NANO – BIO INTERFACES USING AI/ML

Project submitted to the

SRM University – AP, Andhra Pradesh

for the partial fulfillment of the requirements to award the degree of

Bachelor of Technology

In

Computer Science and Engineering

School of Engineering and Sciences

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Nov, 2023

Certificate

Date: 27-Nov-23

This is to certify that the work present in this Project entitled "**NANO – BIO INTERFACES**" has been carried out by **Srikar, Haril, Sravani, Anantha Teja, Pavani** under our supervision. The work is genuine, original, and suitable for submission to the SRM University – AP for the award of Bachelor of Technology in **School of Engineering and Sciences**.

Supervisor

Dr. Sabyasachi Chakrabortty

Associate Professor,

SRM University.

Acknowledgements

As we reach the culmination of our research journey on the intricate topic of "Nano-Bio Interface using AI/ML," I want to extend my heartfelt gratitude to each one of you for the exceptional effort and collective dedication that has defined our collaborative endeavour.

Undertaking this research has been a challenging yet rewarding experience, and it would not have been possible without the commitment and expertise each of you brought to the table. The study of nanoparticle uptake is a complex field, and your individual contributions have been integral to the success of our project.

I would like to express my gratitude to:

- Srikar, Teja: Your meticulous data analysis provided a solid foundation for our research.
- Haril: Your experimental skills and attention to detail in the data were crucial in generating reliable and meaningful results.
- Pavani, Sravani: Your insightful discussions and critical thinking and algorithmic variance, enhanced the depth and quality of our interpretations.

I would also like to extend gratitude to Dr Sabyasachi Chakrabortty that contributed to our research journey.

As we conclude this phase, let's reflect on the significance of our findings and the impact they may have on advancing our understanding of nanoparticle interactions. Our collective effort has not only enriched our knowledge but also positioned us as contributors to the scientific community.

Thank you all for your hard work, passion, and collaborative spirit. Let's celebrate our achievements and look forward to the potential impact of our research in the scientific realm.

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Abstract

Nanomaterials, with at least one dimension smaller than 100 nano-meters, possess unique properties that make them ideal for various biomedical applications. Nanoparticles are a promising tool for revolutionizing the healthcare. Acknowledging the potential benefits of nanomedicine, researchers are attempting to leverage nanotechnology for the purposes of illness prevention, diagnosis, and treatment. However, one of the challenges associated with the use of nanoparticles is ensuring that they are taken up by cells in a safe and efficient manner. This research focuses on optimizing cellular uptake of nanomaterials by investigating the interplay of size, shape, and capping agents, with a primary goal of mitigating toxicity. The impact of nanoparticle size on cellular internalization is systematically explored across a spectrum from nano to microscale dimensions. Findings reveal nuanced relationships between size and uptake efficiency, providing insights into an optimal size range for enhanced cellular interaction while minimizing potential cytotoxic effects. Additionally, the study delves into the influence of nanoparticle shape on cellular uptake dynamics. By synthesizing various shapes, including spheres and rods, we assess their impact on internalization efficiency and potential cytotoxicity, contributing valuable data for the rational design of biocompatible nanomaterials. Capping agents, known stabilizers of nanoparticles, are investigated for their influence on cellular interactions. Examining a diverse range of capping agents, both natural and synthetic, sheds light on their role in shaping uptake efficiency and potential toxicity, offering a comprehensive understanding of their impact on cellular responses.

Statement of Contributions

Pavani: Responsible for Size - Optimized Nanoparticles

Sravani: Responsible for Shape – Dependent Cellular Uptake

Srikar: Responsible for Capping Agent Influence

Anantha Teja: Responsible for Algorithmic, Code Generation

Haril: Responsible for synthesizing the overall findings, interconnected nature of size, shape, and capping agent in nanoparticle design for biological purposes.

Abbreviations

NP - Nanoparticles

AR – Aspect Ratio

Hela – Human Cervical Cancer cells

HEK – Human Embryonic Kidney cells

PEG – Polyethylene Glycol

CTAB - Cetyltrimethylammonium bromide

MUA - Mercaptoundecanoic Acid

List of Tables

Cell Type	Nanoparticle	Functional Group	Capping agent	Size	Shape	Toxicity/Viability	Cellular Uptake
Hela	Au	Thiol	PEG	5.4(AR)	Rod	80pM	11.5 (AR)> 5.4(AR)
				11.5(AR)			
		carboxylic	Citrate	14nm	Sphere	5uM	50nm>14nm
				50nm		40uM	
HEK			Citrate	14nm	Sphere	100ug/ml	20nm>14nm
				20nm			
Hela	Ag	carboxylic	Citrate	70nm	Bell shaped	50ug/ml	70nm has better uptake
				200nm			
				500nm			
			Citrate	10nm		0.0001 - 5 mg/ml	10nm has better uptake
				30nm			
				100nm			
			Citrate	5nm	Sphere	8.6mg/ml	Smaller sizes 5nm,20nm has better uptake than 50nm and 100nm
				20nm		10.2mg/ml	
				50nm		11.8mg/ml	
				100nm		13.4mg/ml	
			Citrate	10nm	Sphere	50ug/ml	Smaller sizes 10nm found to have higher uptake
				40nm			
				75nm			
Hek	ZnS	carboxylic	Citrate	4nm	Sphere	4.75uM	25nm>10nm>4nm
				10nm		2.75uM	
				25nm		<2.75uM	

Cell Type	Nano Material	Fuctional Group	Capping Agent	Size	Shape	Toxicity / Viability	Cellular Uptake
Hela	Gold	Ammonia	CTAB	43nm	sphere	1.9x10^-5M	Sphere > Rods
				17.2 x 37.8nm	rod	9.4 x 10^-6M	
		Carboxylic	Citrate	14nm	sphere	1.9 x 10 ^-5 M	
				17nm			
				14x40nm	rods	1.9 x 10 ^-5 M	
				14x74nm			
				15nm	sphere	0.42 mg/ml	
				25nm	rods	0.32 mg/ml	
		Thiol	PEG	15nm	sphere	1.02 mg/ml	
				25nm	rods	0.78 mg/ml	
		Ammonia	CTAB	50nm	sphere	0.1 mg/ml	Sphere > Rods > Cubes
				10 x 45 nm	rods	0.3 mg/ml	
				50nm	cubes	0.6 mg/ml	
				43nm	sphere	1.5 micmg/ml	sphere > Rods
				38 x 17nm	rods	16 micmg/ml	
hela and hek		Pyrrolidine	PVP	10nm	sphere	>300 mg/ml	spheres has the most cellular uptake
				370nm	flower	100- 200 mg/ml	
				41nm	rod	10 - 20 mg/ml	
				160nm	prism		
				240nm	stars		
Hela		Amide	chitosan	9nm	sphere	127 microM	Sphere > Rods > Stars
				100nm	rods	81.8 microM	
				61nm	stars	8 microM	

Cell Type	Nano Material	Functional Group	Capping Agent	Size	Shape	Toxicity / Viability	Cellular Uptake
Hela	Gold	Thiol	PEG	5-11 nm	Sphere	80pm	PEG>CTAB
		Ammonium	CTAB				
		carboxylic	Citrate	5-20nm		285	
				45nm			
		carboxylic	Citrate	3-10nm		150mg	chitosan > citrate
		Amide	chitosan				
		polyphenol	leaf extract	10-20nm		100mg	
		carboxylic	citrate	14nm		5 micrg/ml	14nm citrate >mua
				50nm		40 micromg/ml	
		alcohol	MUA	14nm		5 micromg/ml	50nm mua > citrate
				50nm		40micromg/ml	
		carboxylic	citrate	15nm		0.42 mg/ml	regardless of shape, size PEG > citrate
		Thiol	PEG		Rod	1.02mg/ml	

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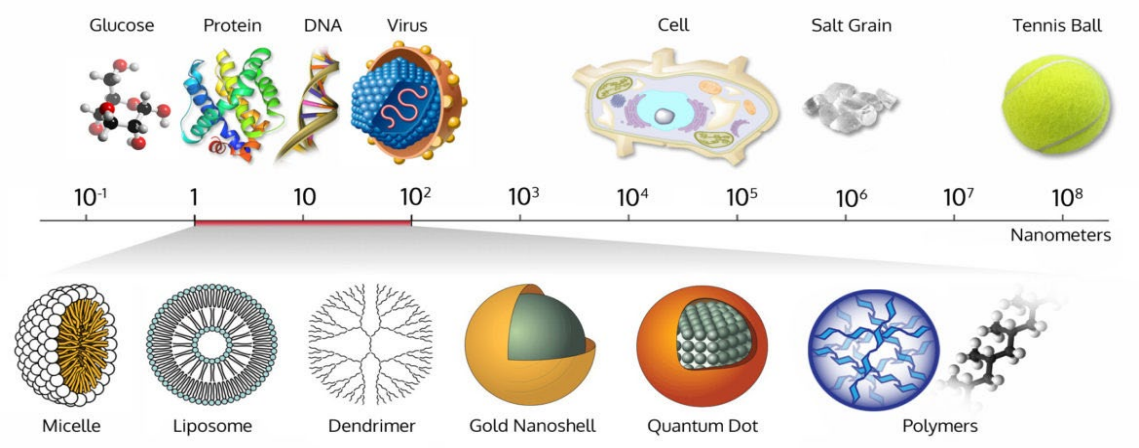
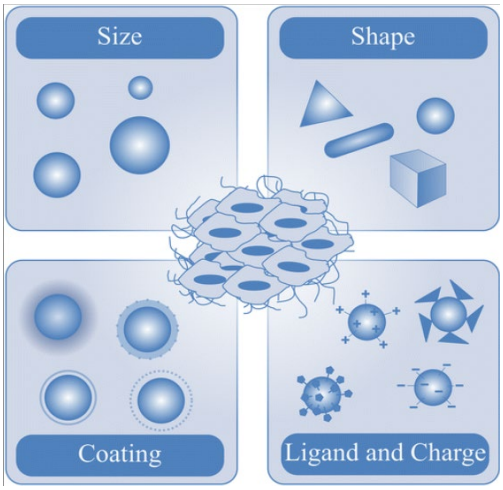


Navigating the Nanoscale: Exploring Cellular Uptake of Nanoparticles [1]

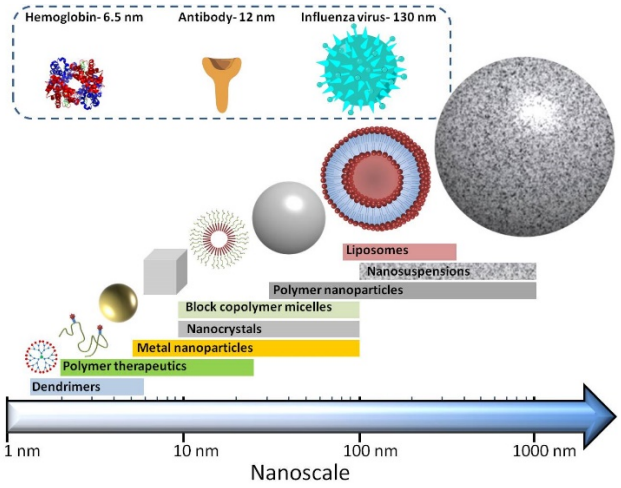
Optimizing Cellular Uptake of Nanoparticles: Size, Shape, and Capping Agent [2]



[3] Applications of Nanotechnology in Pharmaceutical Sciences

1. Introduction

Nanotechnology is emerging as a cutting-edge technology. It is an interdisciplinary field that incorporates a number of academic specialties, including medicine, physics, material science, biology, and chemistry. The word "nano" is derived from the Greek word nanos, which means "dwarf".[4] The vision for nanotechnology was put forth by Nobel Prize-winning physicist Richard P. Feynman, who suggested applying more important items and mechanical tools at a smaller tool and particle scale because he thought that "there is plenty of room at the bottom".[3] Nanoparticles are tiny particles with dimensions typically in the range of 1 to 100 nanometers. To provide a context, one nanometer is equal to one billionth of a meter (10^9m). Engineered NPs have gained great importance in various scientific fields due to their unique and often improved properties compared to bulk materials. As a result, the field of nanotechnology has experienced unprecedented growth, bringing novel solutions and breakthroughs to fields as diverse as medicine, electronics, materials science, and environmental science. The emergence of nanotechnology stems from the remarkable observation that materials, products, and devices manufactured at the nanoscale often exhibit properties that are significantly different from their larger-scale counterparts.[5].This phenomenon is consistent with the fundamental principle of physics and chemistry that the arrangement, size, and shape of atoms within a material directly influence its macroscopic properties. In particular, the integration of nanomaterials into biology and medicine has opened new possibilities for innovative applications. Due to their size, structure, and properties, nanomaterials are well-suited for interactions at cellular and molecular levels, opening opportunities for advances from basic research to clinical applications. Safer and more efficient solutions to numerous medical issues are promised by the development of nanoparticles (NPs) for a broad range of biomedical applications. As with traditional vaccines, new medical products based on nanotechnology are being approved for research and medical use. To deliver drugs to particular cells or tissues with precision and prevent them from degrading, therapeutic substances can be encapsulated in nanoparticles. This precision in cellular targeting holds great promise for personalized medicine, where tailored treatments can be designed based on the specific characteristics of individual patients or diseases. These products include diagnostic tools such as nano-sensors and contrast agents, as well as new drugs and pharmaceutical products such as nanoparticle-based drug delivery. These advances demonstrate that nanotechnology has the potential to significantly improve medicine. However, the effective and maintained controlled entry/trafficking of NPs into the cells remains a major challenge.



Nanoparticles: Diversity in Size and Shape [6]

The unique size and surface characteristics of nanoparticles allow for tailored interactions with biological entities. The cellular uptake takes place in several mechanisms including Endocytosis, Membrane penetration, and Adsorption. The cellular uptake mechanisms, such as endocytosis, facilitate the internalization of these drug-loaded nanoparticles, enhancing the efficiency of treatments while minimizing side effects [7]. The cellular uptake of nanoparticles, a crucial aspect in the field of nanotechnology, refers to the process by which these minute particles are internalized by cells. Moreover, nanoparticles with specific targeting ligands on their surfaces can selectively bind to receptors on the cell membrane, facilitating enhanced uptake by specific cell types. The cellular uptake of nanoparticles also plays an important role in diagnostic applications, where imaging agents and contrast agents can be delivered to specific cells for enhanced visualization and detection. The cellular uptake of nanoparticles is intricately influenced by several key parameters, each playing a critical role in determining the efficiency and specificity of this process [7]. One crucial factor is the size of the nanoparticles, facilitating enhanced interactions with cell membranes. The surface charge of nanoparticles also proves that it has an importance, with positively charged particles often demonstrating increased uptake through electrostatic interactions with negatively charged cell membranes. Surface coating and functionalization contribute to cellular uptake by influencing the recognition of nanoparticles by specific cell receptors, allowing for targeted delivery. The shape of nanoparticles is another determinant, as certain shapes may promote better interactions with cellular structures, influencing uptake efficiency.

Additionally, the hydrophobic or hydrophilic nature of nanoparticles and their concentration in each environment play significant roles, impacting the compatibility with cell membranes and influencing uptake dynamics [8]. Furthermore, the specific cell type targeted is a crucial consideration, as different cell types may exhibit varying uptake behaviors based on their inherent characteristics. Collectively, these findings provide a holistic perspective on tailoring nanomaterials for optimized cellular uptake, fostering safer and more effective applications in drug delivery and biomedical research. The research contributes to the evolving field of nanotechnology, emphasizing the importance of systematically addressing size, shape, and capping agent effects to advance the design and implementation of nanomaterials in biomedical contexts.

In this report, we conducted rigorous research and consulted numerous research papers, articles, and review papers to investigate nano-bio interfaces. Our primary focus was on HELA and HEK cell types, with the main objective being the examination of the cellular uptake of nanoparticles on these cells. Although various factors influence cellular uptake and cytotoxicity, we specifically considered three factors. Our primary goal was to assess how the size and shape of different nanoparticles impact cellular uptake. Recognizing the potential significance of the capping agent, we designated it as the third objective. Each research paper had its own objective and conclusion. Other factors, such as preparation methods, types of solutions used, surface charge, and the ratio of cells to nanoparticle surface area, were not within the scope of our study and could be explored by others in future research.

2. Methodology

This approach involves reading a CSV file containing cytotoxicity data for various nanoparticles on different cell types. The user is prompted to enter the type of nanoparticles (gold, silver, or other) and the cell type (Hek or Hela) they are interested in. The code then filters the data based on the user's input and selects the two most toxic nanoparticles for each unit of measurement. Finally, the code displays the results for each nanoparticle.

The specific steps involved in this approach are as follows:

1. Import pandas and re libraries.
2. Read the CSV file into a Pandas DataFrame.
3. Fill missing values in the 'Nanomaterial' and 'Cell type' columns with empty strings.
4. Get user input for the type of nanoparticles (gold, silver, or other).
5. Create separate DataFrames for gold, silver, and other nanoparticles.
6. Select the DataFrame based on user input.
7. Get user input for the cell type (Hek or Hela).
8. Filter the DataFrame based on the user's input for cell type.
9. Define a function to extract the value and unit from cytotoxicity values.
10. Get unique nanomaterials from the filtered DataFrame.
11. Iterate over the unique nanomaterials.
12. For each nanomaterial, create a DataFrame containing only that nanomaterial.
13. Apply the function to extract the value and unit from cytotoxicity values.
14. Sort the DataFrame by 'Value' in descending order and group by 'Unit'.
15. Select the top two rows from each group.
16. Drop unwanted columns from the DataFrame.
17. Check if the DataFrame is empty.
18. If the DataFrame is not empty, display the results for the nanomaterial.

This approach is effective in identifying the most toxic nanoparticles for each unit of measurement based on the user's input for nanoparticle type and cell type. The code is also well-structured and easy to follow.

Data Research:

The data for this analysis was obtained from a publicly available dataset on cytotoxicity of nanoparticles on different cell types. The dataset is comprised of various nanoparticles and their cytotoxicity effects on HEK and Hela cells. The data is presented in a CSV format, with columns for nanoparticle type, cell type, size, shape, capping agent, cytotoxicity value, and unit of measurement.

Data Cleaning and Preprocessing:

Before analyzing the data, it was necessary to clean and preprocess it to ensure its consistency and accuracy. This involved the following steps:

1. Importing Libraries: The necessary libraries, pandas and re, were imported to handle data manipulation and regular expression operations, respectively.
2. Reading CSV File: The CSV file containing the cytotoxicity data was read into a Pandas DataFrame using the pd.read_csv() function.
3. Filling Missing Values: Missing values in the 'Nanomaterial' and 'Cell type' columns were filled with empty strings for further processing.

User Input and Data Filtering

The code interacts with the user to obtain their desired nanoparticle type and cell type for the analysis. This involves:

1. User Input Prompt: The user is prompted to enter the type of nanoparticles (gold, silver, or other) using the input() function.
2. Nanoparticle Type Selection: Based on the user's input, a separate DataFrame is created for the corresponding nanoparticle type.
3. User Input for Cell Type: The user is prompted to enter the cell type (Hek or Hela) using the input() function.
4. Cell Type Filtering: The filtered DataFrame is obtained by selecting the rows containing the user-specified cell type.

Extracting Value and Unit from Cytotoxicity Values:

The cytotoxicity values are extracted from the 'Cytotoxicity (mg/ml)' column using regular expressions. This involves:

1. Defining the Extract Function: A function extract_value_and_unit() is defined using regular expressions to extract the numerical value and unit of measurement from the cytotoxicity values.

2. Applying Extract Function: The extract_value_and_unit() function is applied to the 'Cytotoxicity (mg/ml)' column to create new columns 'Value' and 'Unit'.

Identifying Most Toxic Nanoparticles:

The code identifies the two most toxic nanoparticles for each unit of measurement based on the filtered DataFrame:

1. Unique Nanomaterials: The unique nanomaterials within the filtered DataFrame are obtained.

2. Iteration over Nanomaterials: For each unique nanomaterial, a separate DataFrame is created.

3. Applying Extract Function: The extract_value_and_unit() function is applied to the extracted cytotoxicities to create 'Value' and 'Unit' columns.

4. Sorting and Top Two Selection: The DataFrame is sorted by 'Value' in descending order and the top two rows for each 'Unit' group are selected.

5. Dropping Unwanted Columns: Unwanted columns like 'Reference' and 'Unnamed: 7' are removed from the DataFrame.

6. Results Display: The results for each nanomaterial are displayed, indicating the nanomaterial type, cytotoxicity value, and unit of measurement.

Overall Methodology:

The code adopts a structured and well-defined approach for analysing cytotoxicity data for various nanoparticles on different cell types. It involves data reading, cleaning, user input, preprocessing, extracting value and unit, identifying the most toxic nanoparticles, and displaying results. The use of regular expressions, Pandas DataFrames, and user input enhances the code's functionality and user-friendliness.

3. Discussion

SIZE:

Cell Type	Nanoparticle	Functional Group	Capping agent	Size	Shape	Toxicity/Viability	Cellular Uptake
Hela	Au	Thiol	PEG	5.4(AR)	Rod	80pM	11.5 (AR)> 5.4(AR)
				11.5(AR)			
		carboxylic	Citrate	14nm	Sphere	5uM	50nm>14nm
				50nm		40uM	
HEK			Citrate	14nm	Sphere	100ug/ml	20nm>14nm
				20nm			
Hela	Ag	carboxylic	Citrate	70nm	Bell shaped	50ug/ml	70nm has better uptake
				200nm			
				500nm			
			Citrate	10nm		0.0001 - 5 mg/ml	10nm has better uptake
				30nm			
				100nm			
			Citrate	5nm	Sphere	8,6mg/ml	Smaller sizes 5nm,20nm has better uptake than 50nm and 100nm
				20nm		10.2mg/ml	
				50nm		11.8mg/ml	
				100nm		13.4mg/ml	
			Citrate	10nm	Sphere	50ug/ml	Smaller sizes 10nm found to have higher uptake
				40nm			
				75nm			
Hek	ZnS	carboxylic	Citrate	4nm	Sphere	4.75uM	25nm>10nm>4nm
				10nm		2.75uM	
				25nm		<2.75uM	

Cellular uptake of nanoparticles is significantly influenced by their size. Extensive research indicates that particles within the medium range (approximately 20-50nm) exhibit optimal uptake compared to sizes either smaller or larger than this range. Notably, within this spectrum, certain sizes demonstrate more efficient cellular uptake. For instance, when comparing sizes like 14nm and 20nm, the latter displays enhanced cellular uptake. Similarly, in a comparison between 50nm and 14nm, the 50nm particles exhibit the highest cellular uptake levels. This emphasizes the critical role of nanoparticle size in determining their cellular uptake efficiency.

Larger nanoparticles are generally not as readily absorbed by cells as smaller ones are. This is due to the fact that smaller nanoparticles have increased surface area to volume ratio, which increases their amount of membrane contact. Furthermore, cells can more readily absorb tiny nanoparticles because they are more flexible than larger ones.

SHAPE:

Cell Type	Nano Material	Fuctional Group	Capping Agent	Size	Shape	Toxicity / Viability	Cellular Uptake
Hela	Gold	Ammonia	CTAB	43nm	sphere	1.9x10^-5M	Sphere > Rods
				17.2 x 37.8nm	rod	9.4 x 10^-6M	
		Carboxylic	Citrate	14nm	sphere	1.9 x 10 ^-5 M	
				17nm			
				14x40nm	rods	1.9 x 10 ^-5 M	
				14x74nm			
				15nm	sphere	0.42 mg/ml	
				25nm	rods	0.32 mg/ml	
		ThioI	PEG	15nm	sphere	1.02 mg/ml	
				25nm	rods	0.78 mg/ml	
		Ammonia	CTAB	50nm	sphere	0.1 mg/ml	Sphere > Rods > Cubes
				10 x 45 nm	rods	0.3 mg/ml	
				50nm	cubes	0.6 mg/ml	
				43nm	sphere	1.5 micmg/ml	sphere > Rods
				38 x 17nm	rods	16 micmg/ml	
hela and hek		Pyrrolidine	PVP	10nm	sphere	>300 mg/ml	spheres has the most cellular uptake
				370nm	flower	100- 200 mg/ml	
				41nm	rod	10 - 20 mg/ml	
				160nm	prism		
				240nm	stars		
Hela		Amide	chitosan	9nm	sphere	127 microM	Sphere > Rods > Stars
				100nm	rods	81.8 microM	
				61nm	stars	8 microM	

One important aspect of NPs' cellular uptake is their shape. Numerous instances indicate that spheres exhibit superior cellular uptake and lower toxicity in comparison to discs. For example, Zhang, S research article demonstrates that while cell viability significantly declines at concentrations of 50 and 400 for spheres, it does not decrease at concentrations of 50 for discs. Therefore spheres are more toxic compared to disc.[9]

Numerous experimental studies have shown that of all the forms compared, sphere-shaped NPs have the maximum cellular uptake, followed by cube- and star-shaped NPs, which have the least amount of cellular uptake. Rod-shaped NPs, on the other hand, have a moderate amount of cellular uptake. Initially, rod-shaped NPs require more time to wrap their membranes than spherical NPs do. Second, surfactant molecules that have adsorbed onto the nanorods' longitudinal axis interfere with the ligand-NP surface binding that promotes cellular uptake. The length to breadth ratio of nanorods, or aspect ratio, has a big impact on how well they are absorbed by cells.

CAPPING AGENT:

Cell Type	Nano Material	Functional Group	Capping Agent	Size	Shape	Toxicity / Viability	Cellular Uptake
Hela	Gold	Thiol	PEG	5-11 nm	Sphere	80pm	PEG>CTAB
		Ammonium	CTAB				
		carboxylic	Citrate	5-20nm		285	
				45nm			
		carboxylic	Citrate	3-10nm		150mg	chitosan > citrate
		Amide	chitosan				
		polyphenol	leaf extract	10-20nm		100mg	
		carboxylic	citrate	14nm		5 micrg/ml	14nm citrate >mua
				50nm		40 micromg/ml	
		alcohol	MUA	14nm		5 micromg/ml	50nm mua > citrate
				50nm		40micromg/ml	
		carboxylic	citrate	15nm		0.42 mg/ml	regardless of shape, size PEG > citrate
		Thiol	PEG		Rod	1.02mg/ml	

The capping agent's action is a crucial component of the NPs' cellular uptake. Numerous studies have demonstrated that the NPs coated with PEG which as thiol functional group has the highest cellular uptake when compared to the chitosan (with amide functional group), CTAB (with ammonium functional group), Citrate (with carboxylic functional group), and MUA (with alcohol functional groups), which have moderate uptake, and the phenol groups which exhibit the lowest cellular uptake.

The following elements generally increase the cellular absorption of capping agents:

- The existence of hydrophilic groups, like amino (-NH2) and hydroxyl (-OH) groups
- Charged groups like sulfonic acid (-SO3H) and carboxylic acid (-COOH) groups are present.
- How the capping agent is smaller in size
- The increased capping agent concentration

The size, shape, and surface charge of the nanoparticle can also have an impact on the cellular uptake of capping agents. Smaller nanoparticles, for instance, are often absorbed by cells more quickly than larger ones. Positively charged nanoparticles are also often absorbed by cells more quickly than negatively charged ones.

The design of nanoparticles for biological purposes must take into account the cellular uptake of capping agents. The size, shape, and surface characteristics of nanoparticles can be altered by capping agents, which can therefore have an impact on the particles' toxicity, biodistribution, and cellular uptake.

4. Concluding Remarks

The cellular uptake of nanoparticles is a critical factor in their effectiveness for various biological applications. Several factors influence the uptake process, including the nanoparticle's size, shape, and capping agent.Particle size plays a pivotal role in cellular uptake. Nanoparticles between 20 and 50 nanometers exhibit the highest uptake efficiency. This size range allows for efficient internalization via endocytosis while avoiding filtration by the kidneys. Nanoparticles smaller than 20 nanometers may be too small for cellular uptake, while those larger than 50 nanometers may be too bulky for efficient transport into cells.Spherical nanoparticles generally demonstrate superior cellular uptake compared to other shapes, such as rod-shaped, cube-shaped, and star-shaped nanoparticles. Spherical nanoparticles have a smoother surface, reducing the likelihood of aggregation or opsonization by blood proteins.The capping agent, a molecule attached to the nanoparticle's surface to prevent aggregation, also influences cellular uptake. Capping agents with thiol functional groups, such as PEG-SH, often enhance uptake the most. Thiol groups can form disulfide bonds with proteins on the cell surface, facilitating nanoparticle entry. Additionally, hydrophilic or charged capping agents can promote cellular uptake by interacting with the cell membrane.When designing nanoparticles for biological applications, carefully consider the size, shape, and capping agent to optimize cellular uptake, minimize toxicity, and achieve the desired therapeutic effect. Balancing these factors is crucial for developing effective nanomedicines.

5. Future Work

Nanomaterials hold significant promise for a variety of biological and industrial applications. Concerns concerning their possible effects on the environment and human health are brought up by their distinct physicochemical characteristics. The future works may include considering may other factors into consideration for the cellular uptake of the NPs Such as surface charge, Hydrophobicity/Hydrophilicity, Temperature and Incubation Time, Steric Hindrance, Preparation methods of the nano particles, Solutions that are used in the preparation methods, etc.

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