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Review Article

Nano drugs in modern drug delivery: advances, application and economic challenges

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ABSTRACT

Nanotechnology has been an influential advancement across all aspects of science, from mechanical technologies to medicine. One of these benefits and impacts is Nano drugs, which, by leveraging nanotechnology, have brought about a remarkable transformation in the diagnosis and treatment of cancer. These drugs, with features such as high surface-to-volume ratio, active and passive targeting, and responsiveness to tumor stimuli, enhance therapeutic efficacy and reduce side effects. In this article, I aimed to first examine the physicochemical principles and mechanisms of action of nanoparticles, including the enhanced permeability and retention (EPR) effect and molecular targeting. Then, clinically approved Nano drugs such as Doxil® and Abraxane® are analyzed in technical detail. Additionally, emerging technologies like smart multi-stimuli systems and CRISPR-Cas9-based gene editing are discussed. Economic challenges along with engineered solutions are presented, and finally, future prospects, including the integration of artificial intelligence and the development of theranostic systems, are outlined. This article provides a comprehensive review of the advancements in cancer Nano drugs, from basic principles to advanced clinical applications.

***Keywords*:** Nanoparticles, Nano Drug, Drug delivery, Cancer , Nano medicine

1. Introduction

Cancer, as one of the most challenging diseases of our time, affects millions of people worldwide every year. Conventional treatment methods such as chemotherapy and radiotherapy, despite their relative effectiveness, come with severe side effects that diminish patients' quality of life. In this context, nanotechnology has introduced innovative solutions, offering new hope for improving cancer treatment. Nano drugs leverage the unique

characteristics of nanoparticles—including their small size, high active surface area, and chemical modifiability—to enable precise targeting of cancer cells while minimizing damage to healthy tissues.

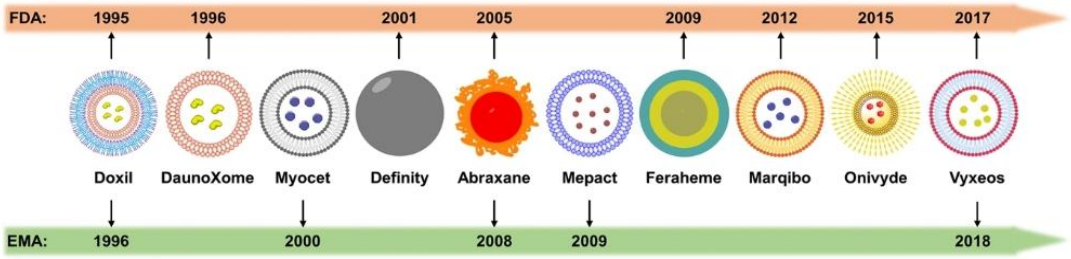

Fig. 1.timeline shows Nano drugs transforming cancer treatment

Recent studies indicate that Nano drugs employ two primary mechanisms for tumor targeting: the enhanced permeability and retention (EPR) effect, which stems from the heterogeneous vascular structure of tumors, and active targeting using specific ligands such as monoclonal antibodies and peptides. Furthermore, recent advancements in nanoparticle engineering have enabled the development of stimuli-responsive systems (e.g., to low pH or specific enzymes). These systems allow for controlled drug release and significantly enhance treatment efficacy.

Despite these achievements, challenges such as protein corona formation, industrial-scale production, and high development costs still require further research. This article aims to comprehensively review recent progress in cancer Nano drugs, from fundamental principles to clinical applications, while examining these challenges and potential solutions to overcome them. Subsequent sections will discuss topics such as drug release kinetics, emerging technologies, and the economic analysis of Nano drug production.

Based on the latest scientific findings and case studies, this article presents a clear picture of the role of Nano drugs in cancer treatment and highlights their potential to revolutionize the future of medicine.

1. Definition and Physicochemical Properties of Nanoparticles

Nanoparticles refer to structures with dimensions of 1-100 nanometers that exhibit unique behaviors due to their extraordinarily high surface-to-volume ratio (approximately 10^8 m^2/m^3) and quantum effects [1]. These characteristics include:

1.1 Advanced Optical and Electronic Properties:

Surface Plasmon Resonance (SPR) phenomenon in metallic nanoparticles such as gold, enabling selective light absorption in the NIR range (700-900 nm) [2]. This property forms the basis for imaging applications and photothermal therapy.

Quantum confinement effect in semiconductor quantum dots (e.g., CdSe/ZnS) that leads to tunable fluorescence emission based on particle size [3].

1.2 Types of Constituent Materials and Specialized Applications:

-Types of Nano-systems: [4]

- Liposomes (phospholipid-based systems)
- Polymeric Nano capsules
- Nano suspensions
- Metallic Nano carriers

Now let's briefly examine some of these systems along with examples of their applications.

- Metallic nanoparticles:

- Gold (AuNPs): In various shapes (spherical, rod-shaped, shell-shaped) for imaging and therapeutic applications [5]

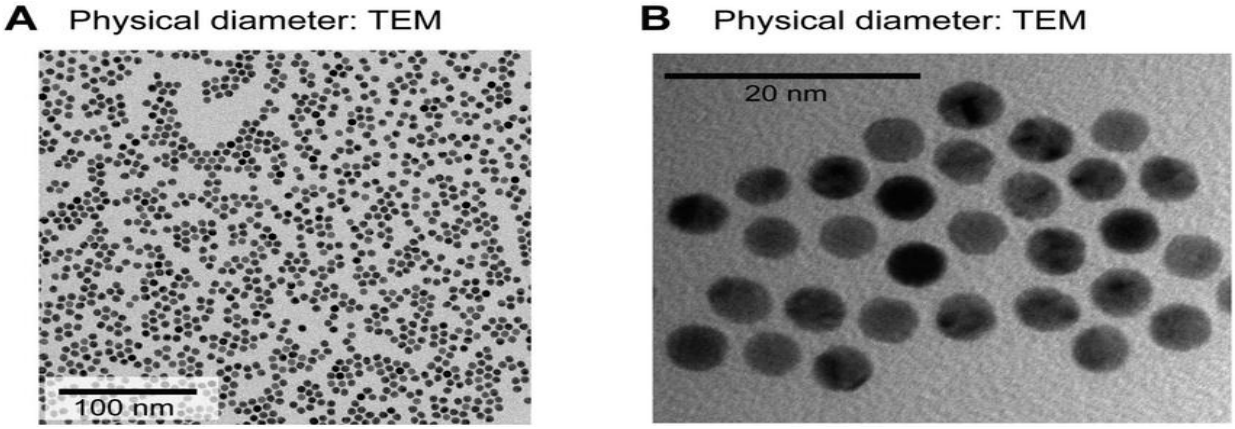

Fig . 2. TEM image of gold nanoparticles with various shapes

- Polymeric nanoparticles:

- PLGA-based systems (poly lactic-co-glycolic acid) with controlled degradation and sustained drug release capabilities [6]
- PAMAM dendrimers with modifiable surface groups for multiple loading [7]

- Lipid-based systems:

- PEGylated liposomes with extended blood circulation stability (up to 72 hours) [8]

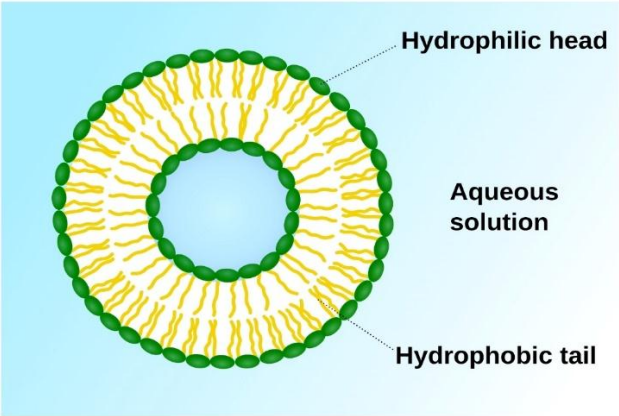

Fig. 3. Schematic of liposome structure with phospholipid bilayer

2. Advanced Molecular-Level Mechanisms

This section discusses "The Role of Technology in Improving Cancer Treatment" and examines technology-driven advancements in cancer treatment methods including photon therapy, charged particle therapy (CPT), and Nano hyperthermia.

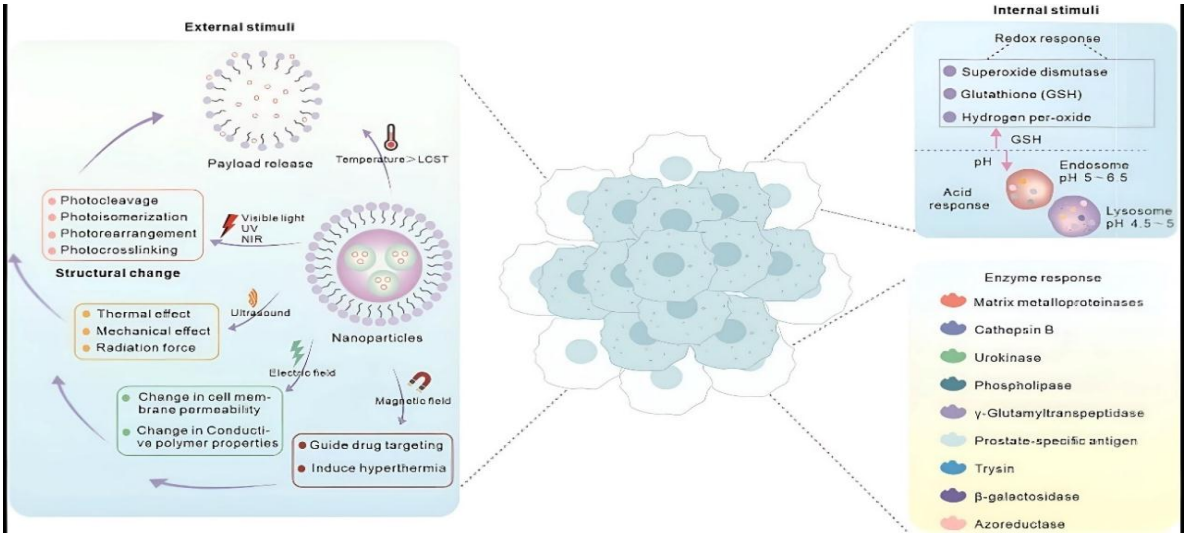

Fig. 4. Stimuli-responsive mechanisms for smart drug delivery systems

2.1 Charged Particle Therapy (CPT):

Due to the physical properties of charged particles, particularly their depth-dose distribution, this method can reduce radiation dose to healthy tissues surrounding the tumor while enabling dose escalation within the tumor. This improves local tumor control and reduces side effects. Carbon ions are particularly suitable for treating resistant tumors due to their lower scattering and higher relative biological effectiveness.

2.2 Nano hyperthermia:

The use of nanoparticles in hyperthermia can enhance thermal effects while protecting healthy tissues. Nanoparticles serve as primary heat sources, creating more localized and safer destructive effects. This method can also be combined with chemotherapy and diagnostic imaging.

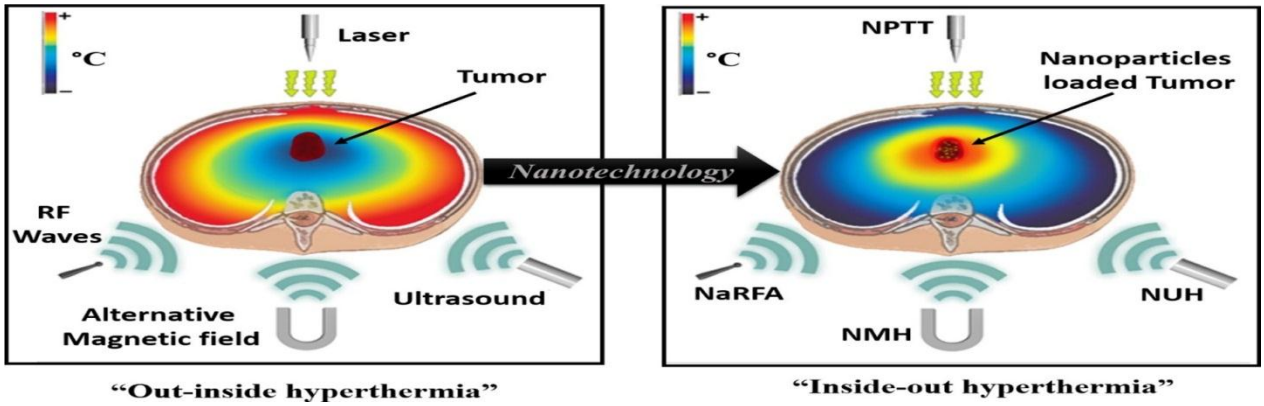

Fig . 5. Nanoparticle-assisted tumor hyperthermia techniques

2.3 Combination of Hyperthermia with Other Methods: Combining hyperthermia with chemotherapy and radiotherapy has shown significant synergistic effects in cancer treatment, increasing the sensitivity of cancer cells to therapy [9].

2.4 Passive Targeting (EPR Effect) with Biological Details

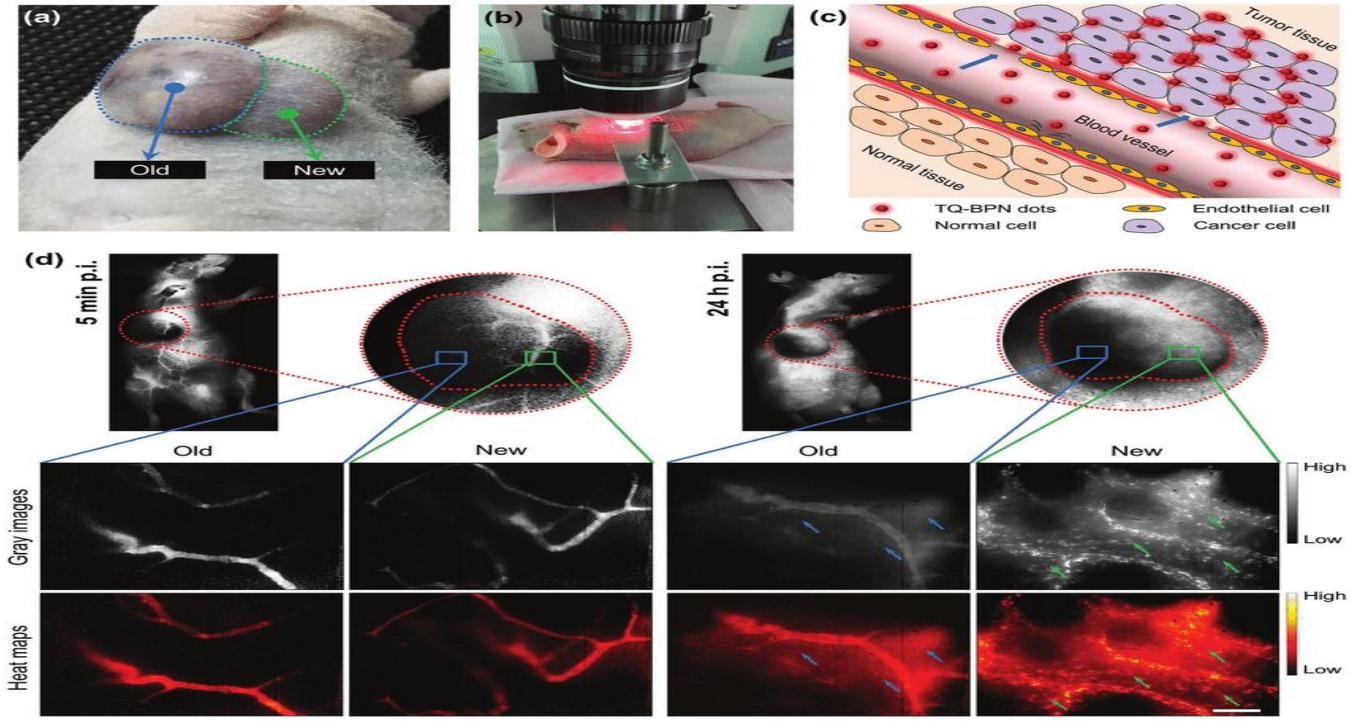

Fig.6. Schematic of smart nanoparticle synthesis for targeted drug/gene delivery

Recent studies indicate that the EPR effect in human tumors is highly heterogeneous and depends on multiple factors including [10]:

- Tumor vascular density (20-200 vessels per mm^2)
- Vascular pore size (200-800 nanometers)[39]
- High interstitial pressure (5-20 mmHg compared to 0-5 mmHg in normal tissue)
- Inefficient lymphatic system (30-50% reduction in lymphatic drainage)

2.5 Active Targeting with Novel Approaches:

- Monoclonal antibodies: Such as trastuzumab (anti-HER2) that binds to membrane receptors [11]
- Targeting peptides: RGD sequence (Arginine-Glycine-Aspartic acid) for integrin αvβ3 in tumor angiogenesis [12]
- DNA/RNA aptamers: With high binding affinity (Kd in nM range) and improved stability [13]

3. Clinically Approved Nano drugs

Now let me briefly introduce to you some of the approved drugs.

Technical and clinical specifications of leading nano drugs:

Table. 1. Comparison of key characteristics of FDA-approved Nano drugs

Parameter	®Doxil	Abraxane®	Onivyde®
Formulation	PEGylated liposome	Nanoalbumin	Liposome
Size (nm)	80-100	130	110
Surface charge (mV)	to 30--50	2-0	+5
Drug loading (%)	8-10	10-12	4.5
Half-life (h)	55	27	39
Clinical application	Ovarian, Kaposi's	Breast, lung	Pancreatic

Comparison of the Efficacy of Doxil® and Free Doxorubicin: [14]

- Study Population: 150 patients with stage III ovarian cancer
- Method ：
  - Group 1: Doxil ® (dose 50mg/m^2 every 4 weeks)

- Group 2: Free doxorubicin (dose 60mg/m² every 3 weeks)

- Results after 6 months:

Parameter	®Doxil	Free Doxorubicin
Complete (%) Response	38	22
Cardiac Toxicity (Grade ≥2) (%)	5	28
Progression-Free Survival (months)	9.2	6.1

4. Emerging Technologies with Clinical Translation Potential

4.1 Multi-Stimuli Responsive Systems [15]:

The new generation of nanoparticles can simultaneously respond to multiple tumor stimuli:

- Low pH (5.5-6.5)

- High reactive oxygen species (ROS) concentration

- Extracellular matrix enzymes (MMP-2/9)

4.2 Advanced Gene Editing Technologies:

- CRISPR-Cas9 Nano carriers: >80% transfer efficiency with reduced toxicity [16]

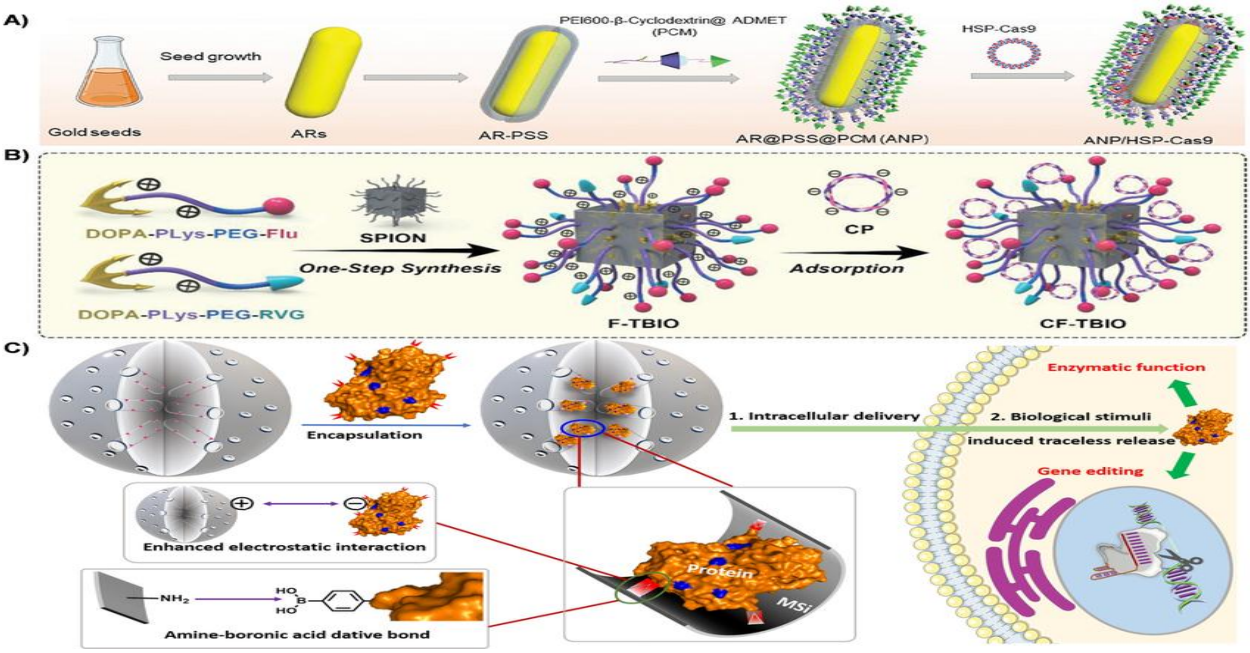

Fig . 7. Analysis of nanoparticle accumulation in cancer vs. normal cells

- RNAi-based systems: siRNA Nano complexes with blood circulation stability up [17]

5. Technical Challenges and Engineered Solutions

5.1 Protein Corona Formation Challenge [18] [42]:

- Serum proteins like albumin and immunoglobulins adsorb onto nanoparticle surfaces [40]
- Innovative solutions:
  - High-density PEG ylation anti-protein adsorption coatings [19]
  - Surface engineering with alternating hydrophobic/hydrophilic peptides

5.2 Industrial-Scale Production Challenges:

- Need for precise parameter control:
  - Size uniformity (PDI < 0.1)
  - Drug loading reproducibility (±2%)
- Production solutions:
  - Automated microfluidic systems with nanometer precision [20]
  - 4D Nano-printing technologies [21]

6. Research-Backed Future Perspectives

6.1 Integration with Artificial Intelligence:

- Computational design of personalized Nano carriers using:
  - Deep Learning algorithms for nanoparticle property prediction [22]
  - Multi-objective optimization for efficacy/toxicity [23]

6.2 Next-Generation Integrated Theranostic Systems [24][41] :

- Multifunctional nanoparticles combining:
  - Multimodal imaging (PET/MRI/optical)
  - Real-time treatment monitoring with biosensors
  - Self-regulating drug release based on biological signals

7. Nano drugs and Chemical Kinetics: From Design to Clinical Performance

7.1 Drug Release Kinetics from Nano carriers:

Kinetic studies show Nano drug release typically follows these models [25]:

- First-order model: Exponential release with rate constant k_1 (for polymeric matrix systems)
- Higuchi model: Diffusion-controlled release (for liposomal systems)
- Korsmeyer-Peppas model: Combined degradation and diffusion (for biodegradable nanoparticles)

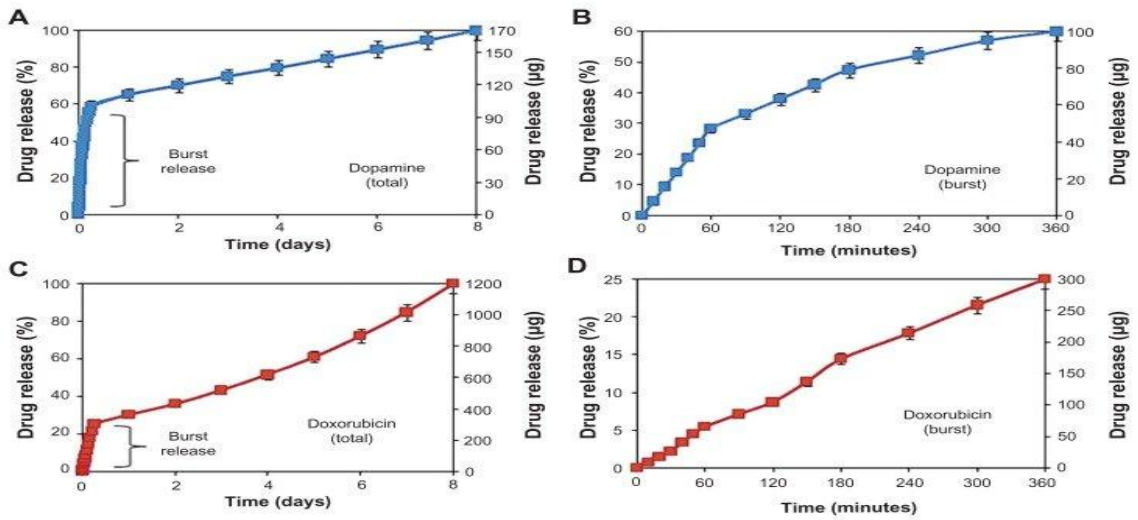

Fig. 8. Drug release kinetics profiles: Burst vs. sustained release of dopamine and doxorubicin

General kinetic equation: $dC/dt = -kC^n$
Where:
- C = Remaining drug concentration
- k = Rate constant
- n = Reaction order (0.5-1.5 for Nano-systems)

7.2 Factors Affecting Release Kinetics[26][27]:

Parameter	Kinetic Impact	Practical Examples
Nanoparticle size	Smaller size → Higher surface area → Faster release	50nm vs 200nm nanoparticles [25]
Polymer nature	Porosity/ crystallinity affects diffusion mechanism	PLGA 50:50 vs 75:25
Environmental pH	Accelerated degradation at acidic pH	Tumor pH (5.5–6.5) release [26]

7.3 Tumor Accumulation Kinetics:

Advanced mathematical models describe nanoparticle accumulation [28]:
- Two-compartment model: Blood circulation ↔ Tumor tissue
- Fractal model: Heterogeneous penetration in tumor matrix

Experimental kinetic data:
- Tumor accumulation half-life: 2-8 hours
- Effective diffusion coefficient ($D_e$ff): 10^{-12} to 10^{-10} cm^2/s

7.4 Metabolism and Clearance Kinetics:

Pharmacokinetic studies show [29]:

- Hepatic clearance: Zero-order for >100nm nanoparticles
- Renal excretion: First-order for <5.5nm nanoparticles
- Biological half-life: 2 hours to 2 weeks depending on surface coating

Table. 2. Kinetic Parameters of Common Nano drugs: [30] [31] [32]

Drug	k_1 (h^{-1})	n	$t_1/_2$ (h)
®Doxil	0.12	0.8	55
Abraxa ®ne	0.25	1.2	27
mRNA-LNPs	0.08	0.6	72

8. Economic Analysis of Nano drug Production vs Conventional Drugs

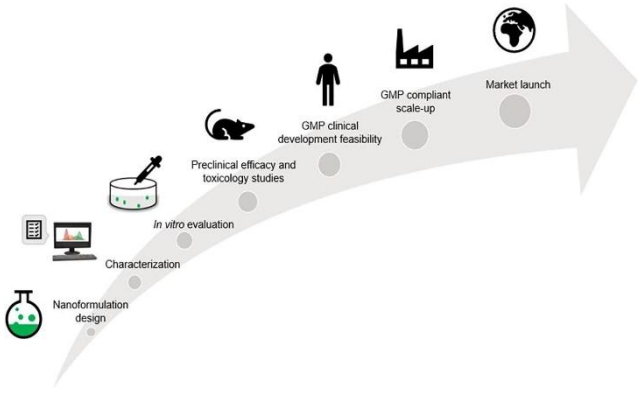

Fig.9. Translation of Nano medicines from research to mass production

8.1 Currency Savings and Cost Reduction:

Iranian Nano drugs (e.g., SinaDoxosome sinaDoxosome , Padinx, Paclinb) have saved $90 million by replacing imports, costing 10× less than foreign equivalents (e.g., Padinx: 9 million Tomans vs $3950) [32] [43]

Insurance companies saved 7000 billion Rials in 7 years using domestic Nano drugs [33]

8.2 Higher Efficacy and Fewer Side Effects:

- Targeted delivery reduces side effects (e.g., hair loss, cardiac issues)
- SinaDoxosome's liposomal coating minimizes healthy tissue damage [34]
- Reduced injection frequency (e.g., DepoStyle's 3-5 month effect) lowers patient maintenance costs

8.3 Pricing and Production Challenges:

Mismatch between pricing and production costs forces discontinuation of vital drugs [35]

However, 96% insurance coverage and tech incubator support (e.g., Tehran University) enable market access

8.4 Global Position and Exports:

Iran exports Nano drugs like SinaDoxosome (1st Middle East anticancer Nano drug) and Lucaza to Syria/Turkey, earning $5 million in 2023 [36]

Knowledge-based companies (e.g., Nano Alvand, Nanodarou) compete with AstraZeneca using indigenous technology

8.5 Economic Future of Nano drugs:

More clinical research investment and international collaboration needed to shorten FDA approval (10-12 years)

8.6 Global Shared Challenges:

- Regulatory hurdles [37]:
- Lack of unified safety assessment standards
- Example: 2-year EMA approval delay for CRLX101
- High clinical trial costs [38]:
- Phase III averages $150M for Nano drugs vs $80M for conventional drugs

9. Conclusion

The current research has comprehensively examined anticancer Nano drugs, illustrating the significant strides this technology has made in transforming cancer treatment. The findings demonstrate that Nano drugs have not only fulfilled their initial promises of more precise targeting and reduced side effects but have also opened new horizons in personalized medicine by pushing the boundaries of scientific knowledge.

Key achievements of nanotechnology and related methodologies:

- Design of intelligent systems responsive to tumor stimuli
- Successful development of Nano drugs with proven clinical efficacy
- Creation of combined platforms for simultaneous diagnosis and treatment

Among the challenges ahead, we can mention:

- Need for improvement in industrial-scale production methods
- Necessity of standardizing safety evaluations
- Management of research and production costs

Recommendations:

1. Development of international collaborations to accelerate research phases
2. Special attention to economic aspects and drug accessibility
3. Investment in training specialists in interdisciplinary fields

This study indicates that cancer Nano drugs stand at the threshold of transitioning from the research phase to widespread clinical applications. Fully realizing this potential requires concerted commitment from researchers, policymakers, and the pharmaceutical industry.

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