Phytochemical antitumor preparation amitozyn with antiviral and immunomodulating action marks the beginning of a new scientific direction of health promotion and environment enhancement on the molecular level

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The late XX and the early XXI clearly showed people the vulnerability of their mental and physical health. Ukraine turned out to be the first victim of the Apocalypse era. The Chernobyl disaster, enduring genocide, ecocide and holocaust undermined reserve, mental, genetic and ecological health of the Ukrainian people. For the last years AIDS has contributed badly to the death toll caused by malignant tumors and tuberculosis. Kiev bears the palm as for the intensity with which this plague of the present time has spread in Europe. Each of 100 residents of Kiev is HIV infected.

Careful and most responsible regulatory impact upon both healthy and sick organisms of living beings long ago ceased to be only the concern of scientists. In the course of the history humanity undoubtedly proved that animate nature possesses inexhaustible self regulating resources.

For over forty years we have been studying problems of regulation of biological processes in the conditions of normal life as well as in disease states especially under stress and induced fatal diseases.

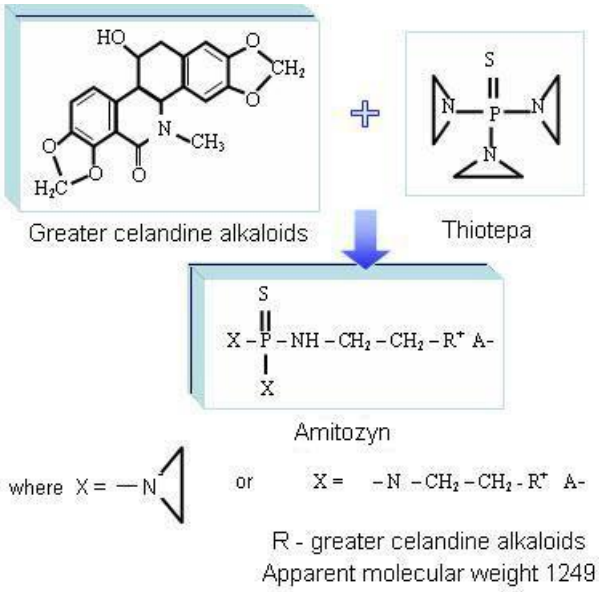
The objects of study are natural substances, synthesized by microorganisms, plants, fungi, insects and animals. These are alkaloids, biogenic amines, amino acids, proteins, nucleic acids as carriers of hereditary traits and their precursors. Due to our new method of a directed change of natural molecules through alkylation, it is possible to enhance the protection of living beings against hazardous environmental factors, to prevent mass virus and microbe diseases, including tumors, immunoagressive and immunodeficiency states. Particularly we should note the possibility of regulatory effect of such substances upon hereditary diseases and radiation damages.

The first substance of this type, together with analogues able to stop this rapid invasion, was antitumor, antiviral and antimicrobial preparation amitozyn, which was devised in 1959 through alkylation of some alkaloids isolated from commonly known and frequently occurred plant greater celandine by antitumors preparation thiophosphamide (thiotepa) (A. I. Potopalsky, 1961). The figure represents the scheme of amitozyn synthesis. For over fifty years this preparation has been used independently and in many complexes for malignant tumors treatment.

The clinical test of amitozyn, conducted in 1967-1968 in former USSR, proved its high medicinal properties in tumors of larynx, neck of womb, prostate, ovaries, pancreas and mammary gland, urinary bladder, melanoblastoma etc., as well as in non-malignant growths (polyps, papillomas, adenomas, fibromiomas). These data were supported by recent clinical tests of amitozyn, conducted in 1998-2001 according to the Ministry of Health of Ukraine on the basis of the Oncology and medical radiology research Institute of the Academy of Medical Sciences of Ukraine. In collaboration with O.S. Abrahamovich, a doctor from Lviv, amitozyn was proved to possess a high medicinal activity in viral infectious polyarticular rheumatoid arthritis and did not inhibit sanguification and immunity in patients but even increased them mobilizing the organism. It is the first preparation of a new class of phytolytic substances – products of alkylation of amines with various actions.

The approach for obtaining a large group of antitumor products of alkylation of isoquinoline alkaloids of triethyphoms, elaborated in collaboration with M. Turkevich, M. Oliyovskaya, V. Ya. Novitsky in 1969, was patented in 16 countries.

FIGURE Scheme of amitozyn synthesis



Amitozyn has been tested in industrial conditions at battery farms for birds viral laryngotracheitis treatment and also experimentally for pigs viral enteritis. Its high specific activity and economic effectiveness for veterinary have been proved.

Amitozyn was proved to possess antiviral action in myeloblastosis and birds viral laryngotracheitis, lymphatic leukemia in baboons and grippal pneumonia and herpesviral meningitis in mice. Also, together with doctors, we have determined its high effectiveness in viral papilloma, hepatitis, enteritis and arthritis. Especially important is that amitozyn inhibits virus reproduction in acute HIV infection for 2 Lg.

Antimicrobial action of amitozyn was determined on staphylococcus mutant 209 UV-2 and UV-3 , intestinal strain O-111 and Bacillus dysenteriae sonnei.

“Ukrain”, an analogous substance of this group, was patented as antitumor and immunomodulatory preparation in Austria and many other countries in 1979 by our co-author V. Ya. Novitsky. It was approved for application in Ukraine in 1998 and reregistered in 2004. This enabled V. Ya. Novitsky to establish Ukrainian anticancer institute in Vienna and set up his own pharmaceutical company.

The toxicity of amitozyn is several times lower than of some of its components – the sums of greater celandine alkaloids and thiophosphamide. And high antitumor activity of amitozyn in the experiment (Table 1) was proved in its clinical test on patients with fatal forms of malignant tumors (table 2). Complete clinical recovery was observed in 17-18% cases, whereas observed contraction of tumors and life prolongation constituted 75% cases. Complications common to most antitumor preparations such as sanguification inhibition, dyspeptic effects, baldness and others were not observed. At the same time characteristics of immunogram normalized and specific cancerous antigens disappeared or decreased dramatically. Inherited resistance effect in rats race cured from Heren cancer was determined.

Table 1.

Spectrum of antitumour action of amitozyn on experimental tumors of rodents (5 hypodermic injections of 100 mg/kg every other day)

Tumor strain	Rodents group	Day of the treatment beginning	Tumor mass	Therapeutic effect	
				% T	Ief
Sarcoma-37	Control Experiment	- 6th	1,46 ± 0,03 0,20 ± 0,02 p<0,01	75,5	4,08
lymphoma NK/Ly	Control Experiment	- 2nd	0,078 ± 0,099 0,25 ± 0,024 p<0,001	67,25	3,12
Ehrlich's carcinoma	Control Experiment	- 4th	0,80 ± 0,11 0,31 ± 0,018 p<0,05	61,25	2,58
Lymphosarcoma LIO-1	Control Experiment	- 2nd	1,57 ± 0,14 0,66 ± 0,14 p<0,01	57,96	2,38
Melanoma Harding-Passie	Control Experiment	- 6th	0,056±0,017 0,026±0,009 p<0,02	52,60	2,15
Hemocytoblastosis of Tailor-rats	Control Experiment	- 2nd	18,1 ± 1,7 0	100	

Table 2.

Overall result of amitozyn treatment of patients with head and neck malignant tumors. (survival, %)

Survival	Patients group	
	Control group	Main group
2-year	52,2 ± 4,2	91,9±3,5*
3-year	47,0 ± 5,0	70,1±5,0*
5-year	40,2 ± 5,2	66,1±6,6*

Altogether there are over 60 preparations registered as biologically active substances of this new type in the public register of the former USSR. They were created by the author in collaboration with a team of scientists in Lviv and Kiev and protected by 40 author's certificates, 5 patents of Ukraine and 14 international patents.

Among promising alkylated derivatives of alkaloids of plant origin and biogenic amines of animal origin there are preparations berberin, sanguinarine, chelidonine, quinine, vinblastin, salsoline, colchamine, adrenalin, noradrenaline, serotonin and some others.

Especially promising preparations were devised on the basis of alkylated nucleic acids and their precursors and analogues (nucleorhexin, the first preparation of the type, created by A.I. Potopalsky, 1979) and they possess antitumor, antiviral, antibacterial, radioprotective and immunoregulatory actions. The substances of this new class can be used for the correction of severe hereditary diseases and disorders in the creation of novel resistant to hazardous weather conditions plant lines.

Thus, the regulatory action of the new substances have been defined on the molecular, cellular, orgonn, and systems levels that allows to recommend them for the molecular genetic rebirth of people and environment.