADR** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: SA Precirol ATO 5 SPC Liquid lipid: Cremophor ELP Surfactant: Lecithin DDAB Functionalization: HA	Emulsification-solvent evaporation	DLS	Size 103.5 ± 2.2 nm PDI Not informed ZP 12.6 ± 1.2 mV %EE_{BCL} 90.8 ± 1.7% %EE_{DOX} 91.5 ± 1.8% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* anti-tumour efficacy	✓ Improved cytotoxicity with synergistic effect ✓ Improved antitumour efficacy with reduced systemic toxicity	[82]	[97]

DOX + Sclareol (SC)	**MDA-MB-231** and **4T1** cells **4T1** tumour-bearing mice Intravenous	(Natural lipids) Solid lipid: ATO Liquid lipid: OA Peanut oil Surfactant: Tween 80	Sonication or ultra-sonication	DLS Microscopy (PLM) DSC SAXS	Size 104 ± 12 nm PDI 0.23 ± 0.02 ZP -31 ± 2 %EE 97 ± 2% Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Antitumour activity	✓ Improved cytotoxicity DOX-SC synergism ✓ Improved antitumoral efficiency	[83]	[98]
DOX + β-elemene	**A549** and **A549/ADR** cells Tumour xenografts **A549/ADR** in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Miglyol 812 Surfactant: Lecithin Tween 80 Functionalization: mPEG-Hyd-DSPE	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 190 nm PDI 0.2 ZP −30.9 and −41.3 mV $\%EE_{DOX}$ 89.3 ± 3.9% $\%EE_{ELE}$ 87.7 ± 4.2% Stability: 72h	Pharm. Development *In vitro* tests *In vivo:* Antitumour activity	✓ Improved cytotoxicity DOX-β-elemene synergistic effect ✓ Improved antitumoral efficiency	[84]	[99]
DOX +	**MCF-7/ADR** cells	(Synthetic lipids) Solid lipid:	Sonication or ultra-sonication	DLS Microscopy (CLSM / TEM)	Size 100.2 ± 6.8 nm	Pharm. Development	✓ Improved DOX retention in tumour	[85]	[100]

β-Lapachone (LAPA)	**MCF-7/ADR** tumour-bearing mouse Intravenous	GMS ATO Liquid lipid: OA SPC Surfactant P-188 PEG-SA			PDI 0.123 ZP -23.5 ± 3.6 mV %EE 92.3% Stability: Not informed	*In vitro* tests *In vivo:* anticancer efficiency and distribution	✓ Enhanced tumour inhibition		
PTX + CIS	Head and neck cancer (**FaDu**) cell line **FaDu** in mice Intravenous	(Natural lipids) Solid lipid: ATO Liquid lipid: Olive oil Cremophor ELP Surfactant: CTAB Tween 80 Functionalization: FA-PEG-DSPE	Solvent injection (or solvent displacement)	PCS Microscopy (TEM)	Size 127.1 ± 5.1 nm PDI 0.23 ± 0.07 ZP 26.7 ± 2.2 mV $\%EE_{CIS}$ 82.1 ± 3.4% $\%EE_{PTX}$ 79.2 ± 3.1% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Tissue distribution and Anticancer effect	✓ Improved cytotoxicity ✓ Improved tumour regressions	[86]	[101]
PTX +	**A549** cells Xenografts **A549** cells in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid	Emulsification-solvent diffusion	DLS Microscopy (TEM)	Size 131.6 ± 3.5 nm PDI 0.131 ± 0.026	Pharm. Development *In vitro* tests *In vivo:*	✓ Improved cell uptake and the combination treatment ✓ PTX-DMN synergistically	[87]	[102]

5-Demethylnobiletin (DMN)		OA SPC Surfactant: Lecithin DSPE-PEG-Mal DDAB			ZP 19.5 ± 2.7 mV %EE_{PTX} 90.5 ± 4.2% %EE_{DMN} 91.1 ± 3.7% Stability: 90 days	Anti-tumour effects and tissue distribution in mice	decreased cancer cells viability ✓ Improved tumour inhibition efficiency		
CIS + 5-FU	Human gastric cancer (**BGC823**) cell line Mice bearing **BGC823** human GC xenografts Intravenous	(Natural lipids) Solid lipid: GMS Liquid lipid: soybean oil Surfactant: Tween 80 Lecithin DDBA Functionalization: HA and 5-FU linked to SA	Microemulsion technique	DLS Microscopy (TEM)	Size 181.6 ± 3.2 nm PDI 0.21 ± 0.04 ZP 26.3 ± 2.4 mV %$EE_{5\text{-}FU}$ 89.8 ± 2.9% %EE_{CIS} 89.1 ± 2.1% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Efficacy	✓ Strongest antitumour activity	[88]	[104]
TMZ + VCR	**U87 MG** cells **U87 MG** cells in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid:	Emulsification-solvent diffusion	DLS	Size 117.4 ± 2.8 nm PDI 0.09 ± 0.02 ZP 29.8 ± 3.2 mV	Pharm. Development *In vitro* tests *In vivo:* Anti-tumour efficacy	✓ Improved cytotoxicity ✓ Improved tumour inhibition	[89]	[105]

		Cremophor ELP SPC Surfactant: DDAB Lecithin			%EE_{TMZ} 88.9 ± 3.6% %%EE_{VCR} 85.4 ± 2.8% Stability Not informed				
TMZ + VCR	**U87 MG**, human malignant glioma (**T98G**) cell line, and **A549** cells **U87 MG** in mice Intravenous	(Synthetic lipids) Solid lipid: Compritol 888 ATO Liquid lipid: Cremophor ELP Surfactant: DDAB Lecithin Functionalization: Lactoferrin-PEG-DSPE RGD-PEG-DSPE	Emulsification-solvent diffusion	DLS	Size 139.3±4.9 nm PDI 0.187 ± 0.021 ZP 32.4±2.7mV %EE_{TMZ} 81.9 ± 3.4% %%EE_{VCR} 82.2 ± 3.2% Stability 3 months	Pharm. Development *In vitro* tests *In vivo:* Tissue distribution, antitumour activity	✓ Improved cytotoxicity with TMZ-VCR synergism ✓ increased drug accumulation in the tumour ✓ improved tumour inhibition with low systemic toxicity	[90]	-
GEM + PTX	Human pulmonary adenocarcinoma (**A549, LTEPa2**) cell lines Tumour xenograft model of **A549** cells in mouse	(Synthetic lipids) Solid lipid: GMS Liquid lipid: Soy lecithin Surfactant: Sodium deoxycholate	Emulsification-solvent evaporation	DLS Microscopy (CLSM / TEM)	Size 119.6 ± 0.3 nm PDI 0.251 ± 0.03 ZP -20.7 ± .9 mV	Pharm. Development *In vitro* tests *In vivo:* Antitumour effect	✓ Suppression of tumour growth	[91]	-

	Intravenous	Poloxamer 188 Tween 80 Functionalization: NAG (N-acetyl-d-glucosamine), a Glucose receptor ligand.			$\%EE_{GEM}$ 83.7 ± 4.15 $\%EE_{PTX}$ 83.5 ± 2.72 Stability: Not informed				
GEM + PTX (Covalently bound through an ester linker form drug conjugates) associated to NAG-NLC	Cell lines: **A549, NCLH1299** and **LTEPa2**	(Synthetic lipids) Solid lipid: GMS Liquid lipid: Soy lecithin Surfactant: P-188 Tween 80 Functionalization: NAG	Emulsification-solvent evaporation	DLS Microscopy (CLSM / TEM)	Size 120.3 ± 1.3 nm PDI 0.233 ± 0.04 ZP -27.8 ± 3.4 mV %EE Not informed Stability Not informed	Pharm. Development *In vitro* tests	✓ Superior cytotoxicity ✓ High uptake by A549 cells (via glucose receptor-mediated endocytosis)	[92]	-
GEM + BCL	Human pancreatic adenocarcinoma (**AsPC1**) cell line and **HeLa** cells AsPC1 cells in mice	(Synthetic / Natural lipids) Solid Lipid: Precirol ATO-5 Liquid lipid:	Solvent evaporation	PCS H NMR and IR spectroscopy	Size 131.9 ± 3.9 nm PDI 0.12 ± 0.03	Pharm. Development *In vitro* tests *In vivo:*	✓ Significant tumour growth inhibition	[93]	-

	Intravenous	Olive oil Surfactant: Tween 80 DDAB SPC Functionalization: HA			ZP -25.9 ± 1.9 mV %EE_{GEM} 85.1 ± 2.3% %EE_{BCL} 82.9 ± 2.4% Stability 1 month	Antitumour effect Tissue distribution			
PTX + Salinomycin (SAL)	**NCl-H1299** and **S180** cells **S180** cells in mice Intravenous	(Synthetic lipids) Solid lipid: ATO Liquid lipid: MCT Surfactant Polyoxyethylene (40) stearate Solutol HS15 Kolliphor EL Functionalization: DSPE-PEG-TR	Microemulsion technique	DLS Microscopy (CLSM)	Size 128.73 ± 2.09 nm PDI Not informed ZP −28.3 ± 0.4 mv %EE 95.62 ± 1.46% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Antitumour effect	✓ Greater tumour suppression	[94]	-
PTX + SiRNA	**A549** cells Mouse orthotopic model of human lung cancer (**A549**) Inhalation	(Synthetic lipids) Solid lipid: Precirol ATO 5 Liquid lipid: Squalene SPC	Sonication or ultra-sonication	DLS Microscopy (AFM)	Size 110 ± 20 nm PDI 0.4 ZP 60.3 mV	Pharm. Development *In vitro* tests *In vivo:* Efficacy, biodistribution	✓ Improved accumulation in lung cancer ✓ Enhanced antitumour efficiency	[95]	-

		Surfactant Tween-80 DOTAP Lecithin Functionalization: DSPE-PEG-LHRH			%EE Not informed Stability 1 month				
PTX + pEGFP	**NCl-H460** cells **NCl-H460** cells in mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid OA Surfactant: DOTMA Tween-80 Lecithin Functionalization: Tf-PEG-PE	Microemulsion technique	LLS Microscopy (TEM)	Size 133 nm PDI Not informed ZP 19 mV %EE 85.4 ± 2.9% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Antitumour efficacy; gene transfection analysis.	✓ Increased *in vivo* gene transfection efficiency ✓ Improved antitumour efficacy	[96]	-
DOX + Sorafenib (SFN)	Mice drug-resistant oesophagus carcinoma (**AKR/Dox**) cell line AKR/Dox tumour-bearing model in mice. Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid OA Surfactant: Lecithin PC Functionalization: SA-PEG-FA	Emulsification-solvent diffusion	DLS	Size 100 nm PDI Not informed ZP Not informed %EE Not informed Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* anticancer efficacy, immune *activation*	✓ DOX-SFN synergistic effect (improved cytotoxicity) ✓ Strong immune response after treatment	[97]	-

MTX + DTX + DOX	**MCF-7** and **A549** cells	(Synthetic lipids) Solid lipid: GMS SA Liquid lipid: Miglyol 812 Surfactant: Poloxamer 407	Solvent injection (or solvent displacement)	DLS Microscopy (SEM / TEM) FTIR	Size 233.3 nm PDI 0.14 ZP Not informed $\%EE_{MTX}$ 33.73% $\%EE_{DOX}$ 90.48% $\%EE_{DTX}$ 98.95% Stability Not informed	Pharm. Development *In vitro* tests	✓ Increased cell uptake, apoptosis, autophagy, ROS levels ✓ Clonogenicity tests revealed decreased colony formation in MCF-7 cells	[98]	-
DTX + Trastuzumab	Breast cancer **(MDA-MB-468 and BT-474)** cell lines	(Natural lipids) Solid lipid: SA Stearyl amine Spermine Chol Liquid lipid: Castor oil Surfactant Poloxamer F127	Sonication or ultra-sonication	DLS Microscopy (SEM/ TEM)	Size 199 ± 10 nm PDI 0.65 ± 0.05 ZP ~18 mV $\%EE_{DTX}$ 75.5 ± 2.0% Stability Not informed	Pharm. Development *In vitro* tests	✓ Enhanced cellular uptake ✓ Higher cytotoxic effect	[99]	-
DTX	**MDA-MBA-231** cells	(Synthetic lipids)	Sonication or ultra-sonication	DLS Microscopy (SEM)	Size 55 a 110 nm	Pharm. development	✓ Improved cytotoxicity	[100]	-

+ Myricetin		Solid lipid: ATO Liquid lipid: Miglyol 812 Surfactant: Poloxamer 407 Functionalization: Myricetin			PDI 0.19 ZP -12 mV % EE Not informed Stability Not informed	*In vitro* tests	✓ Increase in apoptotic cells		

New approaches in chemotherapy

Curcumin as non-conventional AA encapsulated in NLC Curcumin

Drug	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review
Curcumin (CUR)	Human epithelial ovarian cancer (**A2780S** and **A2780CP**) cell lines	(Synthetic lipids) Solid lipid: ATO Liquid lipid: Captex 355 EP/NF Miglyol 812 Surfactant: SPC Taurocholate	Microemulsion technique	DLS Microscopy (fluorescent) FTIR	Size ~100 nm PDI > 0.2 ZP −30 mV %EE 40% Stability	Development *In vitro* tests	✓ Improved cytotoxicity ✓ Improved inhibition colony formation ✓ No haemolytic effect	[101]	-

					Not informed				
CUR	Human neuroblastoma cell line (**LAN5**)	(Synthetic lipids) Solid lipid: ATO Precirol ATO Liquid lipid: Imwitor 800 Surfactant: Lecithin Taurocholate	Microemulsion technique	PCS Microscopy (fluorescent)	Size 110 − 135 nm PDI 0.2 – 0.3 ZP −24 to − 18 mV %EE Not informed Stability Not informed	Development *In vitro* tests	✓ Improved cytotoxicity	[102]	-
CUR	**A549** cells	(Synthetic lipids) Solid lipid: Monostearin Liquid lipid: Octyl decyl acid triglycerate Surfactant: Lecithin P-188 Tween-80	Microemulsion technique	DLS Microscopy (fluorescent)	Size 99.99 nm PDI 0.158 ZP −19.9 mV %EE 97.86 % Stability Not informed	Development *In vitro* tests *In vivo* test: Pharmacokinetic	✓ Improved cytotoxicity ✓ Increased apoptosis ✓ Improved bioavailability	[103]	-
CUR	**HepG2** cells	(Synthetic lipids) Solid lipid: Monostearin Liquid lipid:	Microemulsion technique	DLS	Size 99.99 ± 1.87 nm PDI 0.158 ± 0.005 ZP	Development *In vitro* tests	✓ Improved cytotoxicity ✓ increased caspase-8 and caspase-3 activities ✓ increased apoptosis	[104]	-

		octyl decyl acid triglycerate Surfactant: Lecithin P-188 Tween-80			−19.9 ± 0.65 mV %EE 97.86 ± 0.72 % Stability Not informed				
CUR	**MCF-7 cells**	(Natural lipids) Solid lipid: Cetyl palmitate Liquid lipid: Cod-liver oil Surfactant: Tween 80 Functionalization: Fe_3O_4 particles	Sonication or ultra-sonication	DLS Microscopy (TEM)	Size 166.7 ± 14.20 nm PDI 0.24 ± 0.14 ZP -27.6 ± 3.83 mV %EE 99.95 ± 0.015% Stability 5 months	Development *In vitro* tests	✓ Improved cytotoxicity	[105]	-
CUR	Human brain cancer cell (**A172**) Mice bearing **A172** xenografts Intraperitoneally	(Synthetic lipids) Solid lipid: Tripalmitin Liquid lipid: OA Surfactant: Tween 80	High-pressure homogenization (HPH)	PCS Microscopy (CLSM /TEM)	Size 214.0 nm PDI Not informed ZP Not informed %EE 88.6% Stability	Development *In vitro* tests *In vivo* test: Tumour regression, plasma concentration and tissue distribution	✓ Improved cytotoxicity ✓ Apoptosis ratio and ROS levels ✓ Higher bioavailability ✓ Significant tumour inhibition	[106]	[108]

					Not informed				
CUR + PDT	**MCF-7** cells	(Natural lipids) Solid lipid: GMO Liquid lipid: Olive oil Surfactant: Tween 80 Lecithin	High-pressure homogenization (HPH)	DLS Microscopy (TEM)	Size 113.94 ± 11.3 nm PDI 0.29 ± 0.05 ZP −47.50 ± 2.69 %EE 82.49% Stability 2 months	Pharm. Development *In vitro* tests	✓ Superior cytotoxicity in breast cancer cells	[107]	-
CUR + Imatinib (monoclonal antibody – IMT)	Non-Hodgkin lymphoma (**Jurkat** and **Ramos** cell lines)	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant: Tween 80 Lecithin Functionalization: Rituximab	Emulsification-solvent diffusion	DLS Microscopy (AFM)	Size 272.0 ± 0.3 nm PDI 0.4 ZP 8.2 ± 0.1mV %EE 100% Stability Not informed	Pharm. Development *In vitro* tests	✓ CUR-NLC showed significant cytotoxic effect ✓ Co-administration with imatinib reduced the imatinib doses.	[108]	[109]
CUR + DTX	**NCL-H460** cells Urethane induced lung carcinoma in mice	(Synthetic lipids) Solid lipid: Glyceryl Palmitostearate Trimyristin	High-pressure homogenization (HPH)	DLS Microscopy (TEM) DSC FTIR PXRD	Size 150.2 ± 5.2 nm PDI 0.263 ± 0.15	Pharm. Development *In vitro* tests In vivo:	✓ Improved cytotoxicity ✓ Significantly *better in vivo* effects than Taxotere® ✓ Lower toxicity	[109] [110]	[110] [91]

	Intravenous	Liquid lipid: MCT Surfactant: Solutol HS15 Lecithin Functionalization: FA			ZP 26.3 ± 5.2 mV %EE_{DTX} 94.4 ± 2.3 % %EE_{CUR} 95.10 ± 2.8% Stability Not informed	Pharmacokinetics studies; Pharmacodynamics study; efficacy, Toxicity			
CUR + TMZ	Glioma (C6) cells C6 in mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: MCT Surfactant: P-188	Microemulsion technique	DLS Microscopy (TEM) DSC	Size 78.49 ± 0.38 nm PDI 0.22 ± 0.01 ZP - 8.54 ± 0.51 mV %EE_{TMZ} 70.90% ± 0.06% %EE_{CUR} 68.17% ± 0.20% Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* Antitumour effect, biodistribution and toxicity in mice	✓ Significant synergistic (CUR/TMZ) anticancer effect *in vivo*. ✓ No toxic effects of on major organs and normal cells at the same therapeutic dose.	[111]	[111]

Photodynamic and photothermal therapy

Photosensitizer	Tumour tested and route	Composition	Preparation method	Characterization	Physical-chemical properties	Tests conducted	Main results	Ref.	Ref. in the review

Chloroaluminum phthalocyanine (ClAlPc)	**A549** and **B16-F10** cells	(Synthetic lipids) Solid lipid: SA Liquid lipid: OA Surfactant: Sodium lauryl sulfate	Emulsification-solvent diffusion	DLS Microscopy (TEM) DSC FTIR SAXS	Size 205.9 ± 22.7 nm PDI 0.46 ± 0.04 ZP −69.1 ± 18.5 mV %EE 95.8 ± 0.03 % Stability 3 months	Pharm. Development *In vitro* tests In vivo: Skin permeation in rat	✓ Improved cytotoxicity ✓ Increased the retained of drug into the skin. ✓ biocompatible	[112]	[123]
IR780	Human epithelial colorectal adenocarcinoma cell line (**Caco-2**) and mouse colon cancer cell line (**CT-26**) **CT-26** in mice Oral	(Synthetic lipids) Solid lipid: Trilaurin Liquid lipid: CT Surfactant: Soy lecithin	Emulsification-solvent evaporation	DLS Microscopy (TEM / CLSM)	Size 170 nm PDI 0.057 ZP Not informed %EE Not informed Stability 2h	Pharm. Development *In vitro* tests *In vivo: Pharmacokinetics, Biodistribution, and Therapeutic Activity*	✓ Enhanced oral absorption ✓ Increased oral bioavailability ✓ Improved antitumour efficacy	[113]	[121]
IR780	**4T1** cells **4T1** in mice Intravenous	(Synthetic lipids) Solid lipid: Trilaurin Liquid lipid:	Emulsification-solvent evaporation	DLS Microscopy (TEM / CLSM)	Size ∼135 nm PDI Not informed	Pharm. Development *In vitro* tests *In vivo:*	✓ Photothermal properties of IR780 were improved ✓ Accumulated at high levels in tumours	[114]	[122]

		MCT Surfactant: PC Functionalization: AMD3100			ZP −12 mV %EE 94.6 ± 1.4% Stability Not informed	Pharmacokinetics, Biodistribution, and Therapeutic Activity	✓ Anti-metastatic efficacy		
Verteporfin (VTP)	Human ovarian cancer cell lines: **SKOV3**, **OVCAR3** and **IGROV1** **SKOV3** in mice Intravenous	(Natural lipids) Solid lipid: Suppocir NB Liquid lipid: Soybean oil Surfactant: Polyoxyethylene 40	Emulsification-solvent evaporation	DLS Microscopy (CLSM)	Size ~47.9 ± 1.0 PDI 0.12 ± 0.02 ZP −3.7 ± 0.9 %EE < 95 % Stability: Not informed	Pharm. Development *In vitro* tests *In vivo:* Pharmacokinetics, Biodistribution, and Therapeutic Activity	✓ Enhanced deleterious effects in ovarian cancer cells cultured in monolayer, in spheroids, and *in vivo* (in tumour bearing mice).	[115]	[124]
Zinc phthalocyanine (ZnPc)	**MCF-7** cells	(Synthetic lipids) Solid lipid: Ethoxylated hydrogenated Castor oil 40 Liquid lipid: capric/caprylic acid triglycerides Surfactant: Pluronic F127	Emulsification-solvent evaporation	DLS Microscopy (CLSM) FTIR NMR	Size 166.7 ± 1.33 nm PDI 0.14 ± 0.018 ZP −16.4 ± 0.45 mV %EE 63.00 ± 1.19% Stability 3 months	Pharm. Development *In vitro* tests	✓ New nanocarrier for photodynamic therapy, rationally designed ✓ The photosensitizer was by first time used in drug delivery tests and MTT assays.	[116]	[120]

		Polyoxyethylene 40 Functionalization: FA							
5-amino levulinic acid (5-ALA)	Vero E6 cell lines	(Synthetic lipids) Solid lipid: Compritol ATO 888 Liquid lipid: OA Surfactant: Tween 20	Microemulsion technique Emulsification-solvent diffusion	DLS Microscopy (CLSM / TEM) DSC	Size 194.16 ± 5.73 nm PDI 0.24 ± 0.03 ZP Not informed %EE 72.84 ± 3.81 % Stability Not informed	Pharm. Development *In vitro* tests *In vivo:* skin permeation studies in rat	✓ Increased concentration in the target skin layers	[117]	[118]
DHX-1	**4T1** cells	(Natural lipids) Solid lipid: ATO Liquid lipid: Babassu oil Surfactant: Kolliphor HS	Emulsification-solvent evaporation	DLS Microscopy (TEM)	Size 92.1 ± 0.7nm PDI 0.215 ± 0.030 ZP -1.12 ± 0.09 mV %EE Not informed Stability Not informed	Pharm. Development *In vitro* tests	✓ *In vitro* demonstration of photosensitizer activity ✓ DDS may serve as a theragnostic agent	[118]	[119]
Chlorin e6 (Ce6) + PTX	**MDA-MB-231** cells	(Synthetic lipids) Solid lipid: Precirol ATO 5	Emulsification-solvent evaporation	DLS Microscopy (CLSM / TEM) DSC	Size 120.79 ± 1.68 nm	Pharm. Development *In vitro* tests	✓ Long circulation and tumour targeting ✓ PDT combined with chemotherapy	[119]	[125]

	MDA-MB-231 in mice Intravenous	Liquid lipid: Cremophor RH40 Surfactant: Cremophor RH40 Functionalization: DSPE-PEG-Ce6		XRD	PDI 0.19 ± 0.01 ZP −38.8 ± 1.5 mV %EE 76.67 ± 0.61% Stability Not informed	*In vivo:* Biodistribution efficacy	produced synergistic effects		
Indocyanine green (ICG) + PTX	**HepG2** cells **HepG2** tumour-bearing mice Intravenous	(Synthetic lipids) Solid lipid: GMS Liquid lipid: OA Surfactant P-188 Functionalization: SA-PEG-FA	Solvent injection (or solvent displacement)	DLS Microscopy (TEM)	Size 92.6 nm PDI 0.115 ZP Not informed %EE Not informed Stability: not informed	Pharm. Development *In vitro* tests *In vivo:* Biodistribution and image	✓ Increased drug intracellular uptake ✓ Increased cytotoxicity in cancer cells (ICG-PTX synergistic effect) ✓ Excellent tumour targetability in tumour-bearing mice	[120]	-

***** *In this report (ref. 76) two NLC formulations, one with DOX and the other containing PTX were tested and compared.*

Abbreviations:

5-ALA – 5 amino levulinic acid; 2-DG – stearyl-2-amino-2-deoxyglucose; 5-FU – 5-fluorouacil; AF4 – asymmetric flow field-flow fractionation; AFM – atomic force microscopy; ApoB – apolipoprotein B-100; ATO – Compritol 888; BCL – baicalein; CBZ – cabazitaxel; Ce-6 – chlorin e6; CHEMS – cholesteryl hemisuccinate; Chol – Cholesterol; CIS – cisplatin; ClAlPc – Chloroaluminum phthalocyanine; CLSM – confocal laser scanning microscopy; CT – capric triglyceride; CTAB – cetyltrimethylammonium bromide; CUR – curcumin; CXCR4 - antagonist of the chemokine receptor; CYT – cytarabine; DCB – decitabine; DDAB – Didecyldimethylammonium bromide; DHA – docosahexaenoic acid; DLS – dynamic light scattering; DMN – 5-demethylnobiletin ; DN – docetaxel complexed with nicotinamide; DNPA – delsa nano particle analyser; DOTMA – N-[1-(2,3-dioleyloxy)propyl]-N,N,Ntrimethyl-ammonium chloride; DOX –

doxorubicin; DSC – differential Scanning calorimetry; DSPE-PEG – Distearoyl-phosphatidylethanolamine; DSPE-PEG-Ce6 – distearoyl-phosphatidylethanolamine-chlorin e6; DSPE-PEG-Mal –distearoyl-phosphatidylethanolamine-Mal; DSPE-PEG-NH2 – 1,2-Distearoyl-sn-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol); DSPE-PEG-TR – distearoyl-phosphatidylethanolamine-targeting peptide TISWPPR; DOTAP – 1,2-Dioleoyl-3-trimethylammoniumpropane; DTX – docetaxel; DZ – dacarbazine; EE – encapsulation efficiency; ELS – electrophoretic light scattering; ETP – etoposide; FA – folate acid; FACS – Fluorescence-Activated Cell Sorting; FA-PEG-DSPE – FA containing polyethylene glycol (PEG)-distearoylphosphatidylethanolamine (DSPE); FA-PEGPCHL – folate-poly(PEG-cyanoacrylate-co-cholesteryl cyanoacrylate); FA-SA – folic acid and stearic acid; Fol-PEG-CHEMS – Folate-polyethyleneglycol-cholesterol hemisuccinate; FTIR – Fourier transform infraRed spectroscopy; GMO – glyceryl monooleate; GMS – glyceryl monostearate; HA – hyaluronic acid; ICG – indocyanine green ; IFOS – ifosfamide; IMT – imatinib; Ir – irinotecan; Lapa – β-lapachone; LbL-PEG – layer-by-layer containing polyethylene glycol; LLS – laser light scattering; LPSA – laser particle size analyser; MCT – Medium fatty acids; MCTN – mechlorethamine; MTX – methotrexate; NAG – N-acetyl-d-glucosamine; NLC – nanostructured lipid carriers; NIR – near infrared; NMR – nuclear magnetic resonance spectroscopy; NTA – nanoparticle tracking analysis; OA – oleic acid; OXA – oxaliplatin; P-188 – poloxamer 188; PC – phosphatidylcholine; PCS – photon correlation spectroscopy; PDI – polydispersity index; PDT – photodynamic therapy; PEG – polyethylene glycol; PEG-40-St – Polyethylene glycol 40 stearate; PEG-FA – Polyethylene glycol-Folic acid; pEGFP – green fluorescence protein plasmid; PL – Platelet; PLM – polarized light microscopy; PRXD – powder X-Ray diffraction; PTX – Paclitaxel; PVA – polyvinyl alcohol; RBCm – Red blood cell-membrane; RDG – Arginine-glycine-aspartic acid peptide; RIPL – IPLVVPLRRRRRRRRC peptide; SA- Stearic acid; SAL – salinomycin; SA-PEG-FA – Stearic acid-PEG-folate; SA-R8– Stearyl-polyarginine; SAXS – Small-angle X-ray scattering; SC – sclareol; SiC – sildenafil citrate; SEM – Scanning electronic microscopy; SFN – sorafenib; SPC – soybean phosphatidylcholine; Stattic- STAT3 inhibitor; STEM-EDS – scanning transmission electron microscopy-energy dispersive X-ray spectroscopy; TAT – cell-penetrating peptide transcription activator; TEM – transmission electronic microscopy; Tf – Transferrin; Tf-PEG-PE – transferrin-Polyethylene glycol-phosphatidylethanolamine; TGA – thermogravimetric analysis; TGI – tumour growth inhibition; THP – pirarubicin; TMZ – temozolamide; TPT – topotecan; TS – α-tocopherol succinate; VCR – vincristine sulphate; VTP – verteporfirin; XRD – X-ray diffraction, XPS –X-ray photoelectron spectroscopy; ZnPc – Zinc phthalocyanine; ZP – zeta potential.

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