10 Innovative Nano Technological Platforms for Transdermal Anti-Psoriatic Drug Delivery

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Abstract

Psoriasis is a long-term inflammatory skin condition linked to poor skin barrier function and excessive keratinocyte proliferation. Conventional treatments often show systemic adverse effects, low bioavailability, and poor skin penetration. Transdermal medication delivery systems based on nanotechnology have become viable alternatives to manage psoriasis. Drug penetration, stability, controlled release, and targeted treatment to psoriatic lesions are boosted by nanocarriers like liposomes, ethosomes, transfersomes, solid lipid nanoparticles, nanostructured lipid carriers, and polymeric nanoparticles. These advances enhance patient compliance, decrease toxicity, and increase therapeutic efficacy. The latest advancements, therapeutic advantages, difficulties, and potential applications of novel nano technological platforms in transdermal anti-psoriatic drug administration are presented in this chapter.

Keywords: Psoriasis, Transdermal Delivery, Nanotechnology, Nanocarriers, Liposomes, Ethosomes, Transfersomes, Solid Lipid Nanoparticles, Polymeric Nanoparticles, Controlled Release, Targeted Therapy, Anti-Psoriatic Therapy.

Introduction

About 2-3% of people worldwide suffer from psoriasis, a common chronic inflammatory skin condition marked by recurring relapses and treatment resistance (Greb et al., 2016). Clinically, it is characterized by distinct erythematous plaques coated in silvery-white scales, which can combine to produce large lesions. While the exact pathophysiology of psoriasis is still unknown, a number of factors have been linked to its development, including smoking, infections, psychological stress, and genetic predisposition (Kamiya et al., 2019). Excessive proliferation of immature keratinocytes, immune cell infiltration, and dilated and twisted blood arteries inside afflicted skin areas are among the histopathological characteristics of psoriasis (Rendon and Schäkel, 2019). There is growing evidence that psoriasis is a systemic

inflammatory disease linked to a number of comorbidities, including obesity, diabetes mellitus, and cardiovascular problems, rather than just a skin condition (Jensen and Skov, 2016).

Furthermore, topical drug delivery systems are frequently chosen because of their convenience, ease of application, increased drug bioavailability, improved therapeutic outcomes, and decreased risk of systemic toxicity. Psoriasis is a chronic condition that usually requires long-term and repeated treatment. For individuals with mild to moderate localized psoriasis, topical therapy is therefore frequently regarded as the first-line treatment (Rapalli et al., 2020). The development of efficient topical antipsoriatic formulations is still significantly hampered by the low ability of many therapeutic agents to permeate the skin barrier.

Table 1: Critical Overview of Nanocarriers and Advanced Drug Delivery Technologies for Topical Psoriasis Therapy

Aspect	Description	References
Controlled and Sustained Drug Release	Nanotechnology-based delivery systems enable controlled and prolonged release of therapeutic agents at predetermined rates, improving therapeutic efficacy and reducing dosing frequency.	Barradas et al., 2018; Langasco et al., 2018; Pukale et al., 2020
Enhanced Skin Penetration	Nanocarriers improve drug permeation across the skin barrier, resulting in increased drug absorption and potentially lower required doses.	Pinto et al., 2014; Mao et al., 2017; Freag et al., 2018
Targeted Drug Delivery	Surface modification of nanocarriers with cell-specific ligands facilitates targeted delivery to diseased tissues, enhancing treatment precision and minimizing adverse effects.	Lapteva et al., 2014b; Shores et al., 2020; Lin Z.-C. et al., 2021
Need for Characterization and Evaluation	Comprehensive physicochemical characterization, safety assessment, and efficacy evaluation are essential for successful clinical translation of nanomedicines.	Various studies
Aim of Current Research and Reviews	To critically evaluate the advantages and limitations of different nanocarriers and delivery techniques, and to highlight the unique properties and therapeutic potential of various nanomaterials for topical psoriasis treatment.	Various studies

Nanoparticles

According to Jeevanandam et al. (2018), nanoparticles are ultrafine structures having at least one dimension smaller than 100 nm. Because of their high surface area-to-volume ratio and nanoscale size, they can undergo substantial surface

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functionalization and multifunctional alterations. Nanoparticles are usually made up of two or more materials arranged into separate structural layers, such as a core, a shell, and an outer surface layer, rather than being straightforward molecular entities (Khan et al., 2019). Large volumes of medicinal substances can be effectively encapsulated or adsorbed by nanoparticles thanks to their special physicochemical characteristics, which also make it easier for them to move throughout biological tissues and organs. Because of this, nanoparticles have shown great promise in a variety of biomedical applications, such as drug delivery, bioimaging, and chemical and biological sensing technologies (McNamara and Tofail, 2017).

Table 2: Classification, Characteristics, and Therapeutic Applications of Nanoparticles in Psoriasis Treatment

Nanoparticle Class	Subtype/ Examples	Key Characteristics	Advantages in Psoriasis Treatment	Limitations/ Considerations
Organic Nanoparticles	**Lipid-based nanoparticles** (e.g., liposomes, solid lipid nanoparticles, nanostructured lipid carriers)	Composed of physiological lipids with high biocompatibility and biodegradability	Excellent skin compatibility, low toxicity, minimal skin irritation, enhanced drug penetration, and improved patient tolerability	Limited drug-loading capacity for some drugs and potential stability issues during storage
Organic Nanoparticles	**Polymeric nanoparticles**	Formulated from natural or synthetic polymers	Highly versatile, tunable physicochemical properties, stimuli-responsive behavior, controlled drug release, and customizable design for specific therapeutic requirements	Complex manufacturing processes and potential concerns regarding polymer degradation products
Inorganic Nanoparticles	**Metal-based nanoparticles (MNPs)** such as gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs)	Metallic nanostructures with unique physicochemical and biological properties	Possess antimicrobial activity, enhance drug delivery, improve skin penetration, and may aid in managing skin infections associated with psoriasis	Potential long-term toxicity, accumulation concerns, and requirement for extensive safety evaluation

- **Lipid-Based Nanoparticles**

Lipids are essential parts of the skin and are mostly derived from sebum and keratinocytes. They are vital for maintaining the skin's overall health, moisture, and structural integrity. Many lipid-based delivery systems, such as liposomes, solid lipid

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nanoparticles (SLNs), nanostructured lipid carriers (NLCs), liquid crystalline nanoparticles (LCNPs), transfersomes, ethosomes, and niosomes, have been developed because the lipid composition of epidermal membranes and lipid-based nanocarriers are so similar. In addition to having superior biocompatibility, these nanocarriers have improved skin-penetrating capabilities that enable therapeutic drugs to successfully pass through the stratum corneum and reach deeper skin layers, enhancing drug penetration and therapeutic results (Shah et al., 2012).

- **Liposomes**

First described by Bangham et al. in 1965, liposomes are spherical vesicles mostly made of natural and/or synthetic phospholipids distributed in an aqueous media (Bangham et al., 1965). Because of their special amphiphilic structure, which consists of hydrophilic head groups and hydrophobic lipid tails organized in bilayer membranes, they can encapsulate lipophilic substances within the lipid bilayer and hydrophilic medicines within their watery core (Allen and Cullis, 2013). Small unilamellar vesicles (SUVs; 25–50 nm), large unilamellar vesicles (LUVs; 50–500 nm), and multilamellar vesicles (MLVs; 500–10,000 nm) are the three main categories of liposomes based on their size and quantity of lipid bilayers.

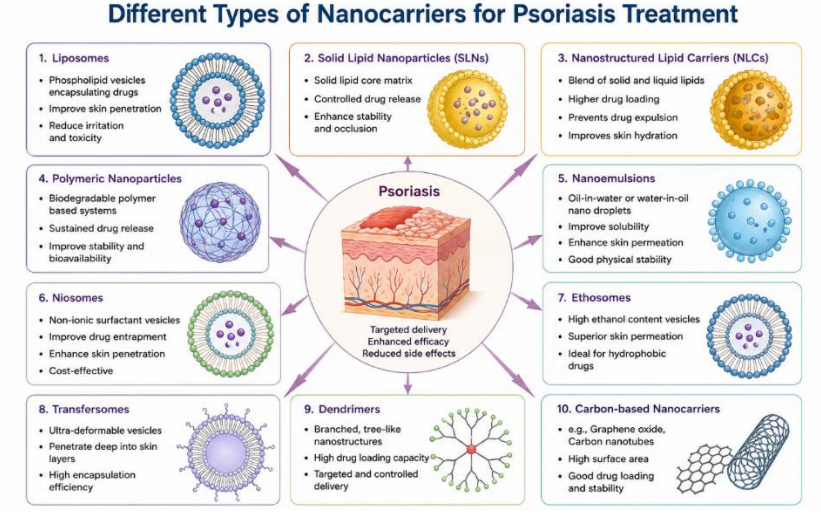

Image 1: Different types of Nanocarriers for Psoriasis Treatment

- **Solid Lipid Nanoparticles**

Solid lipid nanoparticles (SLNs) were first presented as nanosized spherical particles by Gasco and Müller in 1991 as an alternative lipid-based particulate drug delivery platform. In contrast to traditional liposomes, SLNs are made with lipids that stay solid at physiological and room temperature, as well as suitable emulsifying or surfactant agents to stabilize the lipid dispersion (Woo et al., 2014; Amoabediny et al., 2018).

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Table 3: Studies on Solid Lipid Nanoparticles (SLNs) for Topical Psoriasis Treatment

Study	Drug(s) Encapsulated	SLN Preparation/ Approach	Key Findings	Outcome/ Significance
Fang et al., 2008	General SLN systems	Investigation of skin penetration mechanisms	SLNs formed a hydrophobic film on the skin surface, producing an occlusion effect that increased skin hydration and reduced transepidermal water loss.	Enhanced transdermal drug penetration and improved delivery of therapeutic agents into psoriatic lesions.
Sonawane et al., 2014	Betamethasone dipropionate (BD) and Calcipotriol (CT)	Hot-melt extrusion combined with high-shear homogenization	BD-CT-loaded SLNs significantly enhanced dermal absorption of both drugs and inhibited excessive keratinocyte proliferation in rat and human skin models.	Improved antipsoriatic efficacy compared with conventional formulations.

- **Nanostructured Lipid Carriers**

One of the most popular and successful immunosuppressive medications for treating moderate-to-severe psoriasis is methotrexate (MTX), which is usually given orally or intravenously. However, long-term systemic medication is frequently linked to serious side effects, such as liver cirrhosis, hepatotoxicity, anorexia, and bone marrow suppression.

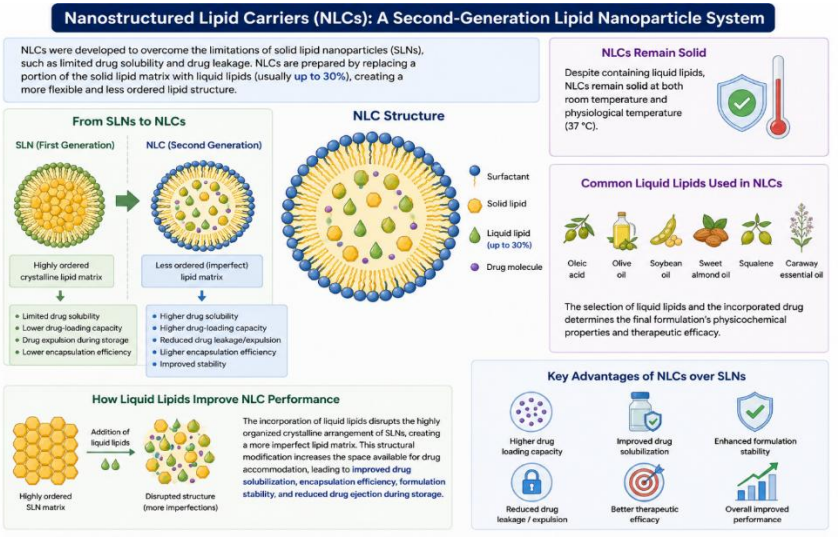

Image 2: Nanostructured Lipid Carriers: A Second Generation Lipid Nanoparticle system

As a safer option, topical MTX delivery has been investigated. However, because of the drug's low penetration of the tightly compacted stratum corneum (SC) that characterizes psoriatic skin, traditional topical MTX formulations have shown little therapeutic efficacy.

- **Transfersomes**

First created by Cevc and Blume in 1992, transfersomes—also referred to as elastic or ultra-deformable liposomes—were later patented by the German business IDEA AG (Cevc and Blume, 1992). Phospholipids, edge activators (EAs), water, and a tiny quantity of ethanol (usually less than 10%) acting as a vehicle make up the majority of these vesicular carriers (Fernández-García et al., 2020).

Table 3: Experimental Studies on Transfersomes for Psoriasis Treatment

Study	Drug/Active Agent	Transferosome Composition	Key Findings	Therapeutic Significance
Jain et al., 2003	Dexamethasone	Transferosomes prepared using different edge activators (EAs): Sodium deoxycholate (SD), Tween 80, and Span 80	Span 80-based transferosomes exhibited the highest deformability and drug entrapment efficiency, while Tween 80-based vesicles showed the lowest deformability.	Demonstrated that the type and concentration of EA significantly influence vesicle flexibility, drug loading, and skin penetration.
Gizaway et al., 2017a	Betamethasone Dipropionate (BD)	Phosphatidylcholine (PC) combined with SD or Tween 80 as edge activators	Optimized formulation showed particle size of 242.8 ± 1.2 nm and remained stable for at least six months at 4°C and 25°C.	Enhanced stability and suitability for long-term storage.

- **Ethosomes**

Phospholipids with a high concentration of alcohol distributed in an aqueous medium are the main components of ethosomes, which are sophisticated ultra-deformable nano vesicular systems. They were initially presented as a new carrier for improved transdermal medication delivery by Touitou and associates in 1996 (Touitou et al., 2000).

Topical application of the MTX-SA-ethosomal gel dramatically decreased the Psoriasis Area and Severity Index (PASI) score in an imiquimod (IMQ)-induced psoriasis model, restoring nearly normal skin architecture with just slight residual keratosis. These findings highlight the potential of ethosomal systems as efficient carriers for enhancing topical administration and therapeutic benefits in the treatment of psoriasis.

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- **Niosomes**

In contrast to liposomes, niosomes are vesicular drug delivery systems made of cholesterol and self-assembled non-ionic amphiphilic surfactants organized into a bilayer membrane with an overall neutral charge (Fang et al., 2008). Niosomes have a number of benefits over traditional liposomal carriers, such as reduced particle size, better uniformity, and increased reproducibility. Furthermore, the addition of non-ionic surfactants like Spans and Tweens gives niosomes advantageous properties like high stability, superior biocompatibility, and cost-effectiveness, making them appropriate for large-scale pharmaceutical manufacture (Lakshmi et al., 2007).

Non-ionic surfactants can interact with the stratum corneum during psoriasis treatment, changing its compact structure and increasing its permeability. In the stratum corneum and epidermal layers, this impact encourages increased drug retention and local drug concentrations (Sinico and Fadda, 2009). Additionally, the skin's moisture condition makes it easier for niosomal vesicles to diffuse through the stratum corneum. As a result, the concentration gradient created during vesicle adherence to or fusion with the skin surface significantly controls the degree of niosomal penetration, allowing for improved transdermal and topical medication administration.

A similar approach was used with acitretin, a systemic retinoid that is only used for severe psoriasis that is resistant to treatment due to its serious side effects, including its teratogenic potential. Using the thin-film hydration technique, Abu Hashim et al. created acitretin-loaded niosomes made of Span 60 and cholesterol (Abu Hashim et al., 2018).

- **Nanofibers**

Because of their unusually high surface area-to-volume ratio, improved porosity, advantageous mechanical properties, and flexible functionalization possibilities when compared to traditional microfibrous materials, nanofibers have become particularly useful drug delivery platforms. Their interconnected scaffolds, which are structurally similar to the native extracellular matrix, offer the perfect conditions for gas exchange, fluid absorption, and moisture regulation—all of which are advantageous for wound healing and skin regeneration (Rasouli et al., 2019).

- **Other Nanocarriers**
  - **Micelles**

Micelles are mainly used in dermatological drug delivery to improve the stability, aqueous solubility, and skin penetration of medicinal medicines that are poorly soluble in water. Research has indicated that the surface charge of micellar systems contributes significantly to transdermal transport by enabling interactions with the stratum corneum (SC), particularly its keratin fibrils and helical filaments, and by

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encouraging the fluidization of SC lipids. Drug penetration through the epidermal barrier may be greatly impacted by these interactions.

- **Nanoemulsions**

Nanocolloidal drug delivery systems called nanoemulsions (NEs) are made up of droplets that are usually between 20 and 500 nm in diameter. They are created by dispersing two immiscible liquids—typically water and oil—into a kinetically stable system in which there is no discernible phase separation. Oil-in-water (o/w), water-in-oil (w/o), and bicontinuous nanoemulsions are the three primary varieties of nanoemulsions, depending on their composition and intended use. High-energy emulsification, low-energy emulsification, or a mix of the two methods can be used to prepare them.

- **Nanogels**

Nanogels, which are created when hydrogels are designed at the nanoscale, offer greatly increased mechanical strength and better drug delivery effectiveness along with decreased swelling behavior. Because of its high drug-loading efficiency, homogenous particle distribution, customizable size, ease of production, and low toxicity, nanogels are used as drug carriers more frequently than traditional hydrogels. Nanogels are attractive platforms for the targeted and regulated delivery of medicinal medicines because of these benefits. Nanogels made from synthetic or natural polymers can be roughly classified as either chemically or physically crosslinked based on the type of crosslinked networks they have.

Physical Transdermal Drug Delivery Systems

- **Non-invasive Delivery**
  - **Iontophoresis**

Iontophoresis (IP) is a non-invasive drug delivery method that uses a low-level electric current, usually between 0.3 and 0.5 mA/cm², to help move ionic drug molecules across the skin (Fukuta et al., 2020). This method uses a programmed electrical system made up of two electrodes to precisely regulate drug administration. The active electrode is the electrode that contains the drug formulation, and the electrical circuit is completed by the return electrode, which is placed close by. Current density, pH, drug concentration, molecule size, and the kind of current application—continuous or pulsed—all affect how effective iontophoresis is (Wang et al., 2021).

- **Invasive Delivery**
  - **Fractional Laser Ablation**

Laser technology, an acronym for Light Amplification by Stimulated Emission of Radiation, enhances transdermal drug delivery by temporarily modifying the skin barrier, thereby facilitating the penetration and absorption of therapeutic agents. Traditional ablative lasers, which treat the entire skin surface, are often associated with

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adverse effects such as erythema, edema, and pain. To minimize these complications, fractional laser ablation (FLA) has been developed as an advanced alternative. In this technique, laser energy is divided into numerous microscopic beams that generate thousands of narrow and deep channels within the skin. By raising the local tissue temperature above 100°C, these microbeams vaporize intracellular water and selectively ablate targeted tissue regions.

- **Microneedle**

By using arrays of tiny needles organized on a tiny patch to deliver medicinal substances into particular skin layers, microneedle technology combines the benefits of transdermal patches with hypodermic injections. According to Waghule et al. (2019), when these micron-sized needles are applied, they form several microchannels across the stratum corneum, allowing for improved medication delivery with no discomfort or tissue damage. Microneedles can be generically classified into solid, coated, dissolving, hollow, and hydrogel kinds based on their design and mechanism of action.

Microneedles are typically thought of as a minimally intrusive and almost painless medication delivery method, despite the fact that they are made up of many needle-like projections. They can only penetrate the skin's outer layers due to their little size; they are unable to reach the deeper dermal areas where pain receptors are mostly found. As a result, using microneedles allows for efficient transdermal drug administration with minimal to no discomfort.

Microneedles have a number of drawbacks despite their many benefits. Because of their tiny size, needle fracture can sometimes happen during application, which raises questions about the skin's ability to retain fractured pieces. Furthermore, vulnerable people may experience allergic reactions, hypersensitivity, or skin irritation, which could limit their use. In order to overcome these obstacles, current research concentrates on creating cutting-edge materials, especially biodegradable and dissolvable polymers, which can improve performance, increase safety, and reduce the possibility of negative side effects related to microneedle-based drug delivery systems (Waghule et al., 2019).

References

1. Abu Hashim, I. I., II, Abo El-Magd, N. F., El-Sheakh, A. R., Hamed, M. F., and Abd El-Gawad, A. E. H. (2018). Pivotal Role of Acitretin Nanovesicular Gel for Effective Treatment of Psoriasis: Ex Vivo-In Vivo Evaluation Study. Int.
2. J. Nanomedicine 13, 1059–1079. doi:10.2147/IJN.S156412 Afsharian, Y. P., and Rahimnejad, M. (2021). Bioactive Electrospun Scaffolds for Wound Healing Applications: A Comprehensive Review. Polym. Test. 93, 106952. doi:10.1016/j.polymertesting.2020.106952
3. Agrawal, U., Gupta, M., and Vyas, S. P. (2015). Capsaicin Delivery into the Skin with Lipidic Nanoparticles for the Treatment of Psoriasis. Artif. Cell Nanomedicine, Biotechnol. 43 (1), 33–39. doi:10.3109/21691401.2013.832683

ISBN: 978-93-49468-33-7

4. Agrawal, Y., Petkar, K. C., and Sawant, K. K. (2010). Development, Evaluation and Clinical Studies of Acitretin Loaded Nanostructured Lipid Carriers for Topical Treatment of Psoriasis. Int. J. Pharm. 401 (1-2), 93–102. doi:10.1016/j.ijpharm.2010.09.007

5. Agrawal, Y. O.,Mahajan, U. B.,Mahajan, H. S., and Ojha, S. (2020). Methotrexate-Loaded Nanostructured Lipid Carrier Gel Alleviates Imiquimod-Induced Psoriasis by Moderating Inflammation: Formulation, Optimization,

5. Characterization, In-Vitro and In-Vivo Studies. Ijn Vol. 15, 4763–4778.doi:10.2147/ijn.s247007

6. Ahmadi, F., McLoughlin, I. V., Chauhan, S., and ter-Haar, G. (2012). Bio-effects and Safety of Low-Intensity, Low-Frequency Ultrasonic Exposure. Prog. Biophys. Mol. Biol. 108 (3), 119–138. doi:10.1016/j.pbiomolbio.2012.01.004

7. Ahmed Saeed Al-Japairai, K., Mahmood, S., Hamed Almurisi, S., Reddy Venugopal, J., Rebhi Hilles, A., Azmana, M., et al. (2020). Current Trends in Polymer Microneedle for Transdermal Drug Delivery. Int. J. Pharmaceutics 587, 119673. doi:10.1016/j.ijpharm.2020.119673

8. Ajeeshkumar, K. K., Aneesh, P. A., Raju, N., Suseela, M., Ravishankar, C. N., and Benjakul, S. (2021). Advancements in Liposome Technology: Preparation Techniques and Applications in Food, Functional Foods, and Bioactive

9. Delivery: A Review. Compr. Rev. Food Sci. Food Saf. 20 (2), 1280–1306. doi:10.1111/1541-4337.12725

10. Alavi, M., Karimi, N., and Safaei, M. (2017). Application of Various Types of Liposomes in Drug Delivery Systems. Adv. Pharm. Bull. 7 (1), 3–9. doi:10.15171/apb.2017.002

11. Albanese, A., Tang, P. S., and Chan, W. C. W. (2012). The Effect of Nanoparticle Size, Shape, and Surface Chemistry on Biological Systems. Annu. Rev. Biomed. Eng. 14, 1–16. doi:10.1146/annurev-bioeng-071811-150124

12. Ali, M. F., Salah, M., Rafea, M., and Saleh, N. (2008). Liposomal Methotrexate Hydrogel for Treatment of Localized Psoriasis: Preparation, Characterization and Laser Targeting. Med. Sci. Monit. 14 (12), Pi66–74.

13. Aljamal, R., and Harrison, D. (2008). Beta1 Integrin in Tissue Remodelling and Repair: from Phenomena to Concepts. Pharmacol. Ther. 120 (2), 81–101. doi:10.1016/j.pharmthera.2008.07.002

14. Allen, T. M., and Cullis, P. R. (2013). Liposomal Drug Delivery Systems: from Concept to Clinical Applications. Adv. Drug Deliv. Rev. 65 (1), 36–48. doi:10.1016/j.addr.2012.09.037

ISBN: 978-93-49468-33-7