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# **Review**

# Implementation of Nanotechnology for Drug Delivery System: Mini Statement

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## Abstract:

Over last four decades, nano-technology is catching up and show no sign of stopping. It has changed the way that all matter of everyday life is affected, from the medical uses to the food industry. The use of nanoparticles since has become crucial for food product (shelf-life extension) as well as intracellular hydrophobic drug delivery, and enhancing the effectiveness of several therapeutic agents, for example anticancer agents; It emphasizes a potential problem and solution related to the extensive use of nanotechnology without interruption, which may lead to continual human contact with nanoparticles.

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## Conflict of interest: Nil

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## Introduction:

Nanotechnology is the plan and control of particulate materials in a condition of  $\sim 1$  nm to 100 nm in size and frame to be used as Nano frameworks with improved usefulness [1]. For instance, nanotechnology arose as a key headway, and its application throughout the last ten years has set Ireland solidly at the cutting edge of logical examination [2]. Nanoparticles are the outcome of the mechanical difference in issue, two or three degrees of size greater than a bit consequence of the treatment of issue in a sub-nuclear scale. Since they are more components like Auto-responsive consistent and self-reassembly, they are really flexible and can be changed to achieve a specific brand name or arranged, for instance, high surface locale when stood out from old approach [3,4].

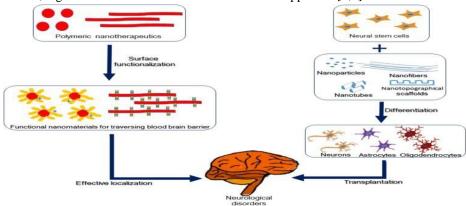


Fig1: Nano-based Medicine in Neurodegenerative disease.

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Nanotechnology is a moderately youthful part of science, drawing in nearer consideration basically throughout recent many years and presently advancing out of the scholarly world and into the business. No place is this more apparent than in nanotechnology, as potential progressions that can be made by this innovation an affect the worldwide economy by about three trillion bucks by 2020 [5] making it an exceptionally impressive contender for financially feasible advancements. These consolidate the extraordinary physical and substance properties of nanoparticles on the constraint of science as well as medicine [7].

Nanotechnology imaginative work is one of the fastest creating lots of legitimate fields with various degrees of progress in different applications. As of now encompassing different fields commonly its own including electrics, energy, materials, bio-prescription, and so on the state of the art in nanotechnology is enormous. Illustrative Picture: Specialists are researching the use of pretty much nothing, extrememly little, semiconductors and various parts to make more humble, speedier and energy satisfactory contraptions in Equipment make new materials and contraptions for reasonable power creation, energy limit and restrict the natural impact of the age and use of energy, some energy warming is used for families.

Nanotherapeutics Better approaches to manage add disposition and potentiate transport of regardless essential medicines integrate assigned treatment and theragnostic. Together, they uncover a field of truly noteworthy dynamism and improvement as addressed by the current status of-the-specialty of nanotechnology.

The more we find out about nanoparticles and nanomaterials then the more extensive their significant applications in medication becomes known. Drug conveyance is one of the most intriguing areas of utilization, on the grounds that nanoparticles can act which present upon them the capacity to target explicit cells types, for example, the infected ones while keeping away from sound cells thus expanding the viability of medications and lessening their secondary effects [6]. Significantly, nanoparticles can likewise give planned arrival of therapeutics, which is urgent for dependable medication conveyance [7-8].

Nanotechnology has by and large affected different regular fields, particularly medicine. One of the most conspicuous responsibilities is the improvement of nanoparticle-enabled drug movement systems for disease treatment. These systems impact the striking properties of nanoparticles to deal with the ampleness and precision of clinical meds. Nanoparticles have obtained popularity in medicine in light of their ability to further develop drug movement. They can be intended to pass medicinal experts clearly on to target districts, thusly extending drug center at the infection site while restricting receptiveness to strong tissues. This assigned methodology can provoke higher treatment ampleness and diminished accidental impacts stood out from standard prescription movement techniques. Despite their promising applications, the wide usage of nanoparticles in drug raises stresses over anticipated

dangerous effects. Nanoparticles can connect with natural structures in sporadic ways, provoking destructiveness and other troublesome effects. Their little size and colossal surface district can achieve extended reactivity and the likelihood to cross normal checks, which could introduce threats to human prosperity.

To address these concerns, the improvement of nanoparticle drug movement structures (DDSs) is based on making safer and more convincing nanoparticles. These degrees of progress integrate arranging nanoparticles with biocompatible materials, updating their size and surface properties to diminish noxiousness, and merging zeroing in on frameworks to ensure they pass their payloads precisely on to the normal site.



Fig.2 Diversity of Nano technology.

## Nanomedicine

In any case, the possibility of nanotechnology was curiously presented in the clinical field by Dr. Richard P. Feynman in the fifties, when he outlined using development to make machines under a disease suitable in planning and prescription. He spread out the picture of nuclear mechanical Machines that are top of the deed of carrying out an operation or those which could be implanted in the body to help utilitarian hurt organs [9]. Nanotechnology is the most pointing subject of the ongoing scene that has by and large impacted prescription and construction how ailments are regulated especially with the curves of state of the art drug movement system from normal as well as produced sources.

For example, specialists at the Wyss Groundwork of Harvard School made a "nano-robot" that is good for recognizing dangerous development cells and conveying carte anticancer. Other almost specialists that are being created integrate nano-robots that can address cardiovascular contaminations which incorporate vein recovering where the nano-robots continue like phony platelets or nano-robots that can treat patients with coronary course obstruction. Nanotechnology can be most important in clinical applications and possibly in drug transport associations. The stream conviction is that most of the normal prescriptions have low levels of bio-openness and dissolvability in water thus acquainting a huge test with their take-up and security in the regular structures [13] Energy tries stay focused in on working on the practicality of most of the standard/customary meds.

Physical and more unassuming in size nanoparticles are considered to have pharmacokinetic properties and can be used to show up at explicit cells to explicitly work in a particle unequivocal way. These particles can quickly cross cell films and be passed on to subcellular compartments to adjust cell pathways, to potentially treat disorders including durable conditions, for instance, diabetes, threatening development and kidney ailments [14]. Besides, the particle sizes of these nanoparticles have been shown to fall inside those predefined in the blueprint under; along these lines, a critical number of these nanoparticles have recently been upheld for use in the middle by the Public authority Drug Association in the US. Notable exploration nanoparticle therapeutics consolidate exemplified mRNA (siRNA) and DNA (in quality treatment), inorganic metal and metal structures, or pharmacologic experts with chemotherapeutic effects [15,16]. A great deal of these nanoparticles, in other words, cross the telephone layer, requiring transport systems to moderate such difficulties. Along these lines, remarkable nanoparticle transport structures, some of which integrate liposomes, micelles, chitosan, and fabricated dendrimers [17-21].

For example, nanoparticles-based transport systems development including liposomes are a profoundly grounded instrument for disorder treatment like DoxilTM (liposomal doxorubicin) embraced by the FDA to treat Kaposi sarcoma and ovarian threatening development. In this manner, liposomal encapsulation fills in as a productive course to redesign the supportive suitability of the medicine. Additionally, by changing the liposomes, tumorous cells inside the body can be reached inactively or really. The effect allowed a useful transport of drugs payload inside the dangerous development malignant growth, while the normal cells would simply be fairly influenced. It chips away at the cytotoxic ability of doxorubicin stacked in the DPPC-based liposome and besides time covers the destructive optional impacts, thusly dealing with the antitumor healing ampleness conversely, with customary doxorubicin [22].

Multifunctional imaging stages like X-beam/optical twofold secluded imaging have been made using iron oxide and silica-based nanoparticles. These stages partake in a couple of high grounds over the continuous positron spread tomography (PET) and handled tomography (CT), the two of which have radiation-related concerns [23-25]. Since iron oxide spoils in normal structures, a magneto responsive metal is similarly biocompatible. It is a radiant X-beam imaging material because of this as well as its optical characteristics. X-beam contrast experts that contain iron oxide nanoparticles have been utilized generally. Since they change the alluring loosening up times of tissues, they are superparamagnetic and can additionally foster difference in X-beam imaging.

This brand name has been applied to clinical imaging for different purposes, for instance, exacerbation imaging, atherosclerosis imaging, and infection acknowledgment. Also, X-pillar contrast experts for CT imaging have moreover been used with silica-based nanoparticles [26]. Because of their high X-shaft debilitating, silica nanoparticles can be used to chip away at the separation in CT pictures, which can be valuable for following and diagnosing different disorders and illnesses, including disturbance and threatening development. A silica-based

nanoparticle with a shining place and a paramagnetic shell was uncovered by Kim et al. [27]. By solidifying the optical property of the nanoparticle focus with the alluring field of the X-beam, this extraordinary nanoparticle gives the likelihood to multimodal imaging. Peptides or other positive combinations can in like manner be used to functionalize the paramagnetic shell. This offers the opportunity to unequivocally zero in on illness cells.

### Physiochemical Properties of Nanoparticles in Medicine

When stood out from more noteworthy particles, the characteristics of nanoparticles think about redesigned pharmacologic approach to acting. To update the potential gains of nanoparticles for clinical applications, a great deal of investigation is being done on changing their size, shape, surface district, and surface science. Different nanoparticles, including liposomes, micelles, and gold nano-shells, can be delivered in different ways, and dependent upon the best helpfulness, the sizes and sorts of these nanoparticles can be changed during the association cycle. During combination, nanoparticles can add up to into greater estimated particles, which, dependent upon their beauty care products, can either augmentation or decrease their cytotoxicity. Assigned drug transport structures can change the surface study of nanoparticles by uniting open get-togethers or iotas, such antibodies, onto their surfaces. Several the physicochemical characteristics of nanoparticles are their charged surfaces, their capacity to bunch together, their capacity to frame various get-togethers to their surfaces, and their controlled association, which simplifies it to make explicit designs and sizes. Considering these properties, nanoparticles can be more responsive in the natural milieu than various types of particles.

#### Size and Surface Region

As recently said, nanoparticles have a high surface region to volume proportion since they are minuscule particles that reach in size from 1 nm to 100 nm. This trademark prompts a few generally latent particles, similar to gold, to become receptive in the nanoscale range in light of the fact that nanoparticles have a higher surface area of contact per mass unit than additional significant particles [27]. Controllably little sizes of nanoparticles give simple entrance of natural liquids and tissues, which would somehow or another be troublesome in mass structure. Basically, the speed at which these nanoparticles are endocytosed, scattered, kept up with, and eliminated inside organic frameworks is affected by their size and surface region [28]. Broad concentrate on the vehicle of nanoparticles into typical and disease cell lines has exhibited that they are consumed by endocytosis processes in a size-subordinate way, since they don't simply diffuse through the cell layer [29.30]. Bigger nanoparticles, ordinarily 500 nm, are known to be consumed by caveolae-interceded endocytosis, while nanoparticles more modest than 200 nm are known to be ingested by clathrin-covered vesicles [31].

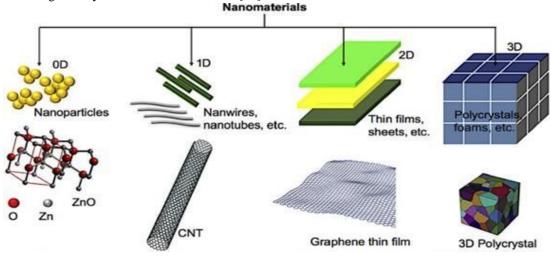
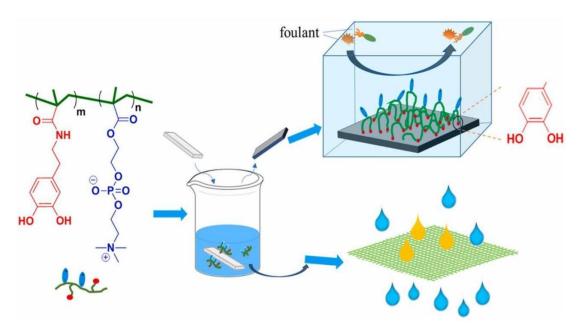
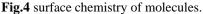


Fig3: Classification and Size of different nanoparticles.

#### Surface Chemistry

The charge or compound gatherings that are connected to the outer layer of nanoparticles assume a critical part in deciding their reactivity, which thus can oversee their capability.





A ton of nanoparticles have had their surface science modified for various purposes. Because of their charge, DNA and pole molded gold nanoparticles (AuNPs) are hard for cells to infiltrate or enter. Lipid layers have been applied to the surfaces of both AuNP and DNA to adjust them, and DNA has likewise been electrostatically coupled to cationic liposomes to help with their vehicle into the phone and improve take-up [31-33]. ZnO2 nanoparticles are generally utilized in sunscreen, because of their UV security properties, yet a few examinations have shown the likely cytotoxicity of the nanoparticles making their application in surface level items troubling.To invalidate this, a few specialists have changed the surface properties, and without a doubt, a review has shown that by surface covering ZnO2 with poly methyl acrylic corrosive (PMAA), the cytotoxicity was decreased the nanoparticles held their UV insurance qualities [34-35].

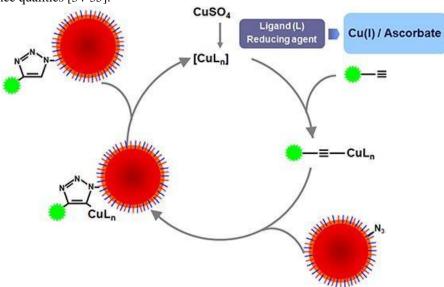


Fig 5. Inorganic properties of Nanoparticle.

## Nanoparticle Cytotoxicity

The development of nanotechnology and its extending use in virtually every part of day to day existence have raised worries about potential dangers related with expanded human openness. The investigation of the perilous impacts or poisonousness of openness to nanoparticles has prompted the advancement of the field of nano-toxicology. This

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field has as of late found that the qualities of nanoparticles that give them fitting pharmacologic activity are likewise responsible for their poisonousness [36]. Various examinations have analyzed the poisonousness of different nanoparticles under different exploratory conditions and with different cell types. For instance, it has been exhibited that the poisonousness of carbon nanotubes influences the assortment of soil microscopic organisms [37], hinders the development of Chlorella vulgaris, Daphnia magna, and Oryziaslatipes [38], and causes oxidative pressure, film harm, and irritation in human A549 lung carcinoma cell line [39-40]. Raised ROS levels cause oxidative pressure, which upsets the phone's normal physiological capabilities and prompts DNA harm, flagging dysregulation, lastly cell demise. Surface-altered nanoparticles are much of the time used to work on their functionalities. Since the surface science of the nanoparticle influences its characteristic poisonousness, this could accidentally prompt an expansion in the cytotoxicity of the molecule. Responsive surface moieties on nanoparticles can respond with different intracellular or extracellular biomolecules relying upon where they are situated inside the natural framework. This can upset the customary cycles that keep tissues or cells in a condition of homeostasis. For instance, it has been exhibited that charged AuNPs are more hurtful than unbiased AuNPs on the grounds that they cause more noteworthy oxidative pressure, which brings down mitochondrial action and increments articulation. It is notable that anionic cyan acrylic nanoparticles are more cytotoxic to macrophages than their cationic partners [42]. The phagocytosis proclivity of the macrophage towards the bacterial cell film, which displays a general negative charge due to the Lipid A particle of the LPS part of the bacterial cell layer, could be the reason for these inconsistencies. Then again, contrasted with a PEGylated variant, agminated iron oxide nanoparticles with a general positive charge have been exhibited to be all the more really incorporated and to cause more noteworthy cytotoxicity in a Chinese Hamster Ovary (CHO-K1) cell line [43]. For a more drawn out enduring impact in vivo, nanoparticles are oftentimes PEGylated to support their retention and lower their immunogenicity [44]

#### **Summary and Future Directions**

There is no dismissing that the gigantic advances in the fields of prescription, food and magnificence care items, and individual tidiness have worked on our perspective on the world. These movements have moreover provoked the improvement of nanotechnology's general business habitats, helping the development's feasibility and monetary impact on nations from one side of the planet to the next. Different standard medications with hazardous auxiliary impacts, such doxorubicin, have been successfully given in segments inside nano-carriers on account of their clinical applications. This hinders unpleasant effects that would some way or another or one more end the association of these prescriptions. Nanoparticles like AgNPs have sincerely committed to food preservation in the food business by growing period of time of convenience and in general incomes. To be sure, even with these advantages, there are detriments. Regularly, nanoparticles are very responsive considering the way that There are various ways that nanoparticles enter the environment, including through aftereffects from homes and associations. This, close by the unfathomable usage of nanoparticles in typically consumed items, raises the opportunity of perilous effects from reiterated receptiveness to these particles. Advocated nanoparticles may not by and by spread the word about any harmful side effects, but long human receptiveness to them through ingestion of things or unusual normal transparency could at last provoke disastrous optional impacts. The safe structure uses different procedures, similar to macrophage phagocytosis, to perceive and discard unwanted particles, including nanoparticles. Along these lines, for successful biomedical applications, strategies including surface adjustment and centering to reduce safe ID and opportunity of nanoparticles are required. Additionally, one huge issue that ought to be agreed to clinical translation is the relentlessness and repeatability of nanoparticles. The approach to acting of nanoparticles in natural systems and the sufficiency of their applications can be impacted by their physicochemical components, which consolidate size, shape, and surface charge. In like manner, the viable usage of nanoparticles in clinical settings requires their mix and depiction to be repeatable. Finally, considering the way that the regulatory opportunity strategy for progressions considering nanoparticles is at this point being made, it will in general be moving for associations and researchers to investigate.

#### **BIBLIOGRAPHY:**

1. 1.Nasrollahzadeh, M.; Sajadi, S.M.; Sajjadi, M.; Issaabadi, Z. An introduction to nanotechnology. In Interface Science and Technology; Elsevier: Amsterdam, The Netherlands, 2019; Volume 28, pp. 1–27.

- Doran, J.; Ryan, G. Does nanotechnology research generate an innovation premium over other types of research? Evidence from Ireland. Technol. Soc. 2019, 59, 101183.
- Cheng, Y.J.; Wolkenhauer, M.; Bumbu, G.G.; Gutmann, J.S. A Facile Route to Reassemble Titania Nanoparticles into Ordered Chain-like Networks on Substrate. Macromol. Rapid Commun. 2012, 33, 218–224.
- Kango, S.; Kalia, S.; Celli, A.; Njuguna, J.; Habibi, Y.; Kumar, R. Surface modification of inorganic nanoparticles for development of organic–inorganic nanocomposites—A review. Prog. Polym. Sci. 2013, 38, 1232–1261.
- 5. Roco, M.C. Overview: Affirmation of Nanotechnology between 2000 and 2030. In Nanotechnology Commercialization: Manufacturing Processes and Products; Wiley: Hoboken, NJ, USA, 2017; pp. 1–23.
- Huang, Q.; Yu, H.; Ru, Q. Bioavailability and delivery of nutraceuticals using nanotechnology. J. Food Sci. 2010, 75, R50–R57.
- Bajpai, V.K.; Kamle, M.; Shukla, S.; Mahato, D.K.; Chandra, P.; Hwang, S.K.; Kumar, P.; Huh, Y.S.; Han, Y.-K. Prospects of using nanotechnology for food preservation, safety, and security. J. Food Drug Anal. 2018, 26, 1201–1214.
- Carbone, M.; Donia, D.T.; Sabbatella, G.; Antiochia, R. Silver nanoparticles in polymeric matrices for fresh food packaging. J. King Saud Univ. Sci. 2016, 28, 273–279.
- 9. Feynman, R.P. There's plenty of room at the bottom. Eng. Sci. 1960, 23, 22-36.
- Douglas, S.M.; Bachelet, I.; Church, G.M. A logic-gated nanorobot for targeted transport of molecular payloads. Science 2012, 335, 831–834.
- Trihirun, S.; Achalakul, T.; Kaewkamnerdpong, B. Modeling nanorobot control for blood vessel repair: A non-Newtonian blood model. In Proceedings of the Biomedical Engineering International Conference (BMEiCON), Amphur Muang, Thailand, 23–25 October 2013; pp. 1–5.
- Cavalcanti, A.; Rosen, L.; Shirinzadeh, B.; Rosenfeld, M.; Paulo, S.; Aviv, T. Nanorobot for treatment of patients with artery occlusion. In Proceedings of the Proceedings of Virtual Concept, Cancun, Mexico, 26 November–1 December 2006.
- Khadka, P.; Ro, J.; Kim, H.; Kim, I.; Kim, J.T.; Kim, H.; Cho, J.M.; Yun, G.; Lee, J. Pharmaceutical particle technologies: An approach to improve drug solubility, dissolution and bioavailability. Asian J. Pharm. Sci. 2014, 9, 304–316.
- 14. Barua, S.; Mitragotri, S. Challenges associated with Penetration of Nanoparticles across Cell and Tissue Barriers: A Review of Current Status and Future Prospects. Nano Today 2014, 9, 223–243.
- 15. Khurana, A.; Tekula, S.; Saifi, M.A.; Venkatesh, P.; Godugu, C. Therapeutic applications of selenium nanoparticles. Biomed. Pharm. 2019, 111, 802–812.
- Sharma, A.R.; Lee, Y.H.; Bat-Ulzii, A.; Bhattacharya, M.; Chakraborty, C.; Lee, S.S. Recent advances of metal-based nanoparticles in nucleic acid delivery for therapeutic applications. J. Nanobiotechnolgy. 2022, 20, 501.
- Park, J.H.; von Maltzahn, G.; Ruoslahti, E.; Bhatia, S.N.; Sailor, M.J. Micellar hybrid nanoparticles for simultaneous magnetofluorescent imaging and drug delivery. Angew. Chem. Int. Ed. Engl. 2008, 47, 7284–7288.
- Wang, X.; Cai, X.; Hu, J.; Shao, N.; Wang, F.; Zhang, Q.; Xiao, J.; Cheng, Y. Glutathione-triggered "offon" release of anticancer drugs from dendrimer-encapsulated gold nanoparticles. J. Am. Chem. Soc. 2013, 135, 9805–9810.
- 19. Sanyakamdhorn, S.; Agudelo, D.; Tajmir-Riahi, H.-A. Encapsulation of antitumor drug doxorubicin and its analogue by chitosan nanoparticles. Biomacromolecules 2013, 14, 557–563.
- Hasan, M.; Belhaj, N.; Benachour, H.; Barberi-Heyob, M.; Kahn, C.; Jabbari, E.; Linder, M.; Arab-Tehrany, E. Liposome encapsulation of curcumin: Physico-chemical characterizations and effects on MCF7 cancer cell proliferation. Int. J. Pharm. 2014, 461, 519–528.

- Koudelka, S.; Masek, J.; Neuzil, J.; Turanek, J. Lyophilised liposome-based formulations of alphatocopheryl succinate: Preparation and physico-chemical characterisation. J. Pharm. Sci. 2010, 99, 2434– 2443.
- 22. Barenholz, Y. Doxil(R)—The first FDA-approved nano-drug: Lessons learned. J. Control. Release 2012, 160, 117–134.
- 23. Lee, N.; Yoo, D.; Ling, D.; Cho, M.H.; Hyeon, T.; Cheon, J. Iron Oxide Based Nanoparticles for Multimodal Imaging and Magnetoresponsive Therapy. Chem. Rev. 2015, 115, 10637–10689.
- 24. Kim, J.S.; Rieter, W.J.; Taylor, K.M.; An, H.; Lin, W. Self-assembled hybrid nanoparticles for cancerspecific multimodal imaging. J.Am. Chem. Soc. 2007, 129, 8962–8963.
- 25. Louie, A. Multimodality imaging probes: Design and challenges. Chem. Rev. 2010, 110, 3146–3195.
- Shirshahi, V.; Soltani, M. Solid silica nanoparticles: Applications in molecular imaging. Contrast Media Mol. Imaging 2015, 10, 1–17.
- 27. Chaloupka, K.; Malam, Y.; Seifalian, A.M. Nanosilver as a new generation of nanoproduct in biomedical applications. Trends Biotechnol. 2010, 28, 580–588.
- Nel, A.; Xia, T.; M\u00e4dler, L.; Li, N. Toxic potential of materials at the nanolevel. Science 2006, 311, 622– 627.
- 29. Powers, K.W.; Palazuelos, M.; Moudgil, B.M.; Roberts, S.M. Characterization of the size, shape, and state of dispersion of nanoparticles for toxicological studies. Nanotoxicology 2007, 1, 42–51.
- Tsai, C.Y.; Lu, S.L.; Hu, C.W.; Yeh, C.S.; Lee, G.B.; Lei, H.Y. Size-dependent attenuation of TLR9 signaling by gold nanoparticles in macrophages. J. Immunol. 2012, 188, 68–76.
- Jiang, W.; Kim, B.Y.; Rutka, J.T.; Chan, W.C. Nanoparticle-mediated cellular response is size-dependent. Nat. Nanotechnol. 2008, 3, 145–150.
- 32. Rejman, J.; Oberle, V.; Zuhorn, I.S.; Hoekstra, D. Size-dependent internalization of particles via the pathways of clathrin- and caveolae-mediated endocytosis. Biochem. J. 2004, 377, 159–169.
- 33. Chithrani, D.B.; Dunne, M.; Stewart, J.; Allen, C.; Jaffray, D.A. Cellular uptake and transport of gold nanoparticles incorporated in a liposomal carrier. Nanomedicine 2010, 6, 161–169.
- 34. Gosangari, S.L.; Watkin, K.L. Effect of preparation techniques on the properties of curcumin liposomes: Characterization of size, release and cytotoxicity on a squamous oral carcinoma cell line. Pharm. Dev. Technol. 2012, 17, 103–109.
- 35. Oh, E.; Delehanty, J.B.; Sapsford, K.E.; Susumu, K.; Goswami, R.; Blanco-Canosa, J.B.; Dawson, P.E.; Granek, J.; Shoff, M.; Zhang,Q. Cellular uptake and fate of PEGylated gold nanoparticles is dependent on both cell-penetration peptides and particle size. Acs Nano 2011, 5, 6434–6448.
- Saucier-Sawyer, J.K.; Deng, Y.; Seo, Y.-E.; Cheng, C.J.; Zhang, J.; Quijano, E.; Saltzman, W.M. Systemic delivery of blood-brain barrier-targeted polymeric nanoparticles enhances delivery to brain tissue. J. Drug Target. 2015, 23, 736–749.
- 37. Suk, J.S.; Xu, Q.; Kim, N.; Hanes, J.; Ensign, L.M. PEGylation as a strategy for improving nanoparticlebased drug and gene delivery. Adv. Drug Deliv. Rev. 2016, 99, 28–51.
- Fillion, P.; Desjardins, A.; Sayasith, K.; Lagace, J. Encapsulation of DNA in negatively charged liposomes and inhibition of bacterial gene expression with fluid liposome-encapsulated antisense oligonucleotides. Biochim. Biophys. Acta 2001, 1515, 44–54.
- Dichello, G.A.; Fukuda, T.; Maekawa, T.; Whitby, R.L.D.; Mikhalovsky, S.V.; Alavijeh, M.; Pannala, A.S.; Sarker, D.K. Preparation of liposomes containing small gold nanoparticles using electrostatic interactions. Eur. J. Pharm. Sci. 2017, 105, 55–63.
- Ewert, K.K.; Kotamraju, V.R.; Majzoub, R.N.; Steffes, V.M.; Wonder, E.A.; Teesalu, T.; Ruoslahti, E.; Safinya, C.R. Synthesis of linear and cyclic peptide-PEG-lipids for stabilization and targeting of cationic liposome-DNA complexes. Bioorg. Med. Chem. Lett. 2016, 26, 1618–1623.
- Pan, G.-H.; Barras, A.; Boussekey, L.; Addad, A.; Boukherroub, R. Alkyl passivation and SiO2 encapsulation of silicon nanoparticles: Preparation, surface modification and luminescence properties. J. Mater. Chem. C 2013, 1, 5261–5271.

- 42. Yin, H.; Casey, P.S.; McCall, M.J. Surface modifications of ZnO nanoparticles and their cytotoxicity. J. Nanosci. Nanotechnol. 2010, 10, 7565–7570.
- 43. Gatoo, M.A.; Naseem, S.; Arfat, M.Y.; Dar, A.M.; Qasim, K.; Zubair, S. Physicochemical properties of nanomaterials: Implication in associated toxic manifestations. BioMed Res. Int. 2014, 2014, 498420.
- 44. 103. Kerfahi, D.; Tripathi, B.M.; Singh, D.; Kim, H.; Lee, S.; Lee, J.; Adams, J.M. Effects of functionalized and raw multi-walled carbon nanotubes on soil bacterial community composition. PLoS ONE 2015, 10, e0123042.
- 45. Sohn, E.K.; Chung, Y.S.; Johari, S.A.; Kim, T.G.; Kim, J.K.; Lee, J.H.; Lee, Y.H.; Kang, S.W.; Yu, I.J. Acute toxicity comparison of single-walled carbon nanotubes in various freshwater organisms. BioMed Res. Int. 2015, 2015, 323090.

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