

Content available at: <https://www.ipinnovative.com/open-access-journals>

IP Indian Journal of Conservative and Endodontics

Journal homepage: <https://www.ijce.in/>

Review Article

Triple antibiotics: A synergistic approach to combating infection

Anukriti Kumari¹, Hemant Sawhney^{1*}, Ritik Kashwani², Geetanjali Gupta³, SJ Das³¹Dept. of Oral Medicine and Radiology, School of Dental Sciences, Sharda University, Greater Noida, Uttar Pradesh, India²Ex -Junior Resident at School of Dental Sciences, Sharda University, Greater Noida, Uttar Pradesh, India³Dept. of Periodontology, Kalka Dental College & Hospital, Meerut, Uttar Pradesh, India

ARTICLE INFO

Article history:

Received 12-10-2023

Accepted 20-11-2023

Available online 16-12-2023

Keywords:

Triple Antibiotic Paste

Metronidazole Ciprofloxacin

Minocycline

Odontogenic Infections

ABSTRACT

The utilization of Triple Antibiotic Paste (TAP) in dentistry has emerged as a significant development in endodontic and odontogenic infection management. With increasing cases of odontogenic infections, particularly in the context of the complex root canal anatomy, the selection of appropriate medicaments and disinfectants has become imperative. (1) In situations where conventional manual preparation and irrigation prove inadequate, TAP stands out as an intracanal disinfectant comprising a combination of three antibiotics, exhibiting a synergistic antimicrobial effect against a wide spectrum of microorganisms. This review outlines the multifaceted applications of TAP in dentistry, from its composition and clinical utility to its potential in preserving the vitality of diseased pulp. It also acknowledges the limitations and drawbacks associated with TAP's application, emphasizing the need for precise administration. Furthermore, it discusses TAP's role in primary teeth, expanding its scope beyond conventional endodontics. This research investigation explores the latest insights and considerations surrounding the "triple antibiotic paste" (TAP) and its applications in the field of dentistry, with a particular focus on endodontics.

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprint@ipinnovative.com

1. Introduction

The use of triple antibiotic pastes in endodontics became popular in the early 2000s. Dr. Mitsuhiro Tsutsui, a Japanese endodontist, is often credited with pioneering its use.¹ He published a study in 1996 in this study, he discussed the use of antibiotic pastes, including triple antibiotic paste, to treat infected root canals. His work laid the foundation for the use of this material in endodontics.² TAP, comprised of a trio of antibiotics - ciprofloxacin, metronidazole, and minocycline has attracted substantial attention especially in the realm of endodontic treatments.³ The utility spans of TAP range from essential pulp therapy to the recently introduced regeneration and revascularization protocols.⁴

Studies have unveiled the paste's ability to effectively exterminate microorganisms within the root canal, creating an optimal matrix for subsequent treatments.⁵ This unique combination exhibits remarkable efficacy in eradicating a diverse range of obligatory and facultative gram-positive and gram-negative bacteria, fostering a milieu conducive to healing.⁶ In cases involving regeneration protocols, TAP plays a pivotal role in establishing a sterile and disinfected root canal system, enabling new tissue infiltration and growth within the radicular area. Moreover, TAP serves as a facilitator for a spectrum of other essential and desired treatments.⁷

TAP constitutes a pharmaceutical synergy comprising ciprofloxacin, metronidazole, and minocycline, each endowing the formulation with distinctive antimicrobial attributes. Metronidazole, a potent nitroimidazole, emerges

* Corresponding author.

E-mail address: hemant.sawhney@sharda.ac.in (H. Sawhney).

Table 1: Composition and indication of triple antibiotic paste

Ciprofloxacin	Metronidazole	Minocycline
Composition: C ₁₇ H ₁₄ FN ₃ O ₃	Composition: CHN ₃ O ₃	Composition: C ₂₃ H ₂₇ N ₃ O ₇
Indication	Indication	Indication
<ul style="list-style-type: none"> • Urinary Tract Infections (UTIs) • Respiratory Tract Infections • Skin and Soft Tissue Infections • Gastrointestinal Infections. • Bone and Joint Infections • Infectious Diarrhea • Typhoid Fever • Anthrax Exposure 	<ul style="list-style-type: none"> • Bacterial Infections • Protozoal Infections • Dental Infections • H. pylori Infection • Rosacea 	<ul style="list-style-type: none"> • Acne • Respiratory Tract Infections • Urinary Tract Infections (UTIs) • Skin and Soft Tissue Infections • Sexually Transmitted Infections (STIs): • Lyme Disease • Malaria

as a focal agent, exerting heightened toxicity selectively against anaerobic microorganisms. This positions metronidazole as a pivotal combatant against protozoa and anaerobic bacterial strains.⁸ Minocycline exhibits bacteriostatic properties and is effective against both gram-positive and gram-negative bacteria. Additionally, it induces an elevation in interleukin-10 levels, an inflammatory cytokine.⁹ Furthermore, ciprofloxacin, a synthetic fluoroquinolone, demonstrates rapid bactericidal action with strong antimicrobial efficacy against gram-negative bacteria, while its impact on gram-positive bacteria is more restricted. It's important to note that ciprofloxacin faces resistance from many anaerobic bacteria.¹⁰ Consequently, it is frequently paired with metronidazole in the treatment of mixed infections to address its restricted scope. Thus, the TAP combination demonstrates efficacy against gram-negative, gram-positive, and anaerobic bacteria, making it effective against a wide range of microorganisms.¹¹ (Table 1)

2. History

Dr. Herbert S. Grossman, a prominent figure in the field of endodontics, did indeed contribute significantly to the development of intracanal medicaments in the mid-20th century. In 1951, he introduced a poly-antibiotic formula known as "PBSC," which was a paste used in endodontics.¹² PBSC stands for "Penicillin, Bacitracin, Streptomycin, and Caprylate Sodium." This medicament was used to treat infected root canals and aimed to combat various microorganisms responsible for endodontic infections. The combination of these antibiotics was intended to provide a broad-spectrum antimicrobial effect.¹³ The inclusion of Caprylate Sodium likely served as a component to enhance the paste's stability and compatibility. Dr. Grossman's work significantly contributed to the development of medicaments for endodontic therapy, and his introduction of PBSC represented an important milestone in the field of endodontics. His contributions have had a lasting impact on the way dental professionals approach the treatment of infected root canals.¹⁴

The poly-antibiotic formula PBSC, comprising Penicillin, Bacitracin, Streptomycin, and Sodium Caprylate, represented a significant milestone in the history of endodontics. Each antibiotic component was carefully chosen for its efficacy against specific types of bacteria and yeasts. While PBSC demonstrated therapeutic results, it had notable limitations, particularly its ineffectiveness against anaerobic microbes, which are key players in endodontic disorders. Furthermore, concerns regarding the risk of sensitization and penicillin allergies prompted the United States Food and Drug Administration (FDA) to ban PBSC for endodontic use in 1975.¹⁵ regulatory action aimed to safeguard patient well-being and encouraged the exploration and development of alternative intracanal medicaments in the field of endodontics, ultimately leading to safer and more effective treatment options for dental professionals and better outcomes for patients. In 2006, the American Association of Endodontics issued an article addressing the use of antibiotics in managing root canal bacteria, which are recognized as key factors in the development and progression of pulpitis. A noteworthy contribution to this field is the Triple Antibiotic Paste (TAP), a specialized antibiotic combination formulated for the purpose of endodontic revitalization¹⁶ and their research team introduced TAP after extensive investigations into its efficacy in eradicating microorganisms from the root canal system. Given its robust antimicrobial properties, TAP offers a wide range of applications within the realm of endodontics, particularly in the treatment of necrotic pulp in teeth with open apices. This advancement has played a significant role in shaping modern endodontic treatment strategies, offering enhanced prospects for successful outcomes in complex cases.¹⁷

3. Composition

The composition of TAP may vary depending on the specific formulation used by a dentist or endodontist. However, in a typical TAP, you might find something like:

Ciprofloxacin: 500mg

Metronidazole: 500mg

Minocycline: 100mg

Vehicle (e.g., propylene glycol or another suitable carrier) to make a paste.

4. Method of Mixing

These two methods describe the proportion of the antibiotics used in TAP, and they offer flexibility based on the clinical situation and the dentist's preference:

4.1. Method (i)

Mixing ciprofloxacin, metronidazole, and minocycline in equal proportions of 1:1:1.

The composition would be ciprofloxacin 33%, metronidazole 33%, and minocycline 34%.

The paste is concentrated at a range of 0.1-1.0 mg/ml using macrogol and propylene glycol as a vehicle.

4.2. Method (ii)

Mixing ciprofloxacin, metronidazole, and minocycline in proportions of 1:3:3.

The composition would be ciprofloxacin 10%, metronidazole 30%, and minocycline 30% and 30 % Carrier substance: (e.g., sterile saline, propylene glycol).

5. Components

The common components of TAP include:

5.1. Ciprofloxacin

Ciprofloxacin is a broad-spectrum antibiotic effective against a wide range of bacteria. Ciprofloxacin is a versatile antibiotic belonging to the fluoroquinolone class, widely used in the treatment of various bacterial infections.¹ Known for its broad-spectrum effectiveness, it targets a diverse range of both gram-positive and gram-negative bacteria. Ciprofloxacin is commonly prescribed to combat infections affecting the urinary tract, respiratory system, skin and soft tissues, bones and joints, and the gastrointestinal tract.¹⁰ It also plays a critical role in post-exposure prophylaxis against anthrax and plague. Its mode of action involves inhibiting enzymes vital for bacterial DNA replication, rendering the bacteria incapable of proliferation. Ciprofloxacin is available in oral and intravenous formulations, providing flexibility in treating infections of differing severities.⁴ As with any medication, it may have side effects and interactions with other drugs, underscoring the importance of responsible use under the guidance of a healthcare professional. Adhering to the prescribed regimen and completing the full course is crucial for effective treatment while minimizing the risk of antibiotic resistance. It is one of the key antibiotics used in TAP to target various bacterial species responsible for endodontic infections.^{6,7}

5.2. Metronidazole

Metronidazole is a versatile antibiotic and antiprotozoal medication with a broad spectrum of applications in the realm of infectious diseases. Its effectiveness extends to bacterial infections of the respiratory tract, skin, and various body systems. What sets metronidazole apart is its exceptional efficacy against anaerobic bacteria, thriving in low-oxygen environments, making it particularly well-suited for infections in the gastrointestinal tract and abdominal regions. Beyond its antibacterial role, metronidazole serves as a reliable treatment for protozoal infections, addressing conditions like trichomoniasis, giardiasis, and amebiasis. Metronidazole is an antibiotic effective against anaerobic bacteria, which are commonly found in dental infections, including root canals. It is another important component of TAP and helps combat anaerobic microorganisms.^{12,13,15}

5.2.1. Minocycline

Minocycline is a tetracycline antibiotic that is effective against both aerobic and anaerobic bacteria. It is used in TAP to provide a broad spectrum of bacterial coverage.

Vehicle: TAP is mixed with a suitable vehicle or carrier to create a paste that can be easily applied within the root canal. Commonly used vehicles include propylene glycol, sterile water, polyethylene glycol, or another carrier that helps create a homogenous paste.¹⁴

6. Conclusion

The utilization of Triple Antibiotic Paste (TAP) in dentistry marks a significant advancement in the management of odontogenic infections, particularly in the context of complex root canal anatomy. As cases of odontogenic infections increase, the need for suitable medicaments and disinfectants becomes paramount. TAP, an intracanal disinfectant comprising ciprofloxacin, metronidazole, and minocycline, offers a potent synergistic antimicrobial effect against a broad spectrum of microorganisms. Its multifaceted applications in dentistry span from essential pulp therapy to innovative regeneration and revascularization protocols, facilitating sterile root canal systems and promoting tissue growth. However, TAP's application requires precise administration, and its role in primary teeth expands its scope beyond traditional endodontics. The history of intracanal medicaments, including the early use of PBSC, laid the foundation for TAP's development. The ban on PBSC in 1975 led to the exploration of safer alternatives, culminating in TAP's introduction, which significantly enhanced endodontic treatment strategies. The composition of TAP can vary slightly, with different proportions of antibiotics, but its core components remain ciprofloxacin, metronidazole, and minocycline. These antibiotics work in synergy to

combat a wide range of microorganisms. The use of TAP in endodontics should be conducted by trained dental professionals, adhering to established guidelines and tailored to individual patient needs and clinical circumstances. TAP stands as an asset in the dental field, offering an effective approach to combat infections and promote dental health.

7. Conflict of Interest

None.

8. Source of Funding


None.

References

1. Parhizkar A, Nojehdehian H, Asgary S. Triple antibiotic paste: momentous roles and applications in endodontics: a review. *Restor Dent Endod.* 2018;43:e28. doi:10.5395/rde.2018.43.e28.
2. Vijayaraghavan R, Mathian V, Sundaram A, Karunakaran R, Vinodh S. Triple antibiotic paste in root canal therapy. *J Pharm Bioallied Sci.* 2012;4(Suppl 2):230–3.
3. Taneja S, Kumari M. Use of triple antibiotic paste in the treatment of large periradicular lesions. *J Investig Clin Dent.* 2012;3(1):72–6.
4. Parhizkar A, Nojehdehian H, Asgary S. Triple antibiotic paste: momentous roles and applications in endodontics: a review. *Restor Dent Endod.* 2018;43(3):e28. doi:10.5395/rde.2018.43.e28.
5. Kashwani R, Bahadur R, Kumari A, Kumar S. Fangs, fur, and dental health: exploring the intricate connection between human oral health and interactions with animals. *J Popul Ther Clin Pharmacol.* 2023;13(2):534–9.
6. Khan AM, Gangoo IKA, Ali NA, Khan M, Javed MQ, Alattas MH, et al. The Effect of Calcium Hydroxide, Triple Antibiotic Paste and Chlorhexidine on Pain in Teeth with Symptomatic Apical Periodontitis: A Randomised Controlled Trial. *Int J Environ Res Public Health.* 2023;20(4):3091. doi:10.3390/ijerph20043091.
7. Kumar NK, Brigit B, Annapoorna BS, Naik S, Merwade S, Rashmi K, et al. Effect of triple antibiotic paste and calcium hydroxide on the rate of healing of periapical lesions: A systematic review. *J Conserv Dent.* 2021;24(4):307–13.
8. Prather BT, Ehrlich Y, Spolnik K, Platt JA, Yassen GH. Effects of two combinations of triple antibiotic paste used in endodontic regeneration on root microhardness and chemical structure of radicular dentine. *J Oral Sci.* 2014;56(4):245–51.
9. Tredoux S, Arnold R, Buchanan G. Triple antibiotic paste in the treatment of a necrotic primary molar: a case report. *South Afr Dent J.* 2018;73(10):624–6.
10. Ghabraei S, Bolhari B, Sabbagh MM, Afshar MS. Comparison of Antimicrobial Effects of Triple Antibiotic Paste and Calcium Hydroxide Mixed with 2% Chlorhexidine as Intracanal Medicaments Against *Enterococcus faecalis* Biofilm. *J Dent (Tehran).* 2018;15(3):151–60.
11. Omaia M, Negm M, Nashaat Y, Nabil N, Othman A. The effect of triple antibiotic paste as an intracanal medication with an anti-inflammatory drug on post-operative pain of asymptomatic uniradicular necrotic teeth: a double blind randomized clinical trial. *F1000Res.* 2022;11:1687. doi:10.12688/f1000research.19699.1.
12. Aujla H. A Review on Triple Antibiotic Paste as an antimicrobial agent in Endodontics. *Int J Dent Med Sci Res.* 2022;4(1):355–9.
13. Chouchene F, Masmoudi F, Baaziz A, Maatouk F, Ghedira H. Antibiotic Mixtures in Noninstrumental Endodontic Treatment of Primary Teeth with Necrotic Pulp: A Systematic Review. *Int J Dent.* 2021;p. 5518599. doi:10.1155/2021/5518599.
14. Jain P, Yeluri R, Garg N, Mayall S, Rallan M, Gupta S, et al. A comparative evaluation of the effectiveness of three different irrigating solution on microorganisms in the root canal: An invivo study. *J Clin Diagn Res.* 2015;9(12):39–42.
15. Prasanti ED, Margono A, Djauharie N. Effect of triple antibiotic paste, calcium hydroxide, ledermix® on viability of pulp mesenchymal stem cells. *Int J Appl Pharm.* 2019;11:49–53. doi:10.22159/ijap.2019.v11s1.164.
16. Akgun OM, Altun C, Guven G. Use of triple antibiotic paste as a disinfectant for a traumatized immature tooth with a periapical lesion: a case report. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;108(2):e62–5. doi:10.1016/j.tripleo.2009.04.015.
17. Acharya S, Gurunathan D, Singh B. Triple Antibiotic Paste-Roles And Applications In Pediatric Dentistry. *J Pharm Negat Results.* 2022;13:1375–8. doi:10.47750/pnr.2022.13.S10.159.

Author biography

Anukriti Kumari, Junior Resident  <https://orcid.org/0009-0001-8434-741X>

Hemant Sawhney, Associate Professor  <https://orcid.org/0000-0002-0862-0760>

Ritik Kashwani, Private Practitioner

Geetanjali Gupta, Post Graduate Student

SJ Das, Dean, Professor and Head

Cite this article: Kumari A, Sawhney H, Kashwani R, Gupta G, Das SJ. Triple antibiotics: A synergistic approach to combating infection. *IP Indian J Conserv Endod* 2023;8(4):189-192.