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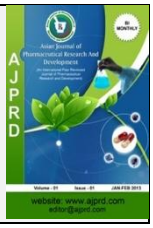

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Review Article

Role of Chewable Tablets: An Overview

Santosh Kumar Bhatt, Kedarnagalakshman M, Mukesh Sharma

Department of pharmaceutics, Oxbridge college of Pharmacy, Bengaluru -560091, Karnataka, India

A B S T R A C T

Chewable dosage forms for example tablets, delicate, pills, gums, chewable squares is long piece of drug specialist armamentarium. They are required to be break and bit in the middle of the teeth before administration. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. These tablets are intended to disintegrate smoothly in the mouth at a moderate rate either with or without actual chewing, characteristically chewable tablets have a smooth texture upon disintegration, are pleasant tasting and leave no bitter or unpleasant taste. Geriatric and pediatric patients and travelling patients who may not have ready access to water are most need of easy swallowing dosage forms like chewable tablets. The major formulation factors are flow, lubrication, disintegration, organoleptic properties, compressibility, compatibility and stability, which are common to regular (swallowed) and chewable tablets; however, organoleptic properties of the active drug substances are primary concern here. A formulator may use one or more approaches to arrive at a combination of formula and process that result in product with good organoleptic properties.

Keywords: chewable tablet, lubrication, disintegration, compressibility etc.

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***Address for Correspondence:**

Santosh kumar Bhatt, Department of pharmaceutics, Oxbridge college of Pharmacy, Bengaluru -560091, Karnataka, India

INTRODUCTION

Oral route is most commonly employed route of drug administration. Although different routes of administration are used for the delivery of drugs, due to flexibility in dosage form design and patient compliance oral route is preferred. The popularity of the oral route is attributed to ease of administration, patient acceptance, accurate dosing, cost effective manufacturing method and generally improved shelf-life of the product. There are several techniques of conventional drug delivery systems where tablets, capsules, pills, liquids, are used as drug carrier. Among them, solid formulations do not require sterile conditions and are therefore, less expensive to manufacture.[1]

Solid oral dosage forms: [2,3,4]

Oral solid dosage forms such as tablets and hard gelatin capsules, which have been in existence since 19th century, remain the most frequently used dosage forms. Oral route of delivery is a route that the patient understands and accepts. For the manufacturer solid oral dosage forms offer many advantages: they utilize cheap technology, are generally the most stable forms of drugs, are compact and their appearance can be modified to create brand identification.

Tablets and capsules are very versatile. When formulating any pharmaceutical dosage form, it is important to remember that there is equilibrium between the bioavailability of the product, its chemical and physical stability and the technical feasibility of producing it. Tablets and capsules represent unit dosage forms in which one usual dose of drug has been accurately placed. By comparison liquid forms such as syrups, suspensions, emulsions, solutions and elixirs are usually designated to contain one medication in 5-30ml, such dosage measurements are typically error by a factor ranging from 20 -50%, when the drug is self-administered by patient.

Types of Solid Dosage Forms:[4,5,6]

There are many different types of tablets which can be designed to fulfil specific therapeutic needs.

Table 1: Types of solid dosage forms

Formulation type	Description
Immediate release tablets	The dosage form is designed to release the drug substanceimmediately after ingestion.
Chewable tablets	Strong, hard tablets to give good mouth feel.
Lozenges	Strong, slowly dissolving tablets for local delivery to mouth or
Buccal tablets	Tablets designed to be placed in buccal cavity of mouth for rapid
Effervescent	tablets
Dispersible tablets	Tablets taken in water, the tablet forms a suspension for ease of
Soluble tablets	Tablets taken in water, the tablet forms a solution for ease of
Hard gelatin capsules	Two-piece capsule shells, which can be filled with powders, pellets,semisolids or liquids.
Soft gelatin capsules	One-piece capsules containing a liquid or semisolid fill.
Pastilles	Intended to dissolve in mouth slowly for the treatment of localinfections. Usually composed of a base containing gelatin and glycerin.

TABLETS:[1,4]

In 1843, the first patent for a hand operated device used to form a tablet was granted. Tabletsare defined as solid dosage forms each containing a single dose of one or more activeingredients, obtained by compressing uniform volumes of particles. They are intended for theoral administration, some are swallowed whole, some after being chewed. Some aredissolved or dispersed in aqueous phase before being administered and some are retained inthe mouth, when the active ingredients are "liberated".Tablets are used mainly for systemic drug delivery but also for local drug action. Forsystemic use drug must be released from tablet that is dissolved in the fluids of mouth,stomach and intestine and then absorbed into systemic circulation by which it reaches its siteof action.

The tablet is composed of the Active Pharmaceutical Ingredient (active drug) together with various excipients. These are biologically inert ingredients which either enhance the therapeutic effect or are necessary to construct the tablet. The filler or diluents (e.g. Lactose or Sorbitol) are a bulking agent, providing a quantity of material which can accurately be formed into a tablet. Binders (e.g. methyl cellulose or gelatin) hold the ingredients together so that they can form a tablet. Lubricants (e.g. magnesium stearate or polyethylene glycol) are added to reduce the friction between the tablet and the punches and dies so that the tablet compression and ejection processes are smooth. Disintegrants (e.g. starch or cellulose) are used to promote wetting and swelling of the tablet so that it breaks up in the gastrointestinal tract; this is necessary to ensure dissolution of the API. Superdisintegrants are some times used to greatly speed up the disintegration of the tablet. Additional ingredients may also beadded such as coloring agents, flavoring agents and coating agents. Formulations are designed using small quantities in a laboratory machine called a Powder Compaction Simulator. This can prove the manufacturing process and provide information.

Advantage of the tablet dosage form:[7]

- They are unit dosage form with great dose precision and the lease content variability.
- Cost is lowest of all oral dosage forms.
- Light and compact.
- Easy and cheap to pack and strip.
- Objectionable odour and bitter taste cab be masked by coating techniques.
- Suitable for large scale production.

Disadvantages of the tablet dosage form:[8]

- Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low density character.
- Drugs with poor wetting, dissolution properties, intermediate to large dosages, optimum absorption high in the GIT or any combination of these features may be difficult to impossible to formulate and manufacture as a tablet that will still provide adequate full drug bioavailability.
- Bitter tasting drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression or the tablets may require coating. In such cases, the tablets may offer the best and lowest cost approach.

Types of tablets:[5,6]

The main reason behind formulation of different types of tablets are to create a delivery system that is relatively simple and inexpensive to manufacture, provide the dosage form that is convenient from patients perspective and utilize an approach that is unlikely to add complexity during regulatory approval process. To perceive each dosage form, tablets here are classified by their route of administration and by the type of drug the delivery system represent within that route.

1. **Oral tablets for ingestion:**
    - Standard compressed tablets
    - Multiple compressed tablets
        - Compression coated tablets
        - Layered tablets
        - Inlay tablets
    - Modified release tablets
    - Delayed action tablets
    - Targeted action tablets
        - Floating tablets
        - Colon targeting tablets
    - Chewable tablets
    - Dispersible tablets

2. **Tablets used in the oral cavity:**
   - Lozenges and troches
   - Sublingual tablets
   - Buccal tablets
   - Dental cones
   - Mouth dissolving tablets
3. **Tablets administered by other routes:**
   - Vaginal tablets
   - Implants
4. **Tablets used for prepare solution:**
   - Effervescent tablets
   - Hypodermic tablets
   - Soluble tablets

CHEWABLE TABLETS: [8,9]

Chewable tablets are tablets that are required to be broken and chewed in between the teeth before ingestion. These tablets are given to children who have difficulty in swallowing and to the adults who dislike swallowing. Chewable tablets are chewed and broken into smaller pieces prior to swallowing and are not to be swallowed intact. In this way, the time required for disintegration is reduced and the rate of absorption of themedicament may increase. For the preparation of chewable tablets, mannitol is used as thebase. These tablets should have acceptable taste and flavour. They should disintegrate in ashort time and produce cool sweet taste.

Manufacturing of chewable tablet is generally done using either wet granulation process or direct compression. Increasingly, micronized and submicron forms of therapeutically and physiologically active substances are incorporated into tablet formulation to take advantage of the enhanced absorption characteristics of these forms. They are also used in the administration of antacids and carminatives. Mannitol is widely used as an excipient in chewable tablet for its non-hygroscopic nature for moisture sensitive drugs. As we know difficulty in swallowing (Dysphasia) is common among all age groups, especially in elderly and in also seen of swallowing of conventional tablets and capsules. The composition of chewable tablet consists of gum core, which may or may not be coated. The core is composed of an insoluble gum base like fillers, waxes, antioxidants, sweeteners, flavouring agents. The percentage of gum base varies from 30-60% depending upon the base used and its properties. A flavouring agent is included to make it more palatable.

Advantages of chewable tablets:[8,9]

Chewable tablets are generally chewed in the mouth prior to swallowing and are not expected to swallow intact. Main purpose of chewable tablet is to provide proper unit dosage form of medication which can easily be administered to children or to the elderly who have difficulty in swallowing a tablet intact. Chewable tablet have some specific advantages:

- Better bioavailability through bypassing disintegration (that increase dissolution).
- Improved patient acceptance (especially pediatric)through pleasant taste.
- Patient convenience; need no water for swallowing.
- Possible to use as a substitute for liquid dosage forms where rapid onset of action is needed.
- Absorption of drug is faster.
- Product distinctiveness through marketing prospective.
- The large size of the dosage form is difficult to swallow. In such cases chewable tablet offers advantages over it.
- Effectiveness of therapeutic agent is improved by the reduction in size that occurs during mastication of tablet before swallowing.

Disadvantages of chewable tablets: [8,9]

There are, of course some limitations to the use of chewable tablets having bad tasting drugs and extremely high dosage level. Some disadvantages of chewable tablet are:

- It contains sorbitol which causes diarrhoea and flatulence.
- Flavouring agents present in chewable tablet may causes ulcer in oral cavity.
- Prolonged chewing of chewable tablet results in pain in facial muscles.
- They are hygroscopic in nature, so must kept in dry place.
- They show the fragile, effervescence granules property.
- Since these tablets have insufficient mechanical strength, so careful handling is required.
- They require proper packaging for safety and stabilization of stable drugs.

General formulation factors for chewable tablets:[8, 9, 10]

There are various factors involved in the formulation of chewable tablets. The major formulation factors are flow, lubrication, disintegration, organoleptic properties, compressibility, compatibility and stability, which are common to regular (swallowed) and chewable tablets; however, organoleptic properties of the active drug substances are primary concern here. A formulator may use one or more approaches to arrive at a combination of formula and process that result in product with good organoleptic properties. Such a substance must have acceptable flow, compressibility and stability characteristics.

Taste and flavours:

Physiologically, taste is a sensory response resulting from a chemical stimulation of the taste buds on the tongue. Salty or sour tastes are derived from substances capable of ionizing in the solution. Many organic medicinal compounds stimulate a bitter response even though they may not be capable of ionizing in an aqueous medium. Most saccharides, disaccharides, some aldehydes and few alcohols give a sweet taste. Substance incapable of producing a sensory stimulation of the buds is known as tasteless. The term flavour generally refers to a specific combined sensation of taste and smell. For example, sugar has a sweet taste, but no flavour, whereas honey has a sweet taste and a characteristics smell.

Aroma:

Pleasant smells are generally referred to as aromas. For example, a well formulated, orange-flavoured chewable tablet should have a characteristic sweet and sour taste and aroma of fresh orange.

Mouth-feel:

This term is related to the type of sensation or touch that a tablet produce in the mouth upon chewing. As such, it has nothing to do with chemical stimulation of olfactory nerves or taste buds. However, for a formulation to be successful, the overall effect in the mouth is important. In general, gritty (e.g., calcium carbonates) or gummy texture is undesirable, whereas soothing and cooling sensation (e.g., mannitol) with smooth texture is preferred.

After effects:

The most common after effect of many compounds is after taste. For example, some irons leave a "rusty" after taste; saccharin in high amounts tends to leave a bitter after taste. Another common after effect is a numbing sensation of a portion of the whole surface of the tongue and mouth. Bitter antihistamines like pyribenzamine hydrochloride and promethazine hydrochloride are typical of this class drugs.

Colouring:

For aesthetic appeal and product differentiation, chewable tablets are often coloured. Colorants can also be used to mask unappealing natural colour, resulting from various raw materials. Colorants can be used for the uniform production of batches if raw materials have a slightly different colour. Colorants in chewable tablets are usually chosen to match the flavour. Colorants are available as natural pigments and synthetic organic dyes. In chewable tablets, the most widely used forms of the colorant are aqueous soluble dyes and lakes made from these dyes.

Chewability:

Acceptability of chewable dosage forms also depends on the chewability of the product. Chewability of a chewable dosage form may be defined as effortless chewing of the product with no desirable gumminess, stickiness, chalkiness or grittiness, yet coupled with a pleasant cooling sensation in the mouth. These properties are imparted by the use of excipients that have inherently good mouth feel and chewability characteristics. Excipients with such properties include mannitol and blends of mannitol, sorbitol, fructose and sucrose.

Need for the Development of Chewable Tablet: [9,10]

The need for non-invasive delivery systems persists due to patients' poor acceptance of, and compliance with, existing delivery regimes, limited market size for drug companies and drug uses, coupled with high cost of disease management.

Patient related factors: Approximately one-third of the patients need quick therapeutic action of drug, resulting in poor compliance with conventional the drug therapy which leads to reduced overall therapy effectiveness. A new dosage form, the immediate release tablets has been developed which offers the combined advantages of ease of dosing and convenience of dosing. These tablets are designed to release the medicaments with an enhanced rate. Chewable dosage forms are particularly suitable for patients, who for one reason or the other; find it inconvenient to swallow traditional tablets and capsules with an 8-oz glass of water.

- Very elderly patients who may not be able to swallow a daily dose of antidepressant.
- An eight-year old with allergies who desires a more-convenient dosage form than antihistamine syrup.

Effectiveness factors: Increased bioavailability and faster onset of action are a major claim of these formulations. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of hepatic metabolism. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism.

Manufacturing and marketing related factors: Developing new drug delivery technologies and utilizing them in product development is critical for pharmaceutical industries to survive, regardless of their size. As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation, value added product line extension and extend patent protection, while offering its patient population a more convenient dosage form. This leads to increased revenue, while also targeting underserved and under-treated patient populations.

General excipients used in the formulation of chewable tablets:[11]

Special consideration, however, needs to be given to those materials that form the basis for chewable tablet formulation. The acceptability in the formulation of chewable tablets will be primarily determined by taste and to a lesser degree, appearance. Therefore, appropriate selection and use of components that impact on these properties are of extreme importance. In the pharmaceutical industry it is a catch all term which various sub-groups comprising diluents or fillers, binders or adhesives, disintegrants, lubricants, glidant, flavors, colours and sweeteners. All of these must meet certain criteria as follows:

- They must be physiologically inert.
- They must be acceptable to regulatory agencies.
- They must be physiologically and chemically stable.
- They must be free of any bacteria considered to be pathogenic or otherwise objectionable.
- They must not interface with the bioavailability of the drug.
- They must be commercially available in the form and purity commensurate to pharmaceutical standards.
- Cost must be relatively inexpensive.
- They must conform to all regulatory requirements.

To assure that no excipient interferences with the utilization of the drug, the formulator mustcarefully and critically evaluate combinations of the drug with each of the contemplatedexcipients and must have certain compliance of each ingredient with existing standards andregulations.The screening of drug-excipient and excipient-excipient interactions should be carried outroutinely in pre formulation studies.

Table 2: List of excipients used in the formulation of chewable tablets

Excipients	Functions	Examples
Diluents	Diluents are fillers used to make required bulk of tablet	Lactose, Microcrystalline cellulose, Mannitol etc.
Binders	Binders are used to impart cohesive qualities to powdered materials.	Gelatin, Glucose, Acacia, ethyl cellulose, hydroxypropylmethyl cellulose, starch, etc.
Superdisintegrants	They facilitate tablet breaking when it comes in contact with water in oral cavity/GIT	Croscarmellose sodium, Crospovidone, Sodium starch glycolate, Starch etc.
Lubricants	These are added to prevent adhesion of tablet material to surface of dies and punches reduces inter particulate friction.	Magnesium sterate, Talc, Paraffin, sodium lauryl sodium, etc.
Glidants	These are added to improve flow characteristics of powder mixture. Glidant minimize the friction between particles.	Colloidal Silicon dioxide(Aerosil), Corn starch, Talc etc.
Sweeteners	These are added to produce a palatable dosage form.	Sucrose, Saccharin, Aspartame, etc.
Flavours	These are added to improve taste of dosage form	Peppermint, Vanilla, Orange, Cinnamon, Mango, Cherry, Menthol, etc
Colours	These are added for better appearance of dosage form	Sunset yellow (Supra),Ferricoxide.

Methods of Manufacturing of chewable tablets:[12]

The Chewable tablets were prepared by using the following methods:

1. Non aqueous Granulation/Dry granulation

2. Aqueous Granulation/Wet granulation

3. Direct compression

Granulation: Granulation is the process in which primary powder particles are made to adhere to form larger, multi-particles entities called granules. Pharmaceutically granules have size range between 0.2 to 4.0 mm. Granulation is used to improve flow and compressibility of powders and to prevent segregation of the blend components. Granulation is mainly done by using two techniques.

Dry granulation: It is the novel method for semi-automatic production of granules. The method is applicable to any solid dosage pharmaceutical products. Dry granulation method replaces existing solid dosage form development and manufacturing technologies offering more rapid development and better quality. In this process, the powder mixture is compressed without the use of heat and solvent. Two methods are used for dry granulation. The more widely used is slugging where the powder is recompressed and the resulting tablet are milled to yield the granules.

Wet granulation: Wet granulation is the most commonly used granulation method. This process involves wet massing of powder blend with a granulating liquid, wet sizing and drying. The granulating liquid contains a solvent which must be volatile so that it can be removed by drying and must be non-toxic in nature. Typical liquid include water, ethanol and Isopropyl alcohol. In the traditional wet granulation method the wet mass is forced through a sieve to produce wet granules which are subsequently dried.

Direct compression: Direct compression is the most popular choice because it provides the shortest, most effective and least complex way to produce tablets. This method is mainly used when a group of ingredients can be blended. This is more suitable for moisture and heat sensitive API's since it eliminates wetting and drying steps and increase the stability of active ingredient by reducing detrimental (harmful) effects. In this process, API mixed with the excipients and lubricant, followed by compression which makes the product easy to process.

Evaluation parameters for chewable tablet:[12]

The variety of evaluation parameters must be kept in mind during the formulation of chewable tablets. These are given as follows:

In-process organoleptic evaluation: This evaluation takes place at various stages in the development of a chewable tablet. These are as follows:

Evaluation of drug itself: It involves characterization and comparison of the substance in an absolute amount or against a known reference standard.

Evaluation of coated drug: It involves comparison against the pure drug as well as different coating treatment.

Evaluation of unflavoured baseline formulation: It involves comparison among different vehicles, proportion of vehicles or other formulation variables in presence of coated drug.

Evaluation of flavoured baseline formulation: It involves comparison among different flavoured formulations.

Evaluation of final selection and product acceptance test: It involves comparison between two formulations or competitive product.

Chemical evaluation of chewable tablets: It involves the following:

1. Assay of drug content.

2. Dosage uniformity.

3. *In-vitro* and *in-vivo* evaluation.

Physical evaluationof chewable tablets: It involves the following:

1. Tablet physical appearance

2. Hardness

3. Friability

4. Disintegration

5. Dissolution

Some marketed formulations of chewable tablet:[12]
Today Chewable Tablet is one of the most popular dosage form, used for delivering the many active components. Some marketed products of chewable tablet are given below in table 3.

Table 3: Marketed formulations of chewable tablets

Brand Name	Active Ingredient	Application
Claritin	Loratadine	Antihistamine
Montair	Montelukast	Asthma
Lamictal	Lamotrigine	Seizures
Mylanta Gas	Simethicone	Gastric relief
Natecal D3	Natecal D3	Osteoporosis
Tylenol	Acetaminophen	Analgesic

DISEASE PROFILE

LOCAL ANAESTHETIC AGENTS:[13-15]

Introduction:

Local anaesthetics are drugs that block conduction of electrical impulses in excitable tissues. These tissues include the nerve cells and myocytes (both cardiac and skeletal muscles). Analgesia and anaesthesia occur as a result of the blockage of electrical impulses. Other local anaesthetics like lidocaine also possess Class I antiarrhythmic properties. Before a detailed venture into the physical-chemical properties and mechanism of action of this class of drugs, a brief overview of the nerve anatomy is discussed. This will aid in the overall understanding of how these agents work and how their efficacy and safety can be improved by the use of appropriate doses and adjuncts.

History:

Cocaine, a compound indigenous to the Andes Mountains, West Indies, and Java, was the first anesthetic to be discovered and is the only naturally occurring local anesthetic; all others are synthetically derived. Cocaine was introduced into Europe in the 1800s following its isolation from coca beans. Sigmund Freud, the noted Austrian psychoanalyst, used cocaine on his patients and became addicted through self-experimentation. In the latter half of the 1800s, interest in the drug became widespread, and many of cocaine's pharmacologic actions and adverse effects were elucidated during this time. In the 1880s, Koller introduced cocaine to the field of ophthalmology, and Hall introduced it to dentistry.

Structure-activity relationship of local anaesthetics:

Local anaesthetics consist of a hydrophilic amine and a lipophilic aromatic ring connected by an intermediate chain. The structural bond in the intermediate chain determines whether the local anaesthetic will be classified as an ester or an amide. Furthermore, the bond in the intermediate chain determines the pathway of metabolism of the compound. Ester local anaesthetics are metabolised by plasma pseudocholinesterases, whereas the amides are metabolised in the liver by the cytochrome family of enzymes.

Mechanism of action of local anaesthetics:

Local anaesthetic blocks the transmission of nerve impulses by reversibly blocking the fast voltage-gated sodium channels, thereby inducing analgesia and anaesthesia. Physicochemically, local anaesthetics are weak bases that are formulated in an acidic milieu, hence containing a larger proportion of the drug in the ionised state. However, it is the unionised fraction that is able to cross the lipid bilayer neuronal membrane and block the voltage-gated sodium channels from the inside of the axoplasm. This blockade renders the sodium channel inactive, and hence, no further conduction of impulses occurs. Diagramatically this is well demonstrated by Figure 1.

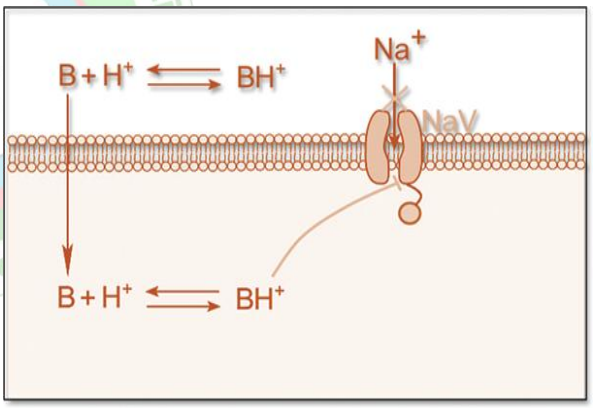

Figure 1: Mechanism of action of local anaesthetics

Determinants of physiological activities of local anaesthetics:

The activity of local anaesthetics is influenced by a number of factors. These include the pH of the surrounding tissue, the lipid solubility of the local anaesthetic, pKa, the bond in the intermediate chain and its length and the protein binding of the particular local anaesthetic in question. Details of how each of these factors influence the activity of local anaesthetics is discussed below:

pKa: The pKa is the pH at which the number of ionised and unionised fractions of the drug is in equilibrium. The lower the pKa, the more the unionised fraction is present for any given pH and hence the faster the onset of action.

pH: The lower the pH, that is, acidic milieu, the less the potency because in acidic conditions the ionised fraction predominates, there is less of the unionised fraction, and

there is less of the local anaesthetic available to cross the lipid bilayer and block the voltage-gated sodium channels. This explains why local anaesthetic does not have much efficacy in reducing pain in infected tissues like abscesses in which the pH of such tissues is much lower than the physiological pH of 7.4.

Lipid solubility: The more lipid soluble the local anaesthetic is, the higher the potency, the faster the onset of action and the longer the duration of action. This is because there are more drug molecules able to cross the lipid bilayer of the neuronal membrane and create a 'depot' of the drug from within the axoplasm.

Intermediate chain: The longer the intermediate chain, the more potent the local anaesthetic. Bupivacaine has a longer intermediate chain compared to lidocaine. Bupivacaine is three to four times more potent than lidocaine.

Protein binding: Local anaesthetics with higher degrees of protein binding have longer duration of action.

Specific local anaesthetics:

Cocaine was first introduced into clinical practice in 1884. It was first used in ophthalmic surgery and later in dental surgery. Currently, it is mainly used topically in ear, nose and throat (ENT) surgeries at a concentration of 4–10%. The onset of action is fast and lasts 20–30 min. Due to its ability to sensitise adrenergic receptors, it is relatively contraindicated in patients known with hypertension and ischaemic heart diseases. Concurrent use of adrenaline is contraindicated because cocaine is a potent vasoconstrictor.

Amethocaine (tetracaine) is another ester used widely in clinical practice. It was introduced in 1930 for ophthalmics/ophthalmology and as a cream for use to locally anaesthetisevenepuncture sites, especially in the paediatric population. The onset of action is relatively fast with a long duration of action. A maximum dose of 1 mg/kg is recommended. It is the least metabolised of ester local anaesthetics and hence possesses a higher risk of toxicity. Other ester local anaesthetics in use include benzocaine, prilocaine and 2-chloroprocaine.

Lidocaine was the first amid local anaesthetics to be introduced in 1948. It remains one of the most widely used anaesthetics as it can be used intravenously, intrathecally and as a local infiltration. It is also a Class 1b antiarrhythmic drug. It has a fast onset of action due to its pKa of 7.8, which is closer to the physiological pH of 7.4, and is moderately water and lipid soluble. It has a moderate duration of action and is the least toxic of all amides probably due to its relatively low protein-binding capacity of 64%.

Mepivacaine is an intermediate duration of action compared to lidocaine and bupivacaine. It was introduced in 1957. It has a pKa of 7.6. It has similar pharmacokinetic and dynamic properties with lidocaine except for some concerns of it being neurotoxic in the neonate. However, its properties of low rates of systemic toxicity, rapid onset and dense motor block make mepivacaine attractive for procedures such as shoulder surgery.

Ropivacainewas introduced in 1976. It has a pKa of 8.2. Its chemical structure is similar to both mepivacaine and bupivacaine. Ropivacaine is available as a pure levorotatory stereoisomer only. It is a pure enantiomer and less cardiotoxic compared with racemic mixtures of other local anaesthetics. With respect to its better safety profile, ropivacaine has become a preferred long-acting local anaesthetics for peripheral nerve blockanaesthesia for many providers.

Bupivacaine exists as levo and dextro enantiomer. Its racemic form was introduced in 1963, while levobupivacaine was introduced in 1995. It has a pKa of 8.1 and a protein binding of 96%. The higher degree of protein binding makes bupivacaine the longest acting and most cardiotoxic local anaesthetic if inadvertently administered intravenously. It has been used successfully over the years since its introduction and has become the yardstick for all other long-acting local anaesthetics.

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