Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

COMPARATIVE LITERATURE REVIEW OF LOCAL ANESTHETICS

[1]Mustanov T.B., [2]Allaeva M.J., [1,2]Djanaev G.Yu.
[1]Alfraganus University, Tashkent, Uzbekistan
[2]Tashkent Medical Academy, Tashkent, Uzbekistan
gayratdjanayev75@gmail.com

Abstract. Anesthetic agents lose local sensitivity. Since this group of drugs primarily relieves the sensation of pain, they are mainly used for the purpose of leaving local pain (anesthesia). As anesthesia deepens, temperature and other types of sensitivity gradually disappear, and lastly, tactile sensation and pressure.
Most anesthetics have 3 main parts: an aromatic structure, an intermediate chain and an amino group. The aromatic structure is lipophilic, and the amino group is hydrophilic. The middle part of the molecule usually consists of an aliphatic chain, composed of complex esters or amides. Considering the structure of anesthetics, it can be assumed that their interaction with the membrane of nerve fibers involves both polar (amino group) and non-polar lipophilic (aromatic) groups. The effect of local analgesics increases under the influence of narcotic drugs, narcotic hypnotics, antipsychotics and opioid analgesics, and decreases when used in combination with MNS-stimulating agents (analeptics).
Key words: Cocaine, Dicaine, Anesthesin, Pyromecaine, Novocaine, Bupivacaine, Articaine, Lidocaine, Trimecaine.

Introduction. Anesthetic agents lose local sensitivity. Since this group of drugs primarily relieves the sensation of pain, they are mainly used for the purpose of leaving local pain (anesthesia). As anesthesia deepens, temperature and other types of sensitivity gradually disappear, and lastly, tactile sensation and pressure.
Anesthetics prevent the generation and propagation of excitatory impulses by affecting sensitive afferent nerve endings and nerve fibers. Their mechanism of action occurs mainly by blocking potential-dependent sodium channels. Hydrophobic (non-ionized) compounds are hypothesized to cross the axon membrane and block sodium channels from the inside. Hydrophilic compounds penetrate through open sodium channels and have a slightly blocking effect. Therefore, the activity of anesthetics, which are weak bases, depends on the pH of the environment, which determines the ratio of ionizable and non-ionizable parts of the drug. In particular, in the case of inflammation, anesthetics are less effective at low pH (acidic environment), because the concentration of non-ionized compounds decreases. Most anesthetics have 3 main parts: an aromatic structure, an intermediate chain and an amino group. The aromatic structure is lipophilic, and the amino group is hydrophilic. The middle part of the molecule usually consists of an aliphatic chain, composed of complex esters or amides.

Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

Considering the structure of anesthetics, it can be assumed that their interaction with the membrane of nerve fibers involves both polar (amino group) and non-polar lipophilic (aromatic) groups[1,2,3].

There are specific requirements for anesthetics. First of all, they should have a high degree of selective action without negative effects on nerve elements or surrounding tissues (tickling, etc.). A short latent period, high efficiency in various forms of local anesthesia, a certain duration of action (convenient for carrying out various manipulations) are properties that an anesthetic agent should have. They should narrow blood vessels (or at least not widen them). This is important because the narrowing of vessels (vasoconstriction) enhances anesthesia, reduces bleeding from tissues, and also delays the absorption of the anesthetic and reduces the possibility of toxic effects. The opposite is observed in the expansion of blood vessels. If the anesthetic does not affect blood vessels or expand them, it is recommended to use it in combination with vasoconstrictors of the adrenomimetic group. Low toxicity and minimal side effects are important features. In such cases, the possibility of a resorptive effect of anesthetics is taken into account, since they can be absorbed from the injection site. Medicines should dissolve well in water, should not be damaged during storage and sterilization [1,4,5].

Local anesthetics are used for various anesthesias. The main ones are:

• **Surface Or Terminal Anesthesia** - in which the anesthetic solution is applied to the surface of the mucous membrane, where it blocks the sensitive nerve endings; in addition, the anesthetic can be applied to the wound, wound surface;

• **Infiltration Or Layer-By-Layer Anesthesia** - in this, the blocking of nerve fibers and sensory nerve endings in these places is achieved by gradually introducing the anesthetic solution into the skin and subcutaneous tissues in the place of operation;

• **Conducting Or (Regional) Area Anesthesia** - in which the anesthetic solution is injected near a certain nerve fiber and blocking of the transmission of nerve impulses to the tissues in the area innervated by this nerve fiber is achieved.

Spinal anesthesia (in which the anesthetic solution is injected subarachnoidally) and epidural or peridural anesthesia (in which the anesthetic solution is injected into the space in front of the dura mater) are distinguished as specific types of conductive anesthesia. In these types of anesthesia, the anesthetic affects the anterior or posterior branches of the gray matter of the spinal cord.

According to their use in practical medicine, local anesthetics can be divided into the following groups:

1. Means used in surface or terminal anesthesia:

Cocaine Dicaine Anesthesin Pyromecaine

2. Means used mainly in infiltration and conduction anesthesia

Novocaine Bupivacaine Articaine

3. Tools used in all types of anesthesia

Lidocaine Trimecaine

Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

The first local anesthetic used in medical practice is cocaine, which is an alkaloid extracted from the Erythroxylon coca plant that grows in South America. It is also isolated from ecgonone by a semi-synthetic method. According to its chemical structure, it is a complex ester of benzoic acid and methylecgonine. It has a very strong anesthetic property, which is several times superior to novocaine, but due to its high toxicity, it is used only in surface anesthesia. Even then, it should be used with extreme caution, as it is easily absorbed through mucous membranes and can cause many side effects and even acute poisoning. Cocaine in its hydrochloride form is mainly used for eye drops in eye practice. In doing so, he narrows the blood vessels of the sclera and dilates the pupil, causing anesthesia that lasts for about 1 hour. Usually the intraocular pressure decreases. However, in some patients there is also a possibility of increased intraocular pressure (apparently due to the difficulty of outflow of intraocular fluid). As a result of its continuous use, it has a negative effect on the epithelium of the cornea, and as a result, the migration of the epithelium and the formation of an ulcer can be observed. If the dose of cocaine is too high, then the MNS will suppress instead of potentiate it. Death occurs as a result of a sharp decrease in the activity of the centers necessary for life (primarily the respiratory center) in the medulla oblongata. The effect of cocaine on adrenergic innervation is specific. It increases the stimulating effects of adrenergic innervation, as well as potentiates the effect of some adrenomimetics[1,6,7].

If cocaine is absorbed through the mucous membranes and has a resorptive effect, then mainly the stimulation of the MNS appears. Initially, a change in the functional state of the cerebral cortex is observed. This includes euphoria1, restlessness, psychomotor agitation, loss of fatigue and hunger, hallucinations2, etc. observed. Cocaine also strengthens the respiratory, cardiovascular and vomiting centers in the medulla oblongata, convulsions may occur. Usually, acute and chronic poisoning with cocaine can be observed. In case of acute poisoning, the main attention should be focused on reducing its absorption from the injection site. If the drug was drunk, then the stomach is washed with a 0.05-0.1 percent solution of potassium permanganate. Adsorbing, wrapping and saline sprays are recommended. If it is introduced through the mucous membranes, then the mucous membranes are washed with an isotonic solution of sodium chloride. But if the drug is injected into the body, then its absorption can be reduced by placing a tourniquet above the injection site. It is also recommended to put an ice pack on the injection site. In case of severe poisoning, it is necessary to be prepared for artificial respiration, tracheotomy when necessary.

Diazepam solution should be injected to eliminate agitation. As a result of continuous use of cocaine (sniffing the powder, chewing the leaves, and sometimes repeated intravenous injection), chronic intoxication occurs. In this case, mental dependence (кокаінизм) appears, and physical dependence does not develop. Habituation does not occur or may occur to a very low degree[1,8,9].

Dikain (tetracaine hydrochloride) is also a tool mainly used in surface anesthesia, and according to its chemical structure, it is a product of paraaminobenzoic acid. It is about 10 times more active than cocaine, and 2-5 times more toxic.

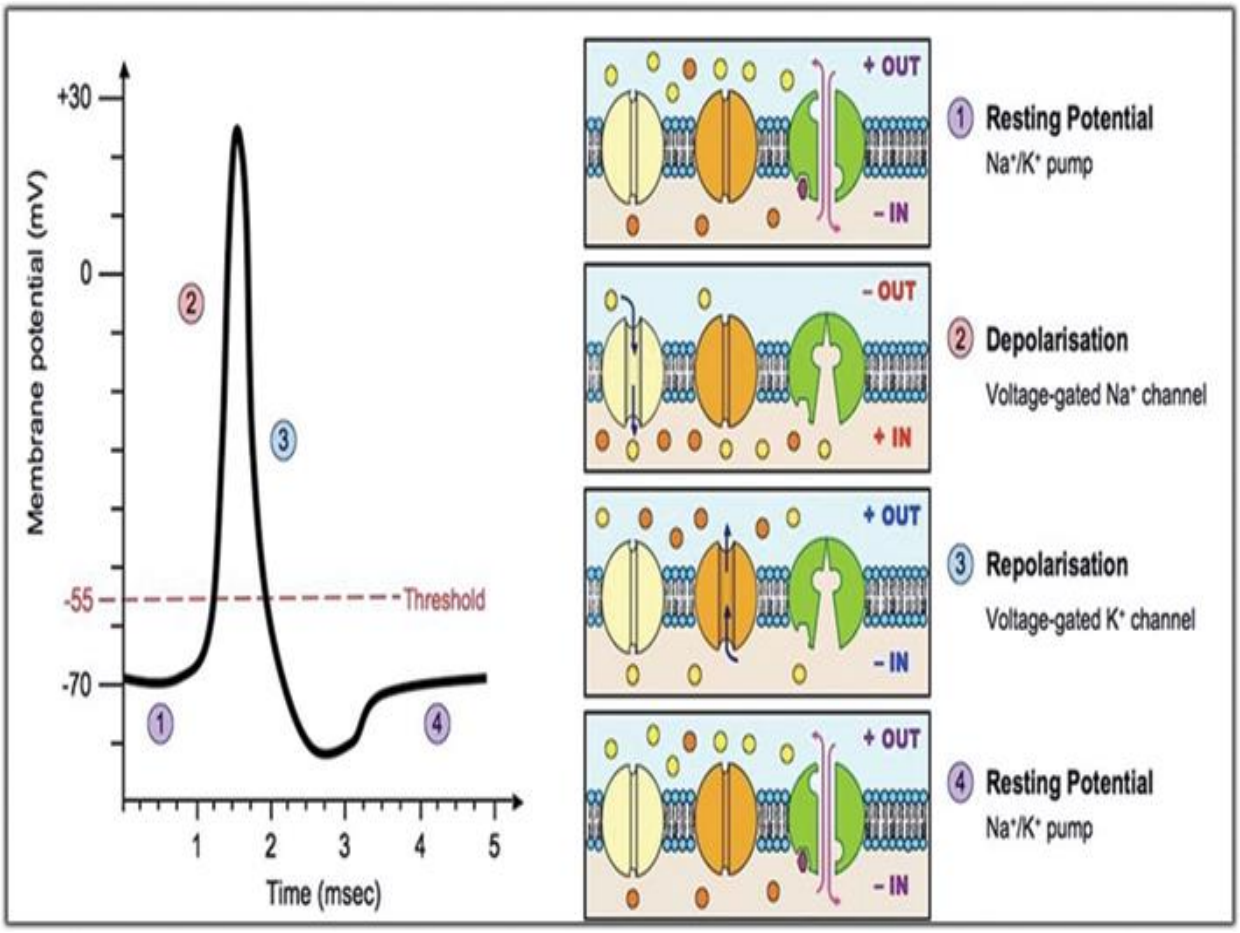
Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

A comparative comparison of some local anesthetics Activity and toxicity (conditional effect units)

Drug	Activity in anesthesia			Toxicity
	Surface	Layer by layer	Conductor	
Cocaine	1	3,5	1,9	3,5
Dikain	10-20	10-20	10-20	10-15
Novocaine	0,1	1	1	1
Trimecain	0,4	3-3,5	2,5-3,5	1,2-1,4
Lidocaine	0,5	2-4	2-3	1,5-2

Dikain does not affect intraocular pressure and accommodation when used in ophthalmic practice, does not dilate the pupil. Can tickle the mucous membrane of the foreskin. Dikain dilates blood vessels, so its solutions should be recommended together with adrenomimetics. Sometimes it is also used for epidural anesthesia. When using dicain, it is necessary to pay special attention to its dose, because it is easily absorbed through the mucous membranes, and there is a possibility of unexpected severe poisoning and even death. For surface anesthesia, p i r o, similar in structure to trimecaine -m e k a i n medicine is also used. Unlike the above drugs, anesthesia is poorly soluble in water, well soluble in alcohol and oils. That is why it is mainly used for sprinkling on the skin and applying it to wounds in the form of ointment and paste, and sometimes it is used in the form of powder, tablets and suspension to numb the mucous membrane in gastrointestinal diseases. It is also used as a suppository for posterior ventral fissures and similar. In all forms of anesthetic use, it is used only to induce surface anesthesia. N o v o c a i n (procaine hydrochloride) is mainly used for layered and transfer anesthesia. It is a complex ester of diethylaminoethanol and paraaminobenzoic acid. It is used in practical medicine in the form of hydrochloride.

Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed



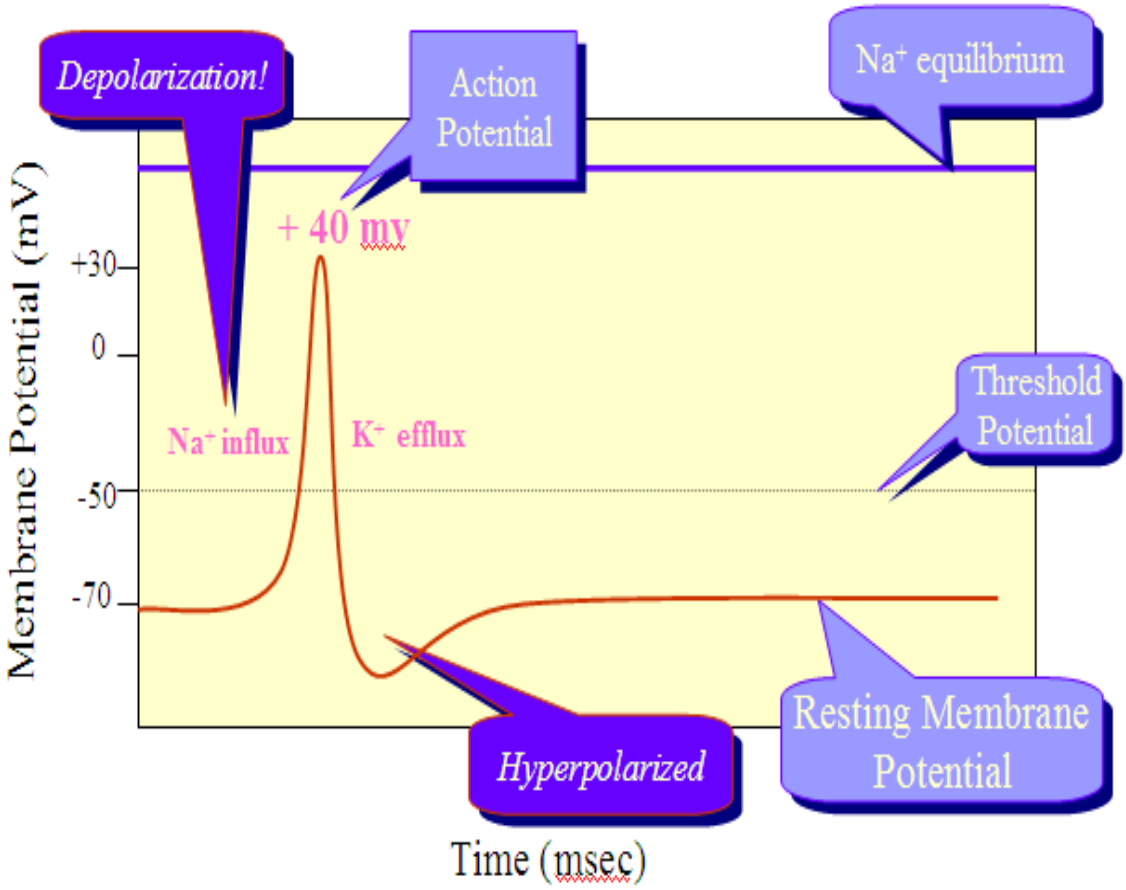
It has a sufficient level of anesthetic properties, but it lags far behind other drugs in terms of this property. The toxicity of it and its metabolites is very low, the duration of the effect is 30-60 minutes[1,10,11].

Novocaine poorly passes through mucous membranes, therefore it can be used in surface anesthesia only in high doses (10% solution in otorhinolaryngology) in rare cases. It slightly dilates the blood vessels. Therefore, it is necessary to add adrenomimetics (for example, 0.1% solution of adrenaline at the rate of 1 drop per 10 ml of novocaine) to its solutions. In this case, adrenomimetics reduce the absorption of novocaine by narrowing blood vessels. As a result, the duration of its effect increases, and its toxicity decreases.As a result of its resorptive effect, novocaine has a depressant and less analgesic effect on the nervous system. Convulsions can occur in high doses.

As a result of its effect on the cardiovascular system, hypotensive (mainly due to weakening of the activity of the MNS and peripheral sympathetic ganglia) and short-term antiarrhythmic (increases the effective refractory period and the time of passage of impulses through the conduction system of the heart, reduces excitability and automaticity) effects are observed. Novocaine is quickly metabolized to diethylaminoethanol and paraaminobenzoic acids under the influence of esterases in the blood plasma. Para-aminobenzoic acid is a competitive

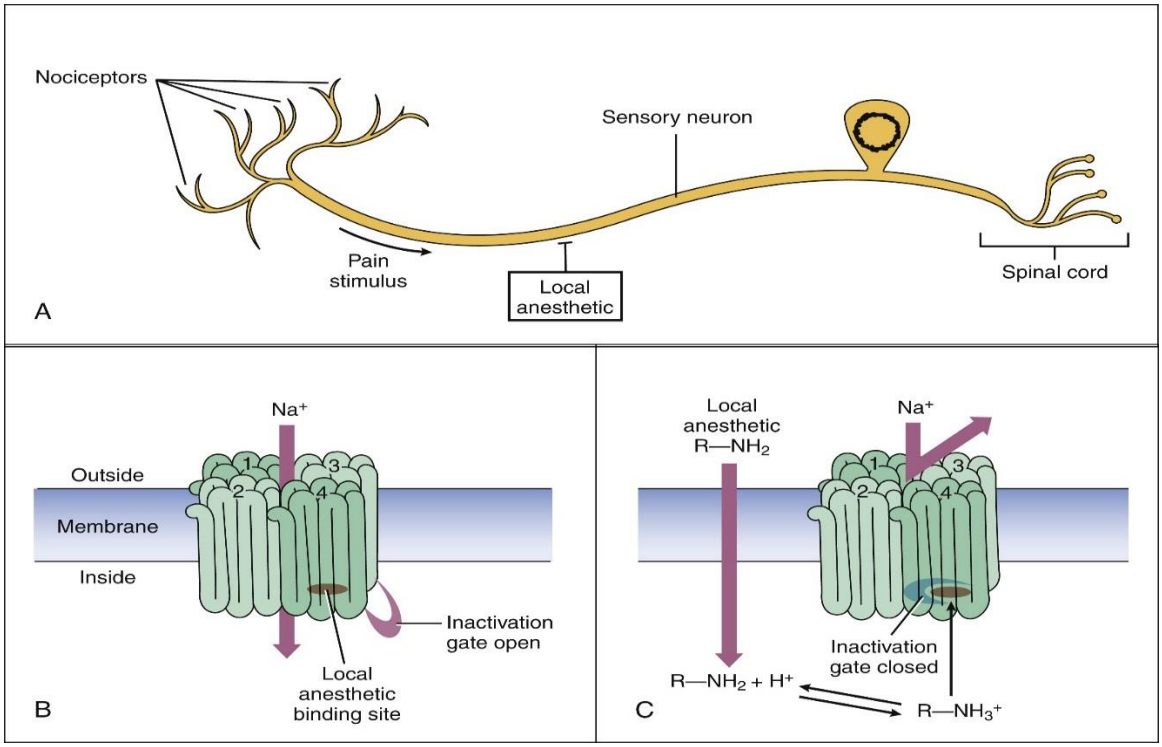
Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

antagonist with sulfonamides and requires that they are not recommended at the same time. Metabolites are excreted by the kidneys.



Bupivacaine hydrochloride (longocaine, mercaine) has been widely used in recent years and is very close to lidocaine in terms of its chemical structure and pharmacological properties. It has high activity and effect. is a long-acting local anesthetic. Mainly used for conduction (spinal) and infiltration anesthesia. The effect appears after 5-10 minutes and lasts 3-4 hours in epidural anesthesia, 7-14 hours in intercostal blockade, and sometimes up to 24 hours and more. In cases of overdose, strong cardiotoxic (ventricular arrhythmias may occur) and neurotoxic (drowsiness, nystagmus, tremor, convulsions, etc.) effects may occur. **Lidocaine** (xycain, xylocaine) is used in all types of local anesthesia. Its anesthetic activity is 2.5 times higher than novocaine, and the duration of action is 2 times longer. If novocaine is used together with adrenomimetics, the duration of action lasts for about 1.5-2 hours, it is 2-4 hours for lidocaine (in 0.5% solutions of both). Toxicity may be almost the same as that of novocaine or slightly higher. Does not have tissue tickling properties. When instilled into the eyes, it does not affect the pupil and blood vessel tension. It is mainly recommended to be used together with a 0.1 percent solution of adrenaline hydrochloride.

Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed



When the dose is exceeded, poisoning occurs and drowsiness, visual disturbances, nausea, tremors, convulsions appear. In severe cases, cardiovascular disorders and shortness of breath may occur.

Unlike other drugs, lidocaine has high efficiency in ventricular arrhythmias.

Trimecain is a drug similar to lidocaine in terms of its chemical structure.

it is also widely used in all types of anesthesia. Its activity is 2-3 times higher than novoka-in, and it is slightly more toxic. The duration of the effect is 2-4 hours. In surface anesthesia, its activity is lower, for this relatively high, 2-5 percent solutions are used. Trimecaine has a strong depressant effect on the cerebral cortex and the ascending reticular formation of the brain stem. That is why it has sedative, hypnotic and anticonvulsant effects. Antiarrhythmic effect occurs when the drug is administered intravenously.

It does not cause side effects from the cardiovascular and respiratory systems when taken in therapeutic doses in layered and conductive anesthesia. Sometimes, as a side effect, a burning sensation in the area where the drug is injected, nausea, vomiting, and clonic seizures may appear in poisonings.

It exhibits antiarrhythmic activity when exposed to the system. For this purpose, it is injected into a vein.

The effect of local painkillers increases under the influence of anesthetics, narcotic hypnotics, antipsychotics and opioid analgesics, and decreases when used in combination with MNS-stimulating agents (analeptics)[1,7,8,11,12].

Western European Journal of Medicine and Medical Science
Volume 2, Issue 1, January, 2024
https://westerneuropeanstudies.com/index.php/3
ISSN (E): 2942-1918 Open Access| Peer Reviewed

CONCLUSION: The effect of local analgesics increases under the influence of narcotic drugs, narcotic hypnotics, antipsychotics and opioid analgesics, and decreases when used in combination with MNS-stimulating agents (analeptics).

List of used literature

1. Харкевич, Д. А. Фармакология / Д. А. Харкевич, Е. Ю. Лемина, В. П. Фисенко, О. Н. Чиченков, В. В. Чурюканов, В. А. Шорр; под ред. Д. А. Харкевича - Москва: ГЭОТАРМедиа, 2014. - 512 с. - ISBN 978-5-9704-2616-6. - URL :https://www.rosmedlib.ru/book/ISBN9785970426166.html (дата обращения: 08.09.2021). - Текст : электронный
2. Skidmore R. A., Patterson J. D., Tomsick R. S. Local anesthetics //Dermatologic surgery. – 1996. – Т. 22. – №. 6. – С. 511-522.
3. Shah J., Votta-Velis E. G., Borgeat A. New local anesthetics //Best Practice & Research Clinical Anaesthesiology. – 2018. – Т. 32. – №. 2. – С. 179-185.
4. Catterall W. A., Mackie K. Local anesthetics //Goodman and Gilman's the pharmacological basis of therapeutics. 11th ed. New York: McGraw-Hill. – 2006. – С. 369-386.
5. Garcia E. R. Local anesthetics //Veterinary Anesthesia and Analgesia, The Fifth Edition of Lumb and Jones. John Wiley & Sons, Inc., Pondicherry, India. – 2015. – С. 332-354.
6. Suzuki S., Gerner P., Lirk P. Local anesthetics //Pharmacology and Physiology for Anesthesia. – Elsevier, 2019. – С. 390-411.
7. Tetzlaff J. E. The pharmacology of local anesthetics //Anesthesiology Clinics of North America. – 2000. – Т. 18. – №. 2. – С. 217-233.
8. Hirschfelder A. D., Bieter R. N. Local anesthetics //Physiological Reviews. – 1932. – Т. 12. – №. 2. – С. 190-282.
9. Golembiewski J. Local anesthetics //Journal of PeriAnesthesia Nursing. – 2013. – Т. 28. – №. 6. – С. 409-412.
10. Tetzlaff J. E. The pharmacology of local anesthetics //Anesthesiology Clinics of North America. – 2000. – Т. 18. – №. 2. – С. 217-233.
11. Butterworth J. F. et al. Clinical pharmacology of local anesthetics //Neural Blockade in Clinical Anaesthesia and Pain Management, 4th Edition. Philadelphia: Wolters Kluwer/Lippincott Wilkins & Williams. – 2009. – С. 96-113.
12. Миронов С. Е. и др. β 3-адренорецепторы–новая мишень лекарственной терапии //Экспериментальная и клиническая фармакология. – 2023. – Т. 86. – №. 8. – С. 29-39.