

Review Article

# Local Anaesthesia (LA): An Overview

Mayure Vijay Kumar\*, V. Sravanthi Department of pharmacology, Maheshwara College of Pharmacy, Hyderabad, Andhra Pradesh, India. \*mayurevijaykumar@gmail.com



### 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 selfexperimentation.

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.



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Table 1: Properties of local anaesthetics:

Drug	Onset	Duration	Tissue	Plasma half-	Main unwanted	notes
			penet	life(h)	effects	
			ration			
Cocaine	Mediu	Medium	Good	-1	CVS and CNS	Rarely used, only
	m				effects owing to	as spray for
					block of amine	upper
					uptake	respiratory tract
Procaine	Mediu	Short	Poor	<1	CNS:	The first
	m				anxiety,	synthetic agent
					Restlessness,	No longer used
					shivering,	
					depression.	
					CVS: Bradycardia,	
					and decrease	
					cardiac output,	
					vasodilatation,	
Lidocaine	Rapid	Medium	Good	-2	Less tendency to	Used intra
					cause CNS effects	venously
						fortreating
						ventricular
						dysrythmias .
Tetracaine	Very	Long	Mode	-1 as	As lidocaine	Used mainly for
	slow		rate	lidocaine		spinal
						andcorneal
						anaesthesia.
Bupivacaine	Slow	Long	Mode	-2	As lidocaine, but	Widely used
			rate		greater	causes less
					cardiotoxicity	cardio
						toxicity(levobupi
						vacaine)
Prilocaine	Mediu	Medium	Mode	-2	No vasodilator	Widely used
	m		rate		activity can cause	
					methaemoglobinae	
					mia	

# 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)	Lidocaine:	Used intravenously	Paraesthesia	Lidoderm



	H A	for the treatment of	Tinnitus	.et.al <sup>[1]</sup>
		ventricular	Tremor	
	Ö	arrhythmias.	Respiratory	
	Trade name: xylocaine	It has been efficient	depression	
	lupac name: 2-(diethylamino)-N-	in refractory cases of	Apnoea	
	(2,6-dimethylphenyl)acetamide.	status epilepticus.	Cardiac arrest	
	Chemical formula: C <sub>14</sub> H <sub>22</sub> N <sub>2</sub> O	Used as an	Bradycardia	
	Mlolecular mass: 234.34 g/mol.	antitussive agent.	Arrhythmias	
2)	Mepivacaine:	It is used in any	Tinnitus	Porto
	Н	infiltration and	Tremor	GG,et.al <sup>[2]</sup>
		regional anaesthesia.	Respiratory	
		It is used widely in	depression	
	Trade name: carbocaine	dental procedures.	Apnoea	
	lupac name: (RS)-N-(2,6-		Cardiac arrest	
	dimethylphenyl)-1-methyl-			
	piperidine-2-carboxamide.			
	Chemical formula: $C_{15}H_{22}N_2O$			
	Mlolecular mass: 246.348 g/mol.			
3)	<u>Prilocaine:</u>	Used for the	Tinnitus	USP
		treatment of	Tremor	convention,
	Ĩ Ì Ì Ĥ ́	paresthesia, it has	Respiratory	et.al
	Trada nama: Citanaat	low cardiac toxicity.	depression	
	Irade name: Citanest.	Commonly used for	Apnoea	
	iupac name: (RS)-N-(2-	intravenous regional	Cardiac arrest	
	metnyiphenyi)-N -	anaesthesia (IVRA).		
	propylalarinamide	Used in patients with		
	Chemical formula: $C_{13}H_{20}N_2O$	hypertension, diabet		
	Milliecular mass: 220.311 g/mol.	es, thyrotoxicosis.		
	LONG ACTING:			
4)	<u>Bupivacaine:</u>	It is indicated for	Cardiotoxic	Rossi S,et.al
		infiltration, nerve	Cardiac arrest	[-+]
		block, epidural, and	Bradycardia	
		intrathecal	Arrhythmias	
	Trade name: Marcaine	anesthesia.	Blurred vision	
	lupac name: (RS)-1-butyl-N-(2, 6-di	It is taken with	Iremor	
	methylphenyl)piperidine-2-	epinephrine to	Dizziness	
	carboxamide.	prolong the duration	Loss of Con -	
	Chemical formula: C <sub>18</sub> H <sub>28</sub> N <sub>2</sub> O	of its action, fentanyl	sciousness	
	Mlolecular mass: 288.43 g/mol.	for epidyral		
		analgesia or glucose.		
5)	Levobupivacaine:	Compared to	Cardiac arrest	Rossi S,et.al
		pupivacaine it is 13%	Bradycardia	[0]
		less potent.Indicated	Arrhythmias	
		tor infiltration, nerve	Blurred vision	



	Trade name: Chirocaine.	block,ophthalmic,	Tremor	
	lupac name: (S)-1-butly-N-(2,6-	epidural, and	Dizziness	
	dimethylphenyl)piperidine-2-	intrathecal	Loss of Con -	
	carboxamide.	Anesthesia in adults.	sciousness	
	Chemical formula:C <sub>18</sub> H <sub>28</sub> N <sub>2</sub> O	And infiltration		
	Mlolecular mass: 288.43 g/mol.	analgesia in children.		
6)	Etidocaine:	It is indicated for	Bradycardia	Duranest
	н	infiltration, nerve	Arrhythmias	Rxlist,et.al.
		block, ophthalmic,	Blurred vision	[6]
	ö	epidural, and	Tremor	
	Trade name: Duranest	intrathecal	Dizziness	
	lupac name: N-(2,6-	Anesthesia	Loss of Con -	
	dimethylphenyl)-2-		sciousness	
	(ethyl(propyl)amino)butanamide.			
	Chemical formula: $C_{17}H_{28}N_2O$			
->	Miolecular mass: 276.42 g/mol.			
/)	<u>Ropivacaine:</u>	It is indicated for	Cardiac arrest	
		Innitration, nerve	Bradycardia	S,et.al
		DIOCK,Ophthalmic,	Armythmias	
	N N	epidurai,anu		
	0	Anosthosia in adults	Dizziness	
	Trada noma. Navanin	and children over 12	Loss of Con -	
	Trade name: Naropin		sciousness	
	lupac name: (5) -N- (2, 6-	years.	30100311033	
	ninetilyipiletiyi)-1-pilopyi			
	Chemical formula: C H N O			
	Molecular mass: $274.4$ g/mol			
8)	Dibucaine:	Use is restricted to	Same as	Martindale
0,	<u>bibucuine.</u>	spinal and topical	bunivacaine	et al <sup>[8]</sup>
		anaesthesia	Cardiotoxic in	ct.ui
		It is a component of	nature	
	N H	the veterinary drug	natarer	
	Ĩ ]	somulose, used for		
		euthanasia of horses		
	Trade name: Cincain	and cattle.		
	lupac name: 2-butoxy -N- [2-			
	(diethylamino) ethyl] quinoline-4-			
	carboxamide.			
	Chemical formula: $C_{20}H_{29}N_3O_2$			
	Miolecular mass: 343.463 g/mol.			
11)	ESTER TYPE:			
0)	SHORT ACTING:			
9)	Procaine:	It is used primarily	Procaine led to	Sawaki,et.al



	H <sub>2</sub> N Trade name: Novacaine Iupac name: 2-(diethylamino) ethyl4-aminobenzoate. Chemical formula: C <sub>13</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> Mlolecular mass: 236.31 g/mol.	used to reduce the pain of intramuscular injection of penicillin, and aldo 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)	Proparacaine: H <sub>2</sub> N H <sub>2</sub> N Trade name: Alcaine Iupac name: 2-(diethylamino)3- amino-4-propoxybenzoate. Chemical formula: C <sub>16</sub> H <sub>26</sub> N <sub>2</sub> O <sub>3</sub> Mlolecular mass: 294.389 g/mol.	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 <sup>[10]</sup>
11)	<u>Chloroprocaine:</u> $H_2N$ Trade name: Nesacaine Iupac name: 2-diethylaminoethyl- 4-amino-2-chloro-benzoate Chemical formula: C <sub>13</sub> H <sub>19</sub> clN <sub>2</sub> O <sub>2</sub> Mlolecular mass: 270.755 g/mol.	It is a local anesthesia given by injection during surgical procedures and labor and delivery.	Same as lidocaine	Hughes,et.al
12)	Butamben: Butamben: O H <sub>2</sub> N Trade name: Butesin lupac name:	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 <sup>[12]</sup>



	Butyl 4-aminobenzoate.			
	Chemical formula: C <sub>11</sub> H <sub>15</sub> NO <sub>2</sub>			
	Mlolecular mass: 193.242 g/mol.			
13)	<u>Benzocaine:</u>	Used in removal of	Increase	Garner,et.al
		excess wax as well as	pulmonary	[13]
		relieving ear	aspiration.	
		conditions such as	Allergic	
	Trade name: Anbesol	Otitis Media and	reactions.	
	lunac name:	swimmers ear.	Methaemoglobi	
	Fthyl 4-aminobenzoate	Used to prevent	naemia.	
	Chemical formula: CooHeeNO	premature		
	Molecular mass: 165, 189 g/mol	ejaculation.		
	INTERMEDIATE ACTING:			
14)	Cocaine:	As ocular	Hemoptysis.	Barnet
,	°, ,CH₃	anaesthetic.	Bronchospasm.	G,et.al <sup>[14]</sup>
	H <sub>3</sub> C-N	As topical	Pruritus.	
		anaesthetic on nose,	Systemic	
		throat, rectum, and	eosinophilia.	
	Trade name: kokain	vigina.	Dyspnea.	
	lupac name: methyl (1R, 2R, 3S, 5S)-	-	Chest pain.	
	3-(benzovloxy)-8-methyl-8-		Asthma.	
	azabicvclo[3.2.1]octane-2-		Mydriasis.	
	carboxvlate.		Tachycardia.	
	Chemical formula: C <sub>17</sub> H <sub>21</sub> NO <sub>4</sub>		Myocardial	
	Mlolecular mass: 303.353 g/mol.		infarction.	
	LONG ACTING:			
15)	Tetracaine:	Topically in	Tremors.	Winthrop,et
	Î l	opnthalmology ans	Drowsiness.	.al <sup>[15]</sup>
		as an antipruritic.	Shallow	
		Used in spinal	breathing.	
	н	anaesthesia.	Headache.	
	Trade name: Ametop		Tingling.	
	lupac name: 2-(dimethylamino)		Blurred vision.	
	ethyl 4-(butylamino) benzoate.		Nausea,	
	Chemical formula: $C_{15}H_{24}N_2O_2$		vomiting.	
	Miolecular mass: 264.363 g/mol.			
16)	Dramovino:	Antipruritic Suphurn	Samo ac	Modling
10)			lidocaine	nlus et al <sup>[16]</sup>
		Poison oak	nuocante.	pius,et.ai
		Poison sumac		
	lupac name: 4- [3- (4-	Minor cuts		
	butoxyphenoxy)propyllmorpholine	Scratches		
	//: = = //:····/·	Juanties		



	Chemical formula: C <sub>17</sub> H <sub>27</sub> NO <sub>3</sub>	Endotracheal.		
	Mlolecular mass: 293.401 g/mol.	Intragastric.		
17)	Dyclonine:	Same as lidocaine	Mouth	N.C.B.infor
			irritation.	mation <sup>[17]</sup>
	N			
		l		
	I rade name: sucrets			
	(1 piperidul) present 1 energy			
	(1-piperidyi) propan-1-one.			
	Chemical formula: $C_{18}H_{27}NO_2$			
10)	Miolecular mass: 289.413 g/mol.		A	C a ift a r
18)		Used in naemorrhoid	Anaestnetizing	Seifter
		pain. Dizzinoss	gastric mucosa.	J,et.al
		Dizzilless.	of gostritic	
		Drowsiness.	OI gastritis,	
	Ý Ť Ť Ť		and Castro-	
	Trade name: oxetacaine.		anu Gastro-	
	lupac name: 2,2'-(2-		rofluy	
	hydroxyethylimino) bis [N- (1,1-		Tenux.	
	dimethyl-2-phenylethyl)-N-			
	methylacetamide]			
	Chemical formula: $C_{28}H_{41}N_3O_3$			
	Mlolecular mass: 467.643 g/mol.			
B)	Mode Of Administration:			
I)	Injectable Anaesthetics:			
	Low Potency And Short Duration:			
19)	Procaine:	It is used primarily	Increases	Sawaki,et.al
		used to reduce the	dopamine and	[19]
		pain of intramuscular	serotonin levels	
	H <sub>2</sub> N	injection of	in the brain.	
	Trade name: Novacaine	penicillin, and aldo	Induces	
	lupac name: 2-(diethylamino)	used in dentistry.	weakening of	
	ethyl4-aminobenzoate.		the myocardium	
	Chemical formula: C <sub>13</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>		leading to	
	Mlolecular mass: 236.31 g/mol.		cardiac arrest.	
20)	Chloroprocaine:	It is a local	Same as	Hughes, et.al
		anesthesia given by	lidocaine.	[20]
	Î	injection during		
		surgical procedures		
		and labor and		
		delivery.		
	I rade name: Nesacaine		1	



	4-amino-2-chloro-benzoate			
	Chemical formula: $C_{13}H_{19}cIN_2O_2$			
	Mlolecular mass: 270.755 g/mol.			
	Intermediate potency and			
	duration:			
21)	Lidocaine:	It is used	Paraesthesia	Lidoderm
		intravenously for the	Tinnitus	.et.al <sup>[21]</sup>
	∣н	treatment of	Tremor	
	$\dot{\mathbf{N}}$	ventricular	Respiratory	
	Γ Υ Υ Ν Υ	arrhythmias.	depression	
	ų k ö k	It has been efficient	Apnoea	
		in refractory cases of	Cardiac arrest	
	Trado namo: vulocaino	status epilepticus.	Bradycardia	
	lupac namo: 2 (diothylamino) N	It is also used as an	Arrhythmias	
	(2.6. dimothylphonyl)acotamido	antitussive agent.		
	Chemical formula: C H N O			
	Molecular mass: $234.24$ g/mol			
221		lised for the	Tinnitus	
22)		treatment of	Tremor	convention
		conditions like	Respiratory	
		naresthesia it has	depression	et.ai
		low cardiac toxicity	Δηγορα	
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	It is commonly used	Cardiac arrest	
	Trade name: Citanest.	for intravenous	Cardiac arrest	
	lupac name: (RS)-N-(2-	regional anaesthesia		
	methylphenyl)-N <sup>2</sup> -	(IVRA) Used in		
	propylalaninamide	natients hypertensio		
	Chemical formula: C <sub>13</sub> H <sub>20</sub> N <sub>2</sub> O	n diabatas		
	Mlolecular mass: 220.311 g/mol.	thyrotoxicosis		
	High Botoncy And Long Duration:			
221	Tetracaine	Tonically in	Tremore	Winthron et
231		onnthalmology and	Drowsiness	al <sup>[23]</sup>
	Ŭ N	as an antinruritic	Shallow	.01
		lised in chinal	hreathing	
		anaesthesia	Headache	
		andestries1a.	Tingling	
	Trade name: Ameton		Blurred vision	
	lunac name: 2-(dimethylamina)		Nausea	
	ethyl A-(hutylamino) benzoste		vomiting	
	Chomical formula: C H N O		vonnting.	
	Molecular mass: $264, 262, a/mol$			
24)	Bunivacaine:	It is indicated for	Cardiotoxic	Rossi S at al
24)	bupivacame.	infiltration nervo	Cardiac arrest	[24]
		innitiation, nerve	Carulac arrest	1



	Trade name: Marcaine Iupac name: (RS)-1-butyl-N-(2, 6- di methylphenyl)piperidine-2- carboxamide. Chemical formula: C <sub>18</sub> H <sub>28</sub> N <sub>2</sub> O Mlolecular mass: 288.43 g/mol.	block, epidural, and intrathecal anesthesia. It is taken with epinephrine to prolong the duration of its action, fentanyl for epidyral analgesia or glucose.	Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Con - sciousness	
25)	Ropivacaine: Ropivacaine: Trade name: Naropin lupac name: (S) -N- (2, 6- dimethylphenyl)-1-propyl piperidine -2- carboamide. Chemical formula: C <sub>17</sub> H <sub>26</sub> N <sub>2</sub> O Mlolecular mass: 274.4 g/mol.	It is indicated for infiltration, nerve block,ophthalmic, epidural,and intrathecal Anesthesia in adults and children over 12 years.	Cardiac arrest Bradycardia Arrhythmias Blurred vision Tremor Dizziness Loss of Con - sciousness	Rossi S,et.al
26)	Dibucaine: Dibucaine: Dibucaine: Trade name: Cincain lupac name: 2-butoxy -N- [2- (diethylamino) ethyl] quinoline-4- carboxamide. Chemical formula: C <sub>20</sub> H <sub>29</sub> N <sub>3</sub> O <sub>2</sub> Mlolecular mass: 343.463 g/mol.	Use is restricted to spinal and topical anaesthesia. It is a component of the veterinary drug somulose, used for euthanasia of horses and cattle.	Relieves pain associated with haemorrhoids. Relieves itch caused by sunburns, insect bites, skin irritation.	Martindale. et.al <sup>[26]</sup>
II)	Surface Anaesthesia:			
	Soluble:			
27)	<u>Cocaine:</u>	As ocular anaesthetic. As topical anaesthetic on nose,throat, rectum.and vigina.	Hemoptysis. Bronchospasm. Pruritus. Systemic eosinophilia. Dyspnea.	Barnet G,et.al <sup>[27]</sup>



	H <sub>3</sub> C-N-CH <sub>3</sub> Trade name: kokain lupac name: methyl (1R, 2R, 3S, 5S)-3-(benzoyloxy)-8-methyl-8- azabicyclo [3.2.1] octane-2- carboxylate. Chemical formula: C <sub>17</sub> H <sub>21</sub> NO <sub>4</sub> Mlolecular mass: 303.353 g/mol.		Chest pain. Asthma. Mydriasis. Tachycardia. Myocardial infarction.	
28)	Lidocaine: H N Trade name: xylocaine lupac name: 2-(diethylamino)-N- (2,6-dimethylphenyl)acetamide. Chemical formula: C <sub>14</sub> H <sub>22</sub> N <sub>2</sub> O Mlolecular mass: 234.34 g/mol.	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.	Paraesthesia Tinnitus Tremor Respiratory depression Apnoea Cardiac arrest Bradycardia Arrhythmias	Lidoderm .et.al <sup>[28]</sup>
29)	Trade name: Ametop Iupac name: 2-(dimethylamino) ethyl 4-(butylamino) benzoate. Chemical formula: C <sub>15</sub> H <sub>24</sub> N <sub>2</sub> O <sub>2</sub> Mlolecular mass: 264.363 g/mol.	Topically in opnthalmology ans as an antipruritic. Used in spinal anaesthesia.	Tremors. Drowsiness. Shallow breathing. Headache. Tingling. Blurred vision. Nausea, vomiting.	Winthrop, et.al <sup>[29]</sup>
	Insoluble:			
30)	Benzocaine:	Used in removal of excess wax as well as relieving ear conditions such as Otitis Media and swimmers ear. Used to prevent premature ejaculation.	Increase pulmonary aspiration.	Garner, et.al <sup>[30]</sup>



	Chemical formula: C <sub>19</sub> H <sub>11</sub> NO <sub>2</sub>			
	Mlolecular mass: 165.189 g/mol.			
31)	Oxethazaine: OH Trade name: oxetacaine. Iupac name: 2,2'-(2- hydroxyethylimino) bis [N- (1,1- dimethyl-2-phenylethyl)-N- methylacetamide] Chemical formula: C <sub>28</sub> H <sub>41</sub> N <sub>3</sub> O <sub>3</sub> Mlolecular mass: 467.643 g/mol.	Used in haemorrhoid pain. Dizziness. Drowsiness.	Anaesthetizing gastric mucosa. To relieve pain of gastritis, Gastric irritation and gastroesophage al reflux.	Seifter J,et.al <sup>[31]</sup>
32)	Butamben:	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 <sup>[32]</sup>

### 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.

## **↓** REFERENCES

1. "Lidoderm". RxWiki.

2. Porto GG, Vasconcelos BC, Gomes AC, Albert D "Evaluation of lidocaine and mepivacaine for inferior thiard molar surgery". Med oral Patol oral cir Bucal January 2007, 12 (1):E60-4.

3. United States Pharmacopial convention. "Revision Bulletin: Lidocaine and prilocaine Cream-Revision to Related compounds Test". Retrieved 10th July 2009.

4. Rossi S, editor, Australian Medicines Handbook Adelaide: Australian Medicines Handbook: 2006.

5. Rossi S, editor, Australian Medicines Handbook Adelaide: Australian Medicines Handbook: 2006.



6. Duranest (RxList)

7. Rossi S, editor, Australian Medicines Handbook Adelaide: Australian Medicines Handbook: 2006.

8. Martindale, The Extra Pharmacopoeia, 30th ed, p 1006.

9. Sawaki, k; and Kawaguchim, M. "some correlations between procaine-induced convulsions and monoamides in the spinal cord of rats". Japanese Journal of pharmacology, 1989, 51 (3), p.369-376.

10. Karen A Russo, ph.D., Scientist Expert Committee: (PA1) pharma.Analysis 1 USP28-NF23 P.1646.

11. Hughes: Anesthesia for pbstetrics, 4th ed, p75.

12. Brill, J.Am.Chem.Soc.43, 1322(1921): adams, volwiler, US1440652 (1923 to abbott); C.A.21, 2478, 1927.

13. Garner, Dwight "Endurance Condoms". The New York Times. 15 Dec 2002.

14. Barnet G, Hawks R, Resnick R. "Cocaine Pharmacokinectics in Humans". J Ethnopharmacol 1981, 3 (2-3): 353-66.

15. Winthrop Chemical Company, Inc US patent 1,889, 645, 1932.

16. nlm.nih.gov/medline plus/druginfo/meds/a642429.html.

17. National Centre for biotechnology information. U>S National Library of Medicine 8600 Rockville Pike, Bethesda MD 20894USA.

18. Seifter J, Glassman JM, Hudyma GM. "Oxethazine and related congeners: a series of highly potent local anaesthetica". Proc soc Exp Biol Med 1962, 109: 664-8.

19. Sawaki, k; and Kawaguchim, M. "some correlations between procaine-induced convulsions and monoamides in the spinal cord of rats". Japanese Journal of pharmacology, 1989, 51 (3), p.369-376 20. Hughes: Anesthesia for pbstetrics, 4th ed, p75.

21. "Lidoderm". RxWiki.

22. United States Pharmacopeial convention. "Revesion Bulletin: Lidocaine and prilocaine Cream-Revision to Related compounds Test". Retrieved 10th July 2009.

23. Winthrop Chemical Company, Inc U.S.patent 1,889, 645, 1932.

24. Rossi S, editor, Australian Medicines Handbook 2006. Adelaide: Australian Medicines Handbook: 2006.

25. Rossi S, editor, Australian Medicines Handbook Adelaide: Australian Medicines Handbook: 2006.

26. Martindale, the Extra Pharmacopoeia, 30th ed, p1006.

27. Barnet G, Hawks R, Resnick R. "cocaine pharmacokinectics in humans". J Ethnopharmacol 1981, 3 (2-3): 353-66.

28. "Lidoderm". RxWiki.

29. Winthrop Chemical Company, Inc U.S.patent 1,889. 1932, 645.

30) Garner, Dwight "Endurance Condoms". The New York Times. 15 Dec 2002.

31. seifter J, Glassman JM, Hudyma GM,. "Oxethazine and related congeners: a series of highly potent local anaesthetica". Proc soc Exp Biol Med 1962, 109: 664-8.

32. Brill, J.Am.Chem.Soc.43, 1322, 1921: adams, volwiler, US1440652 (1923 to abbott); C.A.21, 2478, 1927.