

Cotinus Coggygia Polyphenol Extract in Endodontics: Recent Results of Experimental Study

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ABSTRACT

Background: Endodontic research has always focused on developing methods or endodontic irrigants to remove the bacteria with minimal side effects. Root Canal Persistent Infection microbiome observation advocated the important role of *E. faecalis* in secondary infections. Due to the survival mechanism of resistant endo pathogen - *Enterococcus faecalis*- our research aims to recommend the plant *Cotinus coggygia* Scop. leaves Polyphenolic Extract (CCPE) solutions as an alternative effective antimicrobial endodontic irrigation solution. At the same time, to achieve successful long-term endodontic outcomes, the fluid chemistry of endodontic irrigants represents the most important challenge.

Objectives: The present study aimed to reveal the chemical compatibility of CCPE solution (experimental sample) with the most commonly used irrigants in endodontic practice.

Methods: The evaluation was conducted ex vivo and in vitro by immediately visualizing mixtures of different types of endodontic irrigation solutions.

Results: Chemical Interaction Observation of experimental CCPE solution suggests that cultivated in Georgia, *Cotinus coggygia* Scop. polyphenol extract solution is a chemically compatible and safe endodontic irrigant.

Conclusions: Identified antibacterial activity, unique formulation rich with tannins, and safe interaction with all types of intercanal solutions allow CCPE to provide a uniform irrigation protocol with optimal disinfection effect and maximal safety margins. The in vivo study is in progress, and this novel herbal/bio preparation is recommended as an alternative antimicrobial endodontic irrigant for effective and safe endodontic irrigant for secondary infection prevention.

Keywords: Chemical compatibility; *Cotinus coggygia*; *E. Faecalis*; Endodontic irrigant.

BACKGROUND

Root canal therapy (RCT) eliminates microorganisms from the root canal system and prevents re-infection. One of the most crucial techniques for efficient root canal cleaning and disinfection is root canal irrigation.¹ According to Literature data, the resistance of microbe *Enterococcus faecalis* to the most widely used, "rated" root canal disinfection irrigant - sodium hypochlorite (NaOCl) is a prerequisite for persistent endodontic infection.^{2,3}

In this sense, we recommend the plant *Cotinus coggygia* Scop. polyphenolic extract solutions (CCPE) as alternative herbal/bio antimicrobial endodontic irrigating solution.⁴⁻⁸ The cultivated in Georgia *Cotinus coggygia* Scop. leaves polyphenol extract (CCPE) by the special, patented technology of obtaining biologically active substances was developed at Tbilisi State Medical University (TSMU) Ivel Kutateladze Institute of Pharmacochemistry.⁹ The unique formulation and its purified fraction of various concentrations of aqueous solutions were developed exclusively for endodontic purposes for our research.⁶⁻⁹ Our microbial and safety study established a broad spectrum of antimicrobial activity of even 10% CCPE solution and exhibited the least cytotoxicity.⁶⁻⁸ But as the important part of the irrigation protocol of RCT, the most interesting part of this research step is to determine the chemical interaction of CCPE solution with the most commonly

used irrigants in endodontic practice.¹⁰ Due to the complexity of root canal system morphology and survival mechanism of endo pathogens, the goals of endo irrigation are still complex, including not only antimicrobial, as well as smear layer removal and inorganic and organic tissue-dissolution actions. However, no single irrigant covers all of these functions demanded.¹¹ Thus, irrigation of the canals with different at list two distinct solutions throughout the treatment is beneficial. At the same time, to achieve successful long-term endodontic outcomes, the fluid chemistry of endodontic irrigants represents the most important challenge. Practically all of them, to some extent, have several unfavorable characteristics when combined. The interaction of solutions can be followed by buffering antimicrobial effectiveness and, in some cases, by forming toxic, carcinogenic precipitates. Nowadays, it is known that, during chemical disinfection of the root canal, consecutive application of sodium hypochlorite and chlorhexidine digluconate leads to the formation of an orange-brown precipitate,¹¹ confirmed in our experiment condition (Fig.1). This precipitate is chemically similar to para-chloroaniline (PCA), suspected to have cytotoxic and carcinogenic effects (International Agency for Research on Cancer group 2B)¹² and damages the immune system.¹³ In addition, it is challenging to remove precipitate and can compromise the seal of the obturated canal.¹⁴



Thus, it is paramount to study the chemical reactions/interactions of the experimental CCPE solution with commonly used irrigants (NaOCl, EDTA, CHX, Citric Acid) in the context of chemical compatibility.

FIGURE 1. Brown precipitate formation after consequent use of sodium hypochlorite and chlorhexidine in experimental conditions



The present study aimed to reveal the chemical compatibility of CCPE solution (experimental sample) with the most commonly used irrigants in endodontic practice.

METHODS

The 5ml of experimental 10% CCPE solutions were mixed in glass tubes in a 1:1 ratio with commercially available 5% sodium hypochlorite (NaOCl), 2% chlorhexidine (CHX), 18% ethylenediaminetetraacetic acid (EDTA), 10% citric acid and 95% ethanol at room temperature (230 C) at the preclinical research laboratory of TSMU Ivel Kutateladze Institute of Pharmacochimistry. The tubes with solutions were evaluated visually for color changes, the presence of bubbles, and precipitate formation after being mixed (Fig.2).

FIGURE 2. The visual aspect of the Interaction of CCPE (Cotinus coggygria scop. leaves polyphenolic extract) with NaOCl (sodium hypochlorite), EDTA (ethylenediaminetetraacetic acid), CHX (chlorhexidine), citric acid and ethanol



The evaluation was conducted immediately, after 5 minutes, and after 45 minutes. After that, for the ex-vivo experiment, extracted human teeth were used as a substrate to evaluate the outcome of the interaction of NaOCl, EDTA, CHX, and citric acid. After the tooth was sequentially irrigated with respective irrigants, samples were longitudinally sectioned and observed visually to evaluate the appearance of the mixture in the coronal, middle, and apical thirds. There were no differences in the data compared with the in vitro studies (Fig.3).

FIGURE 3. Ex vivo study of the interaction of CCPE with widely used irrigants



In addition, an ex vivo study revealed that when various irrigants (NaOCl and CHX) are used sequentially in combination to enhance their antimicrobial effect, the precipitation generated in the coronal, middle, and apical thirds has significantly different thicknesses, with a lower rate in the apical third compared to the coronal and middle regions. In the case of CCPE, interaction with any other precipitate irrigant formation was not observed.

RESULTS

Within the limitation of the present study, CCPE, when associated with NaOCl, did not form a toxic, carcinogenic orange-brown precipitate known as parachloroaniline (PCA). Also, no visible precipitate was found in any of the irrigant mixtures tested, except the CCPE and CHX mixture—the mix of CCPE and CHX results in a nondangerous white salty precipitate. Regarding "Iatrogenic Esthetic Endodontics," it must be taken into account that NaOCl violently reacts with organic chemical constituents (biologically active compounds) of CCPE, producing a visible shift to dark color. On the other hand, a mixture of CCPE and ethanol manifests visible translucency and transparency. All the above changes were constant and exhibited instantly after the irrigant's chemical interaction (Tab.1).

TABLE 1. Products formed by the interaction of different types of Irrigants

	Solution 1	Solution 2	Appearance of byproduct
1	5.25% NaOCl	2% CHX	Orange-brown precipitate
2	5.25% NaOCl	17% EDTA	Bubble formation
3	10% CCPE	5.25% NaOCl	Dark solution
4	10% CCPE	2% CHX	White salt precipitate
5	10% CCPE	17% EDTA	Slight yellow-brown solution
6	10% CCPE	95% Ethanol	Transparent, clear solution
7	10% CCPE	0.9% NaCl	Unchanged

Abbreviations: CCPE: cotinus coggygria scop. leaves polyphenolic extract; CHX: chlorhexidine; EDTA: ethylenediaminetetraacetic acid; NaOCl: sodium hypochlorite.

DISCUSSION

Understanding the interaction of various available and commonly used solutions is important for optimal irrigation. The precipitation or discoloration caused by the association of various irrigants can lead to unfavorable endodontic treatment outcomes. To avoid the buffering effect and formation of unfavorable (cytotoxic, carcinogenic) compounds that potentially compromise root canal fillings,¹⁵ current Endodontic Irrigation protocols recommend using intermediate sterile water rinses. Irrigation protocol with multiple irrigation increases chair time and the number of disposable endodontic syringes.¹⁶ Accordingly, Endodontic research must consider refinement of current protocols to achieve easily adaptable, safe, and high-quality cleaning and disinfection of complex root canal system.¹⁷

Respectively, knowing how experimental solutions interact with other proven, commonly used irrigants, chemistry, and characteristics of byproducts can significantly impact designing the procedural guideline. Ultimately, including this experiment step in the suggested solution's overall research is paramount.

CONCLUSIONS

The ex vivo and in vitro study seems encouraging as the antimicrobial 10% CCPE solution (test sample) compatibly blends with lubricants and chelating agents and has no potential to produce dangerous compounds. These results allow a uniform irrigation protocol to achieve an optimal cleansing and disinfection effect with maximal safety margins and discoloration prevention. The in vivo study is in progress for recommending this novel, effective, herbal/bio, safe, biocompatible, and cost-effective preparation for clinical endodontics.

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REFERENCES

1. Arnaldo Castellucci. Endodontics - Volume 1 and 2. EDRA editions. 2022.
2. Haapasalo, M., Shen, Y., Qian, W., & Gao, Y. (2010). Irrigation in endodontics. *Dental Clinics*, 54(2), 291-312.
3. Stuart CH, Schwartz SA, Beeson TJ, Owatz CB. Enterococcus faecalis: its role in root canal treatment failure and current concepts in retreatment. *Journal of endodontics*. 2006; 32: 93-98.
4. Kenan Tunç, Ayşegül Hoş, Bilgen Güneş. Investigation of Antibacterial Properties of Cotinus coggygria from Turkey. Department of Biology, Sakarya University, Sakarya, Turkey Received: 9 October 2012 Accepted: 23 April 2013. *Pol. J. Environ. Stud.* Vol. 22, No. 5 (2013), 1559-1561.
5. Alagl AS, Bedi S and Almas K, Phytosolutions for Enterococcus faecalis in Endodontics: An Update, Oral health and dental management 15(5):332-36, 2016.
6. N. Nizharadze., T. Shavadze, M. Mamaladze, K. Shalashvili, Antimicrobial screening of Cotinus Coggygria Scop. leaves extract for its application in endodontics. *Experimental and Clinical Medicine Georgia*, 2022; (8). <https://doi.org/10.52340/jecm.2022.08.01>.
7. Tamar Shavadze, Natia Nizharadze, Marina Mamaladze, Ketevan Shalashvili, Marine Sulakvelidze, Zh. Novikova, K. Mulkijanian. Comparative safety study of the phenolic constituents of smokebush (Cotinus coggygria) leaves. *Georgian Biomedical News* 2023 <https://www.gbm.org/stomatology>.
8. M. Mamaladze N. Nizharadze T. Shavadze K. Shalashvili. Cultivated in Georgia Cotinus coggygria Scop's Trimli's leaves extract: Study in dentistry. Proceedings of the 1st International Conference on Medicine, Public Health and Biological Science (MPHBS-2016), CASRP Publishing, Tehran, Iran, 18-19 September 2016. DOI:doi.org/10.18869/MPHBS.2016.173.
9. E. Kemertelidze, A. Skhirtladze, K. Shalashvili. Polyphenolic compounds of cultivated Cotinus coggygria leaves. *Proceed. Georg Acad Sci. Chemical Ser.* 2007; 33: 451-460.
10. Prado, M., Júnior, H. M. S., Rezende, C. M., Pinto, A. C., Faria, R. B., Simão, R. A., & Gomes, B. P. (2013). Interactions between irrigants commonly used in endodontic practice: a chemical analysis. *Journal of endodontics*, 39(4), 505-510.
11. Drews, D. J., Nguyen, A. D., Diederich, A., & Gernhardt, C. R. (2023). The Interaction of Two Widely Used Endodontic Irrigants, Chlorhexidine and Sodium Hypochlorite, and Its Impact on the Disinfection Protocol during Root Canal Treatment. *Antibiotics*, 12(3), 589. <https://doi.org/10.3390/antibiotics12030589>.
12. Chhabra RS, Huff JE, Haseman JK, Elwell MR, Peters AC. Carcinogenicity of p-chloroaniline in rats and mice. *Food Chem Toxicol* 1991;29:119-124.
13. Basrani BR, Manek S, Sodhi RN, Fillery E, Manzour A: Interaction between sodium hypochlorite and chlorhexidine gluconate. *J Endod.* 2007, 33:966-9. [10.1016/j.joen.2007.04.001](https://doi.org/10.1016/j.joen.2007.04.001).
14. Bui TB, Baumgartner JC, Mitchell JC: Evaluation of the interaction between sodium hypochlorite and chlorhexidine gluconate and its effect on root dentin. *J Endod.* 2008, 34:181-5. [10.1016/j.joen.2007.11.006](https://doi.org/10.1016/j.joen.2007.11.006).
15. Boutsioukis, C., & Arias-Moliz, M. T. Present status and future directions - irrigants and irrigation methods. *International endodontic journal*, 2022, 55, 588-612. <https://doi.org/10.1111/iej.13739>.
16. Gomes BPPA, Aveiro E, Kishen A. Irrigants and irrigation activation systems in Endodontics. *Braz Dent J.* 2023 Jul-Aug;34(4):1-33. doi: 10.1590/0103-6440202305577. PMID: 37909632; PMCID: PMC10642269.
17. Zehnder M. (2006). Root canal irrigants. *Journal of endodontics*, 32(5), 389-398. <https://doi.org/10.1016/j.joen.2005.09.014>.