ZITA MEDICAL MANAGEMENT

www.hsmc.gr/en/pharmakeftiki-journal/

PHARMAKEFTIKI, 37, 2S, 2025 | 484-487 REVIEW

https://doi.org/10.60988/p.v37i2S.271

Applications of nanoparticles in the transdermal delivery of chemotherapy against breast cancer: a mini-review

Laila A. Alwan[1,*], Shaimaa Nazar Abd Alhammid[2]

[1]Diyala Health Department, Ministry of Health, Baghdad, Iraq
[2]Department of Pharmaceutics, College of Pharmacy, University of Baghdad, Baghdad, Iraq

KEY WORDS:
application; breast cancer; chemotherapeutics; nanoparticles; transdermal

ARTICLE INFO:
Received: January 24, 2025
Revised: February 21, 2025
Accepted: February 21, 2025
Available online: October 10, 2025

ABSTRACT

Transdermal administration represents a promising drug delivery strategy due to its non-invasive nature and potential for controlled, sustained release. By circumventing hepatic first-pass metabolism, it may reduce the need for excessive dosing and enhance therapeutic efficacy. However, the transdermal delivery of chemotherapeutic agents for breast cancer remains challenging, primarily due to the poor skin permeability of most anticancer drugs, which typically exhibit high molecular weight and limited lipid solubility. This mini-review critically examines recent advances in nanoparticle-based systems designed to facilitate transdermal chemotherapy for breast cancer. We categorize the types of nanoparticles employed, discuss their mechanisms of action and therapeutic advantages, and outline future directions for research and clinical translation.

*** CORRESPONDING AUTHOR:**
Laila A. Alwan, Diyala Health Department, Ministry of Health, Baghdad, Iraq;
e-mail: laila.abd2200p@copharm.uobaghdad.edu.iq

1. Introduction

Most transdermal formulations currently available utilize small molecules with a molecular weight below 500 Da and moderate lipophilicity. Transdermal drug delivery offers several advantages, including ease of administration and discontinuation, avoidance of injections and hospitalizations, and protection against drug degradation caused by gastric pH, enzymatic activity, or hepatic metabolism[1]. A strategy to enhance transdermal drug delivery involves the use of nanoparticles and their derivatives. The morphology, size, and surface characteristics of nanoparticles are key determinants of their functionalization with targeting ligands[2].

Recent studies into the transdermal chemotherapy for breast cancer have yielded promising outcomes,

PHARMAKEFTIKI, 37, 2S, 2025 | 484-487

owing to the unique physiological architecture of the breast tissue. The presence of subcutaneous and retromammary adipose tissue, along with internal lymphatic circulation, may facilitate broader distribution of transdermally administered agents. Moreover, the concept of localized transdermal delivery suggests a reduction in systemic adverse effects and an increase in site-specific drug concentration. Such formulations may also prove beneficial in post-radiation and post-surgical contexts[3].

2. Types of nanoparticles used in transdermal delivery (Table 1)

2.1. Vesicular nanocarriers

Vesicular nanocarriers (including liposomes, niosomes, transferosomes, spanlastics, and ethosomes) have emerged as preferred platforms for medicinal delivery. Numerous liposome-based pharmaceuticals are currently approved for clinical use. Liposomes have been proposed as drug delivery systems that enhance therapeutic efficacy while minimizing toxicity. Their biocompatibility and prolonged circulation half-life make them attractive candidates for cancer therapy. However, liposomes are structurally fragile; upon traversing the skin, they tend to adhere to intracellular membranes, leading to phospholipid-associated body collapse and leakage of encapsulated agents. This limits their ability to deliver active compounds to deeper skin layers[4]. Consequently, the use of flexible liposomes – also referred to as "transformable" liposomes – has become a pivotal strategy for achieving effective transdermal drug delivery[5].

2.2. Lipid nanoparticles

Lipid nanoparticles (including solid lipid nanoparticles and nanostructured lipid carriers) are well-suited for transdermal applications. These systems can be engineered in various sizes, and their surface polarity can be modulated to enhance skin penetration. The mechanical flexibility of lipid nanoparticles enables deeper dermal penetration from the epidermal layer[6,7].

2.3. Polymeric nanoparticles

Polymeric nanoparticles (including polymeric micelles and dendrimers) can modulate drug activity, regulate release kinetics, and extend drug residence time within the skin. These nanoparticles serve as reservoirs for lipophilic drugs, thereby facilitating their deposition in the stratum corneum and controlling their transdermal diffusion[8,9].

2.4. Inorganic nanoparticles

Inorganic nanoparticles (including metallic nanoparticles, metal oxide nanoparticles, silica nanoparticles, and quantum dots) exhibit higher cytotoxicity in malignant cell lines compared to healthy cells. Proposed mechanisms of cytotoxicity include reactive oxygen species generation, mitochondrial membrane permeabilization, and targeted DNA cleavage, culminating in cancer cell death *via* necrosis, autophagy, or apoptosis[10]. Chemotherapeutic formulations incorporating these nanoparticles can be topically applied using appropriate excipients and techniques in order to enhance skin permeability.

3. Mechanism of transdermal delivery

Nanoparticles are engineered in order to improve drug penetration through the skin *via* mechanisms such as passive diffusion, follicular transport, and active targeting. Key strategies include: (i) microneedle arrays (which create microchannels in the stratum corneum so as to facilitate deeper nanoparticle penetration), (ii) chemical penetration enhancers (such as surfactants and fatty acids, which disrupt the skin barrier in order to promote absorption), and (iii) sonophoresis and electroporation (which employ ultrasound or electrical pulses in order to transiently increase skin permeability and enhance nanoparticle delivery)[3].

4. Advantages of nanoparticle-based transdermal delivery

The benefits of nanoparticle-mediated transdermal delivery include: (i) enhanced permeability (as nano-

PHARMAKEFTIKI, 37, 2S, 2025 | 484-487

Table 1. Examples of studies on nanoparticle-based transdermal chemotherapeutic systems for the treatment of breast cancer.

Nanoparticle type	Chemotherapeutic agent	Mechanism / features	Reference
Spanlastics	Letrozole and quercetin	Enhanced skin permeation and sustained drug release; decreased drug resistance	Mekkawy *et al.*[5]
Solid lipid nanoparticles	Paclitaxel	Enhanced transdermal delivery of paclitaxel, improving drug stability and controlled release through the skin	Jiang *et al.*[6]
Nanostructured lipid carriers	Tamoxifen	Improved transdermal permeation of tamoxifen, providing a controlled release system for breast cancer treatment	Sani *et al.*[7]
Polymeric nanoparticles	5-Fluorouracil	Increased skin permeation of 5-fluorouracil, allowing for sustained and controlled drug release in breast cancer therapy	Dongsar *et al.*[8]
Polymeric nanoparticles	Anastrozole	Facilitated transdermal delivery and controlled release through the skin	Altameemi and Abd-Alhammid[9]
Gold nanoparticles	Methotrexate	Enhanced transdermal delivery of methotrexate, increasing drug penetration and accumulation in breast cancer cells	Mukhtar *et al.*[10]
Superparamagnetic iron oxide nanoparticles	Doxorubicin	Facilitated transdermal delivery of doxorubicin, enhancing skin penetration and targeting breast cancer cells	Jiang *et al.*[6]

particles improve drug solubility and diffusion across the skin), (ii) sustained release (enabling controlled drug delivery and reduced systemic toxicity), (iii) targeted therapy (wherein functionalized nanoparticles bearing ligands or antibodies selectively accumulate in cancerous tissues *via* active and passive targeting mechanisms), (iv) reduced side effects (due to the avoidance of hepatic first-pass metabolism), and (v) non-invasive administration (which improves patient compliance relative to intravenous chemotherapy)[6].

5. Limitations and challenges

Despite its promise, nanoparticle-based transdermal drug delivery faces several obstacles[4]: (i) the skin's barrier function, particularly the stratum corneum, limits drug permeability, (ii) formulation stability, as maintaining nanoparticle integrity within transdermal systems is essential, (iii) scalability and cost, with manufacturing and commercialization presenting significant challenges, and (iv) long-term safety, as potential toxicity and immunogenicity require further investigation.

6. Anti-cancer properties of nanoparticles: recent innovations

Nanoparticles offer site-specific drug delivery capabilities, and recent innovations include[3]: (i) hybrid nanoparticles, which integrate multiple therapeutic functionalities into a single platform, (ii) smart response systems, which release drugs in response to biological stimuli for precise dosing, and (iii) enhanced imaging modalities, wherein nanoparticles serve as contrast agents to improve cancer diagnosis and treatment monitoring.

7. Future perspectives

Ongoing research aims to optimize nanoparticle formulations for improved efficacy and reduced limitations. Emerging modalities (such as microneedle-assisted delivery and bio-responsive nanocarriers) show potential in overcoming the skin's barrier properties. Further clinical trials are essential in order to be able to translate these advances into practical therapeutic solutions.

8. Conclusion

Nanoparticles represent a promising modality for

transdermal chemotherapy in breast cancer, offering improved therapeutic outcomes and reduced systemic toxicity. Nonetheless, comprehensive research is needed in order to address current limitations and ensure a safe and effective clinical implementation.

Acknowledgements

The authors gratefully acknowledge the Department of Pharmaceutics of the College of Pharmacy of the University of Baghdad.

Conflicts of interest

None exist.

ORCIDs

0009-0003-7198-5177 (L.A. Alwan); 0000-0002-6650-1997 (S.N. Abd Alhammid)

References

1. Fareed N.Y., Kassab H.J. Diacerein loaded novasome for transdermal delivery: preparation, *in vitro* characterization and factors affecting formulation. *Iraqi J. Pharm. Sci.* 32(s), 214–224, 2023. DOI: 10.31351/vol32isssuppl.pp214-224
2. Salih O.S., Al-Akkam E.J. Preparation, *in vitro*, and *ex vivo* evaluation of ondansetron loaded invasomes for transdermal delivery. *Iraqi J. Pharm. Sci.* 32(3), 71–84, 2023. DOI: 10.31351/vol32iss3pp71-84
3. Mukherjee D., Raikwar S. Recent update on nanocarrier(s) as the targeted therapy for breast cancer. *AAPS PharmSciTech* 25(6), 153, 2024. DOI: 10.1208/s12249-024-02867-x
4. Khan S.U., Ullah M., Saeed S., Saleh E.A.M., Kassem A.F., Arbi F.M., *et al.* Nanotherapeutic approaches for transdermal drug delivery systems and their biomedical applications. *Eur. Polym. J.* 207, 112819, 2024. DOI: 10.1016/j.eurpolymj.2024.112819
5. Mekkawy A.I., Eleraky N.E., Soliman G.M., Elnaggar M.G., Elnaggar M.G. Combinatorial therapy of letrozole- and quercetin-loaded spanlastics for enhanced cytotoxicity against MCF-7 breast cancer cells. *Pharmaceutics* 14(8), 1727, 2022. DOI: 10.3390/pharmaceutics14081727
6. Jiang T., Xu G., Chen G., Zheng Y. He B., Gu Z. Progress in transdermal drug delivery systems for cancer therapy. *Nano Res.* 13, 1810–1824, 2020. DOI: 10.1007/s12274-020-2664-5
7. Sani A., Pourmadadi M., Shaghaghi M., Eshaghi M.M., Shahmollaghamsary S., Arshad R., *et al.* Revolutionizing anticancer drug delivery: exploring the potential of tamoxifen-loaded nanoformulations. *J. Drug Deliv. Sci. Technol.* 86, 104642, 2023. DOI: 10.1016/j.jddst.2023.104642
8. Dongsar T.T., Dongsar T.S., Gupta N., Almalki W.H., Sahebkar A., Kesharwani P. Emerging potential of 5-fluorouracil-loaded chitosan nanoparticles in cancer therapy. *J. Drug Deliv. Sci. Technol.* 82, 104371, 2023. DOI: 10.1016/j.jddst.2023.104371
9. Altameemi K.K.A., Abd-Alhammid S.N. Anastrozole nanoparticles for transdermal delivery through microneedles: preparation and evaluation. *J. Pharm. Negat. Results* 13(3), 974–980, 2022. DOI: 10.47750/pnr.2022.13.03.152
10. Mukhtar M., Ezra Manicum A.L., Shojaei Barjouei M., Eshaghi Malekshah R., Behzadmehr R., Rahdar A., *et al.* Nanocarriers for methotrexate delivery/codelivery in the frame of cancer diagnostics and treatment: a review. *Front. Biomater. Sci.* 2, 1200670, 2023. DOI: 10.3389/fbiom.2023.1200670

HOW TO CITE:
Alwan L.A., Abd Alhammid S.N. Applications of nanoparticles in the transdermal delivery of chemotherapy against breast cancer: a mini-review. *Pharmakeftiki* 37(2s), 484-487, 2025.
https://doi.org/10.60988/p.v37i2S.271