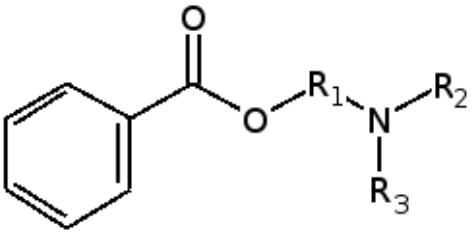
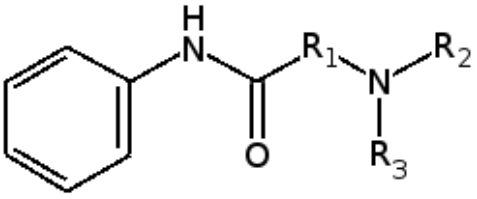
Role of Local Anaesthesia

A **local anaesthetic** (LA) is a medication that causes reversible absence of pain sensation, although other senses are often affected, as well. Also, when it is used on specific nerve pathways (local anaesthetic nerve block), paralysis (loss of muscle power) also can be achieved.

Clinical LAs belong to one of two classes: amino amide and amino ester local anaesthetics. Synthetic LAs are structurally related to cocaine. They differ from cocaine mainly in that they have a very low abuse potential and do not produce hypertension or (with few exceptions) vasoconstriction.



Aminoester



Aminoamide

Types

This LA system is designed to prevent needlestick injury. A cartridge of LA fits into the disposable needle, which can be locked when not in use and can be separated from the handle.

Local anaesthetic solutions for injection typically consist of[1]

- The local anaesthetic agent itself
- A vehicle, which is usually water-based or just sterile water
- Vasoconstrictor possibly

[1] *"Allergic Reactions". Cleveland Clinic. Retrieved 11 April 2014.*

- Reducing agent (antioxidant), e.g. if epinephrine is used, then sodium metabisulfite is used as a reducing agent
- Preservative, e.g. methylparaben
- Buffer

Esters are prone to producing allergic reactions, which may necessitate the use of an amide. The names of each locally clinical anaesthetic have the suffix "-caine". Most ester LAs are metabolised by pseudocholinesterase, while amide LAs are metabolised in the liver. This can be a factor in choosing an agent in patients with liver failure,[2] Although cholinesterases are produced in the liver, physiologically (e.g. very young or very old individuals) or pathologically (e.g. cirrhosis) impaired hepatic metabolism is also a consideration when using amides.

Sometimes, LAs are combined, e.g.:

- Lidocaine/prilocaine (EMLA, eutectic mixture of local anaesthetic)
- Lidocaine/tetracaine (Rapydan)
- TAC

LA solutions for injection are sometimes mixed with vasoconstrictors (combination drug) to increase the duration of local anaesthesia by constricting the blood vessels, thereby safely concentrating the anaesthetic agent for an extended duration, as well as reducing hemorrhage.[24] Because the vasoconstrictor temporarily reduces the rate at which the systemic circulation removes the local anaesthetic from the area of the injection, the maximum doses of LAs when combined with a vasoconstrictor is higher compared to the same LA without any vasoconstrictor. Occasionally, cocaine is administered for this purpose. Examples include:

- Prilocaine hydrochloride and epinephrine (trade name Citanest Forte)
- Lidocaine, bupivacaine, and epinephrine (recommended final concentrations of 0.5, 0.25, and 0.5%, respectively)
- Iontocaine, consisting of lidocaine and epinephrine
- Septocaine (trade name Septodont), a combination of articaine and epinephrine

One combination product of this type is used topically for surface anaesthesia, TAC (5-12% tetracaine, $^{1}/_{2000}$ (0.05%, 500 ppm, ½ per mille) adrenaline, 4 or 10% cocaine).

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[2] *Arnold Stern (2002). Pharmacology: PreTest self-assessment and review. New York: McGraw-Hill, Medical Pub. Division. ISBN 0-07-136704-7.*

Using LA with vasoconstrictor is safe in regions supplied by end arteries. The commonly held belief that LA with vasoconstrictor can cause necrosis in extremities such as the nose, ears, fingers, and toes due to constriction of end arteries, is invalidated, since no case of necrosis has been reported since the introduction of commercial lidocaine with epinephrine in 1948.[3]

Ester group

- Benzocaine
- Chloroprocaine
- Cocaine
- Cyclomethycaine
- Dimethocaine/Larocaine
- Piperocaine
- Propoxycaine
- Procaine/Novocaine
- Proparacaine
- Tetracaine/Amethocaine

Amide group

- Articaine
- Bupivacaine
- Cinchocaine/Dibucaine
- Etidocaine
- Levobupivacaine
- Lidocaine/Lignocaine
- Mepivacaine
- Prilocaine
- Ropivacaine
- Trimecaine

Naturally derived

- Saxitoxin
- Neosaxitoxin
- Tetrodotoxin

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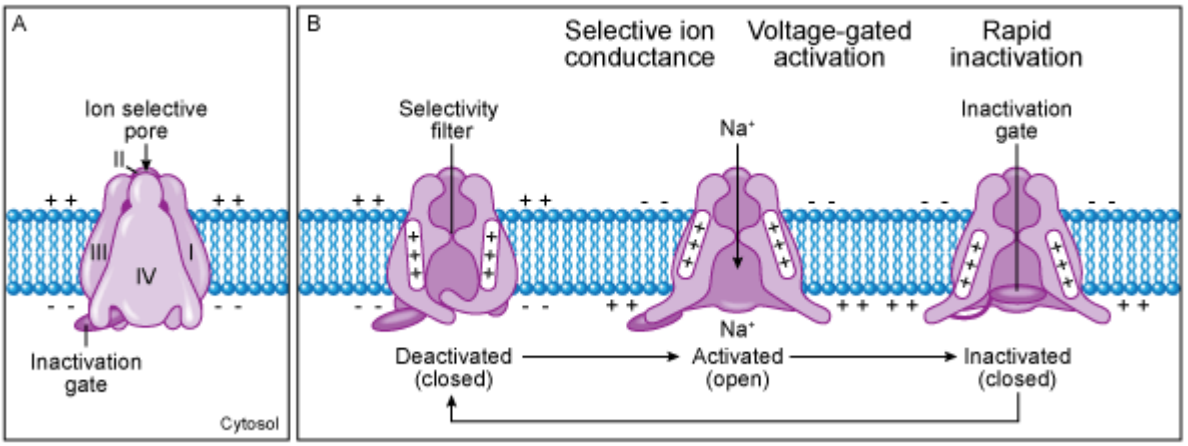
[3] *Nielsen LJ, Lumholt P, Halmich LR (Oct 2014). "[Local anaesthetic with vasoconstrictor is safe to use in areas with end-arteries in fingers, toes, noses and ears.].". Ugeskrift for Lægerer.* ***176****: 44. PMID 25354008.*

- Menthol
- Eugenol
- Cocaine

Naturally occurring local anaesthetics not derived from cocaine are usually neurotoxins, and have the suffix -toxin in their names. [1] Unlike cocaine produced local anaesthetics which are intracellular in effect, saxitoxin, neosaxitoxin & tetrodotoxin bind to the extracellular side of sodium channels.

Mechanism of action

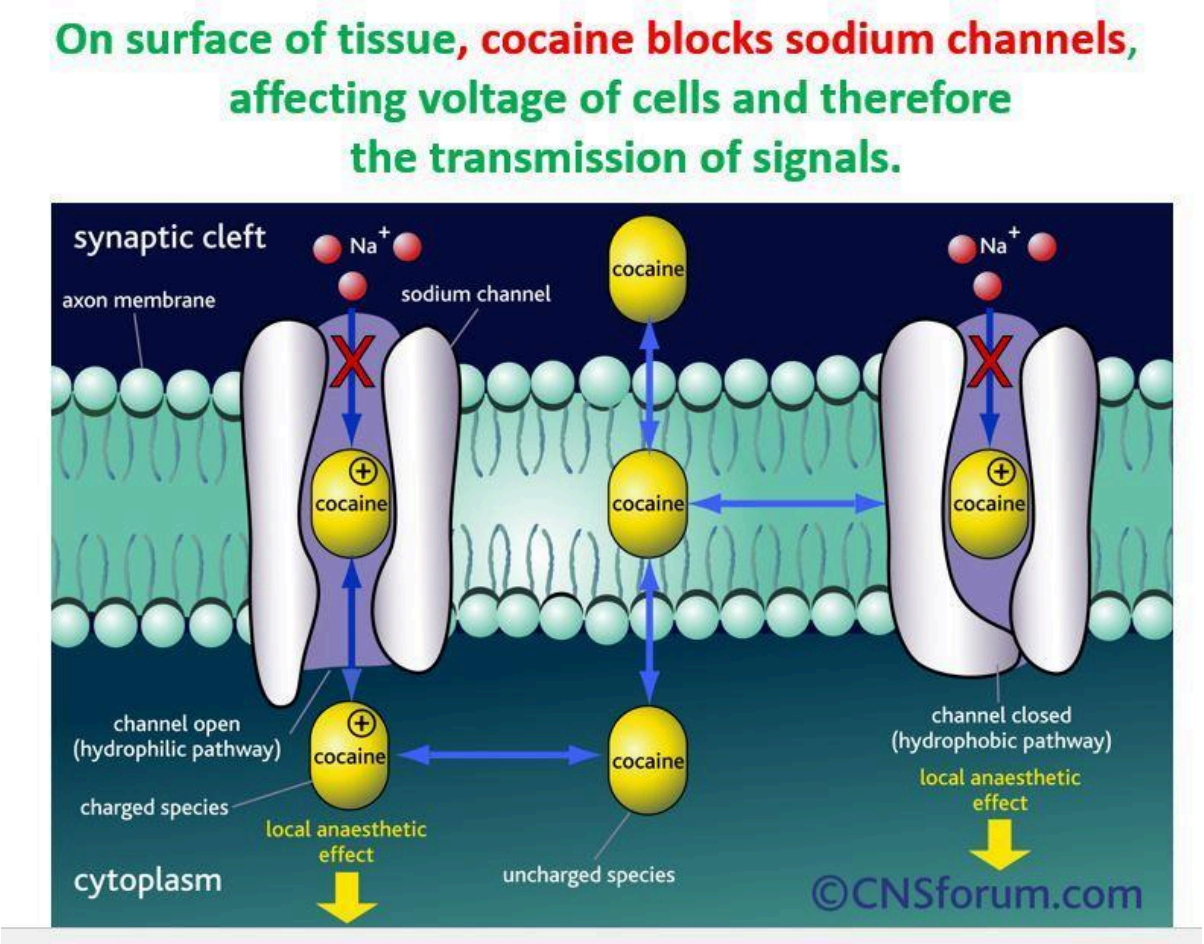
It's a proposed mechanism of action of local anaesthetics



i. Local anaesthetics bind with interior part of voltage gated Na^+ channel
ii. Blockade of the Na^+ channel
iii. Decrease in Na^+ conductance
iv. No Action potential

- ✔ No depolarization
- ✔ No repolarization

v. Conduction blockade
vi. No pain sensation



All Local Anaesthetics are membrane-stabilising drugs; they reversibly decrease the rate of depolarization and repolarization of excitable membranes (like nociceptors). Though many other drugs also have membrane-stabilising properties, not all are used as LAs (propranolol, for example).

LA drugs act mainly by inhibiting sodium influx through sodium-specific ion channels in the neuronal cell membrane, in particular the so-called voltage-gated sodium channels. When the influx of sodium is interrupted, an action potential cannot arise and signal conduction is inhibited. The receptor site is thought to be located at the cytoplasmic (inner) portion of the sodium channel. Local anaesthetic drugs bind more readily to sodium channels in an activated state, thus onset of neuronal blockade is faster in rapidly firing neurons. This is referred to as state-dependent blockade.

LAs are weak bases and are usually formulated as the hydrochloride salt to render them water-soluble. At a pH equal to the protonated base's pKa, the protonated (ionised) and

unprotonated (unionised) forms of the molecule exist in equimolar amounts, but only the unprotonated base diffuses readily across cell membranes. Once inside the cell, the local anaesthetic will be in equilibrium, with the formation of the protonated (ionised form), which does not readily pass back out of the cell. This is referred to as "ion-trapping". In the protonated form, the molecule binds to the LA binding site on the inside of the ion channel near the cytoplasmic end. Most LAs work on the internal surface of the membrane - the drug has to penetrate the cell membrane, which is achieved best in the non ionised form.

Acidosis such as caused by inflammation at a wound partly reduces the action of LAs. This is partly because most of the anaesthetic is ionised and therefore unable to cross the cell membrane to reach its cytoplasmic-facing site of action on the sodium channel.

All nerve fibres are sensitive to LAs, but due to a combination of diameter and myelination, fibres have different sensitivities to LA blockade, termed differential blockade. Type B fibres (sympathetic tone) are the most sensitive followed by type C (pain), type A delta (temperature), type A gamma (proprioception), type A beta (sensory touch and pressure), and type A alpha (motor). Although type B fibres are thicker than type C fibres, they are myelinated, thus are blocked before the unmyelinated, thin C fibre