

The possibility of using phyto-collection in the complex therapy of malignant neoplasms

T.G. Razin¹, E.P. Zueva¹, S.V. Korepanov², S.G. Krylova¹, E.N. Amosova¹, K.A. Lopatina¹
(¹GU Research Institute of Pharmacology, TSC SB RAMS, Tomsk, ²Altai regional phytocenter "Alfit", g. Barnaul)

SUMMARY

In mice with Lewis lung carcinoma, inhibition of tumor growth by phytosanitary (chamomile, plantain, yarrow, licorice, bearberry, St. John's wort) and eleutherococcus extract was found, the possibility of increasing the effectiveness of cytostatic therapy was shown; a decrease in the severity of leukopenia caused by cyclophosphamide was noted.

Key words: transplanted tumors, cyclophosphamide, phyto-collection.

Introduction

Every year, about 500 thousand patients with a diagnosis of cervical cancer (P1PM) are registered in the world, of which more than 12 thousand are registered in Russia. This pathology ranks 7th in the structure of morbidity and mortality from malignant neoplasms. Combined radiation therapy is still one of the main methods of cervical cancer treatment. The results of treatment, due to the relatively slow metastasis and high radiosensitivity of tumor cells, look better than those of other localizations. Thus, the five-year survival rate at stage I of the disease is close to 100%, at stage II it is 85% and at stage III - 68-72% [1]. However, concomitant radiation damage in a number of patients leads to a decrease in the quality of life, sometimes to disability and even death [12, 18, 19, 20, 21].

The use of modern antitumor drugs, which are a powerful stress factor, further aggravates the already existing depletion of the body's resistance system, as a result of which the metastasis process is activated [2, 3]. In addition, both radiation and chemotherapy refer to effects that disrupt the balance of immunity, causing toxic aplasia of hematopoiesis [4]. New concomitant diseases are added and existing concomitant diseases are aggravated.

Therefore, it is urgent to search for drugs that reduce the toxic manifestations of specific tumor treatment. In this case, it is necessary that there is no stimulating effect of such agents on the development of the tumor process. For the prevention and treatment of radiation proctitis, cystitis, vaginitis, the Altai regional phytocenter "Alfit" proposed a collection of pharmacopoeial plants: chamomile, plantain, St. John's wort, yarrow, licorice and bearberry, taken in equal proportions, crushed and shaved. Additionally, the pharmacy extract of Eleutherococcus is recommended as a mild immunomodulator in combination with phyto-collection. Since this complex is supposed to be prescribed before treatment, during treatment and for 3 months as rehabilitation after irradiation, we considered it expedient to test its effect on experimental animals (mice). First of all, to test its effect on tumor growth and development. In the medical environment, including among oncologists, there is an opinion about the possible stimulating effect of phytotherapy, in particular adaptogens, on the tumor process.

Material and methods

The experiments were carried out on 83 female mice of the C57B1 / 6 line with Lewis lung carcinoma (3LL) and melanoma B-16 (B-16) weighing 20 g at the age of 3 months, kept on the usual vivarium regimen. Tumors were grafted according to generally accepted methods [5]. Treatment with phyto-harvest (chamomile, plantain, St. John's wort, yarrow, licorice, bearberry) (LLC "Pharmzavod" Galen", Barnaul) was started from 7 days after transplantation of 3LL and B-16, continuing for 12 days. Phyto-collection was administered to mice by gavage in the stomach, in distilled water at a dose of 100 mg / kg. For carrying out cytostatic therapy, we used cyclophosphamide (CP), manufactured by the industry (JSC "Biochemist", Saransk) in the form of a sterile powder placed in hermetically sealed 0.2 g vials. Cytostatic was injected once intramuscularly at a dose of 125 mg / kg to mice with 3LL and B-16 - for 13-12 days after tumor transplantation. Control animals received equivalent volumes of solvent on the days of drug administration.

At the end of the experiments, the mice were sacrificed following the "Rules for working with laboratory

animals ". The volume and mass of the primary tumor, the mass of the lungs with metastases were determined, the number and area of metastases in the lungs were calculated, the inhibition of tumor growth (TPO,%), the frequency of metastasis, the index of inhibition of metastasis (IMI,%) were calculated [5, 6]. In addition, for 3 days. after the introduction of CP, the number of leukocytes in the peripheral blood of mice was counted. The results were processed using nonparametric Wilcoxon-Mann-Whitney tests and Fisher's exact method [7].

RESULTS AND ITS DISCUSSION

The administration of CP for the treatment of mice with 3LL in the used regimen did not affect the growth of the primary tumor node: its mass was at the level of the control value. Under the influence of cytostatics, inhibition of the process of tumor dissemination was observed: the number of metastases decreased by 7.2 times, and their area - by 14.7 times compared with the control data ($P < 0.01$), the index of inhibition of metastasis was 88%, metastatic nodes decreased by 1.6 times (Table 1). The isolated use of phyto-collection in combination with eleutherococcus extract led to a decrease in the 3LL mass compared to the control (by 1.2 times, $P < 0.05$). At the same time, there was a tendency to a decrease in such indicators of the dissemination process as the number (1.9 times) and area (2.5 times) of metastases in the lungs, the index of inhibition of metastasis in this group of mice was 46%, the lung weight decreased by 1.3 times (Table 1). Against the background of the absence of the effect of cytostatic agents on the primary tumor and the frequency of metastasis when using phyto-collection and eleutherococcus extract in combination with CP, the weight of 3LL was significantly less the control value, and the number of mice with metastatic lesions significantly decreased relative to the control and amounted to 78% (Table 1). In mice receiving combination therapy, the number and 8 times the area of lung metastases decreased by 1.7 times compared with these data in mice treated with CF alone, but these changes were in the nature of a trend. It should be noted that in animals receiving combined treatment, the mass of lungs with metastases was less and with a high level of significance ($P < 0, 01$) differed from this indicator in mice treated with CP only. Integral indicator of the development of the dissemination process - the index of inhibition of metastasis - in this group of animals was the highest and amounted to 94% (table 1).

Table 1

The influence of herbal collection (chamomile, plantain, yarrow, licorice, bearberry, St. John's wort) and Eleutherococcus extract on the development of 3LL in female C57BL / 6 mice and efficacy treatment of CF

Группа наблюдения, доза препарата (количество мышей)	Масса опухоли ($X \pm m$), г	Торможение роста опухоли, %	Частота метастазирования, %	Количество метастазов на 1мышь ($X \pm m$)	Площадь метастазов на 1 мышь ($X \pm m$), мм ²	Масса легких ($X \pm m$), мг	ИИМ, %
1. Контроль (8)	5,58 ± 0,36	-	100	46,88 ± 11,92	105,19 ± 40,58	331,88 ± 41,52	-
2. ЦФ 125 мг/кг х 1 (10)	5,08 ± 0,36	9	90	6,50 ± 2,36 1-2 P < 0,01	7,16 ± 4,20 1-2 P < 0,01	212,30 ± 8,14 1-2 P < 0,01	88
3. Фитосбор 100 мг/кг + элеутерококк 5 мл/кг х 12 (10)	4,56 ± 0,25 1-3 P < 0,05	18	100	25,10 ± 4,05	41,73 ± 13,57	250,60 ± 22,96	46
4. ЦФ + фито-сбор 100 мг/кг + элеутерококк 5 мл/кг х 12 (9)	4,61 ± 0,34 1-4 P < 0,05	17	78 1-4 P < 0,005	3,78 ± 0,97 1-4 P < 0,01	0,90 ± 0,32 1-4 P < 0,01	184,78 ± 4,41 2-4 P < 0,01	94

Note: in this table and below, before the significance level P, the numbers of the compared groups are indicated.

Under the influence of a cytostatic, the number of leukocytes in the peripheral blood of animals decreased 9.5 times compared with the control ($P < 0.01$). With the isolated appointment of phyto-collection and eleutherococcus extract to mice with 3LL, a decrease in the severity of leukocytosis that occurs during tumor development was found: the number of white blood cells decreased by 1.3 times ($P < 0.01$) and approached the norm. It should be especially noted that the combined appointment of phyto-collection and eleutherococcus extract with CP led to a significant increase (2.5 times, $P < 0.01$) in the number of leukocytes in

peripheral blood in comparison with their amount in animals treated with one cytostatic agent (Table 2).

In an experiment on female mice of the C57BL / 6 line, the use of CP led to a significant inhibition of the growth of melanoma B-16: the mass of the primary tumor was 1.4 times less than the control level. However, the cytostatic did not have a significant inhibitory effect on the process of tumor dissemination (Table 3).

The use of phyto-collection and eleutherococcus extract in combination with CP did not significantly change the effectiveness of antitumor therapy. At the same time, there was a tendency towards a decrease in the mass of the primary tumor node, the number of metastatic nodes in the lungs (1.4 times) and the area of metastatic lesions (2.1 times) compared with these indicators in mice treated with a cytostatic (table. 3). If after the introduction of cyclophosphamide the metastasis inhibition index was 6%, then the combined use of a cytostatic and herbal preparations increased it to 32% (Table 3). With the isolated introduction of phyto-collection and eleutherococcus extract into mice, the tendency to a decrease in such indicators of the dissemination process as the amount (by 1.4 times) and area (by 2,

table 2

The content of leukocytes in the peripheral blood of female mice of the C57BL / 6 line with 3LL after therapy with CP, phyto-collection (chamomile, plantain, yarrow, licorice, bearberry, St. John's wort) and Eleutherococcus extract

Группа наблюдения (количество животных)	Количество лейкоцитов на 3 сут после введения ЦФ ($X \pm m$), Г/л
1. Контроль (6)	18,00 \pm 0,66
2. ЦФ (6)	1,90 \pm 0,09 1-2 P < 0,01
3. Фитосбор + экстракт элеутерококка (6)	13,43 \pm 0,42 1-2 P < 0,01
4. ЦФ + фитосбор + экс- тракт элеутерококка (6)	4,77 \pm 0,45 2-4 P < 0,01

Table 3

Effect of phyto-collection (chamomile, plantain, yarrow, licorice, bearberry, St. John's wort) and eleutherococcus extract on the development of B-16 melanoma in female C57BL / 6 mice and the effectiveness of CF treatment

Группа наблюдения, доза препарата (количество животных)	Масса опухоли ($X \pm m$), г	Тормо- жение роста опухоли, %	Частота метаста- зирова- ния, %	Количество метастазов на 1 мышь ($X \pm m$)	Площадь метастазов на 1 мышь ($X \pm m$), мм ²	Масса легких ($X \pm m$), мг	ИИМ, %
1. Контроль (11)	5,33 \pm 0,21	-	45	3,45 \pm 2,13	0,68 \pm 0,53	160,09 \pm 0,17	-
2. ЦФ 125 мг/кг x 1 (14)	3,78 \pm 0,17 1-2 P < 0,01	29	64	2,29 \pm 0,74	0,25 \pm 0,11	190,14 \pm 5,64	6
3. Фитосбор 100 мг/кг + экстракт элеутерококка 5 мл/кг x 12 (10)	5,70 \pm 0,23	+7	40	1,80 \pm 0,18	0,24 \pm 0,13	158,80 \pm 5,73	54
4. ЦФ + фитосбор 100 мг/кг + экстракт элеутерококка 5 мл/кг x 12 (11)	3,57 \pm 0,16 1-4 P < 0,01	33	64	1,64 \pm 0,56	0,12 \pm 0,04	212,00 \pm 7,52 1-4 P < 0,01	32

Thus, the appointment of mice with 3LL phyto-collection (chamomile, plantain, yarrow, licorice, bearberry, St. John's wort) and eleutherococcus extract inhibits tumor growth, which leads to a natural decrease in the severity of leukocytosis; at the same time, a tendency towards inhibition of the process of metastasis was revealed. The combined use of herbal and eleutherococcus extract with CP, which had no effect on the primary tumor, leads to a decrease in its mass. The use of this treatment regimen reduces the incidence of 3LL metastasis, which was not observed in mice treated with cytostatic alone; the weight of the lungs with metastatic nodes is significantly reduced, a tendency was also found

to a decrease in such indicators of the dissemination process as the number and area of metastases. The ability of the studied herbal remedies to reduce the severity of leukopenia that occurs after the administration of CP to animals is essential. When using phyto-collection and eleutherococcus extract for the treatment of female mice of the C57BL / 6 line with B-16 melanoma, a tendency to inhibition of tumor growth and metastases was revealed both when applied alone and in combination with CP. The mechanism of action of the studied herbal collection is determined by its constituent medicinal plants. So, in the experiment it was revealed that plantain juice, having a moderate antitumor activity, has a more significant inhibitory effect on the process of tumor metastasis, increases the effectiveness of chemotherapy, which is consistent with the literature data on its use by traditional medicine for the treatment of lung and stomach cancer [11, 16]. A decrease in the hemato and immunosuppressive effect of chemotherapy with the plantain drug was found [15]. It was shown that the ability of this plant to reduce the toxic effect of cytostatics extends to other actively proliferating tissues of the body - its protective effect on the mucous membrane of the small intestine of mice with Ehrlich's adenocarcinoma damaged by the administration of 5-fluorouracil and rubomycin was found. The plantain drug, by stimulating proliferation processes, normalizes the differentiation and migration of epithelial cells, causing an accelerated restoration of the stationary state of the intestinal epithelium [13]. A decrease in the hemato and immunosuppressive effect of chemotherapy with the plantain drug was found [15]. It was shown that the ability of this plant to reduce the toxic effect of cytostatics extends to other actively proliferating tissues of the body - its protective effect on the mucous membrane of the small intestine of mice with Ehrlich's adenocarcinoma damaged by the administration of 5-fluorouracil and rubomycin was found. The plantain drug, by stimulating proliferation processes, normalizes the differentiation and migration of epithelial cells, causing an accelerated restoration of the stationary state of the intestinal epithelium [13]. A decrease in the hemato and immunosuppressive effect of chemotherapy with the plantain drug was found [15]. It was shown that the ability of this plant to reduce the toxic effect of cytostatics extends to other actively proliferating tissues of the body - its protective effect on the mucous membrane of the small intestine of mice with Ehrlich's adenocarcinoma damaged by the administration of 5-fluorouracil and rubomycin was found. The plantain drug, by stimulating proliferation processes, normalizes the differentiation and migration of epithelial cells, causing an accelerated restoration of the stationary state of the intestinal epithelium [13]. that the ability of this plant to reduce the toxic effect of cytostatics extends to other actively proliferating tissues of the body - its protective effect on the mucous membrane of the small intestine of mice with Ehrlich's adenocarcinoma damaged by the administration of 5-fluorouracil and rubomycin was found. The plantain drug, by stimulating proliferation processes, normalizes the differentiation and migration of epithelial cells, causing an accelerated restoration of the stationary state of the intestinal epithelium [13]. that the ability of this plant to reduce the toxic effect of cytostatics extends to other actively proliferating tissues of the body - its protective effect on the mucous membrane of the small intestine of mice with Ehrlich's adenocarcinoma damaged by the administration of 5-fluorouracil and rubomycin was found. The plantain drug, by stimulating proliferation processes, normalizes the differentiation and migration of epithelial cells, causing an accelerated restoration of the stationary state of the intestinal epithelium [13].

In experiments on animals, inhibition of tumor development and an increase in the effectiveness of cytostatic treatment with licorice were found [23]. It is known that the extract potentiates the antitumor and antimetastatic effect of radiotherapy: its administration to animals after irradiation of the tumor node enhances tumor regression and decreases the average growth rate during the recurrence period, and the radioprotective effect of the extract is due to its stimulating effect on the proliferation of hematopoietic cells [14]. An acceleration of the metabolism of stem cells of the red bone marrow sprout and an increase in the resistance of the animal organism to stress effects under the influence of licorice root extract [9] was found, its antioxidant activity was shown: against the background of CP therapy in mice with P-388, this drug reduces the parameters of lipid peroxidation [22] ... There is evidence that the immunomodulatory effect of licorice extract can be used to correct secondary immunodeficiencies caused by anticancer drugs [24]. The hemostimulating properties of licorice are due to the glycyram in the roots, which contains two residues of D-glucuronic acid in the structure of the molecule: its activating effect on the function of adhesive elements of the hematopoietic microenvironment has been shown [17]. The experiment revealed that yarrow increases the effectiveness of chemotherapy. The combined use of chamomile, St. John's wort and yarrow enhances the anti-inflammatory, antispasmodic, wound-healing effect of each plant [25], which also contributes to the ability of phyto-collection to reduce the toxic effect of specific tumor treatment. Because,

conclusions

1. In an experiment on mice, the ability of phyto-collection introduced together with extract of Eleutherococcus, inhibit the growth of Lewis lung carcinoma.
2. On animals with lung carcinoma Lewis revealed an increase in the effectiveness of treatment cyclophosphamide herbal collection and eleutherococcus extract.
3. Phyto-collection and eleutherococcus extract reduced the severity of peripheral blood leukopenia mice with Lewis lung carcinoma.

Literature

1. Chissov V.I., Daryalova SL. Selected Lectures on Clinical Oncology. - M., 2000 .-- 735 p.
2. Balitskiy K.P., Shmalko Yu.P. Stress and metastasis of malignant tumors. - L., 1987. - 248 p.
3. Katoh C, Kitajima S, Saga Y et al. Assessment of quantitative dualparameter flow cytometric analysis for the evaluation of testicular toxicity using cyclophosphamide- and ethinylestradiol - treated rats // J. Toxicol Sci. - 2002. - Vol. 21. - No. 2. - P.87-96.
4. Ptushkin V.V. Improvement of methods of supportive therapy during

cytostatic treatment // *Modern Oncology*. - 2002. - T.4. - No. 2. - P. 28–30.

5. Sofina ZP, Syrkin A.B., Goldin A., Klein A. Experimental evaluation of antitumor drugs in the USSR and the USA. - M.: Medicine, 1980. -- 296 p.

6. Arkhipov S.A., Juncker V.M. Change in the intensity of metastasis in the lungs of transplanted of tumors in mice depending on the size of the inoculation dose of tumor cells // *Research on induction and metastasis of tumors in experimental animals*. - Novosibirsk, 1984. - S. 14–32.

7. Lakin G.F. *Biometrics*. - M.: Higher school, 1980. -- 293 p.

9. Adamyan Ts.I., Gevorkyan E.S., Minosyan SM. et al. Influence of licorice root on indicators peripheral blood in the dynamics of vibration impact // *Byull. experimental biol. and medicine*. - 2005. - T. 140. - No. 8. - P.164–168.

10. Arkhipov S.A., Juncker V.M. Change in the intensity of metastasis in the lungs of transplanted tumors of mice depending on the size of the inoculation dose of tumor cells // *Research on induction and metastasis of tumors in experimental animals*. - Novosibirsk, 1984. - P.14–32.

11. Balitsky K.P., Vorontsova A.L. *Medicinal plants and cancer*. - Kiev, 1982. -- 376 p.

12. Bardychi M.S., Tsyb A.F. *Local radiation damage*. - Moscow, - Medicine, 1985. - S. 203-214.

13. Borovskaya T.G., Fomina T.I., Yaremenko K.V. Reducing the toxic effect of rubomycin on small intestine of mice with transplanted tumor using rhodiola extract // *Antibiotics and chemotherapy*. - 1988. - No. 8. - P. 615–616.

14. Butorin I.Yu. Radiomodifying activity of licorice root extract during radiotherapy experimental malignant tumors: Dis. ... Cand. honey. sciences. - Tomsk, 2001. -- 145 p.

15. Goldberg E. D., Zueva E. P. Preparations from medicinal plants in complex therapy malignant neoplasms. - Tomsk: TSU Publishing House, 2000. -- 129 p.

16. Goryaev M.I., Sharipova F.S. *Plants with antitumor activity*. - Alma-Ata, 1983. -- 174 p.

17. Zhdanov V.V., Lyubavina P.A., Kirienkova E.V., Dygai AM, Goldberg E.D. About mechanisms hemostimulating effect of glycyram // *Byull. experimental biol. and medicine*. - 1997. - T.123. - No. 5. - P.555–559.

18. Kann D.V., Pronin V.I. *Urological complications in the treatment of pelvic cancer*. - M: Medicine, 1988. - S. 111-140.

19. Kiseleva E.S., Goldobenko G.V., Kanaev SV. *Management. Radiation therapy for malignant tumors*. - M: Medicine, 1996, - C. 439.

20. Maryina L.L., Chekhonadsky V.N., Nechushkin M.I., Kiseleva M.V. *Cancer of the cervix and body of the uterus (radiation therapy)*. - Moscow, - Publishing Center "Ventani-Graf", - 2004. - P. 240–241.

21. Pavlov A.S., Kostromina V.N. *Cervical cancer (radiation therapy)*. - M: Medicine, 1983. - C. 154.

22. Pavlova SI., Sergeev AV, Uteshev BS *Antioxidant properties of licorice root extract on against the background of cytostatic treatment of experimental tumors // Russian Biotherapeutic Journal*. - 2004. - No. 2. - P.29.

23. Razina T.G., Zueva E.P., Amosova E.N. The role of biologically active substances in medicinal plants in increasing the efficiency of cytostatic therapy of transplanted tumors // *Byull. experimental biol. and medicine*, 2005. - App. 1. - P. 35–41.

24. Sergeev A.V., Kabatskaya G.I., Karaseva L.I. and others. *Immunopharmacology of drugs "Kaskarutol" and "Licorice" // Russian Biotherapeutic Journal*, 2004. - No. 2. - P. 9.

25. Sokolov S.Ya. *Herbal medicine and phytopharmacology (a guide for doctors)*. - M., 2000. -- 970 p.

26. Yaremenko K.V. *Natural remedies for cancer*. - SPb, 2001. -- 160 p.

Author's address

Ph.D. Korepanov S.V.

Altai regional phytocenter "Alfit"

656011, Barnaul, st. Matrosova, 13

The possibility of using phyto-collection in the complex therapy of malignant neoplasms / T.G. Razin, E.P. Zueva, S.V. Korepanov, S.G. Krylova, E.N. Amosov, K.A. Lopatina // Traditional medicine. - 2009. - No. 3 (18). - S. 45-49.

[To favorites](#)