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THE STUDY OF THE ACUTE AND CHRONIC TOXICITY OF THE DRUG “DECASAN”

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Key words: decamethoxinum; “Decasan”; rats; acute toxicity; chronic toxicity

The intestinal diseases of bacterial aetiology are characterized by a high prevalence and a severe course, especially at an early age, in concomitant immunity suppression or chronic diseases of the gastrointestinal tract. Therefore, it is expedient to search for new antimicrobial drugs, and it seems promising to use the known antimicrobial agent – decamethoxinum for developing oral medicinal forms, such as “Decasan” – 0.02% decamethoxinum solution for oral use by “Yuria-Pharm”, Ukraine. The aim of the study is to determine the parameters of the acute toxicity of decamethoxinum substance and “Decasan,” as well as to study the possible toxic effects of the latter in chronic administration. The experiments have shown that “Decasan” in the maximum permissible dose of 20 ml/kg does not cause lethality in rats. For decamethoxinum substance LD_{50} equals 586 (484÷588) mg/kg in intragastric administration, and it corresponds to class IV – low toxic substances ($500 \text{ mg/kg} < LD_{50} < 5000 \text{ mg/kg}$). The single intragastric administration of decamethoxinum substance in the dose of 400 mg/kg in 2 days causes moderate reversible changes in the gastrointestinal tract, the thymus and adrenal glands. The intragastric administration of “Decasan” in the doses of 3 ml/kg and 30 ml/kg for 30 days to male and female rats does not cause the pathological changes in biochemical parameters of the blood (only decrease in the content of albumins is observed in male rats receiving the drug in both doses), as well as in the histological structure of the internal organs and functions of the kidney, heart, and CNS.

The problem of intestinal diseases of the bacterial and viral aetiology remains unsolved since there is no distinct decrease in their prevalence, wherein the appearance of serovars causing a severe course of the disease (*Shigella flexneri* 2a, enterohemorrhagic *Escherichia coli* O157, etc.) has been registered. Especially problematic clinical situation develops against the background of immunity deficiency, chronic diseases of the gastrointestinal tract, as well as at an early age. Besides contribution to the acute disease prevalence and lethality, some of the causative agents of acute diarrhoea lead to development of severe, long-lasting complications, such as haemolytic-uraemic syndrome with renal failure (in enterohemorrhagic escherichiosis), Guillain-Barre syndrome in the diseases caused by *C. jejuni*, and malabsorption syndrome (with diarrhoea or without it) in infections induced by enteroaggregative *E. coli*, cryptosporidias and probably, other causative agents of intestinal infections [10, 12, 13].

The choice of an antibacterial drug in acute intestinal diseases of the bacterial aetiology is of special significance since this drug should exert an effective impact on the pathogenic microorganisms without suppression of the highly sensitive and unstable normal intestinal microflora. Moreover, the drug should not be absorbed to the blood, being locally active in the intestine. These requirements are followed if the antimicrobial drug decamethoxinum is used. It is a surface-active cationic detergent with antibacterial, antiviral, antifungal activity of a broad spectrum; it is practically not adsorbed from the gastrointestinal tract. Its additional advantage is the ability to degrade microbial toxins and cause the anti-inflammatory effect. Decamethoxinum is widely used in

infectious diseases in surgery, dentistry, gynaecology, urology, otolaryngology, pulmonology [3, 4, 8, 9, 11]. Thus, development of decamethoxinum medicinal forms for oral administration has been recognized to be expedient and has begun recently with the pharmacological study of “Decasan” – 0.02% decamethoxinum solution for oral use by “Yuria-Pharm” (Kyiv, Ukraine). Still there is a growing concern over the safety of pharmacotherapy, and toxicity studies represent an essential part of the pre-clinical drug research. Therefore, the aim of this study was to evaluate the parameters of acute toxicity of “Decasan” and to determine its possible toxic effects in chronic administration.

Materials and Methods

All the experimental protocols were in accordance with the principles of bioethics as required in the “Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on protection of animals used for scientific purposes”. Albino rats with the body weight of 180-200 g were kept in the Central Research Laboratory of the National University of Pharmacy under the standard conditions. In order to reproduce the clinical signs of the acute poisoning and determine the LD_{50} value the single intragastric administration of “Decasan” in the form of 0.02% decamethoxinum solution was used in rats of both sexes as described in [6]. Taking into consideration that the maximum permissible dose of the liquid oral medicinal forms equals 20 ml/kg and the maximal permissible volume that can be administered intragastrically to a rat with the body weight of 200 g is 5 ml [6, 7] “Decasan” was administered once in the maximum permissible dose of 20 ml/kg. The animals were observed for 14 days after dosing.

Further studies were carried out to determine the LD₅₀ value of the active ingredient of "Decasan" drug – decamethoxinum substance in accordance with the current methodological recommendations using the method of Pastushenko T.V. et al. [6] in rats of both sexes under the conditions of a single-dose intragastric administration. In the preliminary studies, each dose was tested in two animals with the subsequent observations for two weeks. For the exact determination of the LD₅₀ value it was necessary to test several complementary doses and outline the doses causing the effect exceeding 50% (still not reaching 100%) in one of the groups and being less than 50% (but not 0) in another group. This approach allows obtaining reliable toxicological data with the minimal number of animals required from the bioethical viewpoint.

The maximum dose of decamethoxinum without causing lethality was further studied in order to determine the functional state of the organism after the acute intoxication (n = 6 in the groups of male and female rats, as well as in the corresponding intact control groups). After the period of observation for 2 and 14 days, rats were anesthetized; the internal organs were harvested for morphological studies and determination of the relative organ weight. The body weight dynamics was also registered.

In the studies of the chronic toxicity two doses of "Decasan" were administered to rats of both sexes intragastrically (taking into account the possible route of administration). The doses used in this study were chosen in accordance with the current methodological recommendations [1, 6] and equalled 3 ml/kg of "Decasan" or 0.6 mg/kg of decamethoxinum (the result of calculations considering the human therapeutic dose), and 30 ml/kg of "Decasan" or 6 mg/kg of decamethoxinum (the dose exceeding ten times the abovementioned dose). As the maximal permissible volume that can be administered intragastrically to the rat with the body weight of 200 g is 5 ml, the toxic dose of 30 ml/kg was given twice (in the morning and in the evening). The animals of the intact control groups received isotonic saline solution in the dose of 30 ml/kg (n = 6 in each group). The treatment was conducted each day for the period of 30 days (proceeding from the maximal predicted term of the treatment with "Decasan" in clinics that is limited to 3-5 days). The body weight dynamics was registered each week. In 28 days the CNS functional state was assessed using the combined open field test; electrocardiogram was registered on an EKTG-03M apparatus and analysed using generally accepted parameters (including calculation of the heart rate, systolic index as the ratio of QT/RR duration, %); the clinical blood count was performed (with determination of the haemoglobin level, erythrocytes and leucocytes quantity, as well as the ratio of different leucocytes forms by generally accepted methods) [1, 5, 6]. The functional state of the kidney was characterized using the forced diuresis method (the water load at the rate of 2.5% of the body weight followed with the three-hour urine collection). Urine creatinine concentration was measured using Jaffe reaction, urea concentration – by the reaction with diacetyl monooxime, sodium and potas-

sium levels – using the flame photometry method, chloride concentration – using the reaction with mercury(II) thiocyanate. For these metabolites excretion was calculated, as well as urine specific gravity and pH were measured. Plasma creatinine and sodium concentrations were also measured to assess the glomerular filtration rate (GFR), sodium and water reabsorption. The animals were anesthetized, the blood serum and plasma were obtained, and the internal organs were harvested for morphological studies and determination of relative organ weights. Coagulation system characteristics, such as the clotting time, the fibrinogen level in the blood plasma, the prothrombin time were registered. The total protein level in the serum was measured by the biuret method, the content of albumins and globulins – by turbidimetric method, the activity of alanine aminotransferase and aspartate aminotransferase – by the method of S.Reitman, S.Frankel, basic phosphatase – using the reaction with p-nitrophenylphosphate, glucose level – by the glucose oxidase method, urea level – by the reaction with diacetyl monooxime, the creatinine level – by the modified method using Jaffe reaction [5]. Standard kits from "PLIVA-Lachema Diagnostica sro," (Czech Republic), "Filisit-Diagnostika" (Ukraine) were used.

In all of the morphological studies the internal organs were fixed in 10% solution of neutral formalin, dehydrated in ethanol solutions of the augmenting concentration, embedded in celloidin-paraffin. Microtome sections were stained with hematoxylin and eosin, brain tissue sections – by Nissl method [2]. For the analysis a "Mikros 400" microscope and a "Nicon Cool Pix 4500" digital camera were applied. The photographs were processed using Pentium 2.4 GHz computer through a Nikon View 5 program.

Calculation of LD₅₀ was performed as recommended in [6]. Other data were processed using "Statistica 6.0" standard software; dispersion analysis, as well as Newman-Keuls criterion, Kruskal-Wallis method, Mann-Whitney criterion with Bonferroni correction were applied. The level of significance was taken as p≤0.05.

Results and Discussion

LD₅₀ is one of the important characteristics that allows determining the class of toxicity, characterizing the therapeutic window, as well as the ratio of toxicity/safety against the background of the doses exceeding 10-100 times the therapeutic ones. After a single intragastric administration of "Decasan" in the maximum permissible dose of 20 ml/kg no lethality was observed in rats of both sexes during the first three days and the following period up to 14 days. Thus, it was not possible to determine the LD₅₀ value for this medicinal form, and decamethoxinum substance was used in the subsequent studies. As the data in Tab. 1 indicate, this substance leads to the lethality of rats within the range of 500-700 mg/kg. Proceeding from these results, the subsequent doses were determined using the scale recommended in [6]. These results shown in Tab. 2 allowed calculating the LD₅₀ value using the minimal doses causing a certain effect. LD₅₀ for the decamethoxinum substance in rats was 586 (484÷588) mg/kg in intragastric administration. Therefore, according

Table 1

The preliminary results of the acute toxicity studies of decamethoxinum substance in rats in intragastric administration

Dose, mg/kg	Number of animals	The effect observed, dead animals/number of animals in the group
200	2	0/2
400	2	0/2
500	2	1/2
708	2	2/2
1260	2	2/2

to the generally accepted classification (as listed in [6]), the decamethoxinum substance in a single intragastric administration to rats belongs to class IV of low toxic substances ($500 \text{ mg/kg} < LD_{50} < 5000 \text{ mg/kg}$).

The maximum dose of decamethoxinum without causing lethality, namely 400 mg/kg , was further studied in rats. After a single intragastric administration the animals were unkempt, disheveled, suppressed, their food consumption was reduced. Still they normally responded to auditory and visual stimuli; the processes of urination and defecation were normal; respiratory disorders, and seizures were not observed; the reflex excitability of all animals was maintained. Subsequently, starting from the 3-rd day until the end of the observation, the condition of the animals returned to normal, the consumption of water and food in all experimental animals did not differ from those in the intact control groups. As expected, there were no lethality cases in all groups. The body weight dynamics did not have any differences from the intact control values.

The macroscopic examination on day 14 showed no pathological changes in the general state of health and well-being of animals, as well as in the macroscopic structure of the lungs, heart, thymus, peritoneum, liver, pancreatic gland, spleen, kidneys, adrenal glands, gastric mucosa and mucous membrane of different parts of the intestine, and gonads. In the animals taken out of the experiment 2 days after administrating decamethoxinum such changes as transient swelling of the perioral tissues and impurity of the base of the tail were observed. The stomach was distended, filled with poorly digested chyme, its folds were smoothed, and the mucosal surface under chyme had a "gelatinous" form. No visible changes were identified in other organs. The microscopic examination of all samples (obtained within both periods of observation) revealed no pathological changes in the histological structure of the liver, kidneys, myocardium, lungs, spleen, pancreas, testicles, and ovaries.

In the adrenal glands the decrease in saturation of the spongiocyte cytoplasm with lipid droplets was observed in the samples obtained on day 2 compared to day 14. These changes can indicate intensification of the functional activity of the organ with utilization of cholesterol for the synthesis of steroid hormones. On day 2 in the medulla the quantity of the cells with intensely stained

Table 2

The final results of the acute toxicity studies of decamethoxinum substance in rats in intragastric administration

Dose, mg/kg	Number of animals	The effect observed, dead animals/number of animals in the group
398	3	0/3
500	3	1/3
750	3	2/3
1000	3	2/3
1580	3	3/3

cytoplasm was increased; there was also a sign of the reversible enhancement of the organ function, probably developing as a protective reaction to a toxic dose of decamethoxinum. In this period the reversible devastation of the thymus subcortical layer and inversion of the layers were registered in all animals reflecting the organ reaction to the xenobiotic. These changes disappeared after a 14-day period when the morphological structure of the thymus returned to the normal state. In some of the samples, a "starry sky" appearance was present in the cortex.

In 2 days after administration of the decamethoxinum substance the changes in the gastric mucosa were observed both in the fundus and in the pyloric part. Epithelial cells were flattened, intensively exfoliated. The initial stages of formation of superficial erosions were sometimes seen, there also was the subepithelial capillaries plethora. The single cystiform widened glandular tubes were visible. The significant swelling of the submucosa, vascular plethora, sometimes – a distinct subepithelial edema of stroma were seen (Fig. 1, 2). Nevertheless, in 14 days the state of the gastric mucosa in all rats was within the normal physiological range (Fig. 3).

On day 2 there was a slight thickening of the microvilli in the mucosa of the jejunum, the expansion of the stroma, the nuclei of some absorptive cells moved toward their apical part. In 14 days after decamethoxinum administration the state of the microvilli was normal. The number of goblet cells, the state of intestinal crypts during both periods of observation was unchanged. The number of Paneth cells (which mediate the protective mechanisms, including the bactericidal function of the intestine), in 2 days after the administration of the substance studied did not exceed 1-2 per crypt, and in 14 days it ranged from 2 to 4. These short-term changes can be attributed to the certain degenerative manifestations in the microvilli, and signs of dyspepsia observed in the animals in this period. However, the mucous membrane of the large intestine (pelvic colon) was histologically normal.

The results of the chronic toxicity studies of "Decasan" showed that there were no visible changes in the general state of health and their activity; there were no lethality cases in all groups. There were no statistically significant differences between groups in the body weight dynamics in both male and female rats.

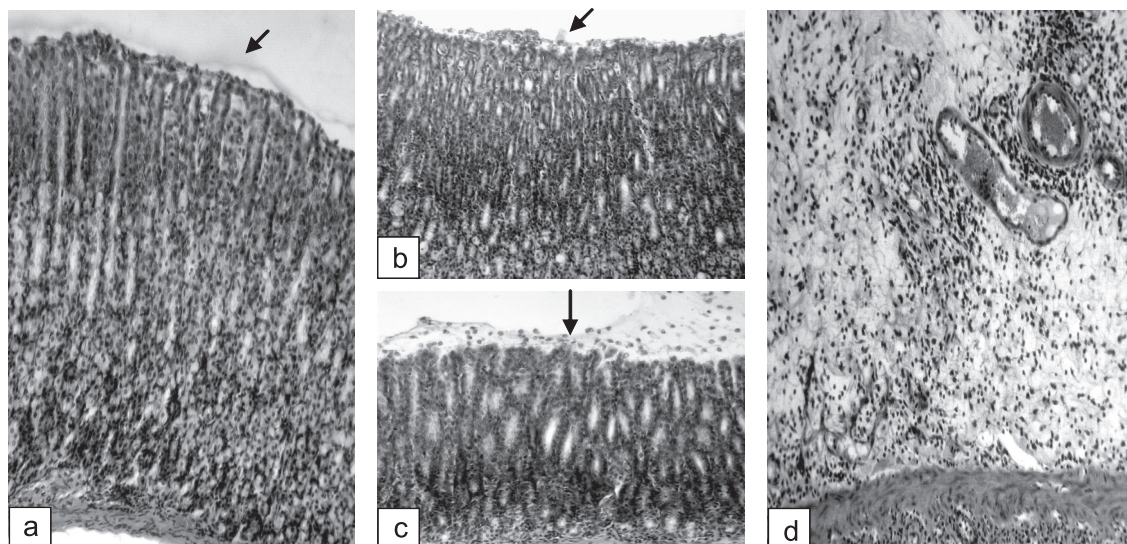


Fig. 1. A photomicrograph of the stomach of the rat in 2 days after intragastric administration of decamethoxinum substance in the dose of 400 mg/kg: a – epithelial cells are flattened in the fundus, subepithelial edema is seen, b-c – desquamated covering cells in the fundus and in the pyloric part, d – edema of the submucosa, thrombosis of blood vessels. Hematoxylin and eosin staining. × 100.

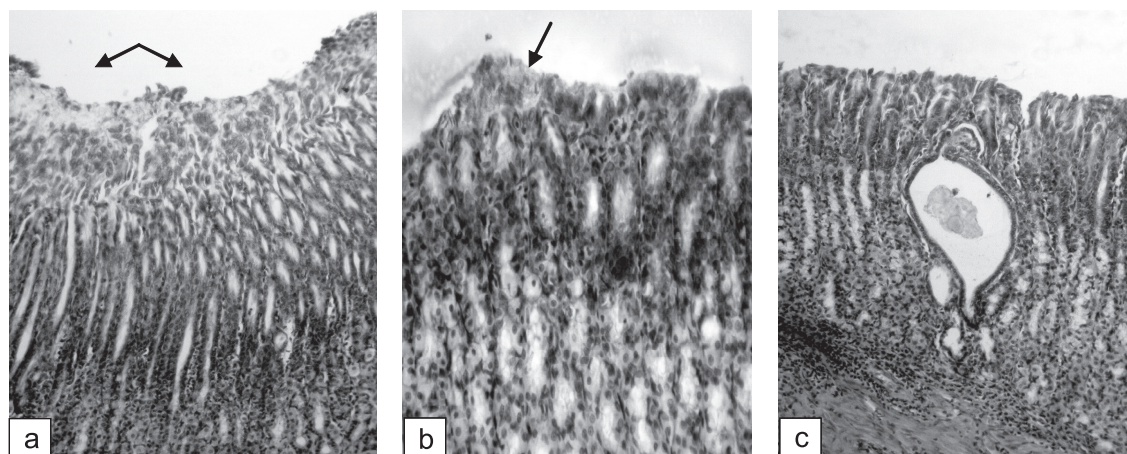


Fig. 2. A photomicrograph of the stomach of the rat in 2 days after intragastric administration of decamethoxinum substance in the dose of 400 mg/kg: a-b – superficial erosion formation in the pyloric part and in the fundus, c – cystiform widening of the gland. Hematoxylin and eosin staining. × 100.

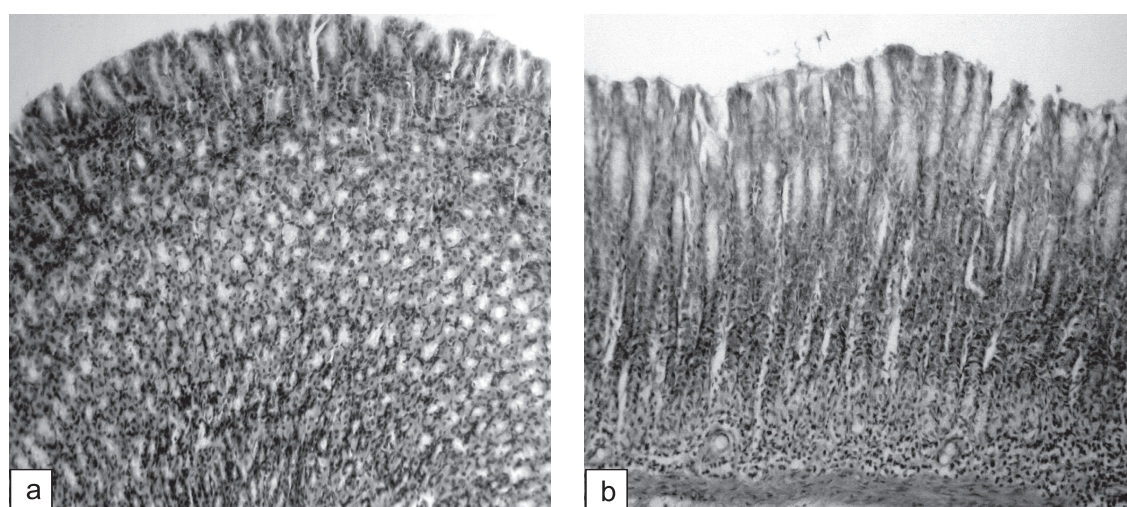


Fig. 3. A photomicrograph of the stomach of the rat in 14 days after intragastric administration of decamethoxinum substance in the dose of 400 mg/kg: the normal state of the mucosa in the fundus (a) and in the pyloric part (b). Hematoxylin and eosin staining. × 100.

The CNS functional state was also not altered under the effect of "Decasan" since all parameters studied using open field test were within the normal physiological range and were not altered. The antimicrobial drug studied did not induce any changes in haemopoiesis in both sexes proceeding from the quantity of erythrocytes and leucocytes, as well as the ratio of different leucocyte forms and the haemoglobin level. No alterations were registered in the coagulation system characteristics. The blood serum biochemical parameters (total protein level, content of globulins, glucose, urea, and creatinine concentration, basic phosphatase, alanine aminotransferase, and aspartate aminotransferase activity) also remained unchanged in all of the groups. The only exception was the significant decrease in the content of albumins: 23.35 ± 1.43 and $26.51 \pm 1.97\%$ of the total protein in the male rats receiving "Decasan" in the doses of 3 ml/kg and 30 ml/kg, respectively, compared to $34.66 \pm 1.58\%$ of the total protein in intact animals ($p < 0.05$ in either case). In female rats no statistically significant changes in albumin level were registered, this value slightly tended to decrease against the background of the high dose of decamethoxinum. The results indicate that administration of "Decasan" for 28 days does not induce cardiotoxic and nephrotoxic effects. Thus, no significant changes were seen in the electrocardiogram parameters (including a marker of intracardiac conduction – PQ interval, as well as the heart rate and normal sinus rhythm) and the excretory renal function indices (including diuresis, urine specific gravity and pH, GFR, sodium and water reabsorption, as well as creatinine, urea, sodium, potassium, chloride excretion).

The macroscopic examination after 28 days of "Decasan" administration in the doses of 3 ml/kg and 30 ml/kg showed no pathological changes in the animals' general state of health, as well as in the macroscopic structure of the thoracic and abdominal cavities, aorta and heart, trachea, larger bronchi and lungs, oesophagus, stomach and intestine, liver, pancreatic gland, spleen, kidneys, adrenal glands, uterus and gonads, brain tissue, meninges and vessels. There were no statistically significant differences between groups in the relative organs weights (namely the liver, kidneys, heart, lungs, spleen, adrenal glands, thymus, brain, testes), and the data were within the normal physiological range inherent in this species and age. Therefore, no abrupt changes in the state of the internal organs were seen under the effect of "Decasan." The

microscopic examination of all samples of male and female animals receiving the drug studied in both doses revealed no pathological changes in the histological structure of the liver, kidneys, myocardium, lungs, thymus, spleen, adrenal glands, pancreatic gland, ovaries and testicles. Proceeding from the possible gastrointestinal irritating properties of decamethoxinum the functional state of the digestive organs was of special interest. It was found that in the doses studied "Decasan" was not able to induce any pathological changes of the histologic features of the oesophagus, stomach and different parts of the intestine. No changes were seen in the sensomotor zones of the cerebral cortex.

CONCLUSIONS

1. The drug "Decasan" in the maximum permissible dose of 20 ml/kg does not cause lethality in rats, not allowing the calculation of LD_{50} . LD_{50} for decamethoxinum substance in rats equals 586 ($484 \div 588$) mg/kg in intragastric administration, and it corresponds to class IV – low toxic substances ($500 \text{ mg/kg} < LD_{50} < 5000 \text{ mg/kg}$).

2. The single intragastric administration of the decamethoxinum substance in the dose of 400 mg/kg in 2 days causes irritation of the gastric mucosa and a slight decrease in the defensive properties of the intestinal mucosa, reactive changes in the thymus and certain exertion of the adrenocorticocytes in the zona fasciculata and chromaffin cells in the adrenal medulla. These changes are reversible and neither observed in 14 days after decamethoxinum administration, nor accompanied with the other pathological signs.

3. The intragastric administration of "Decasan" in the doses of 3 ml/kg and 30 ml/kg for 30 days to male and female rats does not cause the pathological changes in the functional activity of haemopoiesis and blood coagulation, CNS, heart and kidney, as well as in the biochemical parameters of blood serum (only decrease in the content of albumins is observed in male rats receiving the drug in both doses).

4. After intragastric administration of "Decasan" in the doses of 3 ml/kg and 30 ml/kg for 30 days to male and female rats no signs of the cardiotoxic, nephrotoxic, hepatotoxic action of the drug are observed, there are also no reactive changes of the adrenal cortex, no signs of alterations of the structure of the lungs, reproductive system, immune system, sensomotor zones of the cerebral cortex, and no signs of gastrointestinal irritation.

REFERENCES

1. Арзамасцев Е.В., Гуськова Т.А., Березовская И.В. и др. Руководство по экспериментальному (доклиническому) изучению новых фармакологических веществ / Под ред. проф. Р.У.Хабриева. – М.: ОАО Изд-во «Медицина», 2005. – С. 47-54.
2. Волкова О.В., Елецкий Ю.К. Основы гистологии с гистологической техникой. – М., 1982. – 304 с.
3. Декасан: инструкция по применению [Электронный ресурс]. – Режим доступа: <http://tabletki.ua/Декасан>
4. Деркач Н.Н., Штрыголь С.Ю., Койро О.О., Блажеевский Н.Е. // Обзоры по клин. фармакол. и лекарств. терапии. – 2015. – Т. 15, №1. – С. 45-51.
5. Камышников В.С. Справочник по клинико-биохимической лабораторной диагностике: в 2-х т. – Мн.: Беларусь, 2000. – Т. 1. – 495 с., Т. 2. – 463 с.

6. Коваленко В.М. Доклінічні дослідження лікарських засобів / За ред. чл.-кор. НАМН України О.В. Стефанова. – К.: Авіценна, 2001. – С. 74-97.
7. Кожем'якін Ю.М., Хромов О.С., Філоненко М.А., Сайфетдінова Г.А. Науково-практичні рекомендації з утримання лабораторних тварин та роботи з ними. – К.: Авіценна, 2002. – 156 с.
8. Палій В.Г. Автореф. дис. ... канд. мед. наук. – Х., 1999. – 23 с.
9. Палій Г.К., Ковальчук В.П., Деркач Н.М. та ін. // Укр. хіміотерапевт. журн. – 2010. – №1-2. – С. 78-82.
10. Практическое руководство по антиинфекционной химиотерапии / Под ред. Л.С. Страчунского, Ю.Б. Белоусова, С.Н. Козлова. – М.: Боргес, 2002. – 381 с.
11. Фомин П.Д., Лисов А.И., Козлов С.Н. и др. // Ліку України. – 2006. – №12. – С. 74-75.
12. Barr W., Smith A. // Am. Fam. Physician. – 2014. – Vol. 89, №3. – P.180-189.
13. Kosek M., Bern C., Guerrant R.L. // Bull. World Health Organ. – 2003. – Vol. 81, №3. – P. 197-204.

ВИВЧЕННЯ ГОСТРОЇ ТА ХРОНІЧНОЇ ТОКСИЧНОСТІ ПРЕПАРАТУ «ДЕКАСАН»

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Ключові слова: декаметоксин; «Декасан»; щури; гостра токсичність; хронічна токсичність

Захворювання кишечника бактеріальної етіології характеризуються значною поширеністю і тяжким перебігом, особливо у ранньому віці, за супутнього імунodefіциту та хронічних хвороб шлунково-кишкового тракту (ШКТ). Тому є раціональним пошук нових антимікробних засобів та доцільним використання відомого антимікробного засобу декаметоксину для створення лікарських форм для перорального застосування, зокрема «Декасан» («Юрія-Фарм», Україна) – 0,02% розчин декаметоксину для вживання всередину. Мета даного дослідження – визначення показників гострої токсичності субстанції декаметоксину і препарату «Декасан», а також вивчення можливих токсичних ефектів останнього за курсового введення. У досліді на щурах показано, що «Декасан» у максимально допустимій для одноразового введення дозі 20 мг/кг не призводить до загибелі щурів. Для субстанції декаметоксину LD₅₀ становить 586 (484÷588) мг/кг при внутрішньошлунковому введенні, що відповідає IV класу малотоксичних речовин (500 мг/кг < LD₅₀ < 5000 мг/кг). Одноразове внутрішньошлункове введення субстанції декаметоксину в дозі 400 мг/кг через 2 доби спричиняє помірні зворотні зміни з боку ШКТ, тимуса, надниркових залоз. Внутрішньошлункове введення препарату «Декасан» у дозах 3 мг/кг і 30 мг/кг впродовж 30 днів щурам самцям та самкам не призводить до патологічних зсувів біохімічних параметрів крові (за винятком гіпоальбумінемії у самців щурів на тлі обох доз), а також не спричиняє змін гістоструктури внутрішніх органів, функції нирок, серця, ЦНС.

ИССЛЕДОВАНИЕ ОСТРОЙ И ХРОНИЧЕСКОЙ ТОКСИЧНОСТИ ПРЕПАРАТА «ДЕКАСАН»

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Ключевые слова: декаметоксин; «Декасан»; крысы; острая токсичность; хроническая токсичность

Заболевания кишечника бактериальной этиологии характеризуются значительной распространенностью и тяжелым течением, особенно в раннем возрасте, при сопутствующем иммунодефиците или хронических болезнях желудочно-кишечного тракта (ЖКТ). Поэтому рационально изыскание новых антимикробных средств и целесообразно использование известного антимикробного средства декаметоксина для создания лекарственных форм для перорального применения, таких как «Декасан» («Юрия-Фарм», Украина) – 0,02% раствор декаметоксина для приема внутрь. Цель настоящего исследования – определение показателей острой токсичности субстанции декаметоксина и препарата «Декасан», а также изучение возможных токсических эффектов последнего при курсовом введении. В экспериментах на крысах показано, что «Декасан» в максимально допустимой для однократного введения дозе 20 мг/кг не приводит к гибели крыс. Для субстанции декаметоксина LD₅₀ составляет 586 (484÷588) мг/кг при внутривнутреннем введении, что соответствует IV классу малотоксичных веществ (500 мг/кг < LD₅₀ < 5000 мг/кг). Однократное внутривнутреннее введение субстанции декаметоксина в дозе 400 мг/кг через 2 дня вызывает умеренные обратимые изменения ЖКТ, тимуса и надпочечников. Внутривнутреннее введение препарата «Декасан» в дозах 3 мг/кг и 30 мг/кг в течение 30 дней крысам самцам и самкам не приводит к патологическим сдвигам биохимических параметров крови (за исключением гипоальбуминемии у самцов крыс на фоне обеих доз), а также не вызывает изменений гистоструктуры внутренних органов, функции почек, сердца, ЦНС.