Plant Archives Vol. 20 Supplement 1, 2020 pp. 3305-3315 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

LIPOSOME-BASED DRUG DELIVERY SYSTEM FOR CANCER CHEMOTHERAPEUTICS

Sukhbir Singh[1], Neelam Sharma[1]*, Rupanshi Grover[1] and Ikmeet Kaur Grewal[1,2]

[1*]Chitkara College of Pharmacy, Chitkara University, Punjab, India.
[2]Department of Pharmacy, Government Medical College, Patiala, Punjab, India.

Abstract

Liposome-based drug delivery system has emerged as revolutionizing less toxic, biodegradable and biocompatible nano-medicine to overcome adverse side effects produced by conventional cancer treatment approaches. Liposomes are closed spherical bilayer phospholipids vesicles characterised by lipid region incorporating hydrophobic drugs and internal aqueous cavity for entrapment of hydrophilic drugs. Numerous advantages of liposomes over conventional medicines includes increased efficacy, therapeutic index, stability and pharmacokinetic effects; drug targeting to tumour tissue, reduced systemic toxicity, prolonged residence time in blood circulation, modified *i.e.* targeted, controlled and sustained drug delivery to tumour which seize liposome-based drug delivery as blooming field of research. This review briefly summarizes widespread research of liposome-based drug delivery for different cancer chemotherapeutics *i.e.* breast, lung, hepatocellular carcinoma, cervical, pancreatic, gastric, skin, brain, head and neck cancer.

Key words: Liposome, Drug delivery, Cancer, Hepatocellular carcinoma, Chemotherapeutics.

Introduction

Cancer is the uncontrolled development of body cells that are abnormal. The cells that cause cancer are referred to as malignant cells. There are so many ways to treat cancer such as chemotherapy, treatment with radiation, operation and so on (Bardania *et al.*, 2017; Ding *et al.*, 2006; Bulbake *et al.*, 2017). Liposomal drugs have a high capacity for encapsulation, thereby showing significant anticancer activity with preferentially cadiotoxicity reduced toxicity. Liposomes are tiny artificial spherical shaped vesicles that can be formed from cholesterol as well as natural non-toxic phospholipids (Zahednezhad *et al.*, 2019; Marsh, 2012; Koning and Storm, 2003; Daraee *et al.*, 2016). Liposomes are attractive drug delivery mechanisms due to their size, biocompatibility and hydrophobic as well as hydrophilic nature. Advantagesof liposomes include biocompatibility, self-assembly capability, the capacity to bear significant drug payloads and a wide range of physicochemical and biophysical properties that can be changed to monitor their biological characteristics. Moreover, in recent years, a thorough investigation into the liposomal drug delivery system has been established which contributes to the advancement of several liposome-based drug compositions for therapeutic use in cancer treatment (Alavi *et al.*, 2017; Sercombe *et al.*, 2015; Valizadeh *et al.*, 2015). This review summarizes extensive studies into the delivery of liposome-based drugs for various cancer treatments, *i.e.* breast, lung, hepatic, cervical, pancreatic, gastric, skin, brain, head and neck cancer. Lipsomes has been classified into several types on the basis of size and intracellular drug delivery mechanism (Daraee *et al.*, 2016) (Fig. 1).

***Author for correspondence :** E-mail: neelam.sharma@chitkara.edu.in

Applications of liposomes in different cancers

Cancer is one of the major reasons of death globally which can affect any body organ *i.e.* breast, lung, liver, cervical spine, pancreases, stomach, skin, brain, head and neck. Liposome-based drug delivery system has found wide application in several types of cancer therapeutics owing to attainment of tumour targeting, reduced systemic toxicity and prolonged residence time in blood circulation (Fig. 2).

Liposomes in breast cancer

Yang *et al.*, investigated antitumor effect of herceptin conjugated paclitaxel-loaded PEGylated immune liposomes to exclusively distribute paclitaxel to the human epidermal growth factor receptor-2 (HER2)-over

expressing cancer cells and potential approach for tumor-specific therapy (Yang *et al.*, 2007). Coscoa *et al*. investigated effects of synthetic phospholipids of a liposomal multidrug carrier gemcitabine and tamoxifen and *in-vitro* antitumoral activity on diverse breast cancer cell lines and showed a massive degree of cell interaction of liposomal multidrug carrier after just 6 h. (Cosco *et al*., 2012). Rastakhiz *et al*., synthesized nanoliposomes vaccine composed of HER2/neu derived peptide to persuade efficient antigen specific tumor immunity against breast cancer (Rastakhiz *et al.*, 2018). Samson *et al*., developed glucose-regulated protein 78/clusterin targeted DOTAP liposome for co-delivery of camptothecin and GRP78 siRNA/ CLU siRNA for chemosensitivity augmentation in breast cancer stem cells and offers offers extensive prospective for synergistic anti-cancer therapy (Samson *et al.*, 2018). Farzad *et al*., developed P435 HER2/neu-derived peptide conjugated to maleimide-PEG2000-DSPE liposomes containing synthetic phospholipids as successful prophylactic vaccine against HER2-positive breast cancers (Farzad *et al*., 2019). Sun *et al*., investigated novel TN-modified liposome co-loading with curcumin and celecoxib coating with CD44 targeting moiety hyaluronic acid which exhibited prospective for inhibiting tumor development and metastasis in the course of improving inflammatory infiltration of tumor tissue (Sun *et al*., 2019). Xia *et al*., studied anticancer effect of combined therapy using losartan loaded liposomes and paclitaxel pH sensitive TH peptides modified liposomes which could effectively penetrate into solid collagen network in breast tumors without causing hypotension at dosage of 10 mg/kg/d (Xia *et al*., 2016). Ju *et al*., prepared hyaluronic acid customized daunorubicin and honokiol cationic liposomes and evaluated on breast cancer cell lines *i.e.* MCF-7 and MDA-MB-435S breast cancer cells which improved cellular uptake and damaged vasculogenic mimicry channels and shows potential therapeutic strategy for breast cancer treatment (Ju *et al*., 2018). Cao *et al*., synthesized doxorubicin liposomes loaded with thermogel for sustained delivery of doxorubicin for locally breast cancer treatment and better antitumor effectiveness as well as lower side effects (Cao *et al*., 2019). Vaidya *et al*., developed novel tri-functional immunoliposomes of doxorubicin conjugated with trastuzumab and OKT-3 antibodies that target human epidermal growth factor receptor-2 on breast cancer cells and CD3-receptors on T-lymphocytes, respectively which could have prospective to get better clinical outcomes (Vaidya *et al*., 2018). Liposomes that have been successfully employed for treatment of breast cancer have been presented in table 1.

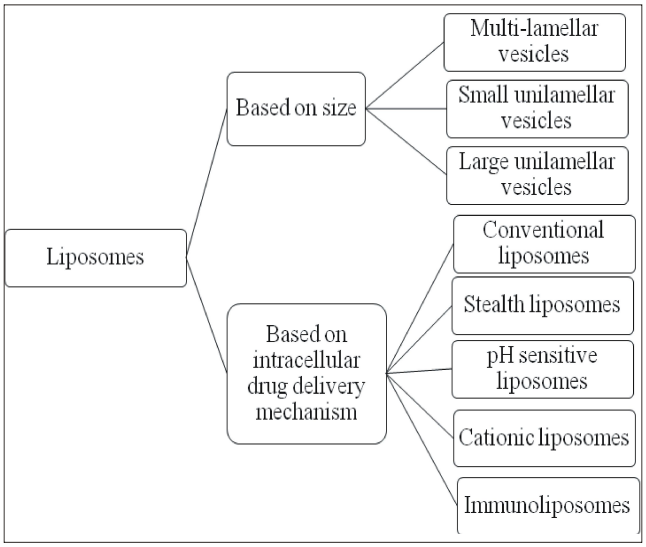

Fig 1: Classification of liposomes.

Liposomes in lung cancer

Cheng *et al*., synthesized Doxorubicin-loaded liposomes containing novel peptide GE11 for targeted deliverance of chemotherapeutic agent to epidermal growth factor receptor-positive non-small cell lung cancer which showed better accumulation and extended retention in tumor tissue (Cheng *et al*., 2014). Cao *et al*., synthesized β-elemene and cisplatin co-loaded liposome to successfully treat lung cancer and exhibited enviable therapeutic outcome in both cell-derived and patient-derived xenografts for successful lung cancer therapy (Cao *et al*., 2016). Gaballua *et al*., prepared liposome and nanostructured lipid carriers of erlotinib to explore anticancer activities and concluded that nanostructured lipid carriers had better anti-cancer activity than liposome (Gaballua *et al*., 2019). Ma *et al*., developed novel

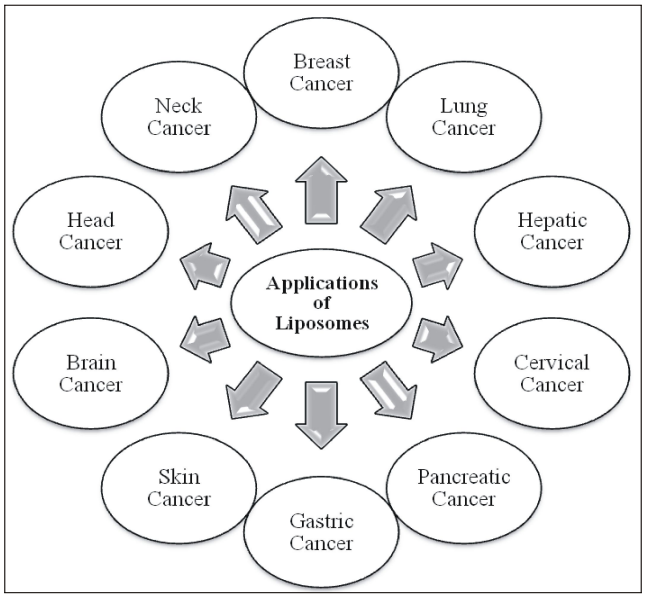

Fig. 2: Application of liposomes into various types of cancer therapeutics.

Table 1: Recent studies in development of liposome-based formulation for breast cancer.

Drug (Technique)	Lipids	Solvents	Reference
Paclitaxel (Thin film hydration)	Soybean phosphatidylcholine, 1,2-distearoyl-sn-glycero-3-phospho-ethanolamine [methoxy (polyethylene-glycol)-2000]	Chloroform	Yang *et al*., 2007
Gemcitabine andTamoxifen (Thin layer evaporation)	Dipalmitoyl phosphatidylcholine, Dimyristoyl phosphatidylglycerol, N-(carbonyl methoxy-polyethylene glycol-2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine, Dioleoyl trimethylammonium propane, Cholesterol	Chloroform Methanol	Cosco *et al*., 2012
HER2/neu derived peptide (Lipid film hydration)	Distearoyl phosphatidylcholine, Distearoyl phosphoglycerol, Cholesterol, Monophosphoryl lipid A, Dioleoyl phosphatidyl-ethanolamine	Chloroform	Rastakhiz *et al*., 2018
Camptothecin and glucose-regulated protein 78 (GRP78)/clusterin (CLU) (Thin film hydration)	Dioleoyl trimethylammonium propane	Chloroform	Samson *et al*., 2018
P435 HER2/neu-derived peptide (lipid film hydration)	Distearoyl phosphatidylcholine, Distearoyl phosphoglycerol, Dioleoyl phosphatidyl-ethanolamine, Distearoyl phosphoethanolamine-N-[maleimide (polyethyleneglycol)-2000]	Chloroform Dimethyl sulfoxide	Farzad *et al*., 2019
Curcumin and celocoxib (Film hydration)	Dioleoyl trimethylammonium propane, Distearoyl phospho-ethanolamine-N-[carboxy (polyethylene glycol)-2000], Distearoyl phosphoethanolamine-N-[maleimide (polyethyleneglycol)-2000], Cholesterol	Chloroform Methanol	Sun *et al*., 2019
Losartan (Thin layer hydration)	Distearoyl phosphoethalamine-N-[methoxy (polyethylene glycol)-2000, Distearoyl phosphoethanolamine-N-[maleimide (polyethyleneglycol)-2000]	Methanol, Chloroform	Xia *et al*., 2016
Daunorubicin hydrochloride (Film dispersion)	Cholesterol, 3β-[N-(N2 ,N2 -dimethyl aminoethane)-carbamoyl] cholesterol, Egg phosphatidylcholine	Chloroform	Ju *et al*., 2018
Doxorubicin (Simple mixing)	Cholesterol, Soybean Phosphatidylcholine	Deuterated Chloroform	Cao *et al*., 2019
Trastuzumab and Doxorubicin (Thin film hydration)	Distearoyl phosphatidylcholine, Distearoyl phosphoethanolamine-N-[methoxy (polyethylene glycol)-2000] (ammonium salt), Distearoyl phospho-ethanolamine-N-[maleimide (poly-ethyleneglycol)-2000], Cholesterol	Chloroform	Vaidya *et al*., 2018

CD133 aptamer modified docetaxel liposome for lung cancer and showed considerable antitumour activity in A549 tumour mice with low systemic toxicity (Ma *et al*., 2017). Xin *et al*., found mitochondria mediated lung cancer apoptosis induced by long circulating targeted liposomes of parthenolide and ginsenoside CK attached with tLyp-1 ligand which exhibits reduced toxicity and superior antitumor effect (Jin *et al*., 2018). Jiang *et al*., developed sustained-release liposomes loaded with paclitaxel and curcumin and modified by arginine, glycine and aspartic acid peptide which exhibited greater anti-proliferative effect on A549 cells for lung cancer therapy (Jiang *et al*., 2018). Poy *et al*., developed carboplatin loaded liposomal nanoparticle with enhanced cytotoxicity on lung cancer (Poy *et al*., 2017). Yanga *et al*., developed tocopheryl polyethylene glycol succinate (TPGS)-modified liposomes loaded with ginsenoside compound K which resulted in enhanced solubility of compound and exhibited targeted drug delivery in A549 cells in lung cancer (Yang *et al*., 2016). Hamzawy *et al*., developed liposome-embedded gold nanoparticle of temozolomide which exhibited enhanced drug distribution and penetration after intra-tracheal inhalation for cancer therapy. Superior synergistic antitumor activity was observed in urethane induced lung cancer in BALB/c mice (Hamzawy *et al*., 2017). Song *et al*., synthesized epirubicin liposomes for safe and proficient treatment of non-small-cell lung cancer and octreotide was modified on liposomal surface and honokiol was integrated into lipid bilayer for inhibiting tumor metastasis and eliminating

Table 2: Recent studies in development of liposome-based formulation for lung cancer.

Drug (Technique)	Lipids	Solvents	Reference
Doxorubicin (Thin film hydration)	Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], Distearoyl-phosphoethanolamine-N-[maleimide (polyethylene glycol)-2000]	Ethanol	Chang *et al*., 2014
β-elemene and cisplatin (Thin film evaporation and ultrasonic hydration)	Phosphatidylcholine, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000]	Chloroform	Cao *et al*., 2016
Erlotinib (Thin layer film and hydration-sonication)	Soybean lecithin, Cholesterol	Ethanol	Gaballua *et al*., 2019
Docetaxel (Thin-film hydration)	Soybean phosphatidylcholine, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], Cholesterol	Chloroform	Ma *et al*., 2017
Ginsenoside CK and parthenolide (Thin-film hydration)	Egg yolk lecithin, Cholesterin, Distearoyl phosphoethanolamine-N-[carboxy (polyethyleneglycol)-2000], Distearoyl phosphoethanolamine-N-[carboxy (polyethyleneglycol)-2000]-tLyp-1	Methanol	Jin *et al*., 2018
Paclitaxel and Curcumin (Solvent evaporation)	Cholesterol, Hydrogenated Soybean phosphatidylcholine, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Chloroform *et al*., 2018	Jiang
Carboplatin (Reverse phase evaporation)	Lecithin, Cholesterol, Polyethylene glycol 3350	Ethanol	Poy *et al*., 2017
Ginsenoside (Thin-film hydration)	D-α-tocopheryl polyethylene glycol l1000 succinate	Dimethyl sulfoxide	Yang *et al*., 2016
Temozolomide (Thin-film hydration)	Phosphatidylcholine, Cholesterol	Chloroform, Ethanol	Hamzawy *et al*., 2017
Epirubicin hydrochloride (Thin-film hydration)	Egg yolk phosphatidylcholine, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000]-NHS,	Chloroform	Song *et al*., 2017
Erlotinib (Single step sonication)	Hydrogenated Soybean phospha-tidylcholine, Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000]	Ethanol Acetone	Mandal *et al*., 2016
Vinblastine (Film dispersion)	Egg yolk phosphatidylcholine, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000]-NHS	Chloroform	Li *et al*., 2015

vasculogenic mimicry channels (Song *et al*., 2017). Mandal *et al*., developed erlotinib loaded lipid-polymer hybrid nanoparticles for deliverance of erlotinib clinically used for treatment non-small cell lung cancer (Mandal *et al*., 2016). Li *et al*., prepared peanut agglutinin modified vinblastine cationic nanostructured liposome for treating non-small cell lung cancer (Li *et al*., 2015). Table 2 depicts various liposomes that have been effectively utilized for treatment of lung cancer.

Liposomes in hepatic cancer

Wei *et al*., developed potential-targeting ligand lactoferrin-modified PEGylated liposomes loaded with doxorubicin for targeting hepatocellular carcinoma (Wei *et al*., 2015). Cheng *et al*., developed cisplatin and curcumin co-loaded nano-liposomes to accomplish synergistic effect for 3-hepatocellular carcinoma (Cheng *et al*., 2018). Jiang *et al*., studied glycyrrhetinic acid-modified curcumin and combretastatin A4 phosphate loaded liver-targeted liposomes which exhibited higher cytotoxicity in BEL-7402 human hepatic carcinoma cells (Jiang *et al*., 2019). Yin *et al*., fabricated sorafenib and ceramide loaded liposomes for achieving synergistic antitumor effect which showed superior cytotoxicity on human liver cancer cell line *i.e*. HepG2 cells (Yin *et al*., 2018). Sarfraz *et al*., studied combination therapy of

Table 3: Recent studies in development of liposome-based formulation for hepatic cancer.

Drug/Technique	Lipids	Solvent	Reference
Doxorubicin (Thin film hydration)	Soybean phosphatidylcholine, Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000]	Dichloro-methane, Ethanol	Wei *et al*., 2015
Cisplatin and Curcumin (Rotary evaporation)	Cholesterol, Dimyristoyl phospha-tidyl choline, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], 1,2-dioleoyl-sn-glycerol-3-phosphate	Chloroform	Cheng *et al.*, 2018
Curcumin and Combretastatin A4 phosphate (Thin film hydration)	l-α-phosphatidylcholine, Cholesterol	Chloroform	Jiang *et al.*, 2019
Sorafenib (Thin-film hydration)	Cholesterol, Lipoid E80, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Chloroform Methanol	Yin *et al*., 2018
Doxorubicin and oleanolic acid (Re-engineered ethanolic injection)	Hydrogenated Soybean Phosphatidylcholine, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Ethanol	Sarfraz *et al.*, 2017
Paclitaxel (Thin-film dispersion)	Soybean phosphatidylcholine, Cholesterol	Chloroform	Zhang *et al.*, 2016
Silibinin and Glycyrrhizic acid (Thin layer film hydration)	DPPC, Distearoyl phosphoethanol-amine-N-[carboxy (polyethyleneglycol)-2000]	Absolute ethanol	Ochi *et al*., 2016

doxorubicin and oleanolic acid loaded liposomes to reduce doxorubicin-induced cardiotoxicity attenuated (Sarfraz *et al*., 2017). Zhang *et al*., investigated hybrid structure comprising of gold nano-particles and liposomes of paclitaxel with unique time-release approach and improved anti-neoplastic activity in hepatic cancer which was studied on xenograft Heps tumor-bearing mice (Zhang *et al*., 2016). Ochi *et al*., studied pegylated nano-liposomes of silibinin and glycyrrhizic acid and assessed cytotoxicity on hepatocellular carcinoma HepG2 and fibroblast cell lines using MTT technique which indicated higher biological activity, stability and synergistic therapeutic effect of herbal therapy (Ochi *et al*., 2016). Table 3, describes several liposomes that have been successfully used for treatment of hepatocellular carcinoma.

Table 4: Recent studies in development of liposome-based formulation for cervical cancer.

Drug/Technique	Lipids	Solvent	Reference
Curcumin (Thin film hydration)	Cholesterol, Soybean lecithin	Chloroform Diethyl ether	Saengkrit *et al.*, 2014
Curcumin (Thin film hydration)	DSPE-PEG(2000) Folate, Distearoyl phospho-ethanolamine-N-[carboxy (polyethyleneglycol)-2000], Cholesterol	Chloroform	Wang *et al.*, 2019
Arsenic trioxide (Thin film hydration)	Soy phosphatidylcholine, Cholesterol, Methoxy (polyethyleneglycol)-2000-distearoyl-phosphatidyletha-nolamine, Distearoyl phosphoethanolamine-N-[folate (polyethyleneglycol)-2000], Distearoyl phosphoethanolamine-N-(folate (polyethylene glycol)-5000]	Methanol, Dichloro-methane	Akhtar *et al*., 2019
Survivin T34A (Thin film hydration)	1,2-dioleoyloxy-3-(trimethylammonio) propane, Cholesterol	Chloroform	Qiu *et al.*, 2018
Cisplatin	Dipalmitoyl phosphatidylcholine, Dipalmitoyl phosphatidyl glycerol (sodium salt), N-(carbonyl-methoxy polyethylene-glycol 2000)-1,2- distearoyl-sn-glycero-3-phospho-ethanolamine (sodium salt), 1-myristoyl-2-stearoyl-sn-glycero-3-phospho-choline or L-α-lysophosphatidylcholine	Chloroform	Dou *et al*., 2017
Epirubicin (Thin film hydration and sonication)	1,2-dioleoyloxy-3-(trimethylammonio) propane, Dioleoylphosphatidyl ethanolamine	Chloroform	Juang *et al*., 2016
Cisplatin and Quaternized N,O-oleoyl chitosan (QCS) (Thin film hydration)	Lecithin, Distearoyl phosphoethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Chloroform Diethyl ether	Saesoo *et al*., 2016

Table 5: Recent studies in development of liposome-based formulation for pancreatic cancer.

Drug/Technique	Lipids	Solvent	Reference
Cromolyn (Reverse phase evaporation vesicle)	Dipalmitoylphosphatidylcholine, Dimyristoylphosphatidylcholine, Distearoylphosphatidylcholine, 1,2-distearoyl-sn-glycero-3-phospho-ethanolamine-N-[methoxy (polyethyleneglycol)-2000]	Chloroform	Kim *et al*., 2012
Curcumin	Dimyristoylphosphatidylcholine, Dimyrsitoylphosphatidylglycerol		Ranjan *et al.*, 2013
Curcumin (Thin film hydration)	1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Chloroform	Bisht *et al.*, 2016
Curcumin	Dimyristoylphosphatidylcholine, Dimyrsitoylphosphatidylglycerol		Mach *et al.*, 2009
Paclitaxel (Thin film hydration)	Egg yolk Phosphatidylcholine, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]	Ethanol	Okamoto *et al*.., 2014
Hyaluronic acid (Thin lipid film-hydration)	Distearoylphosphatidylcholine, Cholesterol, 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[amino (polyethyleneglycol)-2000]	Chloroform	Marengoa *et al.*, 2019
Mcl-1 siRNA and gemcitabine (Thin lipid film-hydration)	Cholesterol, Dimyrsitoylphosphatidylglycerol	Dichloro-methane	Wang *et al*., 2019
Gemcitabine (Thin film hydration extrusion)	Cholesterylhemisuccinate, 1,2-dioleoyl-snglycero-3-phospho-ethanolamine, N-(carbonyl methoxypolyethylene-glycol-2000)-1,2-distearoyl-sn-glycero3-phosphoethanolamine	Phosphate buffer	Hongtao *et al.*, 2016
Paclitaxel and Ellagic acid (Thin film hydration)	Dipalmitoylphosphatidylcholine	Ethanol, Chloroform Methanol	Wei *et al.*, 2017
Curcumin (Thin film hydration with subsequent freeze-thaw, sonication and extrusion)	Cholesterol, Dimyristoylphosphatidyl-choline, Distearoyl phospho- ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000], Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]-Maleimide	Chloroform	Le *et al*., 2018

Liposome in cervical cancer

Casagrande *et al*., developed lipoplatin, novel cisplatin liposomal to diminish cisplatin toxicity and enhanced accretion at tumour site. Antitumoral activity of lipoplatin was analyzed on HeLa and ME-180 cell lines and discovered cisplatin-resistant clone R-ME-180 for potential treatment of cisplatin-resistant cervical cancer (Casagrande *et al*., 2013). Saengkrit *et al*., investigated curcumin-loaded cationic liposomal nanoparticles for enhanced cell uptake against cell lines *i.e.* HeLa and SiHa (Saengkrit *et al*., 2014). Wang *et al*. found greater anti-proliferative effect of folic acid customized curcumin liposomes on HeLa cells for targeted cervical carcinoma therapy (Wang *et al*., 2019). Akhtar *et al*., synthesized folate optimised liposomal encapsulated arsenic trioxide conjugated to polyethylene glycol 2000 and polyethylene glycol 5000 to advance their therapeutic profile for treating high-risk human papilloma virus-positive cervical cancer cells (Akhtar *et al*., 2019). Qiu *et al*., investigated liposome plasmid encoding mutant survivin T34A which inhibited tumor growth of cervical cancer alongwith reduction in angiogenesis and increase in tumor cells apoptosis rate (Qiu *et al*., 2018). Doua *et al*., developed thermosensitive liposome of cisplatin for cervical cancer patients for implementation of custom-made medicine in clinical setting (Dou *et al*., 2017). Juang *et al*., fabricated PEGylated liposomes encapsulating epirubicin as an antineoplastic agent and tilapia hepcidin 2-3, antimicrobial peptides which caused programmed cell death in cervical cancer cells (Jaung *et al*., 2016). Saesoo *et al*., developed surface modified nanoliposome and assessed therapeutic effectiveness using 3-dimensional spheroid cervical cancer model which highlighted apoptosis against cervical cancer (Saesoo *et al*., 2016). Liposomes that have been generously developed for management of cervical cancer have been illustrated in table 4.

Liposomes in pancreatic cancer

Kim *et al*., developed PEGylated liposome of cromolyn to advance antitumor activity for management of pancreatic cancer (Kim *et al*., 2012). Ranjan *et al*., fabricated liposomal formulation loaded with curcumin in human pancreatic tumor xenograft model to perk up

Table 6: Recent studies in development of liposome-based formulation for gastric, skin, brain, head and neck cancer.

Drug/Technique	Lipids	Solvent	Reference
Gastric cancer			
CD44-SATB1-ILs (Lipid film hydration)	1,2-dioleoyloxy-3-(trimethylammonio) propane, Cholesterol, Distearoyl phospho-ethanolamine [methoxy (polyethylene glycol)-2000], Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]-Maleimide	Chloroform	Yang *et al*., 2018
Peptide GX1 (Thin film hydration and sonication dispersion)	Soybean lecithin, Cholesterol, Cholesteryl hemisuccinate	Chloroform	Xiong *et al*., 2015
Skin cancer			
Epigallocatechin gallatein (Film hydration)	Phosphatidylcholine, Cholesterol	Chloroform, Methanol	Marwah *et al*., 2019
Avicequinone-B liposomal formulations (Thin film hydration)	Phosphatidylcholine, Cholesterol	Chloroform, Methanol	Hu *et al*., 2019
Curcumin and STAT3 siRNA (Thin ûlm hydration)	1,2-dioleoyloxy-3-(tri-methylammonio) propane, Dioleoylphosphatidyl ethanolamine	Methanol	Jose *et al*., 2018
Cetuximab and 5-fluorouracil (Thin lipid film hydration)	Distearoyl phosphatidyl-choline, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]-Maleimide	Chloroform	Petrilli *et al*., 2018
Brain cancer			
Carboplatin (Reverse phase evaporation)	Cholesterol, Lecithin, 1,2-distearoyl-sn-glycero-3-phospho-ethanolamine-N-[methoxy (polyethyleneglycol)-2000]	Ethanol	Hassanzade-ganroudsari *et al*., 2019
Cetuximab and Camptosar (Thin-film hydration)	Dipalmitoylphosphatidyl-choline, Cholesterol, Distearoyl phospho-ethanolamine-N-[carboxy (poly-ethyleneglycol)-2000]-NH_2	Chloroform, Methanol	Lu *et al*., 2019
Head and neck cancer			
Dihydroartemisinin (Film dispersion-ultrasonication)	Phosphatidylcholine, Cholesterol	Chloroform	Li *et al*., 2019
Paclitaxel and Ursolic acid (Thin-film dispersion hydration)	Hydrogenated soybean phosphatidyl-choline, Cholesterol and Distearoyl phospho-ethanolamine-N-[carboxy (polyethylene-glycol)-2000]-NH_2	Chloroform	Lv *et al*., 2017

bioavailability and poor aqueous solubility of curcumin (Ranjan *et al*., 2013). Bisht *et al*., developed curcumin analog EF24 liposomal formulation which decreases phosphorylation of I-kappa-B-alpha in xenograft tumor tissues and inhibits pancreatic cancer development (Bisht *et al*., 2016). Mach *et al*., designed curcumin liposomal formulation and concluded that minimum effective dose for liposomal curcumin is 20 mg/kg once daily three times/ week to attain optimal tumor growth inhibition in xenograft human pancreatic cancer model (Mach *et al*., 2009). Okamoto *et al*., prepared paclitaxel-loaded bovine serum albumin encapsulated liposomes using noncovalent binding to albumin for pancreatic cancer (Okamoto *et al*., 2014). Marengo *et al*., prepared hyaluronic acid liposomes comprising diethyl-dithiocarbamate copper to target specific cancer stem cells marker CD44 receptor by ion gradient technique for anti-proliferative action on pancreatic cancer stem cells (Marengo *et al*., 2019). Wang *et al*., developed liposome to co-deliver Mcl-1 siRNA and gemcitabine for pancreatic LP-Gem-siMcl-1 cancer treatment to overcome resistance of gemcitabine (Wang *et al*., 2019). Xu *et al*., fabricated high content gemcitabine pH-sensitive liposomes beneficial over non pH-sensitive liposomes (Hongtao *et al*., 2016). Wei *et al*., prepared paclitaxel and ellagic acid loaded human serum albumin complexes co-encapsulated into thermosensitive liposomes to promote matrix penetration and tumor accumulation (Wei *et al*., 2017). Le *et al*., investigated effect of epidermal growth factor (EGF) conjugated liposomes comprising curcumin on human pancreatic cancer cell lines *i.e.* BxPC-3, Panc-1, Mia Paca-2 and showed targeting of liposomes against human pancreatic cancer cells (Le *et al*., 2018). Table 5, elucidate numerous liposomes that have been effectively applied for curing pancreatic cancer.

Liposomes in gastric cancer

Yhang *et al*., developed CD44-SATB1-ILs antibodies conjugated immune liposomes an imminent approach to enhance therapeutic effect of binding protein-1 against gastric cancer-initiating cells (Yang *et al*., 2018). Xiong *et al*., developed GX1-mediated anionic liposomes carrying adenoviral vectors GX1-Ad5-AL for escalating inhibition effect and suppressing migration of gastric cancer vascular endothelial cells (Xiong *et al*., 2015). Liposomes that have been successfully synthesized for management of gastric cancer have been exemplified in table 6.

Liposome in skin cancer

Marwah *et al*., fabricated tween-20 dependent deformable liposome for dermal cellular delivery of epigallocatechin gallatein which showed superiour drug penetration into dermal cells (Marwah *et al*., 2019). Hu *et al*., synthesized avicequinone-B liposomes which induced apoptosis in cutaneous squamous carcinoma cells (Hu *et al*., 2019). Jose *et al*., synthesized curcumin-loaded cationic liposomes of STAT3 siRNA for iontophoretic administration which showed effectiveness in reducing tumor progression in skin cancer treatment (Jose *et al*., 2018). Petrilli *et al*., developed epidermal growth factor receptors-targeted immunoliposome loaded with 5-ûuorouracil for squamous carcinoma cells (Petrilli *et al*., 2018). Recent works in liposome-based formulation for skin cancer has been represented in table 6.

Liposomes in brain cancer

Hassanzadeganroudsari *et al*., investigated cytotoxic efficacy of PEGylated carboplatin loaded liposomes which hold elevated therapeutic potential for brain cancer therapy (Hassanzadeganroudsari *et al*., 2019). Lu *et al*., developed dual-responsive thermosensitive magnetic liposomes encapsulated with camptosar and magnetic Fe_3O_4 nanoparticles coated with citric acid and conjugated with cetuximab for recognization of over-expressed epidermal growth factor receptors on cancer cell surface (Lu *et al*., 2019). Liposomes that have been effectively manufactured for management of brain cancer have been illustrated in table 6.

Liposomes in head and neck cancer

Hui *et al*., formulated magnetic dihydroartemisinin nanoliposomes to get enhanced targeted delivery for inhibiting head and neck squamous cell carcinomas proliferation (Li *et al*., 2019). Lv *et al*., fabricated paclitaxel and ursolic acid loaded liposome and found increased therapeutic effectiveness in head-and-neck squamous cell carcinoma (Lv *et al*., 2017). Table 6 revealed various liposomes that have been synthesized for management of head and neck cancer.

Conclusion

Liposome-based medications are less toxic, biodegradable and biocompatible nanomedicine having capability of loading hydrophilic as well as hydrophobic drug molecules. Liposome-based drug carriers have been reported to augment drug's efficacy, therapeutic index, stability and pharmacokinetic effects; drug targeting to tumour tissue, reduced systemic toxicity, prolonged residence time in blood circulation, improved safety, therapeutic eûectiveness and patient compliance over conventional medicines. The widespread research of liposome-based drug delivery for different cancer chemotherapeutics *i.e.* breast, lung, hepatic, cervical, pancreatic, gastric, skin, brain, head and neck cancers illustrated that liposomes can be explored as blooming field of investigation.

Acknowledgements

The authors express gratitude to Chitkara College of Pharmacy, Chitkara University, Punjab, India for motivation to compilation of this review.

Conflict of interests

Conflict of interest declared none.

References

Akhtar, A., L. Ghali, S.X. Wang, C. Bell, D. Li and X. Wen (2019). Optimisation of Folate-Mediated Liposomal Encapsulated Arsenic Trioxide for Treating HPV-Positive Cervical Cancer Cells *in Vitro*. *International Journal of Molecular Sciences.*, **20(9):** 1-20.

Alavi, M., N. Karimi and M. Safaei (2017). Application of various types of liposomes in drug delivery systems. *Advanced Pharmaceutical Bulletin.*, **7(1):** 3-9.

Bardania, H., S. Tarvirdipour and F. Dorkoosh (2017). Liposome-targeted delivery for highly potent drugs. *Artificial Cells Nanomedicine Biotechnology.*, **45:** 1478-1489.

Bisht, S., M. Schlesinger, A. Rupp, R. Schubert, J. Nolting, J. Wenzel, S. Holdenrieder, P. Brossart, G. Bendas and G. Feldmann (2016). A liposomal formulation of the synthetic curcumin analog EF24 (Lipo-EF24) inhibits pancreatic cancer progression: towards future combination therapies. *Journal of Nanobiotechnology.*, **14(1):** 1-15.

Bulbake, U., S. Doppalapudi, N. Kommineni and W. Khan (2017). Liposomal formulations in clinical use: an updated review. *Pharmaceutics.*, **9(2):** 1-33.

Cao, D., X. Zhang, M.D. Akabar, Y. Luo, H. Wu, X. Ke and T. Ci (2019). Liposomal doxorubicin loaded PLGA-PEG-PLGA based thermogel for sustained local drug delivery for the treatment of breast cancer. *Artificial Cells Nanomedicine Biotechnology.*, **47(1):** 181-191.

Cao, M., M. Long, Q. Chen, Y. Lu, Q. Luo, Y. Zhao, A. Lu, C. Ge, L. Zhu and Z. Chen (2016). Development of β-elemene

and cisplatin co-loaded liposomes for effective lung cancer therapy and evaluation in patient-derived tumor xenografts. *Pharmaceutical Research.*, **36(8):** 1-14.

Casagrande, N., M.D. Paoli, Marta, M. Celegato, A. Colombatti and D. Aldinucci (2013). Preclinical evaluation of a new liposomal formulation of cisplatin, lipoplatin, to treat cisplatin-resistant cervical cancer. *Gynecologic Oncology*., **131(3):** 744-752.

Cheng, L., F.Z. Huang, L.F. Cheng, Y.Q. Zhu, Q. Hu, L. Wei L. Li and D.W. Chen (2014).GE11-modified liposomes for non-small cell lung cancer targeting: preparation, *in vitro* and *in vivo* evaluation. *International Journal of Nanomedicine.*, **9:** 921-935.

Cheng, Y., P. Zhao, S. Wu, T. Yang, Y. Chen, X. Zhang, C. He, C. Zheng, K. Li, X. Ma and G. Xiang (2018). Cisplatin and Curcumin Co-loaded Nano-liposomes for the Treatment of Hepatocellular Carcinoma. *International Journal of Pharmaceutics.*, **545(1-2):** 261-273.

Cosco, D., D. Paolino, F. Cilurzo and M. Fresta (2012). Gemcitabine and tamoxifen-loaded liposomes as multidrug carriers for the treatment of breast cancer diseases. *International Journal of Pharmaceutics.*, **422(1-2):** 229-237.

Daraee, H., A. Etemadi, M. Kouhi, S. Alimirzalu and A. Akbarzadeh (2016). Application of liposomes in medicine and drug delivery. *Artificial Cells Nanomedicine Biotechnology.*, **44(1):** 381-391.

Ding, B.S., T. Dziubla, V.V. Shuvaev, S. Muro and V.R. Muzykantov (2006). Advanced drug delivery systems that target the vascular endothelium. *Molecular Interventions.*, **6(2):** 98-112.

Dou, Y.N., N. Chaudary, M.C. Chang, M. Dunne, H. Huang, D.A. Jaffray, M. Milosevic and C. Allen (2017). Tumor microenvironment determines response to a heat-activated thermosensitive liposome formulation of cisplatin in cervical carcinoma. *Journal of Controlled Release.*, **262:** 182-191.

Farzad, N., N. Barati, A.A. Momtazi-Borojeni, M. Yazdani, A. Arab, A. Razazan, S. Shariat, M. Mansourian, A. Abbasi, Z. Saberi and A. Badiee (2019). P435 HER2/neu-derived peptide conjugated to liposomes containing DOPE as an effective prophylactic vaccine formulation for breast cancer. *Artificial Cells Nanomedicine Biotechnology.*, **47(1):** 665-673.

Gaballua, F.A., S. Abbaspour-Ravasjanid, B. Mansooria, B. Mansoori, R. Yekta, H. Hamishehkar, A. Mohammadi, G. Dehghan, B. Shokouhi, S. Ghahremani Dehbokri and B. Baradaran (2019). Comparative of *in-vitro* evaluation between erlotinib loaded nanostructured lipid carriers and liposomes against A549 lung cancer cell line. *Iranian Journal of Pharmaceutical Research.*, **18(3):** 1168-1179.

Hamzawy, M.A., A.M. Abo-Youssef, H.F. Salem and S.A. Mohammed (2017). Antitumor activity of intratracheal inhalation of temozolomide (TMZ) loaded into gold nanoparticles and/or liposomes against urethane induced lung cancer in BALB/c mice. *Drug Delivery.*, **24(1):** 599-607.

Hassanzadeganroudsari, M., A. Heydarinasab, P. Chen and M. Soltani (2019). *In vitro* investigation of anticancer efficacy of carboplatin-loaded PEGylated nanoliposome particles on brain cancer cell lines. *Journal of Nanoparticle Research*., **21(6):** 1-12.

Hongtao, X., W. James and Z.W. Paxton (2016). Development of Long-Circulating pH-Sensitive Liposomes to Circumvent Gemcitabine Resistance in Pancreatic Cancer Cells. *Pharmaceutical Research.*, **33(7):** 1628-1637.

Hu, S.C.S., Y.S. Su, Y.C. Lai, C.H. Tseng and F.L. Yen (2019). Liposomal avicequinone-B formulations: Aqueous solubility, physicochemical properties and apoptotic effects on cutaneous squamous cell carcinoma cells. *Phytomedicine.*, **58:** 1-30.

Jiang, H., Z.P. Li, G.X. Tian, R.Y. Pan, C.M. Xu, B. Zhang and J.L. Wu (2019). Liver-targeted liposomes for codelivery of curcumin and combretastatin A4 phosphate: preparation, characterization and antitumor effects. *International Journal of Nanomedicine.*, **14:** 1789-1804.

Jin, X., J. Zhou, Z. Zhang and H. Lv (2018). The combined administration of parthenolide and ginsenoside CK in long circulation liposomes with targeted tLyp-1 ligand induce mitochondria mediated lung cancer apoptosis. *Artificial Cells Nanomedicine Biotechnology.*, **46:** 1-13.

Jose, A., S. Labala, K.M. Ninave, S.K. Gade and V.V. Venuganti (2018). Effective skin cancer treatment by topical co-delivery of curcumin and STAT3 siRNA using cationic liposomes. *American Association of Pharmaceutical Scientists.*, **19(1):** 166-175.

Ju, R.J, L. Cheng, X. Qiu, S. Liu, X.L. Song, X.M. Peng, T. Wang, C.Q. Li and X.T. Li (2018). Hyaluronic acid modified daunorubicin plus honokiol cationic liposomes for the treatment of breast cancer along with the elimination vasculogenic mimicry channels. *Journal of Drug Targeting.*, **26:** 793-805.

Juang, V., H.P. Lee, A.M.Y. Lin and Y.L. Lo (2016). Cationic PEGylated liposomes incorporating an antimicrobial peptide tilapia hepcidin 2-3: an adjuvant of epirubicin to overcome multidrug resistance in cervical cancer cells. *International Journal of Nanomedicine.*, **11:** 6047-6064.

Kanqiu, J., S. Mingjing and X. Weihua (2018). Arginine, glycine, aspartic acid peptide-modified paclitaxel and curcumin co-loaded liposome for the treatment of lung cancer: *in vitro/ vivo* evaluation. *International Journal of Nanomedicine.*, **13:** 2561-2569.

Kim, C.E., S.K. Lim and J.S. Kim (2012). *In vivo* antitumor effect of cromolyn in PEGylated liposomes for pancreatic cancer. *Journal of Controlled Release.*, **157:** 190-195.

Koning G.A. and G. Storm (2003). Targeted drug delivery systems for the intracellular delivery of macromolecular drugs. *Drug Discovery Today.*, **8(11):** 482-483.

Le, U.M., A. Hartman and G. Pillai (2018). Enhanced selective

cellular uptake and cytotoxicity of epidermal growth factor-conjugated liposomes containing curcumin on EGFR overexpressed pancreatic cancer cells. *Journal of Drug Targeting.*, **26(8):** 676-683

Li, H., X. Li, X. Shi, Z. Li and Y. Sun (2019). Effects of magnetic dihydroartemisinin nano-liposome in inhibiting the proliferation of head and neck squamous cell carcinomas. *Phytomedicine.*, **56:** 215-228.

Lu, Y.J., E.Y. Chuang, Y.H. Cheng, T.S. Anilkumar, H.A. Chen and J.P. Chen (2019). Thermo sensitive magnetic liposomes for alternating magnetic ûeld inducible drug delivery in dual targeted brain tumor chemotherapy. *Chemical Engineering Journal.*, **373:** 720-733.

Lv, B.H., W. Tan, X. Shang and L. Zhang (2017). Evaluation of clinical effectiveness of paclitaxel and ursolic acid co-loaded liposomes as enhanced treatment for head and neck squamous cell carcinoma. *Tropical Journal of Pharmaceutical Research.*, **17(11):** 2115-2121.

Ma, J., H. Zhuang, Z. Zhuang, Y. Lu, R. Xia, L. Gan and Y. Wu (2017). Development of docetaxel liposome surface modified with CD133 aptamers for lung cancer targeting, *Artificial Cells Nanomedicine Biotechnology.*, **46(8):** 1864-1871.

Mach, C.M., L. Mathew, S.A. Mosley, R. Kurzrock and J.A. Smith (2009). Determination of minimum effective dose and optimal dosing schedule for liposomal curcumin in a xenograft human pancreatic cancer model. *Anticancer Research.*, **29(6):** 1895-1899.

Mandal, B., H. Bhattacharjee, N. Mittal, H. Sah, P. Balabathula, L.A. Thoma and G.C. Wood (2016). Development and *in vitro* evaluation of core-shell type lipid-polymer hybrid nanoparticles for the delivery of erlotinib in non-small cell lung cancer. *European Journal of Pharmaceutical Sciences.*, **81(4):** 162-171.

Marengoa, A., S. Forcinitib, I. Dandob, E. Dalla Pozza, B. Stella, N. Tsapis, N. Yagoubi, G. Fanelli, E. Fattal, C. Heeschen and M. Palmieri (2019). Pancreatic cancer stem cell proliferation is strongly inhibited by diethyldithio-carbamate-copper complex loaded into hyaluronic acid decorated liposomes. *Biochimica* et *Biophysica Acta General Subjects.*, **1863(1):** 61-72.

Marsh (2012). Thermodynamics of phospholipid self-assembly. *Biophysical Journal.*, **102(5):** 1079-1087.

Marwah, M., Y. Perrie, R.K.S. Badhan and D. Lowry (2019). Intracellular uptake of EGCG-loaded deformable controlled release liposomes for skin cancer. *Journal of Liposome Research.*, **7:** 1-42.

Ochi, M.M., G. Amoabediny, S.M. Rezayat, A. Akbarzadeh, B. Ebrahimi (2016). *In-vitro* co-delivery evaluation of novel pegylated nano-liposomal herbal drugs of silibinin and glycyrrhizic acid (nano-phytosome) to hepatocellular carcinoma cells. *Cell Journal.*, **18(2):** 135-148.

Okamoto, Y., K. Taguchi and M. Sakuragi (2014). Preparation, Characterization and *in Vitro/in Vivo* Evaluation of Paclitaxel-Bound Albumin-Encapsulated Liposomes for the Treatment of Pancreatic Cancer. *ACS Omega.*, **4:** 8693-8700.

Petrilli, R., J.O. Eloy, F.P. Saggioro, D.L. Chesca, M.C. de Souza, M.V. Dias, L.P. Luis, R.J. Lee and R.F. Lopez (2018). Skin cancer treatment effectiveness is improved by iontophoresis of EGFR targeted liposomes containing 5-FU compared with subcutaneous injection. *Journal of Controlled Release.*, **283:** 151-162.

Poy, D., H. Ebrahimi Shahemabadi, A. Akbarzadeh, H. Moradi-Sardareh and M. Ebrahimifar (2017). Carboplatin liposomal nanoparticles: preparation, characterization and cytotoxicity effects on lung cancer *in vitro* environment. I*nternational Journal of Polymeric Materials and Polymeric Biomaterials.*, **67:** 367-370.

Qiu, F. and X. Zhao (2018). *In vivo* antitumor activity of liposome plasmid DNA encoding mutant survivin T34A in cervical cancer. *Molecular Medicine Reports.*, **18:** 841-847.

Ranjan, A.P., A. Mukerjee, L. Helson, R. Gupta and J.K. Vishwanatha (2013). Efficacy of Liposomal Curcumin in a Human Pancreatic Tumor Xenograft Model: Inhibition of Tumor Growth and angiogenesis. *Anticancer Research.*, **133(9):** 3603-3610.

Rastakhiz, S., M. Yazdani, S. Shariat, A. Arab, A.A. Momtazi-Borojeni, N. Barati, M. Mansourian, M. Amin, A. Abbasi, Z. Saberi, S.A. Jalali, A. Badiee and M.R. Jaafari (2018). Preparation of nanoliposomes linked to HER2/neu derived (P5) peptide containing MPL adjuvant as vaccine against breast cancer. *Journal of Cellular Biochemistry.*, **13:** 1-10

Saengkrit, N., S. Saesoo, W. Srinuanchai, S. Phunpee and U.R. Ruktanonchai (2014). Influence of curcumin-loaded cationic liposome on anticancer activity for cervical cancer therapy. *Colloids and Surfaces B*: *Biointerfaces.*, **114:** 349-356.

Saesoo, S., S. Bunthot, W. Sajomsang, P. Gonil, S. Phunpee, P. Songkhum, K. Laohhasurayotin, T. Wutikhun, T. Yata, U.R. Ruktanonchai and N. Saengkri (2016). Phospholipid-chitosan hybrid nanoliposomes promoting cell entry for drug delivery against cervical cancer. *Journal* of *Colloid and Interface Science.*, **480:** 240-248

Samson, A.A.S., S. Park, S.Y. Kim, D.H. Min, N.L. Jeon and J.M. Song (2018). Liposomal co-delivery-based quantitative evaluation of chemosensitivity enhancement in breast cancer stem cells by knockdown of GRP78/ CLU. *Journal of Liposome Research.*, **29(1):** 1-9

Sarfraz, M., A. Afzal, S.M. Raza, S. Bashir, A. Madni, M.W. Khan, X. Ma and G. Xiang (2017). Liposomal co-delivered oleanolic acid attenuates doxorubicin induced multi-organ toxicity in hepatocellular carcinoma. *Oncotarget.*, **8(29):** 47136-47153.

Sercombe, L., T. Veerati, F. Moheimani, S.Y. Wu, A.K. Sood and S. Hua (2015). Advances and challenges of liposome assisted drug delivery. *Frontiers in Pharmacology.*, **6:** 1-13.

Song, X.L., R.J. Ju and Y. Xiao (2017). Application of multifunctional targeting epirubicin liposomes in the treatment of non-small-cell lung cancer. *International Journal of Nanomedicine.*, **12:** 7433-7451.

Sun, Y., X. Li, L. Zhang, X. Liu, B. Jiang, Z. Long and Y. Jiang (2019). Cell permeable NBD peptide-modified liposomes by hyaluronic acid coating for the synergistic targeted therapy of metastatic inflammatory breast cancer. *Molecular Pharmaceutics.*, **16(3):** 1140-1155

Vaidya, T., R.M. Straubinger and S. Ait-Oudhia (2018). Development and evaluation of tri-functional immunoliposomes for the treatment of HER2 positive breast cancer. *Pharmaceutical Research.*, **35(5):** 1-14.

Valizadeh, H., S. Ghanbarzadeh an P. Zakeri-Milani (2015). Fusogenic liposomal formulation of sirolimus: improvement of drug anti-proliferative eûect on human T-cells. *Drug Development and Industrial Pharmacy.*, **41(9):** 1558-1565.

Wang, W.Y., Y.X. Cao, X. Zhou and B. Wei (2019). Delivery of folic acid-modified liposomal curcumin for targeted cervical carcinoma therapy. *Drug, Design, Development and Therapy.*, **13:** 2205-2213.

Wang, Y., F. Gao, X. Jiang, X. Zhao, Y. Wang, Q. Kuai, G. Nie, M. He, Y. Pan, W. Shi and S. Ren (2019). Co-Delivery of Gemcitabine and Mcl-1 SiRNA via Cationic Liposome-Based System Enhances the Efficacy of Chemotherapy in pancreatic Cancer. *Journal of Biomedical Nanotechnology.*, **15(5):** 966-978.

Wei, M., X. Guo, L. Tu, Q. Zou, Q. Li , C. Tang, B. Chen, Y. Xu and C. Wu (2015). Lactoferrin-modified PEGylated liposomes loaded with doxorubicin for targeting delivery to hepatocellular. *International Journal of Nanomedicine.*, **10:** 5123-5137.

Wei, Y., Y. Wang and D. Xia (2017). Thermosensitive Liposomal Co-delivery of HAS paclitaxel and HSA-ellagic Acid Complexes for Enhanced Drug Perfusion and Efficacy against Pancreatic Cancer. *Applied Materials and Interfaces.*, **9:** 25138-25151.

Xia, T., Q. He, K. Shi, Y. Wang, Q. Yu, L. Zhang, Q. Zhang, H. Gao, L. Ma and J. Liu (2016). Losartan loaded liposomes improve the antitumor efficacy of liposomal paclitaxel modified with pH sensitive peptides by inhibition of collagen in breast cancer. *Pharmaceutical Development and Technology*, **23(1):** 13-21.

Xiong, D., Z. Liu, T. Bian, J. Li, W. Huang, P. Jing, L. Liu, Y. Wang and Z. Zhong (2015). JGX1-mediated anionic liposomes carrying adenoviral vectors for enhanced inhibition of gastric cancer vascular endothelial cells. *International Journal of Pharmaceutics.*, **496(2):** 699-708.

Xue-tao, Li., H. Mei-li, Z. Zhi-yan, Y. Jiang and L. Cheng (2015). The antitumor activity of PNA modified vinblastine cationic liposomes on Lewis lung tumor cells: *In vitro* and *in vivo* evaluation. *International Journal of Pharmaceutics.*, **487(1-2):** 223-233.

Yang, F., Z. Zheng, L. Zheng, J. Qin, H. Li, X. Xue, J. Gao and G. Fang (2018). SATB1 siRNA-encapsulated immunoliposomes conjugated with CD44 antibodies target and eliminate gastric cancer-initiating cells. *OncoTargets and Therapy.*, **11:** 6811-6825.

Yang, L., J. Xin, Z. Zhang, H. Yan, J. Wang, E. Sun, J. Hou, X. Jia and H. Lv (2016). TPGS-modified liposomes for the delivery of ginsenoside compound K against non-small cell lung cancer: formulation design and its evaluation *in vitro* and *in vivo*. *Journal of Pharmacy and Pharmacology.*, **68(9):** 1109-1118.

Yang, T., M.K. Choi, F.D. Cui, S.J. Lee, S.J. Chung, C.K. Shim and D.D. Kim (2007). Antitumor effect of paclitaxel-loaded PEGylated immunoliposomes against human breast cancer cells. *Pharmaceutical Research.*, **24(12):** 2402-2411.

Yin, X., Y. Xiao, L. Han, B. Zhang, T. Wang, Z. Su and N. Zhang (2018). Ceramide-Fabricated Co-Loaded Liposomes for the Synergistic Treatment of Hepatocellular Carcinoma. *American Association of Pharmaceutical Scientists.*, **19:** 2133-2143.

Zahednezhad, F., M. Saadat, H. Valizadeh, P. Zakeri-Milani, and B. Baradaran (2019). Liposome and immune system interplay: Challenges and potentials. *Journal of Controlled Release.*, **305:** 194-209.

Zhang, N., H. Chen, A.Y. Liu, J.J. Shen, V. Shah, C. Zhang, J. Hong and Y. Ding (2016). Gold conjugate-based liposomes with hybrid Cluster Bomb structure for liver cancer therapy. *Biomaterials.*, **74:** 280-291.