



Received on 11 January 2020; received in revised form, 08 April 2020; accepted, 14 May 2020; published 01 October 2020

APPLICATION OF NANOTECHNOLOGY FOR TREATMENT OF ANGINA PECTORIS AS CARDIOVASCULAR DISEASE: A REVIEW

Hitesh Kumar Dewangan* and Anuj Garg

Institute of Pharmaceutical Research, GLA University, NH-2 Mathura Delhi Road, P.O.- Chaumuhan, Mathura - 281406, Uttar Pradesh, India.

Keywords:

Angina, Nanoparticles, Heart, Cardiovascular disease, Nanotechnology

Correspondence to Author:

Dr. Hitesh Kumar Dewangan

Assistant Professor,
Institute of Pharmaceutical Research,
GLA University, NH-2 Mathura Delhi
Road, P.O.- Chaumuhan, Mathura -
281406, Uttar Pradesh, India.

E-mail: hiteshdewangan.hd@gmail.com

ABSTRACT: Angina Pectoris is the medical term for chest pain or discomfort due to coronary heart disease. The drawback of the marketed formulation is required repeated administration of the drug due to low bioavailability. Therefore, it utilized a nanotechnology technique for prevention of drawback of marketed formulation. Polymeric nanoparticles have been in preferential list when it comes to nano-drug delivery *via* oral route. Recent advances in lipid-reducing treatment, statins clinical research suggests that antimicrobial therapy is important to continue reducing cardiovascular events, beyond lipid-reducing therapy. A potential therapeutic choice for the residual risk is to intervene directly in the inflammatory process through a drug delivery system based on the nanotechnologies. Different nano-sized materials, including micelles, liposomes, polymer nanoparticles, dendrimers, carbon nanotubes, and metal nanoparticles, are currently developed as by nanotechnology. It is a viable strategy since the inflammatory environment enhances the integration of nano-sized materials into a mononuclear phagocytic process. We have recently developed a polymeric nano pharmaceutical statin in order to optimize its anti-inflammatory properties. In the present review, we present the current development of nanotechnology and future prospects on the treatment of life-threatening cardiovascular disease by anti-inflammatory nanomedicine.

INTRODUCTION: Angina is also called angina pectoris, which is the medical term for chest pain experienced when heart muscles (*i.e.*, myocardial muscles) do not get enough blood supply. It is usually described as squeezing, pressure, heaviness, tightness in the chest. This happens because of the narrowing or blockage of one or more coronary arteries¹. The reduction in blood supply creates ischemic conditions in the heart.

Angina is a common disabling disorder that is caused by myocardial ischemia; (an imbalance between myocardial oxygen supply and myocardial oxygen consumption). This increases the workload of the heart, which results in increased heart rate. Angina usually causes fullness, uncomfortable pressure, and pain in the chest, the discomfort of neck, jaw, shoulder, back, and arm.

Some people suffering from angina described angina as feeling like a vise is squeezing their chest or feeling as if a heavyweight has been placed on their chest^{2, 3}. Angina may be a new pain that needs evaluation by a doctor, or reoccurring pain that goes away with treatment. Although angina is relatively common, it can be hard to differentiate from other types of chest pain, such as the pain or

QUICK RESPONSE CODE 	DOI: 10.13040/IJPSR.0975-8232.11(10).4884-95
This article can be accessed online on www.ijpsr.com	
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(10).4884-95	

discomfort from indigestion. If you have unexplained chest pain, pursue medical attention right away⁴.

Angina is a Coronary Heart Disease (CHD), which is epidemic in most countries, including India. The deaths and disabilities due to CHD continue to increase in developing countries, whereas declining in developed countries⁵. According to The Registrar General of India, deaths due to CHD in 2001-2003 were 17% of total deaths in the country, which gets increased to 23% in 2010-2013. According to the World Health Organization (WHO), the South Asia region has one of the highest CHD mortality rates in the world^{6, 7}. The WHO report says that in 2010, cardiovascular disease mortality rates in India were 349/100,000 in men and 265/100,000 in women. These rates are 2-3 times higher than the United States, where rates were 170/100,000 in men and 108/100,000 in women. According to the Global Burden of Diseases (GBD), deaths, as well as disability in India due to CHD, have been doubled in the last 30 years^{5, 8}. Nowadays, nanotechnology had been utilized for the treatment of various heart diseases. Different nano-sized materials, including micelles, liposomes, polymer nanoparticles, dendrimers, carbon nanotubes, and metal nanoparticles, are currently developed as by nanotechnology. The application of nanotechnology to the coronary artery disease is an effective method. We have recently developed a polymeric nano pharmaceutical statin that has nano-sized and studied in clinical implementation for the treatment of multiple disease models, myocardial ischemia-reperfusion injury, and acute myocardial infarction.

This review article summarizes the application of nanotechnology in angina pectoris and various heart diseases. I also studied the development of nanotechnology and prospects on the treatment of life-threatening cardiovascular disease.

Stable Angina (Classical): It is the common form of angina in which the patient has episodes of chest pain. This form is usually predictable and manageable. Attacks are provoked by emotion, exercise, heavy meals, coitus, and exposure to very hot or cold temperatures. Stable angina is usually generated by physical exertion. When you hike stairs, exercise, or walk, your heart needs more

blood, but it's harder for the muscle to get enough blood when your arteries are narrowed. Other factors, such as emotional stress, low temperature, heavy meals, and smoking as well as physical activity, also can narrow arteries and activate angina^{9, 10}. The following symptoms are observed during stable angina:

- This occurs when the heart must work harder, usually during physical exercise.
- It does not come as a surprise, and episodes of pain tend to be similar.
- Usually lasts a short time (5 minutes or less)
- It occurs even at rest condition
- Frequent feeling of gas or indigestion.
- Felling of chest pain that spreads to the arms, back, and other areas.
- It can be similar to the pain to previous types of chest pain you've had.
- Disappear with use of angina medication.
- The severity, duration, and type of angina can vary.

Unstable Angina: It is the uncommon form of angina which comes as a surprise and usually occurs while resting and cause unaccepted chest pain. It is sometimes also called acute coronary syndrome. The atherosclerosis plaque ruptures and cause injury to coronary vessel result in blood clotting, which blocks blood flow¹¹. This type of attack should be treated as an emergency. The pain is due to spasm in the coronary artery. If fats deposits in a blood vessel rupture or blood clot forms, it can quickly block or decrease blood flow through a narrowed artery, suddenly the flow of blood is decreased to heart muscle^{9, 10}. Unstable angina can also be caused by blood clots that block or block partially your heart's blood vessels. Unstable angina gets worse and is not relieved by rest or usual medications. If the blood flow does not improve, the heart is depressed of oxygen, and a heart attack occurs. Unstable angina is dangerous, so it requires emergency treatment¹¹. The following symptoms are found during Unstable Angina:

- The pain or discomfort.
- It generally occurs while resting, sleeping, or with little physical exercise.
- Comes as a surprise.

- May last longer than stable angina (up to 15 minutes).
- Rest or medicine usually does not relieve it.
- May get worse over time.
- Is a change in your usual pattern of angina.
- Is unexpected.
- Might signal a heart attack.
- It can lead to a heart attack and death.
- May not disappear with rest or use of angina medication.

Prinzmetal's Angina: This type of angina is caused by a spasm in a coronary artery in which the

artery temporarily narrows. This narrowing decreases blood flow to your heart, causing chest pain. Emotional stress, smoking, and use of the drug cocaine or morphine may activate this type of angina^{9,10}.

Pathophysiology of Angina pectoris: Angina results when there is an imbalance between the heart's oxygen demand and supply. This imbalance can result from an increase in demand without a proportional increase in supply. The detailed pathophysiology of angina is shown in **Fig. 1**.

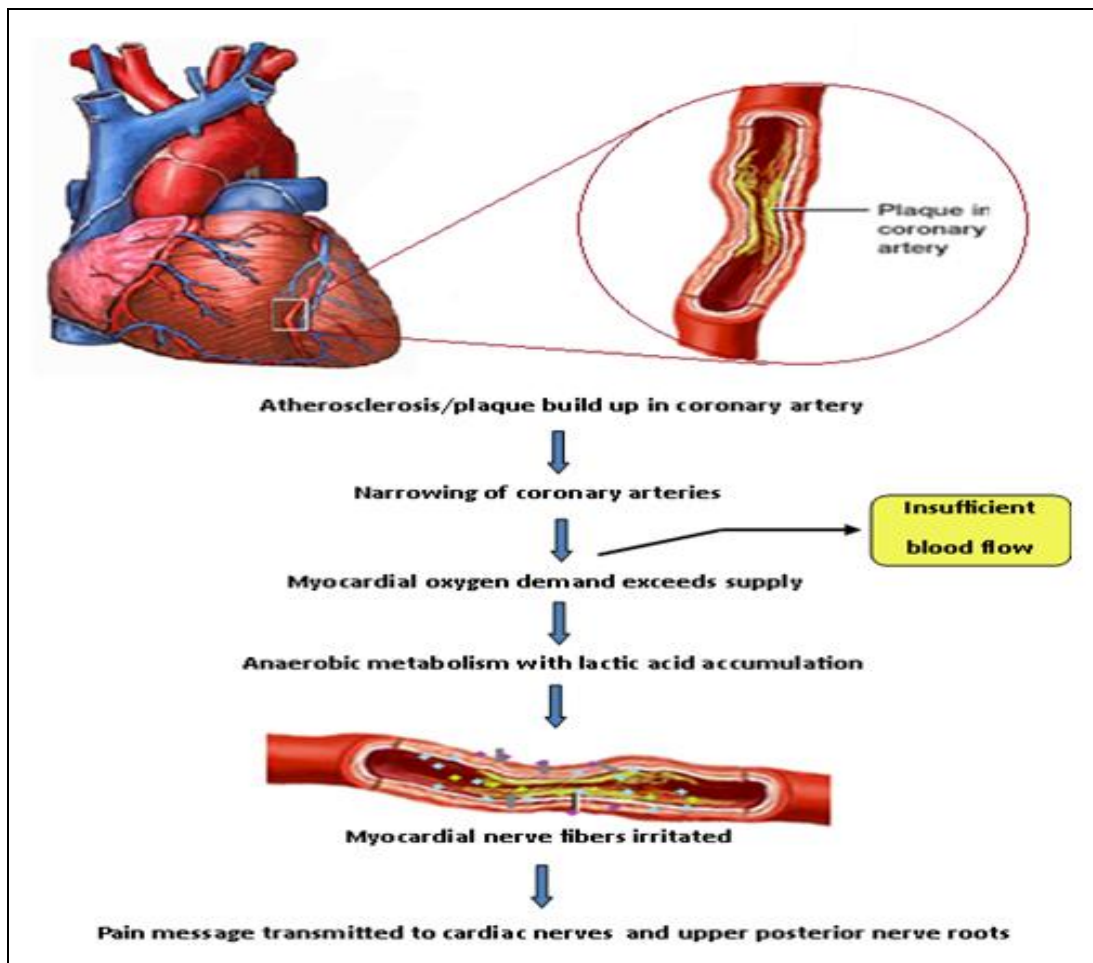


FIG. 1: FLOW CHART SHOWING THE PATHOPHYSIOLOGY OF ANGINA PECTORIS

Causes/risk factors of Angina Pectoris:

- **Atherosclerosis:** In this disease, plaque builds up inside the coronary arteries. Plaque is made up of cholesterol, fat, calcium, and other substances found in the blood. Plaque narrows the coronary arteries and reduces blood flow to heart muscles. This causes a shortage of oxygenated blood in the heart muscles that may lead to Angina^{13,31}.
- **Hypertension:** High blood pressure can cause thickening and hardening of the arteries (atherosclerosis), which can lead to angina, heart attack, stroke, or other complications^{7,58}.
- **Obesity:** Fat builds up in the blood vessels and coronary artery, which leads to increased blood pressure and ultimately raises the risk to angina^{4,15}.

- **Diabetes Mellitus:** Hyperglycemia may damage blood vessels through a process called "atherosclerosis," or clogging of arteries. This narrowing of arteries leads to decreased blood flow to the myocardium, causing angina and eventually heart attack¹⁷. It is the inability of the body to produce enough or respond to insulin properly. Insulin, a hormone secreted by your pancreas, allows your body to use glucose, which is a form of sugar from foods. Diabetes increases the risk of coronary artery disease, which leads to angina and heart attacks by speeding up atherosclerosis and increasing your cholesterol levels^{18,19}.
 - **Dyslipidemia:** hypertriglyceridemia, increased small and dense low-density lipoprotein (LDL) particles, low high-density lipoprotein cholesterol (HDL-C) levels, and elevated apolipoprotein B increases the chances of cardiovascular diseases (Dyslipidemia, Kidney Disease, and Cardiovascular Disease in Diabetic Patients)⁷.
 - **High Blood Pressure:** blood pressure is determined by the amount of blood your heart pumps and the amount of resistance to blood flow in your arteries. Over time, high blood pressure damages arteries by accelerating the hardening of the arteries.
 - **High Blood Cholesterol or Triglyceride Levels:** cholesterol is a major part of the deposits that can narrow arteries throughout your body, including those that supply your heart. A high level of the wrong kind of cholesterol, known as low-density lipoprotein (LDL) cholesterol (the "bad" cholesterol), increases your risk of angina and heart attacks. A high level of triglycerides, a type of blood fat related to your diet, also is undesirable²⁷.
 - **Obesity:** Obesity raises the risk of angina and heart disease because it's associated with high blood cholesterol levels, high blood pressure, and diabetes. Also, your heart has to work harder to supply blood to the excess tissue.
 - **Psycho-social stress:** Chronic stress and depression are associated with an increased risk of cardiovascular disease. Stress can increase your risk of angina and heart attacks. Too much stress, as well as anger, also can raise your blood pressure. Surges of hormones produced during stress can narrow your arteries and worsen angina^{19,28}.
 - **Family History of Heart Disease:** If a family member has coronary artery disease or has had a heart attack, you're at a greater risk of developing angina.
 - **Older Age:** Men older than 45 and women older than 55 have a greater risk than do younger adults.
 - **Lack of Exercise:** An inactive lifestyle contributes to high cholesterol, high blood pressure, type 2 diabetes, and obesity. However, it is important to talk with your doctor before starting an exercise program.
 - **Smoking:** The amount of oxygen available to the muscles, brain, and blood is reduced due to carbon monoxide produced from smoking. Also, the High levels of CO, together with nicotine, cause the hardening of arteries. This increases the workload of the heart. Over time this may cause airways to narrow and blood pressure to rise, which can lead to angina and ultimately heart attack³⁶.
 - **Tobacco Use:** Chewing tobacco, smoking, and long-term contact to used smoke damage the interior walls of arteries-including arteries to your heart -allowing deposits of cholesterol to collect and block blood flow.
- Diagnosis of Angina Pectoris:**
- Electrocardiogram (ECG):** In this test, the electrical activity of the heart is recorded, which is used to diagnose heart abnormalities such as arrhythmias or ischemia (lack of oxygen and blood) to the heart. In angina pectoris, there is the depression of the ST-wave segment of the ECG graph. The amplitude of depression reflects the worsening of angina.
- Stress Test without Imaging:** This test helps to evaluate how well the heart works with activity. During a stress test, the person is asked to do the physical exercise of walking, running, and treadmill. An ECG is recorded during the exercise

period. The ECG is then assessed by the doctor, and the condition is explored to the patient.

Blood Tests: The concentration of an enzyme called “troponin” starts increasing in blood after the heart has suffered from angina or heart attack. The blood test can also help in the measurement of elevated cholesterol, LDL, and triglycerides that increase the chances of coronary artery disease and, ultimately angina²⁵.

Chest X-ray: This imaging test helps the doctor find out other sources of chest pain such as pneumonia.

CT of the Chest: It is a more sensitive test than a chest x-ray that can identify other causes of chest pain such as aortic disease or blood clots in the blood vessels of the lungs⁴².

Coronary Computed Tomography (CT) Angiography: The decrease in blood flow is the result of narrowing of the coronary artery due to plaque buildup or due to other reasons, can be known for this imaging test⁴².

Magnetic Resonance (MR) Imaging/Angiography: The primary purpose of this test is to determine whether there is good blood flow to the heart muscle. If the areas of bad blood flow are found, this could indicate plaque with blood vessel narrowing. This test is carried out after exercise to know the effect of exercise on blood flow and at rest to know the resting blood flow¹⁶.

Treatment of Angina Pectoris: There are various synthetic drugs that can manage angina pectoris and heart attack. They generally work by dilating the blood vessels and arteries. This helps in fulfilling the oxygenated blood supply to the heart muscle and relieves angina pain. Angina is the most common symptom of ischaemic heart disease. Approximately 9 million patients in the USA suffer from angina. The traditional system of treatment for angina is focused on:

- Improving the balance between myocardial oxygen delivery and consumption through heart rate and blood pressure or afterload reduction
- Enhancement of coronary flow by vascular (coronary) muscle relaxation.

As known that Heart rate is the major determinant of oxygen consumption, so attacks of angina are preceded by an increase of heart rate, and Heart rate is the major determinant of oxygen consumption⁴⁷.

The drugs can be classified in two ways: first-line and second-line medications for patients who have contraindications to first-choice agents or do not tolerate them, or remain symptomatic.

First-line treatment

- (a) Beta-blocker
- (b) Calcium channel blocker
- (c) Short-acting nitrates

Second-line treatment

- (a) Ivabradine
- (b) Nicorandil
- (c) Ranolazine
- (d) Long-acting nitrates
- (e) Trimetazidine

Based on Alteration in Physiological Condition:

(A) Drugs that Reduce Heart Rate: It contains three classes of drugs like beta blocker, ivabradine, non-dihydropyridine calcium antagonists, ex-verapamil and diltiazem.

(B) Drugs that induce vascular Smooth Muscle Relaxation: Mainly reduces vascular smooth resistance and causes arteriolar and coronary artery dilatation. In this class included dihydropyridine calcium channel blockers, nitrates, nicorandil.

(C) Metabolic Modulators and Late Sodium Current Inhibitor: piperazine derivatives drugs belong to this class, in which two agents are clinically available such astrimetazidine and ranolazine.

Roll of Nanomaterial and Application in Angina Pectoris: Nanomaterials displayed exceptional open doors for beating the breaking points of ordinary biological materials. An advancement of nanostructured surfaces, nanoparticles, as well as nanocomposites might enormously advance that showing off the traditional biomaterials. Besides, the advancement in the field of nanomaterials can rouse various new restorative procedures that might change the cure for cardiovascular diseases.

Nanomaterials have magnitude highlights going from the level of proteins to the level of cells that imitating extracellular network as well as microenvironment for structure of tissue at distinct leveled and cells^{46, 49}. Then again, nanomaterials have essentially unique physicochemical properties contrasted and even materials. Due to high surface to volume proportion, high surface vitality and movement, just as adjusted wettability could significantly impact on proteins bonds⁵. Besides, nanomaterials can accomplish certain helpful capacities that would be somewhat hard to accomplish utilizing traditional biomaterials.

Nanoparticles, for example, can go about as medication transporter that can go through the endothelium of veins. If appropriately functionalized, they can likewise enter cells through the disguise procedures and, after that convey the pre-stacked medications or qualities. Also, some nanoparticles can be utilized as different operators for attractive reverberation MRI as well as many other bioimaging advances^{37, 38, 48}.

Nanomaterials are especially helpful in heart disease, and they showed possibilities over a few applications. Controlling geographical signals of nanostructured surfaces can specifically coordinate cell exercises. This ability of cell direction is exceptionally valuable in convinced heart utility where advancing elements of special kind of cell while smothering exercises of another sort of cells are liked. For instance, the implantation of coronary stents generally prompts neointimal hyperplasia^{8, 40}. Advancing grip and elements of cells such as endothelial cells and stifling the cell of smooth muscle that will encourage recuperating procedure and endothelial layer development and hindering extreme neointimal arrangement; in this way, particular cell incitement could conceivably prompt a superior and quicker endothelialization.

Notwithstanding nanoscale surface highlights, nanoparticles can fill in as a stage conveying various practical gatherings and give energizing chances to potential heart applications. Such nano-stage can coordinate the elements of focusing on, imaging, and therapeutic in a single molecule^{29, 52, 57}. Also, as of late, created nanocomposites can utilize nanoparticles as a key segment to enormously upgrade the mechanical and natural

exhibitions of current cardiovascular inserts as well as gadgets.

Nanoparticles demonstrated guarantees an assortment of circulatory uses because of their one of a kind character. Not at all like mass inserts, nano molecules exist portable in intra as well as in extravascular frameworks that made this appropriate for specifically conveying medications along with filling in as imaging specialists. A similar different nano constituent, nanoparticles have the unique character radically particular to their traditional partners^{23, 24}. Nano molecules have high surface vitality because of their high surface territory to volume proportion. Therefore, nanoparticles which having the high vitality take care to a lot together to lessen vitality. Subsequently, essential estimates will be taken for settling nanoparticles, these actions incorporate the utilization of surfactant, stabilizer, topping reagents, or changing the dissolvable conditions, for example, pH as well as hydrophilic/lipophilic of an administering media^{6, 51}.

These may regularly be utilized, such as stages that are modified with different particles. Various capacities could coordinate with the one Nano molecule. The nanoparticle can be conjugated by focusing on legends, for example, peptides that will be targeted bleak locales. Nanoparticles are conjugated with the practical legends that will keep away from quick freedom and phagocytosis. For focused medication conveyance, the conjugated gathering nano-molecule ought to discharge in a well-regulated style, which wants unique techniques for structuring as well as designing of Nanoparticle^{22, 46}. Also, nanoparticle which is utilized to improve biomedical imaging. For instance, attractive Nanoparticle (MNPs) as complexity operators would recover attractive reverberation MRI^{24, 53}.

Any type of nanoparticle intended for medical uses, their communications through cells, as well as take-up by cells necessity explicitly measured and deliberately examined. When the Nanoparticle can enter into the human cells, novel uses, for example, Ribonucleic acid locations, as well as intracellular deoxynucleic acid conveyance, become conceivable. The distinctive nanoparticle has the different components that will able to entering into

the different cells. When all is said in done, cells can be disguising nano molecules by using a procedure such as endocytosis, phagocytosis as well as pinocytosis, which are complete, evaluated somewhere else⁵⁹. Endocytosis, as well as phagocytosis, is the particular paths reliant on micro molecules such as protein as well as peptide and receptors, whereas pinocytosis is a non-explicit path that occurs while cells assimilate adjacent fluid. The nearness explicit as well as non-explicit disguise path demonstrates that many nanoparticles can be entered into the cells exist the two instances of disguised nanoparticles situated within the cells. Adequacy of cell take-up of a nanoparticle relies upon numerous elements, including surface charge, width, decoration, measure, size, etymology, mass of nanoparticles, etc. It observed that the shape and state of gold nanoparticles influenced cell take-up by HeLa cells, as appeared in^{11, 61}. The size and angle proportion were found to incredibly impact the take-up of gold nanoparticles in the HeLa cells, through the greatest takes-up were come at a size range of 50 nanometers as well as perspective proportion of 1:1.

Application of Nanoparticles for Angina and Cardiovascular Disease: Acquainting nano-structured surface with ordinary materials that have been utilized in FDA-affirmed restorative inserts and gadgets is additionally viewed as less dangerous while keeping their ideal remedial capacities, from the administrative perspective, for example, FDA, when contrasted and a pristine material which are not utilized in endorsed inserts. In the advancement of novel materials and medications, as a rule, includes high dangers and requires huge endeavors towards the FDA endorsement. For instance, recent medication eluting stents face the late difficulties on account of the symptoms of calming and against proliferative medications which postpone endothelialization^{34, 56}. For this situation, in the case of nanopatterning on an outstanding safe material (endorsed by FDA for medicinal uses) could conceivably supplant counter proliferative medications and not without a doubt merits concentrated examinations.

Physicochemical Properties of Nanostructured Surfaces: This is an outstanding that nano-molecules are an essentially expanded level zone to the volume proportion just as level vitality when

contrasted and regular materials. For the nano-molecules & nanoparticulate, to instance, the surface zone increment in a few requests of greatness when the size element of unit Nano-molecule lessens from full-scale size level down to nano-estimate level while the mass and concoction creation stay unaltered. The surface vitality will likewise increment as an outcome of more prominent surface region and increasingly break the bonds to the level of nano-surfaces and nearness of nano characteristic would likewise fundamentally increment in nano-scale unpleasantness^{20, 30}. Wettability is another significant behavior that may alter for the most part by the surface of nano molecules' surface. Wettability, hydrophilic as well as lipophilic nature can be evaluated by the contact of water point estimations. Essentially expanded surface harshness could effectively affect the wettability of the particle surface. Accounts on the certain molecules recommended that contact with the water edge as a rule increments on more unpleasant planes in a specific dimension, yet aimed at exceptionally hydrophilic surfaces are more, unpleasant to the planes at the nano-range that would prompt lesser contact point. Making small range means nanostructures on the non-polar molecules that would mark them progressively non-polar, whereas making small/nano range includes on polar molecules would make them increasingly polar^{32, 43}.

Creation ways to deal with the architect from the nano-range to sub-micron range constructions on the surface of molecules have been created, which considered intended for a long time, yet most strategies have been centered around or started from electrical molecules. It has been a meadow of biomolecules. The nano-arranged surface used as a developing zone that has pulled for expanding the consideration as of late, for example, creating an increasingly sensitive, well-characterized and requested structure, micro, as well as nanofabrication systems initially settled for electric uses displayed extraordinary possibilities.

Nanostructured Surface and Cell Behavior: In the body, cells normally collaborate to his encompassing condition, for example, extracellular network. The substance synthesis, physicochemical properties, and land signals of the encompassing

condition all assume significant jobs in cell material associations. Nanostructured plane, their different attributes can intervene macromolecules like as proteins that influence the cell grip, expansion, separation as well as phenotype^{23, 35}. Such qualities incorporate superficial vitality, superficial zone, superficial unpleasantness, wettability, electrical charge, geography, morphology, compound piece, and manual characteristics. For instance, a nano-irregular surface was originating to pull in extra vitronectin/fibronectin on superficial, brought about more noteworthy cell bond. With regards to explicit applications, such impacts ought to be considered completely and appropriately^{44, 60}.

For instance, upgraded attachment of specific cells could be an ideal or an antagonistic occasion contingent upon the uses. For CVS stats, expanded bond present in the cell of endothelial is wanted to quick endothelialization, whereas advanced grip, development of smooth muscle cells may prompt intemperate arrangement of neointima/noontime that could square vessel lumen. Every one of these elements ought to be thought about when planning nanostructures for cardiovascular applications⁴⁸.

Notwithstanding changes in physicochemical things by nanostructured, geography has natural impacts which have been known himself. Numerous examinations have been completed to uncover the organic impacts of geologies on various materials. The Pt-covered 50 Nanometer nanodot exhibit on Si wafer incredibly expanded dispersion region as well as the expansion of cardiomyoblasts, which contrasted and level the Si substrate even though firm Si wafers are not good substrates for CVS uses. Unmistakably, an examination of nanostructures has the clinical significant biomolecules application when examined that could be increasingly helpful for the clinical uses^{12, 41}. Aimed at the instance examined that equivalent depression designs of Ti substrates, which obtained to be the grip of bone marrow stromal cell enormously expanded in examples through notch thickness of 500 Nanometer or 750 Nanometer, 5 mm wide-furrow was the best in arranging cell headings. They clarified that two sorts of followed cells coincided: the cells followed onto numerous scores in which cells are bounded in the particular depression. It observed that the cells

would in general, spread over numerous furrows after score thickness has been littler to 5 mm. It was additionally uncovered that the cells scatter above numerous scores were progressively equivalent adjusted with the section once furrow thickness littler than 5 mm. This system may likewise help disclose endothelial cell reactions toward the scored examples on Ti revealed by other examinations. The two examinations demonstrated expanded cell expansion score thickness diminished towards the micro level to micron range^{39, 54}.

When all is said in has done in what way nanotopography impacts cell practices which have been not completely settled to CVS applicable biomolecules. Then the examination and systems where think about taking place to different biomaterials on cell and biomolecular stages are essential. That one is additionally critical toward thinking about the job of physicochemical characteristics, compound syntheses, and manual characteristics in host cells as well as in the tissue reactions. Such as crucial area of CVS biomaterials as well as nanotopography cell connections that can be considered and examined In vitro as well as In vivo to various CVS uses. A single case of In-vitro uses would nano designed platforms for the development of the tissue in bioreactors to treat the cells. Intended for the *in-vivo* investigations otherwise, medical uses, CVs gadgets, for example, stands and stream diverters that this may be embedded in the body would exploit nano molecules on the way to accomplish attractive cell reactions and tissue mending in the host or patients. In *in-vitro* uses of nano molecules, which will be progressively unsurprising in addition to the after-effects of an *in-vitro* investigation increasingly repeatable whereas *in-vivo* uses until looking colossal difficulties because of the unpredictability of human system and which also requires comprehensive investigation later on.

Nanoparticles for the Determination of Cardiovascular Sicknesses: Nanoparticles are utilized in numerous symptomatic uses of cardiovascular diseases because it very well may be designed to target explicit sullen destinations while being recognized. A model is the utilization of Nano molecules in the determination of atherosclerosis. Atherosclerosis frequently prompts

myocardial localized necrosis as well as stroke, yet this should be recognized in beginning time through identifying incendiary level. Achievement of initial finding greatly relies upon the noninvasive analysis in the beginning time. To accomplish this objective, monocrystalline attractive multivalent nanoparticles for distinguishing vascular cell attachment atom 1 (VCAM-1), a pointer of irritation. The multivalent nanoparticles these investigation was embellished through peptide that will be focus on multivalent nanoparticles to cells that will communicate VCAM-1. Multivalent nanoparticles will decide if irritation is happening and what will be the level, giving a chance to recognize atherosclerosis in its beginning period^{14,45}.

In the zone of MRI conclusion, the benefits nanoparticle has been misused too. Nanoparticles will be perfect differentiation specialists for MRI, which has the focus on capacity. By using the MRI nanoparticles objective, thickness, as well as position can be identified. X-ray innovation joined through nanoparticles is fewer obtrusive by the customary biopsy technique. A fruitful model was the imaging of removal place when transplantation of rodent cardiovascular allograft. The novel nanoparticle and which will be covered by dextran and known as ultra-small superparamagnetic iron oxide particles. The macrophage was effectively named through the multivalent nanoparticles, & sign produced through demonstrated area and level of dismissal. Considering that the macrophages will be effectively identified outside body reactions and provocative reactions might likewise be assessed in numerous other cardiovascular relevant environments later on utilizing comparative methodologies. This will be protected on the way to state the nanoparticles take gigantic possibilities to empower fresh, indicative strategies for heart and cardiovascular uses²⁶.

Nanoparticles for Focused Medication

Conveyance: The stage of Nanoparticle can acknowledge focused on medication conveyance for their unrivaled multi-usefulness. Conveying and discharging drug, and focusing on the sullen site are the most fundamental capacities for an effective focused on medication conveyance nanoparticle. For instance, manufactured of functionalized gold nanoparticles for the proscribed arrival of the NO

and accomplished the tunable discharging outline by picking distinctive ligand^{35, 50}. Nitric monoxides can interact endothelium as well as vascular smooth muscle cells capacities. It has been demonstrated that Nitric monoxide discharging polymers repress the deoxynucleic acid blend of the smooth muscle cells. Nanoparticle consolidating imagings, as well as remedial capacities, were regularly named theranostic nanoparticle that should understand the idea of customized medication. They are typically structured like a stage through practical gatherings incorporated. For instance, mixed with the photosensitizer to a dextran covered magneto fluorescent Nanoparticle, which will focus on the plaque macrophages, and it will discharge endless oxygen supplies of particular wavelength go, and this discharged oxygen would execute the macrophages^{3,21}.

Aside from conjugating remedially utilitarian gatherings to the medication stacking nanoparticle, this medication likewise epitomized by nanoparticle. Liposomes are a perfect contender for embodying therapeutics molecules. Some nanoparticles themselves have remedial viability. For instance, silver nanoparticles were accounted for to be hostile to platelet, contingent upon molecule estimate; Magnesium oxide nanoparticles were found that it will have the antibacterial character and which diminish diseases related to therapeutic inserts as well as gadgets. Such nanoparticles are utilized as remedial operators and conveyed with the network resources^{14,26,55}.

FUTURE PERSPECTIVES: In particular, medical technologies and treatments for CVDs have advanced considerably intending to improve the quality and length of life. Better solutions are required for the treatment of CVD since the current practice recommendations are estimated to support just 15% with high-quality evidence^{7,58}. Improved lifestyle, food, medical intervention, earlier detection, prevention strategies, and better living standards all contributed to improved prognosis. Many premature deaths below the age of 75 years are due to CVDs in persons who are residents of the European Union. It is, therefore crucial for quick and effective treatment of the pandemic to be sought to prevent approximately 80 percent of all cardiovascular diseases using nanotechnologies.

A study in 2014 showed 122, of which 17 were in phase II or III trials³³, clinically developing nanomedications. 70 drugs were based on oncology, 19 were focused on infectious diseases, and only 7 were based on cardiovascular medicine. It underlines the urgent need for more research and development.

Current and on-going studies are being performed in cardiovascular therapy use nanotechnology, in particular with the European Commission financed another project. This Phase I trial has been successful in the imaging of thromboses and the treatment of vulnerable plaques by new carriers. Still, in the form of breathing samples and nanomaterial-based detectors, and investigating the possibility of diagnosing heart failure. In nanotechnology applications of drug resulting stents in contrast to bare metal stents further, clinical studies are being carried out: participant size of 8000 and thus far has demonstrated promising results (National Institute for Health and Care Excellence) was found in research.

CONCLUSION: In this study, the evidence demonstrates that the promise of nanotechnology for the treatment of CVD is shown by translation clinical trials. With increased investment in nanotechnology and appropriate infrastructures globally, the rigorous clinical trial process is only time to be completed and introduced onto the market by nanomedicine, nanomaterial equipment, and other related technology. Nanotechnology, of course, promises to improve patient health and well-being. Any progression on current therapies will have a positive effect on patients' lives worldwide. More *in vivo* experiments and clinical tests will have to be performed to clarify the action of nanoparticles systemically to have the greatest impact on medicine as possible.

When medical technology's potential is increasingly based on personalized medicine, nanotechnology could be best placed for this aim of responding to individual conditions. In addition to these exponential increases, higher cost of health care means that alternative solutions to current pharmacological and surgical treatment must be sought. However, there is substantial evidence to support the concept that nanotechnology is yet to make its full impact to revolutionize medicine.

ACKNOWLEDGEMENT: The authors acknowledge to Institute of Pharmaceutical Research (IPR), GLA University, Mathura, India, for provided necessary facility.

AUTHOR CONTRIBUTION: All authors contributed to the idea and design of the review, with drafting of the article, and revision of the article.

CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest.

REFERENCES:

1. Sharma V, Dewangan HK, Maurya L, Vats K, Verma H and Singh S: Rational design and *in-vivo* estimation of Ivabradine Hydrochloride loaded nanoparticles for management of stable angina. *J Drug Del Sci Tech* 2019; 54: 101337-48.
2. Chandarana M, Curtis A and Hoskins C: The use of nanotechnology in cardiovascular disease. *Applied Nanosci* 2018; 8: 1607-19.
3. Katsuki S, Matoba T, Koga J, Nakano K and Egashira K: Anti-inflammatory nanomedicine for cardiovascular disease. *Frontiers in Cardiovascular Med* 2017; 4: 87-96.
4. Gupta R, Mohan I and Narula J: Trends in coronary heart disease epidemiology in India. *Annals of global health* 2016; 82: 307-15.
5. George A, Mensah MD, Gregory AR and Valentin F: The global burden of cardiovascular diseases and risk factors 2020 and beyond. *J American College of Cardiology* 2019; 74: 2529-32.
6. GBD Healthcare Access and Quality Collaborators. Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease Study in 2016. *Lancet* 2018; 391: 2236-71.
7. Califf R: The future of cardiovascular medicine from the regulatory perspective. *J Am CollCardiol* 2016; 68: 766-69.
8. Prabhakaran D, Jeemon P and Roy A: Cardiovascular Diseases in India Current Epidemiology and Future Directions. *Circulation* 2016; 133: 1605-20.
9. Rousan TA and Thadani U: Stable angina medical therapy management guidelines: a critical review of guidelines from the European society of cardiology and national institute for health and care excellence. *Eur Cardiol* 2019; 14(1): 18-22.
10. Rousan TA, Mathew ST and Thadani U: Drug Therapy for Stable Angina Pectoris. *Drugs* 2017; 77(3): 265-84.
11. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Mureretto C, Valgimigli M, Achenbach S and Bax JJ: 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 2020; 41, 407-77.
12. Rousan TA, Mathew ST and Thadani U: The risk of cardiovascular side effects with anti-anginal drugs. *Expert Opin Drug Saf* 2016; 15(12): 1609-23.

13. Ferrari R, Pavasini R, Camici PG, Crea F, Danchin N, Pinto F, Manolis A, Marzilli M, Rosano GMC, Lopez-Sendon J and Fox K: Anti-anginal drugs-beliefs and evidence: systematic review covering 50 years of medical treatment. *Eur Heart J* 2019; 40: 190-4.
14. Banik BL, Fattahi P and Brown JL: Polymeric nanoparticles: the future of nanomedicine. *WIREs Nanomed Nanobiotechnol* 2016; 8: 271-99.
15. Ferrari R, Camici PG, Crea F, Danchin N, Fox K, Maggioni AP, Manolis AJ, Marzilli M, Rosano GMC and Lopez-Sendon JL: Expert consensus document: A 'diamond' approach to personalized treatment of angina. *Nat Rev Cardiol* 2018; 15: 120-32.
16. Pisano U, Deosaran J, Leslie SJ, Rushworth GF, Stewart D, Ford I and Watson AJ: Nicorandil, gastrointestinal adverse drug reactions and ulcerations: a systematic review. *Adv Ther* 2016; 33: 320-44.
17. Thadani U: Management of stable angina-current guidelines: a critical appraisal. *Cardiovasc Drugs Ther* 2016; 30(4): 419-26.
18. Moss AJ, Williams MC, Newby DE and Nicol ED: The updated NICE guidelines: cardiac CT as the first-line test for coronary artery disease. *Curr Cardiovasc Imaging Rep* 2017; 10: 09-15.
19. Ambrosio G, Mugelli A, Lopez-Sendón J, Tamargo J and Camm J: Management of stable angina: A commentary on the European Society of Cardiology guidelines. *Eur J Prev Cardiol* 2016; 23(13): 1401-12.
20. Ambesha P, Campiab U, Obiagwuc C, Bansald R, Shetty V, Hollanderc G and Shani J: Nanomedicine in coronary artery disease. *Indian Heart J* 2017; 69(2): 244-51.
21. He W, Liu X, Kienzle A, Muller W and Feng Q: *In-vitro* uptake of silver nanoparticles and their toxicity in human mesenchymal stem cells derived from bone marrow. *J Nanosci Nanotechnol* 2016; 16(1): 219-28.
22. Fuster V, Frazer J, Snair M, Vedanthan R and Dzau V: The future role of the United States in global health emphasis on cardiovascular disease. *J Am CollCardiol* 2017; 70: 3140-56.
23. Califf R: The future of cardiovascular medicine from the regulatory perspective. *J Am CollCardiol* 2016; 68: 766-69.
24. Jiang W, Rutherford D, Vuong T and Liu H: Nanomaterials for treating cardiovascular diseases: A review. *Bioactive Materials* 2017; 2: 185-98.
25. National Institute for Health and Care Excellence (NICE). Stable angina: management. Clinical guideline [CG126]. <https://www.nice.org.uk/guidance/cg126> (28 March 2019).
26. Jiang W and Liu H: Nanocomposites for bone repair and osteointegration with soft tissues, nanocomposites musculoskeletal. *Tissue Regen* 2016; 5: 241-52.
27. Katsuki S, Matoba T, Koga J, Nakano K and Egashira K: Anti-inflammatory Nanomedicine for Cardiovascular Disease. *Frontiers in Cardiovascular Med* 2017; 4: 87-96.
28. Zimmermann FM, Omerovic E, Fournier S, Kelbaek H, Johnson NP, Rothenbuhler M, Xaplanteris P, Abdel-Wahab M, Barbato E, Hofsten DE, Tonino PAL, Boxma-de Klerk BM, Fearon WF, Kober L, Smits PC, De Bruyne B, Pijls NHJ, Juni P and Engstrom T: Fractional flow reserve-guided percutaneous coronary intervention vs. medical therapy for patients with stable coronary lesions: meta-analysis of individual patient data. *Eur Heart J* 2019; 40: 180-86.
29. Al Meslmani B, Mahmoud G and Bakowsky U: Development of expanded polytetrafluoroethylene cardiovascular graft platform based on immobilization of poly lactic- co -glycolic acid nanoparticles using a wet chemical modification technique. *Int J Pharm* 2017; 529: 238-44.
30. Bejarano J, Navarro-Marquez M, Morales-Zavala F, Morales JO, Garcia-Carvajal I, Araya-Fuentes E, Flores Y, Verdejo HE, Castro PF, Lavandero S and Kogan MJ: Nanoparticles for diagnosis and therapy of atherosclerosis and myocardial infarction: evolution toward prospective theranostic approaches. *Theranostics* 2018; 8(17): 4710-32.
31. Reeh J, Therming CB, Heitmann M, Hojberg S, Sorum C, Bech J, Husum D, Dominguez H, Sehested T, Hermann T, Hansen KW, Simonsen L, Galatius S and Prescott E: Prediction of obstructive coronary artery disease and prognosis in patients with suspected stable angina. *Eur Heart J* 2018; 40: 1426-35.
32. Davidson SM, Takov K and Yellon DM: Exosomes and Cardiovascular Protection. *Cardiovasc drugs Ther* 2016; 31: 77-86.
33. Konigstein M, Giannini F and BanaI S: The Reducer device in patients with angina pectoris: mechanisms, indications, and perspectives. *European Heart J* 2018; 39(11): 925-33.
34. Bobo D, Robinson KJ, Islam J, Thurecht KJ and Corrie SR: Nanoparticle-based medicines: A review of FDA-approved materials and clinical trials to date. *Pharm Res* 2016; 33: 2373-87.
35. Sun ZL, Yang LY, Chen KF, Chen GW, Peng YP, Chen JK, Suo GL, Yu LT, Wang WC and Lin CH: Nano zerovalent iron particles induce pulmonary and cardiovascular toxicity in an *in-vitro* human co-culture model. *Nanotoxicology* 2016; 10(7): 881-90.
36. Motwani M, Swoboda PP, Plein S and Greenwood JP: Role of cardiovascular magnetic resonance in the management of patients with stable coronary artery disease. *Heart* 2018; 104: 888-94.
37. Chuang K, Lee K, Pan C, Lai C, Lin L, Ho S, Ho K and Chuang H: Effects of zinc oxide nanoparticles on human coronary artery endothelial cells. *Food Chem Toxicol* 2016; 93: 138-44.
38. Nemmar A, Beegam S, Yuvaraju P, Yasin J, Tariq S, Attoub S and Ali BH: Ultra small superparamagnetic iron oxide nanoparticles acutely promote thrombosis and cardiac oxidative stress and DNA damage in mice. *Part Fibre Toxicol* 2016; 13: 11-23.
39. Singh B, Garg T, Goyal AK and Rath G: Recent advancements in the cardiovascular drug carriers. *Artificial Cells Nanomedicine, and Biotechnology* 2016; 44: 216-25.
40. Giannouli M, Karagkiozaki V, Pappa F, Moutsios I, Gravalidis C and Logothetidis S: Fabrication of quercetin-loaded PLGA nanoparticles *via* electrohydrodynamic atomization for cardiovascular disease. *Mater Today Proc* 2018; 5: 15998-005.
41. Paul TK, Sivanesan K and Schulman-Marcus J: Sex differences in non obstructive coronary artery disease: recent insights and substantial knowledge gaps. *Trends Cardiovasc Med* 2016; 27: 173-79.
42. Myerson JW, Anselmo AC, Liu Y, Mitragotri S, Eckmann DM and Muzykantov VR: Non-affinity factors modulating vascular targeting of nano- and microcarriers. *Adv Drug Deliv Rev* 2016; 99: 97-112.
43. Barabadi Z, Azami M, Sharifi E, Karimi R, Lotfikhshai N, Roozafzoon R, Joghataei MT and Ai J: Fabrication of hydrogel-based nanocomposite scaffold containing bioactive glass nanoparticles for myocardial tissue engineering. *Mater Sci Eng C* 2016; 69: 1137-46.

44. Murphy A, Casey A, Byrne G, Chambers G and Howe O: Silver nanoparticles induce pro-inflammatory gene expression and inflammasome activation in human monocytes. *J Appl Toxicol*. 2016; 36: 1311-20.
45. Ahadian S, Huyer LD, Estili M, Yee B, Smith N, Xu ZS, Sun Y and Radisic M: Moldable elastomeric polyester-carbon nanotube scaffolds for cardiac tissue engineering. *Acta Biomater* 2017; 52: 81-91.
46. Jiang W, Ford DR, Vuong T and Liu H: Nanomaterials for treating cardiovascular diseases: A review. *Bioactive Materials* 2017; 2(4): 185-198.
47. Ng ACT, Prihadi EA, Antoni ML, Bertini M, Ewe SH, Marsan NA, Leung DY, Delgado V and Bax JJ: Left ventricular global longitudinal strain is predictive of all-cause mortality independent of aortic stenosis severity and ejection fraction. *Eur Heart J Cardiovasc Imaging* 2018; 19: 859-67.
48. Turnbull IC, ELtoukhy AA, Fish KM, Nonnenmacher M, Ishikawa K, Chen JQ, Hajjar RJ, Anderson DG and Costa KD: Myocardial delivery of lipidoid nanoparticle carrying mod RNA induces rapid and transient expression. *Mol Ther* 2016; 24(1): 66-75.
49. Guo J, Shi T, Cui X, Rong Y, Zhou T, Zhang Z, Liu Y, Shen Y and Chen W: Effects of silica exposure on the cardiac and renal inflammatory and fibrotic response and the antagonistic role of interleukin-1 beta in C57BL/6 mice. *Arch Toxicol* 2016; 90(2): 247-58.
50. Saxena U and Das AB: Nanomaterials towards fabrication of cholesterol biosensors: Key roles and design approaches. *Biosens Bioelectron* 2016; 15(75): 196-05.
51. Chan JW, Lewis DR, Petersen LK, Moghe PV and Uhrich KE: Amphiphilic macromolecule nanoassemblies suppress smooth muscle cell proliferation and platelet adhesion. *Biomaterials* 2016; 84: 219-29.
52. 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 and Schiffelers RM: Liposome encapsulated berberine treatment attenuates cardiac dysfunction after myocardial infarction. *J Control Rel* 2017; 247: 127-33.
53. El-Gendy MA, El-Assal MIA, Tadros MI and El-Gazayerly ON: Olmesartan medoxomil-loaded mixed micelles: preparation, characterization and *in-vitro* evaluation. *Future J Pharm Sci* 2017; 3: 90-94.
54. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P and Widimsky P: ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018; 39: 119-77.
55. Ahadian S, Yamada S, Ramon-Azcon J, Estili M, Liang XB, Nakajima K, Shiku H, Khademhosseini A and Matsue T: Hybrid hydrogel-aligned carbon nanotube scaffolds to enhance cardiac differentiation of embryoid bodies. *Acta Biomater* 2016; 31: 134-43.
56. Ma R, Ma ZG, Zhen CL, Shen X, Li SL, Li L, Zheng YF, Dong DL and Sun ZJ: Design, synthesis and characterization of poly(methacrylic acid-niclosamide) and its effect on arterial function. *Mater Sci Eng C* 2017; 77: 352-59.
57. Park JH, Dehaini D, Zhou J, Holay M, Fang RH and Zhang L: Biomimetic nanoparticle technology for cardiovascular disease detection and treatment. *Nanoscale horizons* 2020; 1: 1-17.
58. Gupta P, Garcia E, Sarkar A, Kapoor S, Rafiq K, Chand HS and Jayant RD: Nanoparticle Based Treatment for Cardiovascular Diseases. *Cardiovasc Hematol Disord Drug Targets* 2019; 19(1): 33-44.
59. Fares AR, El Meshad AN and Kassem MAA: Enhancement of dissolution and oral bioavailability of lacidipine *via* pluronic P123/F127 mixed polymeric micelles: formulation, optimization using central composite design and *in-vivo* bioavailability study. *Drug Deliv* 2018; 25: 132-42.
60. Matoba T, Koga JI, Nakano K, Egashira K and Tsutsui H: Nanoparticle-mediated drug delivery system for atherosclerotic cardiovascular disease. *J Cardiol* 2017; 70: 206-11.
61. Kapil N, Datta YH, Alakbarova N, Bershad E, Selim M, Liebeskind DS, Bachour O, Rao GHR and Divani AA: Antiplatelet and Anticoagulant Therapies for Prevention of Ischemic Stroke. *Clin Appl Thrombosis/Hemostasis* 2017; 23: 301-18.

How to cite this article:

Dewangan HK and Garg A: Application of nanotechnology for treatment of angina pectoris as cardiovascular disease: A review. *Int J Pharm Sci & Res* 2020; 11(10): 4884-95. doi: 10.13040/IJPSR.0975-8232.11(10).4884-95.

All © 2013 are reserved by the International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **Android OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)