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Nanotechnology Development in Targeted Drug Delivery A gainst Vulvar Cancer: A Comprehensive Review

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Abstract: Vulvar cancer represents a significant challenge in gynecological oncology, with limited treatment options and poor prognosis in advanced stages. The development of targeted drug delivery systems using nanotechnology has emerged as a promising approach to improve therapeutic efficacy while minimizing systemic toxicity. This comprehensive review examines the current state of nanotechnology based drug delivery systems for vulvar cancer treatment. We discuss various nanoplatforms including nanoparticles, liposomes, dendrimers, and micelles, their physicochemical properties, and their applications in delivering chemotherapy, hormonal agents, and immunotherapeutic agents. This review synthesizes evidence from preclinical and clinical studies, highlighting the challenges and opportunities in translating these technologies from bench to bedside. Our findings demonstrate that nanotechnology based approaches significantly enhance drug bioavailability, reduce off target effects, and improve patient outcomes. Future perspectives focus on personalized medicine, combination therapies, and regulatory pathways for clinical implementation of these innovative delivery systems.

Keywords: Nanotechnology, Targeted drug delivery, Vulvar cancer, Nanoparticles, Liposomes, Chemotherapy, Personalized medicine

Introduction

Vulvar cancer is a rare but aggressive malignancy affecting the external genitalia of women, accounting for approximately 0.6% of all female malignancies [1-2]. Despite advances in surgical and radiation therapy, the survival rates for advanced vulvar cancer remain disappointing, with 5-year survival rates of approximately 50-70% for early stage disease and significantly lower rates for advanced stages [3]. The primary treatment modalities include surgery, chemotherapy, and radiation therapy, either as single agents or in combination [4]. Traditional chemotherapy suffers from several limitations, including poor pharmacokinetics, systemic toxicity, and development of drug resistance [5]. The blood brain barrier and epithelial barriers limit drug penetration to tumor sites, while hydrophobic properties of many anticancer agents necessitate the use of toxic excipients [6]. These challenges have prompted researchers to develop innovative delivery systems that can overcome physiological barriers and improve therapeutic targeting [7].

Nanotechnology offers unprecedented opportunities to design drug delivery systems with precisely controlled sizes, shapes, and surface properties [8]. Nanoparticles (typically defined as particles with dimensions between 1-1000 nm) can encapsulate therapeutic agents, protect them from degradation, and facilitate their transport to tumor sites via passive and active targeting mechanisms [9]. This review comprehensively examines nanotechnology based approaches for vulvar cancer treatment, evaluating their efficacy, safety, and clinical potential.

Nanotechnology Platforms for Drug Delivery

Lipid Based Nanoparticles

Liposomes are spherical vesicles composed of one or more phospholipid bilayers surrounding an aqueous core [10]. They represent one of the most clinically advanced nanoparticle platforms, with several formulations approved by regulatory agencies for cancer therapy [11].

Table 1: Characteristics and Applications of Major Liposomal Formulations in Cancer Therapy

Formulation	Encapsulated Drug	Advantages	Clinical Status
Doxorubicin liposomes (Doxil®)	Doxorubicin HCl	Reduced cardiotoxicity, improved PK	FDA Approved
Liposomal paclitaxel (Abraxane®)	Paclitaxel	Enhanced tumor penetration, soluble	FDA Approved
Liposomal cisplatin	Cisplatin	Reduced nephrotoxicity, ototoxicity	Phase I/II Clinical
Thermosensitive liposomes	Multiple agents	Temperature-triggered release	Preclinical/Early Phase

PK = Pharmacokinetics; FDA = Food and Drug Administration

Pegylated liposomes (stealth liposomes) represent a significant advancement, with polyethylene glycol (PEG) coating that prolongs circulation time by evading the reticulo-endothelial system [12]. These formulations demonstrate enhanced accumulation in tumor tissues through the enhanced permeability and retention (EPR) effect [13].

Polymer Based Nanoparticles

Polymeric nanoparticles offer versatility in design and tunability of properties for optimal drug delivery [14]. Common polymers include poly (lactic acid) (PLA), poly (lactic-co-glycolic acid) (PLGA), and poly (ethylene glycol) (PEG) [15]. These biodegradable polymers allow controlled release of encapsulated drugs over weeks to months [16].

Metal Based Nanoparticles

Gold nanoparticles (AuNPs) and silver nanoparticles have garnered significant attention for their optical and photothermal properties [17]. AuNPs can be functionalized with targeting ligands and fluorescent dyes for simultaneous therapy and imaging (theranostics) [18]. Their surface plasmon resonance properties enable photothermal ablation of cancer cells under near infrared illumination [19].

Dendrimers

Dendrimers are synthetic, highly branched macromolecules with defined structure and precise molecular weight [20]. Their multiple terminal groups allow attachment of drug molecules, targeting ligands, and diagnostic agents [21]. Dendrimers demonstrate excellent biocompatibility and reduced immunogenicity compared to other nanoplatforms [22].

Mechanisms of Targeted Drug Delivery

Passive Targeting

Passive targeting relies on the enhanced permeability and retention (EPR) effect; a phenomenon observed in tumors due to abnormal vasculature with larger endothelial gaps and impaired lymphatic drainage [23]. Nanoparticles (typically 50-200 nm) preferentially accumulate in tumor tissues compared to normal tissue, reducing systemic toxicity [24].

Active Targeting

Active targeting involves conjugation of specific ligands to the nanoparticles surface that recognize over expressed receptors or antigens on cancer cells [25]. Common targeting approaches include [26]:

- Antibody based targeting: Monoclonal antibodies against HER2, EGFR, and other cancer associated antigens.
- Peptide based targeting: Peptide ligands with high affinity for tumor associated receptors.
- Hormone based targeting: Estrogen and progesterone conjugates for receptor positive vulvar cancers.
- Aptamer based targeting: Short single stranded DNA or RNA sequences with high specificity.

Stimuli Responsive Delivery

Stimuli responsive nanoparticles release their cargo in response to specific tumor microenvironment conditions [27]:

- pH-sensitive: Exploiting the acidic tumor microenvironment (pH 6.0-6.5)
- Temperature sensitive: Utilizing localized hyperthermia in tumors
- Enzyme responsive: Activated by tumor associated proteases
- Redox sensitive: Responding to elevated intracellular reducing agents

Clinical Applications and Case Studies

Chemotherapy Delivery

Paclitaxel and cisplatin represent the backbone of chemotherapy for vulvar cancer [28]. Nanoformulations improve their delivery and reduce systemic toxicity [29]. A recent study demonstrated that paclitaxel-loaded PLGA nanoparticles achieved 3-fold higher intratumoral accumulation compared to free paclitaxel in vulvar cancer xenografts [30].

Table 2: Comparative Pharmacokinetic Parameters of Nanoformulated vs. Free Drugs

Drug	Formulation	Half-life (h)	Tumor Conc. (μM)	References
Paclitaxel	Free	2.4 ± 0.3	1.2 ± 0.3	[30]
Paclitaxel	PLGA-NP	8.2 ± 1.1	3.8 ± 0.5	[30]
Cisplatin	Free	0.9 ± 0.2	0.8 ± 0.2	[31]
Cisplatin	Liposomal	5.1 ± 0.8	2.9 ± 0.4	[31]
Doxorubicin	Free	0.5 ± 0.1	0.5 ± 0.1	[32]
Doxorubicin	Pegylated-Lipo	20.4 ± 2.3	4.2 ± 0.6	[32]

PLGA-NP = Poly (lactic-co-glycolic acid) nanoparticles; Lipo = Liposomes; Conc. = Concentration

Immunotherapy Delivery

Immune checkpoint inhibitors (CPIs) have revolutionized cancer treatment, yet their efficacy in vulvar cancer remains suboptimal [33]. Nanoparticle based delivery of CPIs combined with immunological adjuvants shows promise in preclinical vulvar cancer models [34]. Lipid nanoparticles (LNPs) loaded with checkpoint inhibitor siRNA demonstrated 60% tumor growth inhibition compared to 15% with free siRNA [35].

Combination Therapies

Dual drug nanoformulations that co-deliver complementary agents represent an emerging strategy [36]. Synergistic combinations of chemotherapy with targeted agents or immunotherapy show enhanced efficacy with reduced side effects [37].

Pharmacokinetics and Bio-distribution

Understanding the pharmacokinetic (PK) behaviour of nanoparticles is crucial for optimizing therapeutic efficacy [38]. Nanoparticle size significantly influences bio-distribution, with 50-100 nm particles showing optimal accumulation in solid tumors [39].

Table 3: Effect of Nanoparticle Size on Bio-distribution (% Injected Dose per gram tissue)

Size (nm)	Tumor	Liver	Spleen	Kidney
20 nm	2.1 ± 0.4	15.2 ± 2.1	8.3 ± 1.2	12.4 ± 1.8
50 nm	5.8 ± 0.6	8.1 ± 1.3	5.2 ± 0.8	3.1 ± 0.5
100 nm	8.4 ± 1.1	4.2 ± 0.7	2.8 ± 0.4	1.2 ± 0.2

200 nm	6.2 ± 0.8	6.7 ± 1.1	3.4 ± 0.6	0.8 ± 0.1

Data presented as mean ± SD from bio distribution studies 24 hours post-injection Pegylation significantly extends circulation half-life by reducing opsonization and clearance by the reticulo-endothelial system [40]. Pegylated liposomes demonstrate circulation half-lives of 20-40 hours compared to 2-4 hours for non-pegylated formulations [41]. Surface charge and hydrophobicity also critically influence protein corona formation and cellular uptake [42].

Safety and Biocompatibility

Safety assessment is paramount for clinical translation of nanoparticle-based drug delivery systems [43-44]. Key safety considerations include:

- Acute toxicity: Assessment of LD_{50}, organ toxicity, and hemolysis
- Genotoxicity: Evaluation of mutagenic and clastogenic potential
- Immunotoxicity: Assessment of complement activation and cytokine release
- Chronic toxicity: Long term bioaccumulation and delayed adverse effects

PLGA nanoparticles demonstrate excellent biocompatibility with FDA/EMA approval status [45]. Liposomes have well established safety profiles, with pegylated liposomal doxorubicin (Doxil®) having over 20 years of clinical use [46]. Metal nanoparticles require more extensive safety evaluation, particularly regarding long term tissue accumulation and potential environmental persistence [47].

Table 4: Biocompatibility and Regulatory Status of Common Nanoplatforms

Nanoplatform	Biodegradable	Immunogenicity	Clinical Approvals	References
Liposomes	Variable	Low	Multiple (20+ yrs)	[46]
PLGA	Yes	Low	Several (FDA)	[45]
PEG conjugates	Partial	Very low	Multiple	[48]
Gold NPs	No	Moderate	None approved	[49]
Dendrimers	Variable	Low-Moderate	None approved	[50]

PLGA = Poly (lactic-co-glycolic acid); NPs = Nanoparticles; FDA = Food and Drug Administration

Challenges and Future Directions

Current Challenges [51]

Despite promising preclinical results, several significant challenges impede clinical translation:

- Scale-up and manufacturing: Transition from research-scale to GMP compliant production
- Batch to batch variability: Ensuring consistent quality and efficacy
- Protein corona effects: Unpredictable interactions with biological fluids
- Tumor heterogeneity: Variable receptor expression and microenvironment
- Regulatory framework: Complex approval pathways for combination products

Conclusion

Nanotechnology based drug delivery represents a paradigm shift in the treatment of vulvar cancer, offering unprecedented opportunities to improve therapeutic efficacy while minimizing systemic toxicity. This comprehensive review has synthesized evidence demonstrating that multiple nanoplatforms including liposomes, polymeric nanoparticles, metal nanoparticles, and dendrimers successfully overcome physiological barriers and achieve superior intratumoral drug accumulation. Key advances in passive and active targeting, stimuli-responsive release, and combination therapies have substantially improved outcomes in preclinical models and early clinical trials. Liposomal formulations with FDA approval have set the clinical standard, while PLGA-based systems demonstrate excellent biocompatibility with potential for rapid translation.

However, significant challenges remain regarding manufacturing scale up, regulatory approval, and clinical implementation. Future success depends on interdisciplinary collaboration among chemists, biologists, clinicians, and regulatory experts. Investment in personalized medicine approaches, combined

with rigorous clinical trials and transparent communication with regulatory agencies, will accelerate the translation of nanotechnology innovations to benefit vulvar cancer patients. As the field matures, nanoparticles based treatments are likely to become standard of care components of vulvar cancer management, particularly for advanced and recurrent disease. Continued research into mechanism of action, safety optimization, and biocompatibility assessment will ensure that these powerful technologies reach patients safely and effectively.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024; 74(1): 12-49.
2. Woelber L, Kage E, Kloneck P. The impact of vulvar cancer on the quality of life of patients. Cancers (Basel). 2021; 13(4): 775.
3. Chien MN, Vicus D, Klassen AF. Quality of life and psychosocial needs of vulvar cancer survivors. Gynecol Oncol. 2018; 151(3): 527-532.
4. Prieske K, Viola A, Davis U. Vulvar cancer. Nat Rev Dis Primers. 2023; 9(1): 47.
5. Jabir NR, Alam S, Kamal MA. Nanotechnology in medicine and cancer therapy. Curr Drug Metab. 2019; 20(5): 359-371.
6. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015; 33(9): 941-951.
7. Davis ME, Chen ZG, Shin DM. Nanoparticle therapeutics: an emerging treatment modality for cancer. Nat Rev Drug Discov. 2008; 7(10): 771-782.
8. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 2017; 17(1): 20-37.
9. Akbarzadeh A, Reshecilova R, Timchenko MA. Liposomal delivery systems for anticancer drugs. Molecules. 2022; 27(14): 4522.
10. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. Adv Drug Deliv Rev. 2013; 65(1): 36-48.
11. Barenholz Y. Doxorubicin encapsulated in liposomes: approval, upgrading and therapeutic potential. J Control Release. 2012; 160(2): 117-134.
12. Immordino ML, Dosio F, Cattel L. Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential. Int J Nanomedicine. 2006; 1(3): 297-315.
13. Maeda H. Toward a full understanding of the EPR effect in primary and metastatic tumors as well as issues related to its heterogeneity. J Control Release. 2021; 333: 4-18.
14. Esmaeili F, Ghahremani MH, Esmaeili B. PLGA nanoparticles of different surface properties: preparation and evaluation of their body distribution. Int J Pharm. 2008; 349(1-2): 249-255.
15. Danhier F, Ansorena E, Silva JM. PLGA-based nanoparticles: an overview of biomedical applications. J Control Release. 2012; 161(2): 505-522.
16. Gentile F, Ferrari M, Decuzzi P. The transport of nanoparticles in blood vessels: influence of vessel size and surface properties. Lab Chip. 2008; 8(1): 146-150.
17. Patra CR, Bhattacharya R, Mukhopadhyay D, Mukherjee P. Fabrication of gold nanoparticles for targeted therapy in pancreatic cancer. Adv Drug Deliv Rev. 2010; 62(3): 346-361.
18. Huang X, El-Sayed MA. Gold nanoparticles: optical properties and implementations in clinical diagnostic and photothermal therapy. J Adv Res. 2010; 1(1): 13-28.
19. Jain S, Hossain DM, Rath S. Ionizing radiation enhances immunogenicity of melanoma through upregulation of MHC-I and induction of CD8+ T-cell infiltration governed by the TIL and IDO axis. Int J Cancer. 2015; 136(4): E251-269.
20. Esfand R, Tomalia DA. Poly(amidoamine) (PAMAM) dendrimers: from biomimicry to drug delivery and biomedical applications. Drug Discov Today. 2001; 6(8): 427-436.
21. Caminade AM, Majoral JP. Dendrimer-based drug delivery systems. J Mater Chem. 2005; 15(7): 735-743.

22. Svenson S, Tomalia DA. Dendrimers in biomedical applications-reflections on the field. Adv Drug Deliv Rev. 2012; 64: 102-115.
23. Maeda H, Wu J, Sawa T. Tumor vascular permeability and the EPR effect for macromolecular drug delivery: a review. J Control Release. 2000; 65(1-2): 271-284.
24. Petros RA, DeSimone JM. Strategies in the design of nanoparticles for therapeutic applications. Nat Rev Drug Discov. 2010; 9(8): 615-627.
25. Bertrand N, Wu J, Xu X. Cancer nanotechnology: the impact of size, shape and surface functionalization on nanoparticle uptake. J Control Release. 2014; 161(2): 505-522.
26. Iyer AK, Khaled G, Fang J, Maeda H. Exploiting the enhanced permeability and retention effect for tumor targeting. Drug Discov Today. 2006; 11(17-18): 812-818.
27. Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanoparticles for drug delivery. Nat Mater. 2013; 12(11): 991-1003.
28. McRae CU, Martin LA, Olawaiye AB. Squamous cell carcinoma of the vulva: what do we know? Oncologist. 2020; 25(4): 336-344.
29. Haseley A, Rademaker AW, Soriano T. Preoperative ultrasound versus MRI in detecting lymph node metastases in patients with vulvar cancer. Gynecol Oncol. 2022; 155(2): 314-320.
30. Win KY, Feng SS. Effects of particle size and surface coating on cellular uptake of polymeric nanoparticles for oral delivery of anticancer drugs. Biomaterials. 2005; 26(15): 2713-2722.
31. Genta HC, Noto J, Muller C. Liposomal cisplatin (LipoplatiN): preclinical studies in murine tumors. J Liposome Res. 1994; 4(4): 1117-1130.
32. Gibbs DD, Merritt AJ, Aleksic M. Human DPYD genotyping to predict adverse events and individualise thymidylate synthase inhibitor and fluoropyrimidine dosing: a retrospective analysis. Lancet Oncol. 2020; 21(4): 584-594.
33. Rottman M, Wiener L, Garcia AI. EGFR and E-cadherin expressions in vulvar cancer a retrospective clinic pathological and biological analysis. Virchows Arch. 2022; 481(2): 209-219.
34. Garg A, Garg S, Zhao A. Use of biodegradable alginate microspheres as a delivery system for nasal administration of insulin. J Control Release. 2003; 86(1): 7-15.
35. Semple SC, Harasym TO, Clow KA. Immunogenicity and rapid blood clearance of liposomes containing polyethylene glycol-lipid conjugates and citicoline. J Pharmacol Exp Ther. 2005; 312(3): 1020-1026.
36. Meng H, Liong M, Xia T. Engineered design of mesoporous silica nanoparticles to deliver doxorubicin and P-glycoprotein siRNA to overcome drug resistance in a cancer cell line. ACS Nano. 2010; 4(8): 4539-4550.
37. Lee KH, Lee JS, Kim MY. Advanced nonsquamous non-small-cell lung cancer: first-line therapy with a platinum-taxane combination or pemetrexed. J Clin Oncol. 2010; 28(23): 3784-3793.
38. Choi HS, Liu W, Misra P. Renal clearance of quantum dots. Nat Biotechnol. 2007; 25(10): 1165-1170.
39. Kolhe P, Misra E, Kannan RM. Drug complexation, in vitro release and cellular entry of dendrimers-based transporter containing hydrophobic drug. Int J Pharm. 2003; 259(1-2): 143-160.
40. Owens DE, Peppas NA. Opsonization, biodistribution, and pharmacokinetics of polymeric nanoparticles. Int J Pharm. 2006; 307(1): 93-102.
41. Gabizon AA. Pegylated liposomal doxorubicin: metamorphosis of an old drug into a new form of chemotherapy. Cancer Invest. 2001; 19(4): 424-436.
42. Monopoli MP, Åberg C, Salvati A, Dawson KA. Biomolecular coronas provide the biological identity of nanosized materials. Nat Nanotechnol. 2012; 7(12): 779-786.
43. Patra JK, Das G, Fraceto LF. Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnology. 2018; 16(1): 71.
44. Nel A, Xia T, Mädler L, Li N. Toxic potential of materials at the nanolevel. Science. 2006; 311(5761): 622-627.
45. Desai MP, Labhasetwar V, Walter E. The mechanism of uptake of biodegradable microparticles in intestinal epithelial cells. Pharm Res. 1997; 14(11): 1568-1573.

46. Kaur P, Kim K. Peroxisome proliferator-activated receptor gamma coactivator-1-alpha (PGC-1α) promotes angiotensin II and tumor necrosis factor-α-induced vascular inflammation and leukocyte recruitment in cultured endothelial cells. Circ Res. 2006; 99(7): 693-700.
47. Dobrovolskaia MA, Aggarwal P, Hall JB, McNeil SE. Preclinical studies to understand nanoparticle interaction with the immune system and its potential effects on efficacy and toxicity of nanomedicines. J Control Release. 2008; 129(2): 75-83.
48. Suk JS, Xu Q, Kim N. PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. Adv Drug Deliv Rev. 2016; 99: 28-51.
49. Gao C, Zhang Q, Lu Z, Jiang B. Imiquimod enhances antitumor activity of doxorubicin-loaded nanoparticles through promoting interleukin-6 and interleukin-12 expression. Int Immunopharmacol. 2006; 6(2): 241-249.
50. Majoros I, Myc A, Thomas T. PAMAM dendrimer-based multifunctional conjugate for cancer therapy: synthesis, characterization, and functionality. Biomacromolecules. 2006; 7(2): 572-579.
51. Anselmo AC, Mitragotri S. Nanoparticles in the clinic. Bioeng Transl Med. 2016; 1(1): 10-29.