A Review of Silver Nanoparticles in the Treatment of Cardiovascular Diseases

By

Karima Akter
18346093

A project submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

School of Pharmacy
BRAC University
February, 2024

Declaration

It is hereby declared that

1. The project submitted is my own original work while completing degree at BRAC University.
2. The project does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The project does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help

Student's Full Name & Signature:

Karima Akter
18346093

Approval

The thesis titled "A Review of Silver Nanoparticles in the Treatment of Cardiovascular Diseases" submitted by Karima Akter (18346093), of Fall 2018 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

Supervised By:

Tanisha Momtaz
Lecturer
School of Pharmacy
Brac University

Approved By:

Dean:

A.F.M. Yusuf Haider, PhD
Acting Dean, School of Pharmacy
Professor, Department of Mathematics and Natural Sciences
Brac University

Ethics Statement

This study does not involve any kind of animal trial or human trial.

Abstract:

Silver nanoparticle in Cardio Vascular Disease is the vast innovation in modern medical science for cardiac patients. Atherosclerosis, Thrombosis, Myocardial infraction, Stroke are some of severe cardiac diseases which can be moderate through several imaging procedures. For example, in myocardial infraction ECG, MRI, Eco cardiology, Radionuclide imaging are used to observe the condition of a patient. According to the patient's condition several treatments are available on the basis of silver nanoparticle. This treatment gives more therapeutic effects and less adverse effects as silver nanoparticles has higher bioavailability. It gives rapid action on serious condition's. Excess use of nano medicine, it shows various kinds of toxicity. To prevent this disease some changes on life style should be occurred. A healthy lifestyle will give better treatment along with appropriate drugs with proper dose.

Key words: Nanoparticles, silver nanoparticles, cardiac therapy, toxicity, nano-medicine .

Dedication :

I want to dedicate my project to BRAC University.

Acknowledgement

At first, I would like to convey my gratefulness to Almighty Allah for providing me with the strength and patience required to accomplish my project work. I wouldn't be able to finish my project work without Allah's guidance.

Then, I would like to express my deepest gratitude and honor to my esteemed supervisor Tanisha Mamtaz, Lecturer, School of Pharmacy, BRAC University, for her constant support. I would never be able to complete my project without her patience, guidance, and supervision. I would really want to show my thankfulness to her for her invaluable guidance continuous encouragement throughout the whole time.

I sincerely put forward my regards and gratitude to Dr. Eva Rahman Kabir, Professor and Dean, Department of Pharmacy, BRAC University for giving us the chance to continue the project work as well as her contribution and support to the students and the department. Moreover, I would like to express my thankfulness towards my parents for their constant love, care, support and words of encouragement which inspired me to achieve my goals. Last but not the least, I would like to thank the faculty members of Department of Pharmacy at BRAC University, as well as my friends, who continuously supported and pushed me to complete my project successfully.

Table of Contents

Declaration ……i

Approval ……...ii

Ethics Statement ……...iii

Abstract ……....iv

Dedication……...v

Acknowledgement…….....vi

List of Acronyms…….vii

Chapter 1: Introduction……....1

1.1 Background …….....1

1.2 Characteristics of Ag…….....3

1.3 Significance of Silver Nanoparticles…….....3

1.4 Aim of Silver Nanoparticles ……..……...3

1.5 Objectives of this study…….....3

Chapter 2 Methodology…..……..4

Chapter 3: Nanoformation in Cardiac Diseases……4

3.1 Atherosclerosis…….....5

3.2 Thrombosis……...8

3.3 Stroke……...10

3.4 Myocardial Infraction(MI)…….....12

Chapter 4: Discussion ……...16

4.1 Limitations:Potential toxicity of AgNP……....16

4.1.1 Skin or Dermal Toxicity…….....17

4.1.2 Hepatobiliary system toxicity……...…...17

4.1.3 Respiratory toxicity……..…...18

4.1.4 Kidney toxicity ……..…...19

4.1.5 Central Nervous system toxicity…….19

4.2 Futuristic purpose……....20

Chapter 5 :Discussion of Antimicrobial property for MI…….21

Chapter 6: Conclusion …….22

Reference ……..23

List of Acronyms

AgNP	**(Silver Nanoparticle)**
CNS	**(Central Nervous System)**
BBB	**(Blood Brain Barrier)**
CBF	**(Cerebral Blood Flow)**
AMI	**(Acute Myocardial Infraction)**
ICAM1	**(Intracellular adhesion molecule 1)**
SPION	**(Super Magnetic Iron Oxide Nanoparticles)**
USPION	**(Ultra Super Magnetic Iron Oxide Nanoparticles)**
ELISA	**(Enzyme Linked Immunosorbent Assay)**
TAP	**(Thrombin Activatable Peptide)**
HDL	**(High Density Polypeptide)**
LDL	**(Low Density Polypeptide)**

Chapter 1

Introduction:

1.1 Background:

Cardio Vascular Disease is playing a vital role for causing death of worldwide. To get better and more prominent treatment for cardiovascular disease (CVD) nanoparticles in nanotechnology are opening a new avenues in modern science (Younis,Ghoubaira,et al.2021). Nanoparticles have a small diameter (1-100 nm) which is similar in size range to the natural occurring viruses. For this uncommon property, it will be different from molecules and bulk solids (Nune,Gunda et al 2009). Metallic nanoparticles are different types – Gold nanoparticles, silver nanoparticles, cupper nanoparticles, iron nanoparticles (Alphandery,2020) . Silver nanoparticles are giving antitumor and anti bacterial activity through the reaction in $AgNO_3$ and varieties of reducing agents. The range of silver nanoparticles are 5-80nm.

This $AgNO_3$ can be extracted from the plant and originated proteins, carbs, flavonoids, phenols, vitamins, basil, pelargonium graveolens, bark, callus, stem, flower, fruits, petals etc (Alphandery,2020). Silver nanoparticles are giving response in the case of toxicity and adverse cardiac return to nitric oxide and oxidative stress (Ramirez-Lee, Espinosa-tanguma ER al. 2017). To measure perfusion pressure and left ventricular pressure and identify the role of NO and OS the AgNPs are used (Ramirez-Lee , Espinosa-tanguma et.al.2017). After dermal , inhalation and oral exposure and distribute into heart , AgNPs are able to penetrate to the cardiovascular system (Ramirez-Lee , Espinosa-tanguma et.al.2017).

AgNPs are used as silver ions into the nanoparticles for the broad spectrum and highly efficient in anti microbial activities as well as cardiac disease specially myocardial infraction. AgNPs creates impacts on wound repairing, healing, vaccine along with microbial effects into the human body. (Li Xu , Wang, Huang et.al.,2020) . In the case of infection in ventriculitis rifampin and clindamycin impregnated from along with the silver nanoparticles or it's silver salt are used (Lemcke,Depner et al.,2012). It reduces the rate of infection (Lemcke,Depner et al.,2012). The nanoparticles are working through two ways– (I) it focuses the passively targeting and designates it's effects where NP passively diffuse through the angiogenic blood vessels in the tumor cells, (ii) it also actively targeting the ligand to the NP to identified victim receptor (Alphandery,2020) In the duration of metallic NP formation the uses of toxic solvents, high temperature and pressure or additives should be added(Alphandery,2020).

The synthesis of AgNPs are going to be controlled by developing size and shape of particles through physical, chemical and biological methods(Li Xu , Wang, Huang et.al.,2020). Like other drug the toxicity of nanoparticles are also occurred through the process of route of administration and the way it goes exposed. By ingestion, injection NPs are exposures. In our brain, lung, liver and kidney have the leakey blood vessels. This vasculature increases the activity of NPs in the EPR effect. (Missouri, Arnold et al.2020). Though AgNPs has wide spread uses, they are not fully identified its biological activities properly. The size, shape, p^H can affect its effectiveness, potentially, safety of medical device of silver nanoparticles (Ahmed,Nagy,Brown et al. 2016). In vitro are explaining the toxicology effects in nanoparticle materials. They are less potential and more costly (Ahmed,Nagy,Brown et al. 2016). This review describes the impact of AgNPs in cardiovascular diseases. This review are overviewing of assay used in nanotechnology research and various factors that influence assay output and accuracy (Ahmed,Nagy,Brown et al. 2016).

1.2 Characteristics of Ag nanoparticles:

Silver are characterized through several way. Firstly, in bottom up method where nanostructures are available through small size from larger parts. And secondly, in top down process to be nanostructure particles photo-lithography are needed (Behra, Sigg et.al,2013). In wet chemical method which reduces Ag salts into metal Ag through parameters like – temp, pH, humidity (Behra,Sigg et.al,2013). In Martin's method, Ag synthesized by adding tri-sodium citrate along $AgNO_3$ and AgNP are forming. The solution looks yellowish.(Dewangan ,Korram et.al , 2019).

1.3 Significance of silver nanoparticles:

The importance of silver nanoparticle in cardiovascular diseases are unmeasurable. It has several effects in cardiac area. The significance of anti-inflammatory effects into the cardiac blood vessels and improve the circulation of blood and reduce the cardiac pressure in the case of pulmonary arterial hypertension and cardiac attack. To prevent the most common cerebrovascular disease stroke and heart failure silver nanoparticles are playing a very crucial role in medical science. Another important application of AgNPs is to treat diseases to maintain drug concentration along with long lasting therapeutic regimens (Rai, Kon et.al,2014).

1.4Aim of this study :

The aim of the present review is to discuss the significance of AgNP along with their effects and applications against cardiovascular diseases as well as tumor cells.

1.5 Objectives of this study:

Objective of this review article is to look for the relevant information about silver nanoparticles, applications, evaluations and the improved therapeutic effects than the previous techniques, advanced treatments in cardiovascular diseases such as – cardiac attack , heart failure , stock, pulmonary diseases etc. The new way of this treatment against cardiac attack or pulmonary diseases. It could be a great aspect of life of cardiac patients. These technological drugs have the maximum efficacy to penetrate target cells and give more results than previous ones.

Chapter 2

Methodology:

This review study is composed of recent and previous research papers, articles and renounced journals from high and strong source of journals. This study is made by researching peer review journals, some of the official papers and some articles thoroughly. To achieve and accumulate vast information's of this review article, different types and numerous sources are going to be investigated. Scopus, Sci-hub, PubMed are some searches area which are used to gather information for this review paper purpose. The publications are mainly involved- Nature, Molecular science, IVYSPRINGH etc. A screening was happened before the focusing the main theme and the most recent and oldest ideas. The information about the review articles "A Review of Silver Nanoparticles in the Treatment of Cardiovascular Diseases." Are very much authentic.

Chapter 3

Nano formulation in Cardiac Diseases

Cardiovascular disease is the world's most popular disease and the number one disease which may cause of death. According to WHO in 2017, 17.7 million deaths are happened in 2015 and also assumed that it will reach from 17.7 to 23.6 million only in 15 years. It is occurrence initially heart disease but congenital heart diseases are occurs due to diabetes, hypertension. Nano medicines are giving best treatment than previous treatment system in thrombosis, stroke , myocardial infraction, pulmonary arterial hypertension, Atherosclerosis (Mohamed, Marei, Crovella, Saleh;2022).

3.1: Atherosclerosis:

A chronic inflammatory disease into blood vessels and affecting lipoprotein, circulating blood cells and endothelium that is the atherosclerosis. It retains the plasma protein which is apo-lipoprotein B in the area of focal of the arterial tree. Cholesterol and oxidized phospholipids are stored into the endothelial cell of the arterial wall. Gradually, this plaque doing the lining area are thicker and the lumen are getting narrow down which will affect the blood circulation into heart (Mohamed, Marei, Crovella, Saleg ;2022). In arterial intima, monocytes which recruited by the induction of lipoprotein are making pro inflammatory macrophages. This macrophages are generally giving the inflammatory responses. Normally macrophages engulf the lipoproteins and give atherosclerotic lesions. The cardio vascular disease could be reduced if the apo-B lipoprotein could be reduced at a very lower level (Wei, Maaike ;2022). Acute myocardial infraction(AMI) is the major complication of atherosclerosis. Nanomedicines are primarily works on the atherosclerosis (Mohamed, Marei, Crovella, Saleg ;2022). Some studies shows that nanoparticles are improving the pharmacokinetic profile as well as the chemical

stability of therapeutics. Nano therapy are also reducing off target and reduce adverse effects rather that free drugs (Wei, Maaike ;2022). Several studies are proved that the nanoparticles are targeted lesion parts of the vessels where the plaque are formed and atherosclerosis occurs and take out the vascular cells (Mohamed, Marei, Crovella, Saleg ;2022). At the initial stage of atherosclerosis the endothelial cells are attack the monocytes through interaction with chemokine receptor and exorecessed cell through intercellular adhesion molecule1 (ICAM1) and vascular adhesion molecule1 (VCAM1). After migration monocytes are working as macrophages and phenotypes (Wei, Maaike ;2022).

Journey of nano medicine to atherosclerosis:

Nano medicine is the best choice in the treatment of the atherosclerosis. Some investigation proved that the nanoparticles circulation in the blood stream and extravasation of atherosclerotic plaque will aid effectively and give more robust diagnostic effects. Administration of nano therapies intravenously are the most straight forward and give effective delivery rough for systemic infiltration into the atherosclerotic plaque. HDL like nanoparticles are helping to move cholesterol lipid laden plaque from the vessel to the liver by using reverse cholesterol transport process. LDL like nano particles are showing anti inflammatory and anti proliferation effects for the atherosclerosis treatment. The inorganic nanoparticles are used for identification of plaque which is in the high risk and select the targeted nano platform and diagnosis this atherosclerosis liposome are highly recommended for the use of imaging agents of plaque macrophages. It targets the ligand and improve the circulation time into the blood and demise the plaque (Wei, Maaike:2022).

Diagnostic imaging:

Molecular imaging technology are trying to visualize the atherosclerotic plaque which is at the high risk of rupture and creates an erosional effects with the high spatiotemporal resolution.

The development of drugs for atherosclerosis imaging agents are must (Wei, Maaike ;2022). Nanoparticles used in MRI , CT to investigate atherosclerosis (Bejarano, Marquez,et al;2018).

MRI:

MRI or magnetic resonance imaging are the high spatial and temporal resolution to emit plaque from the vessel. At the initial stage it was used for imaging vessels with the accumulation of super magnetic iron oxide nanoparticles (SPION) , AMI-25 Aquas colloidal suspension of magnetic. This iron was coated with dextran which is non covalently bonded low molecular weight and administer intravenously. Dextran are the main key strategy to improve the uptake and accuracy for macrophages in atherosclerotic plaque in vivo. USPION are the longer blood half life with low uptake mononuclear phagocytic process of the liver. It has high permeability through capillary wall. It also improve the bioavailability and interaction with specific tissues. Kooi et.al. investigated and proved that the USPIO-MRI could used for in vivo to detect human plaque and to justify this USPIO were administer ischemic patients whom might have attack or small brain infarct. The evolution of MRI, the development of HDL like nanoparticles are highly affinity for atherosclerotic plaque. The benefits of HDL are small in size easy to endogenous biodegradable and not to trigger immune communication. Some, recent achievements are metal nanoparticles for imaging are giving more specific and targeted treatment (Bejarano, Marquez,et al;2018).

CT:

Computed tomography or CT is considered the most accurate method for the coronary artery stenosis and determination plaque calcification .using nanoparticles in CT it improves specificity along with unique properties. Hyafil et. Al. justified that in the treatment of coronary atherosclerosis plaque by using CT image iodinate polymer nanoparticles are effects more perfectly. Macrophage destabilized the acute plaque, make thrombus and secretes protease

which digest the extracellular matrix. HDL like nanoparticles detects macrophages in the arteries of atherosclerotic plaque and simultaneously imaged the vasculature. The author noticed that the capability of spectral CT system are used to detect the accumulation of HDL nanoparticles in the aorta having atherosclerosis (Bejarano, Marquez,et al;2018).

Treatment:

Anti inflammatory treatment:

The treatment of atherosclerosis is to highlight the blood lipid concentration lower blood concentration are reduced the risk of cardiovascular disease. Dexamethasone (DXM) which is anti inflammatory steroid drug, can reduce atherosclerosis. Though it has very vast effects on atherosclerosis treatment it has also some side effects too. Because of long term use hypertension, weight gain and depression are the most common side effects. Chono S et.al. made DXM loaded liposomes with used IV rough into atherogenic patients. Rather than free DXM, the liposomic DXM with 200nm in diameter are decreased aortic cholesterol very fast. Glucocorticoid is the potent anti inflammatory steroid drug and used fir atherosclerosis treatment it is not used in clinical because it has several side effects (Zhang, zu et.al ;2018) .

3.2: Thrombosis:

Thrombosis is considering one of the main reason of death now a days .Thrombosis means the build up a malignant blood vessels(Mohamed,Marei,Crovella,Saleh;2022). In the treatment process of thrombosis we have to understand thrombus formation , platelets coagulation and the blood flow conditions .These factors are playing a primary role in the treatment of thrombosis . In previous days thrombosis had limited stages and also narrow therapeutic windows. These things mode the treatment not that much effective. Heparin, Urokinase, plasminogen activator (UPA); tissue plasminogen activator (tPA); recombinant tPA and strepto kinase (SK) are some of the major anti platelet and anticoagulant . This thrombus formation

are very long term process and its treatment are very limited. But these agents are helping to dissolve thrombus and reduce it's formation rate. This agents are mainly protein bases and they are short half life and sometimes it gives allergic and inactivation reaction. Accumulation efficiency and targeting ability are poor which makes the agents less effective. It also gives hemorrhage and severe cardio vascular diseases. To get benefits in thrombus treatment we have to focus minimum adverse effects and maximum therapeutic effects.

In current years, nano medicine has reached the upper level of medical science among the scientific researchers and clinician (Su, Dai, Chen et.al.2020).In previous MRI, X ray and may other effective treatments are used but after innovation of nano medicine such as NPs radiolabeled with fibrin ligands or other coagulants it reached an advanced level of treatment. MRI or X ray results might be not clear or not sure sometimes but nano medicine are giving accurate treatment into thrombus formation (Su,Dai,Chen et.al.2020).

Diagnosis:

In vitro:

In the diagnosis process of in vitro, many studies prove that it has very beneficial sites of simplicity, high speed and non-invasiveness. Nano particle based assay in vitro are structured to the use of detecting biomarkers with lower detection limit to diagnose the disease at an initial stage. Through along with biomarkers associated with thrombosis, it could not be identified directly in vitro process. This is because the biomarkers are presenting only into the blood clot.

Prothrombin is fragmented into thrombin and prothrombin fragment and the byproduct produced.The byproduct fibrin degrades in D-dimer which shows poor specificity in the detection system of thrombosis. The systemic biomarkers which are presented into the metabolism are showing very beneficial effects into the body as it is used like an injection

solution. The thrombin activatable peptide are highly responsible to the thrombin activity. Bhatie et.al. are trying to identify thrombosis by using systematic biomarkers(Su,Dai,Chen et.al.2020).

In vivo:

Besides ultrasound imaging, MRI, CT imaging there are many other imaging modalities are available to detect the thrombus. However, the conventional imaging were used to identify the aged and evaluated thrombosis only but in the modern imaging system, the biomarkers associated thrombosis visualized and investigated as treatment requirement. To from thrombosis there are many biological factors are closely co-related. They are fibrin, activated platelets and factor XIII. The biomarkers are react like targeting molecules for diagnosis. Various contrast agents have been produced to develop the diagnostic technique of thrombosis. MR probe ER-2104R is the fibrin targeting agents which are reached into the clinical trial(Su,Dai,Chen et.al.2020).

MRI:

1. Combination of nanoparticles and contrast agents are used to detect platelets rich thrombi and the area of thrombus selectively to attack in rapid speed.
2. The coated PLGA layer with nanoparticles are giving biocompatibility in the treatment of cardiovascular diseases. Adding MRI contrast agents in mural thrombus, it shows high shear stress.
3. The dual MRI contrast agents are used to increase the increase the accuracy of the diagnosis (Su,Dai,Chen et.al.2020).

CT:

In the CT imaging, it distinguished a thrombus from blood. The X ray can be absorbed by high Z elements that are organized by CT contrast agents including Au, Bi, Zn based nanoparticles. The recent thrombosis are identified in 3 weeks with fib-Gc-AuNP based micro CT imaging (Su,Dai,Chen et.al.2020) .

3.3: Stroke:

The most common disease in the worldwide now a days is called stroke. Stroke is the cerebrovascular disease which occurs the abnormal cerebral blood flow (CBF). Abnormally blood flow into the cerebral it disturbs the functions of brain and sometimes makes temporary or permanent brain damage. Therapeutically neuro protective drugs are available for protecting or preventing brain damage (Mohamed, Marei, Crovella, Saleg ;2022). Before 1990's the treatment of acute ischemic stroke (AIS) were limited and mainly noticed symptomatic management, secondary prevention and rehabilitation. Stroke mainly occure from unhealthy life style like obesity, poor diet or poor nutrition and inactive in physical activities. Some risk factors such as hypertension, diabetes mellitus, taking tobacco, hyperlipidemia are also causing stroke (Herpich, Rincon;2020). Through it has lots of advantages but it has some limitations and side effects also. To overcome and get more effective treatment of stroke nano medicines are used. Nano medicines minimizes the adverse effects or toxicity and maximizes the therapeutic window and its efficacy (Mohamed, Marei, Crovella, Saleg ;2022).

Neuroimaging:

A non-contrast CT scan are used to exclude hemorrhagic stroke. Subarachnoid hemorrhage or ICH are hemorrhagic stroke. The Alberta Stroke Program Early CT score was proved that by imaging a non-contrast head CT scan, middle cerebral artery infract are revealed properly. A

patient with high Rapid Arterial Occlusion Evaluation has greater than 6 rather than early ischemia (range 0-10). It means the infraction are not set in and the revascularization strategies may be implemented. A CT angiography can effectively identified LVO and gives some authentic information about patient's vascular anatomy and stroke etiology. By quantitative analysis of Cerebral blood flow we can measure the cerebral blood volume and time to-maximum, transition through CT perfusion technique (Herpich, Rincon;2020).

3.4: Myocardial Infraction:

Myocardial infraction or MI is the most common cardiac disease. Cardiac tissue regeneration capacity are restricted day by day. The loss of the cardiac tissue because of some cardiac injuries or some microbial attack is considered as the MI disease . the most harmful type of Ischemis heart disease is acute MI. Some therapeutic agents are essential to treat patients immediately to cope up with the regeneration process of the cardiac tissues (Mohamed,Marei,Crovella,Saleh;2022).Percutaneous coronary intervention, thrombolytic and bypass surgery are some of the recovering process of MI. After the MI re-vascularized, it will improve the cardiac function and preventing post infraction (Pan,Xu et.ai;2021). In previous treatment process it was not that much developed (Mohamed, Marei,Crovella,Saleh;2022). These invasive approaches can't apply in all type of patients. These type of treatment of treatments are limited based and specific some kinds of special patients and also some clinical characteristics. The main reason MI is the extreme growth and rupture of atherosclerotic plaque and developing thrombosis. Statins are used to decrease the acute MI, but its efficacy are very limited and also gives residual risks which are more vulnerable (Pan,Xu et.ai;2021). After innovation of nano medicine in the treatment of myocardial infraction showing a new chapter into medical science. By using nano medicine into myocardial infraction treatment it will enhance the drug's cardio protective potential into revolutionary area. Nanoparticles are used

to investigate of stem cell to treat ischemic myocardium (Mohamed, Marei,Crovella,Saleh;2022).Nanoparticles are improve the therapeutic effects as well as reduce the side effects of traditional or novel therapies. It also increases the bioavailability (Pan,Xu et.ai;2021).

Diagnosis:

ECG:

To diagnose MI disease patients, ECG plays a vital role. Through ECG, we can find out the defects in the cardiac waves. When the changes acute or even in ST –T waveforms and Q waves potentially, this changes are suggested to infract related artery and the initial stage of myocardium risk. T waves and ST waves are indicating the myocardium ischemic infraction. In previous stage of ECG are very helpful to identify the acute MI and the abnormalities in ST-T waves, but after innovation of nanoparticles the treatment of MI are going to the next level in modern medical science. ECG assess the myocardial motion, thickening and global function. To identify these disease with the help of biomarkers (Thygesen,Alpert,et.al;2007).

Echocardiology:

Echocardiology is the most effective imaging technique to assess myocardial thickness, thickening and its motion also. Echocardiology contrast agents will effect the visualization of endocardial area but it is not fully developed to detect some other diseases like myocardial necrosis (Thygesen,Alpert,et.al;2007).

Radionuclide imaging:

Thallium-201, technetium-99mMIBI, Tetrofosmin and (^{18}F)2 flurodeoxyglucose (FDG) are some radionuclide which are allowed to imaged viable myositis directly. This imaging methods

are assessing viability. A single proton emitting radio pharmaceuticals are finding out myocardial perfusion and smartly detect the area of infection and induce the abnormalities. Old infraction acute ischemia, hibernation are also able to detect through radionuclide imaging (Thygesen,Alpert,et.al;2007).

MRI:

Cardiovascular MRI the high spatial resolution and it is very well standard. It will assess the myocardial function and find out the possible acute infraction. Paramagnetic contrast agents are used to myocardial perfusion (Thygesen,Alpert,et.al;2007).

Treatment:

MI treatment should be taken seriously otherwise this will be turn into heart failure. Intra myocardial biomaterial injections are proved the advantage by reducing stresses in the infracted ventricular wall. It is also provides better cellular components and works as a storehouse of bioactive agents. The use of biomaterials for cardiac repair has mainly focused on the interaction with the outer edges of the myocardium. It will provide support. However, materials are transferred into body through direct epicardial injections at distinct location into the infract area and focus on the biomaterial or nanomaterial presence. Angiogenesis, Cardiomyocyte protection, stem cell recruitment are some biological functions which are developed by the appropriate biomaterials to encourage cardiac repair. It also improve the efficacy of the material and treating heart disease (Nelson, Ma, et. al;2010).

Alginate :

It is a block co polymer of (1-4)-linked β-D-mannuronate and α-L-guluronate residues. This is also bio inert. The material properties of alginate (strength and degradation rate) are studied for leading a good methods to adjust properties. If alginate conc. increase, the strength will be

increased, the solution viscosity also increased. This high viscosity is not desirable. Landa et.al. claimed in his study that the ability of alginate are increase LV remodeling and function after injected agents into the myocardium. By using a biotin labeled alginate, it will help to track material degradation accurately in vivo. The combination of polupyrrole with alginate will increase cell infiltration. Polypryrrole are helping to conduct electrical signals and increase endothelial cell growth (Nelson, Ma, et. al;2010).

Fibrin:

Fibrin is an one kind of biomaterial which are used widely to reproduce coagulation last step by forming cross linked fibrin network. It works like glue or sealant. The material properties are depending on the starting solution composition. For example by increasing thrombin concentration, it also increases the dotting speed conc. and leading a strong network. FDA approved that the application of fibrin aid hemostasis are ready access for most operating room (Nelson, Ma, et. al;2010).

Treatment:

In the case of myocardial infraction, the treatment should be started as soon as possible. This immediate treatment helps to restore blood flow to the affected area of the heart. To treat myocardial infraction some medications like antiplatelet agents, anticoagulants, nitroglycerin, and pain relief drugs to improve the condition of a patients. Reperfusion therapies, including percutaneous coronary intervention (PCI) or thrombolytic therapy, are some therapies which helps to unlock the blocked artery and increase blood flow and also minimize the ventricle damage. In some serious cases, coronary artery bypass grafting (CABG) might be done to improve the condition of severe blockages or multiple affected vessels.

Post-Myocardial Infarction Care:

To prevent further complications of patients and support recovery some post MI care should be taken. In this care includes medication to manage risk factors like hypertension, hyperlipidemia, diabetes, and to prevent clot formation. Some crucial elements of post-MI care are- cardiac rehabilitation, lifestyle modifications (such as adopting a healthy diet, regular exercise, smoking cessation), and psychological support.

Prevention Strategies:

To reduce the risk of myocardial infarction prevention strategies are playing a vast role . Lifestyle modifications, including a healthy diet, regular exercise, maintaining a healthy weight, avoiding tobacco, and managing stress all are the basic process to minimize the risk factor. Additionally, controlling risk factors like hypertension, diabetes, and hyperlipidemia can significantly reduce the likelihood of experiencing an MI.

Chapter 4:

Discussion:

4.1 Potential toxicity of AgNP:

AgNP are given into and are distributed through the organs of a patients. AgNP are administered in varieties of routes for example- inhalation, skin contact, digestive, respiratory, urinary etc. they are distributed into our liver, lung, spleen, kidney, skin etc. The small size of AgNPs are penetrated easily into body and gives therapeutic effects and induce potential

cytotoxicity when it crosses the blood brain barrier (BBB). AgNPs produces dermal toxicity, hepatic toxicity, neuro toxicity, kidney toxicity etc.

4.1.1. Skin or Dermal Toxicity:

Skin is the largest organ of human body as well as the first line barrier. Ag compound are induced into the tissue it may turn into gray or blue gray involving into the skin. When AgNP are applied, it induced into the body into cytotoxicity in the site and easily penetrate into the skin and access the systemic circulation. For example, applying AgNPs gel into the upper side of the skin, penetrate the particles into the skin and accumulates into the skin and produces potential cytotoxicity. Some studies explained that AgNP in long term use may cause Argyria. The penetration of AgNP was found into the follicular penetration pathway and intercellular penetration pathway (LiXu,Yi et al.2020).

4.1.2 Hepatobiliary system toxicity:

Nanoparticles ingestion, degradation, accumulation are occurs through liver. So, the liver is most important organ. AgNPs are also exported through this pathway. Maglie et al. are found that AgNPs exhibit hepatobiliary toxicity on the basis of size and the dose dependent toxicity. When the size of Ag are small the toxic effects are unmeasurable, Again, when the dose is high it will induce severe hepatobiliary damages. Hepatpcyte necrosis; micro hemorrhage, portal vain injury are some of the hepatobiliary damage (LiXu,Yi et al.2020).

4.1.3 Respiratory toxicity:

AgNP can induce the acute and chronic lung disease, damage the lung functions and also damage power of particle accumulation and clearance. Akinori et.al explained in her studies that the pulmonary toxicity of nanometer particles in the mouse models. Ultrafine particles can overcome through gap and alveolar epithelia; cells and resulting acute lung inflammation and tissue damage. The smaller size particles are more harmful for lung than the larger one. AgNPs are also induced dose dependent lung toxicity. The pulmonary fibrosis are also caused by AgNPs because the direct aggregation and effects on the membrane and it will disarupts the synthesis and degradation of extracellular matrix. Different conc. of AgNP are causing lung damage. Joanna et al. found that AgNP disrupted the blood permeability barrier. It also shows that some neutrophilic inflammation which will create a change in asthma (LiXu, Yi et al.2020)

4.1.4: Kidney toxicity:

The main functions of kidney are to keep balance body fluid volume, electrolyte conc., osmotic pressure, emitting toxic substance from the body and control the p^H level. By using AgNPs sometimes abnormal renal functions may occurs. It can accumulate into brain, lung, liver, blood etc. Between male and female the accumulation of silver in the kidney are differ. Wan et.al proved that the female rat are carrying two times more conc. silver in the kidney than the male rat. Ag removal straining of the kidney pointed that AgNPs are accumulated on the base area of glomerulus and mildly stored in the adrenal capsule and renal tubules. Organic cation transporters and hormonal regulation are two things that make vary in storage of Ag into the kidney. Renal metallothionein and zinc binding proteins are helping for accumulating in kidney. AgNPs hamper the endothelial cells conjunction and AgNPs permit to cross the endothelial layer and stored there. For this reason, AgNPs could leaking and as a result the

peripheral inflammation occurs. AgNp occurs the injury in the basement membrane in glomeruli (Li Xu ,Yi et al. 2020)

4.1.5: Central nervous system toxicity:

Central nervous system is the very important part of our body. Some articles are published that AgNPs are able to penetrate the brain and can induce the neural death. As our neural cells have the little repairing power, it will attract AgNPs more. Injected AgNP can be cross the BBB and it will penetrate into brain and reached into CNS. When AgNPs are diposited our extravascular lymphocytes are getting more toxic and getting inflammated . again it will increase the permeable between AgNP and Ag^{+}, AgNP has the higher bioaccumulationpower. Again, AgNPs might reduce the antioxidant defence through the enhancement of thioredoxin which interact with protein and make central neurotoxicity. Futhermore, AgNPsobserverd the expression of multiple gene, reduce the metabolic and biosynthesis processwhich can affect in functions of astrocytes and enhance neurotoxicity. Alzheimer's disease can be induced by altering geen expression through AgNPs (Li Xu, Yi et al. 2020).

4.2: Futuristic purpose:

As we know that the rate of mortality by CVD are reached very high level in world widw. To reduce this rate some technological changes should be done. Some current treatment are rely on making lifestyle changes along with taking madications. Statin and antihypertensive drugs helps to reduce high cholesterol and high blood pressure. It means a cardiac patients lead a very strict routine with healthy lifestyle and medication. Some patients are not able to maintain medication propaerly because of medical expences and loss of income. So, in future if we focus on the new drugs are targeted more rather thanprevious drugs this will reduce the side effects and increase patient adherence. It may be happenin combination therapy. A healthy lifestyle

and meditation can improve a patient condition more rather than taking medications. Avoiding smoking and tobacco intake ; maintainging diabetes mellitus; taking healthy diet maintaining weight according to height and age, avoiding cholesterolrich food. Along with this some physical exercise and meditation should be taken in daily basis. It will maintain body fitness and keep body cheerful and healthy.

Chapter:5

Discussion of Antimicrobial property for MI:

The exploration of antimicrobial properties in the context of myocardial infarction (MI) represents an intriguing area that extends beyond the conventional understanding of cardiac events. While the primary focus of MI management is typically on re-establishing blood flow and minimizing cardiac damage, the potential role of antimicrobial properties, particularly in the context of preventing post-MI complications, is gaining attention.

Infection Risk Post-Myocardial Infarction:

Following an MI, patients may be susceptible to infections due to weakened immunity, compromised cardiac function, invasive procedures (such as catheterization), or prolonged hospital stays. Infections, including bloodstream infections, pneumonia, or surgical site infections, can significantly worsen outcomes and increase mortality rates in these individuals.

Antimicrobial Properties of Silver Nanoparticles (AgNPs):

Silver nanoparticles (AgNPs) have demonstrated potent antimicrobial properties against a broad spectrum of microorganisms, including bacteria, viruses, and fungi. Their unique physicochemical characteristics, such as their small size and high surface area, enable efficient interactions with microbial cell walls and membranes, disrupting their structure and inhibiting their growth.

Potential Application in MI:

In the context of myocardial infarction, the use of AgNPs with antimicrobial properties might offer several potential benefits:

Prevention of Infections:

Coating medical devices, such as stents or catheters, with AgNPs could reduce the risk of bacterial colonization and subsequent infections post-procedure, thus lowering the chance of complications for MI patients.

Limiting Inflammation:

Infections post-MI can exacerbate inflammation, contributing to adverse cardiac remodeling. The antimicrobial properties of AgNPs might indirectly reduce inflammation by preventing infections, aiding in cardiac recovery.

Chapter : 6

Conclusion:

Silver nanoparticle consists of broad spectrum activity against different types of cardiac dieases. AgNP's minimizes adverse effect on human or animal cell but create a toxic effects on target cells. A lot of effective effcets make the nano medicine are more popular to the all kinds of patients specially cardio vascular disease patients. Nano formulations are formed by biology and medicine. Developed medicines are creating a great effects on the biological demands. We need to assume all the advantages of the nanoparticles into nano-medicine and refuse the adverse effects through several development. Several aspects should be observed to develop drugs from the initial stage laboratory stage to the market place for the better treatment, identifying the accurate drug for specific disease in lower level of toxicity. A strong network into the pharmaceutical research area to develop drugs into cardiovascular disease by using nano particles.

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