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Study of Embryotoxic and Teratogenic Action of the Medicinal Form of Capsule “UROCONITE-0.2 G”

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Abstract: ***The authors studied the embryotoxic and teratogenic effects of the capsule "Uroconite-0.2 g." The results of the study proved that the studied capsule - "Uroconite-0.2 g" in doses of 100 and 500 mg/kg does not adversely affect the development of the fetus in experimental animals. Therefore, the capsule "Uroconite-0.2 g" does not involve embryotoxic and teratogenic effects.***

Keywords: “Uroconite-0.2 g”, embryotoxicity, teratogenicity, fetus, pathology and anomalies

1. Introduction

According to the rules of the preclinical safety assessment of pharmacological agents (GLP), each new drug must be examined for embryotoxicity and teratogenicity. In addition, testing the embryotoxic effect of drugs is one of the measures for the prevention of embryopathy and congenital malformations in human development. Therefore, before admission to clinical trials, each drug prescribed to women in the reproductive period should be tested for embryotoxic effects in animal experiments.

Teratogenic is the effect of chemicals on the body of the mother or fetus, accompanied by a significant increase in the likelihood of structural and functional disorders in the offspring. Substances with teratogenic activity are called teratogens.

A large number of substances introduced into the mother’s body at different periods in large doses can cause teratogenesis. Only those substances that penetrate the placental barrier well have a teratogenic effect on the fetus.

There are four types of pathologies of fetal development: death, deformities, growth retardation, functional disorders.

The action of the substance, accompanied by the death of the embryo, is often referred to as embryotoxic [2].

The aim of the study is to study the embryotoxic properties and teratogenic effects of the dosage form of the capsule “Uroconite-0.2 g”.

2. Materials and Methods

The experiments were conducted on clinically healthy animals that were quarantined for at least 10-14 days. To study the state of the fetuses at the end of the antenatal period, we used 27 white rats (out of 18 sexually mature females and 9 males) weighing 180-220 g. To study the state of offspring in the postnatal period of life, we used 45 white mice (15 males and 30 sexually mature virgin females), weighing 18-22 g. Experimental as well as control animals were kept in optimal vivarium conditions, i.e. providing temperature and light conditions, good nutrition, protected from noise and other adverse factors. The females were planted in males in the ratio of 1: 2 to the afternoon. The next day in the morning, a vaginal smear was taken for examination, and when spermatozoa were detected, this indicated the first day of pregnancy in the female.

From the first day of pregnancy and for 20 days, the experimental animals were injected with a probe once, orally, the Uroconite-0.2 g dosage form in the form of a suspension in doses of 100 mg / kg and 500 mg / kg. Also, distilled water was injected into the control animals in the same volume. At the time of administration, the Uroconite-0.2 g dosage form recorded the status and behavior of the females. Conducted daily monitoring of the general clinical condition of the animals. Pregnant animals were weighed weekly (at 1, 8, 14, and 21 days of gestation).

On the 21st day of the experiment, pregnant rats were decapitated and the abdominal uterus was opened, the extracted ovaries were placed in a Petri dish with physiological saline. In the ovaries, the number of corpus luteum, the number of live and dead fruits, as well as the site of implantation and resorption of the embryos were calculated. An external examination of the eyes, brain, facial skull, limbs, spine, tail, and abdominal wall of the fetus was performed. To identify the pathology of internal organs, 1/2 of the fetus was stored for 2 weeks in a Buen solution, after which it was checked by the Wilson method [5]. To examine the condition of the skeleton, the remaining 1/2 part of the fetus was fixed with 96% ethanol for 7 days, according to the Dawson method [6]. The pre-implantation death rate of the embryo was calculated as the difference between the number of yellow bodies and the implantation sites, referred to the number of yellow bodies taken as 100%. The post-implantation death rate was determined as the difference between the number of implantation sites and live fetuses, referred to the number of implantation sites taken as 100%. The female experimental mice remained until delivery.

One of the main studies that are conducted in the study of offspring in the postnatal period of life is the study of animal behavior. These studies must begin immediately after birth, but not earlier than after 24 hours, and continue until 2-3 months of age [1].

3. The Results of the Study

During the autopsy of pregnant females, live fetuses were found, after which they were separated from the uterus. Then weighed the fruits and the placenta. The experimental results are shown in Table 1.

Table 1: The results of a study of the embryotoxic effect of the capsule "Uroconite-0.2 g"

Indicators	Uroconite-0.2 g		Control
	100 mg/kg	500 mg/kg	
The number of pregnant females	6	6	6
The number of yellow bodies	58	57	59
The number of implantation sites	58	56	59
The number of live embryos	58	55	59
Numberofdeadembryos	0	1	0
Totalfetalmortality%	0	3,5	0
Preimplantationdeath%	0	1,7	0
Postimplantationdeath%	0	1,8	0
The mass of the fetus, g	4,5±0,37	4,9±0,33	5,1±0,41г

In the control and experimental groups ("Uroconite-0.2 g" at 100 mg / kg), the number of yellow bodies of pregnancy coincided with the number of fetuses, and this indicated that before and after implantation, death did not occur. The average number of fetuses in rats was 9 ± 1 pc. Using a magnifier, we studied the appearance of the fetus, the development of the head, brain, facial skull, limbs, spine, tail, abdominal wall and legs, which showed the absence of birth defects. An anatomical study of the internal organs and the skeletal system revealed no developmental defects in the fetus, which also indicated the absence of embryotoxic action. The laying and length of the ossification sites of the studied bones did not differ between the experimental and control groups. As a result, pathological changes in the fetus were not recorded. The general clinical condition of the experimental animals did not differ from the control.

In female mice, offspring appeared on time. The results of a study of postnatal development of mice are shown in table 2.

Table 2: The results of the study of the teratogenic effect of the capsule "Uroconite-0.2 g"

Indicators	Uroconite-0.2 g		Control
	100 mg/kg	500 mg/kg	
Numberofanimals	10	10	10
Pregnancyduration	23,0±0,1	22,1±0,2	23,0±0,2
The number of mice born	76	75	80
Stillborn	-	-	-
Safety on the 20th day after birth	100	100	100
Auricledetachment, day	3	3	3
The appearance of a coat, day	5	5	5
Teething, day	9	9	9
Opening of the palpebral fissure, day	14	15	14
The mass of mice on the seventh day, g	3±0,2	3±0,1	3±0,1

During the postnatal study, in particular the analysis of: tooth, skin coatings, external genitalia, muscle development, absorption and movement reflexes, indicated that all indicators were well developed.

4. Conclusions

Therefore, the substance uroconite in the form of a capsule in the therapeutic (100 mg / kg) and maximum doses (500 mg / kg) does not have a negative effect on the growth and development of the fetus. The drug does not lead to topological changes and abnormalities of the fetus. Based on the foregoing, we can say that "Uroconite-0.2 g" in the form of a capsule does not have embryotoxic and teratogenic effects.

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