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# Comparison of the Antitumor Effect of Kolhiprit-Neo with the Effect of Commercial Drugs

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**ABSTRACT**

***Objective:*** *In this study, mice with transplanted Sarcoma 180 and Solid Ehrlich tumors (SET) were used to test the antitumor activity of oral K-20 (colchiprit-neo) against different cytostatics.* ***Methods:*** *Antitumor activity was tested in outbred mice with transplanted tumors, treated orally with K-20 and XELODA, and intraperitoneally with doxorubicin, taxol, etoposide, or other cytostatics. Treatment was began on the 4th-5th day post-transplantation, delivered daily for 10 days. Tumor growth inhibition (TGI), animal body and spleen weight, and hematopoietic indices were measured, with statistical significance set at* $p < 0.05$. ***Results:*** *While other treatments showed significant reductions in hematopoietic parameters, K-20 treatment did not significantly affect body or spleen weight or leukocyte levels. K-20 showed superior antitumor activity, inhibiting tumor growth by 92-94% in Sarcoma 180 and SET models, outperforming doxorubicin (90%) and taxol (84-88%), and demonstrating 27% greater efficacy than XELODA.* ***Novelty****: In contrast to conventional cytostatics, K-20's oral administration demonstrated strong anticancer effects along with a good safety record and little influence on hematopoiesis or organ weights.*

## INTRODUCTION

Experience in chemotherapy shows that all preparations evaluated as active in experimental systems also exhibit antitumor activity in the treatment of human tumors. However, not all substances, both those submitted for clinical trials and those evaluated positively in the experiment, are then proposed for widespread use. The decision on the inexpediency of introducing them into practice is usually made not because of the lack of antitumor properties, but because the preparations have no advantages over those already in existence.

In this regard, the aim of the study comparison of the effect of the new drug colchicine- neo with the effect of commercial drugs of similar tubulin-interactive action (etoposide and taxol), as well as drugs of alkylating action - doxorubicin and cisplatin, as well as with the oral drug xeloda.

## RESEARCH METHOD

The object of the study was the drug K-20, synthesized from colchicine at the Republican Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan and studied with intraperitoneal and

oral administration to mice daily for 10 days in single doses of 3 and 100 mg/kg, which showed the best results in terms of efficacy and tolerability in studies.

The following drugs were used as comparison drugs:

1. Taxol (Intaxel, DaburPharmaLTD, India). Mice were injected intravenously taxol at a dose of 12 mg/kg on days 2-3 after tumor transplantation into mice in parallel with the introduction of the test substances 10 times
2. Etoposide (Etoposide phosphate, from Bristol - MyersSquibb). Mice were injected intravenously etoposide at a dose of 15 mg/kg, 10 times;
3. Doxorubicin (Doxorubicin-Ebewe, Ebewe Arzneimittel, Austria) was administered intravenously at a dose of 1.5 (total dose 15) mg/kg to mice in parallel with the introduction of the test substances
4. Cisplatin (CISPLATIN NAPROD, Naprod Life Scitnces Pvt/Ltd, India). Mice were administered cisplatin intravenously at a dose of 6 (total dose 60) mg/kg 10 times in parallel with the administration of the test substances.
5. Ks e loda (Roche) was administered at a dose of 1200 mg/kg to mice orally

In this work, 44 outbred mice bred in the vivarium of the SES MH RUz were used. The animals were kept in groups of 4-6 individuals under natural lighting conditions with free access to water and food. In each experiment, there were 4 animals in the experimental groups and 6 animals in the control group (with the introduction of a physiological solution).

Tumor strains were obtained from the Blokhin Russian Cancer Research Center of the Russian Academy of Medical Sciences and passaged on donor mice according to the protocol for each strain. Tumor inoculation was performed according to generally accepted methods: tumors were inoculated subcutaneously with a tumor cell suspension of 30-60 mg in 0.3-0.5 ml of a nutrient medium per mouse [1]. Animal treatment was started 3-4 days after tumor implantation. The new drug and Xeloda were administered orally once a day for 10 days in the doses indicated above; other cytostatics were administered intraperitoneally. Animals in the control groups received an adequate volume of the solvent on the days of drug administration. Animals were sacrificed no earlier than 7 days after the last administration of the drug using humane methods of working with laboratory animals. Animal body weight was determined before administration and at the end of the experiment. To study the dynamics of tumor growth in mice and rats of the treated and control groups, the tumor volume was measured in 3 projections at the beginning of the experiment and then every 5 days until sacrifice. Tumor growth inhibition was calculated using formulas [1] for the volume (V) and mass (M) of the removed tumor. The tolerability of the treatment was judged by the death of mice; for an indirect assessment of possible hematotoxicity, the spleen mass and some hematological indices were determined in dead and sacrificed mice. The data obtained were statistically processed using the Student-Fisher method, as applied to experimental

studies [ Lakin G.F., 1973] as modified by M.D. Mashkovsky. The results were considered reliable if $p \leq 0.05$.

## RESULTS AND DISCUSSION

In the experiment with the treatment of the tumor Sarcoma 180 (Table 1) a new drug colchiprit-neo at a single dose of 100 mg/kg (total dose 1000 mg/kg) was more effective (92/90%) than xeloda (65/62%), doxorubicin (88/90%) and

**Table 1.** Antitumor activity of drugs on strain C -180 (early period)
(treatment with 2 days after tumor transplantation: 10 injections of substances, slaughter on the 2nd day)

| Groups animals, doses (mg/kg) and quantity introductions | Quantity here you go nyh | Weight stomach nykh to experience, G | Animal mass after experience, G | Weight tumors, G | Tumor volume, (a x b x c)cm | | | % TPO | | Weight village - eyes, G | Hemoglob | Erythocytosis | Leukoc |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 5 day | 10 Day | 20 day | V | M | | | | |
| 1. Control | 6 | 22.3 ± 0.8 | 24.0 ± 0.8 | 2.1 ± 0.3 | 0.04 ± 0.01 | 0.7 ± 0.1 | 2.6 ± 0.3 | | | 318 ± 29 | 117± 1 | 4.4±0.3 | 7.5 ± 3.5 |
| 2. K -20 Perrault (100-10-kr) | 4 | 24.5 ± 1.8 | 27.7 ± 2.6 | 0.2 ± 0.1* | 0.06+ 0.04 | 0.3 ± 0.08 | 0.21± 0.08* | 92 | 90 | 350 ± 57.7 | 101 ± 1 | 3.4 ± 0.03 | 6.6 ± 2.6 |
| 3. Xnloda (1200-10-cr) | 4 | 24.5+ 0.9 | 26.8 ± 1.1 | 1.3+0.21 * | 0.2+0 .07 | 0.8+0 .12 | 0.9 ±0 .14 * | 65 | 62 | 281+22 | 102+4 | 3.3+0 .03 | 4.1+1 .9 |
| 4. Doxorubicin | 4 | 26.0 ± 1.4 | 24.0 ± 0.8 | 0.2+0.05 * | 0.3+0 .05 | 0.2+0 .009 | 0.3 ± 0.2 * | 88 | 90 | 230+10 | 104+ 6 | 3.5+04 15 | 4.7+0 .2 |
| 5. Cisplatin | 4 | 33.7+2.3 | 29.3 ± 2.2 | 0.3+0.08 * | 0.3 ± 0. | 0.4 ± 0.11 | 0.3 +0 .080* | 82 | 86 | 227+8 | 98+2 | 3.3+04 03 | 4.1+0 .7 |

Note: in treatment groups n = 4, in control n = 6; * differences are statistically significant compared to control at $P \leq 0.05$.

Cisplatin (82/86%). Under the influence of colchiprit-neo no side effects were observed, except for a decrease in hematopoietic indices: the level of leukocytes by 12 %, the level of erythrocytes by 22% and hemoglobin by 3% compared to the control. Xeloda did not reduce body weight, reduced spleen weight by 12% and, comparable to colchiprit-neo, reduced hematopoietic indices, more significantly the level of leukocytes - by 45%.

Doxorubicin and cisplatin were less well tolerated by animals, which was manifested in a decrease in body weight, a decrease in spleen weight by 27-28% compared to the

control, and a decrease in hematopoietic indices: hemoglobin by 13 and 11%, respectively, the level of erythrocytes by 20 and 27%, the level of leukocytes by 37% and 45%.

Thus, the comparison of the action of colchiprit neo with three drugs showed that the activity of colchiprit - neo in comparison with doxorubicin and taxol is higher by 4-10%, the activity of xeloda is higher by 27%, however, colchiprit-neo, in addition, revealed such advantages as a smaller decrease in side effects, such as the effect on the mass of the spleen and spleen and a smaller decrease in hematopoietic indices.

in the treatment of mice with the esr strain (table 2), the p- reparat colchiprit-neo in a single dose of 100 mg/kg was compared with such drugs as taxol and etoposide. Colchiprit-neo was administered orally at a dose of 100 mg/kg and suppressed tumor growth by 97/94 %, with 25% tumor regression. The drug did not reduce the body and spleen weight of mice and the level of leukocytes, compared with the control group. In the experimental groups with intraperitoneal application of etoposide and taxol, their activity was 84/84 and 88/81%, respectively, both drugs caused 25% regression. In animals of these groups (3rd and 4th), the body and spleen weight did not decrease, but the level of leukocytes decreased by 28-30%.

**Table 2.** Antitumor activity of the drug colchiprit -neo (K-20) in comparison with xeloda, taxol and etoposide on the ESR strain
(treatment from 4 days after tumor transplantation: 10 injections of substances, slaughter on day 2 (1)

| Groups Animals | Dose (mg/kg), route of administration | Animal weight (g) | | Weight Spleen (G) | Volume Tumors ($cm^3$) | Weight Tumors (G) | Leukocytes | % slows down - Nia | | % regression | Leukoc |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Before experience | After experience | | | | | By volume | By weight | | |
| 1.Control Phys.r -r | | 30,0 ± 1,3 | 31.5 ± 1.2 | 0.3 ± 0.022 | 3.2F ± 0.4 | 3.1 ± 0.3 | 4.2 ± 0.2 | | | | 4.2 ± 0.2 |
| 2. K-20 | 100 Per " os | 27.8 ± 1 , 03 | 30.3 ± 1.1 | 0.4 ± 0.019 | 0.1 ± 0.03 * | 0.2 ± 0.085 * | 4.2 ± 0.4 | 97 | 94 | 25 | 4.2 ± 0.4 |
| 3. Etoposide | 15 (in/br) | 26 , 5 ± 1 , 2 | 2 8 , 0 ± 1 ,0 8 | 0.4 ± 0.07 | 0 , 5 ± 0.17* | 0 , 5 ± 0.16* | 3.0 ± 0.5 | 84 | 84 | 25 | 3.0 ± 0.2 |
| 4. Taxol | 12(v/br) | 24.3 ± 0.8 | 24, 0 ± 1.6 | 0.4 ± 0.05 | 0,4 ± 0,14 * | 0.6 ± 0.22 * | 3.2 ± 0.2 | 88 | 81 | 25 | 3.2 ± 0.2 |

Note: in treatment groups n = 4, in control n = 6; * differences are statistically significant in comparison with control at $P \leq 0.05$.

As can be seen from the results, oral K-20 therapy causes both more significant antitumor activity and fewer side effects than the drugs used.

## CONCLUSION

**Fundamental Finding:** According to the study, oral colchiprit-neo has better antitumor activity than a number of widely used cytostatics, such as doxorubicin, cisplatin, taxol, etoposide, and the oral medication XELODA. Additionally, colchiprit-neo exhibits a better safety profile with negligible effects on hematopoietic indices and spleen weight. **Implication:** According to these results, colchiprit-neo may present a viable substitute for the cytotoxic treatments currently in use. By lowering the possibility of serious side effects that are frequently connected to traditional treatments, colchiprit-neo may enhance the quality of life for cancer patients undergoing treatment. **Limitation:** The use of animal models, which might not accurately represent the complexities of human cancer and treatment responses, is one of the study's limitations. Long-term safety and effectiveness data in a wider range of tumor types are also required. **Future Research:** Future investigations should focus on clinical trials to assess the efficacy of colchiprit-neo in people, explore its molecular mechanisms of action, and evaluate its long-term safety profile in diverse cancer types. Further study into its conjunction with other medicines could further boost its medicinal potential.

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