Encapsulation methods of active molecules for drug delivery

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OUTLINE

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Abstract

Recent years have witnessed the emergence of nanotechnology in the medicinal field in order to improve existing treatments and develop novel and efficient therapies. Nanostructured systems have attracted unprecedented interest in drug delivery due to their ability to overcome difficulties linked to conventional drug delivery systems. Nanocarriers increase drug solubility and permeability, improve bioavailability, reduce side effects and enhance the therapeutic efficiency, whilst providing a preferential accumulation of active molecules at specific tissue sites or cells. The present chapter highlights the different elaboration processes leading to the development of two main groups of organic nanocarriers; lipid based-nanocarriers (including liposomes and solid lipid nanoparticles) and polymer based-nanocarriers (including polymeric nanoparticles). These carriers are used to encapsulate and to deliver active molecules or in some cases, for in vitro diagnosis and more recently in theranostics applications.

Keywords: nanocarriers, polymeric nanoparticle, liposome, solid lipid nanoparticle, drug delivery.

1. Introduction

Over the past few decades, enormous efforts have been devoted to developing nanotechnology as a novel platform to bypass most common hurdles encountered in traditional drug delivery such as poor stability, low bioavailability, poor solubility and the bitter taste of active agents [1]. Nanotechnology, a buzzword of this era, has transformed the face of research in numerous sectors, such as textiles [2], electronic engineering [3], agriculture [4], food [5] and pharmaceutical/biomedical fields [6], [7]. The application of nanotechnology for diagnosis, treatment, monitoring, and control of biological systems promotes the concept of nanomedicine, an extensively studied field, in which many colloidal drug carriers have been designed, in particular, nanoparticles [6], [8], [9]. Nanoparticles (NPs) are nano-sized structures dedicated to: i) carry the pharmaceutical agent to a specific tissue, ii) protect the drug from premature degradation, iii) lower the required dose for effective therapy, iv) minimize side effects and thereby v) increase the safety profile and therapeutic index of drugs [10]. Moreover, NPs are employed as an approach to increase the bioavailability of pharmaceutical ingredients by improving the cellular uptake, especially in cancer treatment. For instance, doxorubicin, a well-known anticancer drug, suffers from its poor

pharmacokinetics behavior including poor bioavailability after oral administration. Khdair et al. displayed that encapsulating doxorubicin in chitosan-based-NPs enhances its uptake by MCF-7 and Caco-II tumor cell lines [11]. Regarding the cutaneous administration, NPs enhances the skin penetration of drugs. A recent study revealed that the encapsulation of psoralen, widely used for psoriasis treatment, in liposomal carriers, increases the skin permeation by 5 fold and reduced the cytokine levels of psoriasis [12]. Other drugs like docetaxel suffer from their low aqueous solubility which hinders their clinical uses. The nanoencapsulation could also hinder the low aqueous solubility. Qureshi et al. demonstrated that the incorporation of docetaxel in lipid nanocarriers leads to a 686 times increase in water solubility [13].

Depending on the preparation methods, nanocarriers can be broadly divided into two main categories: polymer-based nanocarriers and lipid-based nanocarriers [10]. Amongst the several nanoparticulate systems investigated in drug delivery, polymeric nanoparticles (pNPs), liposomes and solid lipid nanoparticles (SLNs) have received much attention [14]–[19]. In this context, this chapter highlights the recent development of nanocarrier systems for drug delivery with a focus on the principal properties and preparation methods of the main polymer based-nanocarriers (polymeric nanoparticles) and lipid based-nanocarriers (such as liposomes and solid lipid nanoparticles). Furthermore, the current status of their therapeutic applications is also presented and shortly discussed.

2. Polymer-based nanoparticles

During the last decades, polymeric nanoparticles have drawn tremendous attention owing to their peculiar characteristics and behaviours arising from their small size [20]. As demonstrated by different authors, these nanoparticulate systems show prospects for a wide range of applications due to their substantial benefits including upraised drug stability against photo- or chemical degradation, controlled drug release, increased drug-tissue interaction and consequently decreased adverse effects and improved therapeutic index [14], [21]–[23]. Polymer-based nanoparticles are spherical in shape with a size range ranging from 10 to 1000 nm. They can exist in two different forms, a polymeric layer surrounding a hollow core (nanocapsules), or a polymeric matrix extended from the core to the surface (nanospheres). The localization of the active molecule within these two forms depends on its chemical structure. In some cases, the drug can also be adsorbed or grafted onto the surface of the

particles [14], [24], [25]. Based on the origin of the polymer intended for NPs formulation, two types are used: natural and synthetic polymers. Their main features are their biodegradability and biocompatibility [26]. The most widely explored natural polymers are chitosan, alginate and proteins such as albumin [27]. Amongst the various synthetic polymers, polylactide–polyglycolide, polylactide, polycaprolactones, and polyacrylates have been extensively used [28]. For the preparation of polymer-based particles, various methods have been developed. The choice of the appropriate method depends on many factors such as solubility of the drug in water and organic solvents, physicochemical properties of the polymer and the target carrier specifications (i.e., size, size distribution, surface charge nature, surface porosity, etc...) [20], [29]. The most commonly reported processes used for polymer particles formulations are shown in Figure 1.

Figure 1. Schematic illustration of nanoprecipitation, simple emulsion evaporation, and double emulsion evaporation processes.

2.1. Nanoprecipitation method

Nanoprecipitation is a one-step process allowing the instantaneous and reproducible generation of narrow distribution of submicron particles[1]. It was first reported by Fessi et al. [30]. In this process, an organic solution containing a non-water-soluble polymer (solvent phase) is mixed with water (non-solvent phase). It is interesting to notice that both phases are miscible, and the mixture of the two phases becomes a bad solvent of the selected polymer leading to its precipitation via an instantaneous solvent diffusion mechanism [31]. For nanocapsules preparation, the same process is used except for adding oil to the organic phase in order to form an inner oily core [32]. The benefits of the nanoprecipitation technique include facility, rapidity, reproducibility, and scalability [33], [34]. Moreover, in this technique, the use of a stabilizer, in the case of charged polymer, or high production energy is avoided [35]. The main drawback of this method is low loading efficiency for hydrophilic drugs due to the hydrophobicity of a nanoparticle matrix [31]. Nonetheless, several strategies have been asserted to enhance the loading of these molecules [36].

2.2. Simple emulsion evaporation method

A simple emulsification evaporation method has been developed by Vanderhoff et al. to design polymeric nanoparticles [37]. In this process, the polymer and the drug are first dissolved in a volatile water-immiscible organic solvent. Ethyl acetate, owing to its better toxicological profile, has been widely used as a solvent instead of chloroform and dichloromethane [38]. The organic polymer solution is emulsified with an aqueous phase containing a suitable stabilizer under high shear stress (e.g. by homogenization or ultrasonication) [31]. The organic solvent is then evaporated by continuous stirring at room temperature or under reduced pressure leading to polymer precipitation and nanoparticle formation. The benefits of using this encapsulation method are high encapsulation efficiency of hydrophobic drugs, easy to process and good reproducibility. However, some disadvantages are related to this process; in particular, the poor encapsulation efficiency of hydrophilic drugs, the possible coalescence of droplets during evaporation which may lead to polydisperse polymer particles and the need for a high shear process in order to obtain submicron size with a narrow size distribution [1], [20].

2.3. Double emulsion evaporation method

The double emulsification evaporation method has been proposed as an alternative to nanoprecipitation and simple emulsification evaporation methods in term of encapsulation of hydrophilic drugs [39]. For instance, this technique, consisting of two-step emulsification, can encapsulate both hydrophobic and hydrophilic drugs because of the presence of several water and oil layers [40]. In the first step, the water-in-oil emulsion is formed after the homogenization of an aqueous phase (W1) containing the hydrophilic drug with an oily phase (O) that is generally a polymer solution dissolved in an organic solvent containing the necessary hydrophobic drug. The second step is the emulsification of the first W1/O emulsion in another aqueous phase (W2) containing an appropriate stabilizer, under high shear homogenization or low power sonication to form a double emulsion (W1/O/W2). Although this method can encapsulate both hydrophilic and hydrophobic drugs, it presents several drawbacks such as: low colloidal stability of the resulting particles, high shear stirring that may induce emulsion fragmentation, foam formation, and above-micron size polydisperse particles [1].

2.4. Ionic gelation

The ionic gelation method has been developed by Calvo et al. as a novel approach that avoids harmful organic solvents or high shear forces [41]. Among the different natural polysaccharides such as chitosan, some polyelectrolytes and alginates are widely used in the ionic gelation based process. These polyelectrolytes can be crosslinked by electrostatic interaction with an added oppositely charged molecules or macromolecules that can ultimately lead to ionic gelation and therefore to polysaccharide particles formation [42]. The ionic gelation consists of the transition from a liquid to gel state upon complexation between the positively charged amino group of chitosan and the negatively charged tripolyphosphate compound widely used as a polyanion crosslinker leading generally to submicron particles [43]–[45]. The main benefits of this method are in particular the use of aqueous solvents instead of organic solvents. Moreover, ionic gelation is simple, reproducible and a scalable process [46], [47].

2.5. Supercritical fluid method

All the above methods often involve the use of toxic solvents and / or surfactants that are dangerous to the environment as well as to physiological systems [48]. Consequently, current research has been directed to explore safer techniques to develop carriers of

Supercritical fluids have fascinated the interest of many researchers as they are environmentally friendly solvents [49]. Supercritical CO₂ is the most frequently used supercritical fluid due to its low price, abundance, non-flammability and non-toxicity. In the supercritical antisolvent process, the drug and the polymer are dissolved in a liquid solvent such as methanol that is totally miscible with the supercritical fluid. A supercritical antisolvent, A supercritical antisolvent is then added to the solution in a closed chamber, at ambient pressure. The insolubility of the solute in the fluid results in the instant precipitation of the solute, leading to particles formation [15]. Despite the advantage of using environmentally safe materials, some drawbacks are linked to this method since it requires special equipment and is very expensive to be developed as a routine technique [50].

3. Liposomes

Liposomes were first described by Alec Bangham in 1961 [51], [52]. Liposomes are vesicles which are made of one or more lipid bilayers. They can be classified into 3 categories: small unilamellar vesicles (SUV), large unilamellar vesicles (LUV) and multilamellar vesicles (MLV). Liposomes can also be classified according to their surface charge. In fact, they can be non-charged (zwitterionic), cationic or anionic.

The interest of liposomes is related to their ability to contain hydrophilic molecules in their aqueous phase and lipophilic molecules in their lipid bilayers as illustrated in Figure 2 [53]. Furthermore, liposomes bear a good cell affinity and biodegradability. Lipid bilayers are constructed of phosphatidylcholine and cholesterol. The latter ensures the physical stability of the bilayers.

Figure 2. Liposomes containing hydrophilic and hydrophobic active drug.

3.1.Hydration of a Thin Lipid Film

Thin lipid film hydration is the first process used for liposomes preparation. This method consists of the dissolution of lipid ingredients in an organic solvent such as; ethanol, methanol or chloroform in a round-bottom flask [54]. Subsequent evaporation of the obtained phospholipids solution allows the formation of a lipid film. Its hydration by water or a buffer solution enables the formation of liposomes dispersion (see Figure 3). Sonication, homogenization or extrusion may also be performed to ensure size reduction and particles uniformity [55].

Figure 3. Hydration of a thin lipid film (example of a hydrophobic drug incorporated in cyclodextrins).

3.2.Detergent Dialysis

Detergents at their critical micelle concentrations (detergent concentration above which micelles begin to form) can be used to solubilize lipids (see Figure 4). In the detergent dialysis method, phospholipids are solubilized by detergent micelles in an aqueous phase. After detergent removal by dialysis, phospholipid-rich micelles coalescence is obtained, and liposomes are formed. Advantages of this technique include good reproducibility and size uniformity. However, residual detergent retention represents the main drawback [55]. Dialysis can be performed with a commercial device called LipoPrep (Diachema AG, Switzerland) can also be obtained in dialysis bags engrossed in large detergent free buffers [56]. There are

other ways to using dialysis to remove detergent molecules such as chromatographic methods.

Figure 4. Detergent dialysis method.

3.3.Solvent Injection Technique

In the solvent injection technique, phospholipids are dissolved in an organic solvent such as ethanol or ether, then, this solution is slowly injected into an aqueous buffer solution. SUV dispersion is then obtained. Self-assembly of lipids in the aqueous phase to form liposomes occurs following either ethanol dilution in water or ether evaporation (See Figure 5) [57].

The ethanol injection method was first described in 1973 [58]. The main advantage of this method is that narrow size distribution of submicron liposomes (generally under 100 nm) could be obtained without extrusion or sonication [59].

The ether injection method differs from the ethanol injection method since the ether is immiscible with the aqueous phase. The relevance of this method compared to the ethanol injection solvent removal from the product which allows the process to run for an extended period. A more prolonged process was shown to form concentrated liposomes suspension with high loading efficiency [59].

Figure 5. Solvent injection technique.

3.4.Reverse-Phase Evaporation Technique

The reverse phase evaporation method enables the preparation of liposomes with high aqueous space-to-lipid ratio. This allows a large percentage of aqueous material to be loaded. The technique is based on the creation of inverted micelles [56]. The latter are formed when phospholipids solution in an organic phase is hydrated by the addition of water with vigorous mixing. This results in the formation of a water-in-oil emulsion. Subsequent evaporation of the organic phase results in the micelles transformation into a gel-like dispersion (Figure 6). At some point, the gel state collapses and the excess of phospholipids in the environment leads to an aqueous liposomes suspension containing both LUV and MLV [60].

Figure 6. Reverse phase evaporation technique

3.5. Membrane contactor technology:

Membrane contactors are used to mix two materials [61]. This property is used to enable the mixing of the lipid and the water phase to obtain liposomes (see Figure 7). Jaafar-Maalej et al. used a membrane contactor where phospholipid solution in ethanol was extruded into an aqueous phase [62]. The obtained liposomes were prepared by a modified ethanol injection method. In this study, a tubular Shirazu porous glass (SPG) membrane with a mean pore size of 900 nm was used. Laouini et al., 2011, used polypropylene hollow fibers which allowed access to larger membrane areas and uniform flows thus, improving efficiency [63]. Thi Thuy Pham et al. reported the use of membrane contactor technology to produce liposomes on an industrial scale. Their product could be obtained in a very reproducible manner [64]. Advantages of the membrane contactor technique include greater control of liposome size, high encapsulation efficiency, continuous operation and scale-up of the process [55].

Figure 7. Membrane contactor technique

4. Solid lipid nanoparticles

Solid lipid nanoparticles (SLNs) are other lipid-based carriers that have emerged as a less toxic, more biocompatible alternative for polymeric based nanoparticles. Moreover, it has been claimed that SLNs actually unite the benefits of lipid emulsion systems, liposomes, and

polymeric nanoparticles, while sweeping away temporal and in vivo stability [65]. The general chemical composition of these particles are surfactants and sometimes co-surfactants and a lipid matrix that acquires a solid-state at physiological temperature. The lipid matrix of SLNs should be composed of lipids that have good biocompatibility and a melting point above body temperature. With these characteristics, the commonly used materials to structure the lipid core are fatty acids, fatty alcohols, waxes, and triglycerides. In fact, the crystal structure of the lipid core is critical for the feasibility of SLN systems since it may affect controlled drug release and colloidal stability of the dispersion. The formation of a solid core is determined by components ratio and the choice of the preparation method [66].

Different preparation methods were used in the literature to prepare SLNs such as high-pressure homogenization, microemulsion, solvent emulsification evaporation, and solvent emulsification diffusion [67]. These techniques are differentiated by the complexity of their execution and the characteristic of their final product [68].

4.1.High-pressure homogenization

High-pressure homogenization (HPH) is widely used in the pharmaceutical industry since it is easy to scale-up and produce high-quality products with small particle size and higher homogeneity. HPH uses a sophisticated device (high-pressure homogenizer) that is able to push liquids through a narrow gap (micron size) with high pressure (from 100 to 2000 bar) creating an acceleration over a very short distance [69].

In brief, the lipid is heated at 5 to 10°C above its melting point, and the drug is dissolved within. After that, two different approaches can be undertaken One approach is hot homogenization, in which the drug-lipid melt is dispersed in a hot aqueous surfactant solution under stirring at the same temperature creating the pre-emulsion. Then, a hot oil-in-water (O/W) nanoemulsion is formed by homogenization using a piston-gap homogenizer. This nanoemulsion is then cooled to room temperature allowing the formation of lipid crystals creating SLNs [70].

Another approach is cold homogenization that is started with cooling down the drug-lipid melt allowing the formation of solid lipid microparticles (between 50 and 100 nm) that are then dispersed in a cold surfactant solution shaping a pre-suspension. This pre-suspension is on its turn and is strongly homogenized, breaking down the microparticles and forming SLNs. The cold HPH approach is used in the case of thermosensitive drugs where at cold conditions,

lipid melting is minimized and therefore prevents the diffusion of hydrophilic drugs into the water phase [71].

4.2. Microemulsion

This method was first developed by Gasco [72]. It is based on the precipitation of lipid particles by diluting the system with water. Briefly, a microemulsion is formed by adding a mixture of water, surfactant, and co-surfactant to the lipid melt. Taking into account that the water mixtures should be heated to the same temperature as the lipid and added under mild stirring. The formed microemulsions are then diluted in a cold aqueous phase which causes their precipitation into SLNs.

Different types of surfactants and co-surfactants were used in this method such as lecithin, biliary salts, and alcohols. In addition, it is important that during the precipitation step, mixing should be done by mild mechanical agitation to guarantee that the small size of the obtained SLNs is due to precipitation and not agitation. This method has the advantages of being a solvent-free process with gentle preparation conditions. Making it suitable for the encapsulation of various therapeutic peptides and active molecules [69].

4.3. Emulsion methods

Emulsion-diffusion (ED) requires the use of three different liquid phases. The organic phase in which the lipids and the lipophilic drug are dissolved (solvent) and generally miscible with the aqueous phase. An aqueous phase containing a stabilizing agent (non-solvent) and a dilution phase that usually involves a large amount of water. Solvent and non-solvent phases are mutually saturated. The organic phase is emulsified in the water phase under high shear stirring. After that, the water dilution phase is subsequently added allowing the diffusion of the organic solvent to the outer water resulting in the precipitation of lipids and the formation of SLNs. The obtained SLNs by this method are diluted, therefore, a concentration step is followed by ultra-filtration or freeze-drying. The advantage of this technique is the avoidance of temperature use which reflects better stability of the system in general and the drug encapsulated in particular [73], [74].

Emulsion-evaporation (EE) is differentiated from ED by the fact that the non-solvent used should be immiscible with the solvent. In addition, it is critical that the evaporation temperature of the solvent is lower than the non-solvent. After the formation of a simple emulsion, the organic solvent is evaporated leading to the precipitation of the lipids in the

non-solvent phase and formation of nanoparticles that are stabilized instantaneously by surfactants. This leads to the formation of O/W nanoemulsion and in some cases, a double emulsion can be done leading to the formation of W/O formulations. A major drawback of EE is the use of a water-immiscible solvent that can be harmful for human administration [69], [75]. Figure 8 shows the different preparation techniques of solid lipid nanoparticles.

Figure 8. Preparation methods of solid lipid nanoparticles

5. Therapeutic applications:

Numerous active molecules have been encapsulated in nanomaterials to obtain various therapeutic applications. This has led to the emergence of nanomedicine, which is the field that combines nanotechnology with pharmaceutical and biomedical sciences. For instance, polymeric nanoparticles represent the simplest form of soft materials used for nanomedicine applications. This is due to their easy synthesis and wide biomedical applications. In fact, two of the top 10 best-selling drugs in the US in 2013 were polymeric drugs (Copaxone® and Neulasta®), [76], [77]. Liposomes also represent another feature of nanomedicine. Until today, around 20 liposomal products have been approved by regulatory agencies, especially for cancer management. Other therapeutic indications of liposome-based products include antifungal and antibacterial drugs, analgesics, vaccines, and photodynamically active agents [78]. In addition, lipid-based carriers have been evidenced to be attractive candidates for active encapsulation. In fact, lipid materials could circumvent barriers associated with the oral administration of poorly soluble drugs or drugs with intestinal permeability issues. Such properties could be conferred by solid lipid nanoparticles or nanostructured lipid carrier [79]. The following Table 1 shows some examples of nanomedicine-based formulations.

Table 1. Examples of therapeutic indications of liposome-based formulations

Method	Materials	Encapsulated molecule	Size	Zeta	Application	Reference
<i>Polymer-based nanoparticles</i>						
Nanoprecipitation	Eudragit S100 and Hydroxypropylmethylcellulose phthalate	Pantoprazole	299 to 639 nm	-	Acid-related disorders and Helicobacter biliary infections	[80]
Nanoprecipitation	Poly-(D, L-lactic-co-glycolic acid)	Itraconazole	176 nm	-24 mV	Fungal infections	[81]
Nanoprecipitation	Poly-(D, L-lactic-co-glycolic acid)	Cisplatin	126 nm	-12 mV	Ovarian cancer	[82]
Simple emulsion	Poly-(D, L-lactic-co-glycolic acid) and Gly-L-Phe-DThr-Gly-L-Phe-L-	Curcumin	200-250 nm	-22 mV	Alzheimer's disease	[83]

	Leu-LSer(O-b-D-Glucose)-CONH ₂ (g7)					
Simple emulsion	Poly-(D, L-lactic-co-glycolic acid) and carboxymethyl-poly(ethylene glycol)-b-poly(lactic acid)	Irinotecan derivative (SN-38)	269-276 nm	-20-(-26) mV	Cancer	[84]
Double emulsion	Poly-(D, L-lactic-co-glycolic acid)-PEG	Gemcitabine and betulinic acid	195 nm	-4 mV	Cancer	[85]
Double emulsion	Poly-(D, L-lactic-co-glycolic acid)	Doxorubicin	199 nm	-38 mV	Cancer	[86]
Double emulsion	Poly-(D, L-lactic-co-glycolic acid)	Frovatriptan Succinate	264 nm	-35 mV	Migraine	[87]
Ionic gelation	<i>N</i> -succinyl-chitosan and <i>N</i> -glutaryl-chitosan	Paclitaxel and docetaxel	300-350 nm	25-31 mV	Cancer	[88]
Ionic gelation	Chitosan	Letrozole	20-80 nm	-	Breast cancer	[89]
Ionic gelation	Chitosan	Carvedilol	102 nm	32 mV	Hypertension	[90]
Supercritical fluid method	Chitosan	Doxorubicin hydrochloride	120-250 nm	50 mV	Cancer	[91]
<i>Liposomes</i>						
Thin film hydration	Phosphatidylcholine, cholesterol, Dicetylphosphate	5-FU	108 to 234 nm	-2.3 to -16.3 mV	Colorectal cancer	[92]
Thin film hydration	Pure phosphatidylcholine enriched phospholipids, cholesterol	Celecoxib	95 nm	- 42,8 mV	Inflammatory diseases	[93]
Modified thin-film hydration	Soybean phosphatidylcholine, cholesterol	Brinzolamide	96 nm	-1 mV	Glaucoma	[94]
Modified lipid hydration and extrusion	dipalmitoyl-glycero-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] and dipalmitoyl-glycero-phospho-(rac-glycerol)	Bevacizumab	100 - 200 nm	-	Ocular angiogenesis	[95]
Thin film hydration	Dipalmitoylphosphatidylcholine, distearoylphosphatidylethanolamine And Cholesterol	5-FU	174 nm	-	Cancer	[96]
Thin film hydration	Soybean phosphatidylcholine and cholesterol	Timolol maleate	129-437 nm	7-19 mV	Glaucoma	[97]
Thin film hydration	Hydrogenated soy phosphatidylcholine and cholesterol	Doxorubicin and Lovastatin	147 nm	-	Liver cancer	[98]
Thin film hydration	Di-(octadecenoyl)-glycero-phosphoethanolamine , dioleoyl-glycerotrimethylammonium propane (DOTAP), and	Si-RNA	206 – 360 nm	30 – 60 mV	Ocular keratitis	[99]

	distearoyl-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]					
Lipid film hydration	Distearoyl-glycero-phosphocholine	5-Fluorouracil and apigenin	105 nm	-3 mV	Colorectal cancer	[100]
Lipid film hydration	Dipalmitoyl-glycero-phosphocholine, distearoyl-glycero-phosphoethanolamine-[methoxy(polyethylene glycol)-2000], distearoyl-glycero-phosphoethanolamine-N-[maleimide(polyethylene glycol)-2000], and cholesterol	Gemcitabine and paclitaxel	168 nm	-	Pancreatic cancer	[101]
<i>Solid lipid nanoparticles</i>						
High pressure homogenization	Lipid 71 Compritol 88 ATO	Ezetimibe	156 nm	-20 mV	Hyperlipidemia	[102]
High pressure homogenization	Imwitor® 900K, Tagat® S and Sodium deoxycholate	Risperidone	114-195 nm	-	psychological disorders	[103]

Conclusion

Nanomedicine offers an enormous outlook for upgrading current therapies and emerging new treatment tools for illness previously assumed difficult or impossible to treat. Nanostructured systems have shown exciting benefits due to their size and shape since they can reach areas which are inaccessible using other conventional drug delivery systems protect the drug molecules from premature degradation, sudden clearance, and toxic manifestations. Nanostructured systems can also deliver the drug to a specific tissue site or cell leading to increased drug amounts at a local site hence enhancing the therapeutic profile. In this chapter, we spotlight recent advances of both lipid and polymer based-nanocarriers such as liposomes, solid lipid nanoparticles and polymeric nanoparticles in the emergence of new concepts for the efficient transport of drug molecules. The first section of this review has provided information about the properties and recent developments in the synthesis of these nanosystems. Several methods have been explored for nanocarrier preparation, nonetheless, the choice of the appropriate approach is a crucial key to gain specific requirements. Additionally, this paper has reviewed current applications of these carriers. The discussed nanostructured systems provide interesting perspectives for applications in several fields such as drug and gene delivery, biomedical imaging, diagnosis, and theranostics. The specific functionalization of the carrier surface can enhance its biodistribution to target cells and limit its delivery into healthy ones. Consequently, engineering nanocarriers with specific surface

receptors can be considered to be the turning point leading, in the future to a potent use of these systems in large-scale therapeutic applications.

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