

Local Anaesthesia (LA): An Overview

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ABSTRACT

The anaesthetic agents are the drugs which causes anaesthesia-reversible loss sensation. It deals with the property of relieving the pain without eliminating sensation. These drugs are generally administered to facilitate surgery. It can be described by two main classes. General anaesthetic, which causes a reversible loss of consciousness, and local anaesthetics, which causes a reversible loss of sensation for a limited region of the body while maintaining consciousness. Here I explain about the Local anaesthetics agents that prevent transmission of nerve impulses without causing unconsciousness. They act by binding to fast sodium channels from within in an open state.

BACKGROUND: The purpose of this Review article is to summarize the Local anaesthetics agents, general mechanism, structures, therapeutic uses, adverse effects and also explains their properties.

Keywords: Local Anaesthesia, relieving pain, nerve impulses

INTRODUCTION (General)

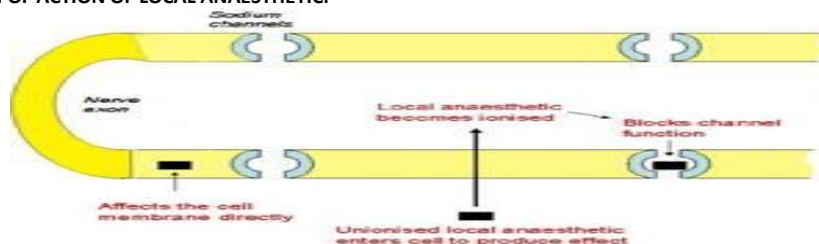
Cocaine is a naturally occurring compound indigenous to the Andes Mountains, West Indies, and Java. It was the first anaesthetic to be discovered and is the only naturally occurring Local anaesthetic; all others are synthetically derived. Cocaine was introduced in to Europe in the 1800s following its 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. Halsted was the first to report the use of cocaine for nerve blocks in the US in 1885 and also became addicted to the drug through self-experimentation.

Procaine, the first synthetic derivative of cocaine, was developed in 1904. Lofgren later developed lidocaine, the most widely used cocaine derivative, during World War II in 1943.

GENERAL MECHANISM OF ACTION OF LOCAL ANAESTHETIC:



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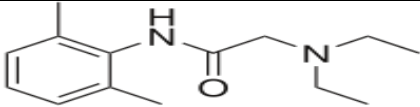
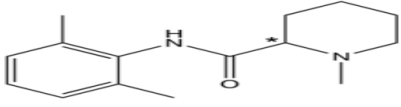
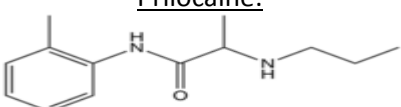
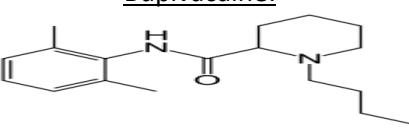
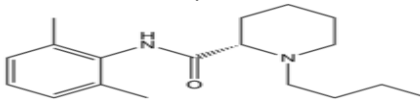
Table 1: Properties of local anaesthetics:

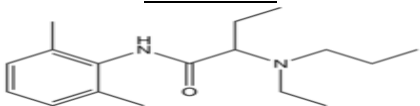
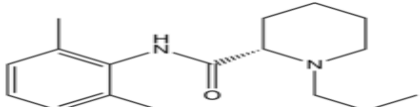
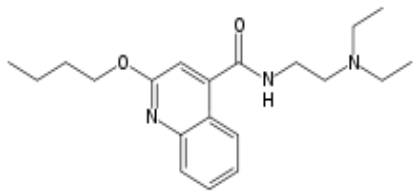
| Drug | Onset | Duration | Tissue penetration | Plasma half-life(h) | Main unwanted effects | notes |
|-------------|-----------|----------|--------------------|---------------------|--|--|
| Cocaine | Medium | Medium | Good | -1 | CVS and CNS effects owing to block of amine uptake | Rarely used, only as spray for upper respiratory tract |
| Procaine | Medium | Short | Poor | <1 | CNS: anxiety, Restlessness, shivering, depression. CVS: Bradycardia, and decrease cardiac output, vasodilatation, | The first synthetic agent No longer used |
| Lidocaine | Rapid | Medium | Good | -2 | Less tendency to cause CNS effects | Used intravenously for treating ventricular dysrhythmias . |
| Tetracaine | Very slow | Long | Moderate | -1 as lidocaine | As lidocaine | Used mainly for spinal and corneal anaesthesia. |
| Bupivacaine | Slow | Long | Moderate | -2 | As lidocaine, but greater cardiotoxicity | Widely used causes less cardio toxicity (levobupivacaine) |
| Prilocaine | Medium | Medium | Moderate | -2 | No vasodilator activity can cause methaemoglobinemia | Widely used |

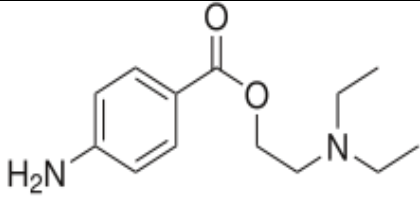
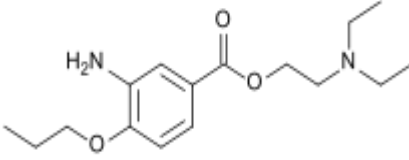
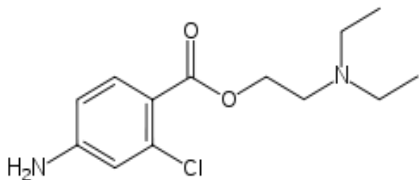
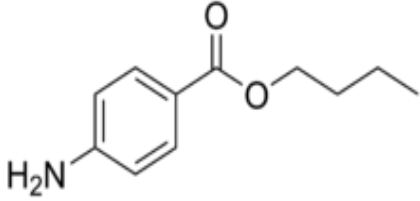
Table 2: local anaesthetics:

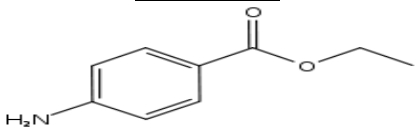
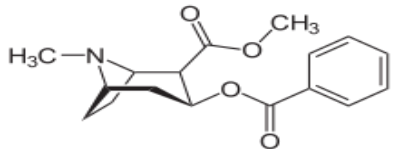
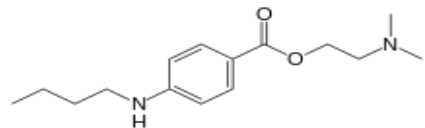
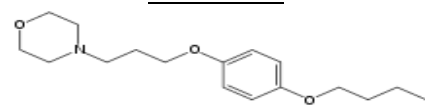
The below list/table are the drugs belonging to local anaesthetics their therapeutic use, adverse effects and structures in pharmaceutical field:

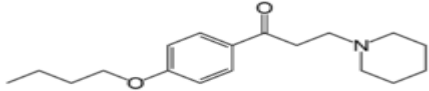
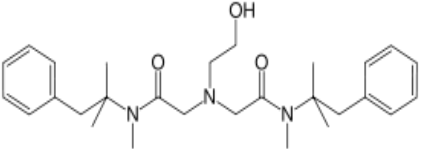
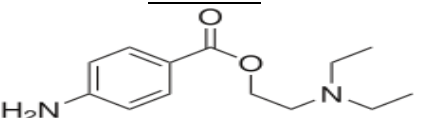
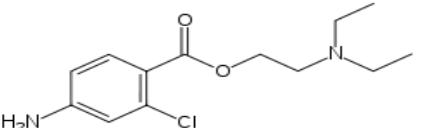
| S.No | Structure of (LA) Drug | Therapeutic Use | Adverse Effect | Reference |
|------|----------------------------------|--------------------|----------------|-----------|
| A) | Based On Chemical Nature: | | | |
| I) | Amide Type: | | | |
| | Intermediate Acting: | | | |
| 1) | <u>Lidocaine:</u> | Used intravenously | Paraesthesia | Lidoderm |

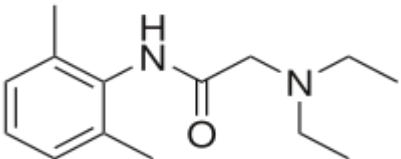
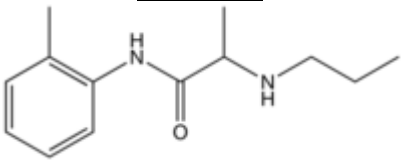
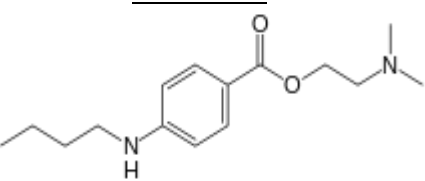
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| |  <p>Trade name: xylocaine Iupac name: 2-(diethylamino)-N-(2,6-dimethylphenyl)acetamide. Chemical formula: $C_{14}H_{22}N_2O$ Molecular mass: 234.34 g/mol.</p> | <p>for the treatment of ventricular arrhythmias. It has been efficient in refractory cases of status epilepticus. Used as an antitussive agent.</p> | <p>Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest Bradycardia Arrhythmias</p> | <p>.et.al ^[1]</p> |
| 2) | <p>Mepivacaine:</p>  <p>Trade name: carbocaine Iupac name: (RS)-N-(2,6-dimethylphenyl)-1-methylpiperidine-2-carboxamide. Chemical formula: $C_{15}H_{22}N_2O$ Molecular mass: 246.348 g/mol.</p> | <p>It is used in any infiltration and regional anaesthesia. It is used widely in dental procedures.</p> | <p>Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest</p> | <p>Porto GG,et.al ^[2]</p> |
| 3) | <p>Prilocaine:</p>  <p>Trade name: Citanest. Iupac name: (RS)-N-(2-methylphenyl)-N²-propylalaninamide Chemical formula: $C_{13}H_{20}N_2O$ Molecular mass: 220.311 g/mol.</p> | <p>Used for the treatment of paresthesia, it has low cardiac toxicity. Commonly used for intravenous regional anaesthesia (IVRA). Used in patients with hypertension, diabetes, thyrotoxicosis.</p> | <p>Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest</p> | <p>USP convention, et.al ^[3]</p> |
| | <p>LONG ACTING:</p> | | | |
| 4) | <p>Bupivacaine:</p>  <p>Trade name: Marcaine Iupac name: (RS)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide. Chemical formula: $C_{18}H_{28}N_2O$ Molecular mass: 288.43 g/mol.</p> | <p>It is indicated for infiltration, nerve block, epidural, and intrathecal anesthesia. It is taken with epinephrine to prolong the duration of its action, fentanyl for epidural analgesia or glucose.</p> | <p>Cardiotoxic Cardiac arrest Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Consciousness</p> | <p>Rossi S,et.al ^[4]</p> |
| 5) | <p>Levobupivacaine:</p>  | <p>Compared to bupivacaine it is 13% less potent. Indicated for infiltration, nerve</p> | <p>Cardiac arrest Bradycardia Arrhythmias Blurred vision</p> | <p>Rossi S,et.al ^[5]</p> |

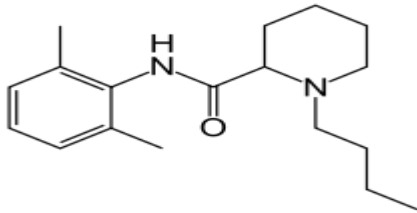
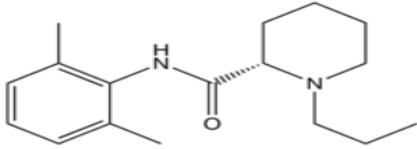
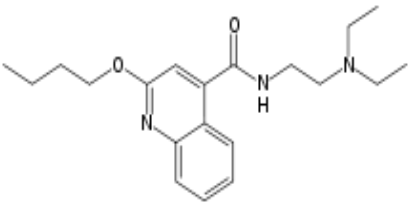
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| | <p>Trade name: Chirocaine. Iupac name: (S)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide. Chemical formula: $C_{18}H_{28}N_2O$ Molecular mass: 288.43 g/mol.</p> | <p>block, ophthalmic, epidural, and intrathecal Anesthesia in adults. And infiltration analgesia in children.</p> | <p>Tremor Dizziness Loss of Consciousness</p> | |
| 6) | <p><u>Etidocaine:</u></p>  <p>Trade name: Duranest Iupac name: N-(2,6-dimethylphenyl)-2-(ethyl(propyl)amino)butanamide. Chemical formula: $C_{17}H_{28}N_2O$ Molecular mass: 276.42 g/mol.</p> | <p>It is indicated for infiltration, nerve block, ophthalmic, epidural, and intrathecal Anesthesia</p> | <p>Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Consciousness</p> | <p>Duranest Rxlist, et al. ^[6]</p> |
| 7) | <p><u>Ropivacaine:</u></p>  <p>Trade name: Naropin Iupac name: (S)-N-(2,6-dimethylphenyl)-1-propylpiperidine-2-carboxamide. Chemical formula: $C_{17}H_{26}N_2O$ Molecular mass: 274.4 g/mol.</p> | <p>It is indicated for infiltration, nerve block, ophthalmic, epidural, and intrathecal Anesthesia in adults and children over 12 years.</p> | <p>Cardiac arrest Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Consciousness</p> | <p>Rossi S, et al.^[7]</p> |
| 8) | <p><u>Dibucaine:</u></p>  <p>Trade name: Cincaïn Iupac name: 2-butoxy-N-[2-(diethylamino)ethyl]quinoline-4-carboxamide. Chemical formula: $C_{20}H_{29}N_3O_2$ Molecular mass: 343.463 g/mol.</p> | <p>Use is restricted to spinal and topical anaesthesia. It is a component of the veterinary drug somulose, used for euthanasia of horses and cattle.</p> | <p>Same as bupivacaine. Cardiotoxic in nature.</p> | <p>Martindale. et al.^[8]</p> |
| II) | ESTER TYPE: | | | |
| | SHORT ACTING: | | | |
| 9) | <u>Procaine:</u> | It is used primarily | Procaine led to | Sawaki, et al |

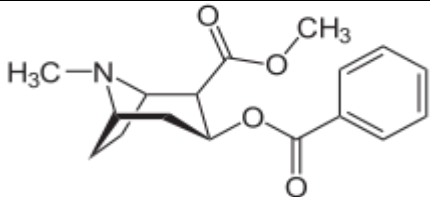
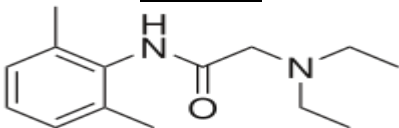
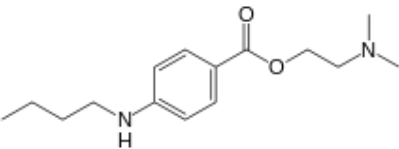
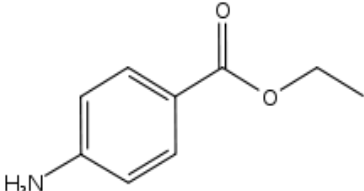
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| |  <p>Trade name: Novacaine Iupac name: 2-(diethylamino)ethyl 4-aminobenzoate. Chemical formula: $C_{13}H_{20}N_2O_2$ Molecular mass: 236.31 g/mol.</p> | used to reduce the pain of intramuscular injection of penicillin, and also used in dentistry. | the increase of dopamine and serotonin levels in the brain. It also induces weakening of the myocardium leading to cardiac arrest. | ^[9] |
| 10) | <p><u>Proparacaine:</u></p>  <p>Trade name: Alcaine Iupac name: 2-(diethylamino)ethyl 3-amino-4-propoxybenzoate. Chemical formula: $C_{16}H_{26}N_2O_3$ Molecular mass: 294.389 g/mol.</p> | It is indicated for procedures such as tonometry, gonioscopy, removal of foreign bodies, or other similar procedures requiring topical anaesthesia of the cornea and conjunctiva. | Papillary dilation. Lacrimation. Stinging. Increased winking. keratitis. Descemetitis. | Karen A Russo, et al. ^[10] |
| 11) | <p><u>Chloroprocaine:</u></p>  <p>Trade name: Nesacaine Iupac name: 2-(diethylamino)ethyl 4-amino-2-chlorobenzoate Chemical formula: $C_{13}H_{19}ClN_2O_2$ Molecular mass: 270.755 g/mol.</p> | It is a local anesthesia given by injection during surgical procedures and labor and delivery. | Same as lidocaine | Hughes, et al. ^[11] |
| 12) | <p><u>Butamben:</u></p>  <p>Trade name: Butesin Iupac name:</p> | It is used in minor skin Wound Pain Medications. Poison ivy. Poison oak. Itching. | Allergic reactions. Burning irritation. Tenderness. Swelling blisters. Oozing | Brill, et al. ^[12] |

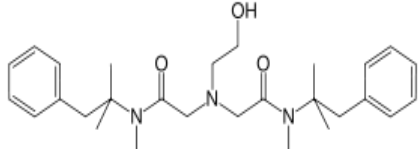
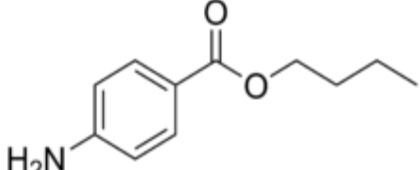
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| | <p>Butyl 4-aminobenzoate. Chemical formula: $C_{11}H_{15}NO_2$ Molecular mass: 193.242 g/mol.</p> | | | |
| 13) | <p><u>Benzocaine:</u></p>  <p>Trade name: Anbesol. IUPAC name: Ethyl 4-aminobenzoate Chemical formula: $C_{19}H_{21}NO_2$ Molecular mass: 165.189 g/mol.</p> | <p>Used in removal of excess wax as well as relieving ear conditions such as Otitis Media and swimmers ear. Used to prevent premature ejaculation.</p> | <p>Increase pulmonary aspiration. Allergic reactions. Methaemoglobinemia.</p> | <p>Garner, et al.^[13]</p> |
| | <u>INTERMEDIATE ACTING:</u> | | | |
| 14) | <p><u>Cocaine:</u></p>  <p>Trade name: kokain IUPAC name: methyl (1R, 2R,3S,5S)-3-(benzoyloxy)-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate. Chemical formula: $C_{17}H_{21}NO_4$ Molecular mass: 303.353 g/mol.</p> | <p>As ocular anaesthetic. As topical anaesthetic on nose, throat, rectum, and vagina.</p> | <p>Hemoptysis. Bronchospasm. Pruritus. Systemic eosinophilia. Dyspnea. Chest pain. Asthma. Mydriasis. Tachycardia. Myocardial infarction.</p> | <p>Barnet G, et al.^[14]</p> |
| | <u>LONG ACTING:</u> | | | |
| 15) | <p><u>Tetracaine:</u></p>  <p>Trade name: Ametop IUPAC name: 2-(dimethylamino)ethyl 4-(butylamino) benzoate. Chemical formula: $C_{15}H_{24}N_2O_2$ Molecular mass: 264.363 g/mol.</p> | <p>Topically in ophthalmology and as an antipruritic. Used in spinal anaesthesia.</p> | <p>Tremors. Drowsiness. Shallow breathing. Headache. Tingling. Blurred vision. Nausea, vomiting.</p> | <p>Winthrop, et al.^[15]</p> |
| | <u>MISCELLANEOUS:</u> | | | |
| 16) | <p><u>Pramoxine:</u></p>  <p>IUPAC name: 4-[3-(4-butoxyphenoxy)propyl]morpholine</p> | <p>Antipruritic. Sunburn. Poison ivy. Poison oak. Poison sumac. Minor cuts. Scratches.</p> | <p>Same as lidocaine.</p> | <p>Medline plus, et al.^[16]</p> |

| | | | | |
|-----------|--|--|---|-----------------------------------|
| | Chemical formula: $C_{17}H_{27}NO_3$ Molecular mass: 293.401 g/mol. | Endotracheal. Intragastric. | | |
| 17) | <p><u>Dyclonine:</u></p>  <p>Trade name: sucrets Iupac name: 1-(4-butoxyphenyl)-3-(1-piperidyl) propan-1-one. Chemical formula: $C_{18}H_{27}NO_2$ Molecular mass: 289.413 g/mol.</p> | Same as lidocaine | Mouth irritation. | N.C.B.information ^[17] |
| 18) | <p><u>Oxethazaine:</u></p>  <p>Trade name: oxetacaine. Iupac name: 2,2'-(2-hydroxyethylimino) bis [N-(1,1-dimethyl-2-phenylethyl)-N-methylacetamide] Chemical formula: $C_{28}H_{41}N_3O_3$ Molecular mass: 467.643 g/mol.</p> | Used in haemorrhoid pain. Dizziness. Drowsiness. | Anaesthetizing gastric mucosa. To relieve pain of gastritis, Gastric irritation and Gastro-esophageal reflux. | Seifter J,et.al ^[18] |
| B) | Mode Of Administration: | | | |
| I) | Injectable Anaesthetics: | | | |
| | Low Potency And Short Duration: | | | |
| 19) | <p><u>Procaine:</u></p>  <p>Trade name: Novacaine Iupac name: 2-(diethylamino) ethyl 4-aminobenzoate. Chemical formula: $C_{13}H_{20}N_2O_2$ Molecular mass: 236.31 g/mol.</p> | It is used primarily used to reduce the pain of intramuscular injection of penicillin, and also used in dentistry. | Increases dopamine and serotonin levels in the brain. induces weakening of the myocardium leading to cardiac arrest. | Sawaki,et.al ^[19] |
| 20) | <p><u>Chlorprocaine:</u></p>  <p>Trade name: Nesacaine Iupac name: 2-diethylaminoethyl-</p> | It is a local anesthesia given by injection during surgical procedures and labor and delivery. | Same as lidocaine. | Hughes,et.al ^[20] |

| | | | | |
|-----|--|---|--|--|
| | 4-amino-2-chloro-benzoate Chemical formula: $C_{13}H_{19}ClN_2O_2$ Molecular mass: 270.755 g/mol. | | | |
| | <u>Intermediate potency and duration:</u> | | | |
| 21) | <p><u>Lidocaine:</u></p>  <p>Trade name: xylocaine Iupac name: 2-(diethylamino)-N-(2,6-dimethylphenyl)acetamide. Chemical formula: $C_{14}H_{22}N_2O$ Molecular mass: 234.34 g/mol.</p> | <p>It is used intravenously for the treatment of ventricular arrhythmias. It has been efficient in refractory cases of status epilepticus. It is also used as an antitussive agent.</p> | <p>Paraesthesia Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest Bradycardia Arrhythmias</p> | <p>Lidoderm .et.al ^[21]</p> |
| 22) | <p><u>Prilocaine:</u></p>  <p>Trade name: Citanest. Iupac name: (RS)-N-(2-methylphenyl)-N²-propylalaninamide Chemical formula: $C_{13}H_{20}N_2O$ Molecular mass: 220.311 g/mol.</p> | <p>Used for the treatment of conditions like paresthesia, it has low cardiac toxicity. It is commonly used for intravenous regional anaesthesia (IVRA). Used in patients with hypertension, diabetes, thyrotoxicosis.</p> | <p>Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest</p> | <p>USP convention, et.al ^[22]</p> |
| | <u>High Potency And Long Duration:</u> | | | |
| 23) | <p><u>Tetracaine:</u></p>  <p>Trade name: Ametop Iupac name: 2-(dimethylamino) ethyl 4-(butylamino) benzoate. Chemical formula: $C_{15}H_{24}N_2O_2$ Molecular mass: 264.363 g/mol.</p> | <p>Topically in ophthalmology and as an antipruritic. Used in spinal anaesthesia.</p> | <p>Tremors. Drowsiness. Shallow breathing. Headache. Tingling. Blurred vision. Nausea, vomiting.</p> | <p>Winthrop, et.al ^[23]</p> |
| 24) | <p><u>Bupivacaine:</u></p> | <p>It is indicated for infiltration, nerve</p> | <p>Cardiotoxic Cardiac arrest</p> | <p>Rossi S, et.al ^[24]</p> |

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| |  <p>Trade name: Marcaine lupac name: (RS)-1-butyl-N-(2, 6- dimethylphenyl)piperidine-2- carboxamide. Chemical formula: $C_{18}H_{28}N_2O$ Molecular mass: 288.43 g/mol.</p> | <p>block, epidural, and intrathecal anesthesia. It is taken with epinephrine to prolong the duration of its action, fentanyl for epidural analgesia or glucose.</p> | <p>Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Consciousness</p> | |
| 25) | <p><u>Ropivacaine:</u></p>  <p>Trade name: Naropin lupac name: (S) -N- (2, 6- dimethylphenyl)-1-propyl piperidine -2- carboxamide. Chemical formula: $C_{17}H_{26}N_2O$ Molecular mass: 274.4 g/mol.</p> | <p>It is indicated for infiltration, nerve block, ophthalmic, epidural, and intrathecal Anesthesia in adults and children over 12 years.</p> | <p>Cardiac arrest Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Consciousness</p> | Rossi S, et.al ^[25] |
| 26) | <p><u>Dibucaine:</u></p>  <p>Trade name: Cincaïn lupac name: 2-butoxy -N- [2- (diethylamino) ethyl] quinoline-4- carboxamide. Chemical formula: $C_{20}H_{29}N_3O_2$ Molecular mass: 343.463 g/mol.</p> | <p>Use is restricted to spinal and topical anaesthesia. It is a component of the veterinary drug somulose, used for euthanasia of horses and cattle.</p> | <p>Relieves pain associated with haemorrhoids. Relieves itch caused by sunburns, insect bites, skin irritation.</p> | Martindale. et.al ^[26] |
| II) | Surface Anaesthesia: | | | |
| | Soluble: | | | |
| 27) | <p><u>Cocaine:</u></p> | <p>As ocular anaesthetic. As topical anaesthetic on nose, throat, rectum, and vagina.</p> | <p>Hemoptysis. Bronchospasm. Pruritus. Systemic eosinophilia. Dyspnea.</p> | Barnet G, et.al ^[27] |

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| |  <p>Trade name: kokain Iupac name: methyl (1R, 2R, 3S, 5S)-3-(benzoyloxy)-8-methyl-8-azabicyclo [3.2.1] octane-2-carboxylate. Chemical formula: $C_{17}H_{21}NO_4$ Molecular mass: 303.353 g/mol.</p> | | <p>Chest pain. Asthma. Mydriasis. Tachycardia. Myocardial infarction.</p> | |
| 28) | <p><u>Lidocaine:</u></p>  <p>Trade name: xylocaine Iupac name: 2-(diethylamino)-N-(2,6-dimethylphenyl)acetamide. Chemical formula: $C_{14}H_{22}N_2O$ Molecular mass: 234.34 g/mol.</p> | <p>It is used intravenously for the treatment of ventricular arrhythmias. It has been efficient in refractory cases of status epilepticus. It is also used as an antitussive agent.</p> | <p>Paraesthesia Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest Bradycardia Arrhythmias</p> | <p>Lidoderm .et.al ^[28]</p> |
| 29) | <p><u>Tetracaine:</u></p>  <p>Trade name: Ametop Iupac name: 2-(dimethylamino) ethyl 4-(butylamino) benzoate. Chemical formula: $C_{15}H_{24}N_2O_2$ Molecular mass: 264.363 g/mol.</p> | <p>Topically in ophthalmology and as an antipruritic. Used in spinal anaesthesia.</p> | <p>Tremors. Drowsiness. Shallow breathing. Headache. Tingling. Blurred vision. Nausea, vomiting.</p> | <p>Winthrop, et.al ^[29]</p> |
| | <p>Insoluble:</p> | | | |
| 30) | <p><u>Benzocaine:</u></p>  <p>Trade name: Anbesol. Iupac name: Ethyl 4-aminobenzoate</p> | <p>Used in removal of excess wax as well as relieving ear conditions such as Otitis Media and swimmer's ear. Used to prevent premature ejaculation.</p> | <p>Increase pulmonary aspiration.</p> | <p>Garner, et.al ^[30]</p> |

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| | Chemical formula: $C_{19}H_{11}NO_2$ Molecular mass: 165.189 g/mol. | | | |
| 31) | <p><u>Oxethazaine:</u></p>  <p>Trade name: oxetacaine. Iupac name: 2,2'-(2-hydroxyethylimino) bis [N-(1,1-dimethyl-2-phenylethyl)-N-methylacetamide] Chemical formula: $C_{28}H_{41}N_3O_3$ Molecular mass: 467.643 g/mol.</p> | Used in haemorrhoid pain. Dizziness. Drowsiness. | Anaesthetizing gastric mucosa. To relieve pain of gastritis, Gastric irritation and gastroesophageal reflux. | Seifter J,et.al ^[31] |
| 32) | <p><u>Butamben:</u></p>  <p>Trade name: Butesin Iupac name: Butyl 4-aminobenzoate. Chemical formula: $C_{11}H_{15}NO_2$ Molecular mass: 193.242 g/mol.</p> | It is used in minor skin Wound Pain Medications. Poison ivy. Poison oak. Itching. | Allergic reactions. Burning irritation. Tenderness. Swelling blisters. Oozing | Brill,et.al ^[32] |

CONCLUSION

Understanding the pharmacology of local anaesthetics enables the anaesthetist to predict the potency, speed of onset, duration of action and safety of a specific drug in a given clinical situation, this maximises the opportunity for safe and effective use of local anaesthesia in a wide variety of contexts. The review here illustrates general mechanism, chemistry and therapeutic uses as well as side effects of the local anaesthetic agents including properties and their usage to the future aspects (anaesthetics) and make aware about the types and benefits of local anaesthetic agents.

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