ERURJ 2025, 4,4, 3238-3269

(Review Article)

Targeting Prostate Cancer with Lipid Nanoparticles: A Comprehensive Review of Current Advances and Future Prospects

Mohamed A. Ali [1*], Toka Tharwat [2], Tassneim M. Ewedah [1]

[1]*Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Egyptian Russian University, Cairo, Egypt.*

[2]*Department of Pharmaceutical Organic Chemistry, Faculty of Pharmacy, Cairo University, Cairo, Egypt.*

*Corresponding author: Mohamed A. Ali, E-mail: mohamd-ali@eru.edu.eg,

Tel: +201008566449

Received 13th May 2025, Revised 20th July 2025, Accepted 27th July 2025

DOI:10.21608/erurj.2025.384731.1280

ABSTRACT

A key characteristic of prostate cancer (PCa) is the age-correlated rise in 5α-reductase conversion of testosterone to highly active DiHydroTestosterone (DHT). DHT stimulates the uncontrolled growth of prostate gland cells by binding to androgenic receptors. For its management, a variety of treatment approaches have been devised, from surgical treatments to herbal remedies, including chemotherapeutic drugs, which are thought to be the most prevalent form of management. Chemotherapeutic agent administration has demonstrated a number of limitations, chief among them being tissue resistance and non-selectivity, which can be addressed by incorporating the agents into a variety of nanocarriers. Nanotechnology, a fast evolving field, has demonstrated great potential for the creation of innovative medications and diagnostic instruments for a variety of diseases, including cancer. Lipid-based nanoparticles (LNPs), one of the most popular nano-transporters, have several benefits due to their controlled drug release patterns, low toxicity, and excellent compatibility with biological systems. Many

medications that are included into LNPs can have their safety, stability, and solubility significantly enhanced. Recent research has used lipid nano-capsules, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLC), and other LNPs. The most popular treatment choices for PCa are discussed in this narrative overview, along with the many lipid nanoparticles and how they were developed. There is also literature-based support for PCa management medications that were successfully incorporated into lipid nanoparticles.

Keywords: Prostate carcinoma, Lipid nanoparticles, Solid lipid nanoparticles, Nanostructured lipid carriers.

1. Introduction

Under the effect of the underlying mesenchyme, the prostate gland matures from epithelial invaginations from the posterior urogenital sinus during the third month of pregnancy. 5α-dihydrotestosterone, which is made from fetal testosterone by 5α-reductase, is essential for the prostate gland to form normally. The human prostate's composition is essentially unchanged during the prepubertal stage, but once puberty sets in, it starts to change morphologically to take on the characteristics of an adult. The gland grows steadily until it reaches its adult weight of about 20 g by the time it is 25–30 years old. The base of the prostate is at the bladder neck and the apex at the urogenital diaphragm (1). McNeal established the current and most widely accepted concept of various zones rather than lobes of the prostate (2).

Globally, prostate cancer (PCa) is ranked as the second most common kind of carcinoma and the fifth leading cause of cancer-related mortality in men. More than 50% of men who are 50 years of age or older have clinical and/or histological indications of benign prostatic hypertrophy (BPH) (3). The prevalence of PCa varies greatly around the globe, with the USA and Europe having higher incidences than South and East Asia. There are an estimated 119.9 patients per 100,000 in the USA and 1.6 patients per 100,000 in China, respectively, according to estimates of frequency rates. Metastases were discovered in almost 20% of the 191,000 PCa cases that were identified in the USA in 2020 alone. The primary feature of both PCa and BPH is the unchecked growth of carcinogenic cells in the prostatic tissue, which is influenced by testosterone and 5α-dihydrotestosterone (DHT) on androgenic receptors (4).

Numerous treatment options are available based on the disease stage, including phyto-medicines, chemotherapy, and surgery. Phytoremedies can be used to treat mild to moderate cases of PCa, but chemotherapeutics may be required for more severe cases. The two main problems that individuals undergoing chemotherapy encounter are high toxicity and significant side effects (5). As a result, the difficulty lies in delivering anticancer to the targeted area at a therapeutically suitable dosage while avoiding serious adverse effects (6).

Advanced diagnostic methods and therapies for numerous illnesses, including cancer, have been successfully developed by nano-science (7,8). In addition to having controlled drug release properties, enhanced cellular absorption, and a notable ability to suppress tumor cell proliferation, nano-transporters are effective drug delivery vehicles with sizes ranging from 0.01 to 1 micron (8). Due to their low toxicity, outstanding compatibility with biological systems, and regulated drug release patterns, lipid-based nanoparticles are among the most widely used nano-transporters and offer a number of advantages (9). Lipid nano-transporters have the potential to effectively improve the safety, stability, and solubility of several drugs when added into them (10). Lipid nano-capsules, nanostructured lipid carriers (NLC), solid lipid nanoparticles (SLNs), and other lipid nanoparticles (NPs) have all been employed in studies recently (11). Most SLNs are composed of solid lipids, including waxes or high-melting-point glycerides, which take the role of liquid lipids in emulsions. SLNs are thought to be the original class of lipid nano-transporters because of their ability to bind pharmaceuticals firmly, stop them from degrading, and release them under controlled conditions. Nonetheless, certain limitations persist, such as limitations on medication loading capacity and drug ejection during storage. Consequently, a novel and enhanced generation of lipid nanoparticles known as the NLC was created (8,12,13).

The aim of our review article is to focus on the different types of lipid-based nanoparticles and their potential role in the management of prostate cancer with several examples from the literature.

2. Prostate gland

2.1. Typical structure of the prostate gland

The prostate's base is located at the neck of the bladder, while its apex is located at the urogenital diaphragm. The prostate and seminal vesicles are located in front of the rectum, separated by the Denonvilliers fascia, a thin, film-like layer of connective tissue. The urogenital

diaphragm's skeletal muscle fibers reach into the prostate at its apex and up to the mid-prostate anteriorly. The prostate gland previously thought to be divided into various lobes, a concept that rejected later on by McNeal that suggest the concept of various zones rather than lobes of the prostate as shown in Figure 1 (14,15). The entire prostatic glandular tissue at the apex and all of the tissue posteriorly, close to the capsule, are included in the peripheral zone. Post-inflammatory atrophy, chronic prostatitis, and cancer are comparatively more common in this zone than other zones. The adult gland's core zone is fashioned like a cone, with the tip of the cone located at the verumontanum, where the ejaculatory ducts and the prostate urethra converge. The midgland's transition zone is made up of two equal sections of glandular tissue that are lateral to the urethra. This area of the prostate has a role in the development of less often occurring adenocarcinoma and age-related benign prostatic hyperplasia (BPH). The anterior external surface's convexity is formed by the anterior fibromuscular stroma (AFMS). This region's apical half is dense with striated muscle, which melds with the pelvic diaphragm's gland and muscle. Smooth muscle cells proliferate toward the base and merge with the bladder neck's fibers. While the proximal part of the AFMS is crucial for involuntary sphincter functions, the distal section is vital for voluntary sphincter functions (1).

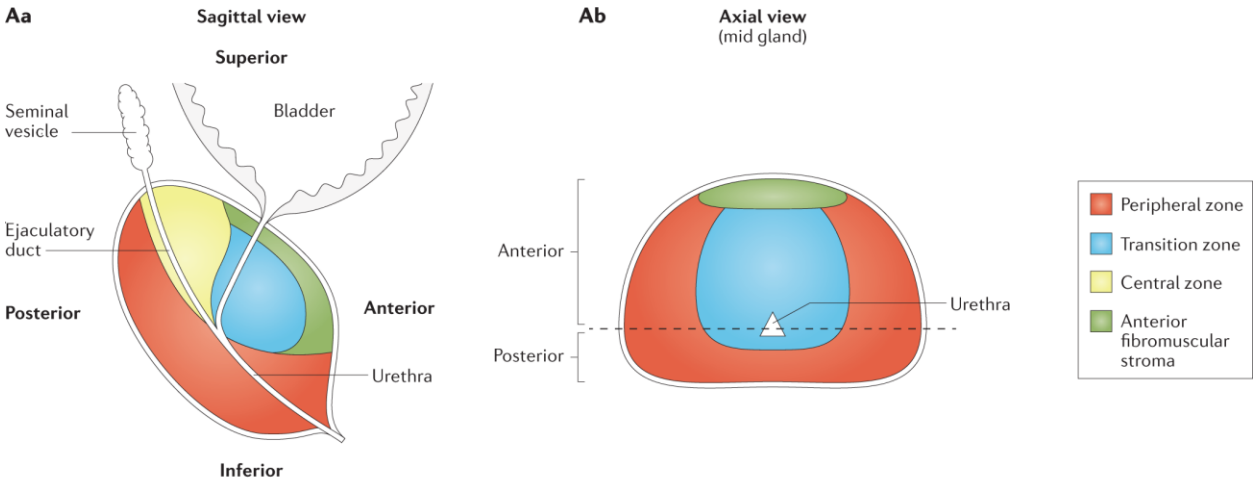


Figure 1Aa: represent sagittal view of the prostate gland while **Figure 1Ab:** represent axial view of the prostate gland. In the young man, the transition zone makes up only 5–10% of the glandular tissue. The ejaculatory ducts pass through the central zone, which is a portion of the prostate's base. The peripheral zone, especially that which is distal to the verumontanum, makes up the prostate (15).

2.2. Androgen production and action

Androgens bind to the androgen receptor (AR) in the hypothalamus to increase the release of luteinizing hormone (LH)-releasing hormone (LHRH). After arriving in the pituitary, LHRH binds to LHRH receptors. LH is released in response to this contact. The pituitary gland secretes LH, which binds to LH receptors (LH-R) in the testes to stimulate the synthesis of testosterone from cholesterol. As testosterone reaches prostate cells, the enzyme 5α-reductase transforms it into dihydrotestosterone (DHT) (16). After forming a strong bond with AR, DHT moves into the cytoplasm and the complex moves to the nucleus, where it stimulates the transcription of genes that control cell division and survival. Through negative-feedback loops, increased testosterone levels can also reduce the generation of LHRH and LH, keeping serum testosterone levels at physiological levels as shown in Figure 2. Androgens can also be produced by the adrenal gland (14).

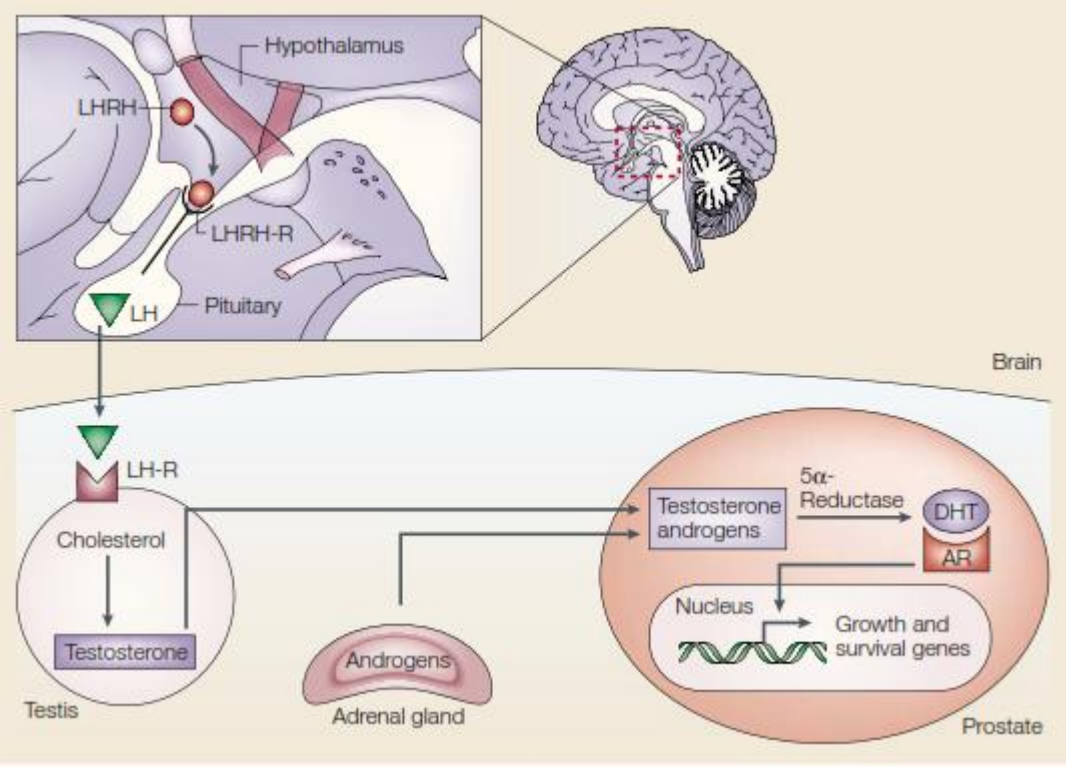


Figure 2. The secretory pathway of the testosterone and dihydrotestosterone starting form hypothalamus ending with prostate gland (14).

2.3. Androgenic receptors and its role in prostate cancer

Prostate development and normal function are dependent on androgens acting through the androgen receptor (AR). A pathway that includes the production of testosterone in the testicles, its delivery to the intended tissues and its transformation by 5 α-reductase into the more potent metabolite 5 α-dihydrotestosterone (DHT) is thought to underpin androgen activity as revealed in Figure 3. Testosterone and DHT bind to AR and activate AR transcription to produce their biological effects. AR's interaction with co-regulators and the phosphorylation of both AR and AR co-regulators in response to growth factors (1–4) regulate the androgen-induced transcriptional activation of AR (2,17). When a prostate cancer is first diagnosed, 80–90% of cases are androgen-dependent. The goal of endocrine therapy for prostate cancer is to lower blood androgen levels and inhibit AR (17,18). The prostate cancer advances to a hormone-refractory stage, though, as androgen ablation therapy eventually fails. In most individuals with hormone-refractory illness, AR is expressed throughout the course of prostate cancer and endures. Notably, transcriptional activity is exhibited by the majority of AR mutations seen in hormone-refractory prostate cancer. The findings indicate that AR-negative prostate cancer cells do not exhibit a significant growth or survival advantage, and that loss of AR activity is not a major reason of androgen ablation failure (2).

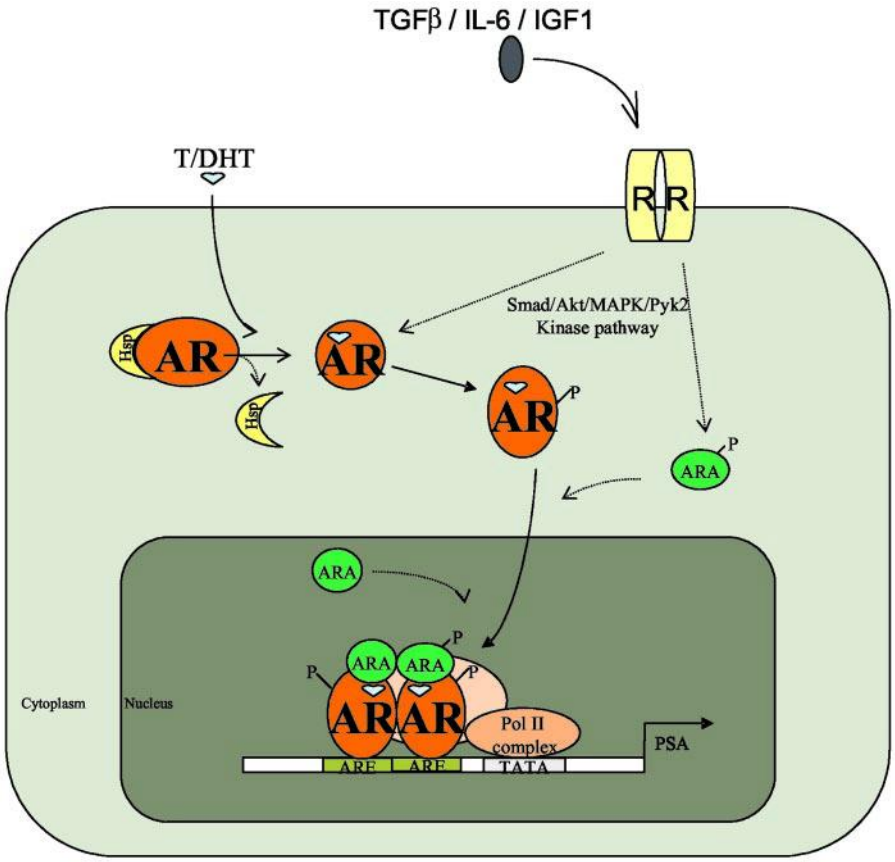


Figure 3. Prostate androgen-AR interaction. DHT and testosterone (T) attach to AR and encourage the binding of AR coregulators (ARAs). After translocating to the nucleus, AR interacts to AREs in target gene promoter regions to trigger both apoptosis and cell division. By phosphorylating AR and/or ARAs, other signal transduction pathways, like those involving TGF, IL-6, and IGF-I, can also increase AR activity. Heat shock protein (Hsp); membrane receptor (R); and protein phosphorylation (P) are the terms used (2).

3. Prostate carcinoma (PCa) and Benign Prostatic Hyperplasia (BPH)

3.1. Diagnosis

The clinical history and digital rectal examination, which is the initial stage in determining whether the prostate's dimensions are abnormal in any way, are used to make the diagnosis of benign prostatic hyperplasia (BPH). In the fifth decade of a man's life, a digital rectal examination is recommended; nevertheless, the results are not as accurate as trans-rectal ultrasound. An additional method for tracking BPH is the American Urology Association

Symptom Index (AUASI) questionnaire (17). It consists of seven questions covering the primary symptoms associated with BPH. Each segment has a score range of 0 to 5, with a maximum score of 35 points possible overall. Three categories exist for the severity of symptoms: mild (0–7 points), moderate (8–19 points), and severe (20–35 points). There is a strong association between the patient's level of urine issues and the AUASI (17). Patients with BPH should be particularly concerned about lower urinary tract symptoms (LUTS) as they negatively impact their quality of life in terms of health. The two types of LUTS symptoms; obstructive and irritative are brought on by the compression and mass effect of nearby tissues like the urethra and nerve tissue. Urethral compression makes it difficult to urinate, and as a result, it can lead to bladder obstruction and incontinence (19).

PSA readings greater than 4.0 ng/mL are frequently utilized as the initial indicator of PCa, primarily in cases where the anomalous result is verified twice. To screen for early PCa, which is typically asymptomatic, PSA levels are paired with digital rectal examination and prostate imaging studies, just like with BPH. Conversely, the gold standard diagnostic method for identifying PCa is prostate biopsy (20). An essential part of PCa diagnosis, the Gleason scoring system is frequently utilized to inform choices. Using five grades-one for the Gleason grade of the main pattern plus another for the grade of the second most prevalent pattern-uch a scoring system quantifies the histological prostate pattern. A Gleason score of less than six is categorized as grade 1, which has the lowest clinical magnitude; a score of seven with the number three as a predominant pattern (3 + 4 = 7) is categorized as grade 2; a total of seven with the number four as a predominant pattern (4 + 3 = 7) is categorized as grade 3; a Gleason score of more than seven with grades four and five indicates poorly differentiated tumors and the worst prognosis (17).

3.2. Management

Alpha-adrenergic drugs, such as doxazosin, and 5-alpha-reductase inhibitors, such as finasteride and dutasteride, are used in the treatment of BPH. These pharmaceuticals improve LUTS while slowing the growth of BPH. Accordingly, there is a warning for TRT in patients with BPH or an elevated risk of BPH initiation because DHT blockage is a therapeutic strategy intended to reduce the extent of prostate hyperplasia patterns. Serum T and DHT concentrations

do not seem to be higher in men who have BPH, despite the fact that androgen deprivation in adulthood causes the prostate tissue to involute (4,21).

Important considerations in PCa treatment are the patient's preferences, the existence or lack of symptoms, and other related illnesses. Radiation therapy with or without androgen deprivation therapy, active surveillance, and radical prostatectomy are the available treatment options for localized prostate cancer, depending on the cancer severity and risk group as revealed in Table 1.

Table 1: Androgen-ablation therapy using different medications

Class	Drugs	Mechanism of action	Advantages	Disadvantages
Estrogen replacement therapy	Diethyl stilbesterol (DES)	Suppression of the hypothalamo-testicular axis.	Used to treat advanced prostate cancer when other treatments are not suitable or no longer working.	Substantial toxicity to the heart and thromboembolism
LHRH agonists	Leuprolide (Lupron), Goserelin (Zoladex), Buserelin and Nafarelin	Long term treatment lead to down-regulation of the pituitary gland receptors for LHRH that eventually leads to diminishing the levels of both FSH and LH.	Reducing blood testosterone levels without causing the rise in thromboembolic incidents linked to estrogen treatment	Induce a "Testosterone flare," a brief spike in serum testosterone levels that results in pain and obstructive symptoms.
LHRH antagonists	Cetrorelix, Abarelix and Orgalutran	Suppress LH and testosterone synthesis by directly blocking the LHRH receptor.	Rapidly lowering testosterone levels without causing the initial "flare" or surge in testosterone seen with agonists.	Injection site reactions, and potential cardiovascular risks.

Anti Androgens	Steroidal (Cyproterone)	Blocks the negative feedback of androgens at the hypothalamic–pituitary level by competitively inhibiting the binding of testosterone or DHT to androgen receptors in brain and pituitary as well as the androgen receptors present in the prostate gland (22).	Preventing tumor flare when starting LHRH agonists and can be used as monotherapy for advanced prostate cancer.	Loss of sexual arousal and desire, also was accompanied by hepatic hypertrophy.
	Non-steroidal (Flutamide, Biclutamide, and Nilutamide) (23)	Inhibits testosterone or DHT binding to androgen receptors exclusively in the prostate gland in a competitive manner.	They had no effect on potency or libido.	Hot flashes, and gynecomastia (breast enlargement)
5α-Reductase inhibitors	Finasteride and Dutasteride	Prevent testosterone from being converted to DHT.	Also used to treat benign prostatic hyperplasia (BPH), helping to alleviate urinary symptoms associated with an enlarged prostate	Increased risk of high-grade prostate cancer, and sexual dysfunction.

4. Brief history of development of lipid-based nanoparticles

Given the variety of colloidal carrier systems available, it is unclear which one would be best suited for the intended use. Naturally, there's no easy response to this query. Among the things to think about are: ① drug entrapment capacity, ② drug targeting potential, ③ carrier's *in vivo* fate, ④ different toxicities (acute and chronic), ⑤ Production scaling, ⑥ stability (both physically and chemically), and ⑦ total costs.

4.1. Polymers based nanoparticles

Artificial and natural sources of polymers have been employed. Nanospheresicles, polymer nanocapsules, and water soluble polymer–drug conjugates are examples of polymer-based systems with submicron sizes. The abundance of potential chemical alterations, such as the creation of block- and comb-polymers, is one benefit of polymer systems while the cytotoxicity of polymers, the scaling up of production processes, and residues from organic solvents used in the process are the main causes of problems with polymer-based nanoparticles. The concentration of nanoparticles in most production processes is minimal, usually not more than 2%. It is important to consider polymer hydrolysis during storage, and lyophilization is frequently necessary to stop polymer deterioration (24).

4.2. Liposomes

Phospholipid bilayers (phosphatidylcholine, in most cases) combine to form spherical vesicles known as liposomes. Hydrophilic medications are dissolved in the inner water core, whereas lipophilic pharmaceuticals can be integrated into lipid bilayers. The intravenous injection of lipophilic medications with extremely low water solubility, such as amphotericin B (AmBisome), is also made possible using liposome-based drug carriers. Comparing the liposome system to a commercial version of amphotericin based on micelles, the toxicity is a tenth. Issues with chemical and physical stability may cause liposomes to aggregate and drugs to degrade while being stored, which would impair the effectiveness of liposome-based drug carriers.

4.3. Nano-suspensions

Colloidal particles made up solely of the medication and emulsifier are called nano-suspensions. High pressure homogenization and ball milling are two examples of potential industrial processes used in their preparation.

4.4. Nanoemulsions

In the 1950s, lipid nano-emulsions were developed for parenteral feeding. The lipid phase, which makes up around 10–20% of the emulsion, is composed of middle chain triglycerides or fatty vegetable oils like soy oil. Phospholipids (stabilizers, 0.6–1.5%) and glycerol (osmolarity control, 2.25%) are additional components. They have several benefits, such as high lipid phase content, high pressure homogenization for large-scale production, and toxicological safety. The small size and liquid nature of the carrier in nano-emulsions limits the potential for controlled medication release. For the majority of medications, there will be a quick release of the medication. According to estimates, extremely lipophilic drugs-their octanol/water partition coefficient should be more than 1,000 000:1-are needed for delayed drug release (25).

4.5. Lipid-based nanoparticles

Pharmacists have long been aware of the use of solid lipid matrices—lipid pellets, specifically—for the extended release of pharmaceuticals. With this in mind, it was a matter of time until lipid microparticles were produced, for example, using spray-congealing as done by Speiser et al (12). The first generation of lipid nanoparticles, or so-called lipid nanopellets for oral delivery, were created in the following stage. There was a reason why this development was stopped. The second generation, known as solid lipid nanoparticles (SLN), was created at the start of the 1990s. The liquid lipid used in emulsions is replaced by a solid lipid including high-melting point glycerides or waxes to produce SLN for pharmaceuticals and cosmetics (26).

5. Different types of lipid nanoparticles

5.1. Solid lipid nanoparticles (SLN)

Solid lipid particles (SLN) are defined as particles comprise lipids that are solid at both room and body temperatures and stabilized by surfactant(s). By definition, the lipids can be complicated glyceride combinations, very pure triglycerides, or even waxes. They can be formed

via dispersing the drug in the melted solid lipid, and then the drug-lipid melt dispersed in heated aqueous surfactant solution to obtain a primary emulsion which is finally homogenized at temperatures over the lipid's melting point to give the final SLN product (13).

It has been stated that SLN avoids the drawbacks of other colloidal carriers while combining their benefits (27). Among the suggested benefits are (28):

1. Regulatory approved and well-tolerated excipients generally recognized as safe (GRAS) can be used to manufacture SLN (no use of toxic organic solvents) and so the carrier isn't a bio-toxic (SLN are ten to one hundred times less cytotoxic than their **polymeric equivalents**) (6).
2. SLN have a broad range of possible applications, including topical, intravenous, cutaneous, and peroral (29).
3. Using solid lipids rather than liquid oils (as in **nano-emulsions**) are a very appealing approach to accomplish controlled drug release due to drug mobility in a solid lipid should be significantly lower than in liquid oil (30).
4. Provide a chemical protection against labile drug's degradation (31).
5. Enhancement of oral and parenteral bioavailability via modification of the rate at which encapsulated drug being dissolved and also via enhancing tissue distribution (10).
6. Drug delivery to specific targeted tissues as shown in Figure 4.
7. Possibility to incorporate both hydrophilic and lipophilic medications.
8. Large-scale production and sterilization are not problematic.

Despite the huge advantages mentioned above, however they are still have several drawbacks (28,32–34):

1. The ability to incorporate drugs is naturally limited by the creation of more or highly organized lipid crystals. While the lipid molecules are chemically similar, perfect lipid crystals can form. For example, while producing lipid particles, highly purified tristearine can be used.
2. Drug ejection and drug crystals in the aqueous SLN dispersion can result from more perfect crystalline β-modifications that can occur during storage—sometimes in as little as a few days or hours (a phenomena that occurs in suppositories synthesized from fatty bases like cocoa butter) as shown in Figure 7.
3. SLN dispersions contain high amount of water (70-95%) (35).

Consequently, lipid particles—also known as NLC—were created, offering a unique nanostructure with improved drug accommodation capability.

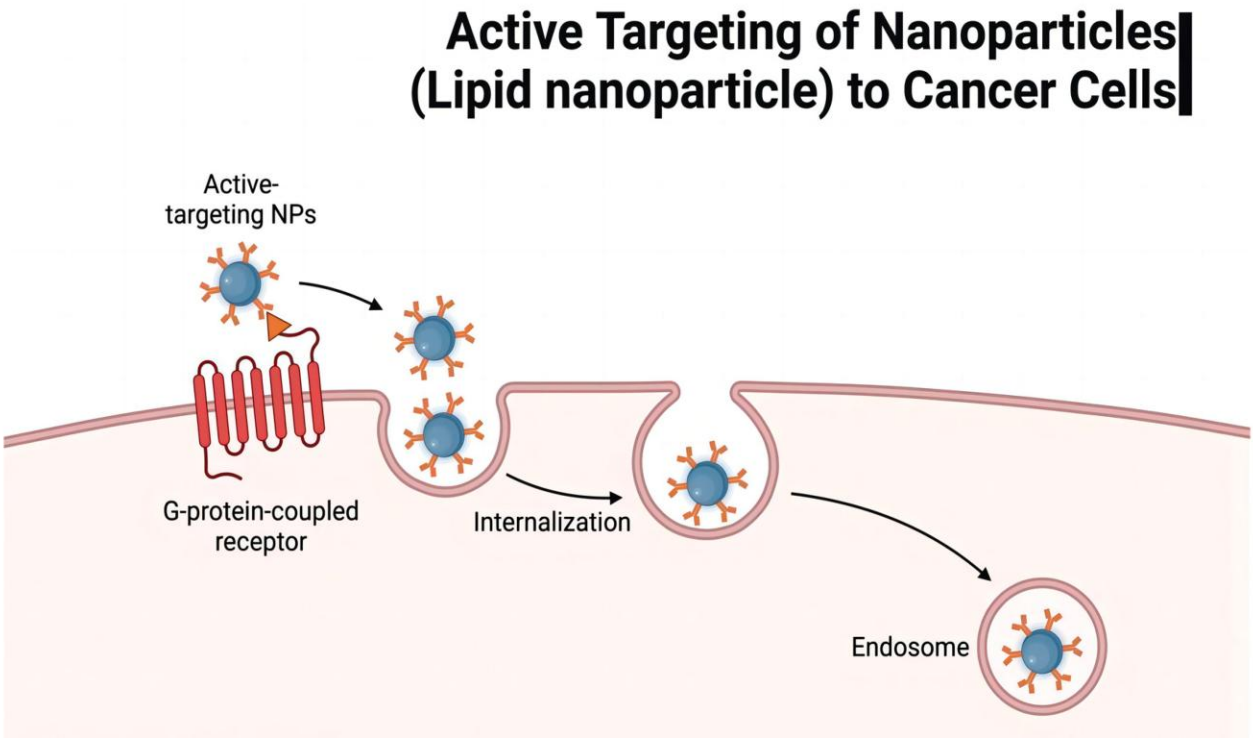


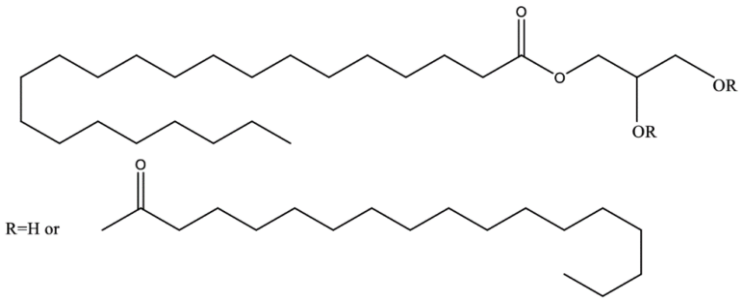
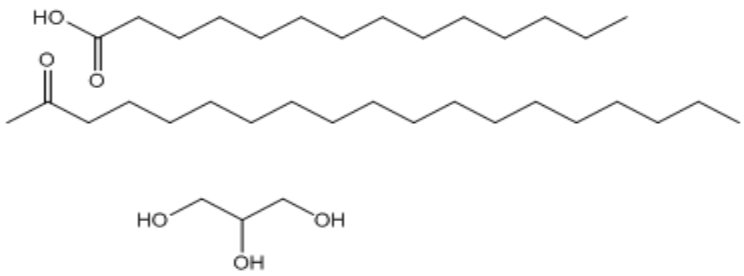
Figure 4. LNP interaction with tumor cells (36).

5.2. Nanostructured lipid carriers (NLC)

They are considered as the second generation of lipid nanoparticles that attempt to circumvent the SLN's drawbacks via applying the several principles depending mainly on providing crystallographic defects in the lipid structure to afford a space accommodate amorphous drug clusters (9,12). There are several types of nanostructured lipid carriers that represented diagrammatically in Figure 7 and Table 2; which can be summarized into (13,27,37,38):

Table 2: Different types of NLC

Type	Principle to provide greater space to accommodate the drug
1) Imperfect NLC	• Mixing spatially dissimilar lipids, such as glycerides made of various fatty acids, results in imperfections in the crystal order. Thus, the use of glycerides made of highly dissimilar fatty acids can result in a substantial increase in

	the distance between fatty acid chains. The drug's molecular shape and amorphous clusters are accommodated by the flaws in the matrix(39). • **Examples of glycerides:** a. Compritol® or glyceryl behenate (mixture of mono-, di-, and tribehenate esters of glycerol).  **Figure 5.** Chemical structure of Compritol® b. Precirol® or glyceryl palmito-stearate (mono-, di-, and triglyceride esters -mainly diglycerides-of palmitic and stearic acids).  **Figure 6.** Chemical structure of Precirol® • The biggest drug payload can be obtained by mixing small volumes of chemically extremely dissimilar liquid lipids (oils) with solid lipids to achieve the highest level of incompatibility.
2) Structure-less or amorphous NLC	• Mixing solid lipids with distinct lipids as **isopropyl myristate**, **Hydroxy-octacosanol-hydroxystearate**, or **medium chain triglycerides as Miglyol 812**, might result in this type of NLC. Since NLC are solids in an amorphous but not crystalline form, the unique structure of the lipid matrix prevents drug ejection caused by the process of crystallization to β forms during storage (40,41).

3 Multiple O/F/W NLC	• Particular kind of NLC, which is caused by high oil concentrations that surpasses its solubility in solid lipid that. In this instance, the drug becomes encapsulated in the oily nano-compartments due to its higher solubility in the liquid lipid than the solid one. • **Advantages:** This makes it possible for more advantageous, better-arranged integrated molecules, improved packaging, improved controlled release profiles, and a reduction in cargo expulsion that occurs too soon. • **Example:** The formation of nano-compartments as small as 200 nm within a nanoparticle is not achievable through mechanical means. Instead, a miscibility gap is used in the phase separation process during particle production. For instance, when Compritol is mixed with a higher percentage of Miglyol 812 (e.g., ~30%), the mixture is used for particle production using the hot homogenization method. In the hot state, the two lipids form one phase, and during the cooling process, phase separation takes place, resulting in the precipitation of tiny Miglyol droplets.

5.3. Lipid drug conjugates (LDC)

While hydrophilic medicines can be included by SLN and NLC, lipophilic substances are better suited for their incorporation. To improve drug loading rates for hydrophilic medicines, LDC were created in the late 1990s. The process of making them involves attaching the medication to the lipid before the O/W emulsion is formed (42).

The drug and lipid are first conjugated by salt formation or covalent bonding, and then the drug-lipid complex is homogenized with a surfactant aqueous solution by HPH to create LDC (43).

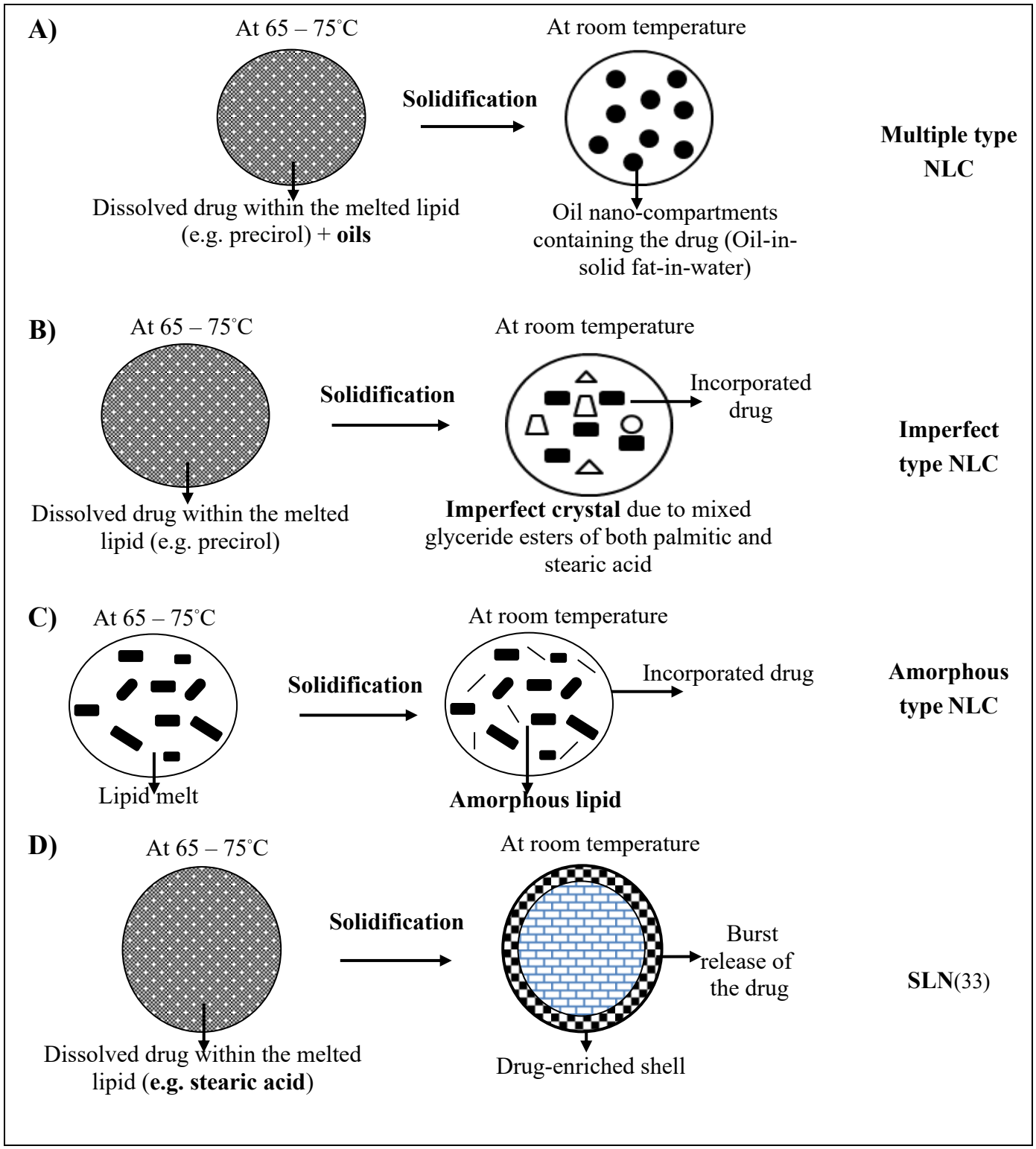


Figure 7. Diagrammatic representation showing different types of NLC: A) Multiple O/F/W type, B) Imperfect type, and C) Amorphous type, while D) represents SLN.

6. Different approaches for developing SLN and NLC

6.1. High-pressure homogenization (HPH)

The primary method that has been established for producing SLN and NLC is high-pressure homogenization. This method has benefits that go beyond its quick turnaround time. Additionally, this technique makes it simple to transfer laboratory-scale production to large-scale production. In addition, this method is widely employed in many industries due to the avoidance of organic solvents, the production of average particle sizes in the submicron zone, and the availability of affordable homogenizer models and brands. Nevertheless, because it's a high-energy intensity technique, it raises the samples' temperature, which isn't good for substances that react negatively to heat. Using this method, the high-pressure sample is forced into a tiny opening that is only a few microns across. Both high and low temperatures (hot and cold homogenization, respectively) can be achieved using high-pressure homogenization of SLN and NLC, but it's crucial to remember that for both methods, the medication must dissolve or spread at a temperature that's roughly 5°C above its melting point (9,44). The hot and cold homogenization techniques are summarized in Table 3.

Table 3: Main differences between Hot and Cold homogenization techniques

Hot homogenization	• Procedures: the whole process is done at temperatures higher than the lipid's melting point. a. First, high-speed stirrer is used to create a pre-emulsion of the drug-loaded lipid melt and the aqueous emulsifier phase (5–10°C above lipid melting point). b. The heated pre-emulsion is homogenized at a regulated temperature and high pressure (one cycle is enough to create a hot emulsion with particles between 250 and 300 nm in size however the literature recommends doing three homogenization cycles at 500 bar). Generally the number of cycles will depend on the emulsion lipid concentration as the energy needed to chop the lipid mass is directly proportional to its concentration in the formulation. • Drawbacks: a. More homogenization cycles promote coalescence due to

	increasing particle's kinetic energy and so producing particles with larger sizes. b. The technique is limited by the temperature used in the process, particularly for chemicals that are hydrophilic and extremely sensitive to temperature which can partition from the lipid phase to the aqueous phase at the high temperature.
Cold homogenization	• <u>Procedures:</u> a. Firstly; dissolving the active ingredient in the melting lipid phase. b. Then; the melting mixture is then quickly cooled using dry ice or liquid nitrogen to a solid form (the uniform distribution of the active component in the lipid phase is favored by this quick cooling). c. The resulting solid is chopped into micro-particle powder; it is shook vigorously in a cold aqueous surfactant solution to form a pre-emulsion. Finally; to create the lipid nanoparticles, the dispersion is homogenized at room temperature or lower, typically for five cycles at 500 pressure. • <u>Advantages:</u> it was emerged as a solution to the hot homogenization issues, for chemicals that are hydrophilic and particularly sensitive to temperature, this procedure is greatly suggested. However this method reduces temperature exposure but does not completely eliminate it as the temperature is needed in the first step as previously mentioned. • <u>Drawbacks:</u> a. The extreme homogenization step's significant energy need. To put it another way, this procedure is not energy-efficient. b. Larger and more poly-disperse particles are seen in cold HPH as opposed to hot HPH.

6.2. Micro-emulsion technique

With this technique, the lipid (or lipid blend) is melted and the surfactant-containing aqueous phase is heated to the same temperature. The surfactant solution is added to the lipid phase while being gently stirred to create the micro-emulsion. By dispersing the micro-emulsion in cold water (2–10°C) while stirring, lipid nanoparticles are produced. Ultimately, the apparatus undergoes a distilled water wash, filtration to eliminate bigger particles, and lyophilization to eliminate surplus water (10,11). This method enables the production of nanoparticles in mildly heated environments. However, the drawbacks include the requirement for comparatively high surfactant concentrations, the particle suspension's significant dilution upon dissolving the micro-emulsion in water; yield a suspension with a very little concentration (38,39,45).

6.3. Emulsification-solvent diffusion

By using a slightly water-miscible, low-toxicity solvent, this technique generates an oil-in-water (O/W) emulsion. Water miscibility in these solvents—which contain the drug—is the basis for the procedure. After creating this temporary O/W emulsion, it is added to water and continuously stirred, allowing the solvent to permeate into the outer phase and solidify the dispersed phase while also forming nanoparticles. Among advantages of this technique are its versatility, reproducibility, ease of implementation, lack of need for high-energy sources, avoidance of temperature stress and agitation, and narrow size distribution. However, the lipid nanoparticle dispersion needs to be concentrated and cleaned up (39,41,45).

6.4. Emulsification-solvent evaporation

This method involves dissolving the lipid matrix in an organic solvent that is water immiscible before the aqueous phase emulsifies it. By evaporating the solvent at a lower pressure, the aqueous medium is more prone to the generation of nanoparticle dispersion by lipid precipitation. With this completely heat-free method, nanoparticles as small as 100 nm can be produced, depending on the ingredients. The use of organic solvent, which may leave hazardous residues in the sample, is a limitation (43).

6.5. Injection of solvent (or displacement of solvent)

This method involves dissolving the lipid matrix in a water-miscible solvent and quickly injecting the mixture into an aqueous phase that contains surfactant through an injection needle. The method for creating lipid nanoparticles is simple to use, adaptable, and effective. However, there is a drawback to using organic solvent (13).

6.7. Inversion of the phase

The formulation components (lipid matrix, drug, water, and surfactant) are mixed using magnetic stirrer in this solvent-free method, and three temperature cycles (85-60-85-60-85°C) are applied to reach the inversion process. The mixture is then diluted in cold distilled water to apply a thermal shock that causes the development of lipid nanoparticles. This method merely involves brief heating times and does not require the use of organic solvents. It takes a while to complete and involves multiple steps (9).

6.8. Sonication or ultra-sonication

This is a dispersion technique, similar to high shear homogenization. In order to create an emulsion, the lipid matrix (containing the medication) is melted 5–10°C above its melting point and then dispersed in an aqueous phase containing surfactant at the same temperature while being vigorously stirred. After that, this is cooled gradually to create the nanoparticle dispersion and sonicated to reduce droplet size. One benefit is the use of a very common apparatus in the laboratories. Nonetheless, lengthy sonication durations are necessary to produce lipid nanoparticles, which raise the possibility of metal pollution from the probe. Furthermore, because of the sample's non-uniform energy distribution, the resultant particles are extremely poly-disperse (37).

6.9. Membrane contactor method

Lipid nanoparticles can be produced on a massive scale using this technology. Pressurization is applied to the drug-containing molten lipid matrix, via a porous membrane (typically with a pore diameter of 50 nm) into aqueous surfactant solution kept at the same temperature of lipid melt, as the mixture cools down to room temperature, the lipid droplets that were formed during the lipid's passage through the pores precipitate as lipid nanoparticles. Using membranes with

varying pore sizes allow for particle size control, also the approach is straightforward, and scalable (7,46).

6.10. Recent formulation techniques

One thing that all of the previously listed methods have in common is the use of thermal or conductive heating. This also makes up the conventional method of developing an organic synthesis. In most cases, conductive heating is applied to formulation ingredients using an external heating source, such as an oil or water bath. Because this kind of heating is dependent on the thermal conductivity of each material, the mixture's temperature will always be uneven and the container's inside will always be hotter than its exterior. As a result, there is very little energy transfer efficiency, which results in particles with irregular qualities (27). The recent techniques are summarized in Table 4.

Table 4: Main difference s between microwave-assisted and ultrasound-assisted synthesis of lipid nanoparticles

	A) Microwave-Assisted Synthesis (MAS)	**B) Ultrasound-Assisted Synthesis (UAS)**
Principle	• Because the nature of this heating is dielectric, meaning that it is dependent on the dielectric characteristics of materials. • Using this method, microwaves link with particles that are in the formulation container, which causes a sharp increase in temperature. Dipole polarization and/or ionic conductance will happen instantly due to overheating because there is no reliance on the reaction vessel's thermal conductivity and so the produced formulations will be with improved qualities and increased uniformity.	• Based on the emission of sound waves at various intensities and frequencies that are higher above the human hearing range (>16 kHz). Since these intensities are inversely correlated with frequency and can be categorized as: ***1.*** *Low-intensity ultrasound:* does not result in physicochemical changes that include destruction because its frequencies range from 1 – 10 MHz and its energies are very low (<1 W/cm^2). In the environment, this kind of ultrasonography is employed for both diagnosis and detection. ***2.*** *High-intensity ultrasound:* operates at powers of 10 – 1000 W/cm^2 with frequencies from 16 – 100 kHz. It is frequently used to change a material's characteristics in a way that favors a physical transformation, as when making emulsions, depolymerizing, deflocculating, and reducing particle size.
Advantages	1. Considered a rapidly formulation method. 2. Regular heating (microwave reactor temperature control, increased energy efficiency). 3. Reduced sizes of the particles. 4. Distributions that are less poly-disperse.	1. Outstanding ability to avoid particle aggregation. 2. Increased energy effectiveness. 3. Reduced sizes of the particles.

Disadvantages	1. Uncommonly employed and little-known techniques for the creation of SLN and NLC. 2. It hasn't been industrially used yet due to its novelty as an SLN and NLC formulation approach.	1. Its novelty as SLN and NLC formulation technique has prevented it from being industrially scaled up to this point. 2. Largely reliant on how the equipment is configured.

7. Literature used lipid nanoparticles as a cargo for prostate cancer treatments

Several drugs had been included into different lipids as a drug cargo that can be summarized in Table 5.

Table 5: literature-based evidences of anti-prostate cancer agents that successfully incorporated into lipid nanoparticles.

Drug	Type of nano-particle	Problem of drug necessitates incorporation into lipid nanoparticle	How the nanoparticle overcome that problem	Design used	Reference
Biclutamide (Anti-androgen)	NLC	Low solubility in water (5 mg/L) and a high lipophilicity (log P = 2.92), so it is poorly soluble at physiological pH and so decreased GIT limiting its oral bioavailability.	NLC were shown to enhance the solubility and so the oral bioavailability	Box-Behnken design	(47)
Tamsulosin (α-blocker)	NLC	Tamsulosin formulation currently goes through a drug release phase when there is water present, which results in a greater drug release profile in the gut and stomach. Oral administration of Tamsulosin has been	Fabrication of a new formula including Tamsulosin & 2 oils having prostate activity (saw palmetto and Pumpkin) was found to enhance its	Central composite design	(48)

		found to elevate the risk of syncope, orthostatic hypotension, dizziness, and postural hypertension.	topical bioavailability in a trial to decrease its oral side effects		
Tadalafil (Alleviation of lower urinary tract symptoms)	SNEDDSs	Tadalafil is Class II biopharmaceutical classification system with poor aqueous solubility and hence low bioavailability	Improve the efficacy of Tadalafil via combination with 2 oils having prostate activity (saw palmetto and Pumpkin)	Mixture design	(19)
Curmumin (Down regulation of androgen receptors)	NLC	Lower oral bioavailability	NLC efficiently enhance oral bioavailability and also drug targeting	-	(49)
Doxorubicin (Induce apoptosis of cancer cells)	NLC	Doxorubicin has been connected to a few side effects as heart disorders and baldness.	NLC effectively target Doxorubicin to prostate cancer cells without harming the normal one.	Box-Behnken design	(50)
Docetaxel (microtubules de-polymerization inhibitor)	PEGylated -SLNs	Poor bioavailability was demonstrated by low water solubility, short circulation time, quick reticulo-endothelial system absorption, and high renal clearance.	Enhancement of the biopharmaceutical characters of Docetaxel & overcome the poor solubility.	-	(51)
Retinoic acid (binding to	SLNs	Poor water solubility and also blood concentration of	Improvement of retinoic acid water	-	(52)

retinoic acid receptors the nuclear membrane of cancer cells leading to inhibition of the growth)		the drug is gradually decreases via induction of cytochrome P-450 liver enzymes	solubility and bioavailability		

8. Conclusion

The goal of this review was to describe the fundamental therapies specialized in the cure of prostate cancer and benign prostate hypertrophy with brief clarification of the disease and its pathophysiology. Also focus on lipid nanoparticles; history of their development, different types recently used in the research and the ways of their manufacture with the principal idea of the treatment options for the prostate cancer that is effectively incorporated into solid lipid nanoparticles and nanostructured lipid carriers that show enhancement in different ways related to the drugs that being incorporated as improvement of the oral and also topical bioavailability, improvement of water solubility for poorly water soluble drugs belonging to BCS class II, drug targeting to the specific tissue being treated which efficaciously decrease the adverse drug actions of the chemotherapeutic agents, and finally improve drug protection from being metabolized in liver. All the aforementioned advantages encourage further trials for the incorporation of many other medications into lipid nanoparticles not only for the treatment of prostate cancer but also for other ailments.

- **Conflict of Interest**

The authors declare no conflict of interest.

9. References

1. Hammerich KH, Ayala GE, Wheeler TM. Anatomy of the prostate gland and surgical pathology of prostate cancer. Prostate Cancer. 2008;(November):1–14.
2. Heinlein CA, Chang C. Androgen receptor in prostate cancer. Endocr Rev. 2004;25(2):276–308.
3. Ali MA, Mohamed MI, Megahed MA, Abdelghany TM, El-Say KM. Cholesterol-based nanovesicles enhance the in vitro cytotoxicity, ex vivo intestinal absorption, and in vivo bioavailability of flutamide. Pharmaceutics. 2021;13(11):1–22.
4. Leisegang K, Jimenez M, Durairajanayagam D, Finelli R, Majzoub A, Henkel R, et al. Phytomedicine Plus A systematic review of herbal medicine in the clinical treatment of benign prostatic hyperplasia. Phytomedicine Plus [Internet]. 2022;2(1):100–53. Available from: https://doi.org/10.1016/j.phyplu.2021.100153
5. Csikós E, Horváth A, Ács K, Papp N, Balázs VL, Dolenc MS, et al. Treatment of benign prostatic hyperplasia by natural drugs. Molecules. 2021;26(23):1–32.
6. Shete HK, Selkar N, Vanage GR, Patravale VB. Tamoxifen nanostructured lipid carriers: Enhanced in vivo antitumor efficacy with reduced adverse drug effects. Int J Pharm [Internet]. 2014;468(1–2):1–14. Available from: http://dx.doi.org/10.1016/j.ijpharm.2014.03.056
7. Chamundeeswari M, Jeslin J, Verma ML. Nanocarriers for drug delivery applications. Environ Chem Lett [Internet]. 2019;17(2):849–65. Available from: https://doi.org/10.1007/s10311-018-00841-1
8. Zhang Y, Zhang P, Zhu T. Ovarian carcinoma biological nanotherapy: Comparison of the advantages and drawbacks of lipid, polymeric, and hybrid nanoparticles for cisplatin delivery. Biomed Pharmacother [Internet]. 2019;109(1):475–83. Available from: https://doi.org/10.1016/j.biopha.2018.10.158
9. Nguyen CN, Nguyen TTT, Nguyen HT, Tran TH. Nanostructured lipid carriers to enhance transdermal delivery and efficacy of diclofenac. Drug Deliv Transl Res. 2017;7(5):664–73.
10. Carbone C, Campisi A, Musumeci T, Raciti G, Bonfanti R, Puglisi G. FA-loaded lipid drug delivery systems: Preparation, characterization and biological studies. Eur J Pharm Sci [Internet]. 2014;52(1):12–20. Available from:

http://dx.doi.org/10.1016/j.ejps.2013.10.003

11. Vidlářová L, Hanuš J, Veselý M, Ulbrich P, Štěpánek F, Zbytovská J. Effect of lipid nanoparticle formulations on skin delivery of a lipophilic substance. Eur J Pharm Biopharm. 2016;108:289–96.
12. Müller RH, Radtke M, Wissing SA. Nanostructured lipid matrices for improved microencapsulation of drugs. Int J Pharm. 2002;242(1–2):121–8.
13. Üner M. Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): Their benefits as colloidal drug carrier systems. Pharmazie. 2006;61(5):375–86.
14. Denmeade R Samuel, Issacs T John. History of prostae cancer. Nat Rev Cancer. 2002;2(5):389–96.
15. Ali A, Du Feu A, Oliveira P, Choudhury A, Bristow RG, Baena E. Prostate zones and cancer: lost in transition? Nat Rev Urol. 2022;19(2):101–15.
16. Tavano L, Muzzalupo R, Mauro L, Pellegrino M, Andò S, Picci N. Transferrin-conjugated Pluronic niosomes as a new drug delivery system for anticancer therapy. Langmuir. 2013;29(41):12638–46.
17. Rizzuti A, Stocker G, Santos HO. Exploring the Role of Testosterone Replacement Therapy in Benign Prostatic Hyperplasia and Prostate Cancer : A Review of Safety. 2022;30–9.
18. An J, Id HK. Comparative application of testosterone undecanoate and / or testosterone propionate in induction of benign prostatic hyperplasia in Wistar rats. 2022;1–13. Available from: http://dx.doi.org/10.1371/journal.pone.0268695
19. Alhakamy NA, Fahmy UA, Ahmed OAA. Attenuation of benign prostatic hyperplasia by optimized tadalafil loaded pumpkin seed oil-based self nanoemulsion: In vitro and in vivo evaluation. Pharmaceutics. 2019;11(12):1–13.
20. Brody H. Prostate cancer. Nature. 2015;528(7582):S117.
21. Blair HA. Hexanic Extract of Serenoa repens - (Permixon ®): A Review in Symptomatic Benign Prostatic Hyperplasia. Drugs Aging [Internet]. 2022;39:235–43. Available from: https://doi.org/10.1007/s40266-022-00924-3
22. Bondì ML, Craparo EF, Giammona G, Cervello M, Azzolina A, Diana P, et al. Nanostructured lipid carriers-containing anticancer compounds: Preparation,

characterization, and cytotoxicity studies. Drug Deliv. 2007;14(2):61–7.

23. Elgindy N, Elkhodairy K, Molokhia A, Elzoghby A. Lyophilization monophase solution technique for improvement of the physicochemical properties of an anticancer drug, flutamide. Eur J Pharm Biopharm [Internet]. 2010;74(2):397–405. Available from: http://dx.doi.org/10.1016/j.ejpb.2009.11.011
24. Mulik RS, Mönkkönen J, Juvonen RO, Mahadik KR, Paradkar AR. ApoE3 mediated polymeric nanoparticles containing curcumin: Apoptosis induced in vitro anticancer activity against neuroblastoma cells. Int J Pharm. 2012;437(1–2):29–41.
25. Qadir A, Faiyazuddin MD, Talib Hussain MD, Alshammari TM, Shakeel F. Critical steps and energetics involved in a successful development of a stable nanoemulsion. J Mol Liq. 2016;214:7–18.
26. Mehnert W, Mäder K. Solid lipid nanoparticles: Production, characterization and applications. Adv Drug Deliv Rev [Internet]. 2012;64(SUPPL.):83–101. Available from: http://dx.doi.org/10.1016/j.addr.2012.09.021
27. López KL, Ravasio A, González-Aramundiz JV, Zacconi FC. Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC) Prepared by Microwave and Ultrasound-Assisted Synthesis: Promising Green Strategies for the Nanoworld. Pharmaceutics. 2023;15(5):1–26.
28. Aslam R, Tiwari V, Upadhyay P, Tiwari A. Original Article REVOLUTIONIZING THERAPEUTIC DELIVERY : DIOSGENIN-LOADED SOLID LIPID NANOPARTICLES UNLEASH ADVANCED CARRIERS. 2024;16(1).
29. Dolatabadi S, Karimi M, Nasirizadeh S, Hatamipour M, Golmohammadzadeh S, Jaafari MR. Preparation, characterization and in vivo pharmacokinetic evaluation of curcuminoids-loaded solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLC). J Drug Deliv Sci Technol [Internet]. 2021;62(September 2020):102352. Available from: https://doi.org/10.1016/j.jddst.2021.102352
30. Khames A, Khaleel MA, El-Badawy MF, El-Nezhawy AOH. Natamycin solid lipid nanoparticles - sustained ocular delivery system of higher corneal penetration against deep fungal keratitis: Preparation and optimization. Int J Nanomedicine. 2019;14:2515–31.
31. Elgindy NA, Elzoghby AO, Helmy MW, Samy WM. Novel ionically crosslinked casein nanoparticles for flutamide delivery : formulation , characterization , and in vivo

pharmacokinetics. Int J Nanomedicine. 2013;8:1721–32.

32. Lin X, Li X, Zheng LQ, Yu L, Zhang Q, Liu W. Preparation and characterization of monocaprate nanostructured lipid carriers. Colloids Surfaces A Physicochem Eng Asp. 2007;311(1–3):106–11.
33. Chalikwar SS, Belgamwar VS, Talele VR, Surana SJ, Patil MU. Formulation and evaluation of Nimodipine-loaded solid lipid nanoparticles delivered via lymphatic transport system. Colloids Surfaces B Biointerfaces [Internet]. 2012;97:109–16. Available from: http://dx.doi.org/10.1016/j.colsurfb.2012.04.027
34. Jahangir MA, Khan R, Sarim Imam S. Formulation of sitagliptin-loaded oral polymeric nano scaffold: process parameters evaluation and enhanced anti-diabetic performance. Artif Cells, Nanomedicine Biotechnol [Internet]. 2018;46(sup1):66–78. Available from: https://doi.org/10.1080/21691401.2017.1411933
35. Patra S. Original Article DEVELOPMENT , CHARACTERIZATION AND PHARMACOKINETIC EVALUATION OF OPTIMIZED VILDAGLIPTIN SUSTAINED RELEASE MATRIX TABLET USING BOX-BEHNKEN DESIGN. 2024;16(1).
36. Wu L, Li X, Qian X, Wang S, Liu J, Yan J. Lipid Nanoparticle (LNP) Delivery Carrier-Assisted Targeted Controlled Release mRNA Vaccines in Tumor Immunity. Vaccines. 2024;12(2).
37. Gugleva V. Recent Progress of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers as Ocular Drug Delivery Platforms. 2023;
38. Agrawal Y, Petkar KC, Sawant KK. Development, evaluation and clinical studies of Acitretin loaded nanostructured lipid carriers for topical treatment of psoriasis. Int J Pharm [Internet]. 2010;401(1–2):93–102. Available from: http://dx.doi.org/10.1016/j.ijpharm.2010.09.007
39. Chinsriwongkul A, Chareanputtakhun P, Ngawhirunpat T, Rojanarata T, Sila-on W, Ruktanonchai U, et al. Nanostructured Lipid Carriers (NLC) for Parenteral Delivery of an Anticancer Drug. AAPS PharmSciTech. 2012;13(1):150–8.
40. Araújo J, Gonzalez-Mira E, Egea MA, Garcia ML, Souto EB. Optimization and physicochemical characterization of a triamcinolone acetonide-loaded NLC for ocular antiangiogenic applications. Int J Pharm. 2010;393(1–2):168–76.

41. Kumbhar DD, Pokharkar VB. Engineering of a nanostructured lipid carrier for the poorly water-soluble drug, bicalutamide: Physicochemical investigations. Colloids Surfaces A Physicochem Eng Asp [Internet]. 2013;416(1):32–42. Available from: http://dx.doi.org/10.1016/j.colsurfa.2012.10.031
42. Aboud HM, El MH, Ali AA, Menshawe SF El, Elbary AA. Development , Optimization , and Evaluation of Carvedilol-Loaded Solid Lipid Nanoparticles for Intranasal Drug Delivery. AAPS PharmSciTech [Internet]. 2016;17(6):1353–65. Available from: http://dx.doi.org/10.1208/s12249-015-0440-8
43. Lasa-Saracibar B, Estella-Hermoso De Mendoza A, Guada M, Dios-Vieitez C, Blanco-Prieto MJ. Lipid nanoparticles for cancer therapy: State of the art and future prospects. Expert Opin Drug Deliv. 2012;9(10):1245–61.
44. Hosny KM, Aljaeid BM. Sildenafil citrate as oral solid lipid nanoparticles: A novel formula with higher bioavailability and sustained action for treatment of erectile dysfunction. Expert Opin Drug Deliv. 2014;11(7):1015–22.
45. Walbi IA, Ahmad MZ, Ahmad J, Algahtani MS, Alali AS, Alsudir SA, et al. Development of a Curcumin-Loaded Lecithin/Chitosan Nanoparticle Utilizing a Box-Behnken Design of Experiment: Formulation Design and Influence of Process Parameters. Polymers (Basel). 2022;14(18):1–17.
46. W C. Ageing effects in parenteral fat emulsions : the role of fatty acids. 1987;39:33–7.
47. Kudarha R, Dhas NL, Pandey A, Belgamwar VS, Ige PP. Box-Behnken study design for optimization of bicalutamide-loaded nanostructured lipid carrier: Stability assessment. Pharm Dev Technol. 2015;20(5):608–18.
48. Bakhaidar RB, Hosny KM, Mahier IM, Rizq WY, Safhi AY, Bukhary DM, et al. Development and optimization of a tamsulosin nanostructured lipid carrier loaded with saw palmetto oil and pumpkin seed oil for treatment of benign prostatic hyperplasia. Drug Deliv [Internet]. 2022;29(1):2579–91. Available from: https://doi.org/10.1080/10717544.2022.2105448
49. Akanda M, Getti G, Douroumis D. In vivo evaluation of nanostructured lipid carrier systems (NLC) in mice bearing prostate cancer tumours. Drug Deliv Transl Res [Internet]. 2023;13(8):2083–95. Available from: https://doi.org/10.1007/s13346-021-01095-1
50. Zhang HW, Dang Q, Zhang ZW, Wu FS. Development, characterization and evaluation of

doxorubicin nanostructured lipid carriers for prostate cancer. J BUON. 2017;22(1):102–11.

51. Korake S, Bothiraja C, Pawar A. Design, development, and in-vitro/in-vivo evaluation of docetaxel-loaded PEGylated solid lipid nanoparticles in prostate cancer therapy. Eur J Pharm Biopharm. 2023;
52. Akanda MH, Rai R, Slipper IJ, Chowdhry BZ, Lamprou D, Getti G, et al. Delivery of retinoic acid to LNCap human prostate cancer cells using solid lipid nanoparticles. Int J Pharm. 2015;