UDC 615. 276. 2/4. 015. 44

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Research of the new myelostimulators among of herbal preparations, derived from plants growing in arid zone of Kazakhstan

Research of the new myelostimulators among of herbal preparations, derived from plants growing in arid zone of Kazakhstan under the following Identifier codes: Halostachys caspia (aqueous extract) – IES.SPP.401R, Holostachys caspia (50% water – ethanol extract) – IES.SPP.401R.SE, Sueda microphylla (aqueous extract) – SIE.SM.401R , Sueda microphilla (50% water – ethanol extract) – SIE.SM.401R.SE, Climacoptera obbtusifolia (70% water – ethanol extract) – $G.COE_X$, Climacoptera lanata (70% water – ethanol extract) -$G.CLE_X$, Climacoptera subcrassa (aqueous extract) -A.SKF, Climacoptera subcrassa (50% water – ethanol extract) -$A.CSE_X$. The highest myelostilating results were from compound SIE.SM.401R.SE.
Keywords: myelostimulator, herbal preparations, leucopoies, lymphopoies, myelopoies.

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Пиперидин туындылардың арасында жаңа миелостимулдаушы перапатарды іздеу

БИВ лабораторлық шифрмен анықтылатын β-циклодекстрин комплекс түрінде би- және моноциклдық пиперидин қосылыстарды зерттелген. Нәтижесінде ең жақсы лейкопоэзді стимулдайтың қосылыс БИВ-69 көрсетті. Қосылыстар БИВ-68 және БИВ-71 лимфопоэзды стимулдады. Ал миелопоэзді БИВ-69 және БИВ-71 қосылыстар белсендетті.
Түйін сөздер: би- және моноциклдық пиперидин қосылыстар, лейкопоэз, лимфопоэз, миелопоэз.

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Поиск новых миелостимуляторов среди растительных препаратов, полученных из растений, произрастающих в аридных зонах Казахстана

Проведен поиск новых миелостимуляторов среди растительных препаратов, полученных из растений, произрастающих в аридных зонах Казахстана под следующими шифрами: Halostachys caspia (водный экстракт) – IES.SPP.401R, Holostachys caspia (50% водно-спиртовой экстракт) – IES.SPP.401R.SE, Sueda microphylla (водный экстракт) – SIE.SM.401R , Sueda microphilla (50% водно-спиртовой экстракт) – SIE.SM.401R.SE, Climacoptera obbtusifolia (70% водно-спиртовой экстракт) – $G.COE_X$, Climacoptera lanata (70% водно-спиртовой экстракт) -$G.CLE_X$, Climacoptera subcrassa (водный экстракт) -A.SKF, Climacoptera subcrassa (50% водно-спиртовой экстракт) -$A.CSE_X$. Высокую миелостимулирующую активность показало соединение SIE.SM.401R.SE.
Ключевые слова: миелостимуляторы, растительные препараты, лейкопоэз, лимфопоэз, миелопоэз.

Currently in medical clinical practice using drugs with myelosuppressive effects. In particular, all cytotoxic agents, which are assessed in oncology practice, the anti-tubercular drugs (streptomycin tiacetazon, isoniazid, p -aminosalicylic acid, dimetilkarbazin), Shtorddart solution, trinitrotoluol, pesticides, especially organochlorines drugs, lindane (gamma – hexachlorocyclohexane) and DDT (di chlorodiphenyltrichloroethane) also cause severe pancytopenia. But the choice of effective drugs

myelostimulatores is very limited. Furthermore, myelostimulators are widely used in ophthalmology, surgery, cosmetics and biotechnology. Thus, pharmacological screening of drugs myelostimulive relevant today.

Materials and Methods

We used healthy adult animals – laboratory rats of both sexes, the age: 10-15 weeks, body weight: 210-280 g. Before and during the experiment in the control and experimental animals were kept under the same standard conditions and for a standard diet, for 6 animals per cage. Blood sampling was performed from the orbital vein of rats anesthetized with ether anesthesia weak at 09.00 am. A blood test was performed on a hematology analyzer for laboratory animals «Abacus junior vet» (made in Denmark, Diatron). Myelosuppressiv syndrome induced by intramuscular administration of cytostatic cyclophosphamide sodium in the dose 30 mg/kg of weight of an animal. Experimental groups of animals were administered compound at a dose of 10 mg/ml (solvent physiological solution) intramuscularly at a volume of 0.5 mL daily for 3 days, 3 days after the last administration was determined number of cells in the peripheral blood. Control animals were administered of the physiological solution. The compounds were investigated under the following Identifier codes: Halostachys caspia (aqueous extract) – IES. SPP.401R, Holostachys caspia (50% water – ethanol extract) – IES.SPP.401R.SE, Sueda microphylla (water extract) – SIE.SM.401R , Sueda microphilla (50% water – ethanol extract) – SIE.SM.401R.SE, Climacoptera obbtusifolia (70% water – ethanol extract) – $G.COE_X$, Climacoptera lanata (70% water – ethanol extract) -$G.CLE_X$, Climacoptera subcrassa (aqueous extract) -A.SKF, Climacoptera subcrassa (50% water – ethanol extract) -$A.CSE_X$ (table 1). The comparator was pantogematogen.

Table 1 – Active compound

Connection Identifier	Herb	Biological active compounds
IES.SPP.401R	Halostachys caspia (aqueous extract)	Flavonoids glycosides, carbohydrates, polysaccharides, amino and organic acids, vitamin C, saponins
IES.SPP.401R.SE	Halostachys caspia (50% water – ethanol extract)	Aglycones flavonoids, carbohydrates, polysaccharides, amino and organic acids, vitamin C, coumarins, alkaloid saponins.
SIE.SM.401R	Sueda microphylla (water extract)	Flavonoids glycosides, carbohydrates, polysaccharides, amino and organic acids, vitamin C, saponins
SIE.SM.401R.SE	Sueda microphylla (50% water – ethanol extract)	Aglycones flavonoids, carbohydrates, polysaccharides, amino, and organic acids, vitamin C, coumarins, alkaloid, saponins
$G.COE_X$	Climacoptera obtusifolia (70% water – ethanol extract)	Fenolacid, flavonoids, saponins, carbohydrates, amino acids
$G.CLE_X$	Climacoptera lanata (70% water – ethanol extract)	Fenolacid, flavonoids, saponins, carbohydrates, amino acids
A.SKF	Climacoptera subcrassa (aqueous extract)	Fenolacid, flavonoids, saponins, carbohydrates, amino acids
$A.CSE_X$	Climacoptera subcrassa (50% water – ethanol extract)	Fenolacid, flavonoids, saponins, carbohydrates, amino acids

Results and discussion

Already on the first day after administration of the cyclophosphamide sodium could be recorded of the immunosuppression with the defeat as leukocyte cells and red blood cells. For control of the level of destruction of hematopoietic pools was taken on the third day after the administration of an immunosuppressant. In the hemogramm was revealed that more suffered of the leukocyte pool. Overall leucocytical indicators with level of the intact animals $(9,15 \pm 1,36) \cdot 10^9$/L blood fell to $(2,371 \pm 0,16) \cdot 10^9$/L to 3.86 time ($P \leq 0,05$). In leucogramm absolute and relative indicators of the agranulocyte leukocytes and granulocyte leuko-

cytes were decreased. Among agranulocytes absolute values of lymphocytes with the values (5,46 ± 0,18) ·10^9/L blood fell to (1,60 ± 0,2) ·10^9/L, of 3.41 times. The relative values of the agranulocytes with the values (68,03 ± 12,3)% of blood fell to (47,2 ± 1,8)% of blood, only 1.44 times. A similar trend is observed for the other cell subpopulations.

Absolute values fell by more than by 2 time and the relative values decreased less than by 1.5 time. For example, the absolute values of monocytic cells with the value (0,5 ± 0,02) ·10^9/L blood decreased to a value (0,12 ± 0,10) ·10^9/L of blood, i.e. more than by 4.17 time ($p \leq 0,05$), whereas a relative value (6,28 ± 1,24)% dropped to a (4,9 ± 1,3)%, which was only 1.28 time difference in values. Granulocytic cells with values (3,64 ± 1,22) ·10^9/L fell to (0,65 ± 0,3) ·10^9/L, i.e. by 5.6 time ($p \leq 0,01$). A relative value of granulocytes with values (40,0 ± 8,36)% reaching values (26,18 ± 4,5)%.

Evidently, than absolute indicators decrease more considerably, than relative. Absolute data of cells are dependent from of the general leucocytic indicators which quickly falls at an immunosuppression.

Changes in the values of erythrocyte and platelet cells were detected, but more than 2- time reduction was not registered. Level erythrocyte cells (6,5 ± 1,56) ·10^{12}/L blood reached the value (4,93 ± 1,3)·10^{12}/L of blood, i.e. decline was 1.32 times . Hemoglobin level fell to 4.51 times. In intact animals it was 140,7 ± 16,7 g / L of blood. And after intoxication fell to 90,75±12,0 g / L of blood. But hematocrit value from the value (39,8±6,3) fell 2.88 times ($p \leq 0,05$) times, reaching values (21,21±2,58).

Critical decrease of platelets was observed. Level intact animals was (660,25 ± 91,21) ·10^9/L blood and artificially induced Immunosuppressive syndrome was (70,5 ± 43,2) ·10^9/L blood, which was more than 9,36 – fold reduction ($p \leq 0,01$).

Causing artificial immunosuppressive syndrome treated animals novel compounds of plant origin. The compounds were investigated under the following Identifier codes: Halostachys caspia (aqueous extract) – IES.SPP.401R, Holostachys caspia (50% water – ethanol extract) – IES.SPP.401R.SE, Sueda microphylla (water extract) – SIE.SM.401R, Sueda microphilla (50% water – ethanol extract) – SIE.SM.401R.SE, Climacoptera obbtusifolia (70% water – ethanol extract) – G.COE$_X$, Climacoptera lanata (70% water – ethanol extract) -G.CLE$_X$, Climacoptera subcrassa (aqueous extract) -A.SKF, Climacoptera subcrassa (50% water – ethanol extract) -A.CSE$_X$.

After analyzing the data obtained can should high activity next connection SIE.SM.401R, SIE. SM.401R.SE derived from plants Sueda microphilla. It should be noted that the activity is significantly distinguished by compounds obtained aqueous – extraction with ethyl plants than aqueous extraction. Blood counts of animals receiving compound SIE. SM401R.SE. It should first be noted that the level of leukocyte cells grown to (5,64 ± 0,03)·10^9/L of blood against the values of the control animals (2,79 ± 0,65) ·10^9/L of blood, i.e. 2.02 times. It should be noted that the compound SIE.SM.401R.SE significantly stimulated the division of granulocytes than agranulocytes. SIE.SM.401R.SE had little effect on the values of lymphocyte cells. After the treatment compound absolute lymphocyte was (1,49 ± 0,02) ·10^9/L blood against the reference value (1,55 ± 0,25) ·10^9/L blood , i.e. even higher than the reference value . A relative values of lymphocytes in the group administering the compound SIE.SM.401R. SE even were 1.93 times less than the control (26,27 ± 2,28)% vs (50,65 ± 8,36)%. But the level of granulocytic leukocytes, both absolute and relative values significantly increased in the group administering the compound SIE.SM.401R.SE. The absolute value of granulocytes in the group administration of the compound was SIE.SM.401R.SE (26,27 ± 2,28) ·10^9/L to control value (1,13 ± 0,0)·10^9/L blood, i.e. to 23.25 times ($p \leq 0,01$) exceeding control. The relative importance of the introduction of the compound in the group SIE.SM.401R.SE also exceeded the control values by 1.45 times.

Significant differences in the values of erythrocyte cells have not been reported, nor in the general index of erythrocyte or hemoglobin, hematocrit, etc. It should be noted changes in the level of platelet cells, against the benchmark (447,0 ± 127,2) ·10^9/L blood administration group SIE.SM.401R.SE he was (600,0 ± 90,1)·10^9/L blood.

Indicators hemogram administration group aqueous analogue SIE.SM.401R were not what higher than the control group, and even a few parameters below in 1.3-2.4 times. Such as leukocyte count in the group administration of the compound was SIE.SM.401R (1,31 ± 0,33) ·10^9/L blood against the reference value (2,79 ± 0,56) ·10^9/L blood. Also, all the indicators leucogramm, both relative and absolute, inferior control values. A similar pattern was

observed in the values of red blood cell and platelet cells.

Absolutely similar pattern can be seen in groups of administration of the compounds IES.SPP.401R. SE. Leukocyte common score in the administration IES.SPP.401R.SE was (4,96 ± 1,23) $\cdot 10^9$/L blood against the reference value (2,79 ± 1,23) $\cdot 10^9$/L blood. The relative importance of granulocytes was (51,53 ± 2,53)% against the benchmark (43,35 ± 3,35)%. Significant differences in terms of monocytes and lymphocytes were reported.

Note the following compounds G.COEx a total leukocyte index (4,71 ± 1,21) $\cdot 10^9$/L blood against the reference value (2,79 ± 1,23) $\cdot 10^9$/L blood. But no significant increase agranulocytes or granulocytes was not registered. Only 2-7% different values in the group administering the compound $G.COE_X$, surpassing the control group. And the level of red blood cell and platelet cells was even lower than the control values. Especially hemoglobin level was (23,29 ± 2,31) g / L of blood against the reference value (96,0 ± 12,2) g / L of blood. Platelet count was (393,33 ± 121,2) $\cdot 10^9$/L blood against the control group (447,0 ± 92,1) $\cdot 10^9$/L blood.

Among the compounds of plant origin worst results myelostimulate compound showed activity $A.CSE_X$. Values leukocyte, erythrocyte, thrombocyte cells was lower in the control group 3,21-27,84 times ($P \leq 0,01$). To a large extent affected platelet cells, as well as the level of trombokrit respectively. It can be assumed that this compound possesses a cytostatic effect, which aggravated and immunosuppressant effect. Also, it can be assumed that compounds $A.SKF. G.CLE_X$ inhibit the proliferative activity of hemopoietic bone marrow pools, which resulted in a decrease in the level of peripheral blood cells even below the level of the control group. Thus, alcoholic extracts of plants Halostachys caspia and mixed have myelostimulating effect on granulocytic leucocytes. No effect on lymphocyte indicators. Compounds derived from plants Climacoptera obtusifolia, woolly, have the opposite effect – suppress the proliferative activity of the cells, i.e. have a cytostatic effect.

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