

RESEARCH ARTICLE

The effect of Sclerosing drugs on the *Tunica albuginea* (Experimental study)

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ABSTRACT:

Background: The relevance of the stated research subject is determined by the need to conduct an experimental study of the effects of various dosages of sclerosing drugs, such as aethoxysklerol, kanamycin, 70% ethyl alcohol on the general condition of the tissues of the *Tunica albuginea*. The main purpose of this research is to analyse the degree of influence exerted by sclerosing drugs on the *Tunica albuginea* when conducting studies using rabbits, as the only laboratory rodents with which it is possible to obtain recombinant pharmaceutical proteins, conduct oral studies, or inject dosage forms into the stomach without violating the integrity of the tablets. **Materials and Methods:** The leading approach in this research is a practical study performed on 19 rabbits aged 7-8 months, with their division according to the principle of analogues into several main groups (three rabbits in each of them and one rabbit separately) with the introduction of the experimental data obtained in special tables. **Results:** The results obtained in this research indicate that there are considerable prospects for studying the effect of sclerosing drugs on the *Tunica albuginea*, from the standpoint of the practical application of the data obtained during the experiment for the treatment of a number of serious diseases in stationary conditions. **Conclusion:** The study results and the conclusions formulated on their basis have a practical value from the standpoint of obtaining the necessary evidence of the safety of advanced sclerotherapy, which is: improvement of hemodynamic parameters of the testicular parenchyma, the complete absence of structural changes in its tissues and the epididymis in conditions of preserving the full course of spermatogenesis.

KEYWORDS: Sclerotherapy, Aethoxysklerol, Kanamycin, Ethyl Alcohol 70%, Sclerosing Drugs, *Tunica albuginea*.

INTRODUCTION:

In various areas of modern biology and experimental medicine, sclerosing drugs are widely used, the main conditions for the use of which should be considered: their sensitivity to specific biological and physical factors, predisposition to storage conditions, availability, and relatively low price¹⁻².

To determine the ultimate effectiveness of the practical use of sclerosing drugs and to establish their toxicity, their various dosages were selected, which were conditionally divided into two main groups. Therewith, rabbits were used as the most common model objects. Rabbits are typical biological models for the study of the characteristic features of drugs (in particular: toxicity, pharmacokinetics) and for the development of certain models of pathologies of humans and some animals, both received at birth and acquired. In addition, rabbits are actively used for the development and research of a number of new surgical

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methods, physiological tests, and for the study of various types of toxicity for drug testing^{3,4}.

As objects of modelling the determination of the mechanism of action of aethoxysklerol, kanamycin, 70% ethyl alcohol on the *Tunica albuginea*, 19 rabbits were adopted, white Californian breeds, weighing 3-3.5kg at the age of 7-8 months. To avoid the painfulness of procedures performed with animals, all experiments complied with the "rules for the conduct of animal experiments". Furthermore, each animal was subjected to a general examination to detect visible changes in the skin, the condition of the mucous membranes, and to detect visible damage of any kind^{5,6}. For anaesthesia of rabbits, the rometar was used, which was administered intramuscularly at the prescribed dosage of 4.0-6.0 mg/kg, then, after 20 minutes, anaesthesia was performed by intramuscular administration of zoletil-50 at the prescribed dosage of 5-10mg/kg. The established combination of drugs allows obtaining stable and sufficient analgesia and relaxation for half an hour. To date, the problem of the occurrence and development of hydrocele disease (accumulation of fluid around a testicle within the scrotum causing swelling) in children from 2-18 years old, mainly under the age of 10 years inclusive, remains highly relevant, which is explained by the wide spread of this disease and the lack of a clear opinion on the choice of treatment tactics. These circumstances explain the increased interest in this subject among a large number of researchers who conducted scientific developments in this area.

Therewith, qualitative checks of the toxic effect on the testicular membranes and the development of the spermatogenesis (the process of sperm cell production and development within the male reproductive system) process were not performed⁷. The choice of rabbits of this breed is explained by the desire to study the toxic effect of sclerosing drugs used in various dosages to effectively determine the degree of influence on the cells of the vaginal layer of the scrotum. During the experiment, aethoxysklerol, kanamycin, 70% ethyl alcohol were injected into the scrotum of rabbits. Despite the seeming "harmlessness", hydrocele is often expressed as a cosmetic defect, can be manifested by discomfort during movements, urination, and sexual intercourse, is also associated with painful sensation, which considerably worsens the life of patients. Strained hydrocele associated with impaired blood supply to the testicle can cause severe pain, which may cause an urgent need for a revision of the scrotum^{8,9}. An important circumstance is a violation of the blood supply to the testicle and lymph flow due to hydrocele, which, negatively affecting the secretory function of the testicles, in 20-30% of cases causes changes in the ejaculate and the development of serious structural

disorders in the testicular tissues. Therewith, it is believed that hydrocele, in combination with other factors, creates conditions for the development of a predisposition to malignant tumours on the testicle¹⁰. In the last few years, a large amount of information has appeared regarding the manifestations of the abdominoscrotal form of hydrocele (a type of hydrocele with fluid extending from the abdomen into the scrotum through an open passage between the two anatomical regions), which has attracted close attention due to the prospect of the development of numerous complications¹¹. Rare complications of hydrocele are also real, in particular, testicular rupture due to traumatic effects.

The aim of this study is to investigate the effects of sclerosing agents on the testicular corpus callosum using a rabbit model. Some research objectives include:

- Compare the effects of various types and dosages of sclerosing drugs on testicular membrane integrity during an extended study period. This study primarily examined short-lived edema effects within 17 days of injection. Prolonged analyses can indicate whether particular routines cause late-onset testicular damage.
- Investigate the fertility and successful pregnancy rates after administering the most effective aethoxysklerol sclerotherapy methods. This would offer clinical proof of maintained reproductive capacity, rather than solely sperm production.
- Determine the most effective method for delivering aethoxysklerol into the *tunica albuginea* using novel vehicles and sustained release. This could enhance the safety profile of the therapy by increasing its precision while maintaining efficacy.
- Expand the trials to further established human hydrocele models, such as rats and dogs, in addition to the current usage of rabbits. This approach considers potential anatomical and physiological discrepancies between species.
- Investigate the effects of blending aethoxysklerol at 0.2 mL with other benign sclerotherapy agents like tetracycline. Find the optimal proportion of the mixture to achieve maximum hydrocele closure while maintaining patient health standards.

MATERIALS AND METHODS:

The basis of the methodological approach in this research is an experimental study involving 19 rabbits aged 7-8 months, divided into four groups according to the principle of analogy (three rabbits in each of them and one rabbit separately). Rabbits were selected as animal models for this experiment for several critical reasons:

1. Rabbits are commonly used as biological models to study drug effects and toxicity. Additionally, they

can be utilized to produce recombinant pharmaceutical proteins, undertake oral studies, or administer injections without harming the integrity of tablets.

2. Rabbits also possess resilient health and docile temperaments, rendering them ideal for biomedical research conditions. The document states that the White Californian breed was specifically chosen for its uniformity in age and weight, thereby enabling consistent experimental results.
3. The study was focused on investigating the effects of sclerosing drugs on testicular membranes and spermatogenesis. Rabbits were a suitable choice for the study since they are the only laboratory rodents that allow for the examination of a complete course of spermatogenesis after drug administration.
4. The rabbits selected were aged between 7 and 8 months and weighed between 3 and 3.5 kg. The uniformity of age and weight amongst subjects was aimed at minimizing the variability of the results.
5. In brief, White Californian rabbits of similar age and weight were selected as commonly utilized disease and drug models, allowing for specialized testing of pharmaceutical proteins, oral drug administrations, and monitoring of reproductive effects such as spermatogenesis. Their consistent health and temperament also make them excellent candidates for precise biomedical research.

All procedures performed using animals were revised and approved by the Scientific Committee of Ethics of the Khoja AkhmetYassawi International Kazakh-Turkish University, Republic of Kazakhstan. Authorization N° 10–31. For premedication, rabbits from the first group were injected with 0.2ml of aethoxysklerol into the scrotum to a depth of 1.0-1.5cm. Rabbits from the second group were injected with 500 mg of kanamycin into the scrotum to a depth of 1.0-1.5 cm. Rabbits from the third group were injected with 0.5 ml of 70% ethyl alcohol into the scrotum to a depth of 1.0-1.5cm. Rabbits from the fourth group were injected with 0.3ml of aethoxysklerol into the scrotum to a depth of 1.0-1.5cm. The theoretical basis of this study was the research of numerous national and foreign authors devoted to the influence of sclerosing drugs on the *Tunica albuginea*, including a number of issues related to the stated research subject. To ensure a full perception of the information provided and to create a qualitative picture of research, all the developments of foreign authors, taken for the citation and presented in this study, have been translated into English.

To observe the general condition of the experimental rabbits divided into four groups, they were constantly monitored for one experimental week. During the observations, no pathological changes were detected in

rabbits. An additional study was performed on nine rabbits aged 7-8 months, which were previously divided into three groups according to the principle of analogues (3 rabbits in a separate group). During this scientific experiment, the following drugs were used:

1. Aethoxysklerol – 0.2ml.
2. Ethyl alcohol 70% – 0.5ml.
3. Kanamycin 500mg.
4. Hematoxylin-eosin staining increase – 100 (10x10).

Based on the results of the experiments, tables containing the main experimental data were compiled. The tables consistently reflect the division of experimental rabbits into specific groups, the name of the drug, and their dosage. In addition, the overall picture of research is supplemented with drawings showing the sequence of research and photographs of the drugs used at the time of their application. The sequence of the description of the experimental procedure is also preserved, indicating the operations performed and all the results obtained during the study. At the final stage, based on the results obtained, final conclusions were formulated, acting as a logical reflection of these results and summarising the final results of the entire complex of research activity performed. The results of this experimental work and the conclusions formulated on their grounds can subsequently serve as a qualitative theoretical basis for further research on the issues of the effect of sclerosing drugs on the *Tunica albuginea*, which in general will contribute to creating the necessary conditions for preventing the development of diseases of the genitourinary system of varying severity.

RESULTS:

The study of the effect of sclerosing drugs on the *Tunica albuginea* led to the following results. The rabbits taken for the experiment were divided into several main groups according to the principle of analogy. Table 1 presents data on the selected division of 19 experimental rabbits into groups and indicates the drugs used during the experiment and the dosage.

Table 1: Distribution of 19 experimental rabbits into groups based on drug type and dosage used

Groups	Number of rabbits in a group	Drug	Dosage
1	3	Aethoxysklerol	0.2ml
2	3	Kanamycin	500mg
3	3	Ethyl alcohol 70%	0.5ml
4	1	Aethoxysklerol	0.3ml

Source: Compiled by the authors.

Figure 1 illustrates a critical phase in the experimental procedure, demonstrating the administration of an ethanol solution as an injectable drug directly into the rabbit's scrotum. This step is imperative in studying the effects of sclerosing agents on testicular tissue with the objective of developing innovative treatments. The

meticulous administration guarantees precise dosing and minimal discomfort to the animal subject.

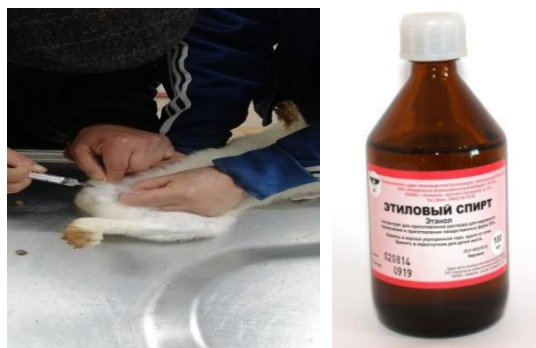


Fig. 1: The drug utilized in the experiment and its injection into the scrotal sac

Source: Compiled by the authors.

During the experiment, the rabbits were divided into four groups, the number of which is shown in Table 1, after which the groups were monitored for one week. Therewith, no pathological changes were noted in rabbits. Then, a second examination was performed, in which nine rabbits were involved, divided according to the principle of analogy. In each of the groups there were three animals aged 7-8 months. Rabbits from the first group were injected with 0.5ml of aethoxysklerol into the scrotum to a depth of 1.0-1.5cm. Rabbits from the second group were injected with 500mg of kanamycin into the scrotum to a depth of 1.0-1.5cm. Rabbits from the third group were injected with 1.0ml of 70% ethyl alcohol into the scrotum to a depth of 1.0-1.5 cm. During the experiment, after the administration of these drugs, the animals were monitored for ten days. No pathological changes were detected in rabbits during the observations. The results of this phase of the experiment are presented in Table 2.

Table 2: Examination results: nine rabbits grouped by drug type and dosage.

Groups	Number of rabbits in a group	Medication	Dosage
1	3	Aethoxysklerol	0.5ml
2	3	Kanamycin	500mg
3	3	Ethyl alcohol 70%	1.0ml

Source: Compiled by the authors.

After the experimental rabbits were injected with these drugs, a 17-day control was established for the animals. Observations have shown that rabbits have correct posture, eat well, and the examination did not reveal any leakage of fluids from their openings. The skin of rabbits was shiny, no pathologies were found on it. The genitals do not have any deformities. During the examination of the scrotum of rabbits divided into four experimental groups, slightly noticeable edema and infiltration in the tissues of the scrotum of rabbits of the first and second groups were observed that completely disappeared within a week; in the scrotum of rabbits of

the third and fourth groups, edema and infiltration were not observed. No harmful effects on testicular tissues were noted. At the end of the 17-day period, the experimental rabbits, which were conditionally divided into four and additionally into three groups, had their testicles removed, which were subsequently placed in a 10% formalin solution. All the requirements of antiseptics during the performance of this surgical operation were met. The moment of removing the testicles and placing them in a formalin solution is shown in Figure 2.



Fig. 2: The removal of the testicles and their placement in a formalin solution

Source: Compiled by the authors.

All the materials prepared for the experimental study were brought for histological, morphological examination to the children's anatomic pathology department of the state municipal enterprise under the right of operational control of the regional pathological anatomical bureau of the health department of the Turkistan region. In histological preparations No.1-9, the structures of testicular tissue, protein membranes, adipose tissue, and connective tissue membranes were presented. The structures of straight, convoluted, efferent tubules with signs of spermatogenesis do not have signs of interstitial tissue edema and various changes associated with the course of inflammatory processes. In histological preparation No. 10, the tissue structures of the right and left testicles of rabbits with an injection site of aethoxysklerol were presented. The tissues of the serous membrane, mesothelium, and *Tunica albuginea* were represented by dense fibrous connective tissue, which had no signs of sclerotic changes. The process of spermatogenesis was preserved. No pathological changes were observed in this case. The results of the experiment are presented in Figures 3-5.

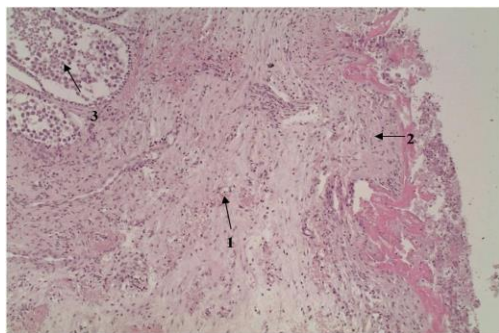


Figure 3: Tissue of an intact rabbit testicle

Note: 1 – Seminiferous tubules; 2 – Seminiferous epithelium; 3 – seminiferous tubules (H&E staining increase of 100).

Source: Compiled by the authors.

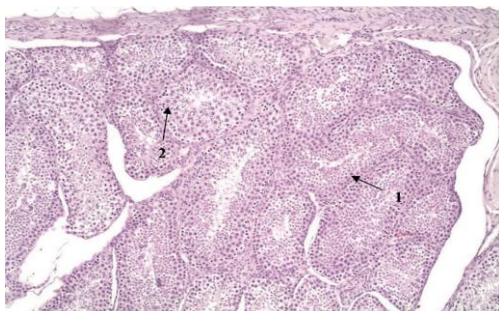


Fig. 4: Rabbit testicle tissue seven days after the administration of aethoxysklerol

Note: 1 – Granulation tissue; 2 – Junction zone.

Source: Compiled by the authors.

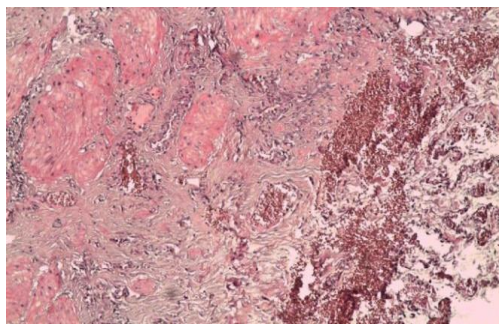


Figure 5: Rabbit testicle tissue ten days after the administration of aethoxysklerol

Note: Connective tissue edema, slight focal lymphoid inflammatory infiltration of a mild course with an admixture of single leukocytes.

Source: Compiled by the authors.

Displayed in Figure 6 is a group of White Californian rabbits, each aged between 7 to 8 months and weighing approximately 3 to 3.5 kilograms, housed within a research enclosure. These rabbits are part of a controlled experimental study, selected for their uniformity in age and weight to ensure consistent results. The facility has been purpose-built to replicate a comfortable and standardized habitat, providing an accurate view of the behavioural and physiological responses of White Californian subjects in experimental conditions. This breed is commonly favoured for their resilient health and docile nature in the context of biomedical research.



Fig. 6: White Californian rabbits in a controlled experiment setting

Source: Compiled by the authors.

Currently, the most common methods of surgical treatment of hydrocele are considered to be open operations performed by means of an incision on the scrotum. The urgency of this problem and the need for its practical resolution are undoubtful since in a number of states the percentage of hydrocele diseases among the male adult population reaches 33-35% and continues to grow steadily¹². The situation is complicated by the fact that the most private consequences of such operations are severe edema, combined with infiltration of the scrotum, the duration of which reaches one month or more. In addition, operations of this kind are very dangerous due to the possibility of injury, can cause complications such as hematomas, bleeding, swelling of the scrotum of varying severity, wound abscess, lymphostasis, postoperative epididymitis and orchitis, in some cases there is a risk of occurrence and development of relapses¹³. All such complications considerably increase the total time of incapacity and the duration of the patient's stay in a hospital-type institution. Lord's surgery, which, unlike Bergman and Winkelman's surgery, does not involve the excision of the hydrocele sac from the surrounding tissues, allows reducing the wound surface and almost completely eliminating damage to blood and lymph vessels, lowering the possible percentage of postoperative complications¹⁴.

Unsatisfactory consequences of the conventional type of surgery, coupled with great difficulties in choosing the method of performing the operation in the presence of concomitant diseases in patients and a necessity to operate on elderly patients allowed the use of not only scroscopic and video endoscopic operations, but also laser and radio wave scalpels¹⁵. One of the minimally invasive methods is sclerotherapy, since, according to the literature, the practical use of a sclerosing agent is completely safe. The mechanism of sclerotherapy is similar to the wide use of sclerosants and is directly related to the stimulation of an inflammatory cellular reaction by a foreign substance, which leads to the adhesion of the sheets of the vaginal membrane¹⁶. Aethoxysklerol, kanamycin, and 70% ethyl alcohol have

shown particular effectiveness as the main sclerosing drugs. It has been experimentally established that sclerosants virtually do not cause severe pain, necrosis, and inflammation of the testicular scrotum tissues, in addition, drugs of this kind are not of considerable toxicity. It should also be considered that in young people, reproductive function remains an important circumstance after the administration of sclerosant.

In summary, the experiments using a rabbit model indicate that low doses of aethoxysklerol sclerotherapy is the most safe and effective treatment for hydrocele. Injecting 0.2 mL of aethoxysklerol into the *Tunica albuginea* only caused minor and temporary edema that resolved within a week. This treatment did not have any discernible effects on the health of testicular tissue or the progression of spermatogenesis. In contrast, administering larger volumes of aethoxysklerol (0.5 mL) combined with 70% ethyl alcohol (1 mL) triggered more significant inflammation and adverse effects on the testicular membranes, which persisted for ten days. Kanamycin, on the other hand, did not lead to any tissue abnormalities. However, considering the lower risk of side effects with aethoxysklerol at 0.2 mL, it appears to offer the benefits of sclerotherapy with fewer chances of complications.

DISCUSSION:

Exposure of cells to helium plasma for one-minute leads to a notable decrease in enzymatic activity. A considerable decrease in the activity of acid phosphatase (an enzyme found inside macrophages that plays a role in their bacterial killing capacity by promoting lysosomal digestion) of phagocytes at such exposure correlates with the previously obtained information regarding the suppression of intracellular digestion of bacteria by macrophages (process in which specialized immune cells called macrophages engulf and break down bacterial pathogens within digestive compartments inside the cell) under the considered conditions^{17, 18}. The positive effect of sclerotic drugs is often associated with their antimicrobial and anti-inflammatory effects, the ability to considerably reduce temperature and enhance tissue regeneration processes. Therewith, various aspects of the effect of such drugs on the body have not yet been fully disclosed. Mononuclear phagocytes are of considerable importance in the creation of high-quality antimicrobial protection to prevent the development and spread of various inflammations in the tissues of the body¹⁹. The consistent implementation of effector and regulatory functions of macrophages largely ensures their propensity to produce highly reactive oxygen metabolites capable of inducing chemiluminescence (light production from a biochemical reaction). Chemiluminescence should be considered the most sensitive and informative method of functional

assessment of phagocytic cells²⁰. The effect of helium plasma on peritoneal macrophages occurs against a constant change in the activity of acid phosphatase of the intercellular space, the area of which and the degree of its development is determined by the final exposures of irradiation of cells. The results obtained in the course of practical experiments should be considered when using helium plasma in clinical research practice. Such studies suggest irradiation of cells for a period of no more than half a minute, while stimulation of chemiluminescence of peritoneal macrophages takes place, which is the evidence of a considerable increase in the formation of active oxygen radicals by phagocytic cells under the influence of helium plasma under low temperature^{21, 22}. Irradiation of cells with helium plasma from one to three minutes consistently reduces chemiluminescence of abdominal macrophages, which is a reflection of a decrease in the rate of production of reactive oxygen metabolites by cells and is essentially a consequence of the cytotoxic effect of plasma flow on phagocytes under final exposure conditions²³.

The above testifies to the determination of the dependence on the exposure of the effect, whereas low-temperature helium plasma has the ability to stimulate and suppress the production of reactive oxygen species by macrophages, contributing to the modification of the existing bactericidal potential. The results obtained in such studies should be considered when using helium plasma in clinical trials. To date, hydrocele is common in 15-33% of adult men. This disease has an extremely negative effect on the overall quality of patients' lives since it can be expressed not only by a cosmetic defect but also cause discomfort during movement, urination, and a short duration of sexual intercourse²⁴. Therewith, hydrocele negatively affects the function of the testicles, disrupting blood supply and lymph outflow. It is generally believed that hydrocele may be a predisposing factor to the development of malignant tumours on the testicles²⁵. To date, the most effective methods of treating hydrocele are considered to be open operations, such as Bergman, Winkelmann, Lord ones, plasma coagulation of the tunica vaginalis, and minimally invasive–video-assisted excision of the testicular membranes, sclerotherapy²⁶. Surgical methods for solving the described problem have demonstrated high efficiency, combined with a considerable percentage of complications, such as epididymitis, orchoepididymitis, hematomas after surgery, and swelling of the scrotum tissues; the type of specific complication that occurred in a particular case is determined by the type of specific surgical intervention²⁷. The probability of complications during the operations of the above types ranges from 11 to 34% of the total number of cases of surgical intervention.

Sclerotherapy has proven to be highly effective in the treatment of hydrocele despite the minimal invasiveness. All available information regarding the practical use of minimally invasive methods of treating hydrocele of the scrotum (puncture and alcohol sclerotherapy) is a clear demonstration of the fact that as the volume of the hydrocele increases and in the case of recurrent hydrocele, the frequency of complications increases exponentially and the frequency of alcohol injection into the scrotum cavity also increases up to four times. When performing hydrocele diagnostics, it is mandatory to collect anamnesis, conduct a general medical inspection, diaphanoscopy, and ultrasound examination. The most considerable from a practical standpoint in the diagnosis of the disease in question should be a comprehensive ultrasound examination, which allows timely, quickly, efficiently, and completely safely obtaining the necessary information about the pathological changes taking place. In all cases where there is a real need for the diagnosis of hydrocele, the classification should be considered, which is extremely important in predicting the course of this disease and prescribing effective methods of its treatment²⁸. In this case, it is imperative to distinguish between congenital hydrocele, which can be communicating with the organs of the abdominal cavity or not having any communication with it, and acquired hydrocele. The latter type of this disease is divided into primary (idiopathic) and secondary (reactive, symptomatic), the cause of which can be traumatic effects, the development of tumours, infections, inflammatory diseases. In addition, the hydrocele can be conditionally divided into acute and chronic forms, as well as unilateral and bilateral.

During a superficial examination of the scrotum, some swelling was noted, which was pear-shaped and turned downwards. The swelling did not cause painful sensations, palpation revealed its smooth surface and dense, elastic consistency²⁹. The most striking, distinctive feature of diaphanoscopy should be considered the screening of swelling. Urologists have not yet come to a consensus on the choice of treatment for hydrocele. Despite the fact that minimally invasive techniques for the treatment of hydrocele have been successfully introduced into modern clinical practice a long time ago and that this practice has taken place almost all over the world, open surgical interventions are still used in numerous clinics, which are associated with a considerable risk of complications and relapses of this disease³⁰. The difficulties may occur when choosing a treatment method for elderly people. Among the wide variety of methods of treatment of hydrocele, characterised by relatively low traumatism, it is possible to distinguish video-assisted excision of the testicular membranes, as this method of treatment does not involve turning the testicle directly into the wound. The

implementation of this technique can take place with considerable volumes of a hydrocele sac. Pain after the surgical intervention is minor. The frequency of complications, the duration of the patient's stay in the hospital, and the timing of postoperative rehabilitation, in this case, are lower than when performing an open surgical intervention^{31,32}.

Sclerotherapy is a very common method of treating hydrocele³³. The mechanism of the occurrence and subsequent development of sclerotherapy is similar to the wide use of sclerosants and has a direct connection with the stimulation of an inflammatory cellular reaction by a foreign substance, which is one of the causes of the adhesion of the sheets of the vaginal membrane. Therewith, sclerosing substances can be tetracycline, betadine (polyvidone-iodine), polidocanol, sodium tetradecyl sulfate, ethanolamine, phenol, 70 to 96% ethyl alcohol. Therewith, the sclerosants used must meet a number of mandatory conditions: 1) do not cause severe pain; 2) do not be toxic; 3) do not contribute to the development of necrosis and inflammatory processes in the tissues of the scrotum. After a certain period of time post sclerotherapy, usually ranging from six to twelve hours, patients often experienced pain in the scrotum area, which was easily stopped. After hydrocele sclerotherapy, patients stayed in the clinic for an average of about three days³⁴. After hospital discharge, routine examination of patients should be carried out for a period of time from two to three weeks. With the development of relapses, it is necessary to perform an additional session of sclerotherapy. In the vast majority of the cases under consideration, patients recovered. In some patients, a long-term beneficial therapeutic effect was observed immediately after the first session of sclerotherapy³⁵.

Some patients require two sessions of sclerotherapy, and in some cases, patients required three sessions. The time interval between injections of tetracycline solution is approximately 3-5 weeks. According to a number of researchers, this time is required for the attenuation of inflammatory changes and the development of fibrosis. In the case of additional injections of sclerosant, patients stayed in the clinic for one day. Doctors advise carrying out sclerotherapy with tetracycline in cases where there are contraindications to the surgical treatment of hydrocele. Today, surgical methods are widely used to restore the patency of the vas deferens to obtain a natural pregnancy, in addition, methods of assisted reproductive technologies are being developed and implemented, involving the extraction of spermatozoa using testicular biopsy³⁶. The quality and validity of such operations, both in terms of the criterion for obtaining sperm in the ejaculate and in the frequency of pregnancy, differ considerably. Thus, according to the information provided by the American Urological

Association, the effectiveness of vasoepididymoanastomosis can reach 60-87%, vasovasostomy – 70-95%, transurethral resection – 50-75%, while the frequency of natural pregnancy is 20-40, 30-75, and 25% in each case.

A number of researchers give recommendations to perform hydrocele punctures using systems for catheterisation of veins located on the periphery. After the puncture of the hydrocele sac, the needle is released, and a plastic cannula is located in the cavity, through which the contents are removed and novocaine and sclerosant are injected³⁷. Researchers assume that the practical use of a plastic cannula instead of a needle allows avoiding damage to the organs of the scrotum during this procedure³⁸. Modern medicine preserves trends in the development of minimally invasive methods of hydrocele treatment, which are in no way inferior to conventional ones, and hydrocele sclerotherapy can rightfully be attributed to them. The method is accessible, safe, and effective. Therewith, it does not involve the risk of injury and nor does it harm the reproductive health of the patient, which allows maintaining working capacity, which is very important from the standpoint of the prospects for the treatment of men of almost any age.

CONCLUSIONS:

The conducted study of the features of the effect of sclerosing drugs on the *Tunica albuginea* led to the following conclusions. According to the results of the studies, based on the tested four options for performing sclerotherapy of the scrotum on experimental rabbits, the first and fourth options should be given the greatest preference, which involve the administration of aethoxysklerol into the *Tunica albuginea* in a dosage volume of 0.2 ml. In the course of the research, minor edema and infiltration of the soft tissues of the scrotum were removed, it took one week to eliminate these problems. In all probability, such problems occur due to blockage of the slotted opening of the vaginal abdominal membrane. With the administration of 0.5 ml of aethoxysklerol and 1.0 ml of 70% ethyl alcohol, edema and infiltration in addition to a local temperature increase take place for 7-10 days, while there is a negative effect on the testicular membranes, which is not acceptable in the treatment of patients. The administration of the drug leads to the destruction of proteins at the injection sites.

The destruction of the internal (endothelial) lining of the veins causes the narrowing of the blood vessel and its further occlusion with prolonged contact of the walls. Over time, at the site of the vein, which was subjected to sclerosing, only fibrous tissue remains in the form of a characteristic scar. A characteristic feature of the drug should be considered an almost complete blockage of

the transmission of nerve impulses from receptors. Due to this circumstance, the procedure performed, as a rule, does not cause pain. When injected into the walls of the genitals, circumvascularedema is observed in the injection area. As the scar forms around the vessels, the veins are compressed and sclerosed. The administration of aethoxysklerol into the scrotum helps to close the open connection between the abdominal cavity and the scrotum and completely stop the outflow of fluid from the abdominal cavity to the scrotum. The proof of the complete safety of advanced sclerotherapy is the improvement of hemodynamic parameters of the testicular parenchyma, the absence of structural changes in the testicular tissue and epididymis, and the preservation of spermatogenesis.

Ultimately, these controlled experiments establish a crucial foundation for the safe and effective use of sclerotherapy agents such as aethoxysklerol in clinical hydrocele treatment for human patients. The findings confirm the safety of administering the 0.2 mL aethoxysklerol regimen as it preserves testicular function and sperm production in animal models. This research outlines a potential framework for future hydrocele therapies, ensuring a balance between treatment effectiveness and patient health.

This study provides a robust basis showcasing the potential of low-dose aethoxysklerol sclerotherapy for treating hydrocele. However, there are still some issues to be tackled such as conducting longitudinal evaluations to ensure safety and effectiveness during chronic exposure, refining adjustments that correspond to patient factors like hydrocele size and age, demonstrations of preserved fertility beyond just spermatogenesis, and conducting experiments on animal models that are more relevant to humans and acknowledge anatomical disparities compared to rabbits. Overall, the positive outcomes merit further inquiry into the effects of different modes of administration, combined strategies, reproductive results, and usage in other populations similar to the clinical hydrocele cohort. By developing this initial evidence through further optimization and model testing, researchers can help to translate aethoxysklerol injections from well-controlled experiments to widespread, long-term usage, providing patients with safe and reliable resolution of hydroceles.

REFERENCES:

1. Goldman M. Weiss R. Sclerotherapy. Elsevier, Oxford. 2016.
2. Lakshmi SS. Rao YS. Asha D. Kumari PK. Mallikarjun P. Formulation and evaluation of rosuvastatin-calcium drug transdermal patch. Res J Pharm Technol. 2020; 13(10): 4784. <http://dx.doi.org/10.33899/iph.2022.170395>
3. Alavian S. Nabavi S. Silva AS. Influence of nutrients, bioactive compounds, and plant extracts in liver diseases. Academic Press, London. 2020.

4. Mazurkevich A. Stadnyk N. Microscopic changes in experimentally damaged rabbit muscles under the influence of transplanted mesenchymal stem cells. *Ukrainian Journal of Veterinary Sciences*. 2023; 14(2): 96-111. <https://doi.org/10.31548/Veterinary2.2023.96>
5. Dasgupta A. Wahed A. *Clinical Chemistry, Immunology and Laboratory Quality Control*. Elsevier, Oxford. 2021.
6. Maslak K. Favara-Scacco C. Barchitta M. Agodi A. Astuto M. Scalisi R. Italia S. Bellia F. Bertuna G. D'Amico S. La Spina M. Licciardello M. Lo Nigro L. Samperi P. Miraglia V. Cannata E. Meli M. Puglisi F. Parisi GF. Russo G. Di Cataldo A. General anesthesia, conscious sedation, or nothing: Decision-making by children during painful procedures. *Pediatr Blood Cancer*. 2019; 66(5): e27600. <https://doi.org/10.1002/pbc.27600>
7. Pinto AMFR. Oliveira OS. Falcao DSC. Direct alcohol fuel cells for portable applications. *Academic Press*, London. 2018.
8. De Azambuja Borges CRL. Silva NO. Rodriguez MR. Marinho MAG. de Oliveira FS. Mendes C. Hom AP et al. Dimiristoylphosphatidylcholine/genistein molecular interactions: A physico-chemical approach to anti-glioma drug delivery systems. *Chem Phys Lipids*. 2019; 225: 104828. <https://doi.org/10.1016/j.chemphyslip.2019.104828>
9. Kurmanova A. Urazbayeva G. Terlikbayeva A. Salimbaeva D. Ayazbekov A. Diagnostic significance of blood lymphocyte activation markers in pre-eclampsia. *Clin Exp Immunol*. 2024; 215(1): 94-103. <https://doi.org/10.1093/cei/uxad121>
10. Kshirasagar N. Puchchakayala G. Balamurugan K. Comparative Pharmacokinetic Studies of Marketed and Microsponges Gel Loaded with Diclofenac Diethylamine in Rabbits. *Res J Pharm Technol*. 2021; 14(12): 6385-6391. <http://dx.doi.org/10.52711/0974-360X.2021.01104>
11. Dobrovanov O. Králinský K. Kovalchuk VP. Ethiological agents of urinal infections and microbial resistance: Retrospective study. *LekObz*. 2019; (7): 186-190.
12. Dasgupta A. *Alcohol, drugs, genes and the clinical laboratory*. Academic Press, London. 2016.
13. McKeen LW. *Permeability properties of plastics and elastomers*. William Andrew, Oxford. 2016.
14. Marakatham S. Shanmugapandian P. Bioanalytical Method Development and Validation of Doravirine, Lamavudine and Tenofovir Disoproxil Fumarate using HPLC in Human Plasma. *Res J Pharm Technol*. 2021; 14(8): 4087-4091. <http://dx.doi.org/10.52711/0974-360X.2021.00708>
15. Dasgupta A. *Critical issues in alcohol and drugs of abuse testing*. Academic Press, London. 2019.
16. Komariah C. Salsabila R. Hilda Hapsari A. Rizky Kurnia Putri S. Febianti Z. The Anti-inflammatory effect of Onion extract in rabbit with Corneal ulcer. *Res. J. Pharm. Technol*. 2021; 14(4): 1854-1858. <https://doi.org/10.52711/0974-360X.2021.00328>
17. Mazumder A. Kumar N. Das S. Kumar SA. Comparative Study on Mono-therapy and Combination Therapy of Additive Drugs (Rebamipide and Pantoprazole) with Amla and Honey combination for the Treatment of Gastroesophageal Reflux Disease and Intestinal motility. *Res J Pharm Technol*. 2022; 15(9): 4144-4150. <http://dx.doi.org/10.52711/0974-360X.2022.00696>
18. Pokryshko O. Khomenko V. Experimental translocation of intestinal bacteria caused by closed abdominal trauma, acute blood loss, internal haemorrhage. *Bull Med Biol Res*. 2023; 16(2): 15-22. <https://doi.org/10.61751/bmbr.2706-6290.2023.2.15>
19. Lisnyy I. Zakalska O. Dmytriiev D. Dmytriiev K. Dobrovanov O. Pre-emptive analgesia with nonsteroidal anti-inflammatory drugs randomized, double-blind placebo-controlled study. *LekObz*. 2021; 70(5): 195-202.
20. Sen F. *Nanomaterials for direct alcohol fuel cells*. Elsevier, Oxford. 2021.
21. Wahman S. Emara M. Shawky MR. In-Vitro Assessment of Staphylococci Biofilms Formed Under Biologically-Relevant Conditions and Correlation to the Biofilm Genotype. *Res J Pharm Technol*. 2023; 16(5): 2273-2279. <http://dx.doi.org/10.52711/0974-360X.2023.00373>
22. Kovalchuk VP. Nazarchuk OA. Burkot VM. Fomina NS. Prokopchuk ZM. Dobrovanov O. Biofilm forming activity of non-fermenting gram-negative bacteria. *Wia Lek*. 2021; 74(2): 252-256. <https://doi.org/10.36740/wlek202102114>
23. Singh A. *Neurobiology of alcohol and the brain*. Academic Press, London. 2020.
24. Mamontov IN. Results of treatment for Mirizzi syndrome. *Klinkhirurhiia*. 2016; (9): 25-27.
25. Vieira WT. de Farias MB. Spaolonzi MP. da Silva MGK. Vieira MGA. Latest Advanced Oxidative Processes Applied for the Removal of Endocrine Disruptors from Aqueous Media – A Critical Report. *J Environ Chem Eng*. 2021; 9(4): 105748. <https://doi.org/10.1016/j.jece.2021.105748>
26. Aravind M. Kumar PS. Begum SKA. An Overview of Dendrimers as Novel Carriers in Drug Delivery. *Res. J. Pharm. Technol*. 2023; 16(4): 2051-2056. <https://doi.org/10.52711/0974-360X.2023.00337>
27. Inticher JJ. Cabrera LC. Guimaraes RE. Zorzo CF. Pellenz L. Seibert D. Borba FH. Advanced Treatment of Water Contaminated with Atrazine, Difenconazole and Fipronil Mixture, Its By-Products and Bio-Toxicity Levels. *J. Environ Chem Eng*. 2021; 9(5): 105883. <https://doi.org/10.1016/j.jece.2021.105883>
28. Zabaïou N. Fouache A. Trousson A. Baron S. Zellagui A. Lahouel M. Lobaccaro J-M. Biological Properties of Propolis Extracts: Something New from an Ancient Product. *Chem Phys Lipids*. 2017; 207: 214-222. <https://doi.org/10.1016/j.chemphyslip.2017.04.005>
29. Beuscher U. Kappert EJ. Wijmans JG. *Membrane Research Beyond Materials Science*. J Membr Sci. 2021; 9: 56-57. <https://doi.org/10.1016/j.memsci.2021.119902>
30. Kandukoori RN. Yellu RN. Effect of Capsaicin on Pharmacokinetics and Pharmacodynamics of Nateglinide in normal and diabetic rats. *Res J Pharm Technol*. 2023; 16(3): 991-996. <https://doi.org/10.1016/j.memsci.2021.119902>
31. Shaprynskyi V. Nazarchuk O. Faustova M. Mituk B. Dmytriiev D. Dobrovanov O. Kralinsky K. Babina Y. Some aspects of infectious complications in patients with surgical diseases multicentr trials. *LekObz*. 2020; 69(7-8): 257-260.
32. Dmytriiev D. Melnychenko M. Dobrovanov O. Nazarchuk O. Vidiscak M. Perioperative hemodynamic protective assessment of adaptive support ventilation usage in pediatric surgical patients. *Acute Crit Care*. 2022; 37(4): 636-643. <https://doi.org/10.4266/acc.2022.00297>
33. Dias IHK. Ferreira R. Gruber F. Vitorino R. Rivas-Urbina A. Sanchez-Quesada L. Silva JV et al. Sulfate-Based Lipids: Analysis of Healthy Human Fluids and Cell Extracts. *Chem Phys Lipids*. 2019; 221: 53-64. <https://doi.org/10.1016/j.chemphyslip.2019.03.009>
34. Yadav MK. Saidulu D. Gupta AK. Ghosal PS. Mukherjee A. Status and Management of Arsenic Pollution in Groundwater: A Comprehensive Appraisal of Recent Global Scenario, Human Health Impacts, Sustainable Field-Scale Treatment Technologies. *J Environ Chem Eng*. 2021; 9(3): 105203. <https://doi.org/10.1016/j.jece.2021.105203>
35. Mohammed MAQ. Jbori AB. Hepa AAA. The effect of Hyperhomocysteinemia on the Osteoclasts activity in Male New Zealand White Rabbits. *Res J Pharm Technol*. 2022; 15(2): 5443-5448. <http://dx.doi.org/10.52711/0974-360X.2022.00917>
36. Marwarha G. Raza S. Hammer K. Ghribi O. 27-hydroxycholesterol: A Novel Player in Molecular Carcinogenesis of Breast and Prostate Cancer. *Chem Phys Lipids*. 2017; 207: 108-126. <https://doi.org/10.1016/j.chemphyslip.2017.05.012>
37. Sari DS. Sakinah N. Nuri N. Suswati E. Widyawati R. Maduratna E. Chlorogenic Acid Fractionation in Robusta Green Bean Extract as a Combination Agent of Dental Pulp Stem Cells in Periodontal Tissue Engineering. *Res J Pharm Technol*. 2022; 15(11): 5005-5010. <https://doi.org/10.52711/0974-360X.2022.00841>
38. Jatoti AS. Hashmi Z. Adriyani R. Yuniarto A. Mazari SA. Akhter F. Mubarak NM. Recent Trends and Future Challenges of Pesticide Removal Techniques – A Comprehensive Review. *J Environ Chem Eng*. 2021; 9(4): 105571. <https://doi.org/10.1016/j.jece.2021.105571>