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# The Effect of Gemcitabine and Verapamil Hydrochloride on C6 Glioma in Experiments on Rats

**Gridina N Ya[1]*, Khokhlov AG[1], Ushenin Yu V[2] and Khristosenko RV[2]**

*[1]Institute of Neurosurgery Named A.P. Romodanov of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine*

*[2]Institute of Semiconductor Physics Named V. E. Lashkaryova of the National Academy of Sciences of Ukraine, Kyiv, Ukraine*

***Corresponding Author:** Gridina N Ya, Institute of Neurosurgery Named A.P. Romodanov of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine.

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## Abstract

The antitumor effect of gemcitabine and verapamil hydrochloride on the life expectancy of rats with transplanted C6 glioma was studied. It was determined that the effect of inhibition of the growth of C6 glioma was almost the same, the average life expectancy of animals was comparable in both groups of animals. The joint administration of drugs did not lead to the expected increase in the life expectancy of animals.

***Keywords:*** *Glioma C6; Gemcitabine; Verapamil-Hydrochloride; Life Expectancy*

## Introduction

Chemotherapy of malignant gliomas has a large number of unresolved problems. Along with the unsatisfactory antitumor effect on brain gliomas, the high toxicity of chemotherapy drugs during their long-term use is of great concern. There are known cases of death of patients from complications on other organs after chemotherapy, ending in death.

Gemcitabine, an antagonist from the pyrimidine group, blocks DNA synthesis, which leads to the destruction of malignant tumors, including brain gliomas [1-4]. The drug penetrates the BBB and has a photosensitizing effect, however, it has side effects with prolonged use, including a pathological effect on the liver, kidneys, bone marrow, urinary system, etc.

Verapamil hydrochloride has an anti-inflammatory and at the same time antitumor effect on malignant gliomas [5-7], while it has no side effects on other organs and tissues. In the treatment with verapamil hydrochloride, there is no toxic effect on organs and tissues, even with prolonged use.

Of interest is the comparative antitumor effect of gemcitabine and verapamil hydrochloride in an experiment on rats with transplanted C6 glioma.

## Aim of the Study

The aim of the study was to compare the life expectancy of rats with transplanted C6 glioma treated with gemcitabine and verapamil hydrochloride.

## Materials and Methods

33 rats were taken into the experiment, of which 16 rats served as control (group 1)A strain of transplantable rat glioma C6 in the amount of 1 million cells in physiological sodium chloride solution was injected into the left parietal region of the brain. 1 day after the inoculation of strain C6 were administered separately to the same area of 6 rats intraperitoneal injections of gemcitabine 0.25 ml (1000 mg/m2 ) on the 3rd and 10th days after transplantation (2nd group). Verapamil hydrochloride was given to 5 rats at a dose of 0.25 ml daily from the second day after inoculation (a 0.25% solution of verapamil hydrochloride was previously diluted 10,000 times with distilled water) (group 3). The fourth group included animals that received gemcitabine and verapamil hydrochloride simultaneously at the above dosages. The life expectancy of animals after treatment with these drugs was determined.

## Results and Discussion

The life expectancy of rats treated with gemcitabine and verapamil hydrochloride was comparable and amounted to 15.8 ± 4.1 and 15.6 ± 5.8 days, respectively. In the control group, the life span of animals was 11.1 ± 4.5 days. The difference in life expectancy of animals in the experiment with rapidly growing C6 glioma by 4 days in clinical conditions is comparable to months and even years of prolonging the life of patients with gliomas of III and IV grades of malignancy, which was shown by comparative studies of the antitumor effect of verapamil hydrochloride in the experiment and in the clinic.

It should be noted that along with the same effect on C6 glioma at concentrations used comparable to those used in patients with malignant gliomas, verapamil hydrochloride does not have a toxic effect on humans and animals.

The mechanism of action of gemcitabine differs from that of verapamil.

While gemcitabine prevents the synthesis of nucleic acids inside tumor cells, verapamil hydrochloride suppresses manifestations of tumor-associated inflammation [8-11] in the microenvironment of glioma cells.

It is logical to assume that there is a syngeneic effect on the manifestation of the antitumor activity of these two drugs in their joint manifestation. However, the experiment showed that with the combined use of drugs, the life expectancy of rats with C6 glioma not only did not increase, but even amounted to 14.3 ± 3.7 days, which is less than in animals with a separate intake of both drugs, although the data are not reliable.

It was previously shown that the combined use of verapamil hydrochloride and lomustine in patients with glioblastomas increased their life expectancy, while the combined use of verapamil hydrochloride with temozolomide did not lead to an increase in the life expectancy of patients [11,12].

## Conclusion

The paper shows the antitumor effect of verapamil hydrochloride, which turned out to be comparable to the well-known chemotherapy drug gemcitabine, which is widely used in the treatment of various types of tumors, including malignant gliomas.

The co-administration of gemcitabine and verapamil hydrochloride indicates complex interactions between anticancer drugs when this does not lead to the desired effect of increasing antitumor activity. Therefore, these studies should be continued until the mechanisms of the joint action of these drugs on the tumor are fully understood, which may lead to unexpected solutions in the field of treatment of malignant gliomas.

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