World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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Regeneration of pulp using stem cells for oral health renewal: A literature review

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World Journal of Advanced Research and Reviews, 2024, 24(02), 2508–2514

Publication history: Received on 13 October 2024; revised on 25 November 2024; accepted on 27 November 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.24.2.3574

Abstract

Introduction: Root canal treatment is often the last resort for managing severe pulp damage. However, current conventional therapies only focus on replacing damaged tissue without any attempt to regenerate biological tissue. Dental pulp stem cell (DPSCs)-mediated pulp regeneration has emerged as an innovative solution.

Methods: This study involved analyzing references from journals and textbooks within the timeframe 2020-2024 to explore the potential of DPSCs in pulp regeneration.

Discussion: DPSCs possess remarkable regenerative potential with their ability to differentiate into various essential cell types. They also support angiogenesis and neurogenesis to repair pulp tissue. While challenges such as standardization and integration with host tissue exist, research continues to enhance the safety and efficacy of the therapy.

Conclusion: Pulp regeneration using DPSCs offers a natural and effective approach to dental care. Despite remaining obstacles, this research provides a foundation for regenerative therapies that could transform endodontic practices and improve patient well-being.

Keywords: Dental health; DPSCs; Pulp regeneration; Regenerative therapy; Root canal treatment

1. Introduction

Root canal treatment often becomes the last resort for treating severe pulp damage, such as damage caused by infection or trauma [1]. However, this procedure has limitations, including the inability to restore the biological functions of lost pulp tissue. Current conventional endodontic treatments only focus on removing damaged tissue and filling the root canal with biologically inactive materials, without attempting to restore the original biological structure and function of dental pulp. This is because conventional therapy merely replaces damaged tissue rather than regenerating biological tissue [2]. Therefore, dental pulp regeneration through stem cell-based approaches has emerged as an innovative potential solution [3].

Recent research indicates that dental pulp stem cells (DPSCs) possess the capacity to differentiate into various cell types, such as odontoblasts and endothelial cells, which play crucial roles in new tissue formation and revascularization [1]. DPSCs show potential not only for hard tissue regeneration, such as dentin, but also for soft tissue, including blood vessels and nerves that are essential for restoring normal dental pulp function [10]. Furthermore, the ability of DPSCs to interact with biomaterials and growth factors makes them ideal candidates for pulp tissue engineering [2]

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DPSCs possess multipotent stem cells which are capable of differentiating into several different cell types, such as skeletal muscle cells, neurons, adipocytes, endothelial cells, chondrocytes (which form cartilage), and osteoblasts (which form bone). This illustrates the significant potential of DPSCs in the development of regenerative therapy and tissue engineering, as shown in Figure 1 below [29].

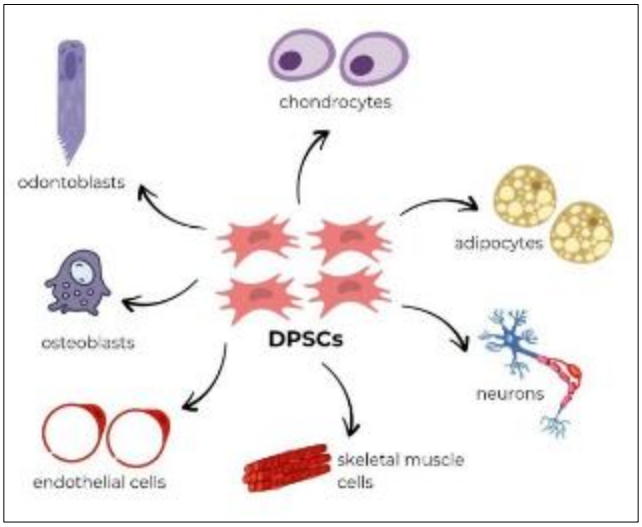

Figure 1 Differentiation potential of DPSCs. Adapted [7]

The significant potential of DPSCs in pulp regeneration is supported by preclinical research demonstrating their ability to promote wound healing and repair damaged tissue in various animal models [4]. Although preclinical results are promising, gaps still exist in the clinical application of this regenerative therapy. Comprehensive clinical trials and further research are needed to ensure its safety and effectiveness in patient care. However, the transition from laboratory to clinical application requires more in-depth research to ensure the safety and effectiveness of this therapy. Thus, this article aims to review the potential of DPSCs in dental pulp regeneration and highlight the progress, challenges, and future prospects in this field.

2. Methods

The method used in this literature review involved collecting references from journals and textbooks within the timeframe of 2020-2024 through electronic databases such as PubMed, ResearchGate, and Google Scholar. Searches were conducted using several keywords, namely: "pulp regeneration", "stem cells", and "dental pulp stem cells". Relevant journals and textbooks were then analyzed to obtain information about the potential of DPSCs in dental pulp regeneration.

3. Results and discussion

3.1. Pulp Definition

Dental pulp is the soft tissue located within the tooth's pulp cavity. It is a vital tissue protected inside the tooth's dentin, but when exposed, it can cause extreme pain and suffering for patients [11]. This tissue consists of blood vessels, nerves, and connective tissue that provide nutrition and sensory response to the tooth. The pulp plays a crucial role in maintaining tooth vitality and providing the ability to sense sensations such as heat, cold, and pressure [12]. Although teeth can continue to function after the pulp is removed and replaced with root canal filling material, pulp plays an essential role in protecting teeth from bacterial invasion. The pulp contains dentinal fluid and odontoblastic processes that help prevent bacteria from entering the dentinal tubules. The pulp can also produce secondary dentin to protect teeth from further damage, such as from caries [13]. Dental pulp has limited regenerative capacity. When damage occurs, such as from caries or trauma, the pulp can respond by producing new tissue like tertiary dentin or reactionary dentin. However, this regenerative ability is limited and often insufficient to repair severe damage [14, 16].

3.2. Etiology of Dental Pulp Disease

Pulp diseases are generally caused by various factors that can affect the health of dental pulp tissue. One of the main causes is dental caries. Caries occurs when acids produced by bacteria in dental plaque damage the enamel and dentin, eventually reaching the dental pulp and causing infection. This process can trigger pulp inflammation known as pulpitis [8, 9].

Besides caries, dental trauma is also a common cause of pulp disease. Trauma can occur due to physical impact, tooth fracture, or even iatrogenic procedures such as aggressive tooth preparation for restoration purposes. This trauma can cause inflammation, necrosis, or even death of the dental pulp. These conditions often require endodontic intervention, such as root canal treatment (RCT), to prevent the spread of infection and further complications [26, 29].

Other factors contributing to pulp disease include chemical irritation from certain materials used in dental treatment, as well as extreme thermal changes. For example, the use of incompatible or overheated filling materials can cause pulp irritation and inflammation. Additionally, systemic diseases such as diabetes mellitus and immunological disorders can affect pulp health by altering the body's immune response to infection and injury [27].

3.3. Root Canal Treatment

Root canal treatment is an endodontic procedure aimed at removing infected pulp tissue. Root canal treatment involves three main stages known as the Endodontic Triad: root canal preparation, sterilization, and filling. The preparation stage includes cleaning and shaping the root canal, followed by sterilization involving irrigation and disinfection, and concluding with filling using specific root canal materials. The goal of this treatment is to maintain tooth functionality and keep it symptom-free [15]. This process involves cleaning, shaping, and filling the root canal to prevent further infection and maintain the function of the affected tooth. This treatment is typically necessary when the pulp experiences severe inflammation or infection caused by caries, trauma, or tooth fractures. Although root canal treatment is effective in eliminating infection and preserving the tooth, this procedure does not restore the biological functions of the pulp. After treatment, the tooth loses its sensory capabilities and nutrition due to the absence of living pulp tissue [28].

3.4. Dental Pulp Stem Cells (DPSCs)

Dental pulp stem cells (DPSCs) are a type of mesenchymal stem cells found in dental pulp tissue. DPSCs were the first stem cells successfully isolated from human permanent teeth [16]. DPSCs have the potential to differentiate into various cell types, including odontoblasts, chondrocytes, osteoblasts, and adipocytes. This multipotent capability makes DPSCs ideal candidates for regenerative therapy in dentistry [5].

DPSCs are found in dental pulp of both deciduous and permanent teeth. DPSCs demonstrate high proliferation capacity and possess the ability to interact with biomaterials and growth factors, which are essential components in tissue engineering. Additionally, DPSCs are capable of producing extracellular matrix rich in collagen and glycoproteins that function as natural scaffolds for new tissue formation [4, 8].

One unique characteristic of DPSCs is their ability to support angiogenesis, or the formation of new blood vessels that is crucial for tissue regeneration requiring good blood supply, including pulp tissue. Research has shown that DPSCs can enhance angiogenesis through the secretion of various angiogenic factors, such as VEGF and bFGF [6, 7].

3.5. Potential and Benefits of DPSCs in Pulp Regeneration

DPSCs undergo multi-lineage differentiation from embryonic stem cells (ESCs) into various cell types. ESCs are obtained from dental pulp, which can then be induced to become various cell types, including neuronal cells, osteoblasts, chondrocytes, adipocytes, and myoblasts. This process allows for the generation of various cell types for therapeutic and research purposes [29]. This can be seen in Figure 2 below

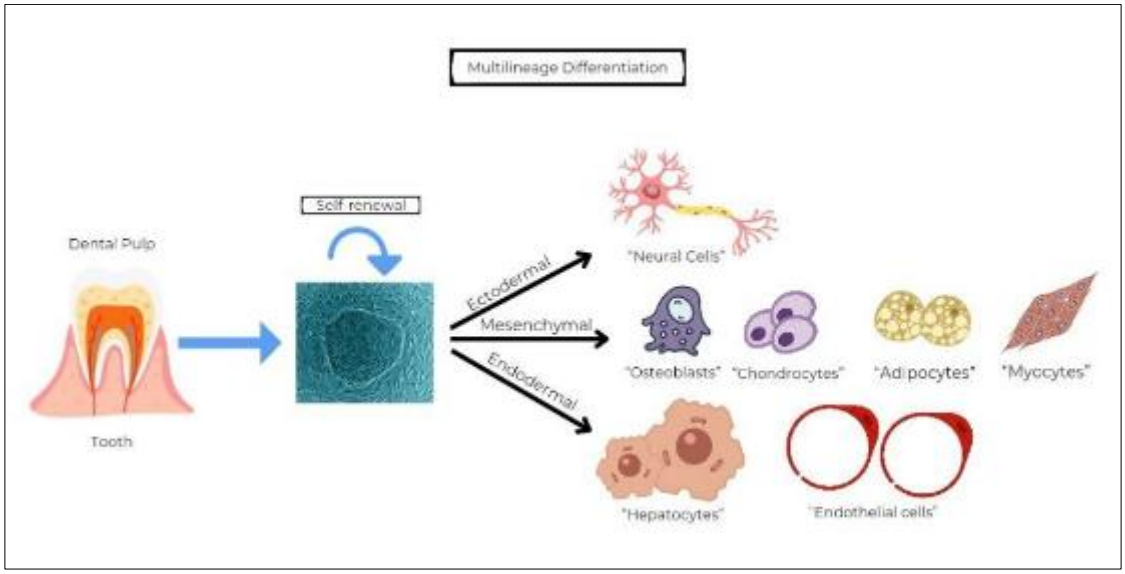

Figure 2 Differentiation process of DPSCs. Adapted [29]

DPSCs have tremendous potential in pulp tissue regeneration due to their ability to differentiate into various cell types, including odontoblasts, osteoblasts, and neurons [4]. This ability not only allows for the repair of damaged tooth structures but also enables a deeper restoration of the biological function of the tooth. DPSCs possess immunomodulatory properties that allow them to reduce inflammation and promote healing [13].

Research has shown that DPSCs can produce various growth factors and cytokines that support tissue regeneration [6]. For example, VEGF secreted by DPSCs can enhance angiogenesis which is essential for blood supply to the tissue [16]. Furthermore, neurotrophic factors such as NGF and BDNF produced by DPSCs can aid in the regeneration of neural tissue, which is crucial for the restoration of sensory function in the dental pulp [7].

3.6. Application Methods of DPSCs and Supporting Biomaterials

One critical aspect in the clinical application of DPSCs is the effective method of applying them to the regeneration site. This technique involves the use of biomaterial-based scaffolds to support stem cell proliferation, differentiation, and integration [17]. Scaffolds serve as a three-dimensional framework that supports stem cells and allows for the growth and formation of new tissue. Scaffolds can also be modified with various bioactive molecules, such as growth factors, to enhance the regenerative capacity of DPSCs [3].

Collagen-based scaffolds are one of the most widely used in pulp tissue regeneration [18]. Collagen, as a major component of the natural extracellular matrix, has biocompatible properties that support cell adhesion and proliferation [19]. Moreover, combining collagen with other materials such as hydroxyapatite or nanofibers can enhance the mechanical and bioactive properties of the scaffold, enabling the formation of hard tissues like dentin. Recent studies indicate that collagen-hydroxyapatite-based scaffolds can enhance the differentiation of DPSCs into odontoblasts, which is essential for the formation of dentin [3].

3.7. Safety and Efficacy of DPSCs-Based Therapies

Safety and efficacy are two key aspects that must be considered in the development of stem cell-based therapies [10]. So far, research has shown that DPSCs have a low potential for causing immunogenicity because they are expressed with an immune profile similar to other mesenchymal cells. This makes them safer for clinical applications as the risk of immune rejection against cell transplantation is low [7].

Furthermore, DPSCs have been proven to have genetic stability, making them less likely to undergo mutations or transformation towards malignancy [28]. Several preclinical studies in animal models have shown that transplantation of DPSCs does not lead to tumor formation, indicating that the risk of carcinogenicity in clinical use is relatively low. This is a significant advantage compared to some other stem cell types which may exhibit higher risks of tumor transformation [9].

However, there are still a few challenges that need to be addressed to ensure the safety of this therapy. One is the control over cellular differentiation and the regulation of the microenvironment [6]. The use of appropriate scaffolds and bioactive molecules is crucial to ensure that DPSCs differentiate in the desired direction and do not cause the formation of unwanted tissues [3].

In terms of efficacy, DPSCs have shown promising results in pulp tissue regeneration, including the formation of new dentin and repair of vascular and neural structures in dental pulp [20]. Initial clinical trials indicate that DPSC-based therapies can promote tissue healing and regeneration more effectively compared to conventional methods such as root canal therapy [21].

3.8. Factors Affecting the Success of DPSCs

Fragile teeth often experience high sensitivity, which can affect the effectiveness of pulp regeneration therapy. This condition is caused by the thinning of enamel and dentin structures, thus reducing protection for the nerves in the pulp. Increased sensitivity in fragile teeth may affect the success of DPSCs therapy because stem cell integration with compromised tissue may not be optimal. Therefore, it is important to consider the condition of fragile teeth in designing more effective and sustainable therapy [22, 27].

3.9. DPSCs Derived from Third Molar Waste

Currently, there are several sources of dental stem cells including:

- Stem Cells from Human Exfoliated Deciduous teeth (SHED): These stem cells are located in the dental epithelial sheath and have the ability to develop into various cell types, including enamel-forming cells, dentin-forming cells, and cementum-forming cells
- Periodontal Ligament Stem Cells (PDLSCs): These stem cells are located in the periodontal ligament and have the ability to develop into various cell types, including periodontal ligament-forming cells, bone-forming cells, and cartilage-forming cells.
- Dental Pulp Stem Cells (DPSCs): These stem cells are located in the dental pulp and have the ability to develop into various cell types, including odontoblasts (dentin-forming cells), osteoblasts (bone-forming cells), and chondroblasts (cartilage-forming cells) [29]. Figure 4 illustrates this.

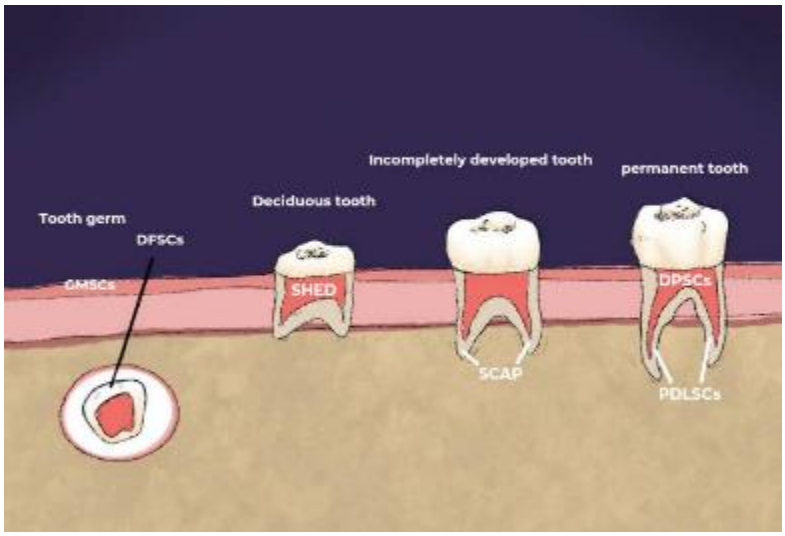

Figure 3 Source of DPSCs. Adapted [21]

DPSCs can also be obtained from third molar waste, which often becomes waste in extraction procedures [23]. Research shows that extracted third molar teeth contain DPSCs that can be isolated and used for regenerative therapy. Using third molar dental waste as a source of DPSCs not only reduces medical waste but also provides a valuable resource for regenerative treatment. By utilizing third molar teeth as a source of DPSCs, the tooth extraction process can be maximized for therapeutic benefits, improving sustainability and efficiency in dental healthcare [24].

3.10. Challenges and Future Directions

Despite the great potential shown by DPSCs in tissue regeneration, there are several challenges that need to be addressed to realize widespread clinical applications [10]. One of the main challenges is the standardization of DPSCs isolation and culture methods. This process can affect the quality and characteristics of the resulting cells, such as proliferation capacity and differentiation potential. This variability can lead to inconsistent results in research and clinical applications [25]. Furthermore, control of the microenvironment is crucial to ensure proper DPSCs differentiation. The use of inappropriate scaffolds and biomaterials can lead to undesirable outcomes, such as the formation of inappropriate tissue or even tumor development [3].

Another challenge is the integration of DPSCs with host tissue. Although DPSCs have good regenerative capabilities, efficient integration with existing tissue remains a problem. This includes ensuring that regenerated cells can connect well with existing vascular and nervous systems to restore normal function. A deeper understanding of the interactions between DPSCs and host tissue, as well as the development of new techniques to improve this integration, is crucial for enhancing the success of DPSCs-based therapy [6, 17].

The future of DPSCs research may also involve multi-disciplinary approaches, such as using gene modification technology and bioinformatics to manipulate specific molecular pathways related to cell differentiation and proliferation [1]. The use of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology, for instance, could enable genetic modification of DPSCs to enhance their regenerative functions or reduce the risk of side effects. Furthermore, further research on the interaction between DPSCs and the immune system can help develop better strategies to reduce the possibility of immune reactions and improve transplant acceptance [12].

4. Conclusion

Pulp regeneration using DPSCs shows great potential in restoring dental pulp function and structure. DPSCs can differentiate into various essential cell types, support angiogenesis and neurogenesis, and interact with biomaterials to promote tissue repair. Although challenges such as standardization and integration with host tissue remain, research must continue to address these barriers and improve the safety and effectiveness of therapy. With these advances, DPSCs offer a more natural and effective approach to dental healthcare that has the potential to transform endodontic practice and enhance patient well-being.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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