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When stem cells meet nanoparticles for biomedical treatments: A mini-review

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Abstract

One of the newest technologies that have been proposed for medical treatments that have attracted a lot of attention is the use of nanoparticles. Today, a wide variety of nanoparticles are known and made. These nanoparticles are used in further research. Especially Nanoparticles have a variety of effects on stem cells. In This mini-review, some applications and effects of nanoparticles in medical treatments have been investigated. First, the toxicity of one of the most common nanoparticles (silver nanoparticle) on stem cells was examined. Also, the potential of several nanoparticles in stem cell differentiation and proliferation and their role in mesenchymal stem cells, neuronal stem cells, and cancer Nanomedicine that has vital in our research was discussed. The purpose of writing this mini-review is to get acquainted with the most common nanoparticles and some of their effects on stem cells for medical treatments. With a better understanding of nanoparticles, they can be better used in clinical treatments or control many deadly diseases.

Keywords: nanoparticles, cancer, stem cells, Toxicity, medical treatment

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1. Introduction

Nanoparticles (NP_S) are small particles that range between 1 to 100 nm. They can classify according to their properties, shapes or size. Fullerenes, metal nanoparticles, ceramic nanoparticles, and polymeric nanoparticles are different groups of nanoparticles. [1] Nanoparticles can use in medical treatment such as Brest cancer or cardiovascular disease. [2] [3] Some of these small particles can also be toxic to stem cells. [4] Stem cell is an undifferentiated cell in the human body. They can differentiate into any cell of an organism. Stem cells are classified as adult stem cells, embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs). [5, 6] Now use of stem cells and nanoparticles in different applications such as medical treatment and tissue regeneration have increased. Nanotechnology has many medical applications. These substances alone can increase the proliferation and differentiation of stem cells or can be toxic to them. [7] In Nanomedicine, drugs can be prevented from degrading by using a nanoparticle coating. Because nanoparticles are so small, they can easily penetrate smaller capillaries and be absorbed by cancer cells.[8]

2. Toxicity of silver nanoparticles in embryonic stem cells.

Today, a lot of application of silver nanoparticles has increased concern about their adverse effect on human health. [4] Silver nanoparticles are one of the most widely used nanoparticles. [9] The toxic effects of silver nanoparticles were determined on human somatic cells. The research shows us that silver nanoparticles can cause transcriptomic changes in mouse embryonic stem cells. For example, in these cells, 5.0 μg/ml of silver nanoparticle after 24 hours gives us 101 differentially expressed genes.[10] Most of the pathways and functions of these genes can be divided into two main groups: embryonic growth and metabolism.[11] However, there is no evidence about pathways related to cancer for silver nanoparticles. But effects of silver nanoparticles on oxidative stress and downstream apoptosis have been well established by flow cytometry analysis. [4] Further, Silver nanoparticles can induce neurotoxicity in neuron and astrocyte networks that are derived from human embryonic stem cells. Indeed silver nanoparticles can change the astrocyte/neuron ratio and affect astrocytic morphology. [9]

3. Potential of nanoparticles in stem cell differentiation and proliferation.

Today, with the advancement in nanotechnology, various nanomaterials are used for multiple applications, such as modulating the behavior of stem cells and therapeutic applications**.** For example, metallic NPs can modulate stem cell differentiation and proliferation. Nanoparticles can potently enhance stem cell differentiation into various lineages, like osteogenic, adipogenic, chondrogenic, neuronal, and hematopoietic differentiation. In addition to stem cells, metallic nanoparticles also affect the differentiation and proliferation of normal and cancer cells. Biodegradable and biocompatible nanoparticles have a role in the intracellular delivery of small molecules such as protein and essential growth factors for cellular differentiation. [7, 12, 13] Nanomaterials have unique properties that allow them to enter the nucleus through various methods. And activate essential transcription factors and molecules associated with signaling pathways. [12] Graphene oxide nanoparticles are another material. [14]This material has unique biophysical and electrical properties and has excellent biological compatibility.[15] Graphene oxide nanoparticles are a promising material for neuronal tissue regeneration by stem cells. [16] Studies show that graphene is applicable in the regulation of human fetal neural stem cells self-renewal and differentiation. [17-19] Several effects of nanomaterials on cell differentiation are shown in Table 1.

Table1. Effect of some of the nanomaterials in cell differentiation

Ag nanoparticles	Osteogenic	Enhance	mesenchymal stem cells	[7]
	Neuronal	Enhance	SH-SY5Y	[20]
	Adipogenic	Enhance	mesenchymal stem cells	[21]
Gold nanoparticles	Osteogenic	Enhance	mesenchymal stem cells	[7]
	Neuronal	Enhance	primary	[7]
	Adipogenic	Suppress	mesenchymal stem cells	[7]
Silica nanoparticles	adipogenic	Enhance	mesenchymal stem cells	[7]
Metallic nanoparticles	Osteogenic	Enhance	Normal and cancer cells	[7]
	Neuronal	Enhance	Normal and cancer cells	[7]
	Adipogenic	Enhance	Normal and cancer cells	[7]
Tio2 nanotube	Osteogenic	Enhance	mesenchymal stem cells	[7]

4. Role of nanoparticles in mesenchymal stem cells.

More than 25 years ago, cells extracted from human and mammalian bone marrow were mesenchymal stem cells. [22] Mesenchymal stem cells are multipotent cells that can self-renewal and differentiate into different types of specialized cells. [23] These cells are also an effective tool in treatment. For example, mesenchymal stem cells are used for cell-based therapy of immune-mediated, inflammatory, and degenerative diseases. [24] In vitro and in vivo experiments show that mesenchymal stem cells introduce iron oxide nanoparticles without adverse effects on cell viability and proliferation.[25] This confirms the biocompatibility of iron oxide nanoparticles. Iron oxide nanoparticles have also been shown to promote the migration of mesenchymal stem cells to sites of inflammation. This illustrates the clinical applications of these nanoparticles and mesenchymal stem cells. [26] [27] In the last decade, there have been many applications for hydroxyapatite nanoparticles in biomedical. [28] Hydroxyapatite is known as the main inorganic substance in bones and teeth. [29] One study found that these nanoparticles could stimulate the osteogenic differentiation of mesenchymal stem cells. It seems that the rate of this differentiation depends on the size of hydroxyapatite nanoparticles. The smaller these nanoparticles cause, the higher rate of differentiation. [28] Gold nanoparticles are another substance that studies in a large number of articles. The applications of these nanoparticles in biomedical are well known. Even the size and shape of gold nanoparticles effectively increase or decrease the osteogenic differentiation of mesenchymal stem cells. [30] Also, silica nanoparticles in three sizes of 50, 200, and 400 nm are effective on this differentiation. [30] The use of silica nanoparticles has increased these days dramatically.[31] These nanoparticles are very stable and have less toxicity. [32] In addition, silica nanoparticles can reduce the adipogenic differentiation of mesenchymal stem cells. This could link this nanoparticles to obesity. [33] Obesity is a complex disease that depends on several factors. The prevalence of this disease has doubled since 1980 in worldwide. In general, the prevalence of this disease is higher in the older person and women. [34]

5. Role of nanoparticles in neural stem cells.

Neural stem cells have received a lot of attention in the last 15 years.[35] These cells are pluripotent and used in neurotoxicity testing, regeneration, repair of neural tissues, treatment of CNS diseases, and personalized medicine. [36] Neural stem cells can differentiate into neurons, astrocytes, and oligodendrocytes. [37] This section discusses the effects of cerium oxide, superparamagnetic iron oxide, graphene oxide, and silver nanoparticles on neural stem cells. Cerium oxide nanoparticles are rare and inorganic nanoparticles that have catalytic antioxidant activity. Research shows that cerium oxide nanoparticles are not toxic to neurons. These nanoparticles also reduce the differentiation of neural stem cells. [38] In research on the applications of superparamagnetic iron oxide nanoparticles in biomedicine, several things are of particular importance. Such as the safety and biocompatibility of these nanoparticles. One study found that the use of superparamagnetic iron oxide nanoparticles was associated with oxidative stress due to an imbalance in the formation of reactive oxygen species. These results indicate that more research is needed to determine the safety and biocompatibility of these nanoparticles. [39] Graphene oxide nanoparticles also affect neural stem cells. The effects of graphene oxide Nanoparticles in different sizes on neuronal stem cells have been tested. This experiment found that nanoparticles in the sizes of 1 and 5 μg have more cytotoxic effects than the sizes of 400 and 700 nm. However, the amount of cytotoxicity in all dimensions was low. Graphene oxide nanoparticles at 417 and 663 nm showed a more remarkable ability to maintain the self-renewal of these cells in the absence of epidermal growth factor (EGF and bFGF) and primary fibroblast growth factor. [37] One of the important physicochemical properties of metallic nanoparticles is their surface structure and differences in surface coating can affect the cytotoxicity and cellular uptake of neural stem cells.[31] The surface structure of silver nanoparticles is an essential and determining factor in the toxicity and cellular uptake efficiency of these nanoparticles in neural stem cells. [40]

6. Role of nanoparticles in cancer Nano-medicine

Cancer is one of the most dangerous and deadly diseases. The death toll from cancer is projected to rise to 13.1 million in the next ten years. [41] Efforts to treat cancer in Nanomedicine have increased since about 20 years ago. Today, about 12 cancer Nanomedicines have been approved. Nanotechnology proposes new solutions for cancer therapeutics. The role of nanoparticle mechanical properties in drug delivery has also been recently identified. Nanoparticles exhibit unique transport, optical, magnetic, biological, electronic, and thermal properties that can be used for therapeutic purposes. These materials can aid in solubilization, imaging, tissue penetration, targeting, and triggered activation.[42] They are also processed differently in the body than conventional drugs. Of course, the delivery of cancer drugs using nanoparticles requires a series of appropriate biological programs. [43, 44] This drug delivery system can prevent rapid drug destruction and increase drug concentration in the target tissues. Therefore, it can minimize the required dose of a particular drug. [41] In cancer, a complete understanding of Nano-bio interactions and the delivery of nanoparticles to tumor cells leads to efficient and safe Nano therapy. [45] As mentioned earlier, finding a way to treat cancer in nanomedicine is significant. In addition to cancer treatment and drug delivery, nanoparticles can also be effective in diagnosing cancer. Rapid detection of cancer-related molecules or detection of molecular changes can lead to new and very effective therapeutic agents. Nanotechnology is likely to provide opportunities for cancer treatment using multifunctional nanoparticles. [46] Many nanoparticles are now found for a variety of nanomedicine applications. Therefore, the development of multifunctional nanoparticle drug delivery systems will be very efficient. And may facilitate cancer treatments. [47] [48] [49]

7. Perspective

A new window into medical treatments will open by reviewing articles and designing new research on nanoparticles and stem cells. Although some nanoparticles can be toxic to some cells, with more knowledge, the toxic effects of these nanoparticles can be minimized and used very well. It seems that the use of nanoparticles in today's medicine can solve many problems, such as cancer treatment. Cancer is affecting more and more people around the world every day. Therefore, a better understanding of the effects of these materials in medical treatments is fundamental.

8. Conclusion

In this mini-review, an attempt has been made to examine the essential properties of nanoparticles in medical treatments. Silver nanoparticles can be toxic to embryonic stem cells. Many nanoparticles increase the proliferation and differentiation of stem cells, including iron oxide, gold, silver, silica, graphene oxide, and metallic nanoparticles. Gold, hydroxyapatite, and iron oxide nanoparticles are beneficial for mesenchymal stem cells. The non-toxicity of cerium oxide nanoparticles for neuronal stem cells has also been identified. In addition, nanoparticles have many applications in Nanomedicine, such as drug delivery, which can accelerate cancer treatment.

Competing interests

The authors declare that no conflict of interest would prejudice the impartiality of this scientific work.

Authors contribution

All authors of this study have a complete contribution for data collection, data analyses, and manuscript writing.

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