# Розділ 6
# ВЕТЕРИНАРНО-САНІТАРНА ЕКСПЕРТИЗА, ГІГІЄНА, ЯКІСТЬ І БЕЗПЕЧНІСТЬ ПРОДУКЦІЇ ТВАРИННИЦТВА

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## APPLICATION OF NEW GENERATIONS ANTIBIOTICS (FLOURCHINOLONES) IN TREATING OF ANIMALS

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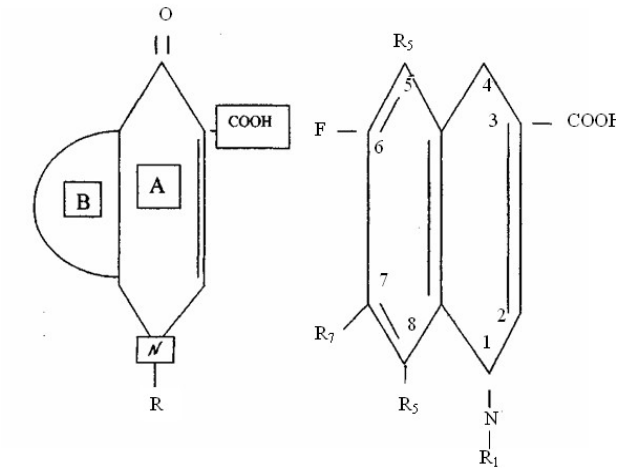
***Summary.*** *On the basis of analysis of professional reports general description of antibiotics of new generation of flourchinolones is presented in domestic and foreign literature.The flourchinolons take main positions in the rank of modern antibacterial means after their qualities, they have unique action mechanism for antimicrobic means – the inhibition of bacterial cells. Flourchinoones antibiotics can be used with another antimicrobical preparation, antibiotics of macrolipid and lincozamid groups. Bacterial activity of flourchinolones rises after complex using them with preparation of aminoglicosydes. Flourchinolones are long-term antibiotics in veterinary medicines during the treatment of animals after bacterial infection.*

***Key words:*** *antibiotics, pharmacology, animals, pharmacokinetics, therapy antibacterial, bacterial cell, flourchilines.*

Antibiotics are very useful in agriculture: as medicines for farm animals: poultry, bees, and plants. When wide using of antibiotics as medicines the microorganisms that are resistant for that preparations appear [6]. The problem of resistance needs more careful study of that question and preparing new and new antibiotics. We have to change one antibiotic with another for struggle with resistant microorganisms.

Last year the antibiotics of flourchinolones group are not used considerably in veterinary medicine because of poor information about scientific researches. Flourchinolones are chemotherapists with general new mechanism of antimicrobial action. They are highly active synthetic chemotherapeutical medicines of wide spectrum of action that are characterized with good pharmaceutical qualities high level of penetration into the tissues and cells. [7].

The history of beginning and evolution of flourchinolones is very interesting. The first flourchinolones was obtained during the process of purification of chloroquine phosphate – the substance with antimalar qualities [3, 11]. It was nalidixic acid.




**Pic. Chemical structure of flourchinolones.**

In principle new compounds were received by introduction the atom of flour into the sixth position of chinolin molecule. The presence of flour atom (one or some) and different groups in different positions marks peculiarities of antimicrobials activity and pharmacokinetic action of medicines [10]. The preparation of flourchinolons group are used in clinical practice in medicine since 80's.

The flourchinolons take main positions in the rank of modern antibacterial means after their qualities [8, 9]: they have unique action mechanism for antimicrobic means – the inhibition of bacterial cells enzyme-DNA-hydras; high level of antibacterial activity; wide spectrum of antimicribic action with Gram-negative and Gram-positive aerobe bacteria (some preparations of flourchinolones are active to anaerobes), Mycobacterium, Chlamydia, Mycoplasma; they have low resistance rate of microorganism to flourchinolones; they high bio penetrating when using inside; they have high penetrating degree into tissues and cells of microorganisms; they have long period of discharge and have postantibiotic effect and because can be used 1 or 2 times per day; they can be used together with another antibacterial preparations 9beta-lactamamys, aminoglycosides, macrolipides, glycopeptides, lincosamides, nitroimidazoles); we proved high efficiency in control clinical researches during the treatment of hospital and out hospital infections of every localization; they can be used for empirical therapy including monotherapy; the medicine has good bearing and low rate of side effects.

There are many classification and chinolones are included into them. One of the main classifications was offered by Quintillion R. (1999) [15, 16]. The classification singles out 4 generations of chinolones; the I (that doesn't fluoridate) chinolones and the II,III,IV- tree generation of chinolones (flourchinolones), that perform fluoridation, among them there are the II generation, - "Gram-negative", the III - "Gram-positive" and the IV- "respiratory" + "antianaerobic" flourchinolones.

The floutchinolones are divided into monofluoridated, diflouridated and triflouridated compounds.

The spectrum of antimicrobic action of flourchinolones includes aerobe and anaerobe bacteria, Mycobacterium, Chlamydia, Mycoplasma, Rickettsia,Borelia and some simple.

Flourchinolones have natural activity to Gram-negative bacteria from families Enterobacteriaceae (Citrobacter, Enterobacter, Escherichiacoli, Klebsiella, Proteus, Providencia, Salmonella, Shigella, Yersinia), Neisseriae (Gonorrhoeae, Meningitides), Haemophilus and Moraxella, they are rather active to Mycoplasma and Chlamydia and show also low activity to nonfermenting Gram-negative bacteria, Gram-positive cocci, micobacteria and anaerobes [12]. Different flourchinolones have different actions as with various groups as with individual species of microbes Flourchinolones II aren't very sensitive to the most streptococci (especially pneumococci), Enterococci, Chlamidia, Mycoplasma. They don't act on Spirochaeta, Listeria and the most anaerobea.

In comparison with the II generation on pneumococci and atypical organism (Chlamidia, Mycoplasma).

Flourchinolones IV are the best in antipneumococci activity and atypical organism according to the previous generation.

All flourchinolones have high level of penetrating into microbial cell, where they choicely oppress the activity of vitally important ferment of microbical cell. The opposite action of superspiralization of DNA Fila is changed after tear up and nest the stitch and restore of DNA structure for replication will be accompical with the development of bactericidal action.

The mechanism of antimicrobial action of flourchinolones is that can oppress the DNA-hydrasa of bacterial cell [1,4] . As a result the ferment activity is broken and superspirilization of chromosome is impossible. It result the breach division, bacteriostasis and the cells death, so the antibacterial action occurs. Hyrasa is absent in mammalian cell and because flourchnolones don't make toxic action on animal body. The availability of flour on chonolon ring in the sixth position and pipereselinum in the eight position provide bacterial action according to Gram-positive and Gram-negative bacteria and radical of cyclopropanole in the first position occurs the death of Pseudomonad, Mycoplasma and Chlamidia.

After breaching with flourchinolones reapplication of DNA, the death of microorganisms depends on some complicated processes that take place in microbial cell. They include the breaching of protein synthesis which defend the cell against preparation on the firth steps. The breaching of cell dividing is the next and then the forming of filamentary forms (in relating to stab neutrophile bacteria) or large changed round forms (in Cocci), Ander such conditions the big morphologic changes occur in the cell and they are incompatible with vital activity of bacterium.

In the mechanism of antimicrobial action its necessary to pay attention also the breaching of structure of microbical cell membrane, and as a result the adhesive features of bacterium are lower, synthesis of exotoxin and exoenzyme is oppressed, virulence of bacteria become lower.

Postanabiotic action of flourchinolones has essential meaning and its length depend on microorganism species and the concentration of preparation. As a result flourchinolons rise sensitivity microorganism to phagocytosis. Pointed ephects of antimicrobical action of flourchinolones make then better according to antibiotics of another groups. Penetrating of flourchinolons into bacterial cell is made through outward membrane of bacterium. The degree of accumulating in the cell depends on microorganism species and because the indicator of preparation penetration can be different in different bacteria. The process of taking out the flourchinolones from the bacterial cell in done by proteins, the carrier. [2,13].

Flourchinolones has high biological access. The preparations have poor absorption in sour stomach medium after peroral introduction, but in the alkaline medium of duodenum only 80-90-100 % of ofloxacinum, enrofloxacinum, lomefloxacinum, pefloxacinum are absorbed. Cyprofloxacinum is absorbed on 60-70% and norfloxacinum – 35-40 %. Adult ruminants intestines can absorb 10 to 35% of the preparation dose [14]. Its important to say that salt of aluminium, magnesium, and calcium in milk make chelates complexes with carboxylium group of flourchinolones, and because resorption of intestinal preparation become lower. It doesn't mater how was preparation of flourchinolones introduced into blood, but in 1 or 2 hours the theurapeutical concentration is prepared and works for 24 hours [13].

Flourchinolones have amphoteric characteristics. They dissolved in water poorly and are not connected with proteins and because are introduced into tissues quickly and high rate of lipidofiles provide their accumulating in liver and kidneys. Entrofloxacinum makes up quickly bacterial concentration in out cellular liquide, it penetrates easily into biological barriers and also hematoencefalic and pacental.

Farmocinetical properties of flourchinolones are characterized by good biological access, bad connecting with blood proteins, long period of taking out from a body, low biotransformation.

Flourchinolones are absorbed quickly from stomach monohastrical animals and in a less amount from ruminant. Calves have biological access of ofloxacynum 80-100 %. During peroral taking of the preparation to cans only 10% of it absorbs. [12].

The intensity of ofloxacynum absorbtion from animal's canal reduces on 30% after using gydrooxidation of aluminium and magnesium and after simultaneous using of iron preparation.

After peroral taking of preparations and hypodermic and intramuscular injections the biological access of ofloxacynum in rabbits consist 61 %, 77 % and 92%.

Maximum concentration of flourchinolones in blood after peroral introduction is making, in 1-3 hours. High concentration in blood is quickly made by cyproflaxynum, perfloxacynum and ofloxacynum are absorbed slowly. In blood they make not high but sufficient concentration for antimicrobical action.

After resorption flourchinolones connect with blood proteins serum only to 40%. Only rufloxacynum is connected with proteins for 60%. Because, according to another antibiotics, they show faint action but it has longer antibacterial action.

Flourchinolones make up bacterical concentration quickly in blood of monohastrical animals with compound stomach. They are introduced into organs and tissues and make up the concentration like in blood but sometimes higher. The introducing of body is done by passive diffusion through the walls of capillaries [12, 17]. Active transportation of flourchinolones is only in kindneys. High rate of diffusion of flourchinolones in tissues is due to lipophilia and some connection them with proteins of blood serum.

Important factor of farmacological properties of flourchinolones group antibiotics is wide absorbtion them into tissues, their easily introduction them through bacterial barrier making high concentration in out cellular liquid and cells cytoplasm. Oflaxacyn in cells make up higher concentration than out cellular liquid that shows a preference for incellular bacteria localization.

Flourchinolones yield metabolism in body partly. They yield to biotransformation only for 6% of taken preparation. It provides long being of preparation in active forming organs and tissues after prescribing therapeutical doses. Some authors say that flourchinolones are yielded to metabolism in bigger amounts. The transformation of flourchinolones molecule is done through carboxyl group and piperazin radical. Pefloxacin is under biotransformation in the biggest amounts. Another flourchinolones are yielded to metabolism from 20 to 30% from taken amount secreted from body in a form of metabolities.

Ofloxynum, lomfaxacynum and temafloxynum yield metabolism less then 10%. Metabolites of antibiotics show low antimicrobic activity.

Flourchinolones are secreted from body slowly. The time of semisecretion of oflaxycinum after peroral introduction for pigs and calves is 7-21 hours, for chickens – 15-19 hours. Slow secretion of flourchinolones from organism gives an opportunity to take them 1-2 times a day. Diflourchinolones have long period of secretion: fleroxacin has 20 hours and rufloxacin has 36 hours.

After peroral introduction 3-4 % of ofloxacynum, fleroxacynum and temafloxacynum are secreted with feces and also 15-20%of norfloxacynum, ciprofloxacynum. [10].

Pharmocinetic of flourchinolones in animal's bodies depends on functional state of kidneys and liver. As liver is the main organ where biotransformations of flourchinolones take place, after functional disorder of liver the Pharmocinetic of oflaxycinum, temafloxacynum, ciprofloxycinum and lomefloxycinum don't change, metabolism in animals in animals body during heparitis.

After low function of kidneys the secretion of ciclofloxacynum and its metabolits became slow. Oflaxacynum secret through kedneys completely in immutable form, because the function of kidneys in secretion of this preparation is too important. If we have disorder of secretion functions of kidneys the length of norfloxacynum action in body becomes longer [5, 9].

The activity of flourchinolones reduce when we use iones of iron, zinc, aluminium and magnesium and chilates complexes are made up. Most flourchinolones show higher antimicrobical activity in alkaline medium [7]. They reduce their activity in sour medium that deal with physical – chemical properties of chinolones compounds. But in practice the activity of flourchinolones remains high when using them in treatment of uresis canals in carnivorous in acid reaction of urine.

Flourchinoones antibiotics can be used with another antimicrobical preparation, antibiotics of macrolipid and lincozamid groups. Bacterial activity of flourchinolones rises after complex using them with preparation of aminoglicosydes. The time of maximum bacterical effect reduce.

In Ukraine 22 preparation of flourchinolones groups are registered and used in veterinary medicine. Among them widely used are enroxyl, enroflox and ofloxacinum. For treatment after bacterial lesion of animal and poultry flourchinolones are takes as an alternative to another antibiotics. Important feature of flourchinolones is their activity to microorganism strains and their persistent to antibacterial preparation.

As many authors say bronchopneumonia in calves takes the second place after the diseases of digestive tract. As bronchopneumonia in calves bring great economical losses and medicines don't supply therapeutical effect, because we have real problem with study of pharmacological action of antibiotics of flourchinolones group on the activity of antioxidation system of calves bodies under catarrhal bronchopneumonia.

So, flourchinolones are long-term antibiotics in veterinary medicines during the treatment of animals after bacterial infection. For wide using antibiotics of flourchinolones group in veterinary medicine, we have to study cumulation, toxicity, accessory action, treatment efficience and influence upon antioxidation defence of body during different bacterial infection in calves. This problem will be studied in our future researches.

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## ЗАСТОСУВАННЯ НОВИХ ПОКОЛІНЬ АНТИБІОТИКІВ (ФЛОРХІНОЛОНІВ) У ЛІКУВАННІ ТВАРИН

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Анотація. На основі аналізу професійних звітів загальний опис антибіотиків нового покоління флорхінолонів представлений у вітчизняній та зарубіжній літературі. Флорхінолони приймають основні позиції в ранзі сучасних антибактеріальних засобів за своїми якостями, вони мають унікальний механізм дії для антимікробних засобів - інгібування бактеріальних клітин. Флорхінолони як антибіотики можуть бути використані з іншим протимікробними препаратами, антибіотиками. Бактеріальна діяльність флорхінолонів піднімається після комплексного використання їх у підготовці з аміноглікозидами. Флорхінолони - довгострокові антибіотики в ветеринарії при лікуванні тварин після бактеріальної інфекції.

Ключові слова: антибіотики, фармакологія, тварини, фармакокінетика, антибактеріальна терапія, бактеріальна клітина, флорхінолони.

## ПРИМЕНЕНИЕ НОВЫХ ПОКОЛЕНИЙ антибиотики (FLOURCHINOLONES) В ЛЕЧЕНИИ ЖИВОТНЫХ

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Аннотация. На основе анализа профессиональных отчетов общее описание антибиотиков нового поколения флорхинолонив представлен в отечественной и зарубежной литературе. Флорхинолоны принимают основные позиции в ранге современных антибактериальных средств по своим качествам, они имеют уникальный механизм действия для антимикробных средств - ингибирование бактериальных клеток. Флорхинолоны как антибиотики могут быть использованы с другим противомикробными препаратами, антибиотиками. Бактериальная деятельность флорхинолонив поднимается после комплексного использования в подготовке с аминогликозидами. Флорхинолоны - долгосрочные антибиотики в ветеринарии при лечении животных после бактериальной инфекции.

Ключевые слова: антибиотики, фармакология, животные, фармакокинетика, антибактериальная терапия, бактериальная клетка, флорхинолоны.