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Cardiac Stem Cells to Cure Heart through Nanotechnology

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Abstract

Loss of heart cells lead to heart attack. The blood flow slows down, eventually pumping gets effected. Several surgeries only weaken the heart. The solution to heart trouble is rather underlying mechanism to derive into regeneration. Several clinical trials have highlighted that stem cells have a promising effect in regeneration. More methods such as cardiac stem cells, bone marrow based cells, mesenchyme stem cells; embryonic stem cells have been effective to an extent. There have been some inconsistencies as well in these methods. Performance of heart has lowered; efficiency to pump blood has influence on selection of type of stem cells. However, future of therapies has to rely on technology. Not just ordinary technology, but nanotechnology. The future of heart repair and advancement of stem cells to cure any heart disease. Nanotechnology helps in understanding cellular layers of heart tissue, which plays a vital role for any heart repair or regeneration. This review discusses the aspects of nanoparticles and nano gel effect in curing heart. Nanoparticles have been effective in drug delivery, targeting particular area of cure. Meanwhile nano gel helps in navigating the drugs and creating a sustainable environment for treatment. Another concept highlighted in this review is nano patch along with nano material or nano cells communication, helping in regenerative therapy. Thus key issues for future prospects are discussed below.

Keywords

Cardiac; Stem cells; Nanotechnology; Heart.

Introduction

Stem cell therapy itself is a success in heart regeneration, but they have few drawbacks as well. To compensate for the disadvantages, nanoparticles or nano cells come into play. Nanotechnology has been a revolution in almost every field of study [1]. The nano cells or nanoparticles measure in nano meters and help in tissue-based engineering for fast diagnosis, efficient drug delivery and stem cell therapy [2,3].

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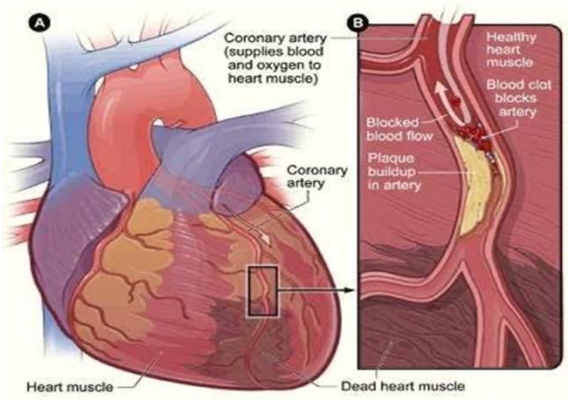
Cardiovascular disease is the most prominent in heart. Usually embryonic stem cells or cardiac stem cells discharge unique method for treatment [5]. They engraft and regenerate heart cells, but drawbacks are visible through transplantation, maturation and formation of aorta [4]. The invention of nanotechnology has become compatible to the field of biology [6]. Nano materials have helped in treatment of coronary heart diseases and resulted in improved drug delivery system and in vivo imaging [7]. Below is a figure to understand the heart and artery blocks [8]. Most importantly it assures a platform for advanced tissue engineering [9].

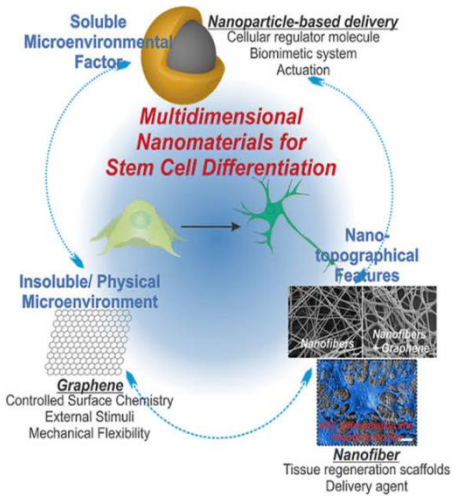
Figure 1: To understand the heart and artery blocks.



Nanoparticles used in therapy

Cardiac therapy has often showed promising results [11]. However the vast technique is injection through myocardium [10]. The poly based nanoparticles injected through intervenes cures heart. Successful delivery of these particles in mice has shown positive results [12]. These nanoparticles have provided protection to heart cells also helped in repairing damaged heart. Their main function is stop thrombus formation [13]. Nano capsules delivered through intravenous injection, has a great phenomenon in targeting the injury specificity of the heart. They are basically carbon based and most suitable to injections [14-17].

Figure 2: The formation of nanoparticles for stem cell differentiation.



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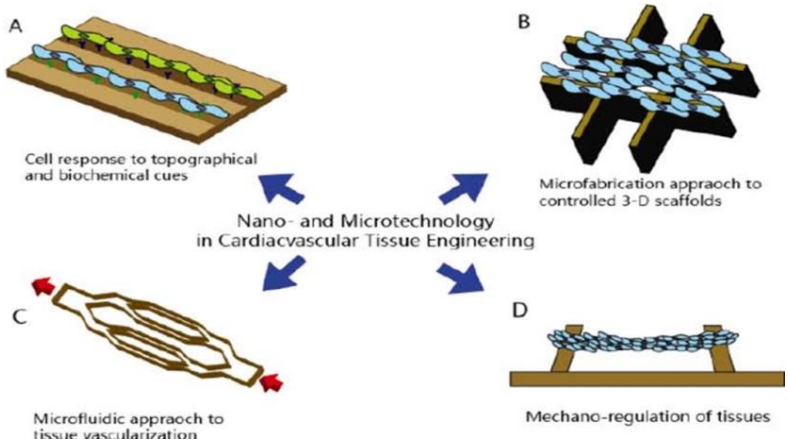
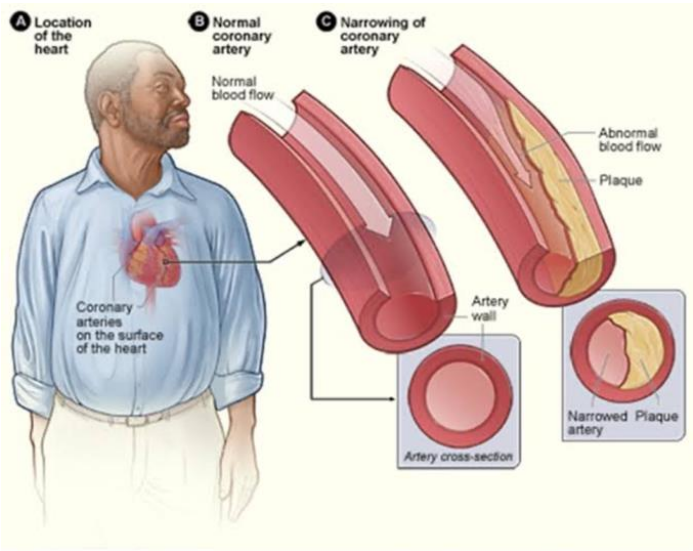
Drugs are usually encapsulated with nanoparticles so therapy can be a success. After encapsulation, therapies have different retention time on molecules [13]. An increased retention time is seen that allows attaining the target and certain sites such as tissues and cells. The surface in which retention takes place can also be customised with polyethylene glycol [14]. Below figure shows the nanotechnology in heart [15]. This polyethylene glycol has shown increased circulation time for drug encapsulation and also stability for nanoparticles to survive [16].

Figure 3: Show the nanotechnology in heart.



The basic concept of nanoparticles is permeability and retention [16]. Drug encapsulated particles actively target the diseased site even without active targeting sites. This is achieved because of retention and permeability effect (RP) [15-17]. Figure shows difference in normal coronary artery and narrowed coronary artery [17]. The RP effect utilises the permeability factor of the drug while targeting the sites. There are certain compounds that help in permeability such as peroxynitrite and nitric oxide [18].

Figure 4: Shows the difference in normal coronary artery and narrowed coronary artery.



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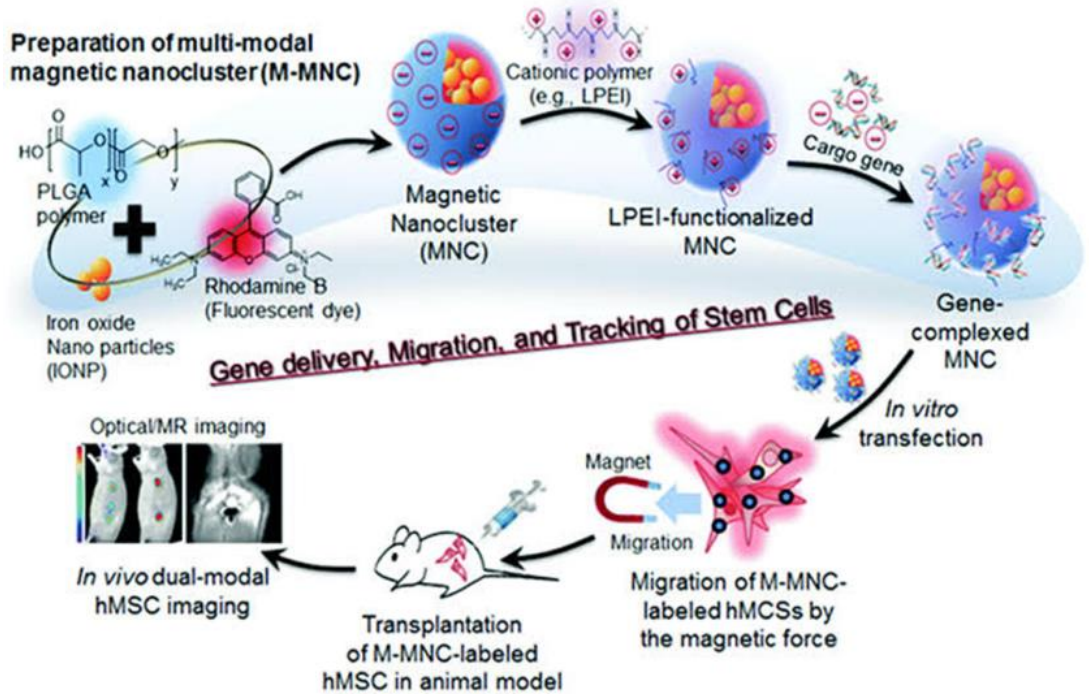
Keeping the above figure in mind we draw to ideas and concepts for Nano gels for cure of heart [19]. Normal functions of nanoparticles are to reach the disease targets. But time plays crucial factor in cure; the window is too short for non-permeable delivery and creates aggregation [20]. The aggregation retains the scaffold to up to 28 days, creating the unregulated matrix. Although it helps in studying the successful delivery during these increased retention time, nanoparticles still have to be performed before RP effect [21]. The usage of antibody in myocardium promotes liposomes in angiogenesis phase. The delivery of drug encapsulated nanoparticle played a successful role in rat models [22]. Figure shows magnetic Nano cluster formation and usage in rat [23].

Figure 5: Magnetic Nano cluster formation and usage in rat.



Higher number of trials has been conducted and significant improvement has been observed. This ensures nanoparticles have been able to reach the heart and increase the therapy.

Nanoparticles for communication of genes and stem cell

Nanoparticles and genes, how do they correlate? Genetic engineering plays an important role in stem cell [24]. Genes are delivered through vectors to have impact on genetically modified stem cells that are ready to repair heart [25-27]. But there is always an impact in culture of cell viability, when accessed by this method [26]. Various studies have shown that traditional method of gene vector highlights stability and excellent gene delivery. However the application to prove these studies has been less [23]. The immune response, transformation due to genes and the volume of genes are abundantly required for cardiac repair through engineered stem cells [25]. In last ten years exclusive sets of nanoparticles have been designed for use as vehicles to therapy, they were also used to deliver genes into cardiac cells

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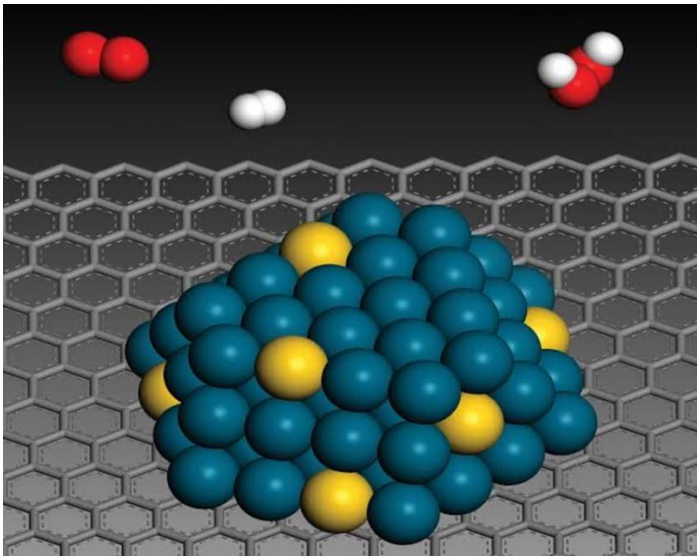
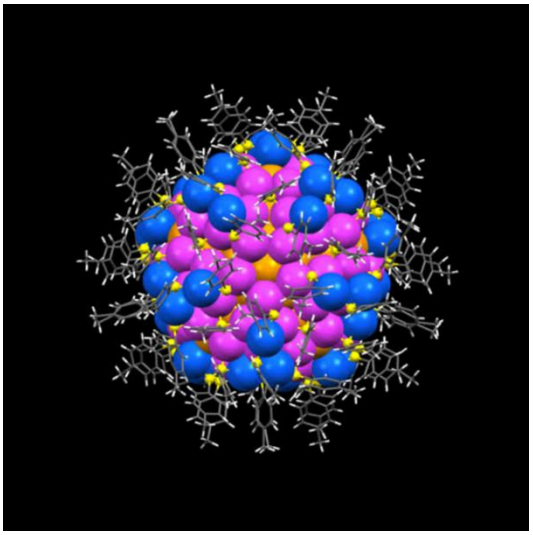
[28,29]. Genetically engineered stem cells have shown progress in ground breaking tissue repair and in clinical trials. These nanoparticles show higher efficiency and play a promising role in tissue repair of heart [30]. Another interesting communication can be established in the bond between nanoparticles, gene and stem cells is through culture. Nano materials can be adapted in culture via direct addition on to the petri dishes [31-34]. The bond between nano materials with cellular components and signalling pathways is a defined pathway to cure of heart [35].

Figure 6: Design of nanoparticles.



Several properties define the nanoparticles like shape, size and durability. Internalization depends on the size and shape of nanoparticles, smaller size ranging from 20-60nm are higher in uptake and sizes ranging from 70-110 nm are less in their uptake [32-34]. They also affect toxicity and cell functions. Above mentioned factors should be analysed for design of nano materials. Figure shows the nanoparticles with protein complexity [35].

Figure 7: Nanoparticles with protein complexity.



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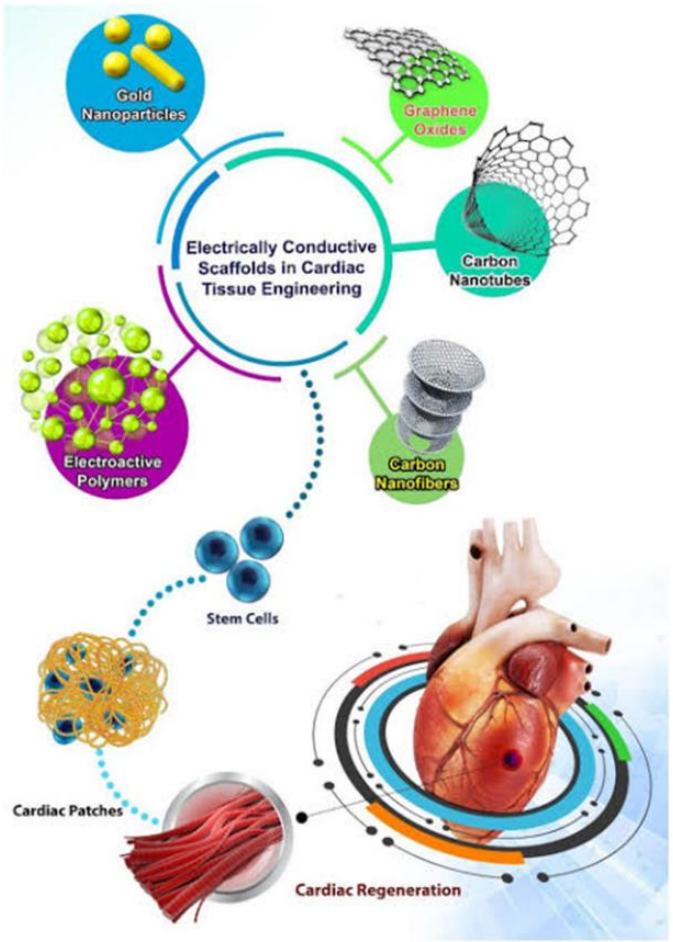
After considerable analyses of shape and size of nano materials, chemical structure is taken into grading. The softness and hydrophobicity of nanoparticle should be high in order for high uptake [37]. Charge variations also play an active role for internalization. If nanoparticles are positive they squeeze through nucleus avoiding degradation and if they are negative or neutral charge they help in localization instead of penetration [36]. The structure of nano materials defines the delusion of self. Engineered nanoparticles with consideration of factors mentioned play a vital tool in heart cure and biomedical application [36].Various studies were done comparing polystyrene nanoparticles with amino content and without amino, amino content nanoparticles had higher uptake [3]. Nano rods with various functional groups such as carboxyl, poly and amino were also done in experiments [37-39]. Each one showed different variations. The higher uptake was with amino based Nano rods followed by carboxyl and finally poly with higher toxicity and less favorability [38]. Therefore design should be in such a manner that particle surface should support the nanoparticles, with adequate cellular uptake and minimal toxicity. Overall nanoparticles with apparent physical composition can help in differentiation of stem cells, initiating heart repair [39]. Figure shows hear regeneration using nanoparticles [42].

Figure 8: Shows hear regeneration using nanoparticles.



Several therapies earlier proved vital in curing cardiovascular diseases, especially protein and cell therapies. But often they had flaws like higher retention in injured sites. Hence nano

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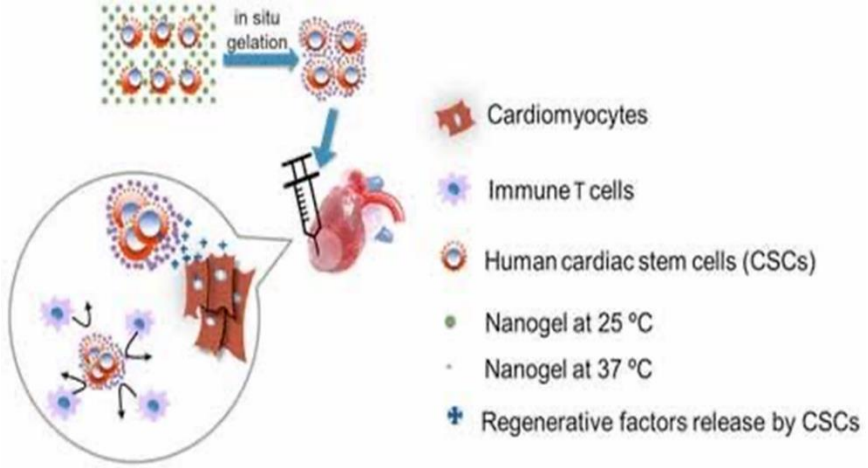
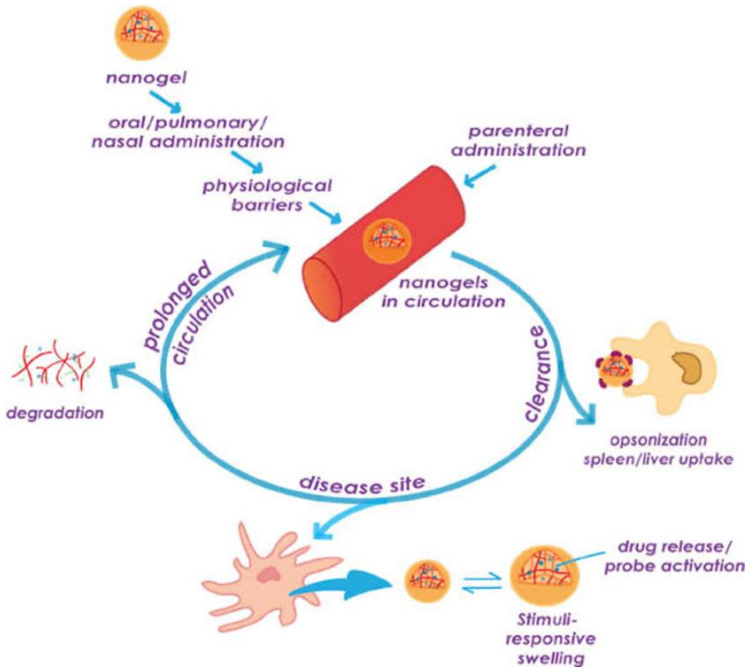
materials were adopted. Nano gel and naopaste also plays a vital role in creating environment for cardiac repairs [28-41]. Figure shows Nano gel and its use in cardiac repair [42].

Figure 9: Shows Nano gel and its use in cardiac repair.



Recent years a group developed drug capturing system with poly hydrogel. It was successful upon injection in heart cells. They help reduce muscle cell death [33]. Another method was tested in pigs, mixtures of nano gels and nano fibers which proved to be effective, thus producing proper functions of systolic cardiac improvement and reduction in size of infract [43]. The nano fibers hold on to environment of damaged site for up to three months and help in repair of cardiac cells [39-41]. Several studies showed nano fibers and nano gels play enhanced role in restoring heart function in long term. Figure represents the nano gel functions in a heart [42].

Figure 10: Represents the Nano gel functions in a heart.



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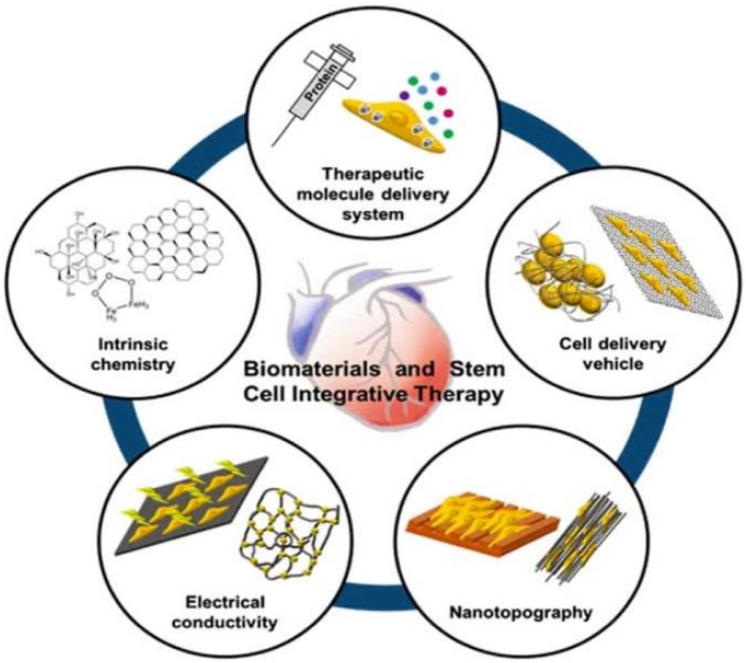
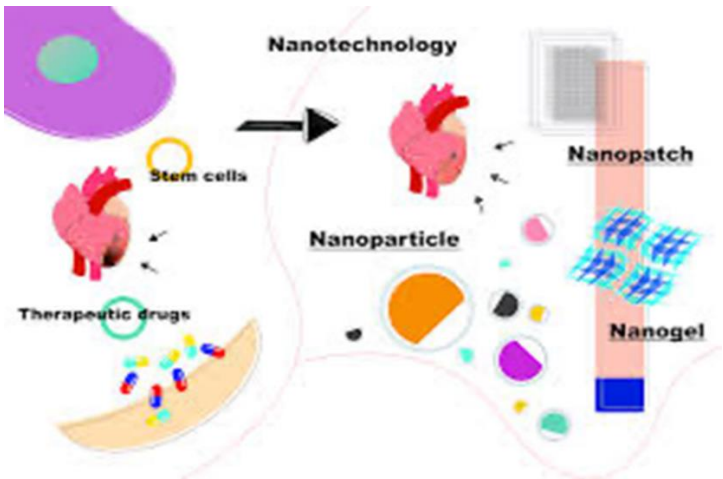
Heavily damaged heart may not only rely on drug treatment because they show less curing rates. Hence transplantation and stem cells are need of the hour [42]. Direct injection system into rat models of nanoparticles show longer retention rates and survival of cellulose matrix. Moreover gene engineered drugs show repair abilities in rat models [40-42]. Figure indicates stem cell therapy with nanoparticles [43].

Figure 11: Indicate stem cell therapy with nanoparticles.



Another important aspect in nano materials is nano patch [39]. Cell sheets in the ventricular walls can be fixed using them. The heart receiving them show improved functions and change in working of left ventricular walls during pumping [40-43]. Figure represents the working of nano gel and nano patch in heart [41].

Figure 12: The working of nano gel and nano patch in heart.



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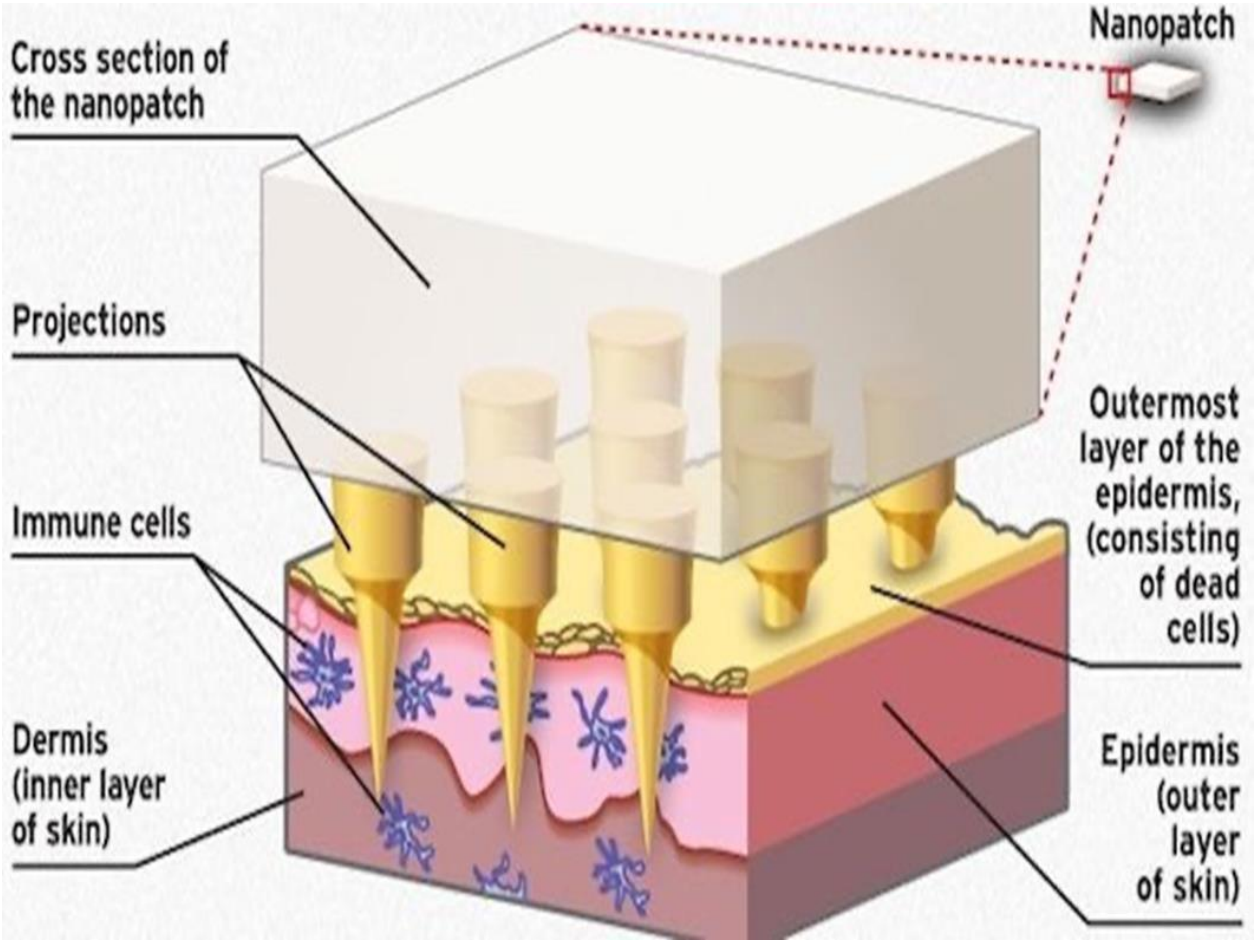
Nano patch usually demonstrates long term retention of drugs on cellulose matrix in rat models, and illustrates survival rate on stem cell differentiation in infract area [25]. Nano patch allows the ventricles to function on par with pre-injury phase of heart. The wall thickness improves, allowing drug from patch to vitalize the cells, resulting in transplantation of sheet to respond to temperature [42]. They also survive the electron spin to align to endothelial cells. This technique generates nano fibers in diameter ranging from 350~40 nm, bringing in variation in orientation in spin less than 10 degrees [45]. Not just the sheet, nano fibers help in providing support to injured heart. Hence more retention time of these fibers show improved cardiac function, this helping circulatory system survive allowing blood to flow normally [42-45].

Figure 13: Shows working of nano patch.



Nano materials design of drug delivery system

Concept of delivery system should be understood in simpler terms. Keeping in mind the barriers of toxicity, levels of toxic layer should be minimum, smooth flow, high retention time and desired target tissue or cell [45]. Always there will two delivery systems, active and passive. Active contributes to specific carriers, drug delivery will be smooth, and they target cells to the point [46]. Meanwhile passive system will have desired effects such as abnormal

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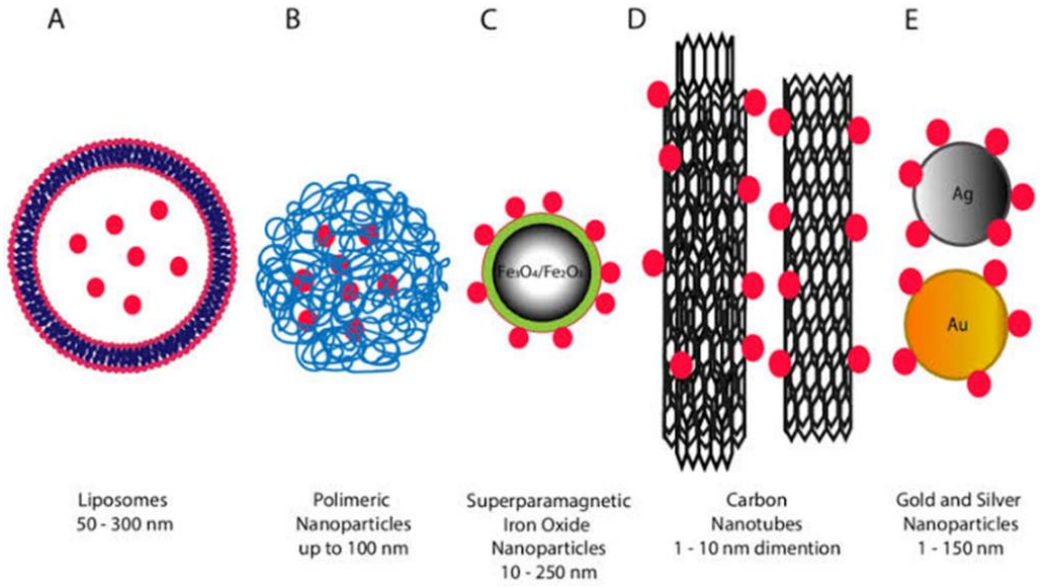
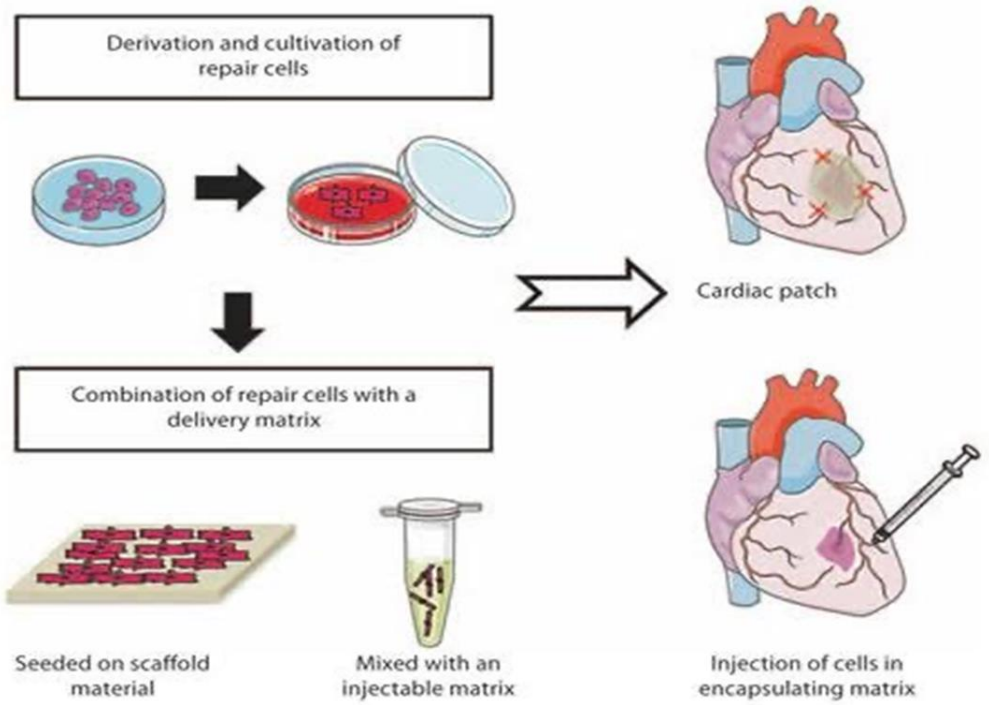
vessel cells, surface deformation and less functional components. Figure shows different nano materials [47].

Figure 14: Shows different nano materials.



Nano materials usually have high efficiency in drug delivery systems. They ensure targeted delivery.

Figure 15: Shows drug delivery system for nano materials.



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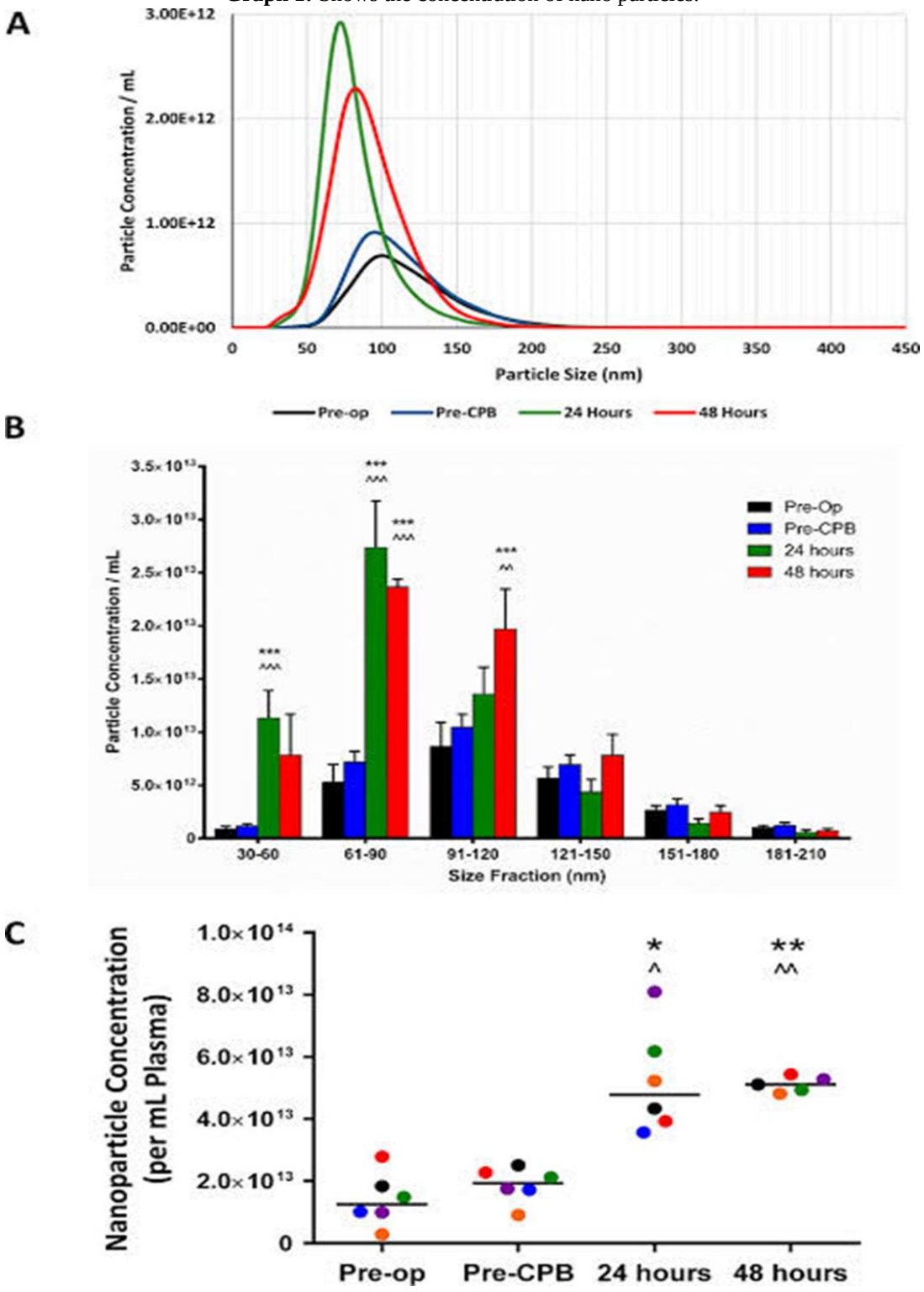
Nanoparticles basically have high rate of migration activity via drugs. The proliferation activity is slower and can be counted by time course nanoparticle uptake [44-47]. Graph shows you the concentration of nanoparticles [48].

Graph 1: Shows the concentration of nano particles.



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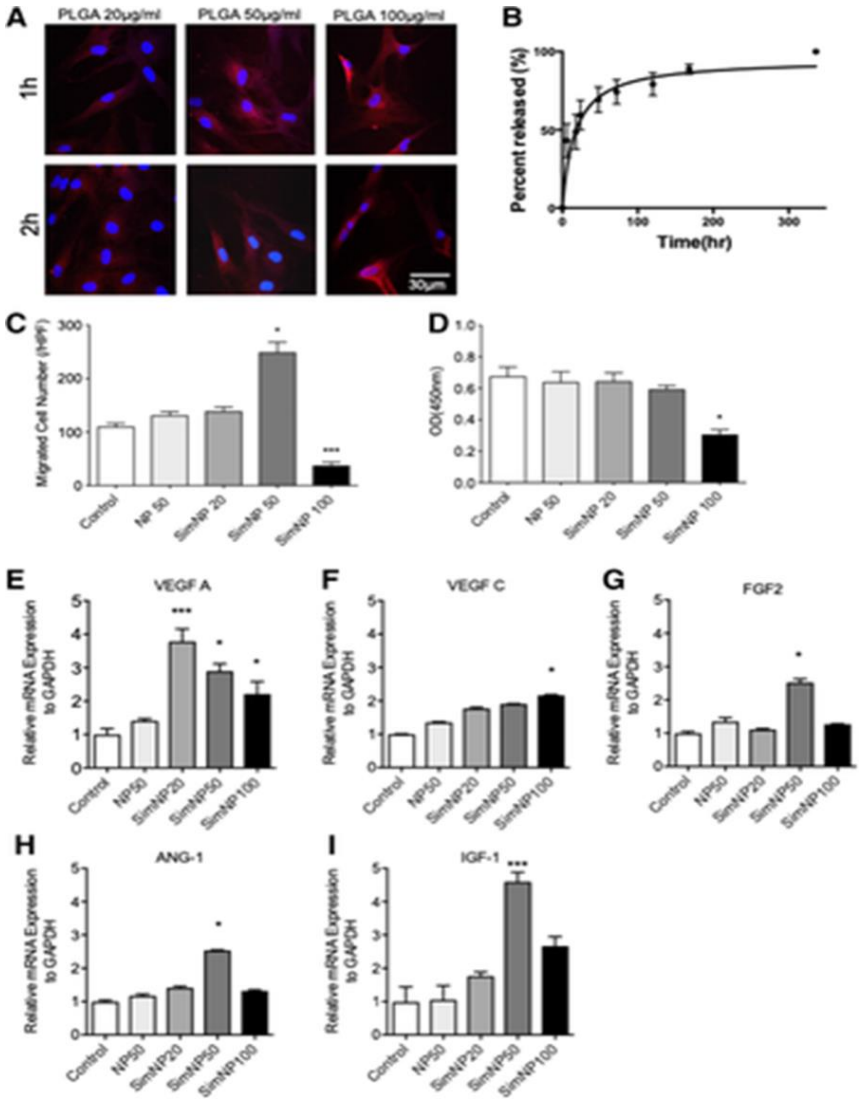
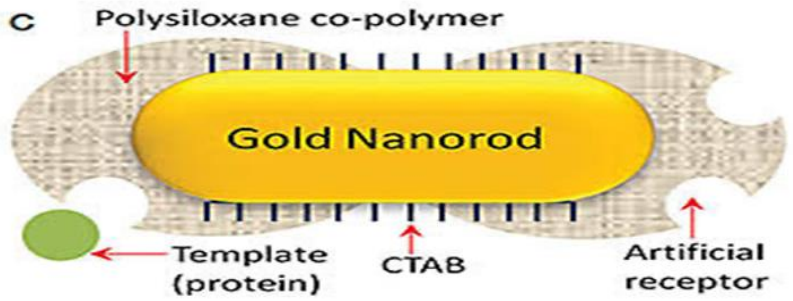
Graph 2: Shown using these characteristics and factors.

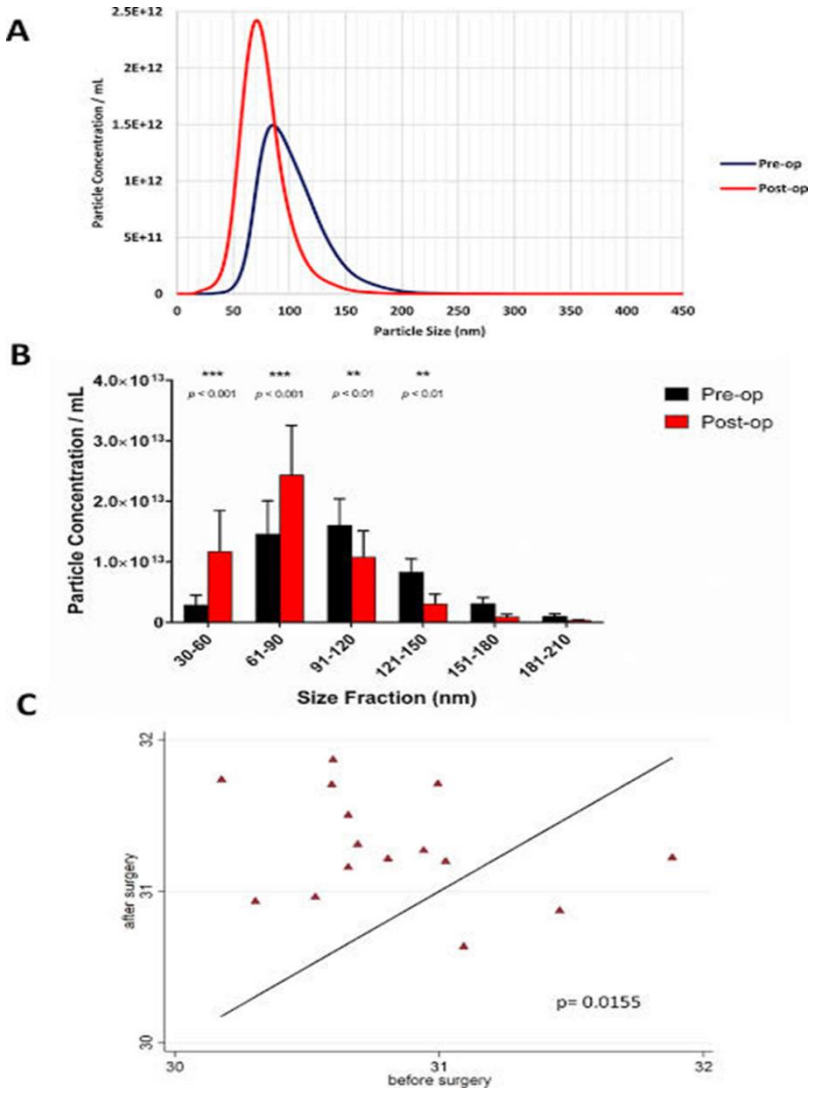


Let us consider the migration and proliferation time of materials. The uptake of nanoparticle also has effects in time zone. The migration induced cells have 20% less follicle bovine serum (FBS). Now for observation of above graph we need to identify characteristics in migration activities. The characteristics such as human adipose derived stem cells (hAdSC) and poly lactic glycolic acid (PLGA). The factor identified is vascular endothelial growth factor (VEGF). A and E factors [38-45]. RT-PCR is used to identify the time. The factor considered shows increased activity of heart when nanoparticles have delivered the drug to the target. Similar results in the graph below shows the activity of nanoparticles [49]. Size and particle concentration is compared and the results are quite similar. When the nano particles size in low, particle concentration is high. The graph below also shows the activity of nanoparticles pre operation and post operation. Before surgery activity is quiet low, after the nanoparticles reach the target the working increases. Hence the result. Figure shows the structure of nano rod used for heart treatment.

Figure 16: The structure of nano rod used for heart treatment.



Graph 3: Shows the activity of nanoparticles pre operation and post operation.



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Conclusion

On the whole, a nano particle helps in targeted drug delivery, and advances the therapeutics in stem cell cure. Nano gel has been in utmost use for environmental stability and also cleaner delivery of targeted drug regions. There also lies a greater navigation of drug to injured sites using nanoparticles. The above graph and figures have shown nano materials help in curing heart muscles and injuries. Nano fibres combined with sheets help in mechanical support to injured region, while nano patch adds electromechanical coupling to heart. This could be a great avenue for further studies. Nanotechnology has been a great paradigm shift in treatment of coronary heart diseases, heart injury, muscle cells improvement, normal functioning of heart after massive injuries. They not only provide a proper medium for drug delivery but also lay a platform for therapy. Nano medicine is another venture to explore, alternative to stem cell therapy. It overcomes several and crucial challenges in cardiac repair. The biological design of nanoparticles has been understood which overrides the drawbacks posed in transformation from animal model to human cells. In future, stem cell tracking can also be researched through nano materials at a larger scale. In this review I tried to highlight nanoparticles for drug delivery, cell communication, use of nano gel, nano patch, and nano materials possessing various functions needed to cure injured heart. Overall stem cells along with nanotechnology shows a promise to cure for all heart related injuries, drug pathways and cell based therapies. It is considered the most effective and safest techniques.

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