

**Keywords**  
Local anaesthesia; Oral mucosa; Anaesthetic effectiveness; Inflammation; Prosthodontics; Restorative dentistry; Orthodontics; Drug diffusion; Pain management; Dental anaesthesia

**Authors**

<sup>1</sup>\*Mr. Nickson Das

PhD Nursing Scholar, Department of Nursing, Specialization in Medical Surgical Nursing, Parul Institute of Nursing, Parul University, Vadodara-391760, India, Orcid Id: 0009-0009-6981-6300  
Email Id: [itsnixon1990@gmail.com](mailto:itsnixon1990@gmail.com)

<sup>2</sup>Dr. Ramachandra S Hooli

Faculty of Nursing, Department of Nursing, Specialization in Medical Surgical Nursing, Parul Institute of Nursing, Parul University, Vadodara-391760, India, Orcid Id: 0009-0004-7985-7580  
Email Id: [ramhooli@gmail.com](mailto:ramhooli@gmail.com)

<sup>3</sup>Dr. Prachi Joshi

Professor, Department of Conservative and Endodontics, Specialisation in Conservative and Endodontics, M.A.Rangoonwalla College of Dental Sciences and Research Centre, Azam Campus, Pune-411001, MUHS, Maharashtra, India  
Orcid Id: 0009-0004-2065-1721, Email Id: [prax\\_in@yahoo.com](mailto:prax_in@yahoo.com)

<sup>4</sup>Dr. Rohini Parui

Postgraduate Trainee, Department of Public Health Dentistry, Specialization in Public Health Dentistry, Kalinga Institute of Dental Sciences (KIDS), Kalinga Institute of Industrial Technology (KIIT) Deemed to be University, Bhubaneswar - 751024, Odisha, India, Orcid Id: 0009-0003-5009-8069, Email Id: [rohiniparui99@gmail.com](mailto:rohiniparui99@gmail.com)

<sup>5</sup>Visali K

PharmD, Department of School of Pharmaceutics, Specialization in Clinical Pharmacy, Vels Institute of Science, Technology and Advanced Studies, Chennai-600066, India, Email Id: [visalikannan93@gmail.com](mailto:visalikannan93@gmail.com), Orcid Id: 0009-0002-8392-4833

<sup>6</sup>Dr. Munish Rastogi

Associate Professor, Department of School of Health Sciences Specialization in MBBS, PHD, Chhatrapati Shahu Ji Maharaj, University, Kanpur-208024, India Email Id: [munishkanuniv@gmail.com](mailto:munishkanuniv@gmail.com) Orcid Id:0009-0004-5745-8853

<sup>7</sup>ABRAHAM.S

Research Scholar, Department of Law, Specialization in Maritime Law, Saveetha School of Law Saveetha Institute of Medical and Technical Sciences (SIMATS) Tamil Nadu-600124, India, Email id: [abrahamlawyer12@gmail.com](mailto:abrahamlawyer12@gmail.com) Orcid Id: <https://orcid.org/0009-0001-7672-7607>

Received Date: 10/04/2026

Revised Date: 26/04/2026

Acceptance Date: 13/05/2026

Doi:

10.1922/ejprd.v34i1s.1368

# Local Anaesthetic Effectiveness in Oral Mucosal Conditions: Clinical Implications for Prosthodontic, Restorative, and Orthodontic Procedures

## Abstract

Local anaesthesia (LA) is one of the elementary aspects of pain control in the field of dentistry; although it is not always reliable due to the variation in the condition of the oral mucosa. The oral mucosa is highly diversified in structure and functions in establishing the pharmacodynamics and pharmacokinetics of the local anaesthetic agents. Epithelial thickness, vascularity, tissue pH, and nerve distribution are such factors that have a significant effect on the diffusion of drugs, onset, and duration of action. There are pathological conditions such as inflammation, ulceration, infection, manifestations of systemic disease, and fibrosis that further complicate the results of anaesthesia. Inflammatory states decrease tissue pH and enhance vascularity, decreasing drug efficacy, and ulcerative and infectious lesions change the mucosal integrity and perception of pain. Systemic factors like xerostomia and diabetes, and fibrotic alterations, add more variability to anaesthetic response. These challenges have important clinical implications across prosthodontic, restorative, and orthodontic procedures, where predictable anaesthesia is essential for successful treatment. Modifications in anaesthetic techniques, appropriate drug selection, and the use of adjuncts such as buffering agents, premedication, and advanced delivery systems can enhance effectiveness. Emerging technologies, including nanocarrier-based systems and liposomal formulations, offer promising avenues for improving drug delivery and prolonging anaesthetic action. This review emphasizes the need for an individualized, evidence-based approach to local anaesthetic administration, taking into account mucosal conditions and patient-specific factors. A comprehensive understanding of these variables is essential for optimizing clinical outcomes and advancing patient-centered dental care.

## 1. Introduction

Local anaesthesia (LA) is an essential part of contemporary dentistry, making it possible to perform a diverse set of procedures in the fields of prosthodontics, restorative dentistry, and orthodontics painlessly. Local anaesthesia has also completely transformed the way patients are handled since its introduction in the field of dentistry, as patients have greatly improved when it comes to compliance, efficiency in the procedure, and treatment outcomes [1]. The capability of the invasive and non-invasive procedures to be done without any discomfort has not only increased the precision of the clinical efforts but has also helped to reduce the level of anxiety the patients may have, hence bringing about better long-term oral health.

Even with all the considerable improvements in pharmacology, modes of delivery, and clinical procedures, inconsistency in anaesthetic success

..... EJPRD

appears to be an issue of constant concern and clinical significance. Particularly, it is not necessarily the predictability of the power of local anaesthetic agents used correctly. This heterogeneity is particularly acute in the case of altered oral mucosal conditions when the local tissue factors and systemic factors may intervene in the expected action of anaesthetic agents.

The oro-mucosal mucosa has a crucial role in the administration, absorption, and diffusion of local anaesthetics. It is an anatomically heterogeneous tissue that is complex and highly specialized, and has significant structural and functional heterogeneity depending on the anatomic location. The oral mucosa is broadly categorized into keratinized (masticatory), non-keratinized (lining), and specialized mucosa. All the types exhibit unique permeability, vascularity, epithelial thickness, and innervation patterns, which determine the pharmacokinetics and pharmacodynamics of the local anaesthetic drug [2]. These differences directly affect the onset, effect, and duration of anaesthetics, and tissue peculiarities are the key to successful clinical practice.

Depending on the density of the epithelium, e.g., on the gingiva and hard palate, keratinized mucosa presents a comparatively impermeable barrier to drug entry. On the other hand, non-keratinized mucosa, such as buccal and labial mucosa, allows quick absorption of the anaesthetic agents. Such variations suggest that one should select the appropriate injection procedures and drug formulations based on the injection site. Moreover, the salivation, mucosa hydration, and the environmental factors also influence drug absorption and efficiency.

One of the most significant factors of the local anaesthetic effect is the condition of the tissue underlying it. In normal mucosa, the traditional techniques will usually give consistent anaesthetic diffusion and nerve blockage. Pathological alterations such as inflammation, infection, ulceration, or fibrosis may, however, have a severe impact on anaesthetic efficacy. An example is that the inflamed tissues are usually of a lower pH due to the concentration of acidic products of the metabolic process. This acidic environment reduces the percentage of the non-ionized form of the anaesthetic necessary to enter the nerve membrane [3]. It consequently leads to the late onset, superficial anaesthesia, or even its total inefficiency in certain clinical situations.

Other than changes in pH, inflammation is also associated with improved vascularity and blood circulation, and this could elevate the rate of systemic absorption and clearance of local anaesthetic drugs. This results in a reduction of the action time and target site effect. Conversely, ailments with thick fibrinous tissue, such as scarring or fibrosis, may impede the diffusion of drugs and thus slow down the onset of the ailment and necessitate some other approach of delivering the drug or an increased dose of the drug [4]. Such physiological and pathologic peculiarities indicate the significance of the knowledge of tissue-specific factors in the context of anaesthetic planning.

These variations have a greater clinical implication in the various dental fields. In prosthodontics, the procedures of tooth preparation, management of soft tissues, and implant placement, among others, require

effective anaesthesia. The existence of flabby ridges, atrophic mucosa, or lesions caused by dentures may affect the method of anaesthetics selected as well as the choice of the right agent [5]. Such conditions usually demand changes in the process of injections to prevent the distortion of the tissues and guarantee comfort to the patient.

On the same note, adequate anaesthesia may be extremely difficult to produce in situations where there is an inflammatory response in the pulpal or periapical areas in restorative dentistry. It is not new that teeth with symptomatic irreversible pulpitis are resistant to the standard anaesthetic methods, and this is mainly attributed to changes in tissue pH and hypersensitization of nociceptors [6]. The clinicians in such situations usually require the use of additional injection methods or additive pharmacological interventions in the attainment of proper pain control.

Although orthodontic procedures are less invasive in nature, they have their own considerations too. Local anaesthesia may be essential in procedures like mini-implant placement, surgical exposure of impacted teeth, treatment of appliance-induced soft tissue irritation, etc. Under such circumstances, the state of the mucosa, the presence of irritation or ulceration, can be of great concern to the comfort of the patient and the effect of anaesthesia. Hence, anaesthetic methods should be evaluated and altered with due attention in order to achieve the best results.

Although local anaesthetics are widely used, there is an increasing awareness that a one-size-fits-all or the same approach cannot be used consistently to produce success. Rather, clinicians should be more individualized and evidence-based in addressing the issue, but they should take into account not only the pharmacological nature of the anaesthetic agent, but also the biological and pathological features of the oral tissues. Age of patients, and health in general, levels of anxiety, and previous anaesthetic experiences are also among such factors that lead to variation in response and should be considered when planning the treatment.

In this respect, it will be necessary to learn about the relationship between oral mucosal states and the efficacy of local anaesthetics in order to optimise clinical results. The combination of the insight into the mucosa anatomy, pharmacology, and disease mechanisms will allow the clinicians to anticipate possible difficulties and make required adjustments to their anaesthetic practice.

This review aims to critically evaluate the influence of oral mucosal conditions on the effectiveness of local anaesthesia and to highlight their clinical implications in prosthodontic, restorative, and orthodontic procedures. By synthesizing current evidence on mucosal biology, pharmacological mechanisms, and clinical practice, this article seeks to provide a comprehensive and practical framework for enhancing anaesthetic success in diverse dental scenarios.

## 2. Anatomy and Physiology of Oral Mucosa Relevant to Anaesthetic Action

Local anaesthetic (LA) agent in dental practice has a close relationship with the physiological and anatomical

nature of the oral mucosa. The mucosa of the mouth is not a uniform tissue, but there is a considerable local difference in its thickness, keratinization, vascularity, and neural distribution. All these factors affect the rate of absorption, diffusion, and the overall effectiveness of local anaesthetic agents.

### 2.1 Types of Oral Mucosa and Their Clinical Relevance

Oral mucosa is widely divided into three categories, namely masticatory mucosa, lining mucosa, and specialized mucosa. Masticatory mucosa, which is present on the gingiva and hard palate, is usually keratinized or parakeratinized and firmly attached to the underlying bone. On the contrary, the lining mucosa, which is located on the buccal mucosa, labial mucosa, and floor of the mouth, is non-keratinized and more elastic. Taste buds are found in specialized mucosa, which is situated on the back of the tongue and has special structural characteristics [2].

The dense layer of epithelium and low permeability of keratinized mucosa increase the resistance to the penetration of drugs. This leads to the topical anaesthetics not being so effective in these areas, and infiltration methods may need more volume or different methods. On the other hand, non-keratinized mucosa permits diffusion of anaesthetic drugs at a faster rate, leading to fast action [7].

### 2.2 Epithelial Thickness and Permeability

The thickness of epithelia is a very important factor in local anaesthetic diffusion. The increasing strength of the epithelium, especially in the tissues that are formed of keratin, restricts the diffusion of the anaesthetic molecules, which are directed towards the nerve endings underneath the tissue. Intercellular lipid composition and tight junctions are also factors that affect the permeability of the oral mucosa [8].

The low density of epithelial cells and the lack of a thick keratin layer in non-keratinized mucosa make such mucosa more permeable. This helps the penetration of lipophilic anaesthetic agents, which improves their clinical efficacy. Conversely, a higher concentration is needed or adjunctive methods to provide sufficient anaesthesia in the keratinized tissues [9].

### 2.3 Vascularity and Its Impact on Anaesthetic Duration

There are two roles of the vascularity of the oral mucosa in the effectiveness of local anaesthetics. On the one hand, a sufficient blood supply provides the drug with rapid spread to the target location. Conversely, the high vascularity of tissues may also result in quicker systemic absorption and clearance of the anaesthetic agent and thus provide a short time of action [10].

As an illustration, in most cases, the lining mucosa is more vascular than the masticatory mucosa, which could lead to reduced anaesthetic length in such areas.

This is especially pertinent in cases where the lasting effect of anaesthesia is necessary, and the introduction of vasoconstrictors, such as epinephrine, is necessary to sustain the effect of the drugs and decrease the uptake into the system [1].

### 2.4 Nerve Supply and Receptor Distribution

Branches of the trigeminal nerve have a dense distribution over the oral mucosa, and the density and distribution of the nerve vary across different parts. Regions that have a higher nerve density might need an anaesthetic delivery that is more accurate to achieve a full nerve block. Also, the effectiveness of infiltration versus the nerve block technique depends on the depth and pattern of branching of the nerve fibers [11].

The perception of pain is based on the free nerve endings that are situated in the epithelium and connective tissue. The topical anaesthetics may be ineffective due to the proximity of the nerve endings to the surface. In areas where the nerve endings are found at a deeper part of the tissue, infiltration anaesthesia is required to obtain sufficient analgesia [12].

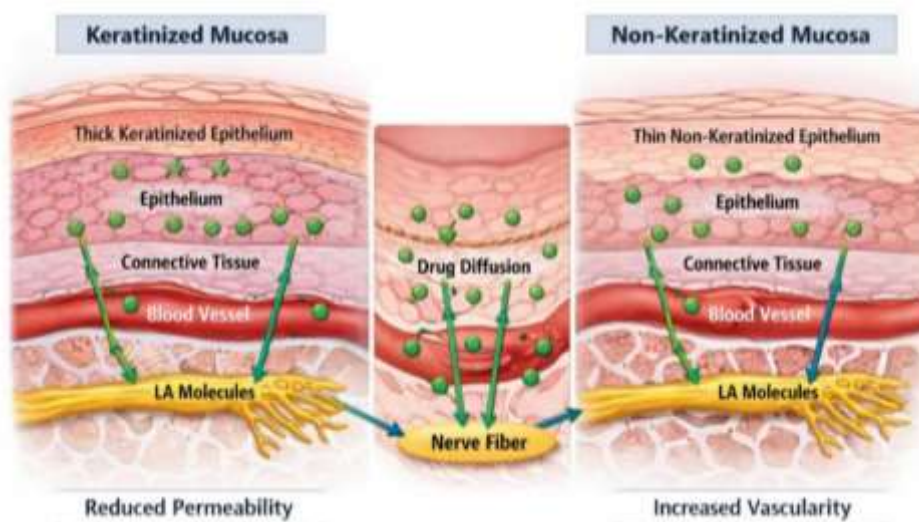
### 2.5 Tissue pH and Microenvironment

The physiological PH of the tissues in the mouth is essential in the determination of the ionization state of the local anaesthetic agents. The majority of the local anaesthetics are weak bases, and they have to be in their non-ionized state to be able to penetrate the nerve membrane. Normal tissue states permit an optimal ratio between ionized and non-ionized states, which enables the nerve blockade to be effective [3].

Yet, it is possible to discuss even slight changes in pH in tissues as factors that affect the effect of drugs. As an example, regions of decreased oxygenation or minor inflammation can have a slight degree of acidity, thereby decreasing the supply of the active form of the anaesthetic. That is where the relevance of the tissue environment of the planned anaesthetic administration is emphasised.

### 2.6 Role of Saliva and Mucosal Hydration

Topical anaesthetic agents are also effective in saliva and mucosal hydration. The mucosal surface is best hydrated to boost the dissolution and absorption (absorption) of drugs, and the dry mucosa can restrict the contact of the drug and thus limit its efficacy. The secretions of saliva may either be a facilitator or offer resistance based on the composition and flow rate [13]. Drying the mucosa before the topical anaesthetic is a common clinical practice to increase the rate of drug adherence and penetration. This is just one of the easily achievable measures to make surface anaesthesia much more effective, especially in non-keratinized areas. As Figure 1 shows, differences in the structure of keratinized and non-keratinized mucosa have a considerable effect on the route of diffusion of local anaesthetic agents.



**Figure 1. Schematic representation of oral mucosal types and pathways of local anaesthetic diffusion**

### 3. Pharmacology of Local Anaesthetics and Mechanisms Affecting Efficacy

One of the significant pillars of dental pain management is local anaesthetics (LA), which work by reversibly inhibiting nerve conduction. Their effect on the human body is explained by the combination of their pharmacological and several physiological and environmental factors affecting onset, deep and pain duration of action. These mechanisms need to be fully understood in order to maximize anaesthetic outcomes, especially when different oral mucosal conditions are involved.

#### 3.1 Classification of Local Anaesthetics

The local anaesthetics are categorized into 4 groups and are classified by the following: The anaesthetics used in the local anaesthetics are categorised into two major groups according to their chemical structures: amide-type and ester-type anaesthetics. The most frequently used in dentistry are the amide anaesthetics, which include lidocaine, articaine, bupivacaine, and mepivacaine, as they are more stable and have lower rates of allergic reactions. The less common types of anaesthetics are the ester anaesthetics, such as procaine and benzocaine, which have more chances of causing hypersensitivity and have shorter action times [3].

The uniqueness of articaine among the amide anaesthetics is that it has an amide linkage as well as an ester group that can be metabolised fast in both the plasma and the liver. This dual metabolism makes it have a good safety profile and increases its diffusion across the soft and hard tissues [14].

#### 3.2 Mechanism of Action

The local anaesthetics work by inhibiting the voltage-gated sodium channels in nerve membranes. This causes the blockage of the activation and spread of action potentials, thus blocking nerve conduction and pain transmission [15].

LA molecules have to diffuse through tissues and cross the nerve membrane to reach the location of their action. This is based on the capacity of the drug to be in a non-ionized (lipid-soluble) state. The ionized form of the neurotransmitter attaches itself to the sodium channel

receptor in the neuron, keeping it in the inactive state. Figure 1 (Section 2) shows that diffusion across the mucosal layers is an important process that affects the efficacy of this process.

#### 3.3 Physicochemical Properties Influencing Efficacy

Several intrinsic properties of local anaesthetics determine their clinical performance:

##### pKa and Onset of Action

The pKa of a local anaesthetic is what dictates the percentage of the drug that exists in the ionic form at a physiological pH. Agents whose pKa is more similar to physiological pH (7.4) contain a larger fraction of non-ionized molecules, which causes accelerated onset of action. For example, lidocaine (pKa 7.9) has a relatively rapid onset compared to bupivacaine (pKa 8.1) [1].

##### Lipid Solubility and Potency

The lipid solubility improves the penetration of the drug into nerve membranes. The lipid-soluble agents are more potent, and they are capable of deeper anaesthesia [16].

##### Protein Binding and Duration

The protein binding levels are associated with the duration of action. The higher the protein binding of the drugs, the longer the drugs stay on the nerve membranes, thus extending the anaesthetic effect. An example is the bupivacaine, which has high protein binding with a long duration of anaesthesia [1].

#### 3.4 Role of Vasoconstrictors

Local anaesthetic solutions are usually supplemented with a vasoconstrictor, i.e., epinephrine, to increase the clinical effects of the local anaesthetic. These are the agents that cause a resultant reduction in the local blood flow, and hence the resultant reduction in systemic absorption and an increase in duration of anaesthesia [17]. Also, vasoconstrictors are used to ensure an elevated concentration of the anaesthetic at the effect site and decrease the amount of bleeding during surgery. These, however, should be used cautiously in patients with cardiovascular diseases or where the tissues are highly vascular, and the excessive vasoconstriction can lead to damage to the tissue health [18].

**3.5 Factors Affecting Onset, Depth, and Duration**

The clinical performance of local anaesthetics is influenced by multiple factors beyond drug properties:

**Tissue pH**

As explained in the above section, tissue pH is an important factor in the performance of anaesthetics. To a larger degree, in acid conditions, like inflamed or diseased tissues, the drug exists in its ionized state and thus has fewer chances to enter nerve membranes. This leads to a slow-acting effect and lower effectiveness [19].

**Tissue Vascularity**

Rapid absorption of the anaesthetic into the systemic circulation is achieved because of highly vascular tissues, and this reduces its duration of action. On the other hand, the less vascular regions will enable the drug to take a longer time to be localized [20].

**Injection Technique**

The procedure (infiltration, nerve block, or intraligamentary injection) adopted has a great influence on anaesthetic success. Increased cortical bone or thick mucosa may infiltrate ineffectively, so nerve block methods may be required [21].

**Dose and Concentration**

Raising the dose and the amount of anaesthetic can enhance its efficacy, but also its toxicity. Thus, determining dosage allows clinicians to use a balance between efficacy and safety [3].

**3.6 Clinical Challenges and Adjunctive Strategies**

The effective anaesthesia of inflamed tissues, including those in irreversible pulpitis, can be regarded as one of the most widespread clinical issues. Conventional methods do not usually work in such cases because the tissue pH is changed, and the nociceptors are more active. Aggarwal et al. (2010) reported that adjunctive strategies such as the use of supplemental injections (i.e., intraosseous or intraligamentary), preoperative analgesics, and buffering of anaesthetic solutions can help to improve success rates [22].

The addition of sodium bicarbonate to buffer local anaesthetic solutions increases the ratio of non-ionized fraction, which increases diffusion and decreases injection pain. On the same note, warming of the anaesthetic solution can enhance comfort and the onset time of the patient, but the evidence is inconsistent [18]. Table 1 summarizes the pharmacokinetic differences of the commonly used local anaesthetics that are common.

**Table 1. Comparison of Commonly Used Dental Local Anaesthetics**

Drug	Type	pKa	Onset Time	Duration (Pulpal)	Protein Binding (%)	Vasoconstrictor Use
Lidocaine	Amide	7.9	Rapid	60–90 min	65	Yes
Articaine	Amide	7.8	Very rapid	60–75 min	95	Yes
Mepivacaine	Amide	7.6	Rapid	20–40 min	75	Optional
Bupivacaine	Amide	8.1	Slow	90–180 min	95	Yes
Prilocaine	Amide	7.9	Moderate	40–60 min	55	Optional

**4. Impact of Oral Mucosal Conditions on Local Anaesthetic Effectiveness**

The condition of the oral mucosa within the location of the local anaesthesia (LA) administration is also a crucial determinant of the success of local anaesthesia (LA) in dental practice. Pathological changes, which include inflammation, ulceration, infection, signs of systemic disease, and fibrosis, may change the tissue properties, thus influencing the pharmacodynamics and pharmacokinetics of local anaesthetic drugs. There are four major changes that mainly affect the diffusion of the drug, ionization, vascular clearance, and neural responsiveness that affect clinical efficacy.

**4.1 Inflammatory Conditions (Gingivitis and Periodontitis)**

The most common causes of local anaesthetic failure are inflammatory conditions (gingivitis and periodontitis). The result of inflammation is the reduction of tissue pH caused by the concentration of acidic metabolites. Because of the weak base nature of the local anaesthetics, an acidic medium makes the drug occupy a higher percentage of ionized form, which reduces its penetrative capacity into the nerve membranes [19]. Also, inflamed tissues are more vascular and thus systemic absorption is quicker and shortens the anaesthetic action. This has especially been noticed in periodontal tissues, where the hyperemia is known to

improve the clearance of any drug at the injection site [23].

Inflammation also sensitizes nociceptors and decreases the pain threshold, resulting in patients being more resistant to standard methods of anaesthetics. Due to this, the administration of more doses or as supplementary injections may be necessary to achieve sufficient analgesia during periodontal procedures [24].

**4.2 Ulcerative Lesions (Apthous Ulcers and Lichen Planus)**

Oral mucosal lesions like recurrent apthous stomatitis and oral lichen planus have special difficulties with regard to the administration of local anaesthetic drugs. These wounds are marked with the rupture of the epithelial layer, the exposure of nerve endings, and the local inflammation, which all lead to an increase in pain sensitivity [25].

Under these circumstances, local anaesthetic agents can be used directly, which can be painful and less effective because of impaired epithelial integrity. Moreover, an inflammatory environment around these lesions may change the diffusion of drugs and decrease the effects of anaesthesia.

Topical anaesthetics can be applied to deal with pain related to ulcerative lesions, but their activity may be reduced due to the salivary dilution and fast disappearance. The infiltration procedures might have to be adjusted so that they do not inject directly into the

ulcerated tissue, but rather at the adjacent healthy mucosa to produce sufficient anaesthesia [13].

#### 4.3 Infectious Conditions (Candidiasis and Viral Lesions)

Local anaesthetic performance can be greatly impaired by infectious diseases of the oral mucosa, such as fungal infections, such as candidiasis, and viral lesions, such as herpes simplex infections. These disorders are normally related to inflammation, damage to the epithelium, and alterations in tissue permeability [26].

As an example, candidiasis causes mucosal erythema and atrophy, and therefore, it can increase the uptake of the drug, but also makes it more sensitive and painful during injection. Viral lesions, especially herpetic ulcers, are very sensitive such that they may inhibit direct anaesthetics administration at the site of the lesions.

In addition, 1 infection may also change local immunity and tissue metabolism, which can impact drug distribution and elimination. Anaesthesia is a potential risk involved in the spread of infection and lack of efficacy when administered in an infected area [27].

#### 4.4 Systemic Conditions Affecting Oral Mucosa (Diabetes and Xerostomia)

Systemic diseases might also occur in the mouth cavity and have an indirect impact on the efficacy of the local anaesthetic effect. An example of microvascular alterations, wound healing impairments, and infection susceptibility is diabetes mellitus. These changes are able to influence drug delivery as well as tissue response to anaesthesia [28].

A diabetic patient can have a slow tissue perfusion, and this may slow the onset of anaesthesia, and it may also increase the duration of anaesthesia because of slower absorption into the system. Nevertheless, the effects can be neutralized by the co-occurring inflammation or infection, with the results being uncertain.

Xerostomia (or dry mouth) can be caused by systemic disorders or by medications, and it influences the hydration of the mucosa. As it is explained in Section 2,

proper hydration is the key to the maximum absorption of drugs, especially topical anaesthetics. Low salivary flow in xerostomic patients may affect the distribution of the drug and anaesthetics' efficacy [29].

#### 4.5 Fibrosis and Scarring

Oral mucosa that has been fibrotic due to trauma, surgery, radiation, or chronic illnesses, e.g., oral submucous fibrosis, may severely hinder the diffusion of local anaesthetic agents. Fibrotic tissues are also defined by excessive collagen deposition, low vascularity, and a lack of tissue elasticity [30].

These alterations result in a physical barrier to the diffusion of the drug, and hence, the anaesthetic finds it hard to reach the target nerve fibers. It might consequently require an additional amount of injection or other methods of injection, like nerve blocks or intraligamentary injection.

Also, due to the decreased vascularity of fibrotic tissues, the time of anaesthesia can be extended, as well as delayed. In these situations, clinicians have to be careful when adjusting their techniques, which will guarantee pain control.

#### Key Mechanisms Affecting Anaesthetic Effectiveness

Across all mucosal conditions, several common mechanisms influence local anaesthetic performance:

- **Altered pH and ionization:** Reduced pH limits the availability of the non-ionized form **necessary** for nerve penetration.
- **Increased blood flow:** Enhances drug clearance, reducing duration of action
- **Pain threshold changes:** Sensitized nociceptors increase resistance to anaesthesia

All these processes are the reason why normal anaesthetic regimes might fail in diseased tissues. The multi-factorial processes, which influence the efficacy of anaesthetics in sick mucosa, are summarized in Figure 2. Table 2 summarizes the interrelationship between the different mucosal conditions and the anaesthetic outcomes.

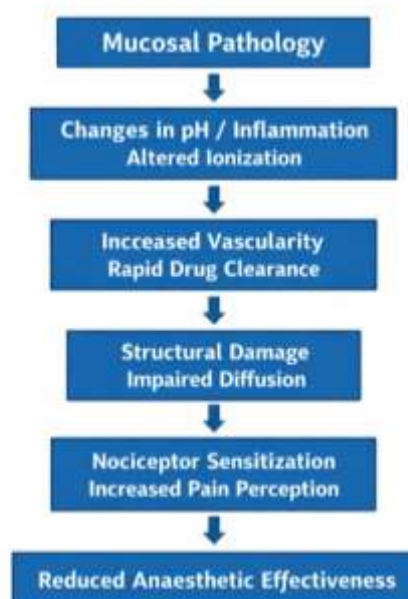


Figure 2. Mechanisms by Which Oral Mucosal Pathology Alters Local Anaesthetic Effectiveness

**Table 2. Effect of Different Oral Mucosal Conditions on Anaesthetic Success**

Condition	Pathophysiology	Effect on LA	Clinical Adjustment
Gingivitis/Periodontitis	Inflammation, ↓ pH, ↑ vascularity	Reduced onset, shorter duration	Use higher dose, nerve block, buffering
Aphthous ulcers	Epithelial loss, exposed nerves	Increased pain, reduced efficacy	Avoid lesion, inject adjacent tissue
Lichen planus	Chronic inflammation, mucosal damage	Variable diffusion	Gentle technique, topical adjuncts
Candidiasis	Erythema, epithelial atrophy	Increased sensitivity	Careful injection, antifungal management
Viral lesions	Ulceration, inflammation	Painful injection, reduced effect	Delay treatment if possible
Diabetes	Microvascular changes	Delayed onset, variable duration	Monitor dose, control systemic condition
Xerostomia	Reduced hydration	Reduced topical effectiveness	Pre-moisturize mucosa
Fibrosis/scarring	Dense collagen, ↓ vascularity	Poor diffusion, delayed onset	Use a nerve block or alternative techniques

### 5. Clinical Implications in Prosthodontic, Restorative, and Orthodontic Procedures

The clinical implication of the variability in local anaesthetic (LA) effectiveness based on oral mucosal conditions has a direct clinical implication in various dental specialties. Each of the processes mentioned in the previous paragraph (prosthodontic, restorative, and orthodontic) is associated with specific challenges, and anaesthetic approaches to these issues need to be customized. Knowing the effects of mucosal properties on drug action will allow clinicians to change procedures, use suitable drugs, and enhance patient outcomes.

#### 5.1 Prosthodontics

##### Denture-Bearing Mucosa

Denture-bearing mucosa is very important in treatment planning and dental procedures in the field of prosthodontics. Long-term use of dentures usually results in changes of this mucosa, including atrophy, thinning, or inflammation. Atrophic mucosa is less resistant and more susceptible, and thus, patients are more prone to discomfort during procedures that need anaesthesia [5].

Such situations could involve the preference of infiltration anaesthesia, as opposed to the use of nerve block to reduce tissue damage. As well, less anaesthetic solution is to be applied to prevent over-pressure of sensitive tissues. Topical anaesthetics may also be useful in minor procedures like adjustments or impression taking, which may cause some discomfort to the patient.

##### Flabby Ridges

Flabby ridges are usually present in edentulous patients, and this tissue is a mobile fibrous tissue that makes both anaesthetic delivery and impression processes difficult. Rapid vascularity and movement of this tissue may result in the quick dispersion of anaesthetic and its reduced efficiency [31].

To attain sufficient anaesthesia, clinicians have to use other methods, including nerve blocks instead of local

infiltrations. Also, the injection technique is to be followed carefully to ensure that the tissue is not distorted, as it may lead to poor results in prosthodontics.

#### Impression Procedures

Topical or minimal infiltration anaesthesia may have to be used in impression procedures, especially in sensitive or inflamed mucosa. Excessive application of anaesthesia will distort contours on tissues and interfere with the accuracy of impressions. As such, there should be a balance between the comfort of patients and the accuracy of the procedure [32].

#### 5.2 Restorative Dentistry

##### Caries with Pulpal Inflammation

The achievement of effective anaesthesia of teeth with pulpal inflammation, including symptomatic irreversible pulpitis, is one of the most important issues in restorative dentistry. In this situation, the traditional inferior alveolar nerve blocks can be ineffective as a result of the changes in tissue pH and the enhancement in nociceptor activity [19].

Additional methods such as intraligamentary, intraosseous, or intrapulpal injections are often necessary. In these situations, articaine has been found to be better than diffusion, especially in combination with nerve blocks as a buccal infiltration adjunct [21].

##### Endodontic Pain Challenges

Anaesthetic management is usually more complicated because, in most cases, endodontic procedures entail a pivotal inflamed or infected tissue. Patients who experience acute pain can also be found to be highly anxious and have lower pain thresholds, which also makes anaesthetic success more complicated.

Nonsteroidal anti-inflammatory drugs (NSAIDs) administration before surgery, buffering of anaesthetics, and higher concentration means of use can be used to achieve better results. Also, the deeper anaesthesia can be obtained with repeated or additional injections [6].

#### 5.3 Orthodontics

**Pain Control During Appliance Placement**

The orthodontic surgery is not very aggressive, but some surgeries, like mini-implantation or surgical exposure of the affected tooth, will need efficient local anaesthesia. Mucosa of orthodontic patients is normally healthy; however, localized irritation or inflammatory response of the appliance can affect anaesthetic output [33]. Infiltration anaesthesia is normally adequate in such cases. Nevertheless, clinicians need to pay attention to the state of the mucosa and change the method. In inflamed or ulcerated places, there may be a need to avoid or use alternative injections, for example.

**Soft Tissue Irritation**

Orthodontic appliances are often noted to induce irritation of the soft tissue, either in the form of localized ulceration or inflammation. Such situations may decrease the topical anaesthetic performance and cause pain to patients during the procedures. The use of topical anaesthetics, protective barriers and patient education are some of the interventions that are important in managing such conditions. When it needs

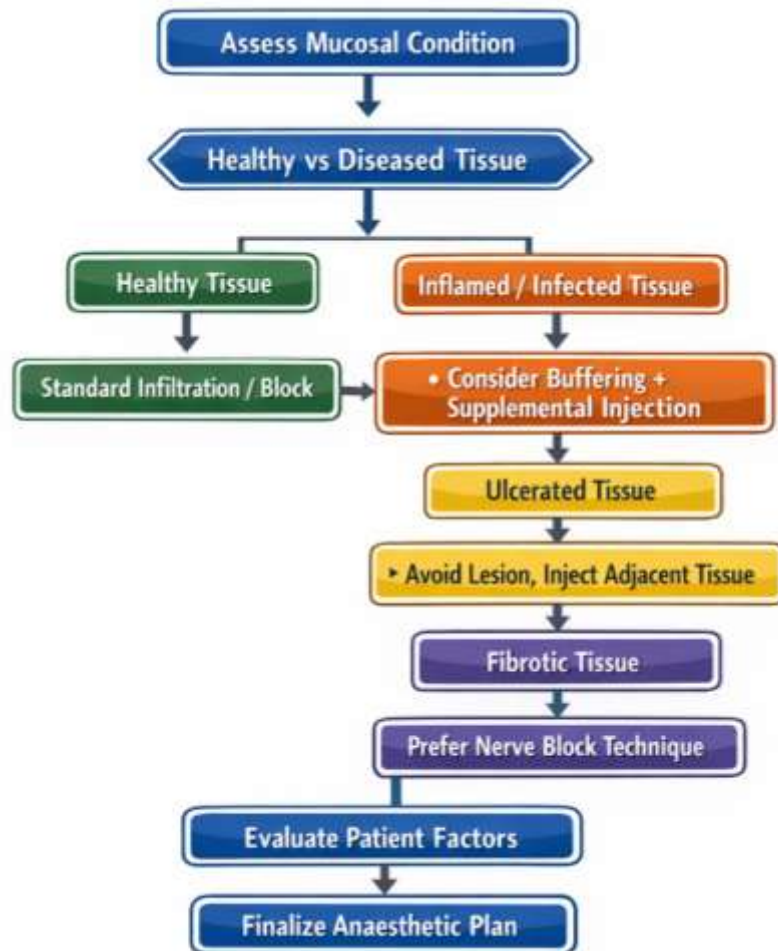
to be intervened with, it is necessary to introduce injections in the surrounding healthy tissue so that it becomes effective and causes minimal pain [34].

**Key Clinical Insights**

Across all specialties, several common principles emerge:

- **Technique modification:** Selection between infiltration and nerve block should be based on tissue condition and anatomical considerations
- **Use of adjuncts:** Buffering, warming, and premedication (e.g., NSAIDs) can enhance anaesthetic success
- **Patient-specific considerations:** Age, systemic health, anxiety levels, and mucosal condition must guide clinical decisions

A systematic mucosal-based anaesthetic selection process, represented in Figure 3, can have an important positive effect on clinical outcomes. Table 3 provides a summary of specialty-specific anaesthetic strategies.



**Figure 3. Clinical Decision-Making Algorithm for Local Anaesthetic Selection Based on Oral Mucosal Condition**

**Table 3. Recommended Anaesthetic Strategies Across Dental Specialties**

Specialty	Condition	Preferred Technique	Drug Choice	Notes
Prosthodontics	Atrophic mucosa	Infiltration	Lidocaine	Use minimal volume
Prosthodontics	Flabby ridge	Nerve block	Articaine	Avoid tissue distortion

Restorative	Irreversible pulpitis	Block + supplemental	Articaine	Consider buffering
Restorative	Endodontic infection	Intraosseous/intraligamentary	Lidocaine	Pre-op NSAIDs helpful
Orthodontics	Mini-implant placement	Infiltration	Lidocaine	Usually sufficient
Orthodontics	Soft tissue irritation	Topical/infiltration	Benzocaine/Lidocaine	Avoid inflamed areas
General	Fibrotic mucosa	Nerve block	Bupivacaine	Longer duration beneficial

## 6. Strategies to Improve Local Anaesthetic Effectiveness and Future Directions

Predictable and effective local anaesthesia (LA) in oral mucosal conditions that change is a major clinical issue. The recent developments in delivery systems, pharmacological adjustments, adjunctive treatment, and newer technologies have tried to overcome these shortcomings. In this part, the author will discuss evidence-based recommendations to improve anaesthetic outcomes and future trends in this dynamic area.

### 6.1 Advanced Delivery Systems

Advancements in systems of aesthetic delivery have made great contributions to accuracy, comfort of the patient, and clinical results. The computer-controlled local anaesthetic delivery (CCLAD) system is one of these developments that has made possible the regulation of flow rates and pressure, which reduces pain on injection. Research has shown that CCLAD systems enhance patient acceptance and anxiety, especially in sensitive mucosal situations [35].

Intraligamentary and intraosseous injection methods are very effective where the normal nerve block methods fail, particularly in inflamed or infected tissues. Such methods enable the delivery of the anaesthetic solution directly or near the target area, bypassing the barrier of a dense cortical bone or fibrotic tissue [18].

Also, needle-free jet injection systems have been investigated as an alternative route of administering anaesthetic agents transmucosally, which decreases fear and pain associated with the use of needles. They have limited clinical applicability, though, because the depth of anaesthesia is inconsistent.

### 6.2 Buffering Techniques and Warming

Local anesthetic solutions have been documented as effective in buffering with sodium bicarbonate. Buffering raises the pH of the solution and sets the equilibrium towards the non-ionized state of the drug, allowing the drug to penetrate the nerve much faster and experience less pain during injection [21].

Likewise, heating of an anaesthesia solution to body temperature has been found to ease discomfort during injection and could minimally improve the onset time. Though the clinical effects are not substantial, this intervention, which is very easy and inexpensive, can improve patient experience, especially in sensitive mucosal conditions [36].

Both buffering and warming are viable examples of practical changes that can be made at the chairside and could be added easily into the everyday dental practice.

### 6.3 Use of Adjuncts (NSAIDs and Sedation)

Pharmacological interventions by adjunctive means are important in enhancing anaesthetic success, particularly in instances where there is inflammation or pain hyperirritability. Use of nonsteroidal anti-inflammatory drugs (NSAIDs) before local anaesthesia has been demonstrated to improve the effect of local anaesthesia by inhibiting inflammatory mediators and sensitisation of nociceptors [37].

Alternative methods of sedation, such as nitrous oxide inhalation sedation and orally administered anxiolytics, may also enhance the comfort of patients and perception of anxiety-related pain. It has been determined that anxiety plays a critical role in determining the pain threshold and anaesthetic success, especially in complicated or lengthy operations [38].

Pharmacological adjuncts coupled with optimised anaesthetic procedures can play a major role in enhancing clinical outcomes in difficult cases.

### 6.4 Emerging Technologies (Nanocarriers and Liposomal Anaesthetics)

The emerging studies have been directed towards improving the pharmacokinetics of the local anaesthetics by developing efficient drug delivery systems, such as nanocarriers and liposomal formulations. Nanocarriers improve the stability of drugs, controlled delivery, and targeted delivery, which may improve efficacy and decrease systemic toxicity [39].

The local anaesthetic profile of liposomal bupivacaine is the longest lasting as the drug is released progressively. These are promising formulations that have demonstrated efficiency in surgical practice and could be used in the future in dentistry, especially in operations that involve prolonged analgesia [40].

These technologies have full potential; however, further clinical validation must be achieved before such new technologies can be widely adopted in dental practice.

### 6.5 Personalized Dentistry Approaches

The idea of personalized dentistry is becoming popular, which is focused on the individualized treatment planning based on the patient-specific factors that are genetic profile, systemic health, and tissue characteristics. The differences in metabolism of drugs, perception of pain, and response of tissues may have a profound impact on anaesthetic results [41].

As an example, the patient's response to local anaesthetic could be changed due to genetic polymorphisms in the function of sodium channels or

the metabolism of the drug. On the same note, systemic disorders like diabetes or chronic inflammation demand specific anaesthetic approaches to enable the best results. Precision medicine can be improved further in the future, thus enabling clinicians to anticipate anaesthetic response and tailor the treatment plans to meet the needs of this response.

### Key Emphasis: Evidence, Gaps, and Future Innovations

Current evidence supports the use of advanced delivery systems, buffering techniques, and adjunctive therapies to improve anaesthetic effectiveness. However, several research gaps remain:

- Limited large-scale clinical trials evaluating emerging technologies
- Inconsistent evidence regarding warming techniques
- Need for standardized protocols in compromised mucosal conditions
- Lack of integration of genetic and personalized approaches in routine practice

The innovations that are likely to be developed in the future are targeted drug delivery, biocompatible carriers, and AI-assisted clinical decision-making, which could redefine anaesthetic management in dentistry

### 7. Conclusion

The effect of excellent local anaesthesia in dentistry is significantly dependent on the pathological and structural specifics of the mucosa of the mouth. As noted in this review, differences in mucosal type, vascularity, pH, and underlying disease conditions can have important effects on the pharmacokinetics and clinical performance of local anaesthetic agents. The inflammatory, ulcerative, infectious, systemic, and fibrotic conditions pose their own problems, which could undermine the success of anaesthetics. In all types of prosthodontic, restorative, and orthodontic procedures, clinicians need to be cognizant of the fact that traditional anaesthetic modalities are not necessarily predictable. Rather, a unique strategy taking into account the condition of the tissues and the specificity of the patient is necessary. Changes to injection technique, choice of suitable anaesthetic use, including adjunctive measures like buffering, premedication, and state-of-the-art delivery devices, can be of significant benefit to clinical outcome. The new technologies, such as nanocarrier-based systems and liposomal formulations, have good potential for enhancing drug delivery and increasing the effects of anaesthesia. Also, the increasing tendency of individual dentistry makes the inclusion of personal patient characteristics in anaesthetic planning important. As much as these have been achieved, more studies should be conducted to help develop a common set of procedures to be used in the management of weakened mucosal diseases and also to confirm the clinical usefulness of new technologies. Research in the future should aim to conduct large-scale clinical trials, molecular pathways of anaesthetic resistance, and the application of precision medicine in dental anaesthesia. In conclusion, optimizing local anaesthetic effectiveness requires a comprehensive understanding

of oral mucosal biology, pharmacology, and clinical adaptability, ultimately enabling more predictable and patient-centered dental care.

### References

1. Becker DE, Reed KL. Essentials of Local Anesthetic Pharmacology. *Anesthesia Progress*. 2006 Jan 1;53(3):98–109. doi:10.2344/0003-3006(2006)53%5B98:EOLAP%5D2.0.CO;2
2. Nanci A. Ten Cate's Oral Histology [Internet]. 2017 [cited 2026 Mar 17]. Available from: <https://shop.elsevier.com/books/ten-cates-oral-histology/nanci/978-0-323-48524-1>
3. Malamed SF. *Handbook of Local Anesthesia*. 2004.
4. Budenz AW. Local anesthetics in dentistry: then and now. *J Calif Dent Assoc*. 2003 May;31(5):388–96. PubMed PMID: 12839231.
5. Carlsson GE, Omar R. The future of complete dentures in oral rehabilitation. A critical review. *J Oral Rehabil*. 2010 Feb;37(2):143–56. doi:10.1111/j.1365-2842.2009.02039.x PubMed PMID: 20002536.
6. Aggarwal V, Singla M, Miglani S. Comparative Evaluation of Anesthetic Efficacy of 2% Lidocaine, 4% Articaine, and 0.5% Bupivacaine on Inferior Alveolar Nerve Block in Patients with Symptomatic Irreversible Pulpitis: A Prospective, Randomized, Double-blind Clinical Trial. *Journal of Oral & Facial Pain & Headache*. 2017 Apr 1;31(2):124. doi:10.11607/ofph.1642
7. Squier CA, Kremer MJ. Biology of oral mucosa and esophagus. *J Natl Cancer Inst Monogr*. 2001;(29):7–15. doi:10.1093/oxfordjournals.jncimonographs.a003443 PubMed PMID: 11694559.
8. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. *J Pharm Pharm Sci*. 1998;1(1):15–30. PubMed PMID: 10942969.
9. Mazzinelli E, Favuzzi I, Arcovito A, Castagnola R, Fratocchi G, Mordente A, et al. Oral mucosa models to evaluate drug permeability. *Pharmaceutics*. 2023;15(5):1559. doi:10.3390/pharmaceutics15051559
10. Hussain N. Contemporary Dental Pharmacology: Evidence-Based Considerations. *Evid Based Dent*. 2024 Dec;25(4):173–173. doi:10.1038/s41432-024-01074-8
11. Renton T, Adey-Viscuso D, Meechan JG, Yilmaz Z. Trigeminal nerve injuries in relation to the local anaesthesia in mandibular injections. *Br Dent J*. 2010 Nov;209(9):E15. doi:10.1038/sj.bdj.2010.978 PubMed PMID: 21072069.
12. Matthews R, Scully C. Oral and Maxillofacial Medicine [Internet]. 2012 [cited 2026 Mar 18]. Available from: <https://shop.elsevier.com/books/oral-and-maxillofacial-medicine/scully/978-0-7020-4948-4>
13. Edgar M, Colin D, Denis O. ResearchGate [Internet]. 2012 [cited 2026 Mar 17]. Saliva and Oral Health | Request PDF. Available from: [https://www.researchgate.net/publication/261061703\\_Saliva\\_and\\_Oral\\_Health](https://www.researchgate.net/publication/261061703_Saliva_and_Oral_Health)

14. Oertel R, Rahn R, Kirch W. Clinical Pharmacokinetics of Articaine. *Clin Pharmacokinet.* 1997 Dec 1;33(6):417–25. doi:10.2165/00003088-199733060-00002
15. Butterworth JF, Strichartz GR. Molecular mechanisms of local anesthesia: a review. *Anesthesiology.* 1990 Apr 1;72(4):711–34. doi:10.1097/00000542-199004000-00022 PubMed PMID: 2157353.
16. Rang HP, Dale MM, Ritter JM, Flower RJ, Henderson G. Rang & Dale's pharmacology [Internet]. Elsevier Health Sciences; 2011 [cited 2026 Mar 17]. Available from: [https://books.google.com/books?hl=en&lr=&id=s2R-ZYz\\_iBYC&oi=fnd&pg=PT26&dq=Rang,+H.+P.,+Dale,+M.+M.,+Ritter,+J.+M.,+Flower,+R.+J.,+%26+Henderson,+G.+\(2020\).+Rang+and+Dale%E2%80%99s+pharmacology+\(9th+ed.\).+Elsevier.&ot s=coDADhR\\_UU&sig=5i9og\\_zRZE\\_qvnYQHGX eudLHioQ](https://books.google.com/books?hl=en&lr=&id=s2R-ZYz_iBYC&oi=fnd&pg=PT26&dq=Rang,+H.+P.,+Dale,+M.+M.,+Ritter,+J.+M.,+Flower,+R.+J.,+%26+Henderson,+G.+(2020).+Rang+and+Dale%E2%80%99s+pharmacology+(9th+ed.).+Elsevier.&ot s=coDADhR_UU&sig=5i9og_zRZE_qvnYQHGX eudLHioQ)
17. Haas DA. An update on local anesthetics in dentistry. *Journal-Canadian Dental Association.* 2002;68(9):546–52.
18. Meechan JG. Supplementary routes to local anaesthesia. *International Endodontic Journal.* 2002;35(11):885–96. doi:10.1046/j.1365-2591.2002.00592.x
19. Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: *Endodontic Topics.* 2002;1(1):26–39. doi:10.1034/j.1601-1546.2002.10103.x
20. Yagiela JA, Dowd FJ, Johnson B, Mariotti A, Neidle EA. Pharmacology and therapeutics for dentistry-E-Book: pharmacology and therapeutics for dentistry-E-Book [Internet]. Elsevier Health Sciences; 2010 [cited 2026 Mar 18]. Available from: [https://books.google.co.in/books?hl=en&lr=&id=utVOHYuhxioC&oi=fnd&pg=PP1&dq=Yagiela,+J.+A.+\(1999\).%0D%0APharmacology+and+Therapeutics+for+Dentistry+\(4th+ed.\).%0D%0ASt.+Louis:+Mosby.&ots=wqRhYyti\\_c&sig=GkTUK E97E3TeLJkFWcv8ycW240](https://books.google.co.in/books?hl=en&lr=&id=utVOHYuhxioC&oi=fnd&pg=PP1&dq=Yagiela,+J.+A.+(1999).%0D%0APharmacology+and+Therapeutics+for+Dentistry+(4th+ed.).%0D%0ASt.+Louis:+Mosby.&ots=wqRhYyti_c&sig=GkTUK E97E3TeLJkFWcv8ycW240)
21. Kanaa MD, Whitworth JM, Meechan JG. A Prospective Randomized Trial of Different Supplementary Local Anesthetic Techniques after Failure of Inferior Alveolar Nerve Block in Patients with Irreversible Pulpitis in Mandibular Teeth. *Journal of Endodontics.* 2012 Apr 1;38(4):421–5. doi:10.1016/j.joen.2011.12.006
22. Aggarwal V, Singla M, Miglani S, Kohli S, Singh S. Comparative Evaluation of 1.8 mL and 3.6 mL of 2% Lidocaine with 1:200,000 Epinephrine for Inferior Alveolar Nerve Block in Patients with Irreversible Pulpitis: A Prospective, Randomized Single-blind Study. *Journal of Endodontics.* 2012 Jun 1;38(6):753–6. doi:10.1016/j.joen.2012.02.003
23. Petersen PE, Ogawa H. The global burden of periodontal disease: towards integration with chronic disease prevention and control. *Periodontology* 2000. 2012;60(1):15–39. doi:10.1111/j.1600-0757.2011.00425.x
24. Meechan JG. Why Does Local Anaesthesia Not Work Every Time? *Dental Update.* 2005 Mar 2;32(2):66–72. doi:10.12968/denu.2005.32.2.66
25. Scully C, Porter S. Oral mucosal disease: Recurrent aphthous stomatitis. *British Journal of Oral and Maxillofacial Surgery.* 2008 Apr 1;46(3):198–206. doi:10.1016/j.bjoms.2007.07.201
26. Akpan A, Morgan R. Oral candidiasis. *Postgrad Med J.* 2002 Aug 1;78(922):455–9. doi:10.1136/pmj.78.922.455
27. Samaranayake L. Essential microbiology for dentistry. 4. ed. Edinburgh: Churchill Livingstone, Elsevier; 2012. 382 p.
28. Iacopino AM. Periodontitis and Diabetes Interrelationships: Role of Inflammation. *Ann Periodontol.* 2001 Dec;6(1):125–37. doi:10.1902/annals.2001.6.1.125
29. Villa A, Wolff A, Narayana N, Dawes C, Aframian D, Lynge Pedersen A, et al. World Workshop on Oral Medicine VI: a systematic review of medication-induced salivary gland dysfunction. *Oral Diseases.* 2016;22(5):365–82. doi:10.1111/odi.12402
30. Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ, Warnakulasuriya S. Oral submucous fibrosis: Review on aetiology and pathogenesis. *Oral Oncology.* 2006 Jul 1;42(6):561–8. doi:10.1016/j.oraloncology.2005.08.005
31. Lynch CD, Allen PF. Management of the flabby ridge: using contemporary materials to solve an old problem. *Br Dent J.* 2006 Mar;200(5):258–61. doi:10.1038/sj.bdj.4813306
32. Zarb GA, Jacob R, Eckert S. Prosthodontic treatment for edentulous patients, 13/e [Internet]. Elsevier India; 2012 [cited 2026 Mar 17]. Available from: [https://books.google.com/books?hl=en&lr=&id=GbfwAwAAQBAJ&oi=fnd&pg=PA303&dq=Zarb,+G.+A.,+Hobkirk,+J.,+Eckert,+S.,+%26+Jacob,+R.+\(2013\).+Prosthodontic+treatment+for+edentulous+patients+\(13th+ed.\).+Elsevier.&ots=q7ztW1nH3\\_&sig=QN6ZqEL3akg\\_240HWGDD\\_ys29D4](https://books.google.com/books?hl=en&lr=&id=GbfwAwAAQBAJ&oi=fnd&pg=PA303&dq=Zarb,+G.+A.,+Hobkirk,+J.,+Eckert,+S.,+%26+Jacob,+R.+(2013).+Prosthodontic+treatment+for+edentulous+patients+(13th+ed.).+Elsevier.&ots=q7ztW1nH3_&sig=QN6ZqEL3akg_240HWGDD_ys29D4)
33. Krishnan V. Orthodontic pain: from causes to management—a review. *Eur J Orthod.* 2007 Apr 1;29(2):170–9. doi:10.1093/ejo/cjl081
34. Proffit WR, Fields H, Larson B, Sarver DM. Contemporary Orthodontics [Internet]. 2018 [cited 2026 Mar 17]. Available from: <https://shop.elsevier.com/books/contemporary-orthodontics/proffit/978-0-323-54387-3>
35. Hochman MN, Friedman MJ, Williams W, Hochman CB. Interstitial tissue pressure associated with dental injections: A clinical study. *Quintessence International.* 2006 Jun 1;37(6):469.
36. Hogan ME, vanderVaart S, Perampaladas K, Machado M, Einarson TR, Taddio A. Systematic Review and Meta-analysis of the Effect of Warming Local Anesthetics on Injection Pain. *Annals of Emergency Medicine.* 2011 Jul 1;58(1):86–98.e1. doi:10.1016/j.annemergmed.2010.12.001
37. Parirokh M, Ashouri R, Rekabi AR, Nakhaee N, Pardakhti A, Askarifard S, et al. The Effect of Premedication with Ibuprofen and Indomethacin on the Success of Inferior Alveolar Nerve Block for

- Teeth with Irreversible Pulpitis. *Journal of Endodontics*. 2010 Sep 1;36(9):1450–4. doi:10.1016/j.joen.2010.05.007
38. Armfield J, Heaton L. Management of fear and anxiety in the dental clinic: a review. *Australian Dental Journal*. 2013;58(4):390–407. doi:10.1111/adj.12118
39. de Paula E, Cereda CMS, Tofoli GR, Franz-Montan M, Fraceto LF, de Araujo DR. Drug Delivery Systems for Local Anesthetics. *Recent Patents on Drug Delivery & Formulation*. 2010 Jan 1;4(1):23–34. doi:10.2174/187221110789957228
40. Chahar P, Cummings KC. Liposomal bupivacaine: a review of a new bupivacaine formulation. *J Pain Res*. 2012 Aug 14;5:257–64. doi:10.2147/JPR.S27894 PubMed PMID: 23049275; PubMed Central PMCID: PMC3442744.
41. Lötsch J. Genetic variability of pain perception and treatment—clinical pharmacological implications. *Eur J Clin Pharmacol*. 2011 Jun 1;67(6):541–51. doi:10.1007/s00228-011-1012-9