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Biocompatibility and Chemical Safety of Pulp Capping Materials: Conventional vs. Natural Alternatives

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ABSTRACT:

Pulp capping materials play a critical role in preserving pulp vitality following carious or traumatic exposure. Conventional agents such as calcium hydroxide and mineral trioxide aggregate (MTA) are widely used due to their bioinductive properties; however, concerns regarding the release of reactive ions, potential cytotoxicity, and long-term chemical safety persist. Recent advancements in natural and biocompatible alternatives, including apitherapeutic formulations, have aimed to minimize chemical hazards while maintaining regenerative potential. This review summarizes the current evidence on the chemical composition, cytotoxicity profiles, and biocompatibility of conventional and natural pulp capping materials. Emphasis is placed on their leachable components, interaction with pulp tissues, and systemic safety implications. The comparative analysis highlights the potential of natural alternatives in reducing chemical health risks, providing a basis for safer clinical application and guiding future research in the development of innovative, biocompatible pulp protective materials.

1. Introduction

Preservation of pulp vitality is a cornerstone of conservative dentistry, aimed at maintaining tooth structure and preventing pulpal necrosis. Pulp capping procedures are indicated when the pulp is exposed either traumatically or during caries removal, with the objective of promoting healing and reparative dentin formation. Traditionally, calcium hydroxide has been the material of choice due to its bioinductive properties, high alkalinity, and ability to stimulate tertiary dentin formation. Subsequently, mineral trioxide aggregate (MTA) and other calcium silicate-based materials have been developed to overcome the limitations of calcium hydroxide, offering superior sealing ability, biocompatibility, and enhanced mineralization potential.

Despite their widespread clinical use, conventional pulp capping agents are associated with chemical health concerns. Leachable ions, high pH, and the release of potentially cytotoxic components can induce localized inflammation and, in some cases, systemic toxicity. These risks have driven interest in biocompatible and natural alternatives, including apitherapeutic formulations such as propolis and royal jelly, which exhibit antimicrobial and anti-inflammatory properties with minimal chemical hazards. This review critically examines the chemical safety, cytotoxicity, and biocompatibility profiles of conventional and natural pulp capping materials, emphasizing their mechanisms of action, clinical relevance, and implications for patient safety.

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2. Conventional Pulp Capping Materials: Composition, Chemical Safety, and Cytotoxicity

2.1 Calcium Hydroxide

Calcium hydroxide has long been regarded as the gold standard for direct and indirect pulp capping. Its mechanism of action involves the release of hydroxyl ions, which create an alkaline environment (pH 12.5), promoting bacterial inhibition and stimulation of pulp repair. Despite these advantages, several chemical health risks have been documented: a)Local cytotoxicity: High alkalinity can cause necrosis of superficial pulp tissue and prolonged inflammation if not applied carefully. b)Solubility and degradation: Calcium hydroxide exhibits gradual dissolution over time, potentially compromising the long-term seal and exposing pulp to harmful byproducts. c)Leachable ions: Calcium ions may diffuse into periapical tissues, occasionally leading to local tissue irritation.
Studies have demonstrated that while calcium hydroxide promotes dentin bridge formation, the chemical stress imposed on pulpal cells can be significant, particularly in cases of prolonged exposure or in immature teeth with open apexes. [1,2]

2.2 Mineral Trioxide Aggregate (MTA)

MTA, a calcium silicate-based cement, was introduced to overcome the limitations of calcium hydroxide. Its advantages include superior sealing ability, bioactivity, and low solubility.[3] MTA's mechanism involves hydration reactions, producing calcium hydroxide in situ, which promotes dentinogenesis. However, chemical safety considerations remain: a)Heavy metal content: Trace elements such as arsenic and lead have been reported in some MTA formulations, though generally below toxic thresholds. b)Alkalinity and cytotoxicity: Like calcium hydroxide, MTA has high pH but is generally better tolerated by pulp tissue. c)Handling and impurities: Variability in manufacturing can affect chemical composition, potentially influencing biocompatibility.
Several in vitro studies report favorable cytocompatibility with MTA, with lower inflammatory responses compared to calcium hydroxide. Nevertheless, prolonged contact with pulpal tissues may cause mild cytotoxic effects, and the material's long setting time can pose procedural challenges. [4–6][7]

2.3 Biodentine and Other Calcium Silicate-Based Materials

Biodentine, a newer calcium silicate cement, has gained popularity for its improved handling, faster setting time, and high biocompatibility. It releases calcium hydroxide during setting, which promotes reparative dentin formation. Toxicological evaluation indicates: a)Reduced cytotoxicity compared to calcium hydroxide and some MTA formulations. b)Limited heavy metal contamination, though careful selection of commercially available products is recommended. c)Alkaline stress on cells is still present but transient and better tolerated. Biodentine has demonstrated promising results in both in vitro and in vivo studies, making it a safer alternative to conventional pulp capping materials while retaining regenerative potential.[4,8,9]

3. Natural and Biocompatible Pulp Capping Alternatives

In response to the chemical risks associated with conventional materials, research has explored natural products and apitherapeutic agents for pulp capping. These materials emphasize minimal chemical hazards, anti-inflammatory properties, and bioactivity.

3.1 Propolis

Propolis, a resinous product collected by bees, contains flavonoids, phenolic acids, and aromatic compounds. Its application in pulp capping is gaining attention due to: a) Antimicrobial activity: Inhibits common oral pathogens, reducing the risk of infection-induced cytotoxicity. b)Anti-inflammatory effects: Reduces inflammatory cytokine production in pulpal cells. c) Biocompatibility: In vitro studies demonstrate high cell viability and odontogenic potential.
Chemical safety is favorable, with low risk of leaching harmful ions. Variability in composition depending on geographic source is a consideration for standardization. [10–13]

3.2 Royal Jelly

Royal jelly, secreted by honeybees, contains proteins, vitamins, and bioactive compounds that promote tissue regeneration. Its advantages include: a) Promotion of pulp stem cell proliferation and differentiation. b) Minimal chemical toxicity, with negligible leachable harmful substances. c) Immunomodulatory properties,

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aiding in reduced inflammatory response. While evidence is emerging, early in vitro and animal studies indicate its potential as a biocompatible pulp capping material. [14–17]

3.3 Combined Apitherapeutic Formulations

Recent innovations include combining propolis, royal jelly, and natural polymers (like keracollagen) to create bioactive pulp capping agents. Benefits observed in preliminary studies: a) Reduced cytotoxicity compared to calcium hydroxide and some MTA formulations. b) Enhanced reparative dentin formation, comparable to conventional materials. c) Chemical safety: No detectable heavy metals or reactive ions, lowering systemic and local risks.
These natural alternatives show promise for clinical translation, offering regenerative benefits with minimal chemical hazards. [14]

4. Mechanisms of Cytotoxicity and Chemical Interactions with Pulp Tissue

Chemical safety of pulp capping materials depends on their interaction with pulpal cells and extracellular matrix. Key mechanisms include: a) Alkaline stress: High pH from calcium hydroxide or MTA can induce necrosis in superficial pulp tissue but also stimulates reparative dentin formation. b) Leachable ions: Calcium, hydroxyl, and trace heavy metals may diffuse into periapical tissues, potentially eliciting inflammatory or systemic effects. c) Oxidative stress: Some materials generate reactive oxygen species (ROS), causing DNA damage in pulp cells. d) Inflammatory cytokine induction: Certain chemical components can upregulate IL-1β, TNF-α, and other inflammatory mediators, prolonging pulp inflammation.
Natural alternatives mitigate these risks through antioxidant, anti-inflammatory, and immunomodulatory effects, promoting a safer environment for pulp regeneration.

5. Comparative Analysis: Conventional vs. Natural Materials

Parameter	Calcium Hydroxide	MTA/Biodentine	Apitherapeutic Formulations
pH	Very high (12.5)	High (10–12)	Neutral–slightly alkaline
Cytotoxicity	Moderate to high	Low to moderate	Very low
Heavy metal risk	Minimal	Trace (As, Pb)	None
Inflammatory response	Moderate	Low	Very low
Dentin bridge formation	Good	Excellent	Promising (emerging evidence)
Handling/Setting time	Easy, fast	Long setting time	Moderate, customizable
Cost	Low	High	Moderate

From a chemical safety standpoint, natural and apitherapeutic materials present minimal risks while retaining regenerative potential, making them attractive alternatives in modern conservative dentistry.

6. Clinical Implications and Safety Considerations

Material selection: Clinicians should balance regenerative potential with chemical safety, especially in pediatric patients and medically compromised individuals. Standardization: Natural formulations must

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be standardized to ensure reproducible chemical composition and consistent biocompatibility. Handling precautions: Even low-risk materials require appropriate handling to avoid contamination or allergic reactions. Monitoring outcomes: Long-term clinical follow-up is necessary to validate the safety and efficacy of novel pulp capping agents.

7. Future Perspectives and Research Directions

Future research should focus on: a) Standardized toxicological profiling for natural pulp capping agents. b) Integration of nanotechnology to enhance bioactivity while minimizing chemical hazards. c) Advanced in vitro and in vivo models to assess systemic safety of leachable components. d) Clinical trials to establish efficacy, safety, and patient-reported outcomes. e) Combination therapies that synergize natural bioactive compounds with conventional materials to optimize pulp healing. The evolving landscape of biocompatible pulp capping materials highlights the potential to reduce chemical health risks while maintaining regenerative outcomes.

8. Conclusion

Pulp capping materials are essential for preserving pulp vitality and promoting reparative dentin formation. Conventional materials like calcium hydroxide and MTA are effective but carry chemical risks, including cytotoxicity and leachable ions. Natural and apitherapeutic alternatives, such as propolis and royal jelly, offer promising biocompatibility with minimal chemical hazards. Incorporating these safer, bioactive materials into clinical practice may reduce chemical health risks while maintaining regenerative potential, highlighting the importance of continued research and clinical validation.

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