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# An Overview of "Stages of Anesthesia and Some Novel Local Anesthetics Drug"

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**Keywords:** Anesthesia; Cocaine; Benzocaine; Chloroprocaine; Procaine; Lidocaine

**ABSTRACT**

Anesthesia means stopping of sensation and feeling. Anesthesia is a state of temporary induced loss of sensation or awareness. It gives analgesia i.e. relief from pain or prevention of pain and paralysis. Local anesthesia involves injections that numb a larger or deeper part of the body. The patient stays conscious but free from pain. Local anesthetics produce anesthesia by inhibiting excitation of nerve endings or by blocking conduction in peripheral nerves. It was achieved or done by anesthetics reversibly binding to sodium channels and inactivating sodium channels. Sodium influx through these channels is necessary for the depolarization of nerve cell membranes and subsequent propagation of impulses along the course of the nerve. When a nerve loses depolarization and capacity to propagate an impulse, the individual loses sensation in the area supplied by the nerve.

## INTRODUCTION:

Anesthesia is a state of temporary induced loss of sensation or awareness. It gives analgesia i.e. relief from pain or prevention of pain and paralysis. A patient under the effects of the anesthetic drug is known as anesthetized. Anesthesia enables the painless performance of medical producers that would cause severe pain to an unanesthetized patient. There are both major and minor risks of anesthesia. Examples of major risks include death, heart attacks and pulmonary embolism and minor risks like nausea and vomiting. Anesthesia means stopping of sensation and feeling. It can be given in various ways and does not always make you unconscious. It includes;

- Local anesthesia
- Regional anesthesia
- General anesthesia

Local anesthesia involves injections that numb a small part of the patient body. The patient stays conscious but free from pain. Regional anesthesia involves injections that numb a larger or deeper part of the body. The patient stays conscious but free from pain.

### Mechanism of Action for Local anesthetics drug:

Local anesthetics produce anesthesia by inhibiting excitation of nerve endings or by blocking conduction in peripheral nerves. It was achieved or done by anesthetics reversibly binding to sodium channels and inactivating sodium channels. Sodium influx through these channels is necessary for the depolarization of nerve cell membranes and subsequent propagation of impulses along the course of the nerve. When a nerve loses depolarization and capacity to propagate an impulse, the individual loses sensation in the area supplied by the nerve.

### Uses of local anesthesia:

- Local anesthesia is used when surgery is minor and does not require general or regional anesthesia
- The procedure can be done quickly and the patient does not need to stay overnight
- The operation does not need the muscles to be relaxed or for the patient to be unconscious

**Stages of anesthesia:**

According to Guedel's classification, it can be divided into four stages of anesthesia**;**

**Stage 1:**

In Stage 1 is the period between the administration of induction agents and loss of consciousness. It is also known as induction. During this stage, the patient progresses from analgesia without amnesia to analgesia with amnesia. Patients can carry on a conversation or talk at this time.

**Stage 2:**

Stage 2 is also known as the excitement stage. It is the period following the loss of consciousness and marked by excited and delirious activity. During this stage, the patient's heart rate may become irregular; uncontrolled movements, vomiting, and pulmonary dilation.

**Stage 3:**

In Stage 3 is also known as surgical anesthesia. During this stage, the skeletal muscles relax, vomiting stops, respiratory depression occurs, and eye movements slow and then stop. The patient is unconscious and ready for surgery. This stage is divided into four planes:

- The eyes roll, then become fixed;
- Corneal and laryngeal reflexes are lost;
- The pupils dilate and light reflex is lost;
- Body paralysis

**Stage 4:**

Stage 4 is also known as overdose. It occurs when too much anesthetic medication is given.

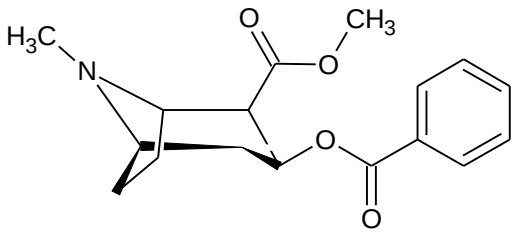
**Classification of local anesthetics Drug:**

- Ester-type local anesthetic
- Amide-type local anesthetic

- Miscellaneous type local anesthetic

**Ester-type local anesthetic drug:**

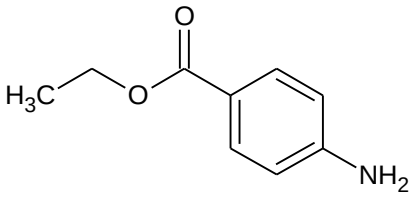
**Cocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • Methyl (1*R*,2*R*,3*S*,5*S*)-3-(benzoyloxy)-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate |

Cocaine is also known as Coke. Cocaine is an example of local anesthetic drug. It is the strong stimulant drug. It is an example of ester type of local anesthetic drug. It is commonly inhaled as a smoke, or as a solution injected into a vein. It gives the feeling of happiness or agitation. It gives its effect by increasing heart rate and large pupils. Cocaine acts by inhibiting reuptake of serotonin, norepinephrine, and dopamine. It can easily cross the BBB i.e. blood-brain barrier. Cocaine is a naturally occurring substance found in the coca plant. Cocaine was first isolated from the leaves in 1860.

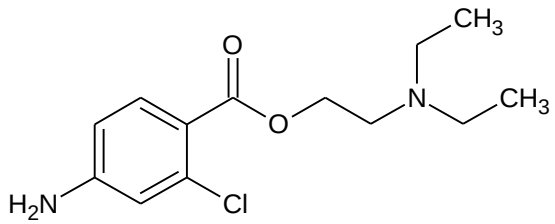
**Benzocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • Ethyl 4-aminobenzoate |

Benzocaine is an example of the local anesthetic drug. It is an example of ester type of local anesthetic drug. It was sold under the brand names like Orajel. It is used in the form of topical pain reliever and also in cough drops. It is also used to control ear pain and remove ear wax.

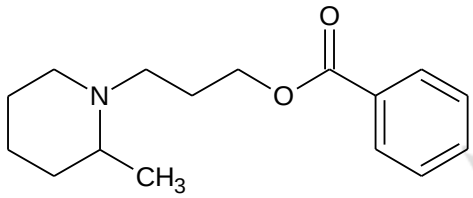
**Chloroprocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • 2-diethylaminoethyl-4-amino-2-chloro-benzoate |

Chloroprocaine is an example of the local anesthetic drug. It is an example of ester type of local anesthetic drug. It is given by injection during the surgical procedure. It is also used in labor pain and delivery. It was sold under the brand names like Nesacaine, and Nesacaine-MPF.

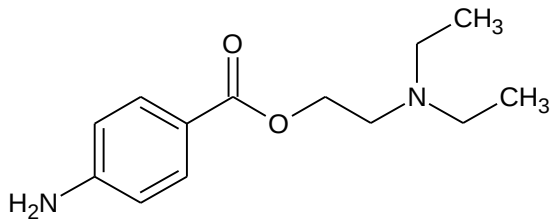
**Piperocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • 3-(2-Methylpiperidin-1-yl)propyl benzoate |

Piperocaine is an example of local anesthetic drug. It is an example of ester type of local anesthetic drug. It was developed in the 1920s. It is used for nerve blocks.

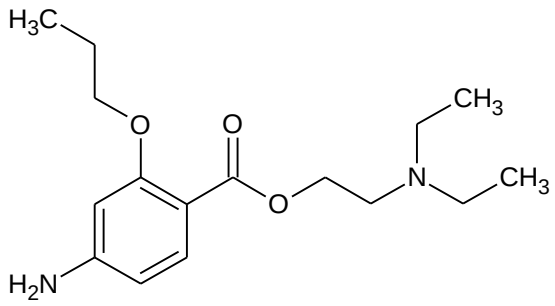
**Procaine:**




| **Systematic (IUPAC) name** |
| --- |
| • 2-(diethylamino)ethyl 4-aminobenzoate |

Procaine is an example of local anesthetic drug. It is an example of amino ester type of local anesthetic drug. It is used primarily to reduce the pain of intramuscular injection of penicillin. It was sold under the trade names like Novocain. It acts mainly as a sodium channel blocker. Procaine was first synthesized in 1905.

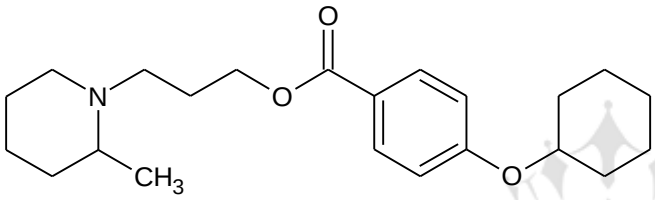
**Propoxycaine:**



| Systematic (IUPAC) name |
|---|
| 2-(diethylamino)ethyl 4-amino-2-propoxybenzoate |

Propoxycaine is an example of local anesthetic drug. It is an example of amino ester type of local anesthetic drug. It is used primarily to treat anesthesia.

**Cyclomethycaine:**

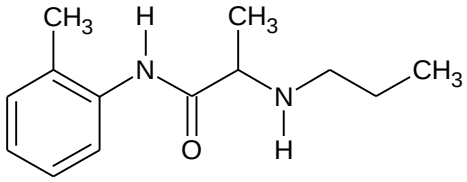


| Systematic (IUPAC) name |
|---|
| 4-(cyclohexyl)benzoic acid 3-(2-methyl-1-piperidinyl)propyl ester |

Cyclomethycaine is an example of local anesthetic drug. It is an example of amino ester type of local anesthetic drug. It is used primarily to treat anesthesia.

**Amide-type local anesthetic drug:**

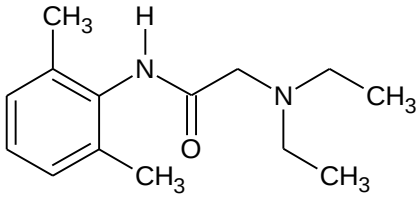
**Prilocaine:**



| Systematic (IUPAC) name |
|---|
| • (*RS*)-*N*-(2-methyl phenyl)-$N^2$-propylalaninamide |

Prilocaine is an example of local anesthetic of the amino amide category. It was discovered by the scientist Claes Tegner and Nils Lofgren. It is available in the form of trade name like Cianest. It is also often combined with Lidocaine as a topical preparation for dermal anesthesia. it is commonly used for intravenous regional anesthesia.

**Lidocaine**:




| **Systematic (IUPAC) name** |
| --- |
| • 2-(diethylamino)-*N*-(2,6-dimethylphenyl)acetamide |

Lidocaine is also known as Lignocaine or Xylocaine. It is a medication used to numb tissue in a specific area. It is also used to treat ventricular tachycardia. It is used to decreases the bleeding. Lidocaine mixed with a small amount of Adrenaline or Epinephrine is used to decrease bleeding. When Lidocaine was used in the form of injectable, then it gives its effects within four minutes and lasts for half an hour to three hours. Lidocaine mixtures may also be applied directly to the skin or mucous membranes to numb the area. Lidocaine was discovered in 1946 and went on sale in 1948. It gives a rapid onset of action and intermediate duration of efficacy. Lidocaine drops can be used on the eyes for short ophthalmic procedures. It is used to treat ventricular arrhythmias for acute myocardial infarction. Inhaled Lidocaine can be used as a cough suppressant. Lidocaine is about 95% metabolized in the liver by the enzyme CYP3A4. It is used in the form of

- Injected local anesthetic
- Dermal patch
- Intravenous injection
- Intravenous infusion
- Nasal instillation/spray
- Oral Gel

- Oral liquid
- Topical Gel
- Topical liquid
- Ophthalmic solution
- Ear drops

**Mechanism of action:**

Lidocaine alters signal conduction in neurons by blocking the fast voltage sodium channels in the neuronal cell membrane responsible for signal propagation. Lidocaine produces anesthesia by inhibiting excitation of nerve endings or by blocking conduction in peripheral nerves. It was achieved or done by anesthetics reversibly binding to sodium channels and inactivating sodium channels. Sodium influx through these channels is necessary for the depolarization of nerve cell membranes and subsequent propagation of impulses along the course of the nerve. When a nerve loses depolarization and capacity to propagate an impulse, the individual loses sensation in the area supplied by the nerve.

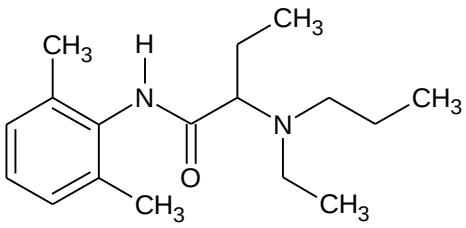
**SAR of Lidocaine:**

- Addition of alkyl group on Aryl group gives increases or enhances the biological activity.
- A steric effect observes between Methyl group and nitrogen, it gives hydrolysis of the amide bond and enhances the distribution.
- Aryl substitution on the aryl ring that enhances Zwitterion formation, it gives more potent compounds.
- Carbonyl group is necessary for biological activity
- The tertiary amine is more effective than secondary or primary amine because secondary or primary amine gives irritation to the tissue.

**Side effect:**

It gives common side effects like sleepiness, muscle twitching, and confusion, changes in vision, numbness, tingling, and vomiting.

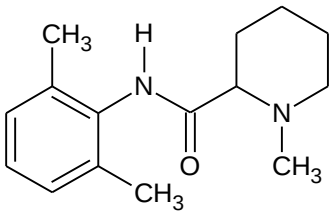
**Etidocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • *N*-(2,6-dimethylphenyl)-2-(ethyl(propyl)amino)butanamide |

Etidocaine is available in the form of trade name like Duranest**.** It is a medication used to numb tissue in a specific area. It is an example of local anesthetic drug. It was given by injection for the surgical procedure. It is used in the labor and delivery. Etidocaine has a long duration of activity, and the main disadvantage of using during dentistry is increased bleeding during surgery

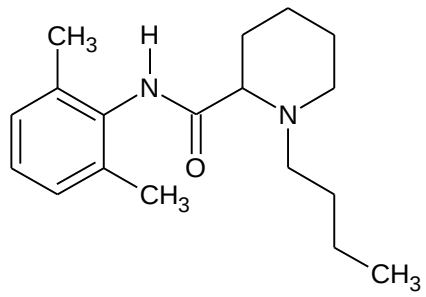
**Mepivacaine:**




| **Systematic (IUPAC) name** |
| --- |
| • (*RS*)-*N*-(2,6-dimethylphenyl)- 1-methyl-piperidine-2-carboxamide |

Mepivacaine is an example of local anesthetic drug. It is an example of amide type of local anesthetic drug. Mepivacaine gives rapid onset and medium duration of action. Mepivacaine is available in the form of trade names like Carbocaine and Polocaine. Mepivacaine is available in the Us from the 1960s. It is used to treat regional anesthesia. It is supplied as the hydrochloride salt of the racemate i.e. racemic mixture. It consists of R(-)-Mepivacaine and S(+)-Mepivacaine in equal proportions.

**Bupivacaine:**



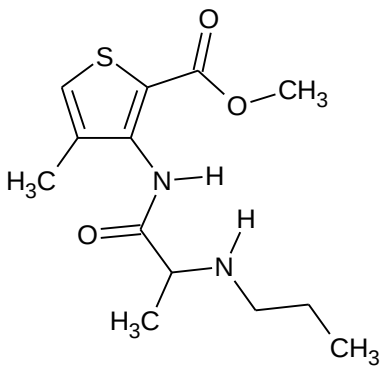

| Systematic (IUPAC) name |
| --- |
| • (*RS*)-1-Butyl-*N*-(2,6-dimethylphenyl)piperidine-2-carboxamide |

Bupivacaine is an example of local anesthetic drug. It is an example of amide type of local anesthetic drug. Bupivacaine is available in the form of the brand name like Marcaine. Bupivacaine is a medication used to decrease the feeling in a specific area. It is available in the form of combination with epinephrine to make the longer action. Bupivacaine typically begins working within 15 minutes and lasts for 2 to 8 hours. It gives side effects like sleepiness, muscle twitching, changes in vision, low blood pressure and irregular heart rate. Bupivacaine was discovered in 1957.

**Mechanism of action:**

Bupivacaine binds to the intracellular voltage sodium channels and blocks sodium influx into nerve cells. It prevents depolarization.

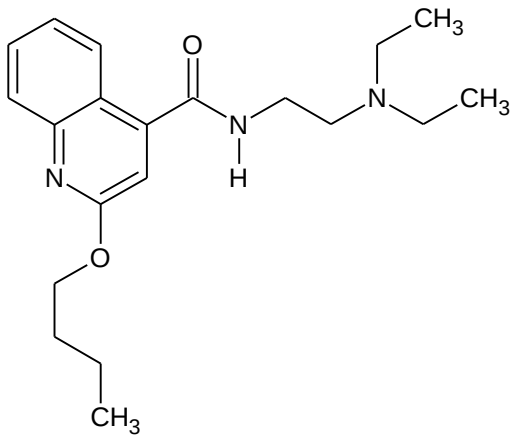
**Articaine:**




| Systematic (IUPAC) name |
| --- |
| • (*RS*)-Methyl 4-methyl-3-(2-propylaminopropanoylamino)thiophene-2-carboxylate |

Articaine is an example of the local anesthetic drug. It is an example of amide type of local anesthetic drug. It is used in the treatment of dental surgery. It is the most widely used local anesthetic in a number of European countries. It contains thiophene ring. This drug was first synthesized by Hoechst AG in 1969 in Germany.

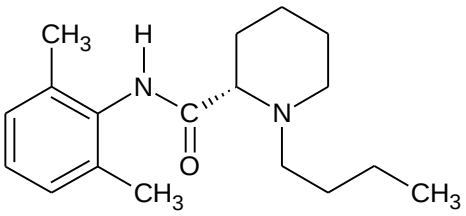
**Cinchocaine:**




| **Systematic (IUPAC) name** |
| --- |
| • 2-butoxy-*N*-[2-(diethylamino)ethyl]quinoline-4-carboxamide |

Cinchocaine is also known as dibucaine. Cinchocaine is an example of the local anesthetic drug. It is an example of amide type of local anesthetic drug. It is the most potent and toxic of the long-acting local anesthetics. The current use of Cinchocaine is generally restricted to spinal and topical anesthesia. It is sold under the brand names like Nupercainal, Nupercaine, and Cocaine.

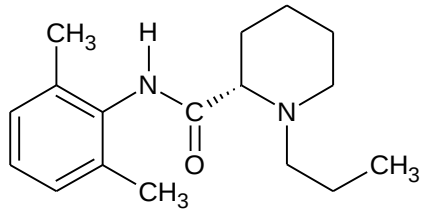
**Levobupivacaine:**




| **Systematic (IUPAC) name** |
| --- |
| • (*S*)-1-butyl-*N*-(2,6-dimethylphenyl) piperidine-2-carboxamide |

Levobupivacaine is an example of local anesthetic drug. It is an example of amide type of local anesthetic drug. It is S-enantiomers of Bupivacaine. Levobupivacaine hydrochloride is commonly marketed by Abbvie Company under the trade name Chirocaine. It is approximately 13 % less potent than racemic Bupivacaine. Levobupivacaine is used for local anesthesia including nerve block and intrathecal anesthesia in adults. It gives some side effects like nervousness, tingling around the mouth, tremor, dizziness, and blurred vision.

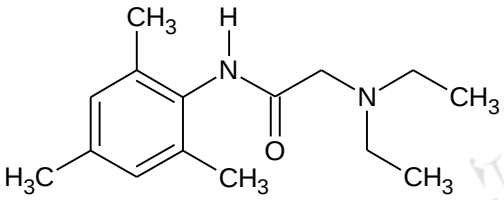
**Ropivacaine:**




| Systematic (IUPAC) name |
| --- |
| • (*S*)-*N*-(2,6-dimethylphenyl)-1-propylpiperidine-2-carboxamide |

Ropivacaine is an example of local anesthetic drug. It is an example of amide type of local anesthetic drug. Ropivacaine hydrochloride is commonly marketed by Astra Zeneca Company under the trade name Naropin. Ropivacaine was found to have less cardiotoxicity than bupivacaine in animal models. This drug was found after Bupivacaine.

**Trimecaine:**

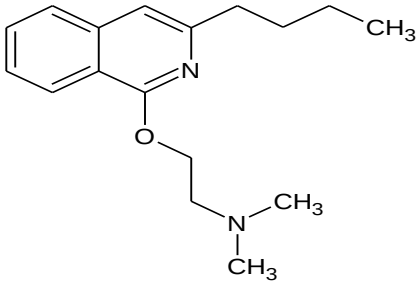



| Systematic (IUPAC) name |
| --- |
| 2-diethylamino-*N*-(2,4,6-trimethylphenyl)acetamide |

Trimecaine is an example of organic compounds. Trimecaine is an example of the local anesthetic drug. It is an example of amide type of local anesthetic drug and cardial antiarrhythmic drug. It is an active ingredient in products available under trademarks Mesdicain, Mesocain, Mesokain and others.

**Miscellaneous type local anesthetic Drug:**

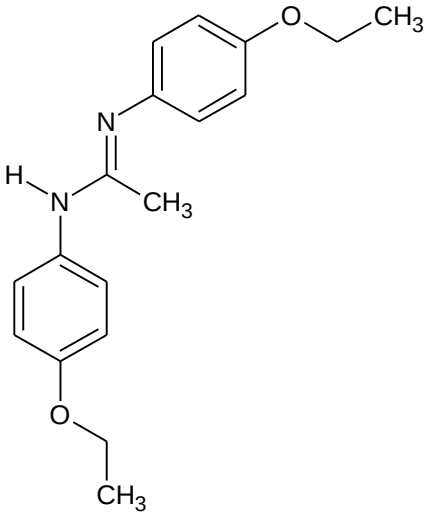
**Quinisocaine:**



| **Systematic (IUPAC) name** |
| --- |
| • (*S*)-*N*-(2,6-dimethylphenyl)-1-propylpiperidine-2-carboxamide |

Quinisocaine is also known as dimethisoquin. Quinisocaine is an example of local anesthetic drug. It is an example of Isoquinoline type of local anesthetic drug.

**Phenacaine:**

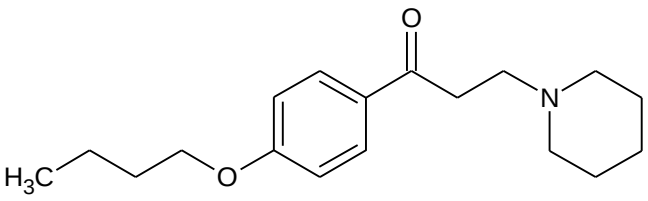


| **Systematic (IUPAC) name** |
| --- |
| (1*E*)-*N*,*N*′-Bis(4-ethoxyphenyl)ethanimidamide |

Phenacaine is also known as holocaine. Phenacaine is an example of the local anesthetic drug. It is the only anesthetic other than cocaine i.e. it was approved for ophthalmic use.

**Dyclonine:**

| **Systematic (IUPAC) name** |
| --- |
| • 1-(4-butoxyphenyl)-3-(1-piperidyl)propan-1-one |




Dyclonine is also known as Dyclocaine. Dyclonine is an example of the oral local anesthetic drug. The product Sucrets was introduced in Maryland by the scientist Sharp and Dohme in 1932.

**CONCLUSION:**

Local anesthesia involves injections that numb a small part of the patient body. Patient stays conscious but free from pain. Regional anesthesia involves injections that numb a larger or deeper part of the body. Patient stays conscious but free from pain. Local anesthetics produce anesthesia by inhibiting excitation of nerve endings or by blocking conduction in peripheral nerves. It was achieved or done by anesthetics reversibly binding to sodium channels and inactivating sodium channels. Sodium influx through these channels is necessary for the depolarization of nerve cell membranes and subsequent propagation of impulses along the course of the nerve. When a nerve loses depolarization and capacity to propagate an impulse, the individual loses sensation in the area supplied by the nerve. There are many drugs which are used to produce anesthesia with the help of Cocaine, Benzocaine, Chloroprocaine, Procaine, Lidocaine, Etidocaine, Mepivacaine, Bupivacaine, Ropivacaine, Quinisocaine, Dyclonine etc.

**ACKNOWLEDGEMENT:**

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