Chapter

Biomimetic Nanomaterials from the Assembly of Polymers, Lipids, and Surfactants

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Abstract

Nanostructured materials require evaluation at a molecular level to become controllable and useful in drug and vaccine delivery. Over the years self-assembled nanomaterials such as nanoparticles and thin films have been prepared, characterized, and used for biomedical applications. In this review meaningful examples of biomimetic nanomaterials and their construction based on intermolecular interactions such as the electrostatic attraction or the hydrophobic effect will be discussed. Emphasis will be placed on the interactions between polymers, lipids, surfactants, and surfaces leading to bioactive supramolecular assemblies such as nanoparticles and coatings. Among the important applications of the self-assembled nanostructures and films to be reviewed are their antimicrobial effect and their adjuvant activity for vaccine delivery.

Keywords: lipid polymer nanoparticles, antimicrobial nanostructures, adjuvants for vaccines, intermolecular interactions, assembly and disassembly

1. Introduction

Life is ephemeral as are the assemblies that make life possible. Among the nanomaterials, the biomimetic nanomaterials mimic the assemblies found in living creatures and may find a myriad of useful applications [1–9]. The bioactive biomimetic nanomaterials encompass a wide variety of hybrid metastable nanostructures keeping different or similar molecules transiently together thanks to weak but frequent intermolecular interactions as are the van der Waals, the hydrogen bridges, the electrostatic and electrolydynamical interactions, and the hydrophobic effect [10, 11]. Among these, one may say that the lipid polymer, the lipid inorganic materials and the coatings with NPs inclusion have been the subject of important developments in drug and vaccine delivery to fight pathogens and prevent, treat or diagnose major human diseases such as cancer. Stimuli responsive assemblies with the use of various triggers such as pH, temperature, light, enzyme, and redox potential are emerging strategies for the effective localization of the bioactives at the tumor site for safe and effective cancer therapy or diagnosis despite all problems with multidrug resistance, long-lasting chemotherapy and low transfection and non-specific immuneresponse after systemic delivery of siRNAs [12]. For example, a biomimetic phospholipid-like amphiphilic prodrug, 1-O-octodecyl-2-conjugated linoleoyl-sn-glycero-3-phosphatidyl gemcitabine (OLGPG) combined with cholesteryl hemisuccinate polyethylene glycol 1500 (CHS-PEG) upon injection in water...
formed the OLGPG and OLGPG/CHS-PEG nanometric spherical vesicles due to the hydrophobic interaction of lipid moieties. Since phospholipase A2 (PLA2) is highly expressed in tumor tissues and specifically degrades the 2-acyl of the phospholipids to lysophospholipids, a PLA2-sensitive OLGPG specific degradation in the tumor tissue was obtained [13]. In this same work, the in vivo experiments with a hepatocellular tumor-bearing mouse model showed that these long-circulating phospholipid-like prodrug nanoassemblies yielded the highest antitumor and tumor targeting effects compared to the other groups [13].

Today (30 November 2018) a search of the literature on lipid polymer coatings in the Scopus database produced 26,123 items whereas a search on lipid polymer nanoparticles resulted in 24,042 publications. I feel somewhat proud to have witnessed and contributed to some of the early and late developments on lipid polymer [14–23] and lipid silica NPs [24–29] that started about 3 decades ago. In particular, cationic lipids by themselves or in combination with other lipids or assemblies can yield interesting microenvironments to accommodate a variety of bioactive molecules such as drugs, antigens, peptides, nucleic acids, etc. [30–37]. The nanometric size and positive charge impart desirable properties for the cationic assemblies after injection via parenteral route in vivo. Good instances are the direct action at the lymph nodes for stimulation of dendritic cells for vaccines [9, 22, 31, 34–37], and the penetration of nasal mucosae to overcome the blood brain barrier releasing drugs into the brain [33]. Other important applications relate to the antimicrobial properties of a variety of cationic assemblies either by themselves such as cationic bilayers or in effective combinations with other antimicrobials such as antibiotics, polymers or peptides [7, 23, 38–45].

This review will discuss mostly seminal and recent contributions regarding applications of biomimetic nanoparticles and coatings in antimicrobial therapy and vaccine development. Emphasis will be placed on lipid polymer NPs and their coatings plus their biomedical applications in drug and vaccine delivery.

2. Lipid polymer nanoparticles: overview on their applications

Lipids and polymers have been yielding a myriad of combinations. From the 24,042 publications on lipid polymer nanoparticles found today, 6173 were review articles. Many of them referred to solid lipid nanoparticles or nanostructured lipid carriers and the associated problems regarding drug location and arrangements of the lipids and the stabilizing agents in the lipid particle nanostructure [46, 47]. These NPs are based on lipid cores stabilized by layers of hydrophilic polymers [48, 49]. They may also assume the form of nanodiscs or open bilayer fragments (BF) [17]. The scaffold is then an organized and open lipid bilayer disk of charged and saturated synthetic lipids [50, 51] or compositions containing polyethylene glycol covalently bound to lipids [52]. Dioctadecyldimethylammonium bromide bilayer fragments (DODAB BF) with two consecutively deposited layers of carboxymethylcellulose (CMC) and polyallyldimethylammonium chloride (PDDA), respectively, were effective microbial assemblies [39, 40]. This activity was associated with the outermost layer of the cationic antimicrobial polymer PDDA [39–41]. The visualization of the lipid or lipid polymer nanodiscs was achieved by advanced microscopy techniques such as shown from cryo-transmission electron micrographs (cryo-TEM) [52] in Figure 1(a), transmission electron micrographs with electronic staining of the nanodiscs in Figure 1(b) or scanning electron micrographs of the DODAB BF/CMC/PDDA nanodiscs in Figure 1(c). It is interesting to notice that the disks could be observed both face-on and edge-on.
Dispersions of phospholipids such as 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) and 1,2-dihexanoyl-sn-glycero-3-phosphocholine (DHPC) can yield also discoidal and open lipid particles; the short-chain components preferentially occupy curved rim environments around bilayer disks of the long-chain components [53, 54]. Cationic peptides such as a lung surfactant protein and the antimicrobial peptide magainin 2 interacted with the DMPC/DHPC neutral bicelles but did not affect their structure as seen from magnetic resonance spectroscopy [53]; for disks containing the anionic 1,2-dimyristoyl-sn-glycero-3-phospho-(1′-rac-glycerol) (DMPG) the peptides lowered the temperature at which the particles coalesced into more extended lamellar structures or promoted partitioning of the zwitterionic and anionic long-chain lipid components into different environments [53].

Other lipid–polymer hybrid nanoparticles consist of a polymer core surrounded by a lipid shell combining properties of both polymeric nanoparticles and liposomes and often referred to as biomimetic nanoparticles [14–23, 55–58]. Sometimes, when the lipid has good affinity for the polymer, it can be embedded in the polymer matrix as was the case of the cationic lipid dioctadecyl(dimethyl ammonium bromide (DODAB) and poly methyl methacrylate (PMMA) polymer for producing microbicidal PMMA/DODAB coatings from spin-coating [59]. In these coatings the cationic lipid DODAB accounted for the microbicidal activity [59]. Hadinoto and co-workers reviewed the literature on lipid-coated polymeric nanoparticles
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(LPNPs) prepared from natural polymers such as chitosan (CS) and the biocompatible and biodegradable poly-lactic-co-glycolic acid (PLGA), and their applications as a delivery platform for cancer therapy [60].

Leaf Huang and co-workers recently gave a comprehensive account on the important role of lipid polymer nanoparticles in combination therapy against cancer including chemotherapy, photodynamic therapy, thermal heating treatments with metals, siRNA delivery and others [61]. Some synergistic combinations of anti-cancer drugs can circumvent resistance to treatment and be effective in anti-cancer therapy. For example,

NPs formulated through self-assembly of the biodegradable PLGA and a cationic, hydrophobic molecule carried siRNA to knock down target oncogenes and to deliver cisplatin prodrug to tumors both in vitro and in vivo [62]. The NPs induced a significant and sustained suppression of genes in a human lymph node carcinoma of the prostate xenograft mouse model for up to 3 days after a single dose. Administering these NPs revealed a synergistic effect on tumor inhibition that was strikingly more effective than cisplatin monotherapy [62]. On reference [62] the cationic molecule was embedded in the PLGA-PEG shell and the cargo of siRNA was in the inner aqueous core.

Messerschmidt and coworkers [63] described another sophisticated system of lipid polymer NPs aiming at cancer combined therapy. Lipid coated -polystyrene NPs endowed with several functions such as targeting to the cancer cells with a single-chain Fv antibody fragment, steric stabilization of the outer lipid layer with polyethylene glycol (PEG) lipids and single chain tumor necrosis factor (scTNF) covalently bound to the polystyrene core [63]. Thereby, the system specifically delivered scTNF to the cancer cells inducing their death by apoptosis without affecting the healthy cells.

Many applications in drug and vaccine delivery for the hybrid polymer lipid NPs called biomimetic nanoparticles were systematically reviewed over the last three decades [7, 8, 17–19, 31, 38, 44, 55–58, 64–66]. In special when either the lipid or the polymer is cationic, lipid polymer NPs display remarkable interactive capability with bioactive molecules and can impart antimicrobial properties to a variety of nanomaterials adding functionality to dispersions, surfaces and coatings and allowing to obtain interesting combinations of bioactive molecules and assemblies. Novel approaches proliferate exponentially for the development of different advanced materials shaped as NPs, hydrogels and surface coatings with effective antimicrobial properties. Bassegoda and coworkers recently gave a comprehensive account on major strategies to prevent the occurrence of resistance against antibiotics by using advanced materials [67]. Advanced materials occur as anti-fouling molecules and surfaces that prevent microorganisms adhesion and formation of biofilms or they are bactericidal materials that cause cell membrane disruption, production of reactive oxygen species with damage to vital biomolecules in the cell or materials that damage vital proteins [67]. They recognized the importance of antimicrobial biomimetics from the need of a new generation of hybrid materials with strong antimicrobial/antifouling activities and improved biocompatibility imparted by “safety design” [67]. In the next section we discuss some of these cationic materials.

3. Cationic lipid polymer nanoparticles, coatings and applications in antimicrobial biomimetics and vaccine delivery

Cationic lipid polymer NPs and coatings are strategic for applications in antimicrobial biomimetics and vaccine design [7, 8, 38–45, 55–59]. Due to the cationic lipid, lipid polymer cationic NPs can combine effectively with antibiotics
like amphotericin B or miconazole [39, 68–70], rifampicin [71], clarithromycin [72], anti-inflammatory hydrophobic drugs like indomethacin [32], nucleic acids [21], oligonucleotides [35, 73, 74], proteins in general including serum proteins, transmembrane proteins, receptors and toxins [75–78], antigens [9, 20, 22, 34–37], peptides [23, 43–45] or polymers [79, 80].

Early work on the affinity between the biocompatible PMMA polymer and the antimicrobial DODAB lipid showed that thin films of PMMA/DODAB casted by spin-coating a chloroformic solution onto silicon wafers were homogeneous and retained the microbicidal activity of DODAB [59]. Figure 2 illustrates the polymer lipid coatings of polystyrene (PS)/DODAB and PMMA/DODAB; whereas DODAB did not mix homogeneously with PS (Figure 2(a), the film resulting from the PMMA/DODAB spin-coating procedure in Figure 2(c) was very smooth and homogeneous as reproduced from reference [59]. The live–dead testing for Escherichia coli showed green, and alive bacteria on the PMMA coating (Figure 2(e) and red, and dead ones on the PMMA/DODAB coating (Figure 2(f)).

Taking advantage of the good compatibility between DODAB lipid and PMMA, Melo and co-workers evaluated the interaction between different quaternary ammonium surfactants and PMMA from spin-coated PMMA/DODAB and PMMA/CTAB films on silicon wafers or glass coverslips [81]. The mobility of CTAB in the coatings allowed this surfactant to leak to the outer medium in contrast with the permanence of DODAB in the coatings and its antimicrobial action by contact [81].

In another meaningful instance, Naves and co-workers synthesized PMMA NPs by emulsion polymerization in the presence of DODAB or CTAB and determined the antimicrobial activity of the dispersions [82]. Loading the biocompatible poly acrylic particles with the quaternary ammonium surfactants was a facile, fast, low-cost approach to obtaining highly efficient antimicrobial nanoparticles which either killed by contact in the case of embedded DODAB or by leakage to the outer medium in the case of CTAB [82].

The biocompatible PMMA polymer and the antimicrobial and cationic polymer PDDA reunited by synthesizing PMMA in the presence of PDDA yielded interesting
NPs [83]. This was a facile alternative approach in comparison to strategies based on the synthesis of block copolymers incorporating both functions. Figure 3 shows the macroscopic and microscopic appearance of the very stable dispersions of PMMA/PDDA and PMMA/PDDA/cationic amphiphile and some of their films obtained

Figure 3.
Stable NPs dispersions of biocompatible polymer (PMMA), antimicrobial polymer (PDDA) and cationic lipid (DODAB) or surfactant (CTAB) in form of NPs dispersions in water just after synthesis (a) and 6 months after synthesis (b). Coatings were obtained by casting and drying NPs water dispersions on polystyrene, silicon wafer or glass coverslip surfaces from left to right (c). The SEM micrograph for the PMMA/PDDA NPs coatings showed the NPs film obtained after drying (d). Reproduced from reference [80].
by casting and drying the water dispersions of NPs onto different surfaces such as polystyrene, silicon wafers or glass coverslips [80].

Against fungus such as *Candida albicans*, the variable antimicrobial activity of the quaternary ammonium nitrogen in lipids, surfactants and polymers was previously established by our group [40, 84–86]. While substantial fungicidal activity was described for the micelle-forming CTAB surfactant, the bilayer–forming DODAB did not show the ability of moving from the bilayer assembly to the fungus cell membrane [85]. As a consequence a poor fungicidal activity of DODAB bilayers assembled as bilayer fragments or as large vesicles was obtained [84, 86]. The microbicidal quaternary nitrogen only kills the fungus if its host molecule has mobility enough to cross the thick and dense layer of glycoproteins at the outer fungus cell wall. Adsorption isotherms of CTAB and DODAB on *C. albicans* were revealing; increasing DODAB concentration reduced its adsorption onto the cells due to the preferential vesicle-vesicle instead of the vesicle-cell interaction [87]. In contrast to other surfactants such as sodium dodecyl sulfate (SDS), CTAB did not disrupt the cell membrane and cell death occurred when the cell became positively charged [85]. Fungus death requires adsorption of the quaternary ammonium moiety to the cell, change in the cell charge and penetration through the cell wall reaching the fungus cell membrane. Since DODAB, in the DODAB bilayer, exists mostly in the rigid gel state there is no penetration of the quaternary ammonium moiety into the fungus cell wall and cytoplasmic membrane what explains the poor DODAB activity against fungus when compared to other micelle-forming surfactants [84, 85]. These considerations directly lead to the prediction that mobile polymers bearing the quaternary ammonium moiety would be efficient antimicrobial agents against fungus. Polymer immobilization, however, would reduce their action and these were indeed the experimental results [40, 83]. Immobilization of PDDA in PMMA/PDDA NPs substantially reduced the PDDA fungicidal action against *C. albicans* [83]. PDDA by itself showed remarkable fungicidal activity (minimal fungicidal concentration of 0.5 μg/mL) in complete absence of toxicity against red blood cells [86]. Very recently, Fait and co-workers comprehensively revised the structure–function activity of cationic surfactants as antifungal agents [88].

For vaccines, cationic nanostructures have been revealing their potential in several instances from combinations with cationic lipids or other hybrid assemblies shaped as microparticles or nanoparticles [7–9, 17–22, 28, 31, 34–37, 55, 58, 64, 66, 76, 78]. The possibility of varying sizes from nanometric to micrometric and the positive charge are major assets for adjuvants since they allow combinations with the vast majority of antigens such as proteins, peptides, haptens, nucleic acids, oligonucleotides or other negatively charged biological combinations such as extracts of pathogens. The nanosize is valuable for localizing the antigen directly in the lymph nodes where capture by antigen presenting cells may elicit suitable humoral and cellular defenses. Manolova and co-workers showed that particles target distinct dendritic cell populations according to their size [89]. Virus-sized NPs with 20–200 nm diameter are captured by dendritic cells (DC) whereas bacteria with 500–5000 nm diameter are captured by phagocytes or macrophages. Whereas images of large particles (500–2000 nm) localized them in DC from the injection site, small (20–200 nm) NPs and virus-like particles (30 nm) were also found in lymph nodes–resident DC and macrophages, suggesting free drainage of NPs to the lymph nodes; particle size determined the mechanism of trafficking to the LN so that only small NPs could specifically target LN-resident cells [89]. Manolova and co-workers [89] considered the mechanism of NPs trafficking from the skin to the draining LN in vivo; the optimal size for lymphatic uptake would be between 10 and 100 nm [89]. The initial lymphatic vessels are lined with overlapping endothelial cells so that DC and fluids from the interstitial space enter lymphatic
vessels through the endothelial cell junctions. Hence, these junctions might act as a molecular sieve and could prevent large particles from entering freely into the afferent lymphatics [89]. In the interstitial space, DC that captured large particles would carry them into the lymphatics. In addition, large particles would remain more tightly trapped in the interstitial space before entering the lymphatics. Their prolonged residence in the interstitium would increase the probability of phagocytosis. The role of NP charge was reviewed [90] and the boosting of cationic NPs for generating antigen-specific CD4(+) T cell proliferation was demonstrated [91].

4. Conclusions

The plethora of biomolecules that can be combined with polymers enables the design of new types of polymer-based NPs and interfaces, for example antimicrobial coatings from hybrid lipid polymer NPs [80, 83], possibly useful in medical devices, which will hopefully provide innovative preventive and therapeutic approaches in medicine.

Future generations of biomimetic systems will involve more complex compositions and combinations, leading to insights into fighting pathological conditions. Future developments in biomimetic assemblies including polymers will certainly improve and expand biomedical applications and significantly advance the treatment of cancer and many other diseases.

Nowadays lipid polymer, positively charged, biomimetic NPs are available over a range of sizes for vaccines design and drug delivery. Biomimetic lipid polymer NPs were first described by our group in the nineties [7–9, 14–16, 92]. The last decades witnessed significant extensions in our repertoire so that lipid-polymer and polymer-lipid dispersions or coatings, nanosized bilayer fragments, bilayer-covered polymeric particles, and layer-by-layer lipid polymer assemblies, most of them cationic, found novel applications as adjuvants for vaccines, as carriers for drug delivery and as antimicrobial assemblies.

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Conflict of interest

The author declares no conflict of interest.
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References

[1] Einfalt T, Witzigmann D, Edlinger C, Sieber S, Goers R, Najer A, et al. Biomimetic artificial organelles with in vitro and in vivo activity triggered by reduction in microenvironment. Nature Communications. 2018;9(1):1127. DOI: 10.1038/s41467-018-03560-x

[2] Garni M, Thamboo S, Schoenenberger CA, Palivan CG. Biopores/membrane proteins in synthetic polymer membranes. Biochimica et Biophysica Acta—Biomembranes. 2017;1859(4):619-638. DOI: 10.1016/j.bbamem.2016.10.015

[3] Schoonen L, van Hest JC. Compartmentalization approaches in soft matter science: From nanoreactor development to organelle mimics. Advanced Materials. 2016;28(6):1109-1128. DOI: 10.1002/adma.201502389

[4] De Martino MT, Abdelmohsen LKEA, Rutjes FPJT, van Hest JCM. Nanoreactors for green catalysis. Beilstein Journal of Organic Chemistry. 2018;14:716-733. DOI: 10.3762/bjoc.14.61

[5] Vonarbourg A, Passirani C, Desigaux L, Allard E, Saulnier P, Lambert O, et al. The encapsulation of DNA molecules within biomimetic lipid nanocapsules. Biomaterials. 2009;30(18):3197-3204. DOI: 10.1016/j.biomaterials.2009.03.009

[6] Groo AC, Matougui N, Umerska A, Saulnier P. Reverse micelle-lipid nanocapsules: A novel strategy for drug delivery of the plectasin derivate AP138 antimicrobial peptide. International Journal of Nanomedicine. 2018;13:7565-7574. DOI: 10.2147/IJNN.S180040

[7] Carmona-Ribeiro AM. Self-assembled antimicrobial nanomaterials. International Journal of Environmental Research and Public Health. 2018;15(7):1408. DOI: 10.3390/ijerph15071408

[8] Carmona-Ribeiro AM. Biomimetic nanoparticles: Preparation, characterization and biomedical applications. International Journal of Nanomedicine. 2010;5:249-259

[9] Carmona-Ribeiro AM. Chapter Thirteen - Nanomaterials Based on Lipids for Vaccine Development. In: Skwarczynski M, Toth I, editors. Micro and Nanotechnology in Vaccine Development. William Andrew Publishing; 2017. pp. 241-257. DOI: 10.1016/B978-0-323-39981-4.00013-0 Available from: http://www.sciencedirect.com/science/article/pii/B9780323399814000130

[10] Israelachvili JN. Intermolecular and surface forces. 3rd ed. San Diego: Academic Press; 2011. p. 674. DOI: 10.1016/B978-0-12-375182-9.10025-9

[11] Israelachvili JN, Mitchell DJ, Ninham BW. Theory of self-assembly of lipid bilayers and vesicles. Biochimica et Biophysica Acta. 1977;470(2):185-201

[12] Jain A, Jain SK. Stimuli-responsive smart liposomes in cancer targeting. Current Drug Targets. 2018;19(3):259-270. DOI: 10.2174/1389450117666160208144143

[13] Zuo J, Tong L, Du L, Yang M, Jin Y. Biomimetic nanoassemblies of 1-O-octodecyl-2-conjugated linoleoyl-sn-glycero-3-phosphatidyl gemcitabine with phospholipase A (2)-triggered degradation for the treatment of cancer. Colloids and Surfaces. B, Biointerfaces. 2017;152:467-474. DOI: 10.1016/j.colsurfb.2017.02.001

[14] Carmona-Ribeiro AM, Midmore BR. Synthetic bilayer adsorption onto polystyrene microspheres. Langmuir. 1992;8(3):801-806. DOI: 10.1021/la00039a013
[15] Carmona-Ribeiro AM, Herrington TM. Phospholipid adsorption onto polystyrene microspheres. Journal of Colloid and Interface Science. 1993;156(1):19-23. DOI: 10.1006/jcis.1993.1074

[16] Carmona-Ribeiro AM, Lessa M. Interactions between bilayer membranes and látex. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 1999;153(1-3):355-361. DOI: 10.1016/S0927-7757(98)00532-9

[17] Carmona-Ribeiro AM. Bilayer vesicles and liposomes as interface agents. Chemical Society Reviews. 2001;30:241-247. DOI: 10.1039/B101608N

[18] Carmona-Ribeiro AM. Bilayer-forming synthetic lipids: Drugs or carriers? Current Medicinal Chemistry. 2003;10(22):2425-1446. DOI: 10.2174/092986703776872925

[19] Carmona-Ribeiro AM. Lipid bilayer fragments and disks in drug delivery. Current Medicinal Chemistry. 2006;13(12):1359-1370. DOI: 10.2174/092986706776872925

[20] Lincopan N, Espíndola NM, Vaz AJ, Carmona-Ribeiro AM. Cationic supported lipid bilayers for antigen presentation. International Journal of Pharmaceutics. 2007;340(1-2):216-222. DOI: 10.1016/j.ijpharm.2007.03.014

[21] Rosa H, Petri DF, Carmona-Ribeiro AM. Interactions between bacteriophage DNA and cationic biomimetic particles. The Journal of Physical Chemistry. B. 2008;112(51):16422-16430. DOI: 10.1021/jp806992f

[22] Lincopan N, Espíndola NM, Vaz AJ, da Costa MH, Faquim-Mauro E, Carmona-Ribeiro AM. Novel immunoadjuvants based on cationic lipid: Preparation, characterization and activity in vivo. Vaccine. 2009;27(42):5760-5771. DOI: 10.1016/j.vaccine.2009.07.066

[23] Xavier GRS, Carmona-Ribeiro AM. Cationic biomimetic particles of polystyrene/cationic bilayer/gramicidin for optimal bactericidal activity. Nanomaterials. 2017;7(12):422. DOI: 10.3390/nano7120422

[24] Rapuano R, Carmona-Ribeiro AM. Physical adsorption of bilayer membranes on silica. Journal of Colloid and Interface Science. 1997;193(1):104-111. DOI: 10.1006/jcis.1997.5060

[25] Rapuano R, Carmona-Ribeiro AM. Supported bilayers on silica. Journal of Colloid and Interface Science. 2000;226:299-307. DOI: 10.1006/jcis.2000.6824

[26] Moura SP, Carmona-Ribeiro AM. Cationic bilayer fragments on silica at low ionic strength: Competitive adsorption and colloid stability. Langmuir. 2003;19(17):6664-6667. DOI: 10.1021/la034334o

[27] Moura SP, Carmona-Ribeiro AM. Biomimetic particles: Optimization of phospholipid bilayer coverage on silica and colloid stabilization. Langmuir. 2005;21(22):10160-10164. DOI: 10.1021/la0504614

[28] Lincopan N, Santana MR, Faquim-Mauro E, da Costa MH, Carmona-Ribeiro AM. Silica-based cationic bilayers as immunoadjuvants. BMC Biotechnology. 2009;9:5. DOI: 10.1186/1472-6750-9-5

[29] Ribeiro RT, Braga VHA, Carmona-Ribeiro AM. Biomimetic cationic nanoparticles based on silica: Optimizing bilayer deposition from lipid films. Biomimetics. 2017;2(4):20. DOI: 10.3390/biomimetics2040020

[30] Sobral CN, Soto MA, Carmona-Ribeiro AM. Characterization of DODAB/DPPC vesicles. Chemistry and
Physics of Lipids. 2008;152(1):38-45. DOI: 10.1016/j.chemphyslip.2007.12.004

[31] Carmona-Ribeiro AM. Chapter Five–The versatile diocadecyldimethylammonium bromide. In: Najjar R, editor. Application and Characterization of Surfactants. Rijeka: InTech; 2017. pp. 157-181. DOI: 10.5772/68020. Available from: https://www.intechopen.com/books/application-and-characterization-of-surfactants/the-versatile-diocadecyldimethylammonium-bromide

[32] Lima EG, Gomes LR, Carmona-Ribeiro AM. Stable indomethacin dispersions in water from drug, ethanol, cationic lipid and carboxymethyl-cellulose. Pharmaceutical Nanotechnology. 2016;4(2):126-135. DOI: 10.2174/2211738504666160304 195436. Available from: http://www.eurekaselect.com/node/140208/article

[33] Pashirova TN, Zueva IV, Petrov KA, Lukashenko SS, Nizameev IR, Kulik NV, et al. Mixed cationic liposomes for brain delivery of drugs by the intranasal route: The acetylcholinesterase reactivator 2-PAM as encapsulated drug model. Colloids and Surfaces. B, Biointerfaces. 2018;171:358-367. DOI: 10.1016/j.colsurfb.2018.07.049

[34] Carmona-Ribeiro AM. Chapter One–Cationic nanostructures for vaccines. In: Duc GHT, editor. Immune Response Activation. Rijeka: InTech; 2014. p. 3-43. DOI: 10.5772/57543. Available from: http://www.intechopen.com/books/immune-response-activation/cationic-nanostructures-for-vaccines

[35] Rozenfeld JH, Silva SR, Ranéia PA, Faquim-Mauro E, Carmona-Ribeiro AM. Stable assemblies of cationic bilayer fragments and CpG oligonucleotide with enhanced immunoadjuvant activity in vivo. Journal of Controlled Release. 2012;160(2):367-373. DOI: 10.1016/j.jconrel.2011.10.017

[36] de Oliveira Santos FA, Lincopan N, De Gaspari E. Evaluation of intranasal and subcutaneous route of immunization in neonatal mice using DODAB-BF as adjuvant with outer membrane vesicles of Neisseria meningitis B. Immunobiology. 2018;223(12):750-760. DOI: 10.1016/j.imbio.2018.07.021

[37] Gaspar EB, Rosetti AS, Lincopan N, De Gaspari E. Neisseria lactamica antigens complexed with a novel cationic adjuvant. Human Vaccines & Immunotherapeutics. 2013;9(3):572-581

[38] Mamizuka EM, Carmona-Ribeiro AM. Cationic liposomes as antimicrobial agents. In: Antonio Méndez Vilas. (Org.). Communicating Current Research and Educational Topics and Trends in Applied Microbiology. 1 ed. Badajoz: Formatex, 2007, v. 2, p. 636-647. ISBN-13: 978-84-611-9423-0. Available from: http://www.formatex.org/microbio/pdf/pages636-647.pdf

[39] Vieira DB, Carmona-Ribeiro AM. Cationic nanoparticles for delivery of amphotericin B: Preparation, characterization and activity in vitro. Journal of Nanobiotechnology. 2008;6:6. DOI: 10.1186/1477-3155-6-6

[40] Melo LD, Mamizuka EM, Carmona-Ribeiro AM. Antimicrobial particles from cationic lipid and polyelectrolytes. Langmuir. 2010;26(14):12300-12306. DOI: 10.1021/la101500s

[41] De Melo Carrasco LD, Sampaio JL, Carmona-Ribeiro AM. Supramolecular cationic assemblies against multidrug-resistant microorganisms: Activity and mechanism of action. International Journal of Molecular Sciences.
2015;16(3):6337-6352. DOI: 10.3390/ijms16036337

[42] Carrasco LD, Bertolucci R Jr, Ribeiro RT, Sampaio JL, Carmona-Ribeiro AM. Cationic nanostructures against foodborne pathogens. Frontiers in Microbiology. 2016;7:1804. DOI: 10.3389/fmicb.2016.01804

[43] Ragioto DA, Carrasco LD, Carmona-Ribeiro AM. Novel gramicidin formulations in cationic lipid as broad-spectrum microbicidal agents. International Journal of Nanomedicine. 2014;9:3183-3192. DOI: 10.2147/IJN.S65289

[44] Carmona-Ribeiro AM, de Melo Carrasco LD. Novel formulations for antimicrobial peptides. International Journal of Molecular Sciences. 2014;15(10):18040-18083. DOI: 10.3390/ijms151018040

[45] Carvalho CA, Olivares-Ortega C, Soto-Arriaza MA, Carmona-Ribeiro AM. Interaction of gramicidin with DPPC/DODAB bilayer fragments. Biochimica et Biophysica Acta. 2012;1818(12):3064-3071. DOI: 10.1016/j.bbamem.2012.08.008

[46] Gordillo-Galeano A, Mora-Huertas CE. Solid lipid nanoparticles and nanostructured lipid carriers: A review emphasizing on particle structure and drug release. European Journal of Pharmaceutics and Biopharmaceutics. 2018;133:285-308. DOI: 10.1016/j.ejpb.2018.10.017

[47] Pereira I, Zielińska A, Ferreira NR, Silva AM, Souto EB. Optimization of linalool-loaded solid lipid nanoparticles using experimental factorial design and long-term stability studies with a new centrifugal sedimentation method. International Journal of Pharmaceutics. 2018;549(1-2):261-270. DOI: 10.1016/j.ijpharm.2018.07.068

[48] Mishra V, Bansal KK, Verma A, Yadav N, Thakur S, Sudhakar K, et al. Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. Pharmaceutics. 2018;10(4). DOI: 10.3390/pharmaceutics10040191

[49] Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery—a review of the state of the art. European Journal of Pharmaceutics and Biopharmaceutics. 2000;50(1):161-177. DOI: 10.1016/S0939-6411(00)00087-4

[50] Andersson M, Hammarstroem L, Edwards K. Effect of bilayer phase transitions on vesicle structure, and its influence on the kinetics of viologen reduction. The Journal of Physical Chemistry. 1995;99(39):14531-14538. DOI: 10.1021/j100039a047

[51] Carmona-Ribeiro AM, Castuma CE, Sesso A, Schreier S. Bilayer structure and stability in dihexadecyl phosphate dispersions. The Journal of Physical Chemistry. 1991;95(13):5361-5366. DOI: 10.1021/j100166a080

[52] Zetterberg MM, Reijmar K, Pränting M, Engström Å, Andersson DI, Edwards K. PEG-stabilized lipid disks as carriers for amphiphilic antimicrobial peptides. Journal of Controlled Release. 2011;156(3):323-328. DOI: 10.1016/j.jconrel.2011.08.029

[53] Miranda C, Booth VK, Morrow MR. Effects of amphipathic polypeptides on membrane organization inferred from studies using bicellar lipid mixtures. Langmuir. 2018;34(39):11759-11771. DOI: 10.1021/acs.langmuir.8b02257

[54] Sanders CR, Prosser RS. Bicelles: A model membrane system for all seasons? Structure. 1998;6(10):1227-1234

[55] Carmona-Ribeiro AM. Lipid-based biomimetics in drug and vaccine
delivery. In: Mukherjee A, editor. Biomimetics Learning from Nature. Olajinica: InTech; 2010. pp. 507-534. DOI: 10.5772/8792. Available from: http://www.intechopen.com/books/biomimetics-learning-from-nature/lipid-based-biomimetics-in-drug-and-vaccine-delivery

[56] Carmona-Ribeiro AM, Barbassa B, Melo LD. Antimicrobial biomimetics. In: Cavrak M, editor. Biomimetic Based Applications. Olajinica: InTech; 2011. pp. 227-284. DOI: 10.5772/14400. Available from: http://www.intechopen.com/books/biomimetic-based-applications/antimicrobial-biomimetics

[57] Carmona-Ribeiro AM. Preparation and characterization of biomimetic nanoparticles for drug delivery. In: Soloviev M, editor. Nanoparticles in Biology and Medicine. Methods Mol Biol. (Methods and Protocols). Vol. 906. Totowa, NJ: Humana Press; 2012. pp. 283-294. DOI: 10.1007/978-1-61779-953-2_22

[58] Carmona-Ribeiro AM. Biomimetic particles in drug and vaccine delivery. Journal of Liposome Research. 2007;17(3-4):165-172

[59] Pereira EM, Kosaka PM, Rosa H, Vieira DB, Kawano Y, Petri DF, et al. Hybrid materials from intermolecular associations between cationic lipid and polymers. The Journal of Physical Chemistry. B. 2008;112(31):9301-9310. DOI: 10.1021/jp801297t

[60] Hadinoto K, Sundaresan A, Cheow WS. Lipid-polymer hybrid nanoparticles as a new generation therapeutic delivery platform: A review. European Journal of Pharmaceutics and Biopharmaceutics. 2013;85(3 Pt A):427-443. DOI: 10.1016/j.ejpb.2013.07.002

[61] Miao L, Guo S, Lin CM, Liu Q, Huang L. Nanoformulations for combination or cascade anticancer therapy. Advanced Drug Delivery Reviews. 2017;115:3-22. DOI: 10.1016/j.addr.2017.06.003

[62] Xu X, Xie K, Zhang XQ, Pridgen EM, Park GY, Cui DS, et al. Enhancing tumor cell response to chemotherapy through nanoparticle-mediated codelivery of siRNA and cisplatin prodrug. Proceedings of the National Academy of Sciences of the United States of America. 2013;110(46):18638-18643. DOI: 10.1073/pnas.1303958110

[63] Messerschmidt SK, Musyanovych A, Altvater M, Scheurich P, Pfizenmaier K, Landfester K, et al. Targeted lipid-coated nanoparticles: Delivery of tumor necrosis factor-functionalized particles to tumor cells. Journal of Controlled Release. 2009;137(1):69-77. DOI: 10.1016/j.jconrel.2009.03.010

[64] Carmona-Ribeiro AM. Chapter Eight–Lipid-based biomimetics: General perspectives in drug and vaccines delivery. In: Souto EB, editor. Lipid Nanocarriers in Cancer Diagnosis and Therapy. Shawbury: Smithers; 2011. pp. 189-226

[65] Petri DFS, Carmona-Ribeiro AM. Biomimetic particles. In: Nalwa HS, editor. Polymeric Nanostructures and Their Applications. Los Angeles: American Scientific Publishers; 2007. pp. 485-530

[66] Carmona-Ribeiro AM. Biomimetic systems in nanomedicine. In: Torchilin V, editor. Handbook of Nanobiomedical Research. 1st ed. Vol. 4. Singapore: World Scientific; 2014. pp. 401-456. DOI: 10.1142/9789814520652_0063

[67] Bassegoda A, Ivanova K, Ramon E, Tzanov T. Strategies to prevent the occurrence of resistance against antibiotics by using advanced materials. Applied Microbiology and Biotechnology. 2018;102(5):2075-2089. DOI: 10.1007/s00253-018-8776-0
[68] Pacheco LF, Carmona-Ribeiro AM. Effects of synthetic lipids on solubilization and colloid stability of hydrophobic drugs. Journal of Colloid and Interface Science. 2003;258(1):146-154. DOI: 10.1016/S0021-9797(02)00103-0

[69] Vieira DB, Pacheco LF, Carmona-Ribeiro AM. Assembly of a model hydrophobic drug into cationic bilayer fragments. Journal of Colloid and Interface Science. 2006;293(1):240-247. DOI: 10.1016/j.jcis.2005.06.046

[70] Lincopan N, Carmona-Ribeiro AM. Lipid-covered drug particles: Combined action of dioctadecyldimethylammonium bromide and amphotericin B or miconazole. The Journal of Antimicrobial Chemotherapy. 2006;58(1):66-75. DOI: 10.1093/jac/dkl153

[71] Barbassa L, Mamizuka EM, Carmona-Ribeiro AM. Supramolecular assemblies of rifampicin and cationic bilayers: Preparation, characterization and micobactericidal activity. BMC Biotechnology. 2011;11:40. DOI: 10.1186/1472-6750-11-40

[72] Carrasco LDM, Santos HCAS, Sampaio JLM, Carmona-Ribeiro AM. Self-assembled antibiotic nanoparticles against intracellular bacteria. Drug Delivery Letters. 2017;7:39. DOI: 10.2174/2210303107666170203163102

[73] Nantes IL, Correa FM, Faljoni-Alario A, Kawanami AE, Ishiki HM, Amaral AT, et al. Nucleotide conformational change induced by cationic bilayers. Archives of Biochemistry and Biophysics. 2003;416(1):25-30. DOI: 10.1016/S0003-9861(03)00280-7

[74] Rozenfeld JH, Oliveira TR, Lamy MT, Carmona-Ribeiro AM. Interaction of cationic bilayer fragments with a model oligonucleotide. Biochimica et Biophysica Acta. 2011;1808(3):649-655. DOI: 10.1016/j.bbamem.2010.11.036

[75] Carvalho LA, Carmona-Ribeiro AM. Interactions between cationic vesicles and serum proteins. Langmuir. 1998;14(21):6077-6081. DOI: 10.1021/la980345j

[76] Tsuruta LR, Quintilio W, Costa MH, Carmona-Ribeiro AM. Interactions between cationic liposomes and an antigenic protein: The physical chemistry of the immunoadjuvant action. Journal of Lipid Research. 1997;38(10):2003-2011. Available from: http://www.jlr.org/content/38/10/2003.long

[77] Sicchierolli SM, Carmona-Ribeiro AM. Biomolecular recognition at phospholipid-covered polystyrene microspheres. The Journal of Physical Chemistry. 1996;100(41):16771-16775. DOI: 10.1021/jp961785r

[78] Lincopan N, Carmona-Ribeiro AM. Protein assembly onto cationic supported bilayers. Journal of Nanoscience and Nanotechnology. 2009;9(6):3578-3586

[79] Carmona-Ribeiro AM, de Melo Carrasco LD. Cationic antimicrobial polymers and their assemblies. International Journal of Molecular Sciences. 2013;14(5):9906-9946. DOI: 10.3390/ijms14059906

[80] Galvão CN, Sanches LM, Mathiazzzi BI, Ribeiro RT, Petri DFS, Carmona-Ribeiro AM. Antimicrobial coatings from hybrid nanoparticles of biocompatible and antimicrobial polymers. International Journal of Molecular Sciences. 2018;19(10):E2965. DOI: 10.3390/ijms19102965

[81] Melo LD, Palombo RR, Petri DF, Bruns M, Pereira EM, Carmona-Ribeiro AM. Structure-activity relationship for quaternary ammonium compounds hybridized with poly (methyl methacrylate). ACS Applied Materials & Interfaces. 2011;3(6):1933-1939. DOI: 10.1021/am200150t
[82] Naves AF, Palombo RR, Carrasco LD, Carmona-Ribeiro AM. Antimicrobial particles from emulsion polymerization of methyl methacrylate in the presence of quaternary ammonium surfactants. Langmuir. 2013;29(31):9677-9684. DOI: 10.1021/la401527j

[83] Sanches LM, Petri DF, de Melo Carrasco LD, Carmona-Ribeiro AM. The antimicrobial activity of free and immobilized poly (diallyl dimethyl ammonium) chloride in nanoparticles of poly (methyl methacrylate). Journal of Nanobiotechnology. 2015;13:58. DOI: 10.1186/s12951-015-0123-3

[84] Campanhã MTN, Mamizuka EM, Carmona-Ribeiro AM. Interactions between cationic vesicles and Candida albicans. The Journal of Physical Chemistry. B. 2001;105(34):8230-8236. DOI: 10.1021/jp003315+

[85] Vieira DB, Carmona-Ribeiro AM. Cationic lipids and surfactants as antifungal agents: Mode of action. The Journal of Antimicrobial Chemotherapy. 2006;58(4):760-767. DOI: 10.1093/jac/dkl312

[86] Carmona-Ribeiro AM, Carrasco LDM. Fungicidal assemblies and their mode of action. OA Biotechnology. 2013;2(3):25. DOI: 10.13172/-2-3-983

[87] Pacheco LF, Vieira DB, Correia FM, Carmona-Ribeiro AM. Interaction between cationic bilayers and Candida albicans cells. In: Surface and Colloid Science. Progress in Colloid and Polymer Science. Vol. 128. Berlin and Heidelberg: Springer; 2004. pp. 175-177. DOI: 10.1007/b97059

[88] Fait ME, Bakas L, Garrote GL, Morcelle SR, Saparrat MCN. Cationic surfactants as antifungal agents. Applied Microbiology and Biotechnology. 2019;103(1):97-112. DOI: 10.1007/s00253-018-9467-6

[89] Manolova V, Flace A, Bauer M, Schwarz K, Saudan P, Bachmann MF. Nanoparticles target distinct dendritic cell populations according to their size. European Journal of Immunology. 2008;38(5):1404-1413. DOI: 10.1002/eji.200737984

[90] Blank F, Fytianos K, Seydoux E, Rodriguez-Lorenzo L, Petri-Fink A, von Garnier C, et al. Interaction of biomedical nanoparticles with the pulmonary immune system. Journal of Nanobiotechnology. 2017;15(1):6. DOI: 10.1186/s12951-016-0242-5

[91] Seydoux E, Rodriguez-Lorenzo L, Blom RA, Stumbles PA, Petri-Fink A, Rothen-Rutishauser BM, et al. Pulmonary delivery of cationic gold nanoparticles boost antigen-specific CD4(+) T cell proliferation. Nanomedicine. 2016;12(7):1815-1826. DOI: 10.1016/j.nano.2016.02.020

[92] Tsuruta LR, Lessa MM, Carmona-Ribeiro AM. Effect of particle size on colloid stability of bilayer-covered polystyrene microspheres. Journal of Colloid and Interface Science. 1995;175(2):470-475. DOI: 10.1006/jcis.1995.1477