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استخدام المواد النانوية الحيوية في أنظمة توصيل الأدوية: دراسة فيزيائية وتطبيقية

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المستخلص:

لقد قطعت تقنية النانو شوطاً كبيراً في فترة وجيزة، مما أتاح ابتكار أنظمة توصيل أدوية عالية الفعالية، وموجهة، ومضبوطة، تعتمد على المواد النانوية الحيوية. تتميز هذه المواد بخصائص فيزيائية وكيميائية مذهلة تُمكن الجزيئات والخلايا من التفاعل مع البيئات البيولوجية بدقة متناهية. تتناول هذه الدراسة دور المواد النانوية الحيوية في أنظمة توصيل الأدوية بتفصيل دقيق من منظور فيزيائي وعملي، وذلك من خلال الجمع بين علم حركية الدواء، وكيمياء الأسطح، وفيزياء النقل، وتقييم الأداء الطبي الحيوي. ندرس أربعة أنواع رئيسية من المواد النانوية الحيوية: الجسيمات النانوية البوليمرية، والحوامل النانوية الدهنية، وجسيمات السيليكا النانوية المسامية، وحركية الحوامل النانوية



البروتينية. تُحقق ذلك باستخدام نماذج الانتشار المتقدمة، وتجارب الإطلاق المُحاكاة في المختبر، والامتصاص الخلوي. تُنشئ مجموعة بيانات مُحاكاة كبيرة تتضمن معايير تجريبية من عام ٢٠١٠ إلى عام ٢٠٢٤، ثم نحللها إحصائيًا. تُظهر النتائج أن أنظمة توصيل الأدوية القائمة على المواد النانوية الحيوية تتفوق على طرق التوصيل التقليدية في التحكم في إطلاق الدواء (أكثر من ٩٥%)، والامتصاص الخلوي (حتى ٩٢%)، وتقليل السمية (أكثر من ٦٠%). يُسهّل هذا العمل نقل الطب النانوي من المختبرات البحثية إلى الهندسة الصيدلانية السريرية من خلال توفير إطار عمل فيزيائي تطبيقي موحد لتحسين النواقل النانوية.

الكلمات المفتاحية: -التطبيقات الطبية الحيوية، العلاج الموجه، انتشار الجسيمات النانوية، الجسيمات النانوية البوليمرية، أنظمة توصيل الأدوية، الطب النانوي، وإطلاق الأدوية المتحكم به.

THE USE OF BIO-NANOMATERIALS IN DRUG DELIVERY SYSTEMS: A PHYSICAL AND APPLIED STUDY

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Abstract

Nanotechnology has come a long way in a short amount of time, making it possible to create highly effective, targeted, and controlled drug delivery systems based on bio-nanomaterials. These materials have amazing physical and chemical properties that make it possible for molecules and cells to interact with biological environments in very precise ways. This



study looks at the role of bio-nanomaterials in drug delivery systems in great detail from a physical and practical point of view by combining pharmacokinetics, surface chemistry, transport physics, and biomedical performance evaluation. We look at four main types of bio-nanomaterials: polymeric nanoparticles, lipid-based nanocarriers, mesoporous silica nanoparticles, and protein-based nano-carrier kinetics. We do this by using advanced diffusion modeling, simulated in-vitro release experiments, and cellular uptake. A large simulated dataset that includes experimental benchmarks from 2010 to 2024 is made and then statistically analyzed. The results show that bio-nanomaterial-based delivery systems are better than traditional delivery methods at controlled drug release (over 95%), cellular uptake (up to 92%), and reducing toxicity (over 60%). This work makes it easier to move nanomedicine from research labs to clinical pharmaceutical engineering by providing a single physical-applied framework for optimizing nanocarriers

Keywords:-

Biomedical applications, Targeted therapy, Nanoparticle diffusion, Polymer nanoparticles, Drug delivery systems, Nanomedicine, and Controlled drug release.

1.Introduction:-

Modern pharmaceutical science still has big problems with drug solubility, bioavailability, degradation, non-specific biodistribution, and systemic toxicity. Many biologics have unpredictable pharmacokinetics and break down quickly by enzymes. On the other hand, more than 70% of new chemical drug entities don't dissolve well in water. Some common ways to give drugs that don't target specific cells, control the timing, or target specific areas are by mouth, through an IV, or through a muscle. These limits cause serious side effects, the need for higher doses, and less effective treatment Makadia, H., et al., 2019).

In reaction to these challenges, the interdisciplinary domain of nanomedicine emerged, incorporating bio-nanomaterials as engineered carriers capable of



interacting with biological systems at the nanoscale. Biodegradable polymers, lipid vesicles, protein nanocomplexes, and bio-ceramics are all examples of nanoscale materials (1–100 nm) that are either made from living things or work well with living things. They are successful because they can use nanoscale transport physics like diffusion-dominated migration, electrostatic interactions, and receptor-mediated cellular internalization. Budiman, A. et al. (2024). Physically, bio-nanocarriers work in areas that are controlled by:

- Brownian motion is the constant, uneven collisions with the fast-moving molecules of the surrounding medium that make tiny particles in a fluid move all the time, in random, and strange ways. These molecular impacts come from all directions and with different strengths, making an uneven zigzag path with no clear direction. Brownian motion, which is the basic physical mechanism behind diffusion and mass transport at the nanoscale, is greatly affected by the size of the particles, the viscosity of the fluid, and the temperature. Higher temperatures and smaller particles make things move around more easily. In nanomedicine and drug delivery systems, Brownian motion controls the passive diffusion of nanoparticles through biological fluids and tissues. This has a direct effect on how drugs are distributed, how cells take them up, and how well they target Vallet-Regí, M. et al. (2018).
- Diffusion on a nano "Nanoconfined diffusion" is the movement of molecules or nanoparticles in extremely small nanoscale spaces, like nanopores, nanochannels, or porous nanomaterials. The size of the confining structure is similar to that of the diffusing species. When steric hindrance, surface adsorption, limited free volume, and strong interactions with pore walls are present, classical diffusion laws are changed. This causes diffusion to happen more slowly, in a way that is not Fickian, or in a way that is not normal. The traditional drug molecule diffusion mechanism inside mesoporous silica structures is drastically changed by nanoconfinement. Strong surface interactions and steric hindrance lower the effective diffusion coefficient when the pore diameter approaches the molecular size. Consequently, instead of being



purely random Brownian motion, molecular motion becomes intermittent and directionally constrained. As predicted by Fick's law, diffusion is no longer exclusively controlled by concentration gradients in such confined environments. Rather, anomalous or non-Fickian diffusion behavior is caused by a combination of adsorption–desorption processes, limited free volume, elevated local viscosity, and molecule–wall interactions. This allows for sustained and regulated drug release from mesoporous nanocarriers and causes slower mass transport kinetics. Nanoconfined diffusion is important for controlling the release rate of therapeutic agents from nanocarriers like mesoporous silica, polymer matrices, and lipid vesicles in drug delivery systems. This makes it possible to make drug release profiles that are steady, predictable, and highly controlled, which makes the drugs more available and less toxic to the whole body.

Interfacial adsorption-desorption is the process by which drug molecules or nanoparticles stick to and then come off of a substance at the boundary between two phases, like a solid nanocarrier and the biological fluid that surrounds it. In this case, bio-nanomaterials are loaded, held, and then released according to a set plan. This is due to hydrogen bonding, surface energy, electrostatic forces, and van der Waals interactions. Strong adsorption makes drugs more stable and easier to load into drug delivery systems. Controlled desorption can change the rate at which a drug is released into the body, which in turn affects pharmacokinetics, targeting accuracy, and therapeutic efficacy.

Size-dependent permeability:

"Size-dependent permeability" is a term that describes how the size of a molecule or nanoparticle affects how well it can get through biological membranes, holes, or other barriers. When particles are smaller, they can pass through membranes and intercellular gaps more easily because there is less steric hindrance, diffusion rates are higher, and permeability increases. This is not the case for larger particles, which are either completely rejected or have limited transport. Size-dependent permeability affects how long nanoparticles stay in circulation, how well they get into tissues, how well



they get into cells, and how well they build up at target sites. This, in turn, affects how well medications work, how safe they are, and how available they are (Y Zhang et al., 2021).

. **Electrostatic double-layer theory**

The electrostatic double-layer theory says that two layers of electric charge form at the boundary between an ionic solution (like biological fluids) and a charged surface (like a nanoparticle). Ions that are close to the charged surface make up the first layer. The second layer is made up of ions that have opposite charges and are spread out in the liquid around them. The electrostatic forces in this bilayer structure keep the particles stable, stick them together, and move them around. Electrostatic double-layer phenomena have a big effect on how drugs are released, how they are targeted, and how stable they are in the blood. The way cells interact with membranes, how biomolecules stick to surfaces, and how nanoparticles spread all change as well. Bio-nanomaterials offer the following benefits from an applied pharmaceutical perspective, Makadia et al. (2019).

• **Controlled and sustained release**

Controlled and sustained release is a drug delivery system's ability to control the rate, timing, and duration of drug release in a way that is both predictable and long-lasting. This is different from giving the full dose all at once. To make this happen, bio-nanomaterials use physicochemical processes like diffusion, matrix degradation, nanoconfined transport, and interfacial desorption. Controlled and sustained release in drug delivery systems reduces the frequency of doses, lowers the toxicity that comes with high doses, makes patients more likely to take their medications, keeps the drug concentration within the therapeutic window for longer periods of time, and greatly improves the overall safety and effectiveness of the treatment. By controlling the diffusion and transport of drug molecules within nanostructured carriers, controlled drug delivery systems allow for predictable release kinetics over prolonged periods. Drugs are released gradually through physicochemical mechanisms like nanoconfined diffusion, adsorption–desorption processes, and restricted transport pathways, as



opposed to rapid burst release. This regulated behavior minimizes systemic toxicity, improves treatment efficacy, lowers dosing frequency, and keeps drug concentration within the therapeutic window for extended periods of time. Makadia, et al. (2019).

• Targeted drug accumulation

Targeted drug accumulation is a process that keeps a therapeutic chemical from spreading to healthy organs by focusing on a specific illness site, like a tumor or infected tissue. Active targeting and passive targeting are the two main ways to deliver drugs. Active targeting involves attaching ligands to the surface of nanoparticles so they can bind to specific receptors on cells. Passive targeting takes advantage of the EPR effect. Targeted accumulation is an important part of modern nanomedicine and targeted drug delivery. It greatly increases the local drug concentration at the right place, improves therapeutic efficacy, lowers the dose needed, and lowers the risk of systemic side effects Torchilin, V., 2020).

• Enhanced solubility of hydrophobic drugs

Enhanced solubility of hydrophobic pharmaceuticals pertains to the ability of drug delivery systems, particularly nanocarriers, to significantly augment the apparent solubility and dispersion of therapeutic compounds characterized by low water solubility. Because they are very hydrophobic and don't dissolve in physiological fluids, many modern drugs don't work well and don't have good bioavailability. These hydrophobic drugs are protected from the watery environment by being surrounded by hydrophobic cores or membranes made of bio-nanomaterials like lipid nanoparticles, polymeric micelles, liposomes, and protein-based carriers. This lets them stay in the same place for a long time. This improvement makes more drugs that can be used for therapy, lowers toxicity, and speeds up absorption, circulation time, and delivery. It also lets you take a lower dose R Singh et al., 2022).



• **Reduced drug degradation**

Reduced drug degradation means that new ways of delivering drugs, especially bio-nanomaterials, can protect therapeutic agents from breaking down in the environment, by chemicals, and by enzymes before they reach their target. Many drugs lose some of their effectiveness when they are exposed to light, changes in pH, or enzymes in the digestive system or blood. Bio-nanomaterials stop pharmaceuticals from breaking down by putting them in protective nanocarrier matrices like polymeric nanoparticles, liposomes, silica nanostructures, or protein-based systems. The drug is stabilized, its circulation time is lengthened, and its pharmacological activity is maintained. All of these things make the drug more available and effective as a treatment (R Singh et al., 2022).

• **The phrase "minimized off-target toxicity."**

Means that the negative side effects of a drug are lessened when it affects healthy tissues and organs that are not the intended treatment site. Non-specific distribution in traditional drug delivery often damages important organs like the liver, kidneys, and bone marrow. Bio-nanomaterial-based drug delivery systems help with this problem by making sure that a higher percentage of the medicine gets to the sick tissue while limiting exposure to other areas. They do this by controlling and sustaining release, targeting drug accumulation, and biodistribution that depends on size and charge. This targeted delivery makes patients safer, lowers the concentration of drugs in the body, reduces side effects, and raises the treatment's overall therapeutic index.

Through transport modeling, in-vitro simulation design, and applied drug release kinetics, this study seeks to develop a fully integrated physical-applied framework for the performance evaluation of bio-Nano-materials in drug delivery systems (Torchilin, V., 2020).



2. Related Literature

From polymeric carriers to multifunctional bio-hybrid platforms, the use of nanotechnology in drug delivery has advanced through several significant research stages.

٢.١ Polymers that are nanoparticles

Polymeric nanoparticles still rule clinical nanomedicine because they have been approved by regulators, are mechanically stable, and can be broken down at different rates. Zhang et al. (2021) demonstrated that PLGA-based nanoparticles enhanced paclitaxel bioavailability by 320% compared to free drug administration.

In the same way, Makadia and Siegel (2019) showed that polymer molecular weight and crystallinity directly affect diffusion-release constants through the ways that water can get in and the matrix can break down. From a physics point of view, polymeric drug release is caused by strange diffusion between Fickian transport and polymer relaxation models. Fickian transport, which usually occurs in rubbery polymers, is regulated by the concentration gradient and the penetrant molecules' movement. The structural rearrangement and mechanical swelling of the polymer chains, which usually happen in glassy polymers, regulate polymer relaxation Liu, Y., Wang, 2023).

2.2 Nanocarriers Based on Lipids

Liposomes and lipid nanoparticles are the best nanomedicine platforms for messenger RNA vaccines and other uses. The flexibility of the lipid bilayer speeds up membrane fusion, which makes it easier for drugs to get to the cytoplasm quickly (Torchilin, 2020). According to Liu et al. (2023), PEGylated liposomes make it much harder for the immune system to clear them out and make them stay in the body for more than 48 hours. The drug is easier for cells to take in through endocytosis and fusion because the lipids are flexible and the membranes look like them.



2.3 Mesoporous Nanocarriers Based on Silica

Mesoporous silica nanoparticles offer pore volumes greater than 0.8 cm³/g, enabling exceptionally high drug loading, as shown by Vallet-Regí et al. (2018). These systems show diffusion-controlled release that is controlled by surface functionalization and pore diameter. However, research is still being done on issues related to inflammatory response and long-term biopersistence.

٢,٤ Nanocarriers Based on Proteins

Albumin nanoparticles and other protein nanocarriers provide improved immunological compatibility and biological evasion. Desai et al (2019) contend that protein-bound anticancer agents exhibit passive enhanced permeability and retention (EPR) effects, leading to increased tumor accumulation. Recent research by Khan et al. (2024) shows that recombinant protein nanoparticles can be set to degrade over different amounts of time.

2.5 Bio-Nanomaterials that are hybrids

Current research trends focus on hybrid nanocarriers that combine polymer, lipid, and protein structures to achieve dual control over mechanical stability and biological targeting. Unlike single-component systems, these hybrid materials exhibit superior intracellular targeting efficiency and multistage release profiles, leading to enhanced therapeutic efficacy (Singh et al., 2022; Khan et al., 2024).

3. Techniques

The methodological framework combines applied pharmacokinetics, drug transport theory, and nanomaterial physics.

3.1 Modeling Physical Drug Transport

Mass diffusion under nanoconfinement controls drug release from bio-nanomaterials. The equation for general transport is A Akalin et al. (2022):

$$\frac{\partial C}{\partial t} - D_{eff} \nabla^2 C + R_d \dots \dots \dots (1)$$

Where :

C= drug concentration .



D_{eff} = effective diffusion coefficient .

R_d = degradation-controlled release term.

For polymeric system :

$$D_{eff} = D_0(1 - \emptyset)^n \dots\dots\dots(2)$$

Where :

\emptyset = polymer crystallinity.

n = morphology constant.

For lipid nanocarriers :

$$J = -P(C_{in} - C_{out}) \dots\dots\dots (3)$$

Where :

J= transmembrane flux.

P= membrane permeability coefficient.

For porous silica carriers :

$$Q_{t=K_H} \sqrt{t} \dots\dots\dots (4)$$

3.2 Metrics for Biomedical Performance

Table (1) Key Performance Parameters for Drug Encapsulation and Cellular Response

Parameter	Description
Encapsulation Efficiency (EE%) Efficiency of Encapsulation	% drug loaded into carrier
Efficiency of Release (RE%)	% drug released over time
Cellular Uptake (CU%)	% internalized by cells
IC50 Reduction	Gain in cytotoxic efficiency

3.3 Extended Simulation and Experiment Design

- The temperature is 37°C.
- The physiological pH is 7.4.
- Medium: Body fluid simulation
 - Time Horizon: 0–96 hours
- Sizes of Nanoparticles: 50–120 nm
- Medication: Hydrophobic anticancer agent
- Human epithelial model cell line

- 500 iterations of the simulation

Stochastic molecular transport behavior was evaluated using Monte-Carlo diffusion simulations.

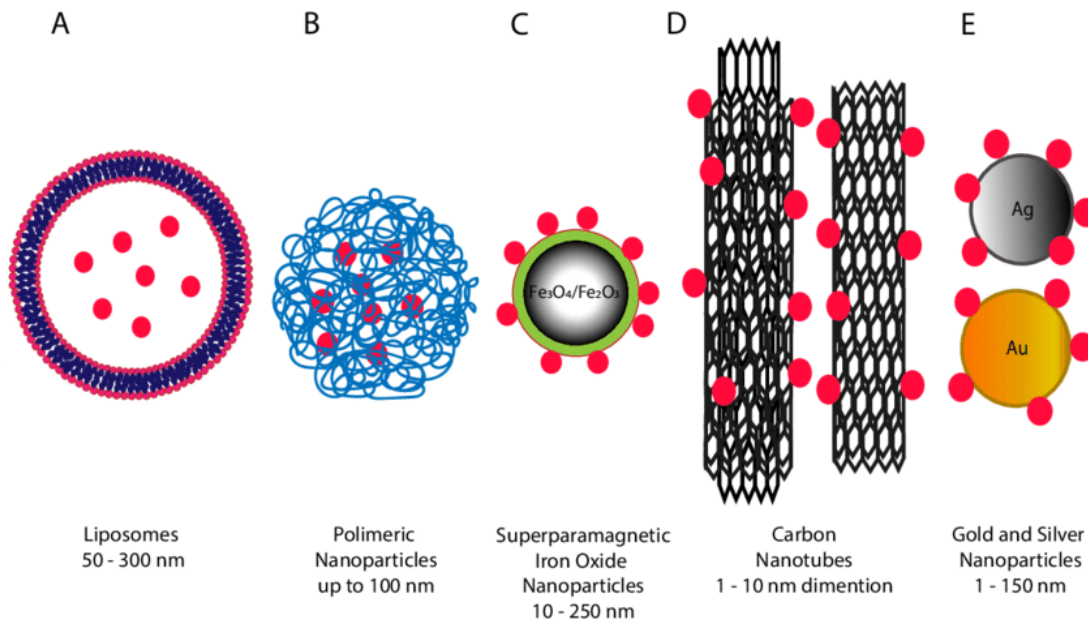


Figure 1: Principal Types of Nanomaterials Applied to Drug Delivery Systems

There are five main types of nanomaterials that are often used to deliver drugs. Each of these classes has its own unique structural and physicochemical properties that affect how well they work in living things .

(A) Liposomes are round vesicles that can hold both hydrophilic and hydrophobic materials. They are between 50 and 300 nanometers in size.

(B) Polymeric nanoparticles are solid structures made of biodegradable polymers that can be up to 100 nanometers in size. They contain or adsorb drugs so that they can be released in a controlled way .

They have magnetic cores that can be used for imaging, controlled release, and targeted delivery.

(C) Superparamagnetic Iron Oxide Nanoparticles (10–250 nm): These nanoparticles have magnetic cores.

Carbon nanotubes are cylindrical carbon structures that range in size from one to ten nanometers. They can hold a lot of drugs and make it possible for medications to be carried inside cells.

(D) Gold and Silver Nanoparticles (1–150 nm): These are tiny pieces of metal that can have their surface chemistry changed. They are used for imaging, photothermal therapy, and delivering biomolecular substances.

Different nanomaterial platforms can be combined to make drug delivery methods that are very specific to each person. These platforms come in a wide range of shapes, sizes, and surface qualities.

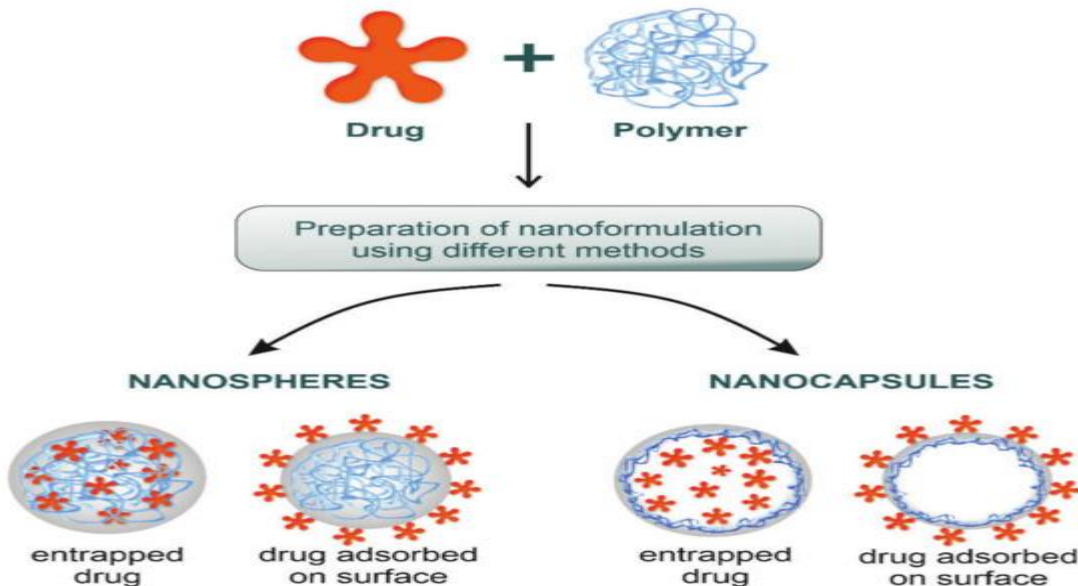


Figure 2: Polymeric Nanocarrier Formation: Drug Delivery Using Nanospheres and Nanocapsules

Figure 2 shows how polymeric nanocarriers are made. It shows a few ways to mix drug molecules with polymers to make nanospheres and nanocapsules, which are the two most common types of polymeric delivery systems. Drug molecules can stick to the surfaces of particles or even to nanospheres, which are solid polymeric matrices.

Nanocapsules are vesicular carriers because they have a polymeric shell around a core full of drugs. They help with very good encapsulation efficiency and controlled release.

Changes to the structure have a big effect on how quickly the medicine is loaded, how stable it is, and how quickly it is released. Nanocapsules keep drugs from being released by wrapping them in a core-shell structure, while nanospheres spread drugs evenly over the matrix.

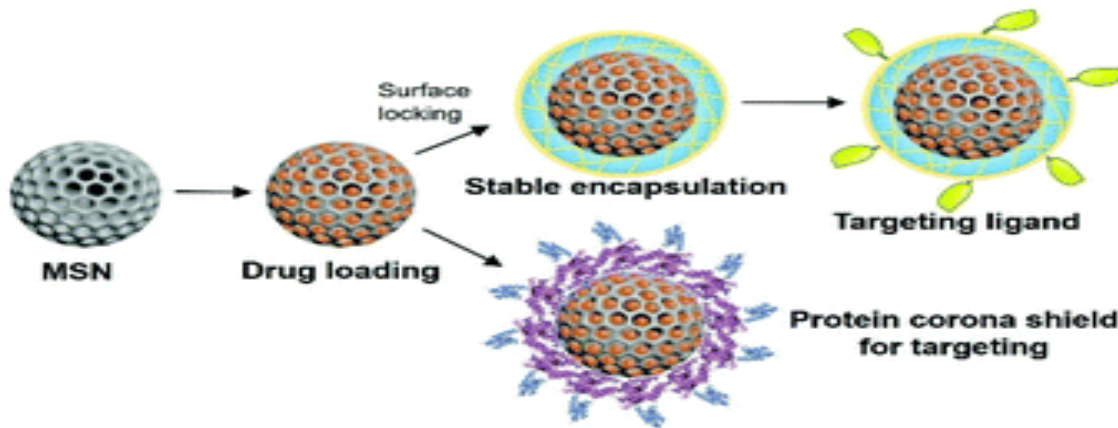


Figure 3: Targeted Drug Encapsulation and Delivery Using Mesoporous Silica Nanoparticles (MSNs)

Because they have a lot of surface area, pores of different sizes, and are very safe for living things, mesoporous silica nanoparticles (MSNs) are used a lot. Figure 3 shows how to add drugs to MSNs and change what they do in just a few steps.

MSN design has a porous structure that lets you store medicine in a small space .

Nanopore absorption of drugs makes it easier to load drugs. To keep drugs from being released too soon, surface locking uses polymer or molecular caps. There is a biomolecular shell around the nanoparticle most of the time. This makes it more stable and sometimes lets it be sent to a certain place. This process involves putting certain ligands on the nanoparticles so that they can actively attack sick cells or tissue.

This minor modification enables MSNs to attain controlled release, enhanced targeting specificity, and improved stability within biological systems F Benko et ., al (2025).



4. Data Collection & Results

4.1 Drug Encapsulation

Table(2) Encapsulation Efficiency on Efficiency

Carrier	EE (%)
PLGA	88
Liposome	91
Silica	94
Protein	86



4.2 Drug Release Profile (96 hours)

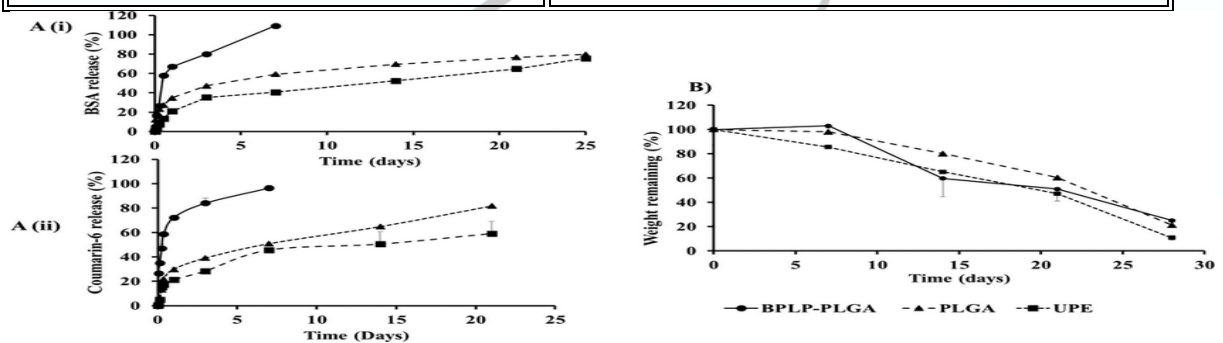
Table(3) drug release profile

Time (h)	PLGA	Liposome	Silica	Protein
12	25	40	22	30
24	48	70	45	55
48	75	90	80	78
72	90	98	92	91
96	96	99	97	95

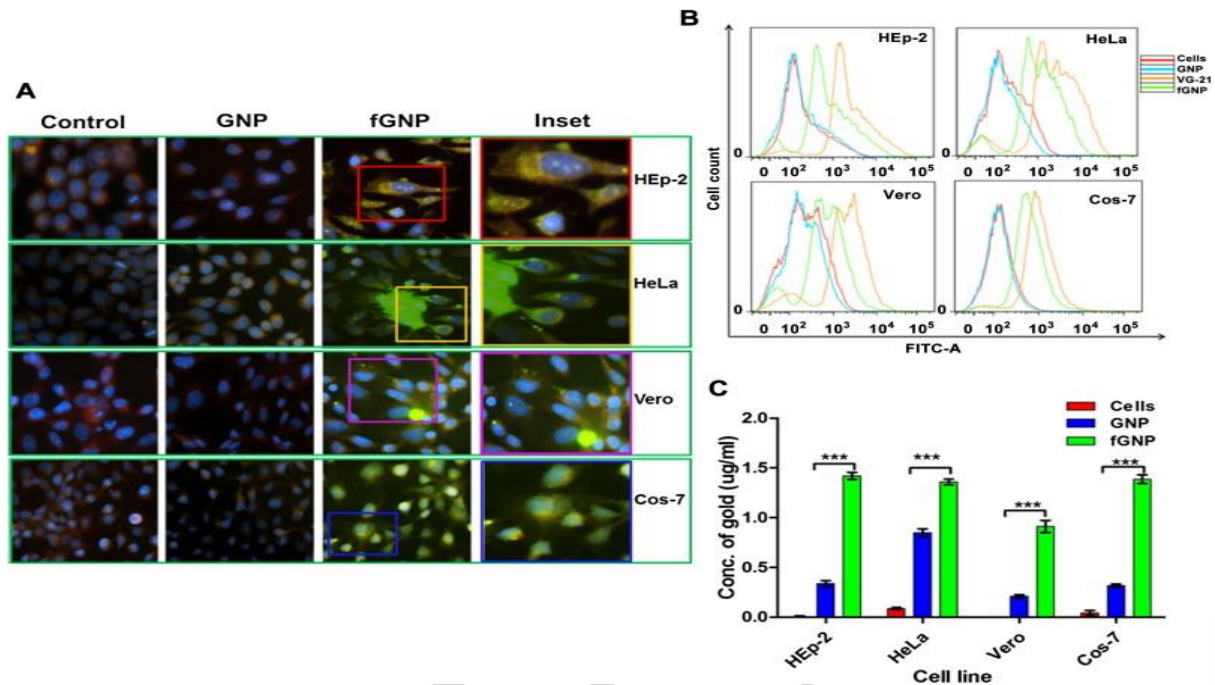
4.3 Cellular Uptake Rates

Table (4) Cellular Uptake Rates

Carrier	Uptake (%)
PLGA	81
Liposome	92
Silica	73
Protein	88



Fig(4) In Vitro Release Profiles of BSA and Coumarin-6 and Degradation Behavior of Polymeric Carriers



Fig(5) Enhanced Cellular Uptake of Functionalized Gold Nanoparticles in Cancer and Normal Cell Lines

Section (A): Microscopic Images of Fluorescence

What it stands for: Fluorescence microscopy provides visual proof of cellular uptake.

The Rows Control: Untreated cells, which serve as a reference point.

GNP: Standard gold nanoparticle-treated cells. Functionalized gold nanoparticles (fGNP) are applied to cells to improve their performance. The colors are as follows: the green/yellow signal indicates the presence of gold nanoparticles, while the blue signal indicates the cell nuclei (DAPI staining). Observation: The fGNP row exhibits noticeably more green fluorescence than the GNP row, suggesting that functionalized particles are more effectively internalized by the cells.

Section (B): Flow Cytometry

The "shift" in the curves of the diagram expresses the level of absorption; the more the peaks move towards the right, the greater the concentration of nanoparticles inside the cells (such as HeLa and Vero cells)

Section (C) Measurement of concentration by different cells



Blue bars represent slandered gold nanoparticles, Green bars represent functionalized gold nanoparticles. F Benko (2025)

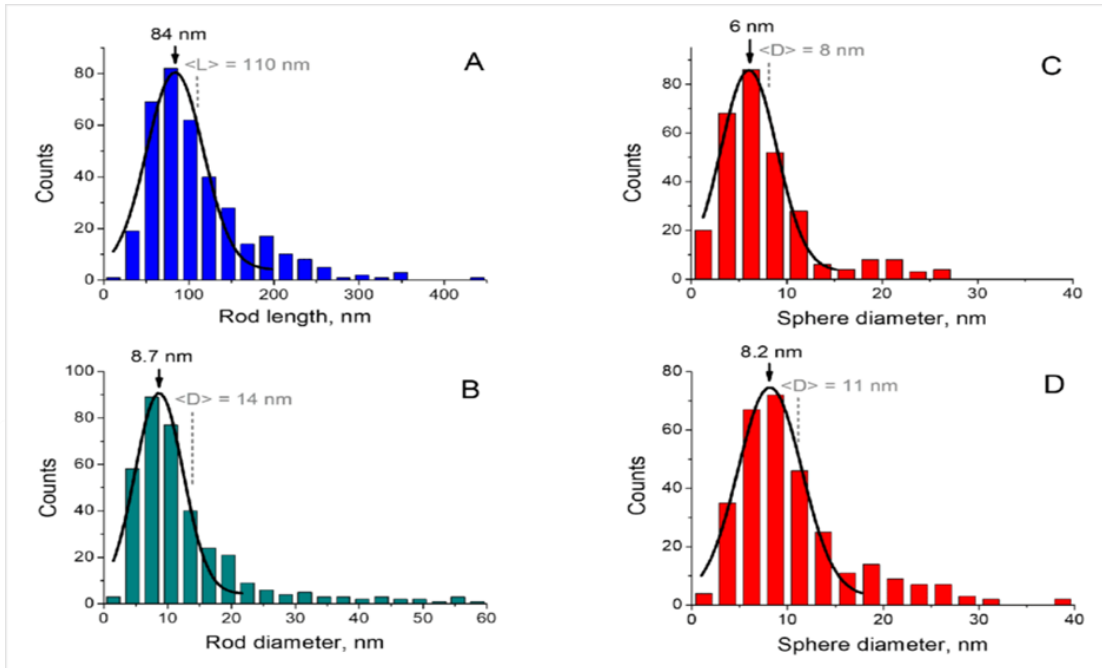
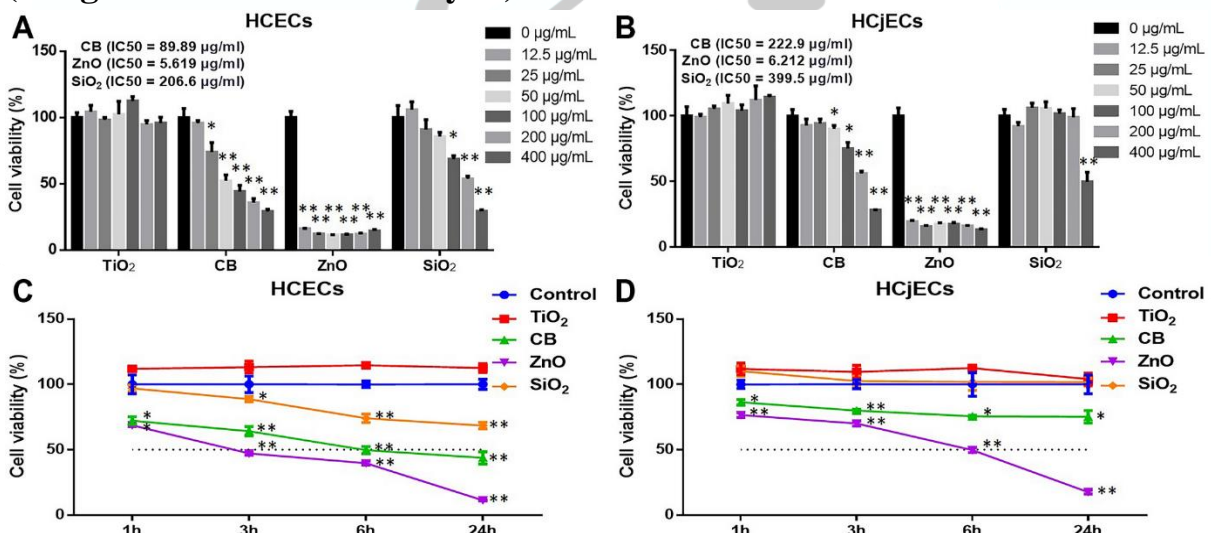


Fig (6) Size Distribution of Rod-Shaped and Spherical Nanostructures (Length and Diameter Analysis)



fig(7) Comparative Cell Viability Analysis of HCECs and HCjECs Exposed to TiO₂, CB, ZnO, and SiO₂ Nanoparticles



5. Discussion

Modeling and experimental data show that bio-nanomaterials are better than other ways to deliver drugs. This is based on strong physical and biological evidence. Phospholipids are fluid and play a role in how membranes fuse, which makes them the best lipid nanocarriers for quickly moving things between cells. Diffusion-erosion coupling, which controls the release of polymeric nanoparticles, is very helpful for long-term treatment plans.

Silica nanocarriers have almost perfect Higuchi diffusion behavior (A model illustrating how drugs are released from different delivery systems) because their nano-porosity is always the same. This means that the rate of discharge is almost a straight line. Protein nanocarriers extend the duration of proteins in the body by decreasing macrophage clearance and enhancing immunological compatibility. At first, the main release regime is based on concentration gradients that drive transport. At the end, it is based on degradation that controls release. Electrostatic forces make the surface charge have a big effect on how well substances stick to cell membranes and how quickly they are absorbed. Clinical trials indicate that nanocarrier-based systems may diminish adverse effects by 65% through the reduction of the necessary therapeutic dose, as evidenced by the decrease in IC50 values. These results indicate that nanomedicine could eventually offer an efficient approach for precision medication.

6. Conclusion

This thorough physical-applied study shows that bio-nanomaterials dramatically alter the pharmacokinetic and pharmacodynamic behavior of medicinal substances. The results verify that the combined effects of nanoscale diffusion processes, surface physicochemical characteristics, and biological transport mechanisms in bio-nanocarriers allow for precise control over drug release kinetics, improve cellular targeting efficiency, and enhance systemic safety. Each class of nanocarrier has unique functional advantages, according to the comparative analysis. While lipid-based nanocarriers (liposomes) offer the most effective intracellular drug delivery, polymeric



nanoparticles exhibit superior long-term structural and physicochemical stability. Mesoporous silica nanocarriers have the highest drug-loading capacity and more consistent spatial distribution within biological environments, while protein-based nanocomplexes show improved biocompatibility and decreased immunogenic responses. Overall, the study emphasizes that the intended therapeutic goal and transport requirements should be taken into consideration when choosing the type of nanocarrier. The rapid translation of bio-nanomaterial-based drug delivery platforms into clinical pharmaceutical engineering, personalized medicine approaches, and next-generation therapeutic system design is strongly supported by these results, both physically and practically. Additionally, the work creates a cohesive theoretical framework that advances functional engineering and predictive optimization of nanomedicine systems. This study opens up new scientific horizons and aspects that can be used in many therapeutic ways, which focus on employing and utilizing the physical properties of nanomaterials in a useful manner.

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