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An Investigation of Antigenotoxic Properties of Plant Extracts of *Chelidonium majus* L., *Plantago major* L. and *Tussilago farfara* L.

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Abstract—The antigenotoxic properties of the sap from three medicinal plants, the greater celandine (*Chelidonium majus* L.), the greater plantain (*Plantago major* L.), and coltsfoot (*Tussilago farfara* L.), were studied using two bacterial test systems (SOS chromotest and Rec assay). It was determined using the combined effect of the plant sap and model genotoxicants on the cells of test strains that the plant sap of the greater celandine reveals a dismutagenic effect decreasing the genotoxic effect of nalidixic acid in the SOS chromotest and furacilin in the Rec assay. The plants sap of the greater celandine and coltsfoot (in 1 : 10 and 1 : 100 dilutions) demonstrated a bioantimutagenic effect in the SOS chromotest because pre-incubation of the *E. coli* PQ37 cells test strain with the sap of these plants resulted in a significant decrease of the genotoxic effect of nalidixic acid. The antigenotoxic effect of the greater plantain sap was not statistically significant in both test systems. Possible mechanisms of determining the antigenotoxic properties of the plant sap from greater celandine and coltsfoot are discussed.

Keywords: plant sap, *Chelidonium majus* L., *Plantago major* L., *Tussilago farfara* L., antigenotoxic effect, SOS chromotest, Rec assay

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INTRODUCTION

At present, the biosphere is progressively accumulating chemical anthropogenic compounds, and many of them possess mutagenic properties (Bochkarev and Chebotarev, 1989). Therefore, search for antimutagens, i.e., synthetic and natural compounds that protect the genetic apparatus of somatic and human germ cells from damage, is required.

Antimutagens can be divided into two general groups: dismutagens and bioantimutagens (Poroshenko and Abilev, 1988). Dismutagens prevent DNA damage by physical and chemical interaction with a mutagen before they enter a cell. Bioantimutagens affect the processes occurring in an organism, such as metabolic activation and detoxication of the mutagen, its transport, and passing across the cell membranes and repair of damaged DNA.

During the past few years, interest in investigation of the antimutagenic activity of plant components related with the possibility of their application for prophylactic action and treatment of oncological and other diseases entailing higher sensitivity of the genome to damage has risen. The plants are a source of various bioactive compounds (vitamins, polysaccharides, saponins, polyphenols, terpenoids, isoflavonoids, indoles, etc.) possessing antioxidative, antimutagenic, anticarcinogenic, and immunomodulating properties (Craig, 1999; Santos-Cervantes et al., 2007).

The advantage of application of the plant drugs in medicine is determined their low toxicity, which is explained by the similar chemical composition of biologically active substances and a certain affinity of metabolism of the plant and animal cell (Kolomiets and Efimov, 2005).

Greater celandine (*Chelidonium majus* L.) is used in traditional and alternative medicine including homoeopathy, treatment of dermal diseases, essential hypertension, stenocardia, and diseases of the liver and stomach (Zuzuk et al., 2006; Taborska et al., 1995; Kim et al., 1997). Several researchers have determined that the plant extract from greater celandine possess anti-inflammatory (Lenfeld et al., 1981), antiviral (Kery et al., 1987), and antimicrobial activity (Colombo and Bosisi, 1996) and reduces the growth of malignant tumors (Panzer et al., 2000; Biswas et al., 2008).

The greater plantain (*Plantago major* L.) is one of most widespread and well-known medical plants. Infusions and extracts prepared from fresh leaves and the sap possess styptic, bacteriostatic, wound healing, expectorative, and hypotensive effects. In addition, aqueous and alcoholic extracts of leaves are an effective drug for difficult forms of stomach ulcers (Samuelsen, 2000; Olennikov et al., 2007).

Coltsfoot (*Tussilago farfara* L.) is a longstanding medical remedy against cough, and the tincture and decoction of leaves provide expectorative, emollient, antiinflammatory, antiseptic, disinfectant, and spasmolytic effects. Leaves of coltsfoot are used as decoctions and infusions in folk medicine for treatment of acute and chronic laryngitis, bronchitis, bronchial asthma, multiple bronchiectasis, and inflammatory diseases of the gastrointestinal tract and urinary tract. Sometimes the sap from fresh leaves is proposed against tuberculosis and prolonged rhinitis (Kirpichnikov, 1981; Coltsfoot – *Tussilago farfara* L., 2010).

The aim of this study was investigation of the antigenotoxic properties of the sap from medical plants of the greater celandine (*Ch. majus* L.), greater plantain (*P. major* L.), and coltsfoot (*T. farfara* L.).

MATERIALS AND METHODS

Plant material. The sap from medical plants of the greater celandine (*Ch. majus* L.), greater plantain (*P. major* L.), and coltsfoot (*T. farfara* L.) were provided by Y.P. Abdrakhimova, Chair of Plant Physiology and Biotechnology, Kazan State University. The samples of the plant sap were obtained by following method: fresh leaves (5 g) were washed in running tap water and pounded. The raw mass was wrapped in gauze and squeezed between two sterile metal plates in vice grips. The sap was centrifuged at 4000 g/min for 10 min, and the supernatant was filtered using a Synpor membrane filter with the pore diameter 0.2 μm. Sterile plant sap was divided into Eppendorf tubes and stored at –20°C. The plant sap samples before investigation were diluted with sterile distilled water to the concentrations 1 : 10 and 1 : 100.

Chemical agents. Ampicillin, furacilin (OAO Sintez, Kurgan), 4-nitrophenyl phosphate and 4-nitrophenyl-β-D-galactopyranoside (Sigma–Aldrich, Germany), and nalidixic acid (Chinoin, Hungary) were used as chemical agents.

Strains of microorganisms. The strain *Escherichia coli* PQ37 with genotype F^- thr leu his-4 pyrD thi galE galK lacΔU169 srl300::Th10 rpoB rpsL uvrA rfa trp::Muc$^+$ sfi A::Mud(Ap, lac)cts, was received from the Institute of General Genetics (Moscow). Strains *E. coli* for Rec assay obtained from the Scientific Research Institute of the Ecology of Microorganisms, Ural Scientific Center, Russian Academy of Sciences (Perm), included the following:

WP2 *trpE65* – wild type;

polA *trpE65 sul malB polA* (no DNA-polymerase I activity);

uvrA *trpE65 sul, uvrA155* (disturbed excision repair);

recA *trpE65 recA* (disturbed postreplication repair, general recombination, SOS response of the cell) (Il'inskaya, 2005).

The antigenotoxic properties of samples of the plant sap samples were evaluated by SOS chromotest and Rec assay.

SOS chromotest was carried out according to the method described by Quilllardet and Hofnung (Quilllardet and Hofnung, 1985). Expression of the β-galactosidase gene *lacZ* in strain PQ 37 due to the "link" *sfi A::lac Z* is controlled by the promoter of the *sfi A* gene, one of components of SOS-regulone of *E. coli*. The index of SOS inducing activity of the studied agents in SOS chromotests is the activity of β-galactosidase, which was evaluated relative to the activity of the constitutive enzyme, i.e., alkaline phosphatase (Quilllardet and Hofnung, 1985). SOS chromotest is widely used for investigation of the genotoxic and antigenotoxic properties of different agents including plant extracts (Bouhlel et al., 2007).

In this study, the tests were carried out according to the following procedure: 18-hours culture of test strain was diluted by the fresh nutrient medium LB (Miller, 1976) with ampicillin (20 μg/ml) in the ratio 1 : 3 and precultivated at 37°C with aeration until an exponential growth phase. The bacterial suspension was diluted by the nutrient medium LB in the ratio 1 : 10 and separated into the tubes. Sterile distilled water was used as a negative control and nalidixic acid (60 μ)g/ml, which is a known inductor of SOS cell response, was used as a positive control. The plant sap samples and nalidixic acid for investigation of the dismutagenic effect were added simultaneously into the tubes with the cell culture *E. coli* PQ37. The bioantimutagenic effect was investigated by simultaneous addition of the plant saps and nalidixic acid after preliminary (for 18 h) treatment of the cells of *E. coli* PQ37 by the plant sap samples (100 μ]l per probe). Mixtures were incubated at 37°C for 2 h. Measurements for each dilution of the plant sap samples and negative and positive controls were carried out in three repeats.

The activity of β-galactosidase was determined according to the method described by Miller (Miller, 1976). Alkaline phosphatase activity was determined according to the method described by Quilllardet and Hofnung (Quilllardet and Hofnung, 1985). The quantity of the SOS response was evaluated by the IF index (induction factor of SOS response of a cell) according to the following formula (Quilllardet and Hofnung, 1985):

$$IF = R(O)/R(C),$$

where

R(O) = β-galactosidase in the experiment/Alkaline phosphatase activity in the experiment,

R(O) = β-galactosidase in the control/Alkaline phosphatase activity in the control.

The induction factor of cell SOS response IF > 2 evidences that the studied compound possesses the genotoxic effect (Mersch-Sundermann et al., 1991; Bouhlel et al., 2007). In our experiments, the induction factor of SOS response of a cell for the model

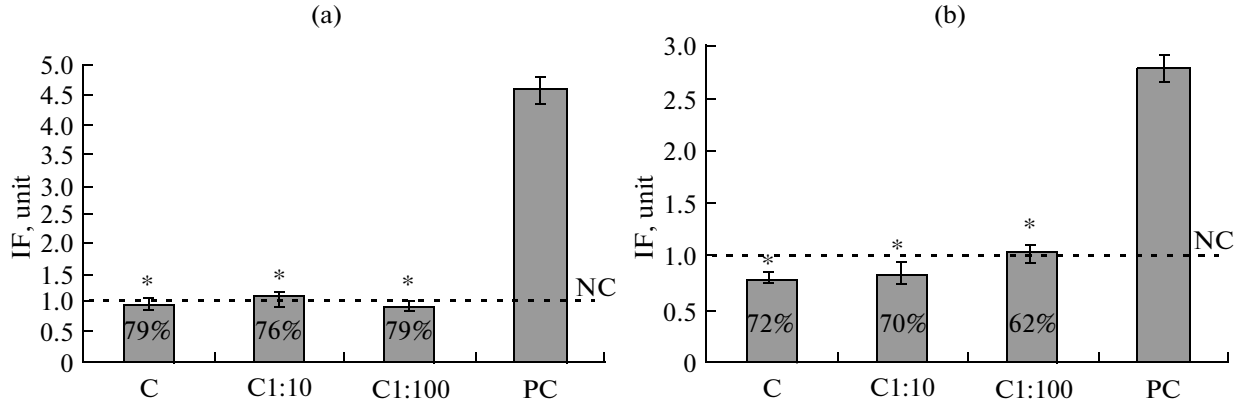

Fig. 1. Antigenotoxic effect of the plant sap of greater celandine *Ch. majus* L. in SOS chromotest. (a) Dismutagenic effect of sap from greater celandine plants, (b) bioantimutagenic effect of sap from greater celandine plants. (C) Sap from greater celandine and nalidixic acid, (C1 : 10) Sap from greater celandine in dilution 1 : 10 and nalidixic acid, (C1 : 100) sap from greater celandine in dilution 1 : 100 and nalidixic acid. NC (dotted line) is the negative control, PC is the positive control (nalidixic acid). %, index of antigenotoxic effect efficiency. * Significantly different from PC, $P \le 0.05$.

genotoxic agent nalidixic acid corresponded to criterion IF > 2.

The antigenotoxic effect of the plant sap samples in the SOS chromotest was evaluated according to the formula (Bouhlel et al., 2007)

$$\mathrm{AE}(\%) = 100 - \frac{\mathrm{IF}_1}{\mathrm{IF}_2} \times 100,$$

where IF_1 is the induction factor of SOS response in the presence of the mutagen and the target extract, and IF_2 is the induction factor of SOS response affected by the mutagen.

The Rec assay allows evaluation of the effect on DNA damage by the studied compound based on comparative analysis of the survival of test bacteria with normal and defective systems of DNA reparation (Slater et al., 1971; Leifer et al., 1981).

The culture of test strains was inoculated from slope agar to 5 ml of nutrient medium LB and incubated at 37°C for 18 h. Petri plates with the whole agar medium were inoculated by a culture of test bacteria. A sterile paper disk (d = 2 cm) was placed on the surface of the culture in the center of the plate. The dismutagenic activity of the plant sap samples was evaluated by 50 μl of furacilin solution and 50 μl of the plant sap in different dilutions placed on the disks.

Distilled water served as the negative control, and furacilin (500 μg/ml), as the positive. Plates were incubated for 24 h at 37°C, and the zone of growth inhibition of test bacteria around the disk, i.e., the distance from the edge of the paper disk to the edge of the growth suppression zone of test bacteria, was measured. The plant sap samples in every dilution and the negative and positive controls were tested in three repeats.

The antigenotoxic effect of plant saps in the Rec assay was determined according to the formula

$$\mathrm{AE}\ (\%) = 100 - \frac{X_a - X_b}{Y_a - Y_b} \times 100,$$

where X_a and X_b are the dimensions of growth inhibition zones around the disk in the strain with defect reparation (X_a) and the wild-type strain (X_b) with the combined effect of furacilin and plant sap, mm; Y_a and Y_b are the dimensions of growth inhibition zones around the disk in the strain with the reparation effect (Y_a) and the wild-type strain (Y_b) affected only by furacilin, mm.

Statistical data analysis was carried out by Students' t-test (Lakin, 1994). The data represented in this study are the average of three independent experiments ± σ (standard deviation). Differences between the data groups were significant at $P \le 0.05$.

RESULTS

Dismutagenic effect of the plant sap.

The dismutagenic properties of the sap of the medical plants greater celandine, greater plantain, and coltsfoot were investigated by SOS chromotest and Rec assay by a combined treatment of test bacteria by plant sap with the classic inductor of SOS response, nalidixic acid, and with the inductor of DNA damage by furacilin.

The results in Fig. 1a show that the plant sap of greater celandine possess a dismutagenic effect decreasing the genotoxicity of nalidixic acid with a combined effect on the cells of *E. coli* PQ37. The efficiency of the antigenotoxic influence of greater celandine sap and its dilutions 1 : 10 and 1 : 100 in the SOS chromotest is 79%, 76%, and 79%, respectively (Fig. 1a).

In contrast to greater celandine, the plant sap of greater plantain caused an insignificant decrease in the genotoxic effect of nalidixic acid and the highest dis-

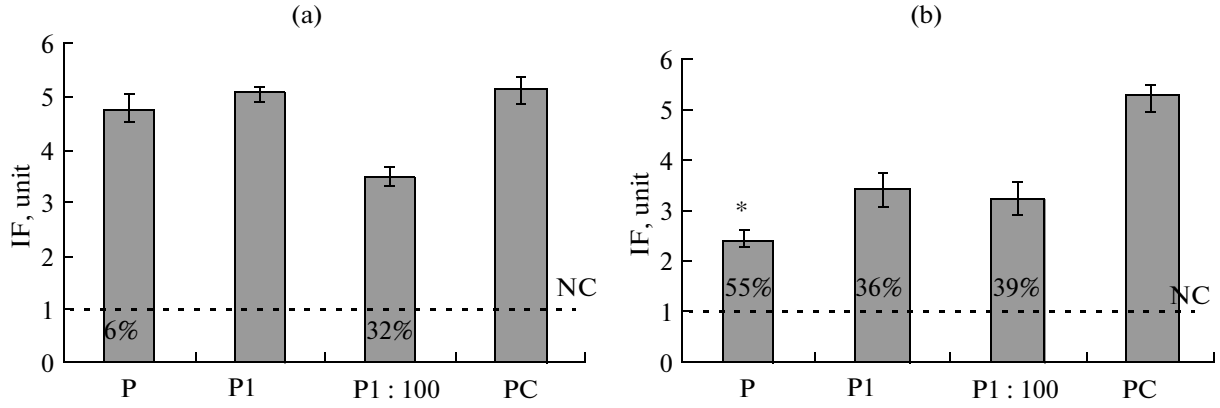

Fig. 2. Antigenotoxic effect of the plant sap from the greater plantain *Plantago major* L. in the SOS chromotest. (a) Dismutagenic effect of sap from greater plantain plants, (b) bioantimutagenic effect of sap from greater plantain plants. (P) sap from greater plantain and nalidixic acid, (P1 : 10) sap from the greater plantain in dilution 1:10 and nalidixic acid, (P1 : 100) sap from the greater plantain in dilution 1 : 100 and nalidixic acid. NC (dotted line) is negative control, PC is positive control (nalidixic acid). %, index of antigenotoxic effect efficiency. * Significantly different from PC, $P \le 0.05$.

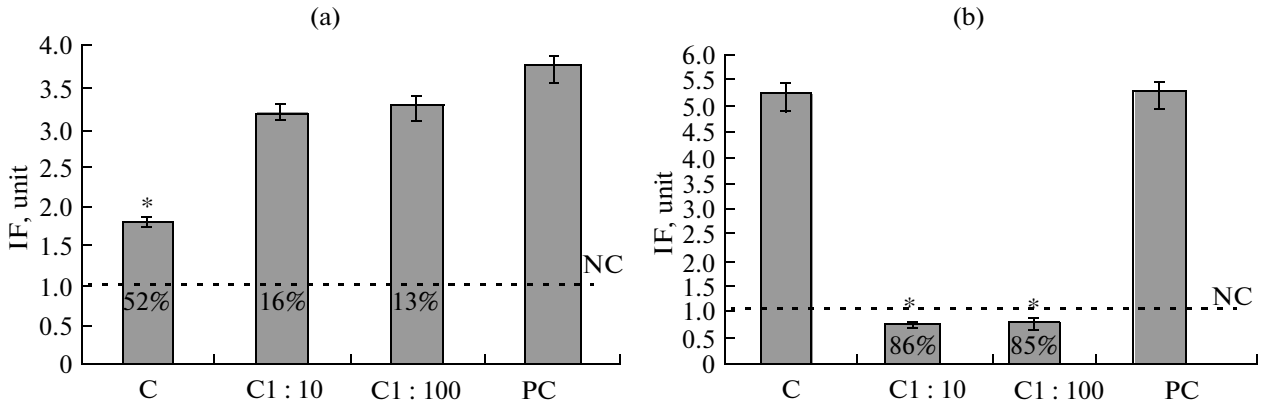

Fig. 3. Antigenotoxic effect of the plant sap from coltsfoot *Tussilago farfara* L. in SOS chromotest. (a) Dismutagenic effect of sap from coltsfoot plants, (b) bioantimutagenic effect of sap from coltsfoot plants. (C) Sap from coltsfoot and nalidixic acid, (C1 : 10) sap from coltsfoot in dilution 1 : 10 and nalidixic acid, (C1 : 100) sap from coltsfoot in dilution 1 : 100 and nalidixic acid. NC (dotted line) is negative control, PC is positive control (nalidixic acid). %, index of antigenotoxic effect efficiency. * Significantly different from PC, $P \le 0.05$.

mutagenic effect (32%) found at a dilution of plantain sap of 1:100 was statistically insignificant (Fig. 2a).

The plant sap of coltsfoot showed a dismutagenic effect and expressed as a decrease in the induction factor of SOS response of *E. coli* PQ37 cells by two times (Fig. 3a). In the next dilution of sap, a dismutagenic effect was not expressed and was 16 and 13% for sap dilutions 1 : 10 and 1 : 100, respectively (Fig. 3a).

Table 1 shows that the sap of greater celandine possesses a dismutagenic effect in the Rec assay. The highest effect was observed under the combined influence of furacilin and the sap of greater celandine on strain

Table 1. Evaluation of the antigenotoxic effect of greater celandine sap in Rec assay

	WP2	recA	polA	uvrA
Furacilin	1.5 ± 0.10	6.5 ± 0.52	5.5 ± 0.35	6.0 ± 0.54
Sap from greater celandine and furacilin	1.0 ± 0.08	5.5 ± 0.45(10%)	1.5 ± 0.12(88%)*	4.5 ± 0.38(23%)
Sap from greater celandine 1:10 and furacilin	1.3 ± 0.12	5.0 ± 0.37(26%)	1.7 ± 0.09(90%)*	3.2 ± 0.30(58%)*
Sap from greater celandine 1:100 and furacilin	0.5 ± 0.03	3.7 ± 0.21(36%)*	1.3 ± 0.11(80%)*	3.0 ± 0.22(45%)*

* Statistically reliable difference from positive control, $P \le 0.05$. Indexes of efficiency of the antigenotoxic effect are shown in brackets, %.

Table 2. Evaluation of antigenotoxic effect of greater plantain sap in Rec assay

	WP2	recA	poA	uvrA
Furacilin	1.7 ± 0.14	5.5 ± 0.48	5.5 ± 0.50	6.5 ± 0.52
Sap from greater plantain and furacilin	1.5 ± 0.12	5.0 ± 0.37(8%)	4.2 ± 0.28(29%)	5.8 ± 0.49(11%)
Sap from greater plantain 1:10 and furacilin	1.5 ± 0.09	5.2 ± 0.50(4%)	4.5 ± 0.34(22%)	6.0 ± 0.48(7%)
Sap from greater plantain 1:100 and furacilin	1.6 ± 0.15	5.0 ± 0.25(11%)	4.0 ± 0.30(36%)*	5.5 ± 0.37(19%)

* Statistically reliable difference from positive control, $P \leq 0.05$. Indexes of efficiency of the antigenotoxic effect are shown in brackets, %.

Table 3. Evaluation of antigenotoxic effect of coltsfoot sap in Rec assay

	WP2	recA	polA	uvrA
Furacilin	2.0 ± 0.16	5.0 ± 0.37	4.8 ± 0.22	5.0 ± 0.44
Sap from coltsfoot and furacilin	1.8 ± 0.09	4.5 ± 0.32(10%)	4.3 ± 0.24(11%)	4.5 ± 0.35(10%)
Sap from coltsfoot 1:10 and furacilin	2.0 ± 0.18	4.5 ± 0.28(17%)	4.5 ± 0.20(11%)	4.5 ± 0.29(17%)
Sap from coltsfoot 1:100 and furacilin	1.8 ± 0.11	4.3 ± 0.30(17%)	4.2 ± 0.33(15%)	4.3 ± 0.21(17%)

Note: Indexes of efficiency of the antigenotoxic effect are shown in brackets, %.

polA defected in DNA polymerase 1, which expressed an significant decrease of the genotoxic effect of furacilin (90%). Meantime, the expressed dismutagenic effect of greater celandine was not determined during tests on the strains uvrA and recA (Table 1).

The evaluation results of the dismutagenic effect of greater plantain in the Rec assay shown in Table 2 indicate that the sap of this plant reveals a weak dismutagenic effect on *E. coli* test strains compared with the sap of greater celandine. The plant sap of greater plantain showed a more significant effect on the strain polA (until 36% in dilution 1 : 100).

The differences in the dimensions of the inhibition zones on plates with normal and defective reparation bacteria were insignificant under the simultaneous influence of the plant sap of coltsfoot and furacilin on test strains *E. coli*. The value of the dismutagenic effect in this case did not exceed 17% (Table 3).

Bioantimutagenic effect of the plant sap.

Preliminary treatment of the cells of test strain *E. coli* PQ37 by the plant sap of greater celandine for 18 h resulted in total removal of the genotoxic effect of nalidixic acid. The induction factor of SOS response was 0.77–1.05 units, while IF in the positive control reached 2.8 units with the addition of nalidixic acid after preliminary incubation of the cells of the test bacteria with the sap of this plant in the studied spectrum of dilutions, which evidences the presence of bioantimutagenic properties in plant sap of *Ch. majus* L. (Fig. 1b).

The results in Fig. 2b show that preliminary incubation of the cells of test bacteria with greater plantain sap decreased the IF of SOS response by 1.6–2 times, although IF of the SOS response induced by nalidixic acid after preliminary incubation with greater plantain sap differed statistically significantly from IF of the positive control in only one case. The antigenotoxic effect of the sap of this plant both undiluted and diluted at 1 : 10 and 1 : 100 was 55, 36, and 39%, respectively.

It was determined during investigation of coltsfoot sap that dilution of sap results in an increase of its bioantimutagenic activity. The plant sap in dilutions of 1 : 10 and 1 : 100 decreased the IF of SOS response induced by nalidixic acid in the cells of *E. coli* PQ37 by 7.2 and 6.8 times, and the efficiency of the antigenotoxic effect reached 86% (Fig. 3b).

Thus, only the plant sap of greater celandine (*Ch. majus* L.) among the three medical plants studied demonstrated a significant dismutagenic effect in both tests and a bioantimutagenic effect in the SOS chromotest. Pre-incubation of the cells of the test strain *E. coli* PQ37 with coltsfoot sap in low doses resulted in decrease in the level of induced SOS response. The sap of greater plantain was not effective as a dismutagen and was less effective as a bioantimutagen in the SOS chromotest and weak dismutagen in the Rec assay.

DISCUSSION

There are several studies that evidence the anticarcinogenic effect of the plant extracts of greater celandine. Kim and Lee (Kim and Lee, 1997) determined that the plant extract of greater celandine inhibits development of stomach tumors. Very small doses of homeopathic preparations *Chelidonium 30* and *Chelidonium 200* showed a therapeutic effect on induced hepatocarcinogenesis in mice (Biswas and Khuda-Bukhsh, 2002). It was determined that extract of *Ch. majus* L. possesses a strong antioxidant effect and

inhibits proliferation of tumor cells (Nadova, 2008). Biswas and coauthors (Biswas et al., 2008) found that the extract of greater celandine possesses an anticlastogenic effect decreasing the frequency of chromosomal aberrations and the number of micronuclei in the cells of mouse marrow. It is known that greater celandine contains a wide variety of biologically active substances such as tannins, flavonoids, saponins, and vitamins A and C; organic acids (1.4–4.32%) are represented by chelidonic, citric, malic, ascorbic, and siccine acids. This plant is characterized by alkaloids (approximately 27 types) with a selective cytostatic effect on human tumor cells in vitro. An extract of the roots and plant leaves contains benzophenantridine alkaloids such as chelidonin, berberin, and others related to anticarcinogenic effects of the extracts from this plant (Barreto et al., 2003; Wolff and Knipling, 1993; Biswas et al., 2008).

The results of SOS chromotest and Rec assay of the plant sap from greater celandine evidence that the anticarcinogenic, anticlastogenic, and antimutagenic effects of this plant sap can be determined by the dismutagenic effect of its bioactive components. The data of the bioantimutagenic effect of greater celandine sap in the SOS chromotest with pre-incubation allow the supposition that the protective effect of biologically active plant compounds is related to the influence on the processes of DNA reparation. The efficiency of the antigenotoxic effect of greater celandine sap in the SOS chromotest without pre-incubation did not depend on the dose: dilution of the sap by 10 and 100 times did not change the effect. The efficiency of the antigenotoxic influence of sap is determined by a complex of substances that can include antioxidants and toxic and genotoxic compounds. Most likely, the different dose-dependent effect of components results in smoothing of the value of the antigenotoxic effect of diluted sap. A certain limitation of penetration of the sap component with the antigenotoxic effect into the bacterial cell is possible, which explains the absence of changes of the antigenotoxic effect value of sap depending on dose.

A significant dismutagenic effect of greater plantain sap in both the SOS chromotest and Rec assay was not determined. There are literature data showing that the extracts of this plant possess genotoxic activity. Basaran et al. (Basaran et al., 1996) determined that the extracts of *P. major* L. cause damage to human lymphocytes (DNA-comet method) although without mutagenic activity in the Ames test using the strains *Salmonella typhimurium* TA98 and TA100. An aqueous extract of greater plantain leaves induces high frequency of recombination in somatic cells of *Drosophila melanogaster* (Pimenta and Nepomuceno, 2005). Most likely, genotoxic effects are determined by toxic compounds of this plant such as nitrates and oxalic and erucic acids (Guil et al., 1997). Compounds such as proteins, hemicelluloses, photosynthetic pigments, alkaloids, tannins, phenolic acids, flavonoids, and derivatives of caffeic acid were determined in greater plantain plants during investigation of the composition of biologically active compounds (Olennikov et al., 2007). One of the important components of the plants from the *Plantago* family is flavonoids, in particular luteolin-7-7-*O*-β-glucoside, the presence of which reveals an anticarcinogenic effect on most species *Plantago* (Kawashty et al., 1994; Galvez et al., 2003; Richardson, 2001; Samuelsson, 2004).

It was determined that aqueous extracts of *Plantago lancelota* L. leaves decrease the mitotic index and frequency of chromosomal aberrations induced by H_2O_2 in the cells of the root meristem of *Allium cepa* (Celik and Aslanturk, 2006). Efimov and coauthors studying the antimutagenic activity of 41 medical plants from Siberia using a micronuclear test showed that the greater plantain belongs to plants with average anticlustogenic activity (Efimov et al., 2004). An extract of this plant decreased the number of micronuclei induced by X-ray radiation in erythrocytes of mouse peripheral blood from 4.8 to 2.95%. The data on the insufficient antigenotoxic effect of the plant sap of the greater plantain in bacterial test systems allow the supposition that the biological activity of antimutagenic components of *Plantago* plants (in contrast to genotoxic substances) is probably related to the regulatory influence on the processes of metabolism of mutagens in the organism.

A significant inhibitory effect of the sap of this plant induced by nalidixic acid in the cells of *E. coli* PQ37 was determined in the study of the bioantimutagenic properties of coltsfoot plant sap. It was noted that the bioantimutagenic activity of the sap appeared at its dilution. An increase in the efficiency of the bioprotector effect with a decrease of the dose was found during study of some biologically active substances in particular antioxidants (Savina et al., 2009).

It is known that leaves of coltsfoot contain bitter glycosides, saponins, carotenoids, gallic acid, malic acid, ascorbic acid, and tartaric acid, sitosterol, mucuses, tannins, traces of essential oils, mineral salts, and the polysaccharides inulin and dextrin (Kirpichnikov, 1981; Coltsfoot – *Tussilago farfara* L., 2010). It is known that inulin is a carbohydrate containing indigestible fructooligosaccharides which positively influences the development of some bacteria of the intestinal microflora and are considered a bifidogenous factor (Mitsuoka et al., 1987). Moreover, some studies showed that butyrate is synthesized during bacterial fermentation of inulin and possesses antitumor activity (Reddy et al., 1997; Valyshev, 2000). The dose of biologically active substances optimal for achievement antigenotoxic effect was achieved with a dilution of coltsfoot sap.

Thus, study of the antigenotoxic properties of the plant saps from greater celandine (*Chelidonium majus* L.), greater plantain (*Plantago major* L.), and coltsfoot (*Tussilago farfara* L.) in bacterial test systems identified a significant dismutagenic effect of greater celan-

dine in SOS chromotest and Rec assay and its bioantimutagenic effect in SOS chromotest, and a bioantimutagenic effect of coltsfoot sap in SOS chromotest. There are several notes in the literature on the antigenotoxic effect of different plant extracts and their single components in the SOS chromotest. Bouhlel et al. (Bouhlel et al., 2007) showed that extracts from leaves of *Acacia salicina* L. plants sufficiently decreased the genotoxic effect of nifuroxazide and promutagen benz[α]-pyrene. The ability to decrease the genotoxic effect of nifuroxazide was identified for essential oils extracted from *Pituranthos chloranthus* plants. Moreover, the studied samples of essential oils demonstrated significant antigenotoxic effect related to hydrogen peroxide on strains of *E. coli* PQ37 and PQ35 in the SOS chromotest (Neffati et al., 2009). Extracts from fruits of bael *Aegle marmelos* L. decreased the IF of the SOS response induced in the cells of test bacteria by hydrogen peroxide and aflatoxin B1 (Kaur et al., 2009). Fuentes et al. found antiradiation activity of the extracts from *Phyllanthus orbicularis* L., ground lemon *Cymbopogon citratus* L., and Caribbean pine *Pinus caribaea* L. on the genotoxic effect of γ-rays in SOS chromotest. Most researchers consider relation of antigenotoxic effect of extracts of different plants with antioxidant effect of the components of plant extracts.

The ability of the sap from greater celandine and coltsfoot plants to reduce genotoxicity of model mutagens may be determined by biologically active substances in the plants such as phenolic compounds, chlorophylls, vitamins, and other secondary metabolites (alkaloids and saponins) (Efimov et al., 2004; Craig, 1999; Martnez et al., 2003; Moura et al., 2007; Santos-Cervante et al., 2007). According to the data on investigation of bioantimutagenic activity of the plant sap, it can be supposed that the sap of greater celandine and coltsfoot either promote blockage of SOS signal induction or activate other systems of reparation promoting correction of damaged DNA.

Further research devoted to elucidation of certain components and mechanisms determining antimutagenic effects of these plants should contribute to strategic development of their rational application for creation of antimutagenic preparations.

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