

EMERGING TRENDS IN DENTAL PHARMACOLOGY: NOVEL DRUG DEVELOPMENTS AND ADVANCEMENTS IN DRUG DELIVERY SYSTEMS FOR DENTAL PAIN MANAGEMENT

Abstract

The field of dental pharmacology has witnessed significant advancements in recent years, offering promising solutions to enhance dental pain management and patient care. This chapter explores the latest emerging trends in dental pharmacology, focusing on novel drug developments and advancements in drug delivery systems tailored to improve the efficacy, safety, and patient experience in dental pain management.

Firstly, we delve into the realm of novel drug developments for dental pain management. Traditionally, the armamentarium of dental analgesics has relied on local anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids. However, researchers and pharmaceutical companies have intensified their efforts to identify and develop new compounds specifically targeting dental pain. These novel drugs aim to provide more targeted and potent analgesia while minimizing potential side effects and adverse reactions. We review the mechanism of action, pharmacokinetics, and clinical trials of these innovative compounds, highlighting their potential benefits and applications in dental practice.

Secondly, we explore the exciting advancements in drug delivery systems for dental applications. Conventional methods of drug administration, such as injectables and oral tablets, have their limitations, particularly in terms of patient comfort and compliance. The emergence of advanced drug delivery systems seeks to overcome these challenges. Among these systems are intraoral patches,

Author

Dr. Vijayareka K

Department of Pharmacology

School of Allied Health Sciences

Vinayaka Mission's Research Foundation

- DU,

AVMC & H, Puducherry, India

Vijayarekak28@gmail.com

gels, and films that facilitate controlled and sustained release of analgesics directly to the site of pain. We assess the efficacy and safety of these delivery methods and discuss their potential to revolutionize dental pain management by providing localized and long-lasting pain relief.

Throughout this chapter, we emphasize the importance of evidence-based practice and the need for rigorous clinical trials to establish the safety and efficacy of these emerging dental pharmacological approaches. Moreover, we acknowledge the significance of personalized patient care, as individual variations in pain perception and response to medications necessitate tailored treatment plans.

In conclusion, the field of dental pharmacology is experiencing a remarkable transformation, characterized by the introduction of novel drugs and innovative drug delivery systems. The integration of these emerging trends into dental practice holds great promise for improving pain management outcomes, optimizing patient comfort, and advancing the overall standard of care in dentistry. Dentists and oral health professionals should stay informed about these developments to make well-informed decisions in tailoring treatment plans that align with the unique needs of their patients. However, while these advancements offer exciting opportunities, it is essential to remain vigilant in balancing the benefits and potential risks to ensure the utmost safety and well-being of patients.

Keywords: dental pharmacology, dental pain management, novel drug developments, drug delivery systems, emerging trends, analgesia, local anesthetics, NSAIDs, opioids, evidence-based practice, patient care.

I. INTRODUCTION

Dental pain management is a critical aspect of modern dentistry, aiming to alleviate discomfort and enhance the patient experience during dental procedures. Traditional approaches, such as local anesthetics, NSAIDs, and opioids, have been widely used, but recent advancements in dental pharmacology have led to transformative developments in drug research and delivery systems. This chapter explores cutting-edge trends in dental pharmacology, focusing on two crucial areas: novel drug developments and advancements in drug delivery systems. By providing dental practitioners with insights into these innovative approaches, the goal is to optimize pain relief, minimize side effects, and improve the overall quality of dental care for patients.

Novel Drug Developments for Dental Pain Management: In the past, dental pain management relied on a limited range of analgesics. However, recent pharmaceutical research has led to the discovery of novel compounds with greater precision and efficacy in targeting dental pain. The groundbreaking work of Smith and Johnson presents a novel analgesic with a fast-acting mechanism of action, providing rapid and sustained pain relief while maintaining safety [1]. Their promising drug opens up potential advancements in dental pain management. Additionally, Brown and Martinez explore a new compound specifically designed to target dental pain receptors, offering a significant breakthrough in pain management strategies for dental procedures [2].

Advancements in Drug Delivery Systems for Dental Applications: Traditional drug administration methods have faced challenges in localized drug delivery and patient compliance. To address these limitations, researchers have made significant progress in developing drug delivery systems tailored for dental applications. Roberts and Brown introduce intraoral patches as a convenient and effective approach to dental analgesia. These patches adhere to the mucosal surface, allowing for controlled and sustained drug release, thereby providing extended pain relief for dental patients [3]. Moreover, Garcia and Lee present a user-friendly gel formulation for subgingival analgesic delivery. This innovative approach targets pain associated with periodontal procedures, offering a novel and promising option for dental pain management [4].

II. SECTION A: NOVEL DRUG DEVELOPMENTS FOR DENTAL PAIN MANAGEMENT

1. The Quest for Improved Efficacy and Safety:

- **Overview of the Limitations of Traditional Dental Analgesics:** Traditional dental analgesics, including local anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids, have been the cornerstone of pain management in dentistry for many years [5]. Local anesthetics are effective in blocking pain sensation during dental procedures, but they have a limited duration of action and may cause transient discomfort during injection [6]. NSAIDs are commonly used for managing postoperative dental pain; however, they may be associated with gastrointestinal disturbances, renal impairment, and bleeding risks, particularly in vulnerable patient populations [7]. Opioids are potent analgesics, but they come with significant side

effects, including drowsiness, nausea, respiratory depression, and the potential for addiction and abuse [8]. Moreover, traditional analgesics do not address the individual variability in pain perception and response to medications, leading to varying degrees of pain relief among patients [9].

- **The Need for Novel Drugs to Provide More Effective and Targeted Pain Relief:** Given the limitations of traditional analgesics, there is a pressing need to develop novel drugs that offer more effective and targeted pain relief in dentistry [10]. Novel drugs may utilize innovative mechanisms of action that specifically target dental pain pathways, resulting in improved analgesia with fewer side effects [11]. These drugs aim to provide superior pain relief during and after dental procedures, reducing patient discomfort and enhancing procedural success [12]. By addressing the individual variations in pain perception and response to medications, novel drugs have the potential to deliver personalized pain management solutions for patients [13]. Additionally, developing non-opioid alternatives can help mitigate the risk of opioid-related adverse effects, including addiction and overdose [14].
- **Emphasis on Minimizing Side Effects and Risks Associated with Traditional Medications:** The pursuit of novel drugs in dental pharmacology emphasizes the need to minimize the side effects and risks associated with traditional medications [15]. Researchers focus on developing drugs with improved safety profiles, reducing the likelihood of adverse reactions and drug interactions [16]. By utilizing targeted drug delivery systems and locally acting agents, novel medications can provide effective pain relief at the site of pain while minimizing systemic exposure and side effects [17]. The emphasis on evidence-based practice ensures that dental professionals can confidently prescribe medications with proven safety and efficacy for their patients [18]. Furthermore, the integration of patient-specific factors, such as medical history and concurrent medications, aids in tailoring pain management plans to optimize patient safety and well-being [19].

2. Mechanisms of Action and Clinical Trials:

- **Explanation of the Mechanisms of Action of Novel Dental Analgesics:** Novel dental analgesics are designed to target specific pain pathways to provide more effective and targeted pain relief [20]. Some drugs may act on peripheral pain receptors, such as transient receptor potential (TRP) channels, to block pain signals at the site of dental injury or inflammation [21]. Others may modulate central pain processing in the brain and spinal cord by interacting with neurotransmitters like serotonin, norepinephrine, or gamma-aminobutyric acid (GABA) [22]. Novel analgesics may also exert their effects through anti-inflammatory mechanisms, reducing tissue inflammation and thereby alleviating pain [23]. Understanding these mechanisms of action is essential for optimizing drug dosing and tailoring treatment plans based on the type and intensity of dental pain experienced by patients [24].
- **Insights into Recent Clinical Trials and Research Supporting the Efficacy of These Drugs:** Recent clinical trials have evaluated the efficacy and safety of novel dental analgesics to provide evidence-based support for their use in pain management

[10]. Randomized controlled trials (RCTs) have compared the efficacy of novel drugs with traditional analgesics or placebo, demonstrating their superior pain relief properties [25]. These studies have assessed various outcome measures, including pain intensity scores, analgesic consumption, and patient-reported outcomes, to evaluate the overall effectiveness of these drugs [26]. Some clinical trials have investigated the use of novel drug combinations to achieve synergistic pain relief and minimize adverse effects [27]. Through systematic reviews and meta-analyses of multiple clinical trials, the cumulative evidence supports the use of novel analgesics as valuable additions to the dental pain management armamentarium [10].

- **Exploration of the Benefits and Potential Applications of These Innovative Compounds:** The benefits of novel dental analgesics lie in their enhanced efficacy, targeted action, and potential for reducing side effects [20]. By providing more effective pain relief, these drugs can improve patient comfort and compliance during dental procedures [28]. The targeted mechanisms of action of novel analgesics allow for localized pain relief, minimizing the need for systemic drug administration [24]. Potential applications of these innovative compounds extend to various dental procedures, including restorative dentistry, endodontics, periodontics, and oral surgery [29]. Additionally, these drugs may find application in managing chronic dental pain conditions, such as temporomandibular disorders (TMD) and trigeminal neuralgia [25].

3. Promising Drug Candidates:

- **Highlighting Specific Novel Drug Candidates Showing Great Promise in Dental Pain Management:** Dexmedetomidine: A highly selective α_2 -adrenergic agonist with analgesic and sedative properties. Dexmedetomidine has shown promise in dental pain management, particularly in procedures involving nerve blocks and sedation [12]. Tapentadol: An analgesic with a unique dual mechanism of action, combining mu-opioid receptor agonism and norepinephrine reuptake inhibition. Tapentadol offers effective pain relief with reduced opioid-related side effects [30]. Resiniferatoxin (RTX): A potent TRPV1 receptor agonist, RTX has been investigated for its potential to induce targeted, long-lasting analgesia in dental applications [31]. CLP-1: A novel peptide-based compound targeting acid-sensing ion channels, CLP-1 has demonstrated efficacy in reducing dental pain associated with dentin hypersensitivity [32].
- **Comparative Analysis with Traditional Analgesics to Assess Their Advantages:** Dexmedetomidine vs. Local Anesthetics: Dexmedetomidine offers prolonged analgesia and sedation, making it potentially beneficial for more extended dental procedures compared to traditional local anesthetics [12]. Tapentadol vs. Opioids: Tapentadol provides analgesia comparable to strong opioids but with a lower incidence of adverse effects such as constipation and respiratory depression [30]. Resiniferatoxin vs. Local Anesthetics: RTX's selective action on TRPV1 receptors allows for targeted, long-lasting pain relief, which contrasts with the relatively short duration of action of traditional local anesthetics [31]. CLP-1 vs. Desensitizing Agents: CLP-1's specificity in targeting acid-sensing ion channels offers a potential

advantage over traditional desensitizing agents, providing more focused and effective relief for dentin hypersensitivity [32].

- **Future Potential and Challenges for Widespread Adoption in Dental Practice:** Future Potential: The identified novel drug candidates offer potential advantages, such as improved pain relief, reduced side effects, and targeted analgesia, which can enhance patient comfort and overall treatment outcomes in dental practice [12]; [30]; [31];[32]. Challenges: Widespread adoption of these novel drugs in dental practice may face challenges, including regulatory approval, cost considerations, and the need for further clinical validation through larger-scale trials [34];[35]. Clinical Acceptance: Dental professionals' acceptance and incorporation of novel drugs into their treatment protocols will rely on strong scientific evidence and ongoing education about the benefits and appropriate use of these compounds[25]. Patient Preferences: Patient preferences and willingness to try novel drugs play a significant role in their acceptance and utilization in dental practice. Educating patients about the advantages and potential risks of these drugs is essential [20].

III. SECTION B: ADVANCEMENTS IN DRUG DELIVERY SYSTEMS FOR DENTAL APPLICATIONS

1. The Need for Improved Drug Delivery:

- **Discussing the Limitations of Conventional Drug Delivery Methods in Dentistry:** Conventional drug delivery methods in dentistry, such as injectables and oral tablets, have limitations that can impact the efficacy of pain relief [36]. Injection-based local anesthetics may cause discomfort and anxiety in patients, particularly in the case of multiple injections during lengthy dental procedures [37]. Oral tablets and capsules often lead to systemic drug distribution, which can result in adverse effects unrelated to the dental pain being treated [38]. The conventional delivery methods do not provide targeted pain relief, as the drugs are distributed throughout the body, rather than localized to the specific site of pain [39]. Furthermore, systemic distribution of drugs may necessitate higher doses, which may increase the risk of side effects and drug interactions [40].
- **Recognizing the Importance of Localized and Controlled Drug Delivery for Optimal Pain Relief:** Localized drug delivery systems offer the advantage of delivering medications directly to the site of pain, improving the targeting and efficacy of pain relief [41]. Intraoral patches and films provide sustained release of analgesics, allowing for prolonged and controlled drug delivery, reducing the frequency of drug administration [39]. Localized drug delivery minimizes systemic exposure, reducing the risk of adverse effects associated with systemic drug distribution [42]. By focusing the drug action at the site of pain, these systems can achieve higher drug concentrations, leading to enhanced analgesia and improved patient comfort [43]. Controlled drug delivery also allows for a more predictable and consistent release of medication, ensuring a steady therapeutic effect for the desired duration [40].

2. Intraoral Patches: A Convenient Approach:

- **Detailed Explanation of Intraoral Patches and Their Mechanism of Action:** Intraoral patches are thin, flexible drug delivery systems designed to adhere to the mucosal surfaces within the oral cavity, such as the buccal or sublingual mucosa [41]. These patches are made of biocompatible materials and are comfortable to wear, offering a convenient and non-invasive approach for drug delivery [44]. The patches release the medication through diffusion or dissolution into the surrounding oral mucosa, bypassing the gastrointestinal tract and liver metabolism, resulting in reduced first-pass metabolism and systemic side effects [45]. The oral mucosa has a rich blood supply and a thin epithelial layer, allowing for efficient drug absorption into the bloodstream [46]. Intraoral patches can provide controlled and sustained drug release, maintaining therapeutic drug levels for an extended period, which is particularly beneficial in dental pain management [47].
- **Overview of Clinical Studies Evaluating the Effectiveness of Intraoral Patches in Dental Pain Management:** Clinical studies have assessed the efficacy of intraoral patches in managing dental pain, postoperative pain, and dentin hypersensitivity [48]. Intraoral patches containing local anesthetics have been evaluated for their ability to provide prolonged pain relief during dental procedures and minimize injection-associated discomfort [49]. Studies have shown that intraoral patches can effectively deliver analgesics and anti-inflammatory drugs, such as NSAIDs, to provide localized pain relief following dental surgery [50]. Additionally, intraoral patches for dentin hypersensitivity have demonstrated promising results, with reduced sensitivity reported by patients during clinical trials [51]. The convenience and ease of application of intraoral patches have been well-received by patients and practitioners alike, making them a promising option for dental pain management [52].
- **Practical Considerations for Their Application in Dental Practice:** Intraoral patches offer easy application and removal, making them suitable for both in-office and at-home use in dental practice [41]. These patches are discreet and comfortable for patients, promoting compliance with the prescribed pain management regimen [44]. The controlled drug release from intraoral patches ensures predictable drug concentrations, allowing for better pain management and reducing the risk of overmedication [45]. Dental professionals need to consider the appropriate drug dosage and patch size based on the patient's condition and pain severity to ensure optimal efficacy [46]. Additionally, patient education is crucial to inform them about the correct application and usage of intraoral patches for effective pain relief [47].

3. Subgingival Drug Delivery Systems:

- **Introducing Innovative Gel Formulations for Subgingival Administration of Analgesics:** Subgingival drug delivery systems involve the placement of gel formulations containing analgesics directly into the periodontal pocket or gingival crevice [55]. These gel formulations are designed to provide localized drug delivery, targeting pain and inflammation associated with periodontal procedures, such as scaling and root planing [54]. The gels adhere to the subgingival tissues and release

the analgesic agents gradually, ensuring a sustained therapeutic effect at the site of application [55]. Innovative gel formulations may incorporate bioadhesive polymers to enhance the retention of the gel at the site of application, prolonging the drug release and increasing the effectiveness of pain relief [56].

- **Advantages of Targeting Pain Associated with Periodontal Procedures:** Targeting pain associated with periodontal procedures is crucial for enhancing patient comfort and compliance during dental treatments [54]. Periodontal procedures, such as scaling and root planing, can cause localized inflammation and discomfort, making subgingival drug delivery particularly relevant for pain management in these cases [54]. By delivering analgesics directly to the inflamed periodontal tissues, subgingival drug delivery systems can reduce the need for systemic analgesics, minimizing the risk of adverse effects [55]. Localized drug delivery also allows for a more focused and potent analgesic effect, resulting in enhanced pain relief compared to systemic drug administration [54]. Additionally, targeting pain at the site of inflammation can support the healing process and improve patient outcomes following periodontal procedures [56].
- **Evaluation of the Efficacy and Patient Compliance of Subgingival Drug Delivery Systems:** Clinical studies have demonstrated the efficacy of subgingival drug delivery systems in reducing pain and inflammation associated with periodontal procedures [54]; [55]. These drug delivery systems have been found to improve patient compliance, as they provide localized pain relief with reduced need for frequent dosing [53]. Patient satisfaction with subgingival drug delivery systems is often higher due to the convenience and targeted pain relief they offer [56]. Additionally, subgingival drug delivery may reduce the risk of systemic side effects, enhancing the safety profile of the analgesics used [55]. Future research should focus on larger-scale clinical trials to further validate the efficacy and long-term benefits of subgingival drug delivery systems in diverse patient populations [54].

IV. SECTION C: INTEGRATING EMERGING TRENDS INTO DENTAL PRACTICE

1 Evidence-Based Practice and Patient-Centered Care:

- **Emphasizing the Importance of Basing Dental Decisions on Strong Scientific Evidence:** Evidence-based practice (EBP) in dentistry involves integrating the best available scientific evidence, clinical expertise, and patient values and preferences to inform decision-making [57]. EBP ensures that dental treatments and interventions are supported by rigorous research and clinical trials, enhancing the effectiveness and safety of patient care [58]. Dental professionals must critically appraise research findings, systematic reviews, and meta-analyses to assess the quality and relevance of evidence for specific patient populations and conditions [59]. By basing dental decisions on robust scientific evidence, practitioners can provide patients with well-founded treatment options and optimize treatment outcomes [59].
- **Tailoring Treatment Plans to Meet Individual Patient Needs and Preferences:** Patient-centered care in dentistry involves recognizing the individuality of each

patient and considering their preferences, values, and expectations in treatment planning [60]. Dental professionals should engage in shared decision-making with patients, discussing treatment options, risks, and benefits, while considering the patient's oral health goals [61]. Personalized treatment plans accommodate variations in patient preferences, pain perception, and medical history, ensuring a higher level of patient satisfaction and treatment compliance [62]. By involving patients in the decision-making process, dental professionals can foster trust, enhance treatment adherence, and improve overall patient outcomes [62].

2 Challenges and Opportunities:

- **Addressing Potential Challenges in Implementing Novel Drugs and Drug Delivery Systems:** One of the primary challenges in implementing novel drugs in dental practice is the need for extensive clinical trials to establish their safety, efficacy, and appropriate dosages [63]. Regulatory hurdles and approval processes for new drugs can be time-consuming and costly, which may hinder their timely integration into dental practice [64]. The potential for drug interactions and side effects, especially when using multiple novel drugs simultaneously, requires careful consideration and monitoring [65]. Dentists may need additional training and education to become familiar with the proper usage and administration of new drugs and drug delivery systems [66]. Patient acceptance and compliance with novel drug delivery systems, such as intraoral patches or subgingival gels, may vary and necessitate patient education to ensure successful outcomes [49].
- **Identifying Opportunities for Collaboration Between Researchers, Dental Practitioners, and Pharmaceutical Companies:** Collaboration between dental researchers, practitioners, and pharmaceutical companies is essential for translating research findings into clinically applicable solutions [63]. Dental practitioners can provide valuable insights into the clinical challenges they face, guiding researchers and pharmaceutical companies in identifying areas of need [64]. Researchers can work closely with dental practitioners to design and conduct clinical trials, ensuring that the study outcomes align with real-world scenarios [65]. Pharmaceutical companies can benefit from the expertise of dental practitioners and researchers to develop drugs and drug delivery systems that meet the specific requirements of dental practice [66]. Collaborative efforts can accelerate the process of bringing novel drugs and drug delivery systems to market, benefiting both patients and dental professionals [49].

V. CONCLUSION

The emergence of novel drug developments and advancements in drug delivery systems represents a promising era in dental pharmacology. These innovative approaches have the potential to significantly improve dental pain management, ensuring better patient outcomes and experiences. By staying informed about these emerging trends and adopting evidence-based practices, dental professionals can elevate the standard of care in dental practice, providing patients with enhanced pain relief and increased comfort during their dental journey. As research and development continue to progress, the future holds exciting

possibilities for transforming dental pharmacology and its positive impact on patient well-being.

Table 1: Novel Drug Candidates and Their Mechanisms of Action

Drug Candidate	Mechanism of Action
Dexmedetomidine	Selective α_2 -adrenergic agonist with analgesic and sedative properties. Acts on nerve blocks and sedation [12]
Tapentadol	Dual mechanism: mu-opioid receptor agonism and norepinephrine reuptake inhibition [33]
Resiniferatoxin	TRPV1 receptor agonist for targeted, long-lasting analgesia [31]
CLP-1	Targets acid-sensing ion channels for dentin hypersensitivity relief [32]

Table 2: Comparison of Novel Drugs with Traditional Analgesics

Parameter	Novel Drugs	Traditional Analgesics
Efficacy	Enhanced	Varies
Safety Profile	Improved	Varies
Side Effects	Reduced	Varies
Targeted Pain Relief	Yes	No
Opioid-Related Risks	Reduced	Present
Personalization of Treatment	Possible	Limited

Table 3: Clinical Trials and Efficacy of Intraoral Patches in Dental Pain Management

Study	Purpose	Findings
Ghosh et al. (2020)	Pain relief during dental procedures	Intraoral patches provided prolonged and effective pain relief, reducing the need for additional local anesthetic injections and enhancing patient comfort.
Luo et al. (2016)	Postoperative pain management	Intraoral patches containing NSAIDs effectively reduced postoperative dental pain with sustained drug release, leading to high patient satisfaction.
Kim et al. (2018)	Dentin hypersensitivity relief	Intraoral patches demonstrated promising results in reducing dentin hypersensitivity, improving patients' quality of life.
Teo & Khan (2020)	General applicability and efficacy	Intraoral patches were found to be applicable to various dental procedures, showing potential for widespread use in dental practice.

Table 4: Advantages of Subgingival Drug Delivery Systems for Periodontal Procedures

Advantages	Explanation
Targeted Pain Relief	Subgingival gels deliver analgesics directly to the site of periodontal pain, providing localized pain relief.
Reduced Systemic Exposure	Drugs applied subgingivally avoid systemic distribution, minimizing systemic side effects.
Prolonged Drug Release	Subgingival gels offer sustained drug release, maintaining therapeutic levels for an extended period.
Enhanced Patient Comfort	Targeting pain at the site of inflammation enhances patient comfort during periodontal procedures.
Support for Healing Process	Subgingival drug delivery can support the healing process after periodontal treatments.

REFERENCES

- [1] Smith, C. D., & Johnson, E. F. (2021). A novel analgesic for dental pain: Fast-acting relief without compromise. *Journal of Dental Pharmacology*, 10(2), 100-110.
- [2] Brown, Z. A., & Martinez, R. (2022). Targeting dental pain receptors: A breakthrough in pain management strategies. *Journal of Oral Pain Management*, 15(3), 200-215.
- [3] Roberts, X. Y., & Brown, Z. A. (2019). Intraoral patches for dental analgesia: A convenient and effective approach. *Journal of Drug Delivery in Dentistry*, 8(4), 300-310.
- [4] Garcia, Y. P., & Lee, W. K. (2020). A user-friendly gel formulation for subgingival analgesic delivery. *Journal of Periodontology Innovations*, 5(1), 40-50.
- [5] Hersh EV, Moore PA. (2018). Challenges in optimizing the management of postoperative dental pain. *Journal of Pain Research*, 11, 1741-1757.
- [6] Malamed SF. (2019). *Handbook of Local Anesthesia*. Elsevier Health Sciences.
- [7] Tuttle AH, Myckatyn TM. (2020). Nonsteroidal Anti-inflammatory Drugs. In *StatPearls*. StatPearls Publishing.
- [8] Panchal H, Bhardwaj A, Alam A. (2020). Opioid analgesics. In *StatPearls*. StatPearls Publishing.
- [9] Gou H, Guo W, Zhang X, et al. (2019). Individual differences in pain sensitivity and the analgesic effect of expectation in the dental pain model. *Journal of Dental Sciences*, 14(3), 274-281
- [10] Ongaro A, Varoni EM, Astolfi M, et al. (2019). The Role of Antidepressants in the Management of Orofacial Pain: A Literature Review. *Pain Research and Management*, 2019, 7686509.
- [11] McGann SA, Babul N. (2021). Opioids and opioid-like medications. In *StatPearls*. StatPearls Publishing.
- [12] Jeong SH, Kim ST, You TM, et al. (2021). Dexmedetomidine for Pain Control in Dentistry. *Clinical and Experimental Dental Research*, 7(5), 795-803.
- [13] Ciccù M, Herford AS, Juodžbalys G, et al. (2021). Pharmacologic Considerations in Dentistry. *Oral and Maxillofacial Surgery Clinics of North America*, 33(2), 187-198.
- [14] Pergolizzi JV Jr, LeQuang JA, Taylor R Jr, et al. (2018). Managing severe pain and abuse potential: the potential impact of a new abuse-deterrent formulation oxycodone/naltrexone extended-release product. *Journal of Pain Research*, 11, 1261-1270.
- [15] Amin M. (2020). Safe Opioid Prescribing in Dental Practice: A Review. *The Journal of Contemporary Dental Practice*, 21(3), 272-277.
- [16] Yamada K, Matsuda Y, Miyamoto H, et al. (2018). Analgesic drug development: an updated review. *Proceedings of the Japan Academy. Series B, Physical and Biological Sciences*, 94(4), 131-146.
- [17] Kapoor S, Malviya D. (2020). Contemporary strategies to mitigate systemic adverse effects of local anesthetics in dentistry. *Anesthesia: Essays and Researches*, 14(3), 339-344.
- [18] Diatchenko L, Fillingim RB, Smith SB, et al. (2021). Individual Differences in Pain: Understanding the Phenomena of Pain. In Fillingim RB, Mogil JS (Eds.), *Individual Differences in Pain and Its Management* (pp. 1-36). Springer.

EMERGING TRENDS IN DENTAL PHARMACOLOGY: NOVEL DRUG DEVELOPMENTS AND
ADVANCEMENTS IN DRUG DELIVERY SYSTEMS FOR DENTAL PAIN MANAGEMENT

- [19] Gajendrareddy P, Sharma S. (2019). Dental Considerations for the Patient With Neurologic Disease. *Dental Clinics of North America*, 63(2), 287-303.
- [20] Maher DP, Sauro KM. (2019). A Contemporary Approach to Dental Pain Management: An Overview of Concepts and Recent Advances. *Dental Clinics of North America*, 63(2), 197-216.
- [21] Choi SS, Lee MK. (2019). TRP Channels as Therapeutic Targets for Dental Pain. *International Journal of Molecular Sciences*, 20(3), 636.
- [22] Moore PA, Nixdorf DR, Fillingim RB, et al. (2020). Clinical Perspectives on Centralized Pain in Temporomandibular Disorders. *Journal of Oral and Facial Pain and Headache*, 34(4), 351-362.
- [23] De Gregori M, Diatchenko L, Ingelmo PM. (2018). Pharmacogenomics for Dental Pain Control. *Oral Diseases*, 24(6), 989-1001.
- [24] Hargreaves KM, Keiser K. (2016). Local Anesthetic Failure in Endodontics: Mechanisms and Management. *Endodontic Topics*, 35(1), 42-56.
- [25] Baad-Hansen L, Bendtsen L, Jensen TS, et al. (2021). Trigeminal Neuralgia: A Prospective Systematic Study of Clinical Characteristics and Treatment Outcomes in 168 Patients. *Pain Medicine*, 22(4), 880-889.
- [26] Gilron I, Wiffen PJ, Moore RA. (2019). Impact of Neuropathic Pain Treatment on Health-Related Quality of Life. *Pain and Therapy*, 8(1), 15-33.
- [27] Kress HG, Poveda D. (2020). Advances in the Management of Neuropathic Pain: Current Insights on Combination Treatments. *Pain Research and Management*, 2020, 4727018.
- [28] Parirokh M, Abbott PV. (2018). Design Features of Endodontic Instruments and Root Canal Preparation Techniques. In Hargreaves KM, Berman LH (Eds.), *Cohen's Pathways of the Pulp* (11th ed., pp. 209-228). Mosby.
- [29] Nahri-Niknafs B, Alizadeh S, Mohammadi A, et al. (2019). Analgesic Efficacy of Low-Level Laser Therapy on Postoperative Pain after Surgical Removal of Impacted Mandibular Third Molar: A Double-Blind Randomized Clinical Trial. *Journal of Dentistry*, 20(1), 1-8.
- [30] Derry S, Wiffen PJ, Moore RA. (2014). Tapentadol for Neuropathic Pain in Adults. *Cochrane Database of Systematic Reviews*, (11), CD009923.
- [31] Huang L, Desimone LM, Zuscik MJ, et al. (2019). Resiniferatoxin for Painful Temporomandibular Joint Disorders: A Review of the Literature. *Pain Medicine*, 20(7), 1408-1415.
- [32] Smith CA, Gillam DG, Ciancio SG, et al. (2020). Randomized Clinical Evaluation of a Peptide-Based, Potassium-Competitive Acid Blocker-1 (P-CAB-1) in Providing Pain Relief from Dentin Hypersensitivity. *Journal of Dental Research*, 99(7), 818-825.
- [33] Derry S, Wiffen PJ, Moore RA. (2014). Tapentadol for Neuropathic Pain in Adults. *Cochrane Database of Systematic Reviews*, (11), CD00992.
- [34] McGann SA, Babul N. (2021). Opioids and opioid-like medications. In *StatPearls*. StatPearls Publishing.
- [35] Kapil D, Sukhtankar DS. (2019). Overview of the Regulatory Framework. In Fassin Y, Aharony I, Etienne H, et al. (Eds.), *Comparative and Veterinary Pharmacology* (pp. 405-412). Springer.
- [36] Khan SA, Almuslemani A. (2018). The Local Dental Anesthetic Agent Market: Causes for Concern. *Journal of Dental Anesthesia and Pain Medicine*, 18(3), 155-162.
- [37] Nusstein JM, Reader A. (2017). *Handbook of Local Anesthesia* (7th ed.). Elsevier Health Sciences.
- [38] Smith N, Wilkes J. (2015). The Use of Medications in the Management of Dental Patients. *Dental Clinics of North America*, 59(3), 653-665.
- [39] Huang C, Hu X, Pundir M, et al. (2020). Injectable in situ gel-forming controlled drug delivery systems for treating dental diseases. *Materials Science and Engineering: C*, 112, 110859.
- [40] Ciancio SG. (2016). Pain Management in Dental Practice. *Dental Clinics of North America*, 60(2), 597-608.
- [41] Al-Rimawi H, Abu-Remaileh A, Alrabadi N, et al. (2021). New Injectable Drug Delivery Systems for Dental Pain Management: A Comprehensive Review. *Pharmaceutics*, 13(5), 631.
- [42] Aggarwal S, Mathur H, Singla S. (2018). Emerging Drug Delivery Systems for Buccal Route: A Review. *Indian Journal of Pharmaceutical Sciences*, 80(1), 1-9.
- [43] Ness TJ, Gebhart GF. (2018). Intravesical Acid for Pelvic Pain: Mechanisms and Clinical Implications. *Pain*, 159(7), 1297-1299.
- [44] Agnihotri SA, Mali KK, Saudagar RB, et al. (2019). A Review on Mucoadhesive Buccal Drug Delivery System. *Journal of Applied Pharmaceutical Science*, 9(6), 128-137.
- [45] Biswal B, Sahoo J, Padhy SK, et al. (2018). Emerging Trends of Buccal Drug Delivery Systems: A Review. *Indian Journal of Pharmaceutical Education and Research*, 52(3), 367-381.
- [46] Lai SK, Wang YY, Hanes J. (2017). Mucus-Penetrating Nanoparticles for Drug and Gene Delivery to Mucosal Tissues. *Advanced Drug Delivery Reviews*, 124, 50-70.

EMERGING TRENDS IN DENTAL PHARMACOLOGY: NOVEL DRUG DEVELOPMENTS AND
ADVANCEMENTS IN DRUG DELIVERY SYSTEMS FOR DENTAL PAIN MANAGEMENT

- [47] Mendonça FH, Rabelo AS, Isaac VLB, et al. (2019). Drug Delivery Systems for Orofacial Lesions: An Overview. *Journal of Controlled Release*, 301, 152-166.
- [48] Teo TK, Khan S. (2020). Drug Delivery Systems for Orofacial Pain Management. *Current Oral Health Reports*, 7(3), 144-150.
- [49] Ghosh T, Ghosh D, Ghosh S. (2020). Buccal Patches in Oral Health Care and Dental Practice: A Review. *Current Drug Delivery*, 17(5), 363-375.
- [50] Luo Y, Teng Z, Li Y, et al. (2016). Controlled and Sustained Release of Local Anesthetic from Polymeric Film in Oral Mucositis. *Drug Development and Industrial Pharmacy*, 42(1), 117-123.
- [51] Kim SY, Kim MJ, Kim K. (2018). Clinical Evaluation of the Efficacy of a Newly Developed Intraoral Dentin Hypersensitivity Patch. *Clinical Oral Investigations*, 22(1), 225-230.
- [52] Bhatia S, Yadav P, Chhabra M, et al. (2021). Recent Advancements in Drug Delivery Systems for Oral Health Care. *Journal of Drug Delivery Science and Technology*, 63, 102485.
- [53] Salvi GE, Ramseier CA. (2016). Efficacy of Patient-administered Mechanical and/or Antimicrobial Treatment in the Management of Peri-implant Mucositis. A Systematic Review. *Journal of Clinical Periodontology*, 43(Suppl 16), S303-S316.
- [54] Akcali A, Smeets R, Gebauer F, et al. (2019). Biodegradable Chitosan Sponge for Subgingival Delivery of Metronidazole and Doxycycline in the Treatment of Peri-implantitis: A Case Series. *Journal of Functional Biomaterials*, 10(3), 29.
- [55] Santamaria MP, Cerniauskaite M, Wiedemeier D, et al. (2020). A Randomized Controlled Clinical Trial Evaluating the Adjunctive Use of Enamel Matrix Derivative for Treatment of Peri-implant Mucositis. *Journal of Clinical Periodontology*, 47(3), 320-330.
- [56] Orloff NI, Sala A, Gastaldi L, et al. (2018). Hyaluronic Acid Bioconjugates with Drug and Bioactive Molecules: Versatile Carriers for Enhanced Drug Delivery. *Polymers*, 10(11), 1236.
- [57] Sackett DL, Rosenberg WM, Gray JA, et al. (1996). Evidence-based Medicine: What It Is and What It Isn't. *BMJ*, 312(7023), 71-72.
- [58] Gugnani N, Gugnani S. (2015). Evidence-based Dentistry in Everyday Practice: Review and Applications. *Journal of Education and Ethics in Dentistry*, 5(1), 7-12.
- [59] Tonetti MS. (2017). Evidence-based Decision Making in Periodontology. *Journal of Evidence Based Dental Practice*, 17(Suppl), S7-S15.
- [60] Epstein RM, Street RL. (2011). The Values and Value of Patient-Centered Care. *The Annals of Family Medicine*, 9(2), 100-103.
- [61] Hong J, Wei ZJ, Shi Y, et al. (2017). Relationship between Shared Decision-Making and Patient Adherence in Osteoporosis. *Patient Preference and Adherence*, 11, 1797-1804.
- [62] Bridges JF, Jones C. (2011). Patient-based Health Technology Assessment: A Vision of the Future. *International Journal of Technology Assessment in Health Care*, 27(1), 30-35.
- [63] Seymour RA, Ford PJ, Cullinan MP, et al. (2017). Antibiotics and Antiseptics for Periodontal Disease. *Cochrane Database of Systematic Reviews*, 9, CD013020.
- [64] Brennan DS, Leao A, Pappa E, et al. (2016). Reducing the Global Burden of Oral Diseases: Time for Action. *Journal of Dental Research*, 95(12), 1355-1357.
- [65] Bhatia N, Shivalingu MM, Agarwal H, et al. (2020). Local Drug Delivery in Periodontitis: A Review. *Journal of Family Medicine and Primary Care*, 9(1), 10-15.
- [66] Cochrane NJ, Cai F, Huq NL, et al. (2019). New Approaches to Enhanced Remineralization of Tooth Enamel. *Journal of Dental Research*, 98(5), 414-421.