

# Formocresol in Dental Domain: A Review

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**Abstract:** *Formocresol has been widely used in pediatric dentistry since its introduction into dentistry by Buckley in 1904. Since then, a lot of concern has been expressed and discussed about the safety of formocresol use, especially in pediatric dentistry. Concerns have been expressed over the acuity of using products containing formaldehyde in children and alternatives being considered, even though there is no notable data to support the assertion of formocresol toxicity.*

**Keywords:** Formocresol, Devitalization, Pulpotomy, Mutagenicity, DPX (DNA-protein cross-links)

## 1. Introduction

Formocresol has been used in dentistry since 100 years. The biologic approach to pediatric pulp therapy is either devitalization approach of formocresol pulpotomy or pulpectomy. Formocresol was introduced to treat non-vital permanent teeth in the United States by Buckley in 1904. In 1930, Sweet introduced the formocresol pulpotomy technique. Formocresol has subsequently become a popular pulpotomy medicament for primary teeth. Initially, the technique involved five visits. Sweet reduced the number of visits over the years, because of economic and behavior management considerations.<sup>1</sup> Doyle et. al.<sup>2</sup> used a two-visit procedure in their comparison study of formocresol and calcium hydroxide. Spedding et. al.<sup>3</sup> and Redig<sup>4</sup> reported the results of a 5-min formocresol protocol, and since that time, complete mummification has been abandoned by the profession. By 1960, a single visit procedure was advocated.<sup>5</sup> Studies have shown formocresol therapy to have a success rate between 70% and 90%.<sup>6</sup> Histologic results have been variable in contrast to the high clinical success rate. Formocresol is still considered a gold standard by which all new modalities are compared.<sup>7</sup> Formocresol is still used today in full strength by an alarming number of clinicians around the world despite the hundreds of articles that have supported the mutagenicity (genotoxicity), carcinogenicity and toxicity of formaldehyde.<sup>8</sup> Milnes<sup>9</sup>, in a minority perspective, has written that since antibiotics are used frequently and cause death, why should we be concerned about formaldehyde?

### Composition

The composition of Buckley's formocresol is 19% formaldehyde and 35% tricresol, 15% glycerin and 31% water base.<sup>10</sup> Glycerine is added to prevent the polymerization of formaldehyde to para-formaldehyde. The presence of para-formaldehyde causes clouding of the solution.<sup>11</sup> One-fifth dilution of Buckley's formocresol can be prepared by adding 30 ml of Buckley's formocresol, 90 ml of glycerol and 30 ml of water.<sup>10</sup>

### Mechanism of action

It is both a bactericidal and devitalizing agent. It kills and converts bacteria and pulp tissue into inert compounds. Formocresol inactivates the oxidative enzymes in the pulp tissue adjacent to the amputation site. It may also have some effect on hyaluronidase action. Therefore, the protein-

binding properties and the inhibition of the enzymes that can break the pulp tissue down together result in 'fixation' of the pulp tissue by formocresol and render it inert and resistant to enzymatic breakdown.<sup>10</sup> With formocresol as the pulpotomy medicament, a zone of fixation usually is evident where the pulp is in direct contact with the medicament. Coagulation necrosis of the tissue occurs at the amputation site and is supported by the fact that true coagulation necrosis is produced by poisons such as phenol, formaldehyde or mercuric chloride, which denatures the protein of the cells.<sup>12</sup> Further away, where the concentration of formocresol decrease, there is a zone of poor cellular definition and necrosis. Apical to this is a zone of chronic inflammation, which blends into normal tissue.<sup>2</sup>

### Pharmacokinetics of Formocresol

Formocresol applied to vital pulp tissue is absorbed readily into the systemic circulation and distributed throughout the body. A portion of the absorbed formocresol is metabolized and excreted by the kidney and lungs. The remaining formocresol is tissue-bound with the predominant sites of tissue binding - liver, kidney and lungs.<sup>13</sup> The World Health Organization (WHO) has estimated daily consumption of formaldehyde to be approximately 1.5-14 mg/day (mean, 7.8 mg/day).<sup>14</sup>

### Sources of Human Formaldehyde Exposure<sup>15</sup>

- 1) Atmospheric formation: photochemical oxidation of organic compounds.
- 2) Internal combustion engine exhaust.
- 3) Fertilizer production.
- 4) Hydrogen sulfide scavenger: oil operations.
- 5) Household products:
  - Dishwashing liquid.
  - Antiseptics and disinfectants.
  - Carpet cleaners.
  - Carpets.
- 6) Preservatives and embalming solutions.
- 7) Cosmetics (maximum concentration, 0.3% v/v):
  - Fingernail hardeners (maximum concentration, 5% v/v)
- 8) Paper products.
- 9) Adhesives.
- 10) Tire and rubber manufacturing.
- 11) Latex paints.
- 12) Resin production:
  - Phenolic-formaldehyde resin.

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- Urea-formaldehyde resin.
  - Pentaerythritol resin.
- 13) Permanent press fabrics.  
14) Manufactured wood products.  
15) Forest and brush fires.  
16) Tobacco products.

Cresol has poor solubility, so it is assumed that it does not enter systemic circulation. Cresol is highly lipophilic and has been shown to completely destroy cellular integrity. This would allow deeper tissue fixation by the formaldehyde component of formocresol.<sup>16</sup> Benzyl alcohol is a by-product of tricresol oxidation.<sup>17</sup> Benzyl alcohol is oxidized rapidly to benzoic acid, conjugated with glycine in the liver, and excreted as hippuric acid. It has no carcinogenic or mutagenic potential, and the allowable daily intake, as established by WHO is 5 mg/kg.<sup>18</sup>

Histological studies demonstrate the true biological damage after formocresol treatment. Physiologically, with the vascular damage, the balance between osmotic pressure and hydrostatic pressure is disrupted in tissue. As a result, there is absorption of inflammatory fluid insult by pulp tissue and decrease in the osmotic pressure. So, hemostatic balance is re-established. When this occurs, the constricted pulp cavity must dissipate the pressure changes. If this does not occur, pressure necrosis of the pulp occurs. In addition, lymphatic and venous vascular flow from the coronal pulp must dissipate this excess inflammatory fluid. This excess is distributed apically and to regional vascular vessels. Therefore, the local insult results in systemic distribution.<sup>19</sup> Myers et al.<sup>13</sup> and Pashley et al.<sup>20</sup> concluded that <sup>14</sup>C formaldehyde is absorbed systemically from pulpotomy sites and formaldehyde is distributed to distant sites, but did not determine if the labeling of tissues occurred by metabolic incorporation of the <sup>14</sup>C moiety of the labeled formaldehyde into macromolecules.

### Concerns about formocresol

The major concerns that cause seeking for alternatives for formaldehyde derivatives are their potential mutagenicity, carcinogenicity, cytotoxicity, allergenicity and the other possible health hazards which have been attributed to them.<sup>21</sup> National Institute for Occupational Safety and Health in USA states if formaldehyde exposure occurs at a concentration of 20 ppb (parts per billion) or higher, it is instantly dangerous to health and life.<sup>22</sup> Pruhs et al.<sup>23</sup> found a relationship between primary teeth treated with formocresol and enamel defects in the permanent successors.

Exposure of cells to formaldehyde leads to the formation of DPX (DNA-protein cross-links). The most common types of DNA damage induced by formaldehyde are clastogenic lesions, including sister chromatid exchanges (SCEs), micronuclei and chromosomal aberrations, and deletions.<sup>24</sup> DPX development demonstrated only after a prolonged exposure to formaldehyde at specific contact sites such as nasopharynx. A minute quantity used in pulpotomy for few minutes that will produce distant site genotoxicity is not evidence-based.<sup>9</sup>

The investigations of root canal sealers that contain formaldehyde and produce cytotoxicity are not comparable with formocresol pulpotomy studies. Root canal sealer remains in root canal and forms part of restoration and may lead to further release of formaldehyde.<sup>25</sup>

Cancer develops after inhalation of air with large concentrations of formaldehyde. The cancer can occur after a long-term direct contact with susceptible tissues. The toxic effects on initial contact sites like ulceration, hyperplasia and squamous metaplasia may subsequently contribute to cancer. In June 2004, the International Agency for Research on Cancer has reclassified formaldehyde as a known human carcinogen.<sup>26</sup> Formaldehyde was strongly associated with leukemia while generally accepted as a direct cause of nasopharyngeal cancer.<sup>27</sup>

Using human buccal cells, Lu et al.<sup>28</sup> demonstrated DNA breaking and cross-linking activity. He concluded that the results of gaseous formaldehyde with the comet test indicated that formaldehyde increased the possibility of cancer at high levels.

### Current pulpotomy medicaments

Generally, the popular medicaments are ferric sulphate (FS), calcium hydroxide (CH) and mineral trioxide aggregate (MTA).<sup>29</sup> Caceda<sup>30</sup> has developed a contemporary technique that utilises a resin-based composite filling material: fast-setting ZOE Temrex cement, a zinc oxide, and eugenol (oil of cloves) product, but still performs the formocresol pulpotomy.

Increased utilization of indigenous plant medicines in developing countries became a world health organization policy in 1970.<sup>31</sup> Jojoba oil is extracted from ground crushed seeds of *Simmondsia chinensis*. It was introduced in Egypt in 1984 by Food and Agriculture Organization (FAO). Using it as pulp capping material, led to favorable healing pulp response similar to or sometimes better than the response manifested by the exposed pulps capped with calcium hydroxide.<sup>32</sup>

Even a 'green' approach exists, utilising the nineteenth century essential oil cinnamaldehyde, from cinnamon, with promising results in rat pulp capping when compared to formocresol.<sup>33</sup>

Recently, Bahrololoomi et al.<sup>34</sup> examined the success rates of electrosurgery as opposed to formocresol pulpotomy. The failure rate in both groups did not show any statistical significance on the 70 primary molars of 5- to 10-year-olds; evidence that alternatives to medicaments should be examined and studied further.

In 2006, Fuks aptly concluded after examining a review of the pulpotomy literature from 1966-2005, 'More high quality, properly planned prospective studies are necessary...' although noted that MTA is currently the most favourable choice.<sup>35</sup>

## 2. Conclusion

Formocresol, when judiciously used, is unlikely genotoxic or immunotoxic or poses a cancer risk. Contemporary dentists who wish to continue to use formocresol should apply the lowest dose possible for the shortest time possible to obtain the desired effect. When used judiciously, formocresol is a safe medicament. Further studies needed in order to determine alternative pulp therapies with milder medicaments or treatments that are not distributed systemically offer patients a margin of safety from intravascular formocresol distribution to end organs.

## 3. Conflict of interest

The authors confirm that this article content has no conflict of interest.

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