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REVIEW ON DIFFERENT APPROACHES OF NANOTECHNOLOGY FOR CARDIOVASCULAR DISEASES

Deep M. Solanki*, Rajashri R. Dhonnar, Rutuja S. Shinde, Shweta S. Shelar, Vaibhavi A. Shirke

Shivajirao S. Jondhale College of Pharmacy, Asangaon, Thane - 421601, India.

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***Corresponding Author**
Deep M. Solanki
Shivajirao S. Jondhale College of Pharmacy, Asangaon, Thane - 421601, India.

ABSTRACT

Cardiovascular diseases claim many lives globally, and a significant portion of these cases could be prevented. The increase in these diseases is closely tied to diets high in saturated fats, salt, and sugar, along with sedentary lifestyles and rising obesity rates. Currently, the available treatments for cardiovascular diseases are limited to oral medications or invasive surgical procedures. Nanotechnology holds the potential to offer more effective treatments with fewer side effects. In this review, we will explore the future prospects of nanotechnology in the field of cardiovascular medicine. A substantial portion of nanomedicine research in the cardiovascular domain has been dedicated to developing specialized nanoparticles that can enhance targeting, thus addressing biological barriers. In the context of heart-related conditions like atherosclerosis, hypertension, and myocardial infarction, various types of nanoparticles have been employed. These include liposomes, polymeric nanoparticles, polymeric micelles, and dendrimers, among others. The advancement of nanotechnology, especially in the realm of nanoparticles for drug delivery, has significantly improved our ability to target drugs more effectively, thereby enhancing therapeutic outcomes. Thorough in vivo studies of nanoparticles are invaluable as they offer insights that can shape future treatments.

KEYWORDS: Nanotechnology, Cardiovascular disease, CNT, Nanoparticles, Liposomes.

INTRODUCTION

Leading cause of death annually. claiming 17.7 Million lives in 2017 & according to WHO CVD will claim 23.6 Million in 2030. Not Limited to Coronary heart disease, Myocardial

infarction (MI), Deep vein thrombosis (In legs Clots formed) all of which lead to Ischemia & tissue death of which MI & heart failure are major condition lead to death.[1]

MI is the result of total occlusion of arteries Supplying blood to heart leading to decrease of blood flow, oxygen & nutrient. Supply An mi result due to ST elevation or non ST-elevation.[1]

The current treatment for MI is reperfusion in short period of time which can be achieved by percutaneous coronary intervention (PCI) coronary artery bypass graft (a new route for blood flow).[2]

Current treatment of CVDS are focussed on restoring normal blood flow through damaged vasculature and prevention of recurrent CV insults" Dual antiplatelets. therapies using anti cyclooxygenase such as inhibitors aspirin & P2Y 12 inhibitor Such as clopidogrel first line treatment are for prevention of CVDS, which aim to reduce clot formation & plate aggregation In addition Some patient do not respond well to antiplatelet therapy (3) Studies Shown that patient who have suffered from (MI) but have low response to clopidogrel are at increased risk of recurrent (CV) Events.[4] This Supports the necessity for advancement in technology & opportunity for nanomedicine.

Nanotechnologies for treatment of cardiovascular disease

The field of nanomedicine comprises diagnosis, treatment, prevention of disease or injury to improve quality of life with use of nanotechnology.[5]

For examples

- A domain of "A nanomedicine to control & manipulate biomacromokaler & aims Supra molecular entities which are vital to human health encompassing DNA, RNA, call membranes, & lipid bilayers.[6]
- Nanoparticles have physical chemicals. properties have high surface area to volume ratio wettability, reactivity, and roughness.[7]
- The British Standard Institute defines nanoparticles with all three dimensionsin nanoscale from 1 to 100 nm.[8]
- Advancement in nanomedicine research have led to better ways to reduce toxicity, prolong the half life of drugs effects through & reduce side effects through alteration of nanoparticle properties.[9] Targeted drug delivery in treatment of disease is possible

through active or by passive means active (conjugation of therapeutic agent to tissue or cell specific ligand) passive (coupling of therapeutic agent to high molecular weight polymer that has enhanced permeation & retention to Vascular tissue).[10]

Nanotechnology: Nanotechnology refers to the branch of science and engineering devoted to designing, producing, and using structures, devices, and systems by manipulating atoms and molecules at nanoscale.[11]

It is multidisciplinary field of science, engineering, and technology that deals with the manipulation and control of matter at the nanoscale. The nanoscale typically refers to structures and systems with dimensions on the order of nanometers, where one nanometer is equal to one billionth of a meter (1 nm = 10^-9 meters). Nanotechnology involves understanding, designing, and using materials and devices at this scale.

Key characteristics and concepts of nanotechnology include

Nanoscale materials: Nanotechnology involves the study and manipulation of materials at the nanoscale, which can lead to unique properties and behaviors due to the quantum and surface effects.

Interdisciplinary: It draws knowledge and techniques from various fields, including physics, chemistry, biology, materials science, and engineering.

Applications: Nanotechnology has a wide range of applications in areas such as electronics, medicine, energy, materials science, environmental science, and more.

Manipulation: Researchers in nanotechnology can manipulate individual atoms and moleculesto create new materials and structures with tailored properties.

Bottom-Up and Top-Down Approaches: Nanotechnology utilizes both "bottom-up" approaches (building structures atom by atom) and "top-down" approaches (scaling down largerstructures).

History of nanotechnology

U.S. physicist Richard Feynman is often credited with laying the foundation for what we now call nanotechnology. In a 1959 talk titled "There's Plenty of Room at the Bottom," he introduced groundbreaking ideas and concepts that form the basis of nanotechnology.

Although Feynman didn't use the term "nanotechnology" in his talk, he described a process in which scientists could manipulate and control individual atoms and molecules, paving the way for nanoscale engineering.

The true emergence of modern nanotechnology occurred in 1981 with the development of the scanning tunneling microscope, a significant breakthrough that allowed scientists and engineers to visualize and manipulate individual atoms. Gerd Binnig and Heinrich Rohrer, scientists at IBM, were awarded the Nobel Prize in Physics in 1986 for their invention of the scanning tunneling microscope. Their groundbreaking work marked a critical milestone in the field. The legacy of their contributions continues at the Binnig and Rohrer Nanotechnology Center in Zurich, Switzerland, which conducts research and explores new applications for nanotechnology.

An iconic moment in the development of nanotechnology was led by Don Eigler at IBM. His team spelled out "IBM" using just 35 individual xenon atoms, showcasing the precision and capabilities of nanoscale manipulation.

By the end of the 20th century, many companies and governments recognized the potential of nanotechnology and began investing in it. Major nanotech discoveries, including carbon nanotubes, were made in the 1990s. By the early 2000s, nanomaterials were already finding theirway into consumer products, from sporting equipment to digital cameras.

Although modern nanotechnology is relatively recent, the use of nanometer-scale materials datesback centuries. As far back as the 4th century, Roman artists discovered that adding gold and silver to glass created a captivating effect: when illuminated from the outside, the glass appeared slate green, but when lit from within, it glowed red. This was achieved by suspending nanoparticles of gold and silver in the glass solution, imbuing it with color. The Lycurgus Cup, a ceremonial vessel, is the most famous surviving example of this ancient nanotechnology.[12]

Fig. 1: A and B.

The Lycurgus cup, renowned for its remarkable optical properties, exhibits a green color when viewed under reflected light (A) and shifts to a red-purple hue when examined under transmitted light (B). This fascinating effect is a testament to early innovations in nanotechnology. (Image source: Reference 43)

Types of nanomedicine

One noteworthy material is **Poly(lactic-co-glycolic acid) (PLGA).** PLGA has gained recognition for its exceptional biocompatibility and minimal cytotoxicity. It stands as one of the most extensively researched biodegradable polymeric materials employed in drugdelivery systems. Regulatory authorities such as the **US FDA and European Medicine Agency** (EMA) have provided their endorsements for its use. The high level of biocompatibility and low cytotoxicity is attributed to the byproducts of its degradation, namely lactate and glycolate, which can be easily assimilated into cellular metabolic processes.[13] Given these highly desirable attributes, PLGA has been the subject of extensive research and exploration for its potential applications in both therapeutic and diagnostic roles in the field of cardiology.[14,15,16]

Additionally, PLGA has garnered significant attention due to the relative ease with which relatively large quantities of nanomedicines can be manufactured through emulsion polymerization. This specific approach has enabled the incorporation of a wide range of water-soluble and -insoluble substances into PLGA delivery systems.

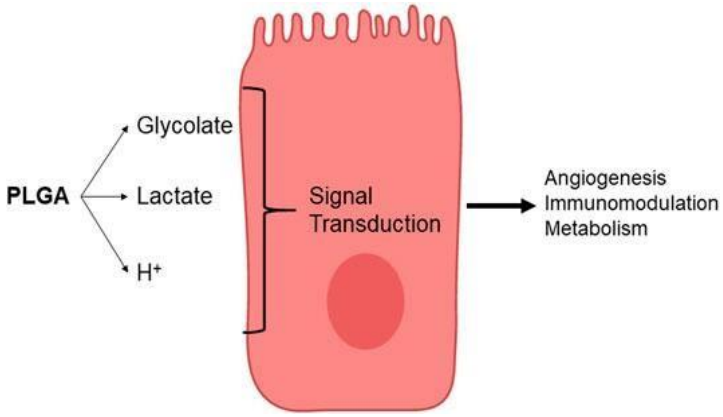


Fig. 2. (2)

Poly(lactic-co-glycolic acid) (PLGA) undergoes degradation, leading to the release of glycolate, lactate, and H+ ions. This process is illustrated in the image adapted from reference.[13]

Carbon nanotubes (CNT), carbon nanotube fibers (CNTf), and graphene oxide (GO) products have captured the interest of the biomedical community due to their remarkably diverse chemical and physical properties, enabling a wide range of versatile applications. Graphene, in particular, possesses intriguing electrical and mechanical characteristics, combining the conductive properties of a metal with the mechanical strength and stiffness of a polymer fiber, while also maintaining high biocompatibility.[17,18,19]

CNT fibers (CNTfs), known for their outstanding physical properties, have been suggested as an alternative to non-conductive fatigue-resistant fibers commonly used as surgical sutures (McCauley et al., 2019). In this approach, CNTfs offer a combination of electrical conduction capabilities, low impedance for ionic charge transfer, biocompatibility, and physiological stability. These qualities make them promising candidates for potential use in repairing myocardial lesions. It has been observed that when CNTfs are sewn across the epicardial scar in a sheep model, they acutely enhance conduction. Additionally, the interface between CNTfs and myocardial tissue exhibits such low impedance that CNTfs facilitate local downstream myocardial activation (Figure 3).

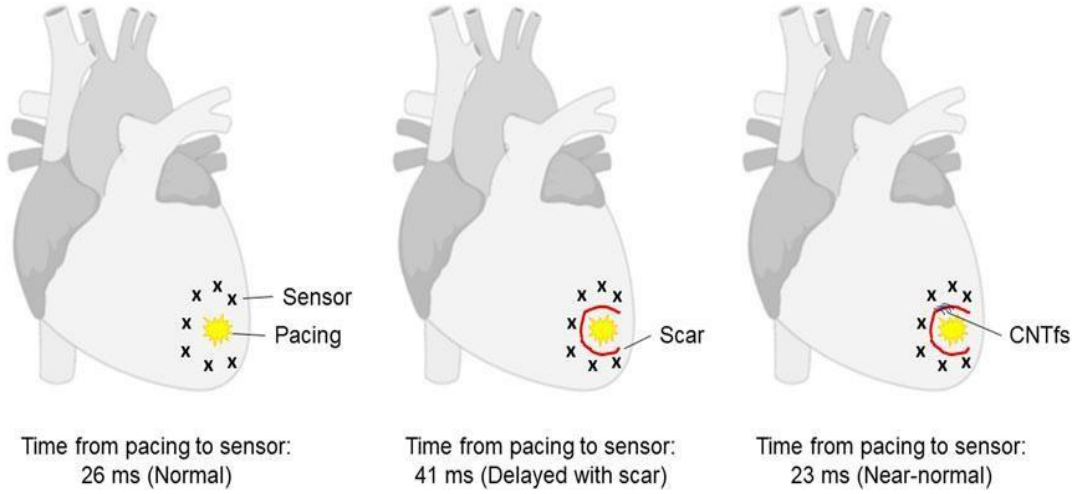


Figure 3

The in vivo restoration of myocardial conduction using conductive carbon nanotube fibers (CNTfs) is a promising approach. When CNTfs are sutured across an obstructed area, they have the potential to markedly reduce conduction time, bringing it closer to normal values. This effectis illustrated in the image adapted from McCauley et al. (2019).

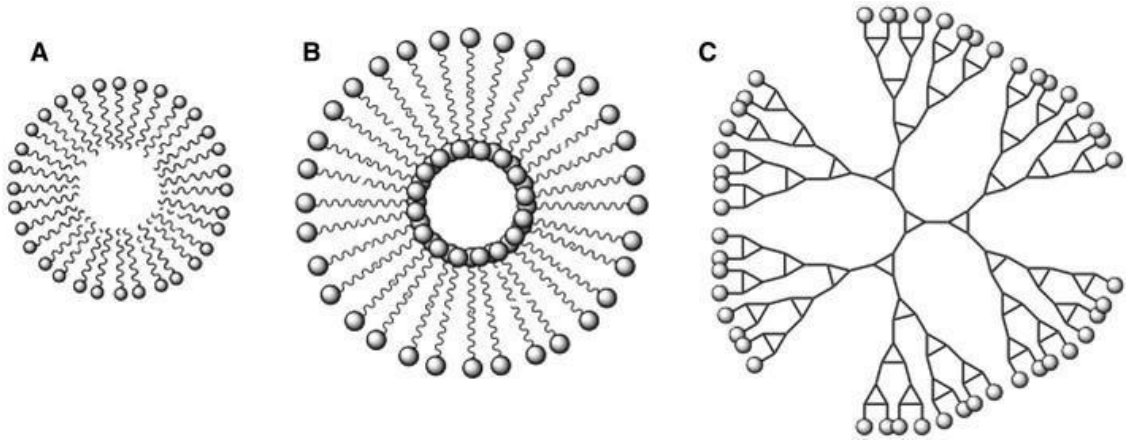


Fig. 4. (1)

Nanocarriers for the delivery of therapeutic agents include:

a) Micelles
b) Liposomes
c) Dendrimers

Different conventional medicines for cvs disease with brand Names and Applications

Medication (Generic Name)	Common Brand Name(s)	Typical Application
Aspirin	Bayer Aspirin	Antiplatelet, reduces the risk of blood clots
Simvastatin	Zocor, Lipitor	Reduces LDL cholesterol levels, lowers heart disease risk
Atenolol	Tenormin	Beta-blocker, lowers heart rate and blood pressure
Lisinopril	Prinivil, Zestril	ACE Inhibitor, controls blood pressure, reduces heart strain
Amlodipine	Norvasc	Calcium Channel Blocker, dilatesblood vessels, reduces blood pressure
Furosemide	Lasix	Diuretic, promotes diuresis, reduces fluid buildup in the body
Isosorbide Mononitrate	Imdur	Nitrate, dilates coronary blood vessels, relieves angina
Warfarin	Coumadin, Jantoven	Anticoagulant, prevents blood clotformation

Nanoparticles classes with their applications[1]

Nanoparticles Class	Application (s)
Liposomes	Thrombosis Atherosclerosis Vasodilation Cardio-protectant
Polymeric nanoparticle	Thrombosis Atherosclerosis Cardio-protectant
Polymeric micelle	Thrombosis Atherosclerosis Cardio-protectantVasodilation
Dendrimer	Thrombosis Atherosclerosis Cardio-protectantVasodilation

liposomes

Liposomes are nanostructures characterized by a phospholipid bilayer that forms a structure of approximately 200 nm in size. These bilayers enclose an aqueous core and often incorporate natural phospholipids like cholesterol.[20] A notable feature of liposomes is their dual nature, possessing both hydrophilic and hydrophobic properties, which makes them highly suitable for use as effective drug delivery systems. Liposomes come in three main classifications, which are determined by their size and the number of bilayers they contain. Various factors, including size, preparation methods, surface charge, and lipid composition, contribute to the distinct properties exhibited by a liposome.[21]

1. **Small Unilamellar Vesicles (SUV):** These liposomes consist of a single lipid bilayer.
2. **Large Unilamellar Vesicles (LUV):** Similar to SUVs, LUVs have a single lipid bilayer.
3. **Multilamellar Vesicles (MLV):** MLVs have multiple lipid bilayers.[21]

Moreover, liposomal surfaces can be modified by attaching antibodies or other targeting moieties to enable specific targeting of particular areas.[22] Platelet-targeted liposomal drug delivery is of interest due to the involvement of platelet aggregation in conditions like myocardial infarction, atherosclerosis, and thrombosis.[23]

Research is currently underway to investigate the liposomal drug delivery of prostaglandin E-1 (PGE-1), marketed under the trade name Liprostin, in phase III clinical trials.[24] Liposomes have also been developed for targeted treatment of thrombosis, a condition associated with blockages in blood vessels, which can lead to conditions like myocardial infarction and stroke. Berberine, a fluorescent isoquinoline quaternary alkaloid, has been encapsulated in liposomes for its potential cardio-protectant properties and enhancement of cardiac function.[25,26,27,28,29]

While liposomes have been used for various drug delivery applications, including those relatedto the cardiovascular system, they do have certain limitations.

These include issues with long-term stability, which can result in premature drug release, and the requirement for increased excipient-to-drug ratios, making them comparatively more expensive and less effective than some polymer-based systems.[1]

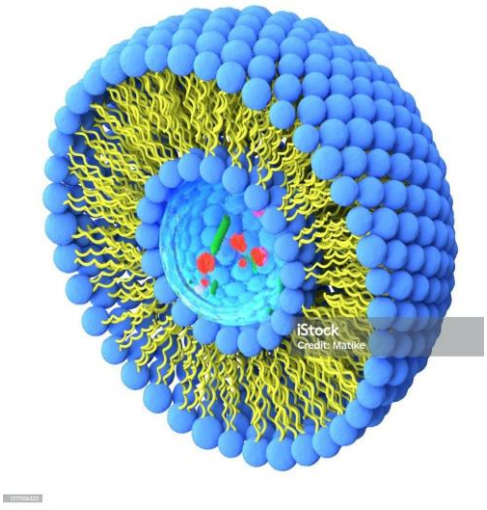
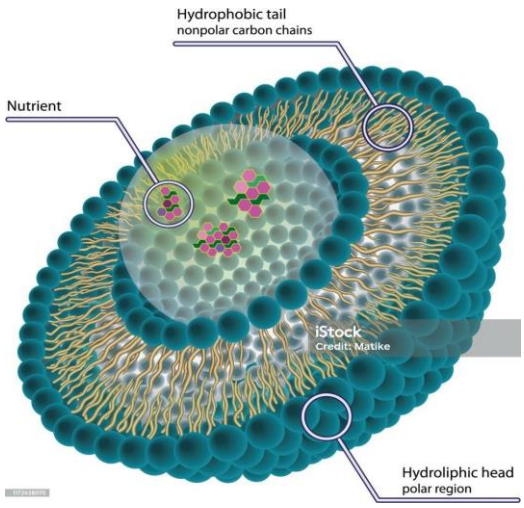


Fig. 3.



Structure for liposomes

Fig. 4.

Polymeric nanoparticles

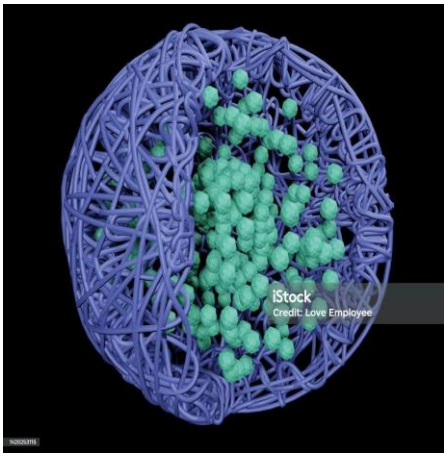
The choice of delivery route for polymeric nanoparticles depends on their intended site of action and the most minimally invasive method for introducing them into the systemic circulation.

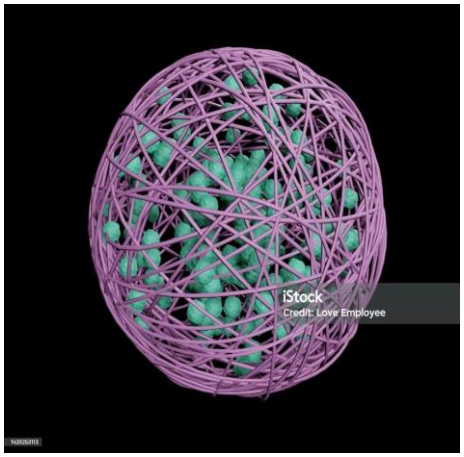
Intravenous injection is the most common method of administration, but oral, mucosal, dermal,or transdermal routes are also viable options.[30]

Polymeric nanoparticles encompass a broad class of systems, which include solid nanoparticles, amphiphilic nanoparticles (forming micelles, vesicles, and rods), dendrimers, and star-shaped systems. Each of these systems possesses its own unique architecture and properties.[31] Generally, polymer-based systems are more cost-effective and easier to manufacture and scale up compared to liposomes, with longer stability profiles.

While there are non-biodegradable polymers such as poly (methyl methacrylate) (PMMA), poly(acrylamide), poly(styrene), and poly(acrylates)[32] studies have shown chronic toxicity associated with the use of these materials. As a result, there has been a shift in focus towards biodegradable polymers.[33] Examples of biodegradable polymers include synthetic polymers such as poly(lactide) (PLA), copolymers like poly(lactide-co-glycolide) (PLGA), and poly(amino acids), among others.[30] Polymeric nanoparticles have demonstrated promising encapsulation efficiencies and drug release profiles, indicating their potential as formulations for protection against cardiovascular diseases (CVDs).[34] Ongoing research aims to explore their invitro and in vivo potential further.

One notable advantage of polymeric nanoparticles is their increased stability compared to low molecular weight surfactants and liposomes, primarily due to the drug-to-excipient ratios. Theiruse of extremely low excipients reduces the risk of systemic toxicity resulting from the carrier vehicle, making them cost-effective.[1]





Structure for polymeric nanoparticles

Fig. 5. **Fig. 6.**

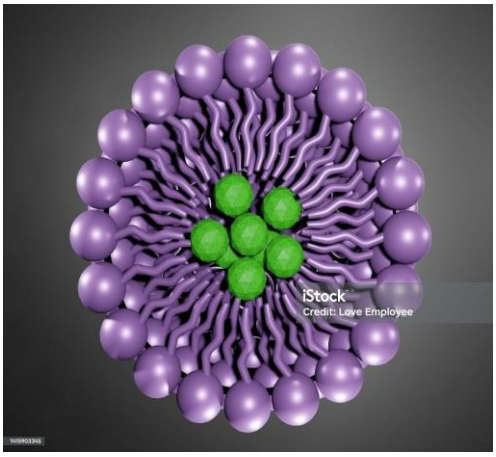
Micelles

Micelles are nanostructures characterized by their amphiphilic nature, featuring hydrophobic cores and hydrophilic shells. They can be formed from either polymer- or lipid-based amphiphilic molecules.[35]

Their small size enables them to penetrate tissues by crossing membranes. However, micelles have a limitation in that they can carry only a small amount of drug compared to larger carrierslike liposomes and dendrimers.[36]

Polymeric nanoparticles, including micelles, possess enhanced stability compared to low-molecular-weight surfactants and liposomes, primarily due to their extremely low excipient-to-drug ratios. This characteristic reduces the risk of systemic toxicity resulting from the carrier vehicle and contributes to their cost-effectiveness.

The synthesis of polymeric nanoparticles is highly controllable, and they can be customized for specific applications, such as by adding targeting ligands or tracking molecules. For micellar drug delivery, polymers typically used are derived from polyesters or poly (amino acids) to create the hydrophobic core.[37] Approved polyester forms for human applications include poly(lactic acid) (PLA), poly(ε-caprolactone) (PCL), and poly(glycolic acid), chosen for their biocompatibility, biodegradability, and structural properties.[37]



Structure of micelles

Fig. 7.

Dendrimers

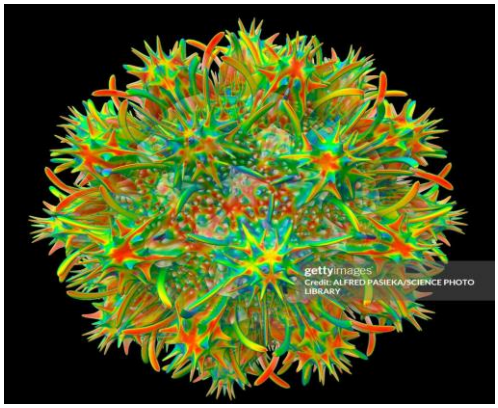
The term "dendrimer" is derived from the Greek word "dendron," which means "tree." This name accurately reflects the structure of dendrimers, which are repeatedly branched molecules.[38] The uniqueness of dendrimers lies in their multibranched, three-dimensional architecture, combined with low polydispersity (a measure of size distribution) and high functionality.[39]

Dendrimers offer several advantages as non-viral vectors for therapeutic purposes compared to other nanotechnologies. They are highly soluble, exhibit greater stability, have minimal immunogenicity (low likelihood of causing an immune response), and are effective at delivering drug molecules, DNA, and RNA. These qualities make them superior to both viral and non- viralalternatives.[40]

However, a potential drawback of dendrimers is that they often have highly charged exteriors due to the numerous branches on their surface, each with its own surface charge. This can resultin a highly cationic (positively charged) or highly anionic (negatively charged) nature, which, if not properly addressed, can lead to toxicity issues.[41]

A recent development in dendrimer technology involves a dendrimer composed of poly(glutamic acid) and poly(ethylene glycol) (PEG), referred to as Gn-PEG-Gn. This dendrimer has been used for the delivery of nattokinase (NK), a thrombolytic drug known for its high safety levels and low side effects. However, NK is sensitive to degradation from the external environment, necessitating careful formulation to ensure its clinical usefulness.

In summary, dendrimers are characterized by their high solubility, greater stability, and their ability to facilitate the effective delivery of drug molecules, making them a promising avenue innanomedicine.[1]



Structure for dendrimers

Fig. 8.

CONCLUSION

The evidence presented in this review underscores the immense potential of nanotechnology in the treatment of cardiovascular disease (CVD). With growing investments in nanotechnology research and development and the establishment of suitable infrastructure on a global scale, it's only a matter of time before nanomedicines, nanomaterial devices, and related technologies successfully navigate the rigorous clinical trial process and become available on the market.

One thing is certain: nanotechnology offers the promise of improving patient health and overallwell-being. Advancements in this field have the potential to enhance existing therapies and positively impact the lives of patients worldwide. To realize this potential in medicine, more invivo studies and clinical trials are needed to gain a comprehensive understanding of how nanoparticulate systems behave within the body.

As the future of therapeutics leans toward personalized medicine, nanotechnology is well-positioned to achieve the goal of tailoring treatments to individual disease states.

Additionally, the increasing costs of healthcare make it imperative to explore alternatives to current pharmacological and surgical management in order to mitigate the escalating expenses.

While there is substantial evidence supporting the transformative potential of nanotechnology inmedicine, it is also clear that this field has yet to fully realize its potential to revolutionize healthcare.[1]

REFERENCES

1. https://link.springer.com/article/10.1007/s13204-018-0856-z#citeas.
2. The physiology of cardiovascular disease and innovative liposomal platforms for therapy Guillermo U Ruiz-Esparza, Jose H Flores-Arredondo, Victor Segura-Ibarra,Guillermo Torre-Amione, Mauro Ferrari, Elvin Blanco & Rita E Serda.
3. Kapil N, Datta YH, Alakbarova N, Bershad E, Selim M, Liebeskind DS, Bachour O, Rao GHR, Divani AA Antiplatelet and Anticoagulant Therapies for Prevention of Ischemic Stroke. Clin Appl Thrombosis/Hemostasis, 2017; 23: 301–318.
4. Geisler T, Langer H, Wydymus M, Gohring K, Zurn C, Bigalke B, Stellos K, May A, Gawaz M Low response to clopidogrel is associated with cardiovascular outcome after coronary stent implantation. Eur Heart J, 2006; 27: 2420–2425.
5. Patil M, Mehta D, Guvva S Future impact of nanotechnology on medicine anddentistry. J Indian Soc Periodontol, 2008; 12: 34–40.
6. Tomalia DA, Reyna LA, Svenson S Dendrimers as multi-purpose nanodevices for oncology drug delivery and diagnostic imaging. Biochem Soc Trans, 2007; 35: 61–67.
7. Jiang W, Rutherford D, Vuong T, Liu H Nanomaterials for treating cardiovascular diseases: a review. Bioact Mater, 2017; 2: 185–198.
8. British Standards Institute, 2011; 71: 2011: nanoparticles-vocabulary. London: BSI. [Online] https://shop.bsigroup.com/upload/Shop/Download/Nano/PAS71.pdf. Accessed 19 Apr 2018.
9. Gupta A, Gupta M Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. Biomaterials, 2005; 26: 3995–4021.
10. Patel D, Bailey S Nanotechnology in cardiovascular medicine. CatheterCardiovasc Interv, 2007; 69: 643–654.
11. https://ec.europa.eu/health/scientific_committees/opinions_layman/en/nanotechnologies/l-2/1-introduction.htm#:~:text=Nanotechnology%20refers%20to%20the%20branch,of%20a%20millimetre)%20or%20less
12. https://education.nationalgeographic.org/resource/nanotechnology/
13. Chereddy, K. K., Payen, V. L., and Préat, V. PLGA: from a classic drug carrier toa novel therapeutic activity contributor. J. Control Release, 2018; 289: 10–13.

doi:10.1016/j.jconrel.2018.09.017

14. Oduk, Y., Zhu, W., Kannappan, R., Zhao, M., Borovjagin, A. V., Oparil, S., VEGF nanoparticles repair the heart after myocardial infarction. Am. J. Physiol. Heart Circ. Physiol, 2018; 314: H278–H284. doi:10.1152/ajpheart.00471.2017
15. Zhang, Y., García-Gabilondo, M., Rosell, A., and Roig, A. MRI/photoluminescence dual-modal imaging magnetic PLGA nanocapsules for theranostics. *Pharmaceutics, 2019;* 12: 16. doi:10.3390/pharmaceutics12010016
16. Fan, C., Oduk, Y., Zhao, M., Lou, X., Tang, Y., Pretorius, D., Myocardial protection by nanomaterials formulated with CHIR99021 and FGF1. JCI Insight, 2020; 5: e132796. doi:10.1172/jci.insight.132796

    Fan, C., Tang, Y., Zhao, M., Lou, X., Pretorius, D., Menasche, P., CHIR99021 and fibroblast growth factor 1 enhance the regenerative potency of human cardiac muscle patch after myocardial infarction in mice. J. Mol. Cell. Cardiol, 2020; 141: 1–10. doi:10.1016/j.yjmcc.2020.03.003
17. Behabtu, N., Young, C. C., Tsentalovich, D. E., Kleinerman, O., Wang, X., Ma, A.W., et al. Strong, light, multifunctional fibers of carbon nanotubes with ultrahigh conductivity. Science, 2013; 339: 182–186. doi:10.1126/science.1228061
18. Liu, J., Cui, L., and Losic, D. Graphene and graphene oxide as new nanocarriers for drug delivery applications. Acta Biomater, 2013; 9: 9243–9257. doi:10.1016/j.actbio.2013.08.016
19. Xu, Z., Liu, Y., Zhao, X., Peng, L., Sun, H., Xu, Y., et al. Ultrastiff and strong graphene fibers via full-scale synergetic defect engineering. Adv. Mater, 2016; 28: 6449–6456. doi:10.1002/adma.201506426
20. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo S, Zarghami N, Hanifehpour Y, Samiei M, Kouhi M, Nejati-Koshki K Liposome: classification, preparation, and applications. Nanoscale Res Lett, 2013; 8: 102.
21. Sahoo S, Labhasetwar V Nanotech approaches to drug delivery and imaging. Drug Discov Today, 2003; 8: 1112–1120.
22. Levchenko TS, Hartner WC, Torchilin VP Liposomes in diagnosis a and treatment of cardiovascular disorders. Methodist DeBakey Cardiovasc J, 2012; 8: 36–41.
23. Ruiz-Esparza G, Flores-Arredondo J, Segura-Ibarra V, Torre-Amione G, Ferrari M,Blanco E, Serda R The physiology of cardiovascular disease and innovative liposomal platforms for therapy. Int J Nanomed, 2013; 8: 629–640.
24. Bulbake U, Doppalapudi S, Kommineni N, Khan W Liposomal formulations in clinical

use: an updated review. Pharmaceutics, 2017; 9: 12.

25. Allijn IE, Czarny SMS, Wang X, Chong SY, Weiler M, da Silva AE, Metselaar JM, Lam CSP, Pastorin G, de Kleijn DPV, Storm G, Wang J-W, Schiffelers RM Liposome encapsulated berberine treatment attenuates cardiac dysfunction after myocardial infarction. J Control Rel, 2017; 247: 127–133.
26. Luo X, Li J, Guo L, Cheng X, Zhang T, Deng Y Preparation of berberine hydrochloride long-circulating liposomes by ionophore A23187-mediated ZnSO4 gradient method. Asian J Pharm Sci, 2013; 8: 261–266.
27. Sailor G, Seth AK, Parmer G, Chauhan S, Javia A Formulation and in vitro evaluation of berberine containing liposome optimized by 32 full factorial designs. J Appl Pharm Sci, 2015; 5: 023–028.
28. Zhang Y, Yang S, Li M, Iqbal J, Bourantas CV, Mi Q, Yu Y, Li J, Zhao S, Tian N, Chen S Berberine attenuates adverse left ventricular remodeling and cardiac dysfunction after acute myocardial infarction in rats: role of autophagy. Clin Exp Pharmacol Physiol, 20147; 41: 995–1002.
29. Huang Z, Han Z, Ye B, Dai Z, Shan P, Lu Z, Dai K, Wang C, Huang W Berberine alleviates cardiac ischemia/reperfusion injury by inhibiting excessive autophagy in cardiomyocytes. Eur J Pharmacol, 2015; 762: 1–10.
30. Elsabahy M, Wooley K Design of polymeric nanoparticles for biomedical delivery applications. Chem Soc Rev, 2012; 41: 2545–2561.
31. Hoskins C, Thoo-Lin PK, Cheng WP A review of comb-shaped amphiphilicpolymers for hydrophobic drug solubilisation. Ther Deliv, 2012; 3: 59–79
32. Banik BL, Fattahi P, Brown JL Polymeric nanoparticles: the future of nanomedicine. WIREs Nanomed Nanobiotechnol, 2016; 8: 271–299.
33. Burman A, Mukherjee R, Khatta D, Mullick S, Jaggi M, Singh M, Kumar M, Prusthy D, Gupta P, Praveen R, Singh S Biocompatible, non-biodegradable, non-toxic polymer useful for nanoparticle pharmaceutical compositions, 2015; 8: 927 - 023 B2.
34. Giannouli M, Karagkiozaki V, Pappa F, Moutsios I, Gravalidis C, Logothetidis S Fabrication of quercetin-loaded PLGA nanoparticles via electrohydrodynamic atomization for cardiovascular disease. Mater Today Proc, 2018; 5: 15998–16005.
35. Gupta A Nanomedicine approaches in vascular disease: a review. Nanomed Nanotechnol Biol Med, 2011; 7: 763–779.
36. Eniola-Adefeso O, Heslinga MJ, Porter TM Design of nano vectors for therapy and imaging of cardiovascular diseases. Methodist DeBakey Cardiovasc J, 2012; 8: 13–17.

37. Gaucher G, Dufresne M, Sant V, Kang N, Maysinger D, Leroux J Block copolymer micelles: preparation, characterization and application in drug delivery. JControl Release, 2005; 109: 169–188.
38. Crampton HL, Simanek EE Dendrimers as drug delivery vehicles: non-covalent interactions of bioactive compounds with dendrimers. Polym Int, 2007; 56: 489–496.
39. Sherje AP, Jadhav M, Dravyakar BR, Kadam D Dendrimers: a versatile nanocarrier for drug delivery and targeting. Int J Pharm, 2018; 548: 7070–7720.
40. Mendes LP, Pan J, Torchilin VP Dendrimers as nanocarriers for nucleic acid and drug delivery in cancer therapy. Molecules, 2017; 22: E1401.
41. Jain K, Keharwani P, Gupta U, Jain NK Dendrimer toxicity: lets meet thechallenge. Int J Pharm, 2010; 394: 122–142.
42. Zhang S-F, Gao C, Lü S, He J, Liu M, Wu C, Liu Y, Zhang X, Liu Z Synthesis of PEGylated polyglutamic acid peptide dendrimer and its application in dissolving thrombus. Colloid Surface B Biointerface, 2017; 159: 284–292.
43. www.britishmuseum.org/research/collection_online/collection_object_details.aspx?objobjec=61219&partId=1 for fig 1.
44. https://www.istockphoto.com/photos/liposome for fig 3,4
45. https://www.istockphoto.com/photos/nanoparticles-for-drug-delivery for fig 5,6
46. https://www.shutterstock.com/search/micelles for fig 7
47. https://www.gettyimages.com/photos/dendrimer for fig 8