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Sulfamethoxazole in Dental Practice: Chemistry, Pharmacology, and Clinical Relevance - A Review

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Abstract:

The article investigate the role of sulfamethoxazole in relieving and alleviating dental pain and discusses its broader implications in clinical practice. Sulfonamide antibiotic functions by inhibiting folic acid synthesis in the bacteria, which is paramount for DNA replication and cell viability. This characteristic goes a long way in supporting its efficacy against infections by different species of bacteria In dentistry, the scope of its application includes treating odontogenic infections, prophylactic measures during oral procedures, and management of systemic complications arising from dental disease .Its dual activity against both Gram-positive and Gram-negative bacteria makes it an important alternative, particularly in cases of resistance to conventional antibiotics. This study highlights the role of sulfamethoxazole in treating dental pain. The active ingredient in the drug, with its unique chemical structure, exerts a therapeutic effect on improving dental health. This study provides an overview of the drug's pharmacological properties, therapeutic application, and clinical outcomes, reinforcing the continued importance of sulfamethoxazole in modern dental practice.

Keywords: Sulfamethoxazole, Dental Diseases, Pharmaceuticals, dental drugs , sulfonamide antibiotic functions.

السلفاميثوكسازول في طب الأسنان: الكيمياء، وعلم الأدوية، والأهمية السريرية

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مستخلص:

تتناول هذه المقالة دور السلفاميثوكسازول في تخفيف وتسكين الام التهاب الأسنان، وتناقش آثاره الأوسع نطاقًا في الممارسة السريرية. يعمل هذا المضاد الحيوي من فئة السلفونواميدات عن طريق تثبيط تخليق حمض الفوليك في البكتيريا، وهو أمر بالغ الأهمية لتضاعف الحمض النووي وبقاء الخلية. تُساهم هذه الخاصية بشكل كبير في فعاليته ضد العدوى التي تسببها أنواع مختلفة من البكتيريا. في مجال طب الأسنان، تشمل استخداماته علاج التهابات الأسنان، والتدابير الوقائية أثناء إجراءات الفم، وإدارة المضاعفات الجهازية الناجمة عن أمراض الأسنان. إن التأثير المزدوج لهذا العلاج ضد البكتيريا موجبة وسالبة الغرام يجعل منه بديلاً هامًا، خاصةً في حالة وجود مقاومة للمضادات الحيوية التقليدية. تسلط هذه المقالة الضوء على دواء السلفاميثاكسازول في معالجة الام الاسنان وذلك بسبب المادة الفعالة الموجودة في الدواء والمتشكلة في التركيب الكيميائي جعلت له تأثير كيميائي طبي في تحسين صحة الاسنان ،. تقدم هذه المقالة نظرة عامة على الخصائص الدوائية والتطبيق العلاجي والنتائج السريرية، مما يدعم استمرار أهمية السلفاميثوكسازول في ممارسة طب الأسنان الحديثة.

الكلمات المفتاحية: سلفاميثوكسازول، أمراض الأسنان، المستحضرات الصيدلانية، أدوية الأسنان، وظائف المضادات الحيوية السلفونواميدية.

Introduction

Sulfamethoxazole is a synthetic antimicrobial agent belonging to the sulfonamide class, its active constituents include a substituted benzene sulfonamide moiety namely N-(5-methylisoxazol-3-yl)-sulfanilamide (Figure.1) which interferes with the normal metabolism of bacterium primarily by inhibiting the enzyme dihydropteroate synthase. The enzyme is essential for the steps that lead to the biosynthesis of dihydrofolic acid an intermediate in the formation of tetrahydrofolate, a key compound for the synthesis and replication of bacterial nucleotides. Sulfamethoxazole is often combined with trimethoprim to create co-trim oxazole, a synergistic antimicrobial regimen that interrupts two sequential steps in the process of folate metabolism. Combination application in the management of infections caused by susceptible Gram-positive and Gram-negative bacteria, especially those affecting the respiratory tract, urinary tract, and infections in immunocompromised patients like Pneumocystis jirovecii pneumonia [1].

Physical, Chemical Properties of Sulfamethoxazole

Sulfamethoxazole presents as a white to off-white crystalline powder. with a relatively stable physical form under standard laboratory conditions[2]. This appearance makes it easy to handle and process during pharmaceutical manufacturing. Low solubility in water (~0.16 mg/mL at 25°C), a characteristic of many sulfonamides.It is more soluble in organic solvents such as ethanol and methanol, indicating its lipophilic tendencies. The solubility in organic media is important for formulation and absorption.This manuscript is designed as a narrative review.

Aim of the Study

This review aims to comprehensively explore the pharmacological and therapeutic properties, focusing on its contemporary relevance in dental medicine. the research underscores the critical role of sulfamethoxazole in combating complex infections addressing the challenges of antimicrobial resistance and adverse effects[1].

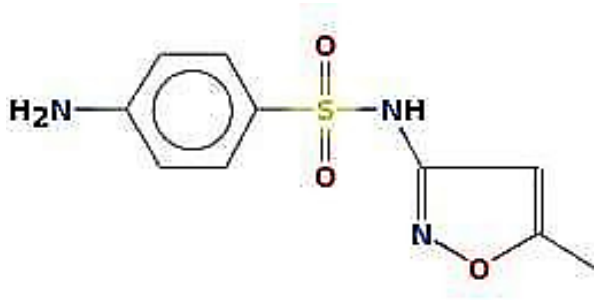

Fig.1: Chemical structure of SMZ

Formulaions and Clinical Accessibility

sulfamethoxazole is available in different formulaions for diverse clinical applications. These include oral tablets, oral suspensions, injectable preparations, and topical preparations. Common sulfa doses known for combined sulfamethoxazole-trimethoprim combination are regular- strength (400 mg/80 mg) and double-strength (800 mg/160 mg) tablets.

The implication of local market data from Iraqi pharmacies (e.g., Baghdad) serves as a representative case study for clinical accessibility. and the following was obtained:

Oral tablets: Cotrimoxazole/TMP SMX 400 mg Sulfamethoxazole / 80 mg trimethoprim (regular strength). 800 mg Sulfamethoxazole / 160 mg trimethoprim (double strength). liquid suspensions for use in pediatric or geriatric patients containing 200 mg of sulfamethoxazole and 40 mg of trimethoprim per 5 ml [13] ,Low-dose therapy (150 mg/m2 of body surface area of trimethoprim and 750 mg/m2 of body surface area of sulfamethoxazole) has been shown in numerous studies to be beneficial in preventing P. carinii infection. Additionally, giving severely neutropenic patients 800 mg of sulfamethoxazole and 160 mg of trimethoprim twice a day was found to significantly protect against sepsis caused by Gram-negative bacteria.

By concentrating the availability of these specific concentrations in local pharmaceutical sectors, the review bridges the gap between theoretical pharmacology and the practical applicability in dental setting.

Methodology

Study desgin

This study is structured as a narrative review.The primary objective was to synthesize current literature regarding the pathophysiology and and management the common oral disease

focusing on dental caries, periodontal disease, gingivitis, and related disease. (5)

Search Strategy and Databases

A comprehensive literature was carried out based on a number of peer-reviewed articles and academic texts the following databases and digital libraries were consulted:

- Google Scholar,
- PubMed,
- British Pharmacological Society,
- International Journal of Dentistry,
- MDPI, and National Library of Medicine.

Search Parameters

Keywords: the search utilized the specific dental terms such as ental caries, periodontal disease, gingivitis, and related disease.

Timeframe: 2020-2025 was selected to ensure the inclusion of contemporary researches and the most recent clinical guidelines.

Inclusion and Exclusion Criteria

To maintain the quality and relevance of the study, the following criterias were used :

Inclusion Criteria: Full-text original research articles, systemic reviews. Studies focusing on the etiology, progression, and pharmacological treatment of the specified dental diseases.

Exclusion Criteria: Duplicate records across different databases , Articles where the full text was unavailable or inaccessible.

Results and discussion

Trimethoprim-sulfamethoxazole (TMP/SMX) in the treatment of acute maxillary sinusitis

Study objective: Trimethoprim-sulfamethoxazole (TMP/SMX) is very effective for resolving the clinical and radiographical findings of acute maxillary sinusitis by comparing 3-day and 10-day TMP/SMX courses

Sample Characteristics:clinical and radiographical findings of patients having acute maxillary sinusitis(12)

Key Findings: found equal clinical outcomes. On the 14th day, symptom resolution or improvement was reported by 77% of patients in the 3-day group and by 76% in the 10-day group. Roentgenographic findings improved similarly for both groups (Figure.2).

The shorter course-the 3-day regimen-was found to demonstrate equal

efficacy with no statistically significant difference in relapse or recurrence rates compared to the longer 10-day course[14].

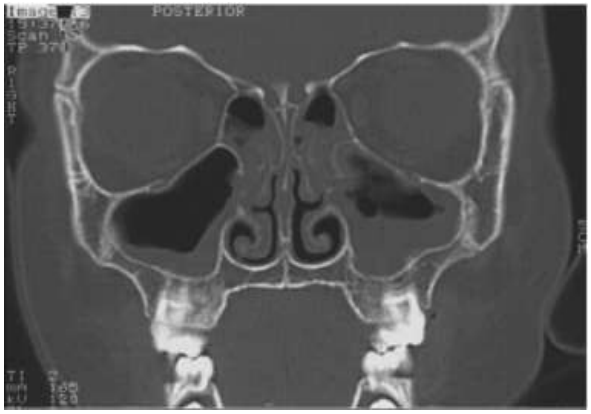

Fig. 2: Maxillary sinusitis

Relevance in Dentistry: TMP/SMX would function similarly effective for shorter durations and be both cost effective and convenient for the management of acute maxillary sinusitis [3] . On the whole, TMP/SMX is a good drug for treating sinusitis, particularly in cases where shorter courses of antibiotic treatment are desirable or needed.

TMP/SMX in the Treatment of Facial Osteomyelitis

Study Objective: To identify the first choice antibiotic protocols and common pathogens associated with facial osteomyelitis.

Sample Characteristics:cases involving bone level infections of the midface and mandible.

Key Findings: Rifampin is the first-choice antibiotic for facial osteomyelitis, along with Sulfamethaxzol and Clindamycin (administered intravenously in the first 1-2 weeks). Anaerobic bacteria and streptococci are the two main opportunistic pathogenic species. Staphylococci and enteric rods are the most specific bacteria that may be isolated from bone or blood in hematogenous osteomyelitis. [4][11].

Relevance to Dentistry: TMP/SMX is a gold-standard pharmacological framework for managing the bone infections that followe the invasive dental procedures or trauma.

Antimicrobial Susceptibility in Peruvian patients with periodontal disease

Study Objective: In order to ascertain the etiology and resistance proile of bacteria identified in a group of Peruvian patients with periodontal disease.

Sample Characteristics: a pilot study titled "Screening and Assess-

ment of Antimicrobial Susceptibility of Periodontopathic Bacteria in Peruvian Patients with Periodontitis" [5] was used. Eight individuals with severe periodontitis had six samples of subgingival plaque was taken.

Key Finding: An initial culture, PCR amplification, and DNA sequencing were used to identify the bacteria. They used the disk diffusion method to assess antibiotic susceptibility. Each of the eight patients had varying levels of oral microbiome diversity. Streptococcus spp. (15/48, 31.3%) was the most commonly detected bacterial genus, followed by Rothia spp. (11/48, 22.9%), Actinomyces spp. (9/48, 18.8%), and Eikenella spp. (4/48, 8.3%). Rothia dentocariosa was the most prevalent species (8/48, 16.7%). The majority of the bacteria, including Eikenella corrodens and Granulicatella adiacens, were also resistant to the widely used antibiotics in dentistry, trimethoprim-sulfamethoxazole (SXT) and clindamycin (CD).

Relevance to Dentistry: to prevent antibiotic resistance and enhance the treatment outcomes for patients with periodontal disease, specific targited antimicrobial therapy is needed.

Possible Adverse Effects on Oral Tissues

The StatPearls summary of trimethoprim-sulfamethoxazole is a useful medication review that lists typical side effects[10]:

General Oral Side Effects

- **Stomatitis**
- **Glossitis** painful or swollen tongue
- **Xerostomia** serious idiosyncratic reactions.[6]

Stevens - Johnson Syndrome

Clinical Presentation: A Case Report on the Unusual Presentation of Stevens - Johnson Syndrome Induced by Trimethoprim-Sulfamethoxazole (2024) , a recent case report that details SJS with noticeable erosions of the oral mucosa following TMP-SMX; it includes clinical photos and a course, which are useful as direct evidence connecting TMP-SMX to severe oral lesions.[7]

Diagnostic Significance: the administration of trimethoprim-sulfamethoxazole may result in fixed drug eruption of the tongue.

Fixed Drugs Eruption (FDE) of the Tongue

Study Objective: To detect the unusual localized reaction to sulfamethoxazole . **Case Summary:** After receiving trimethoprim-sulfamethoxazole (SMX/TMP) for recurrent UTIs, a 21-year-old woman experienced a fixed drug eruption (FDE) on her tongue, according to a case report by Gleeson et al. (2020). The patient had vesicular lesions on the dorsal tongue and a severe pseudomembranous ulcer within 24 hours. figure[3], which recurred on multiple occasions after exposure to the drug. Histopathological analysis confirmed an inflammatory reaction consistent with FDE. **Key Finding:** discontinuation of SMX/TMP led to complete healing, and the patient was advised to avoid sulfonamide antibiotics due to the risk of recurrence[16].

Clinical Significance: This report highlights that while oral FDE is relatively rare, the dorsal tongue is a typical site, and SMX/TMP is among the most frequent antibiotic triggers. Oral lesions may mimic conditions such as aphthous ulcers, candidiasis, herpes simplex infection, or autoimmune blistering diseases, which can complicate diagnosis. Recognition of sulfamethoxazole-induced oral mucosal reactions is therefore clinically important in dentistry, as it prevents misdiagnosis and unnecessary treatments, while emphasizing the need for thorough drug history in patients presenting with unexplained oral ulcers.[8]

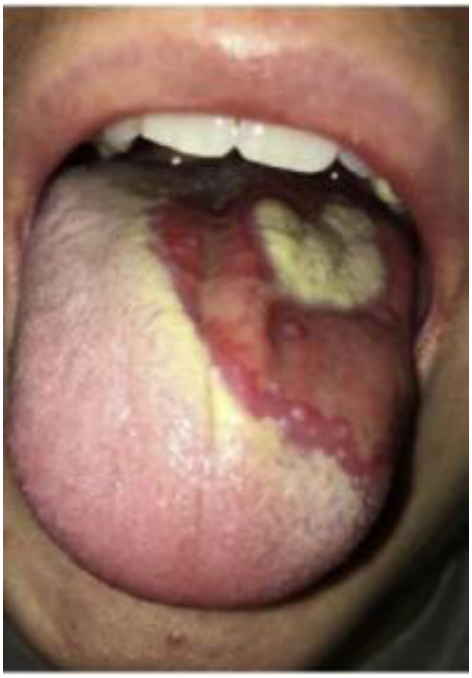

Figure 3.:On the left posterior dorsal part of the tongue, there is a large pseudomembranous ulcer accompanied by several tiny vesicular lesions and a yellowish-white area.

Interpretation of Findings

The results of this review confirm the ongoing clinical significance of

sulfamethoxazole, especially when used in conjunction with trimethoprim.

Mechanism and Efficacy: in the treatment of dental infections. Its broad-spectrum effect against both Gram-positive and Gram-negative pathogens is based on the suppression of folate metabolism. This explains why it is beneficial for odontogenic infections, dental-related maxillary sinusitis[9]

Prophylaxis: SMX-TMP act as a vital preventative measure immunocompromised patients undergoing invasive dental work . Shorter treatment courses have been shown to be successful in treating acute maxillary sinusitis, which further supports their value as an affordable and practical choice and supports ongoing initiatives to limit needless antibiotic exposure.

In osteomyelitis of the facial bones, the integration of sulfamethoxazole with clindamycin and rifampin reflects the need for combination therapy against mixed flora including Streptococcus spp., anaerobes, Staphylococcus aureus, and enteric rods.

Stewardship and Resistance: the review of antimicrobial susceptibility in periodontitis cases highlights the complex microbial diversity within periodontal pockets and raises concern over increasing resistance to TMP/SMX and other commonly prescribed antibiotics.These findings emphasize the necessity of tailored antimicrobial therapy guided by culture and sensitivity testing, rather than empirical use alone[11].

The Adverse Oral Effects associated with sulfamethoxazole, though less frequent than systemic reactions, require particular attention in dental practice. Reported manifestations range from stomatitis and glossitis to severe mucocutaneous reactions such as Stevens–Johnson syndrome. Moreover, the documented cases of fixed drug eruption involving the tongue illustrate the potential for misdiagnosis, as lesions may mimic aphthous ulcers, candidiasis, or viral infections. Early recognition of drug-induced oral pathology is therefore crucial to prevent unnecessary interventions and ensure prompt discontinuation of the offending agent.[14]

Limitations of the Available Evidence: despite the available evidence

on the pharmacology, therapeutic uses, and adverse reactions of sulfamethoxazole, there remains a notable gap in dentistry-specific research. Most of the current literature approaches the drug from a general medical or infectious disease perspective, with only scattered references to oral infections, periodontal therapy, or maxillofacial conditions. Dedicated clinical trials in dental populations are scarce, and much of the evidence used in dental practice is extrapolated from systemic infection studies. This absence of dentistry-focused investigations limits the ability to draw firm conclusions about optimal dosing regimens, comparative efficacy with other dental antibiotics, and long-term safety within the context of oral health care. Future research tailored to dental applications would therefore be of considerable value in guiding clinicians toward more evidence-based use of sulfamethoxazole in dental practice. Collectively, these observations underscore the dual nature of sulfamethoxazole in dentistry: while it remains a valuable antimicrobial option, its clinical use must be balanced against emerging resistance patterns and the possibility of serious adverse effects. Rational prescribing, antimicrobial stewardship, and vigilant monitoring for oral manifestations of drug reactions represent essential components of safe and effective practice.[15]

Conclusion

Clinical Applicability in Dentistry

Sulfamethoxazole still has therapeutic value in dentistry, especially when combined with trimethoprim. It is used to treat odontogenic infections, dental sinusitis, and osteomyelitis. When first-line antibiotics are no longer effective, it is a viable substitute due to its broad antimicrobial activity against both Gram-positive and Gram-negative organisms. However, the medication has several drawbacks. The need for cautious clinical judgment is underscored by the growing number of reports of bacterial resistance, as well as unfavorable oral side effects like glossitis and stomatitis, as well as uncommon but serious reactions like Stevens-Johnson syndrome or fixed drug eruptions.

Principles of Antimicrobial Stewardship

For the dental practitioner, this balance underscores two priorities: the ra-

tional selection of antimicrobials based on culture and sensitivity whenever possible, and vigilance for early signs of adverse oral manifestations. While sulfamethoxazole remains a relevant option within dental pharmacotherapy, its use must be guided by principles of antimicrobial stewardship, patient safety, and awareness of the drug's potential complications. Further dentistry-specific studies are still required to clarify its optimal role and to establish stronger evidence-based guidelines for its safe and effective use in oral health care.

Risk-Benefit Considerations

The clinical decision to prescribe SMX involves an assessment of potential outcomes and the secondary risks:

Benefits: High bone penetration in osteomyelitis cases and a broad antimicrobial reach that provides a "safety net" in complex or refractory infections.

Risks: Dentists must concern the benefit against the risk of severe mucocutaneous reactions, such as Stevens-Johnson syndrome or Fixed Drug Eruptions . Because these can manifest early in the oral cavity as glossitis or stomatitis, the dentist serves as the first line of defense in early diagnosis and drug discontinuation

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