

* Local Anaesthetics:- Drugs that have little/no irritating effects when injected into the tissues & that will temporarily interrupt conduction when absorbed into the nerve. Local Anaesthetic compounds are most widely used in dentistry with the exception of cocaine (seldom used today). They all are synthetic compounds.

* Properties of an Ideal Anaesthetic:-

- ① Action must be reversible
- ② Must be non-irritating to tissues & produce no secondary local reaction.
- ③ Should have low degree of systemic toxicity.
- ④ Should have rapid onset & be of sufficient duration to be advantageous.
- ⑤ Should have potency sufficient to give complete anaesthesia without use of harmful concentrated solutions.
- ⑥ Should have sufficient penetrating properties
- ⑦ Should be free from producing allergic reactions.
- ⑧ Should be stable in solution & undergo biotransformation readily within body.
- ⑨ Should be either sterile / capable of being sterilized by heat without deterioration.

Local Anaesthetics in dentistry can be divided into 2 grps :-

esters
(widely used)
composed of :-
a) Aromatic, lipophilic grp
b) Intermediate chain
(cont. ester linkage)
c) hydrophilic 2°/3° amino grp.

amides
(newest & most popular)
composed of :-
a) aromatic, lipophilic
b) Intermediate chain
c) hydrophilic 2°/3° amino grp.

Injectable Type

contain hydrophilic 2° or 3° amino grp. which forms water soluble salts when combined with acids

Lidocaine, Tetracaine, Bupivacaine

Topical anaesthetics

(lack hydrophilic substituted amino portion)

Cocaine, Benzocaine, Lidocaine

Soluble - Cocaine, Tetracaine, Lidocaine

Insoluble - Benzocaine, Butylamine

→ The synthetic compounds used as Injectable Local anaesthetics are weakly basic in nature & poorly soluble in water & acid in reaction.

→ They have both lipophilic & hydrophilic properties
If too hydrophilic → ability to diffuse into lipid-rich nerves diminished

If too lipophilic → Insoluble in water & unable to diffuse through interstitial tissues, of little clinical value.
Toxicity & potency varies with chemical structure of Local Anaesthetics.

* Common Properties of Injectable Local Anaesthetics:-

- ① They are all synthetic.
- ② They all contain amino acids
- ③ They all form salts with strong acids
- ④ The salts are water soluble
- ⑤ Alkali increases the concentration of free base
- ⑥ Unionized free Base soluble in lipids
- ⑦ Anaesthetic Salts acid in reaction & relatively stable
- ⑧ They are all either hydrolyzed by plasma Cholinesterase / undergo Biotransformation in liver
- ⑨ Actions of all drugs are reversible
- ⑩ Compatible with epinephrine or allied drugs.
- ⑪ Incompatible with metal salts of mercury, silver, etc
- ⑫ affect Nerve Conduction in similar manner
- ⑬ Capable of producing systemic effects when a sufficiently high plasma conc. is reached
- ⑭ little / no irritating effect on tissues in anaesthetic conc.

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* Classifn of Local Anaesthetics

(BASED ON SOURCE OF OCCURRENCE)

(i) Naturally occurring - Cocaine

(ii) Synthetic Compounds

a) Nitrogenous Compounds

- Derivatives of PABA (para amino Benzoic acid)

eg:- Procaine, Benzocaine

- Derivatives of acetanilide

eg:- Lignocaine

- Derivatives of Quinolone

eg:- Cinchocaine

- Derivatives of Acridine

eg:- Bupivacaine

b) Non-nitrogenous Compounds

eg:- benzyl alcohol & propanediol

(iii) Drugs with Local Anaesthetic Action

eg:- Clove oil, phenol, chlorpromazine

Classify of Local Anaesthetics

(BASED ON CHEMICAL STRUCTURE)

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ESTER GROUP

A) Benzoic acid Esters

- i) Cocaine (topical use only)
- ii) Benzocaine (topical use only)

B) PARA - AMINO BENZOIC Acid Esters

- i) Procaine (Novocain)
- ii) Tetracaine (Pontocaine)
- iii) Propoxycaine (Ravocaine)
- iv) 2-Chloroprocaine (Nisocaine) (not marketed in dental cartridge)

NONESTER GROUP

A) Amide (Non ester Type)

- i) Bupivacaine (Marcaine, Sensorcaine)
- ii) Etidocaine (Duranest)
- iii) Lidocaine (Xylocaine)
- iv) Mepivacaine (Carbocaine)
- v) Prilocaine (Citanest)

* Classification of Local Anaesthetics

(BASED ON DURATION OF ACTION)

- Short Acting - articaine, Lidocaine, prilocaine
- Long Acting - Bupivacaine, etidocaine, buvicaine

(i) Ultra - Short acting Agents
DOA < 30 min.

- procaine without Vasoconstrictor
- 2 - Chlorprocaine (1.2 or 3%) without Vasoconstrictor
- 2% Lidocaine without Vasoconstrictor
- 4% Prilocaine without Vasoconstrictor for Infiltration

(ii) Short - acting Agents DOA = 45-75 min.

- 2% Lidocaine with 1:1,00,000 epinephrine
- 2% mepivacaine with 1:2,00,000 levonordefol
- 4% prilocaine for Nerve Block
- 2% procaine

(iii) Medium - acting Agents DOA 90-150 min.

- 4% prilocaine with 1:2,00,000 epinephrine
- 2% Lidocaine & 2% mepivacaine with Vasoconstrictor

(iv) Long - acting Agents DOA > 180 min.

- 0.5% bupivacaine with 1:2,00,000 epinephrine

Pharmacokinetics of Local Anaesthetics:-

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UPTAKE:-

When injected into soft tissue most local anaesthetics produce dilation of vascular bed.

Cocaine, the only local anaesthetic that produces vasoconstriction, which is followed by prolonged vasodilation.

Vasodilation is due to increase in the rate of absorption of local anaesthetic into the blood, thus decreasing the duration of pain control while increasing the blood anaesthetic level & potential for overdose.

ORAL ROUTE:-

Except cocaine, local anaesthetics poorly absorbed from GIIT

Most Local Anaesthetics undergo hepatic first-pass effect following oral administration. 72% of dose biotransformed into inactive metabolites.

TOCAINIDE HYDROCHLORIDE $\rightarrow$ analogue of Lidocaine effective orally

TOPICAL ROUTE:-

They are absorbed at different rates after application to mucous membrane

In Tracheal mucosa, as rapid as i.v. administration

In pharyngeal mucosa, uptake is slow

In bladder mucosa, uptake even slower

④ INJECTION:-

- Rate of uptake related to both vascularity of injection site & vascularity of drug.
- Intravenous administration provides the most rapid elevation of blood levels & used for treatment of Ventricular arrhythmias.

ROUTE	TIME TO PEAK LEVEL (min.)
Intravenous	1
Topical	5
Intramuscular	5-10
Subcutaneous	30-90

⑤ DISTRIBUTION:-

- Once absorbed in blood stream → distributed ^{all tissues} ~~blood~~ brain, heart, kidney have higher blood levels of anaesthetic than less perfused organs.
- All local anaesthetics readily cross the Blood-brain barrier & also placenta.

⑥ METABOLISM (BIOTRANSFORMATION):-

- Ester Local Anaesthetics
 - ① hydrolyzed in plasma by Pseudocholesterases
 - ② Chlorprocaine → rapidly hydrolyzed → least toxic
 - ③ Tetracaine → hydrolyzed 16 times slowly
↳ greatest toxicity

Local Metabolism Site of Pilocaine the EXCRETION Kidneys 1% of urine Procaine Amides in 0

Amide Local Anaesthetics

- Metabolism more
- 1. Sit

1st Site - Liver

ii) Prilocaine - Liver complicated them esters than amides.

EXCRETION:-

Kidneys the 1° organ

% of wine

~~Catecholamine~~ excreted unchanged in urine
Proaine appears in urine

unchanged as PABA (90%) & 2%.

Amides present in urine as parent compound in a greater % than esters.

Drug	Onset	Duration	Tissue Penetration	Unwanted effects	Notes
<u>COCAINE</u>	medium	medium	good	Cardiovascular & CNS effects due to block of amine uptake	Rarely used, only as spray for upper resp. tract
<u>PROCAINE</u>	medium	Short	poor	CNS - restlessness, shivering, anxiety occasionally convulsions followed by resp. depression CVS - bradycardia, ↓ cardiac output, vasodilation	No longer used
<u>EUPHYACINE</u>	slow	long	moderate	greater cardiotoxicity	widely used because of long duration of action
<u>PRILDOCAINE</u>	medium	medium	moderate	No vasodilator activity, can cause methaemoglobin	widely used, not for obstetric analgesia due to risk of Methaemoglobinemia

Drug	Onset	Duration	Tissue penetration	main adverse effects	Notes
LIGNOCAINE (2%)	rapid	medium	good	has tendency to cause CNS effects	widely used for local anaesthesia Also used in

Note

* LIDOCAINE (XYLOCAINE, DENTOCAINE, OCTOCAINE, LTGNOCAINE)
→ First non-ester type of local Anesthetic compound to be used in dentistry.

→ White Crystalline powder, used as a hydrochloride salt.

→ Drug compatible with all vasoconstrictors & withstands boiling & autoclaving.

→ Lidocaine Base slightly water-soluble, but hydrochloride salt readily soluble in water.

① Pharmacology:-

→ half life = 1.6 hrs (90 min.)

→ Distribution = lipophilic, widely distributed into body

→ pH of plain sol. = 6.5

→ pH of vasoconstrictor cont. sol. = 5.0-5.5

→ Onset of action = rapid

→ Pregnancy Classification = B

→ effective Dental Conc. = 2%

→ protein binding = 60-80%

② Max. Recommended Dose

→ Max. manufacturers recommend-

Dose of lignocaine with epinephrine
= 7.0 mg/kg body wt. for adult patient

(not to exceed dose of 500 mg)

4.4 mg/kg body wt. dose of lignocaine without a vasoconstrictor

(not to exceed 300 mg)

A 2% lidocaine sol. contains 2g / 100ml or 2,000mg / 100ml or 20mg/ml of local anaesthetic sol.

* In India, a standard cartridge contains 2ml of Local Anaesthetic sol.

- (iii) @ Recommendations of American Dental Assoc. Dosage suggested by Council of Dental Therapeutics of ADA & United Pharmaceutical Convention, max. dose for lidocaine with / without Vasoconstrictor = 4.4 mg/kg body wt.

Dental Cartridge contains:-

2ml of Local Anaesthetic Sol. → in India

1.8ml of local Anaesthetic Sol. → in USA & Europe

2.2ml of Local Anaesthetic Sol. → in UK & Australia

(iv) Biotransformation:-

→ Metabolism - Metabolized in liver by microsomal fixed function Oxidases

Lidocaine & other amide type Local Anaesthetic agents not affected by enzyme → plasma Cholinesterase. Hence, these are the agents of choice in patients with abnormal insufficient amts. of this enzyme.

→ Excretion - excreted to some extent in urine by kidneys
< 10% unchanged, > 80% by various mechanisms

- Potency - 2 times more potent than Procaine
- Toxicity - 2 times more toxic than Procaine
- Action on Blood Vessels - less than Procaine but more than prilopaine & Mepiracaine
- Time of Onset = rapid (2-3min.)
- Duration of Onset:- depends upon -
 - (i) Type of Injection - Nerve Block has longer duration than Infiltration
 - (ii) Amount of Vasoconstrictor used in sol.

- effective Dental Conc. - 2%
- Anaesthetic half life - 1.6 hrs

Topical Anaesthetic Action - forms an excellent surface anaesthetic. used in following forms topically:-

- (i) 2% in form of jelly
- (ii) 5% in ointment
- (iii) 10% & 15% in form of spray (aerosol)

Lignocaine availability in India for Dentistry
 Dental Cartridge 2% Lidocaine with epinephrine 1:80,000 in India

Viols
 2% Lidocaine without epinephrine (Lidocaine plain)
 2% Lidocaine with epinephrine 1:80,000, 1:100,000 & 1:2,00,000

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vi) Toxicity of Lignocaine

→ Central Nervous System -

Toxic doses first produce stimulation followed by depression. Manifestations of stimulation vary from mild restlessness to severe convulsions. The phase lasts for a brief period. Depression manifested by drowsiness to loss of consciousness.

Lidocaine if administered i.v. capable of producing a degree of analgesia & even general anaesthesia.

→ Cardiovascular System -

a) Moderately Large Doses - produce overall inhibition on contractility of heart muscle in form of:-

- (i) ↓ in electrical excitability
- (ii) ↓ in force of contraction (-ve Inotropic)
- (iii) ↓ in rate of Impulse Conduction (-ve Chronotropic)

b) Large Doses - In large doses, given i.v. during general anaesthesia & surgery to correct ventricular arrhythmia occurring during surgical procedures.

→ Vascularity -

Vasodilation produced by direct relaxing on smooth muscle of vessel walls. In toxic doses - contributes to hypotension & Cardiovascular Collapse.

Respiratory System -

a) In small doses -

b) In large doses - causes Bronchodilation
cause sup. arrest (apnea)

Composition of Lignocaine

Local Anaesthetic Agent - LIGNOCAINE
HYDROCHLORIDE (2%)

Reducing Agent - Sodium Meta-bisulphite
(0.5mg)

These act as preservatives for vasoconstrictor agents. Vasoconstrictors are unstable in solution & may oxidize, esp. on exposure to prolonged sunlight. Sodium Metabisulphite which competes for the available oxygen is added in conc. between 0.05 - 0.1%.

Preservative - METHYL PARABEN (0.1%) (1mg)

Stability of modern L.A is maintained by adding caprylhydrocaryum toxin which includes xylotox & Methyl Paraben. Methyl Paraben can cause allergic reactions.

Diluting Agent - DISTILLED WATER (dissolve the components & maintains desired percentage/comp)

Fungicide - THYMOL (antiseptic, fungistatic & antihelminthic)

Isotonic Solution - SODIUM CHLORIDE / RINGER'S SOLUTION (6mg)

does not cause Burning sensation

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Isotonic vehicle reduces discomfort during injection.

- Vasoconstrictor - ADRENALINE (1:80,000) (D.C.)
- ↓ Blood flow to site of Injection
 - absorption of L.A. by cardiovascular system is slowed
 - ↓ risk of Local Toxicity
 - ↑ Vol. of local anesthetic agent remain in or around the nerve for longer period
 - ↑ Duration of Action
 - also ↓ bleeding at site of administration

→ To adjust pH - SODIUM HYDROXIDE

→ NITROGEN BUBBLE



1-2mm in diameter

present to prevent oxygen from being trapped in cartridge & potentially destroying the Vasopressor

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* VASOCONSTRICTOR CLASSIFICATION

- ① Directly Acting Drugs (Catecholamines)
Stimulate / exert their action directly on
adrenergic receptors
eg:- epinephrine, norepinephrine
dopamine
- ② Indirectly Acting Drugs (Non-Catecholamines)
act by releasing norepinephrine from
adrenergic nerve terminals
eg:- Tyramine, amphetamine, Methamphetamine
- ③ ~~100~~ Mixed Acting Drugs
have both direct & Indirect actions
eg:- ephedrine, metaraminol