EJPMR, 2025, 12(11), 50-56 **Review Article** **Impact Factor 7.065**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

A REVIEW ON REGENERATIVE ENDODONTIC PROCEDURES

[1]K. S. Chandra Babu, [*2]Kata Chandanesh, [3]C. Sunil Kumar, [4]Vamsee Krishna Nallagatla, [5]S. Sunil Kumar, [6]R. Bharathi Suma

[1,5,6]Reader, Department of Conservative Dentistry and Endodontics, CKS Theja Institute of Dental Sciences and Research, Tirupati – 517501, Andhra Pradesh, India.
[*2]Postgraduate, Department of Conservative Dentistry and Endodontics, CKS Theja Institute of Dental Sciences and Research, Tirupati - 517501, Andhra Pradesh, India.
[3]Professor & HOD, Department of Conservative Dentistry and Endodontics, CKS Theja Institute of Dental Sciences and Research, Tirupati – 517501, Andhra Pradesh, India.
[4]Professor, Department of Conservative Dentistry and Endodontics, CKS Theja Institute of Dental Sciences and Research, Tirupati – 517501, Andhra Pradesh, India.

***Corresponding Author: Kata Chandanesh**
Postgraduate, Department of Conservative Dentistry and Endodontics, CKS Theja Institute of Dental Sciences and Research, Tirupati - 517501, Andhra Pradesh, India.

DOI: https://doi.org/10.5281/zenodo.17472193
How to cite this Article: [*]K. S. Chandra Babu, Kata Chandanesh C Sunil Kumar, Vamsee Krishna Nallagatla, S Sunil Kumar, R Bharathi Suma (2025). A Review on Regenerative Endodontic Procedures. European Journal of Pharmaceutical and Medical Research, 12(11), 50–56.

Article Received on 01/10/2025 **Article Revised on 21/10/2025** **Article Published on 01/11/2025**

ABSTRACT
Pulpal and periradicular pathosis, which can be caused by caries, trauma, or dental abnormalities, is a common disease in clinic for dental treatment. Root canal treatment (RCT) is a conventional option to manage the endodontic diseases demonstrating outstanding clinical outcomes. Regenerative endodontic treatments are growing in popularity are creating even more complex treatment protocols, involving revascularization and/or autologous platelet-rich plasma and scaffolds to elicit host stem cell *de novo* tissue formation to re-establish the vitality of teeth. Regenerative endodontics has the unique potential advantage of being able to continue the root development and maintaining vitality of the tooth, thereby potentially saving the teeth for the lifetime of the patient. This review mainly focus on the procedures of regenerative endodontics.

KEYWORDS: Revascularization, Regenerative Endodontics, Stem cells, Triple antibiotic paste, scaffold development, signalling molecules.

INTRODUCTION

Root canal treatment (RCT) is a conventional option to manage the endodontic diseases demonstrating outstanding clinical outcomes.[1] Regenerative endodontics has the unique potential advantage of being able to continue the root development and maintaining vitality of the tooth , thereby potentially saving the teeth for the lifetime of the patient.[2] Immature permanent teeth that have erupted but have not reached the plane have short roots and an open apex , and continue to develop the roots after eruption.[3] Dental trauma amongst children results in pulpal tissue damage, with concerns mainly in the immature tooth, as treatment options are limited in such cases of open apices.[4] Pulp necrosis leads to the interruption of root development and further reduces the physiological function and lifespan of affected teeth.[3] In the year 2001, a new treatment option termed 'revascularization' was introduced in endodontics to manage an immature permanent tooth with apical periodontitis and sinus tract (Iwaya et al).[5] Procedures that involve the usage of materials that encourage healing and repair of the pulp dentin complex after restoring the infectious or diseased tooth tissue are known as regenerative procedures.[4] Regenerative endodontics has introduced numerous procedures such as pulp implantation, revascularization, and postnatal stem cell therapy.[4] Such procedures involve the combination of cells, engineering materials, and relevant biochemical factors to improve or replace biological functions to promote advances in the area of

medicine.[6] Root canal medicaments, particularly antibiotics, have steadily revealed their crucial importance and key role in achieving positive outcomes as an adjunct to clinical therapy.[7] Triple antibiotic paste (TAP) is a combination of ciprofloxacin, metronidazole and minocycline introduced especially for the regeneration and revascularization protocol and the treatment of open apex teeth with necrotic pulp.[8] Regeneration of pulp dentin complex depends upon highly coordinated interaction between three key factors, that often constitute the regenerative endodontic triad, which includes dental stem cells, growth factors, and scaffold.[9] Cell differentiation and the development of new pulp tissue rely on stem cells, which have a high potential for specialization. These stem cells can either be transplanted into the root canal or harvested from local tissues. This leads to two concepts in endodontic tissue engineering: cell transplantation (cell-based) and cell homing (primarily cell-free). In cell-based methods, cells are cultured ex vivo and then introduced into the root canal using scaffolds containing signaling molecules. Clinical translation of this approach poses significant challenges, as it requires donor tissue or cell banks. In contrast, cell-homing methods utilize naturally residing stem or progenitor cells within the body that are locally available, bypassing any ex vivo manipulation. Here, scaffolding materials that are primarily cell-free are placed in the root canal, along with signaling molecules to attract cells from the remaining pulp tissue or the surrounding periapical space.[10]

MATERIALS AND METHODS

An electronic research was done on PubMed, Scopus, Google Scholar and research gate with keywords search of Revascularization, Regenerative Endodontics in immature permanent tooth. Out of 150 articles 22 articles have been chosen which were related to review taken.

Goals Of Regenerative Endodontic Procedures (REPs)

The American Association of Endodontists (AAE 2016) clinical considerations for regenerative endodontic procedures define success by three measures

Primary goal (essential) The elimination of symptoms and the evidence of bony healing.
Secondary goal (desirable) Increased root wall thickness and/or increased root length.
Tertiary goal positive response to vitality testing.[5]

Stem cells

Besides the development and introduction of new techniques, instruments, and medicaments for the clinical management of the dental pulp, the fundamental principles of clinical endodontics today are not drastically different than those of the time when first root canal instruments and gutta-percha were introduced in the 1800s. However, the isolation of clonogenic and highly proliferative stem cells from the dental pulp has the potential to change this scenario. Studies carried out at the National Institutes of Dental and Craniofacial Research (NIDCR) unveiled the stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSC) from permanent teeth.[11] Till now, different populations of adult stem cells have been identified and can be induced to differentiate into odontoblast-like cells in specific conditions, showing their potentials to be used in REPs. These include dental pulp stem cells (DPSCs), stem cells of the apical papilla (SCAPs), periodontal ligament stem cells (PDLSCs), inflammatory periapical progenitor cells (iPAPCs) and bone marrow stem cells (BMSCs).[12]

Osteogenic differentiation of apical papilla stem cells and the formation of osteoblast and osteoblast-like cells have been demonstrated in addition to the formation of new hard tissue.[13] Even when teeth develop pulp necrosis, apical periodontitis or periapical abscess, some residual vital pulp tissues may exist in the apical region, which can be used in REPs to promote tissue regeneration. SCAPs were firstly characterized from the apical tissue in 2006, with capacity of proliferation and odontogenic differentiation that is beneficial for root development.

In addition, in combination with the location proximal to teeth apices, SCAPs would be the most promising stem cell source for REPs. PDLSCs and BMSCs are also the potential stem cell sources for REPs as evoked bleeding from the apical tissue may induce the release of these cells.

Studies have proved an increased expression of marrow stem cells (MSCs) markers in the intra-canal blood induced by over instrumentation into the periapical tissues, both in immature and mature teeth.[1]

Growth factors

Dentin matrix has been considered as a reservoir of growth factors, which may be released through demineralization of dentin matrix by bacterial acid, irrigation with sodium hypochlorite (NaOCl) and ethylenediaminetetraacetic acid (EDTA), stimulation by calcium hydroxide and silica-calcium biomaterials such as Mineral trioxide Aggregate (MTA) and Biodentine. Besides, the blood clot formed during REPs also contains certain growth factors.

The dentin-derived growth factors are believed to play a key role in progenitor cell recruitment, proliferation, differentiation, and promoting tissue regeneration. For example, transforming growth factor-β1 (TGF-ß1) and fibroblast growth factor 2 (FGF2) have been implicated in promoting cell migration and proliferation. Vascular endothelial growth factor (VEGF) plays an important role in cell proliferation and regulation of angiogenesis while bone morphogenetic protein (BMP) and FGF2 mediate the signaling in dentin formation. Non-collagenous proteins (NCPs) including dentin matrix

protein and dentin phosphoprotein maybe involved in odontogenesis.[1]

Scaffolds

A scaffold is a complex three-dimensional material with mechanical and chemical properties that mimic the native extracellular matrix.[6] These materials should have certain characteristics to be able to be used for this purpose, such as providing a support to which the cells can adhere, allowing cell proliferation without affecting cell viability, and inducing their differentiation for the regeneration of the target tissue.[14] Blood clot, autologous platelet concentrates and synthetic biomaterials could serve as the scaffolds of REPs. Among them the blood clot is the most common scaffold used for inducing regeneration which is a relatively straightforward and simple approach. It allows integrators on cell surfaces to adhere to fibrous components and selectively adsorb cells, supplying growth factors to promote tissue regeneration.

Another approach for creating a scaffold is the use of autologous platelet concentrates, including platelet‐rich plasma (PRP), platelet rich fibrin (PRF) and concentrated growth factor (CGF). They consist of three-dimensional fibrin matrix and abundant bioactive molecules and can degrade over time.[1]

Pulp revascularization/revitalization

A necrotic pulp and irreversible pulpitis procedure which disinfects the root canal with antibiotics or/and antimicrobial agents. The periapical tissues are instrumented through the open root apical foramen to cause bleeding into the canal to revascularize it. Thereby, promoting tissue formation within the root canal for the continued deposition of mineral to strengthen dentine and grow the roots of immature teeth.[16]

Regenerative endodontics

A necrotic pulp and irreversible pulpitis procedure which debrides tissues from the root canal, disinfects the root canal, instruments the periapical tissues through the open root apical foramen to cause bleeding into the canal to revascularize. In addition to adding a scaffold or biological procedure within the root canal to promote vital tissue formation which will continue the deposition of mineral to strengthen dentine and grow the roots of immature teeth.[16]

Treatment procedures for CF-REPs

The treatment procedures of REPs is usually done in two appointments (Fig.1).

1st Appointment

Ensure the patient satisfies the case section criteria for regenerative endodontics and obtain patient approval, and parent and guardian consent for the treatment plan.[16]

The tooth must be permanent and very immature with a wide-open apical foramen wider than 1.1 mm and have an injured or exposed pulp. The tooth must have thin walls that will benefit from a continued development of the root, so that it can become stronger and less prone to failure in later life.

No emphasis on the use of vasoconstrictors while using local anesthesia
Isolate the tooth with a rubber dam and cut a root canal access wide enough to see all the walls.
Working length is determined by radiograph with a file positioned at 1mm from apex
Introduce a hand or rotary file into the root canal. Circumferentially “brushing” the canal walls minimal instrumentation without major dentin removal.

Sequence of irrigation

20 ml of 1.25% NaOCl (20 mL per canal, 5 min)
Sterile saline (5mL per canal)
17% EDTA (20 mL per canal, 5 min)

The root canals were dried with paper points to prepare the canals to receive the intracanal medication.[17]

Pack the root canals with calcium hydroxide or a triple antibiotic paste of Ciprofloxacin, Metronidazole, Minocycline to a final concentration of 0.1 mg/ml, for up to 4 weeks and restore the tooth with a temporary restoration. Restoration (cavit or glass ionomer) should be at least 3~4mm.

2nd appointment

AAE recommends the recall of 1~4 weeks after the first visit Complete resolution of signs and symptoms which include pain, swelling, sinus, or fistula was considered success of the first appointment.[18]

Repeat the treatment procedures of the first appointment if there are signs or symptoms of persistent infection.
3% mepivacaine without vasoconstrictor (epinephrine)is administered.

Irrigation, chelation, rinsing and drying root canals

Irrigate the root canal with 20 ml of 1.25% NaOCl and with suction to prevent leakage
Rinse the root canals with a chelating agent of 17% EDTA or Qmix 2in1 for 60 s
Final rinse of root canal with sterile saline
Dry root canal with paper points

Induction of bleeding

Stir periapical tissue with a bent k-file (for example size #25) 3 mm through the root apex to induce bleeding If you wish to use a BCR approach, wait for blood to fill the root canals up to the level of the cementoenamel junction. If you wish to attempt to use PRP or PRF to revascularize the root canal, you should allow an extra 30 min to use phlebotomy to obtain the patient's own blood from a vein in their arm, and to centrifuge it using

a PRP or PRF kit before placing the PRP or PRF into the root canal.

Angiogenesis is defined as the sprouting and dividing of existing vessels to establish new vessels (Bergers & Song 2005). For CF-RET cases, angiogenesis is the process of how vital tissues repopulate in the canal space. Revascularization is not an optimal term for this process. Neo-vascularization is more suited for the revitalization of the tissue in the canal after CF-RET.[19]

The collagen matrix is trimmed into a diameter slightly larger than the coronal part of the root canal. Insert bioabsorbable collagen scaffolds using forceps' to lightly pack the root canal space from the apex to the cementoenamel junction.

Seal root canal orifice with a 2 mm thick layer of white MTA placed in contact with the scaffolds. Capping material should be approximately 2mm underneath the CEJ.

The light cure glass ionomer layer should be at least 3~4mm over the capping material.

Restore tooth with composite resin permanent restoration and check occlusion.

The patients should be reviewed at 3 months, 6 months,12 months, and yearly for a total of 5 years for regular clinical (vitality) and radiographic (root development) examinations.

CBCT is highly recommended for initial evaluation and follow up visits.

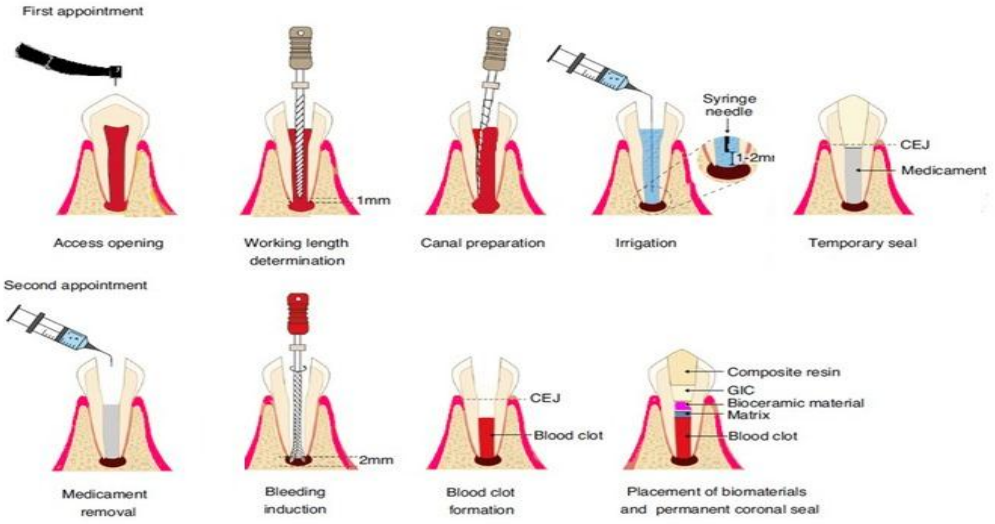

Figure 1: The treatment procedure of Regenerative Endodontic Procedures (REPs).

Antibiotic paste

Approximately 50 percent of root canal peripherals and ramifications may remain uninstrumented during preparation of the root canal. In this condition, the remaining necrotic tissues may act as a nutrition source for the surviving bacteria.[8] Exacerbation of the problem results due to improper cleaning and disinfection of the root canal space. In such cases, manual preparation and irrigation alone will be of no help. The treatment outcome mostly depends upon the correct selection and application of the proper intracanal disinfectant along with the proper choice of medicament.[7] Root canal medicaments, particularly antibiotics, have steadily revealed their crucial importance and key role in achieving positive outcomes as an adjunct to clinical therapy.[7] TAP is a combination of ciprofloxacin, metronidazole and minocycline. Metronidazole, as a nitroimidazole compound, is particularly toxic to anaerobes and is considered an antimicrobial agent against protozoa and anaerobic bacteria. Minocycline is bacteriostatic and shows activity against gram-positive and gram-negative bacteria. It also causes an increase in the amount of interleukin-10, which is an inflammatory cytokine. Moreover, ciprofloxacin — as a synthetic fluoroquinolone — possesses fast bactericidal action and exhibits high antimicrobial activity against gram-negative bacteria, whilst limited activity against gram-positive ones.[8] This mix is potently active against a wide range of bacteria, be it obligatory or facultative, gram-positive or gram-negative, allowing the site to heal. It aids in disinfecting and sterilising the root canal system by making the area free of microbial colonization.[7]

ROLE OF TAP IN REGENERATIVE ENDODONTICS

As it has an antimicrobial effect when used in the root canal, it shows a dual effect - first by acting against *Enterococcus faecalis*, which is the most prevailing microbe in the root canal region, and next by bringing in the stem cells, followed by their proliferation, which helps expand the root length.

ADVERSE EFFECTS

Failed cases are primarily attributed to inadequate removal of biofilm possibly due to minimal instrumentation or inadequate disinfection. Failures were also associated with reinfection of the root canal system, which could also be attributed to failed restorations allowing coronal leakage.[5]

Cell based regenerative endodontic procedures (CB-REPs)

Cell-based REP consists of the implantation of autologous or exogenous DPSC inside the root canal, so that they proliferate and differentiate in the different cellular phenotypes of the dental pulp.[20] The transplanted cells have been removed from the host (autologous) or from other individuals (allogenic) and may have been either minimally processed (separation from tissues) or grown in cultures to expand their numbers.[21] CB-RET is similar to the general understanding of tissue engineering concepts that adopts cell-based therapies. This approach requires a cell source delivered into the host for tissue to regenerate to its original or close to its original state.

Stem cell sources for pulp/dentin engineering and regeneration

To date, 5 different human dental stem/progenitor cells have been isolated and characterized: dental pulp stem cells (DPSCs), stem cells from exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs), stem cells from apical papilla (SCAP), and dental follicle progenitor cells (DFPCs). These post-natal populations have mesenchymal-stem-cell-like (MSC) qualities, including the capacity for self-renewal and multilineage differentiation potential.[12]

Different subpopulations of DPSCs have been identified and used for specific regenerative purposes. A highly angiogenic subfraction of side population cells, CD31−/CD146−, has been isolated from porcine dental pulp expressing CD34 and receptor for vascular endothelial growth factor-2 (VEGFR2), which are similar to endothelial progenitor cells. These cells have MSC properties as well as angiogenic potential demonstrated by mouse hind limb ischemia study models.

DPSCs in the dog root canal after pulpectomy resulted in complete pulp regeneration including nerves and vasculature by day 14, followed by new dentin formation along the dentinal wall by day 35.[21]

From the series of large animal studies, CB-REP has been reported to be capable of complete regeneration of pulp tissue in empty canals with newly deposited dentine-like mineral along the canal wall and/or formation of dentine-bridge-like mineral under the coronal restoration. A layer of odontoblast-like cells was also observed adjacent to the newly produced dentine-like mineral. Thus, CB-RET currently appears to be able to regenerate pulp and dentine in animal models, although challenges lay ahead including absence of dentinal tubule formation and difficulty in dealing with smaller canals due to issues of angiogenesis and vasculogenesis.[19]

In the study by Xuan et al. (2018), the age of the patients ranged from 7 to 12 years. All teeth were traumatized immature permanent teeth diagnosed with pulp necrosis and apical periodontitis. Autologous DPSC aggregates from primary teeth were implanted into the pulpectomized experimental teeth to regenerate the pulp–dentine complex. The stem cell implanted teeth were followed up for 24 months. Radiographic examination indicated continued root maturation. Histological examination of one extracted experimental tooth due to a further traumatic injury revealed regeneration of dental pulp tissue containing an odontoblast layer, connective tissue and blood vessels similar to normal dental pulps.[12]

Cell-based regenerative endodontics is still at the stage of clinical trial. The American Association of Endodontists (AAE) (2018) and European Society of Endodontology (ESE) (2016) have not yet recommended autologous stem cell transplantation in clinical regenerative endodontics, because it involves stem cell isolation, ex vivo expansion, good manufacturing practice facilities, stem cell banks, government regulatory issues, clinician's skill, chair-side assistant's training and comparatively high cost.[19]

Isolation and culturing

DPSCs were isolated from freshly extracted sound third molars the surfaces of the freshly extracted teeth were cleaned and cut at the cementoenamel junction using a sterile fissure bur to reveal the pulp chamber. After gently separating the pulp tissue from the crown and root, it was digested in a solution containing 3 mg/mL collagenase type I and 4 mg/mL dispase for 1 h at 37^{o}C. Then, the cells were passed through a 70-mm strainer to obtain single-cell suspensions. These cells were seeded in 75-cm^{2} culture flasks containing a-minimum essential medium (a-MEM) supplemented with 15% fetal bovine serum, L-ascorbic acid-2-phosphate, 100U/mL penicillin-G, 100 mg/mL streptomycin, and 0.25mg/mL fungizone and cultured under 5% CO2 at 37^{o}C.

Characterization of DPSCs

Before using the DPSCs for experiments, the ''stemness'' of the freshly isolated cells was assessed by flow cytometric analysis of the expression of mesenchymal stem cell markers CD73, CD90, CD105, STRO-1, and hematopoietic marker CD45.

Procedure

The roots of freshly extracted human teeth were cleaned and shaped using rotary instruments These root fragments were soaked at room temperature in 17% ethylenediamine tetraacetic acid (EDTA) for 10min and

then in 19% citric acid for 1 min to remove the smear layer and subsequently treated with betadine for 30min and 5.25% NaOCl for 10–15min to remove the organic component, the debris originating from pulp tissue and microorganisms. The root canal space of the root is loaded with stem cells and coronal end of the root is sealed with MTA.[22]

CONCLUSION

RET is able to eliminate patient's clinical symptoms/signs and resolve apical periodontitis, which is the primary goal of endodontic therapy.[5]

However, unpredictable root maturation of REPs is a major concern raised in the current literature, and evidences suggest that true regeneration of pulp–dentin complex does not occur after REPs. In recent years, the strategies of stem cell transplantation is drawing dramatic attention due to their potential to achieve organized dental pulp regeneration. Pulp/dentin regeneration has been reported in animal studies using exogenously transplanted dental stem cells Despite the excellent effects in resolution of apical lesion, the outcomes of pulp regeneration by REPs are still unpredictable. Stem cells transplantation is currently proposed as the potential ways to regenerate true pulp tissues with scientific validity. However, prospective clinical trials and histological evaluations are necessary to identify their applications in clinical translation, making them achievable and predictable in dental practice.[1]

REFERENCES

1. Wei, X., Yang, M., Yue, L. et al. Expert consensus on regenerative endodontic procedures. Int J Oral Sci, 2022; 14: 55.
2. Saoud TM, Zaazou A, Nabil A, Moussa S, Lin LM, Gibbs JL. Clinical and radiographic outcomes of traumatized immature permanent necrotic teeth after revascularization/revitalization therapy. J Endod., 2014; 40(12): 1946-52.
3. Yang N, Yang W, Shen R, Zhang S, Ma T, Liu Y. In vitro and in vivo evaluation of iRoot BP Plus as a coronal sealing material for regenerative endodontic procedures. Clin Oral Investig, 2024; 28(1): 70.
4. Arshad S, Tehreem F, Rehab Khan M, Ahmed F, Marya A, Karobari MI. Platelet-Rich Fibrin Used in Regenerative Endodontics and Dentistry: Current Uses, Limitations, and Future Recommendations for Application. Int J Dent, 2021; 2021: 4514598.
5. Kim SG, Malek M, Sigurdsson A, Lin LM, Kahler B. Regenerative endodontics: a comprehensive review. Int Endod J, 2018; 51(12): 1367-1388.
6. Yan H, De Deus G, Kristoffersen IM, Wiig E, Reseland JE, Johnsen GF, Silva EJNL, Haugen HJ. Regenerative Endodontics by Cell Homing: A Review of Recent Clinical trials. J Endod, 2023; 49(1): 4-17.
7. Malu K, Khubchandani M. Triple Antibiotic Paste: A Suitable Medicament for Intracanal Disinfection. Cureus, 2022; 14(9): e29186.
8. Parhizkar A, Nojehdehian H, Asgary S. Triple antibiotic paste: momentous roles and applications in endodontics: a review. Restor Dent Endod, 2018; 43(3): e28.
9. Preetham HS, Kumar NK, Brigit B, Swathisha A, Shylaja V. Quantitative assessment of transforming growth factor-β1 release from dentin matrix upon conditioning with ethylene diamine tetra-acetate, doxycycline hydrochloride, and propolis: An in vitro study. J Conserv Dent Endod, 2023; 26(5): 564-568.
10. Widbiller M, Galler KM. Engineering the Future of Dental Health: Exploring Molecular Advancements in Dental Pulp Regeneration. Int J Mol Sci, 2023; 14: 24(14): 11453.
11. Rosa V, Botero TM, Nör JE. Regenerative endodontics in light of the stem cell paradigm. Int Dent J, 2011; 61: 1(Suppl 1): 23-8.
12. Huang GT, Gronthos S, Shi S. Mesenchymal stem cells derived from dental tissues vs. those from other sources: their biology and role in regenerative medicine. J Dent Res, 2009; 88(9): 792-806.
13. Abdelaziz H, Mahran AH, Elsewify T. Osteogenic differentiation and proliferation of apical papilla stem cells using nanoparticles of Neo MTA and bioactive glass. Saudi Dent J, 2024; 36(1): 134-139.
14. López-García S, Aznar-Cervantes SD, Pagán A, Llena C, Forner L, Sanz JL, García-Bernal D, Sánchez-Bautista S, Ceballos L, Fuentes V, Melo M, Rodríguez-Lozano FJ, Oñate-Sánchez RE. 3D Graphene/silk fibroin scaffolds enhance dental pulp stem cell osteo/odontogenic differentiation. Dent Mater, 2024; 40(3): 431-440.
15. Caviedes-Bucheli J, Muñoz-Alvear HD, Lopez-Moncayo LF, Narvaez-Hidalgo A, Zambrano-Guerrero L, Gaviño-Orduña JF, Portigliatti R, Gomez-Sosa JF, Munoz HR. Use of scaffolds and regenerative materials for the treatment of immature necrotic permanent teeth with periapical lesion: Umbrella review. Int Endod J, 2022; 55(10): 967-988.
16. Murray PE. Review of guidance for the selection of regenerative endodontics, apexogenesis, apexification, pulpotomy, and other endodontic treatments for immature permanent teeth. Int Endod J, 2023; 56(2): 188-199.
17. Bartaw RT, Eid MH, Gawad RYAA, Samad AMA. Discoloration after revascularization using calcium phosphosilicate-based bioceramic versus mineral trioxide aggregate in necrotic immature permanent anterior teeth: A Randomized clinical trial. J Conserv Dent Endod, 2024; 27(3): 293-304.
18. Tawfeek HA, El-Bardissy AA, Abou El-Yazeed M, Youssef R, Abd Alsamad AM. Clinical and radiographic evaluation of NeoMTA versus conventional white mineral trioxide aggregate in revascularization of non-vital immature permanent

anterior teeth (A randomized controlled trial). BDJ Open, 2023; 9(1): 17.
19. Lin LM, Huang GT, Sigurdsson A, Kahler B. Clinical cell-based versus cell-free regenerative endodontics: clarification of concept and term. Int Endod J, 2021; 54(6): 887-901.
20. Costa LA, Eiro N, Vaca A, Vizoso FJ. Towards a New Concept of Regenerative Endodontics Based on Mesenchymal Stem Cell-Derived Secretomes Products. Bioengineering (Basel), 2022; 10(1): 4.
21. Huang GT, Al-Habib M, Gauthier P. Challenges of stem cell-based pulp and dentin regeneration: a clinical perspective. Endod Topics, 2013; 28(1): 51-60.
22. Dissanayaka WL, Hargreaves KM, Jin L, Samaranayake LP, Zhang C. The interplay of dental pulp stem cells and endothelial cells in an injectable peptide hydrogel on angiogenesis and pulp regeneration in vivo. Tissue Eng Part A, 2015; 21(3-4): 550-63.