Nanoparticle and Stem Cell Nanotechnology: Interdisciplinary Research Area Involving Pharmacology and Anatomy

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Review Article

Abstract: **Introduction:** Nanoparticles are the particles of nanometer size that are used in various applications while stem cells are pluripotent cells having capacity to proliferate and differentiate in desired manner. Interaction of nanoparticles with stem cells i.e. stem cell nanotechnology has opened the new area of research and application in medical sciences. **Objective:** In this review we aimed to search the pharmacological aspect of nanoparticles in stem cells. **Method:** We searched pubmed, medline, google scholar and other online as well as offline data base with key words of nanoparticle, stem cells, nanotechnology to find the information. Articles were further sorted out regarding the availability of content. Only those articles, which were available by open access either abstract or full paper or both were included in the review. **Result & Conclusion:** We conclude the stem cell nanotechnology is upcoming branch of study in pharmacology. Different pharmacokinetic and pharmacodynmic aspect of nanoparticles as nanodrug has to be explored before using them on wide scale. These data warrant the establishment **of new** a**re**a **of** studies i.e. Stem Cell Nanophrmaceutics to deal with nanodrugs.

Key Words: Nanoparticle, Stem cells, Nanotechnology.

1. Nanoparticles

Every person ingest more than 10 million nanoparticles every day[1].They are physically and chemically different from their parent material either in molecular form or in bulk in following manner[2] - High surface to volume ratio, Surface tailorability, Improved solubility, Multifunctionality, High electrical and heat conductivity, and Improved surface catalytic activity Nanop**articles** have four basic unique effects i.e. surface effects, quantum size effects, small size effects, and tunnel effects[3-4].

2. Types of Nanoparticles

Nanoparticles are classified into two categories on the basis of their origin –

2.1. Carbon-based materials, such as fullerenes and carbon nanotubes i.e. polymeric nanoparticles (such as polyglycolic acid, polylactic acid, chitosan, and gelatins), liposomes, dendrimers, nanotubes and nanocrystals[5].

2.2. Inorganic nanoparticles including

2.2.1. Metal oxides (eg, cerium oxide, iron oxide, titanium dioxide, and zinc oxide,),

2.2.2. Metals (iron, silver, and gold) and

2.2.3. Quantum dots (cadmium selenide and cadmium sulfide).

These Nanoparticles **are of different shape** th**at** integrated into larger systems at nanoscale to form nanomaterials [6].

3. Stem cells

Stem cells are unlimited cell source in stem cell therapy. They are pluripotent cells present in blood, bone marrow, skin, muscle, brain, liver, etc to maintain and replace the body cells [7-10]. They are classified as

3.1. **Embryonic stem cells (ESCs)** - Evans, firstly reported the isolated ESCs in 1981. They are pluripotent and may differentiate into all three primary germ lineages, raising hopes for stem cells-based therapy for degenerative diseases and human injuries[11-12].

3.2. **Especially induced pluripotent stem cells (ips)** – They are controllable man-made stem cells, established in 2007[13-15].

3.3. **Adult stem cells -** They are not pluripotent but multipotent, which differentiate into limited cell types only[16-17]

Mesenchymal stem cells have been researched most due to their differentiation ability into various connective tissue as well as other tissues [18]. Although different adult tissues including adipose tissue, amniotic fluid, dental pulp, liver, muscle, placenta, and umbilical cord blood may provide MSC, they are mainly obtained from bone marrow. In bone marrow their concentration is up to 0.01%, isolated

easily and cultured up to 40 times within ten weeks [19].

4. Isolation of Stem Cells

Isolation of stem cell from multiple type cell mixture is challenging. MNPs labeled stem cells are isolated by flow cytometry or magnetic force in cost effective, fast, and easier way [26].

5. Nanoparticles and stem cells

Nanoparticle interacts with biological system at molecular level more selectively as compare to conventional pharmacological drug to induce desired response with minimal side effects [20]. Biomolecule i.e. antibodies, membrane receptors, nucleic acids, and proteins occurs at sub-nanometer ranges similar to nanoparticles, making use of nanoparticles possible in diagnosis and therapy [21].

New era of upcoming research area is opened to study stem cell and nanoparticle interaction [22] i.e. regenerative medicine[23-24] as nanoparticles override the limitations of stem cell therapy of homing and fixing to desire site[25].

6. Cellular uptake of nanoparticles in stem cells

Nanoparticle uptake by stem cells is depending on size, shape, type, concentration, and surface modification of the nanoparticles. Stem cells utilize different endocytic mechanisms (Clathrin-dependent endocytosis, Caveolae-dependent uptake Non-clathrin/non-caveolae endocytosis, Phagocytosis, Macropinocytosis) or receptor mediated mechanism for the uptake [27].

6.1. **Uptake of Magnetic iron oxide** cationic liposome nanoparticles [28] and superparamagnetic iron oxide was through endocytosis in human mesenchymal stem cells[18]. Iron-oxide-based MNPs, coated with biological polymers internalized or the attached to cell surface receptors. Uptake was variable as per the cell types and particle coatings [29].

6.2. **Nanodiamond particles** in stem cells were taken inside by clathrin-mediated endocytosis and macropinocytosis [30].

6.3. **Mesoporous silica nanoparticles** was taken by both clathrin- and actin-dependent endocytosis into human bone marrow mesenchymal stem cells[31]. It was concentration and time dependent with short incubation period[32]. Dynamic polymerization of actin filaments was crucial and its inhibition by cytochalasin D decreased the uptake[33]. Silica Nanoparticles conjugated with chimeric protein GFP-FRaTide (GFP – biomarker, FRaTide – glycogen synthatase kinase inhibitor) was delivered in human embryonic kidney cell and rat neural stem cell via endocytosis. Successful inhibition of enzyme opened the hopes for intracellular delivery of function protein for signaling pathways and in vivo delivery options [34].

6.4. **Delivery of Quantum dots** into cells is done by electroporation, endocytis, liposome-mediated transfection, microinjection, and special peptide delivery[35]. After the uptake of quantum dots, there is cytoskeletal reorganization i.e. formation of lamellipodia with dense actin network within one day after exposure[36].

7. Nanoparticles inside stem cells

Nanoparticles locate themselves at different sites in cell. For example

7.1. In perinuclear region i.e. forming rings around the cell nucleus

7.2. In cytoplasmic vesicles of stem cells

7.2.1. Polystyrene nanoparticles in cytoplasmic extension pseudopods[1]

7.2.2. Nanodiamond particles as single cluster[30]

7.3. In lysosomes –

7.3.1. Superparamagnetic iron oxide nanoparticles may be degraded to release free iron[37-38]

7.3.2. Quantum dots initially escaped from lysosomal intake but later on all are inside the lysosome due to increased lysosome expression[35]

8. Nanoparticles in biodistribution (i.e., in vivo tracking) of Stem Cells

For stem cell research the major question is to control homing and temporal and spatial migration of these cells, their acceptance and functional capability in grafted site. Tracking was done initially by histopathological studies, later on by cell imaging to obtain real time changes. Stem cells are labeled with fluorescent dyes, reporter genes or contrast genes for cell imaging i.e. supermagnatic iron oxide labeling is done in MRI.

To maximize the therapeutic benefits and minimize side effects, Stem cells should be delivered to target site in sufficient amount with less number to untargeted sites. Tracking of stem cells is must to understand the mechanism to tissue repair in field of developmental biology and tissue regeneration. Reliable cellular imaging techniques are needed to

track density, distribution, proliferation, and differentiation of grafted stem cells[39].

Nanoparticles like quantum dots, MNPs, gold nanorods, mesoporous silica nanoparticles, superparamagnetic nanoparticle iron oxide and light-emitting semiconductors with special physical properties are used as Inorganic probes[36] for imaging and tracing of stem cells[40- 44]

QDs may be designed as multi-functional nanoprobes, modifiable with different biomolecules (liposome, PEG, peptides, or antibody), having own specific functions and used for gene or drug delivery, molecular imaging and tracing[45], cellular imaging[46] etc. Quantum dots conjugated with mortalin protein to form i-QD composites, which were internalized by mesenchymal stem cells (MSCs) to form labeled MSCs cells. These i-QD labeled MSCs differentiated in vitro and in vivo to normal adipocyte, osteocyte, and chondrocyte, suggesting in vivo application in diagnostic imaging and tracing of stem cells [40].

Superparamagnetic iron oxide nanoparticles (SPIO) have been used for molecular imaging and tracing of stem cells,[43-44] stem cell labeling, MRI, and tracking of transplanted stem cells[47]. Fluorescent molecules linked to dextran-coated iron oxide nanoparticles, labeled HSCs to monitor the engraftment process. It eliminated spurious signals from nonsequestered nanoparticle contaminants[48].

Surface modification with poly-L-Lysin (PLL), D-mannose, or polydimethylacrylamid (PDMAAm) of MNPs resulted in better labeling efficiency as compare to dextran-coated SPIO. FluidMAG nanoparticles (ferrofluids with aqueous dispersion of magnetic iron oxides and a starch coating) were used for tracking of MSCs in breast cancer and lung metastases[29].

Iron oxide nanoparticles labeled embryonic stem cells and bone marrow mesenchymal stem cells were administered intracerebrally or intravenously in rats with spinal cord or cortical lesions. Grafted cells were migrated to lesion site within one week and were visible as a hypointense signal on MR images for more than a month. Their studies demonstrated that MRI of grafted stem cells labeled with iron oxide nanoparticles is a useful method for evaluating cellular migration toward a lesion site [23,49].

Feridex-labeled neural stem cells originated from bone marrow stroma cells of the rhesus monkey were autografted into the striatum. In brain, they were survived, differentiated and tracked reliably using MRI [50].

Superparamagnetic nanoparticle iron oxide labeled human mesenchymal stem cells were injected intra-articularly articular cartilage repair and tracked successfully with MRI[18,51].

Mesoporous silica nanoparticles are preferred for stem cell tracking due to better internalization, biocompatibility and durability. Silica coating and polyethylene glycolation of magnetic ferrite nanoparticles provide further stability and biocompatibility[32]

Gold Nanoparticles based surface enhanced Raman scattering were used to track differentiation in mouse embryonic cells. Gold Nanoparticles were delivered inside the cells and tracked by transmission electron microscopy and bright and dark field imaging. Multifunctional nanoparticle-labeled mesenchymal stem cells were tracked successfully in infarcted myocardium enabled us to monitor the fate of transplanted stem cells by MRI [52]. MRI has become the best for cell imaging modality for magnetically nanoparticle-labeled stem cells due to advantages of High spatial resolution with good anatomic background contrast, noninvasive method which is crucial to develop successful stem cell therapies, No exposure to ionic radiation, Cells may be followed up for months, Labeling is non toxic, Does not affect proliferation and differentiation [29, 24, 49, 53].

Disadvantages are – Rate of cell division is difficult to measure, Whether progeny cell have SPIO particle may not be measured, Some cells may lose differentiation capacity in concentration dependent manner, No difference in signals between alive or dead cell, Signals are received from labeled cells or macrophages cannot be determined.

9. Effects of Nanoparticles on proliferation of stem cells

Some nanoparticles may affect viability, morphology, and proliferation of stem cells while some may not.

9.1. ***Mesenchymal stem cells*** – Single walled nanotubes (SWCNTs), multi-walled nanotubes (MWCNTs) and functionalized CNTs did not affect adipogenesis, chondrogenesis, or osteogenesis in hMSCs[54]. Mesoporous silica nanoparticles conjugated with fluorescein isothiocyanate in human bone marrow mesenchymal stem cells did not affect stem cell viability and proliferation[31-32] as silica nanoparticles escaped from endolysosomal degradation but they increase actin polymerization in mesenchymal stem cells[33]. Magnetic nanoparticles can be used to modify mesenchymal stem cells sufficient enough for clinical application[28]. Magnetite iron oxide cationic liposomes change fibroblastic Mesenchymal stem cells into polygonal

when incubated in osteogenic medium. They increase the cell proliferation up to five times with very high survival rate (97%–99%) pointing out no effect on stem cell viability[18,23,38-39]. Ferucarbotran nanoparticles promoted growth of human mesenchymal stem cells due to peroxidase like activity which decreased intracellular H_2O_2 and oxidative stress. Ferucarbotran released free iron from lysosomal degradation that accelerated cell cycle progression by altering iron on protein regulators[24].

9.2. ***Neural stem cells*** – Superparamagnetic iron oxide contrast agent does not affect morphology, cell proliferation, and differentiation of labeled Neural stem cells[50].

9.3. ***Embryonic stem cells*** – Embryonic stem cells were columnar and embryoid body-shaped at low concentration while fibroblast-like and less squamous at high concentration of polystyrene Nanoparticles. In embryonic stem cell, nanoparticles reduced viability and disrupt cytoskeletal development but have no effect on size of nucleus[1]. Single walled carbon nanotubes (SWCNTs) decrease cell proliferation, and cell adhesion in dose/ time-dependent manner in human embryonic kidney cell line HEK293 cells [55].

10. Effect of nanoparticles on differentiation of stem cell

Now, investigation of migration patterns, and targeting of particle-labelled cells to desired locations to initiate activation and differentiation of stem cells is possible [56]. Effects of properties and structure of nanomaterials on stem cell differentiation has developed as new interdisciplinary area in regeneration medicine and material science[57-58]. Superparamagnetic iron oxide labeling inhibits chondrogenic differentiation of in one study[59] while showing no effect on adipogenic, osteogenic, or myogenic differentiation in others[18,23,39]. On other hand, increased proliferation and osteogenic differentiation was seen with Naringin nanoparticles in (1–100 µg/mL) concentrations[60].

In embryonic stem cells, calcium-handling properties of cardiomyocytes was unaffected by Superparamagnetic iron oxide labeling and direct injection into infarcted myocardium caused significantly improved cardiac output. Polystrene nanoparticles minimally affect differentiation and viability of embryonic stem cells [51].

In human mesenchymal stem cells, Mesoporous silica nanoparticles have no affect on regular osteogenic differentiation[33] while *In vitro* osteogenesis was induced successfully in highly chondrogenic synovium[61].

In vitro as well as in *vivo,* Fibrin-polylactide-caprolactone (PLCL) nanoparticles complex in Human adipogenic stem cells induced chondrogenic differentiation by upregulating chondrogenesis marker genes and significantly enhanced chondral extracellular matrix deposition[62].

In contrast, osteogenic differentiation and bone matrix mineralization is impaired in human mesenchymal stem cell by direct exposure to biphasic calcium phosphate particles i.e. calcium-deficient apatite particles due to the Ca^{2+} uptake from culture media [63].

Stem cell differentiation is closely associated with their microenvironment. Regulation of stem cells depends on their interaction with a highly specialized microenvironment or niches [64]. The niche secretes appropriate chemicals to direct the differentiation and development of stem cells. A key challenge in stem cell microenvironment research is to develop an in vitro system that accurately imitates the in vivo microenvironment [65]. Nanotechnology can be utilized to create in vivo-like stem cell microenvironment to determine mechanisms underlying the conversion of an undifferentiated cells into different cell types[66]. A better solution is currently under investigation: growing the stem cells on a so-called “lab-on-a-chip”[67].

11. Effect of 3D Nanostructures in Stem Cell differentiation i.e. Tissue Engineering

The differentiation of stem cells with conjugate 3D materials is currently hotspot in tissue engineering. Various micro-/nanofabrication technologies are used to develop stem cells into 3D biodegradable scaffolds [68-69].

These Nanostructured scaffolds trigger stem cells to develop specialized cell types depositing their own matrix. After degradation of scaffold, they developed as 3D tissue structure mimicking body’s natural tissues i.e. mouse neural stem cell in 3D motif[70].

12. Uses of nanoparticles labeled stem cells

Magnetic nanoparticles (MNPs) for isolation and sorting[26], quantum dots for molecular imaging and tracing[40], nanomaterials i.e. carbon nanotubes (CNTs)[71], fluorescent CNTs[72] and fluorescent MNPs[73], to deliver gene or drugs into stem cells have been used successfully. Superparamagnetic Magnetic nanoparticles (MNPs), i.e. magnetism-engineered iron oxide nanoparticles have been widely researched for application in magnetic resonance

imaging (MRI)[43], hyperthermia[74], tissue repair[75], immunoassay[76], drug/gene delivery[77], cell separation etc. Nanostructures were designed to regulate proliferation and differentiation of stem cells and their application in regenerative medicine. Regenerative medicine is application of stem cells in regenerating the tissues like cadiomyocytes, neurons, bones, cartilage and wound healing. Some of the uses given below:

12.1. **Uses in Nervous system-**Nanofiber conjugated laminin and nerve stem cell differentiated on damage position and generated new neuron. Mouse paralyzed due to spinal cord injury similar to human cord injury due to traffic accident is regenerated on nanofibre scaffold[78] raising the hope of nerve regeneration for Parkinsons, apoplexy, cardiomyopathy and diabetes neuropathy too[79]. Nanofibres, developed as tissue-engineered scaffolds promote adhesion of various cells. Surface modifications, including immobilization of functional cell-adhesive ligands and bioactive molecules such as drugs, enzymes and cytokines are used to increase bioactive or therapeutic properties of nanofibrous scaffolds. Nanofibers prepared by needleless technology have been used as scaffolds to treat spinal cord injury[80].

12.2. **Uses in Cardiovascular system-** Nitric Oxide Combined with nanofiber delivery vehicles has created a novel NO-releasing therapy i.e. self-assembling NO-releasing nanofiber gels to prevent neointimal hyperplasia[81-82]. Endorem-labeled GFP+ MSCs were grafted into experimental stroke model in rats[83]. Lesion was considerably smaller in grafted MSCs suggesting protective effect[84].

12.3. **Uses in musculoskeletal system-** Rabbit bone marrow-derived mesenchymal stromal cells labelled with ferumoxide were injected and directed to Interconnected porous calcium hydroxyapatite ceramic via external magnetic targeting system to evaluate subsequent bone formation. Enhanced bone formation may be translated clinically to treat fractures, bone defects, delayed union and nonunion[85]. Magnetically labeled synovium-derived cells (M-SDCs) with ferumoxides regenerated the articular cartilage which may be beneficial to repair human articular cartilage defects[86]. Rat bone marrow mesenchymal stem cells (BMSCs) were harvested and labeled by (SPIO) super paramagnetic iron oxide and (Dil) 1,1-Dioctadecyl-3,3,3,3-tetramethylindocarbocyanine perchlorate particles. The transplanted BMSCs were observed by fluorescence microscope and traced by magnetic resonance (MR) imaging. Transplanted BMSCs promoted tendon-to-bone tunnel healing and may be useful for earlier rehabilitation for ligament reconstruction surgery[87].

12.4. **Uses in wound healing-** Mesenchymal stem cells are excellent for cell and tissue replacement therapies like wound healing[32,88]. Embryonic stem cells (ESCs) are used in genetic, traumatic, and degenerative conditions due to preserved functional efficacy in vivo[89]. Biomimetic nanofiber scaffolds (NFSs) functionalized with rich attachment of bone-marrow-derived mesenchymal stem cells (BM-MSCs) can promote wound healing in acute full-thickness skin wounds (FTSW). Wounds closed early due to increased epithelial edge in growth and collagen synthesis[90]. Complete Skin regeneration is seen with locally injected nanosized rhEPO via combined expression of EPOR and βCR[91].

12.5. **Uses for Gene Delivery into Stem Cells-** Efficient intracellular delivery is prerequisite to control stem cells. Electroporation and nucleofection have high delivery efficiency but may cause severe damage to stem cells[92]. Viral vectors successfully transfect and manipulate cell differentiation [93] but increased mutagenesis, immunogenicity, and the risk of toxicity preclude their preference. Therefore, polymeric nanoparticles are seen as most promising nanotechnology to convert laboratory results into clinically viable applications with stem cell[94-95] For example, (dMNTs) polyamidoamine dendrimer-functionalized fluorescent multi-walled carbon nanotubes entered into mice embryonic stem cell line efficiently[71,96] and markedly enhanced gene delivery with advantages of simplicity of use, and ease of mass production[97-99]. Protein-conjugated Carbon nanotubes CNTs can penetrate cellular membrane[100-101] and may store gene or peptide for delivery in stem cell[94]. Atomic force microscopy (AFM) and nanoneedle were developed to transfer gene into human MSCs and human embryonic

kidney cells (HEK293)[102]. CNTs are novel and emerging technology in gene or drug delivery, tissue engineering, and regenerative medicine. They may be used for development of nanovehicles and for creation of electroactive CNTs. Being electrically conductive CNTs have huge potential to manipulate MSC's differentiation pathways to create electroactive cells i.e. heart [103-105]. Gene-modified mesenchymal stem cells show superior characteristics of specific tissue differentiation, directional migration and resistance to apoptosis. Polyethylene glycol-grafted polyethylenimine (PEG-PEI) is a valid gene delivery agent with better transfection efficiency in mesenchymal stem cells [106].

12.6. **Uses in drug delivery**-In recent days, drugs are aimed to be given more and more targeted within cells and tissues on individual basis to minimize side effects. Ideally pharmaceutical agents should be delivered to their sites of action within the cell i.e. selective subcellular delivery[5]. The benefits of selective subcellular delivery by drug delivery systems based on nanoparticles are:

12.6.1. Efficient encapsulation of the drug

12.6.2. Successful delivery and release of drug to the targeted region of the body to maximize efficacy

12.6.3. Improved bioavailability of the drug delivery at specific places in the body

12.6.4. Drug action over prolonged period of time[107] due to altered pharmacokinetics and decreased drug clearance of drug

12.6.5. Regulated drug release with minimum tissue damage[108].

12.6.6. Human mesenchymal stem cell (MSC) is most promising to produce exosomes as drug delivery vehicle due to the ready availability, proliferative, immunosuppressive and clinically tested profile [109].

Uses for Stem cell nanotechnology seem never ending. However, several obstacles must be overcome before their therapeutic application can become reality. It needs better understanding and controlled functions of microenvironmental signals and tracking of transplanted stem cells [110-113].

13. Toxicity of nanoparticles in stem cells

Today Nanoparticles in stem cells is becoming an emerging interdisciplinary research area. Nanoparticles must be biocompatibile if desire to be used in biomedicine and has to be evaluated for their potential toxicity by uniform criteria's [33]. Toxicity data of nanoparticles in stem cells are limited and molecular mechanisms of toxicity are still unknown[114]. Nanoparticles may induce cell injury by generating reactive oxygen [115] which may be concentration-dependent[114]. Toxicity of cadmium oxide in germ-line stem cells was evident within 48 hours of exposure showing significant inhibition of mitochondrial function at 1μg/mL and necrosis at 5 μg/mL concentration.

Degree of cytotoxicity in nanoparticle-labeled stem cells varies as per nanoparticles[116]. Silver nanoparticles are most toxic due to oxidative stress imparted by them while Carbon nanomaterials induced cell death and impaired phagocytosis in alveolar macrophages[117].

Hence, toxicity studies, pharmacokinetic and pharmacodynmic studies are critical to establish nanoparticles as reliable treatment modality[118].

14. Limitations of Stem cell Nanotechnology

Further work at multiple centers is required to investigate the effects of different nanoparticles in directing stem cell behavior and should provide valuable information about the impact of nanoparticles in diagnostic and therapeutic applications.

Nanoparticles have wide range of applications in the stem cell field, but information concerning the impact of manufactured nanomaterials on human health and the environment has to be sought before going ahead [114]. Many questions are seeking answer, in regard to Stem cell nanotechnology -

14.1. The mechanism of interaction between nanomaterials and stem cells is still not known in detail.

14.2. How nanomaterials and nanostructures affect stem cells function is yet to be explored.

14.3. How nanomaterials are metabolized inside stem cells, what are the pharmacokinetic profiles is yet to be defined.

14.4. Problems in establishing functional interface between nanomaterials and stem cell have to be overcome.

14.5. More and more information regarding mechanisms regulating nanoparticles on stem cell's surface is also required.

14.6. Utilization of current knowledge and principles to develop nanostructures for clinical application

14.7. Availability of high quality nanomaterials, their processing, characterization and tailoring is a great challenge facing by researchers

15. Conclusion

Nanotechnology uses Nanoparticles to design, and construct nanomaterials [119-120] involving their manipulation, modeling and imaging[121]. Nanoparticles are the particles of nanometer size that are used in various applications while stem cells are pluripotent cells having capacity to proliferate and differentiate in desired manner **Stem cell nanotechnology** is application of nanotechnology in stem cells research and development[122-123]. It is interdisciplinary and multidisciplinary branch of science combining various subfields of material sciences, engineering sciences and medical sciences [121]. Interaction of nanoparticles with stem cells i.e. stem cell nanotechnology has opened the new area of research and application in medical sciences.

We conclude the stem cell nanotechnology is upcoming branch of study in pharmacology. Different pharmacokinetic and pharmacodynmic aspect of nanoparticles as nanodrug has to be explored before using them on wide scale. These data warrant the establishment **of new** a**re**a **of** studies i.e. Stem Cell Nanopharmaceutics to deal with nanodrugs.

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