ХV МЕЖДУНАРОДНАЯ КОНФЕРЕНЦИЯ СТУДЕНТОВ, АСПИРАНТОВ И МОЛОДЫХ УЧЕНЫХ «ПЕРСПЕКТИВЫ РАЗВИТИЯ ФУНДАМЕНТАЛЬНЫХ НАУК»

NANODIAMONDS AS IDEAL NANOCARRIERS FOR CYANCONTAINIG CYTOSTATICS

V. V. Davydova, E.S. Illarionova, <u>M. A.</u> Mar'yasov Scientific supervisor: Professor O. E. Nasakin FGBOU VO "Chuvash state University. I. N. Ulyanov", Russia, 428015, Cheboksary, Moskovsky prospect 15, 428015 E-mail: ecopan21@inbox.

НАНОАЛМАЗЫ КАК ИДЕАЛЬНЫЕ НАНОНОСИТЕЛИ ДЛЯ ЦИАНСОДЕЖАЩИХ ЦИТОСТАТИКОВ

В.В. Давыдова, Е.С. Илларионова, М.А. Марьясов

Научный руководитель профессор О. Е. Насакин

ФГБОУ ВО «Чувашский государственный университет им. И.Н. Ульянова», Россия, 428015,

г.Чебоксары, Московский пр. 15, 428015

E-mail: ecopan21@inbox.rul

Аннотация. Цианосодержащие цитостатики - новый класс открытых нами лекарств, которые благодаря цианогруппам хорошо закрепляются на наноалмазах, с увеличением активности.

Introduction. The problem of cancer is in the most urgent before science and humanity. According to statistics, over the past 15 years, the annual increase in the number of cancer patients is 3.5 - 4%. Global losses of \$ 1 trillion [1, 2] in 2017, more than 17 million people on earth fell ill with cancer and died about 8 million.

Cancer is on the 2nd place in the world in mortality after cardiovascular diseases, and the cost of drugs and treatment courses is definitely on the first.

We carry out screening on clean lines of cancers (more than 80 tests, and much more) in NCI (Maryland, USA). Known. that the average cost of developing only one drug is an astronomical sum of \$ 2 billion! and it takes up to 15 years of work of huge groups of chemists and testers-biologists and only 10 largest international pharmaceutical companies capable of this work.

We developed a completely new concept of creating a "soft" cyanoalanine alkylating agents. Existing substances in this class are descended genetically from lethal toxic compounds of nitrogen mustard. As this compound is lethal to humans, and all the other extremely deadly.

These anticancer drugs are able to connect with DNA and interfere with the reading of the cell genome during its division. As a result, the synthesis of elements stops, and the cell dies. These drugs have a very effective effect on all rapidly multiplying cancer cells. Unfortunately and on healthy, too. Such drugs include, for example: cyclophosphamide, mielosan, novemberin, nitrosomethylurea. They are extremely toxic, cancero and teratogenic, so much of the treatment of patients simply can not withstand chemo.

We drew attention to the hundreds of synthesized structures, often highly complex structure (400 SAR). All these transformations unites unusual for compounds of possible ensembles carbonitrile (cyanegroupe) to different types of coordination in organic structures. This phenomenon is preceded by a very rapid speed interactions (comparable to the speeds of catalytic and enzymatic) processes of change of ceanography involving nucleophilic

207

208 XV МЕЖДУНАРОДНАЯ КОНФЕРЕНЦИЯ СТУДЕНТОВ, АСПИРАНТОВ И МОЛОДЫХ УЧЕНЫХ «ПЕРСПЕКТИВЫ РАЗВИТИЯ ФУНДАМЕНТАЛЬНЫХ НАУК»

centers of the molecules. Such "push-pulse reactions" lead to the fact that in one technological stage in a split second proceed (in our cases) up to 12 chemical intramolecular processes with a total yield (often) 90-98%!

Materials and methods of research. Our attention is focused on natural and synthetic cyanide derivatives. Nanotechnology is currently one of the most promising areas of development of modern science, technology and medicine a significant role in the properties of the substance begins to play the state of the surface of the nanoparticles of the material. The development of these concepts has developed in a new direction of science-nanomedicine, in which one of the main tasks is the creation of drug delivery systems (LV) addition to the obvious increase in the activity of organic compounds as anti-cancer substances, cyanogen group is ideal for fixing substances on nanowires, it is compact (3,5 A), does not create steric obstacles, has the highest adhesion to almost all materials. It is known that many of the obtained nanoparticles (more than 400) have the ability to penetrate into the cells through the shell.

In conventional medicines, only one molecule of 10,000 reaches the target, and the rest are neutralized by the body or harm it. Nanoparticles same 1-2 orders of magnitude more markers. the pharmaceutical industry for several drugs based on liposomes are produced: "Lipodox" (liposomal doxorubicin), "Lipin" (antihypoxic), "Laoliu" (hepatoprotective). Studies conducted on carbon nanotubes of CNTS with incorporated molecules of antitumor compounds, such as doxorubicin [3, 4], 10-hydroxycamptothecin [5], paclitaxel [6], metatrexate [7] and cisplatin [8], showed a decrease in cytotoxic action and preservation of pharmacological activity of drugs. Begin clinical trials of three drugs: "Antilipase" (Antihemorrhagics), "Belacan" (wound healing) and "Chlorophillipt" (anti-inflammatory). Biological tests are "Aminophosphate" (against hemolytic disease of the newborn), "Betws" (antimelanoma), "Fotos" (anticancer), "Rifamycin" and "Isocyanide" (TB).

Results. In the literature it is indicated that nanodiamonds (N) is an ideal method of drug delivery [9]. It is established that H does not possess carcinogenic, mutagenic action, they are nontoxic and biocompatible. In a number of works [9.10] it is shown that the bottom has the least toxic effect among carbon nanostructures. Recently, the interest of researchers in choosing the optimal carrier for LV shifts from the above carbon nanostructures to the bottom die to the optimal complex of its physico-chemical, biopharmaceutical and pharmacological and Toxicological characteristics. Getting nanodiamonds in parallel solves the problem of disposal of huge stocks of explosives/ accumulated even with world wars, which are calculated not tons and TRAINS! They often detonate for no apparent reason (the latest explosions in Abkhazia, Ukraine, the far East, etc.), causing incalculable material and human losses, permanently paralysing the economic activities of entire regions. Nanodiamonds are easily obtained by utilization of the above explosives on an industrial scale. This results in ultrafine carbon nanomaterials with an average size of 5 nm, which consist of a diamond core, the surface layer of which is formed by different functional groups. They have already been proposed to be used as galvanic coatings, lubricants, biologically active compounds, etc. It is important that only in 2015 they began to be involved as delivery systems of biologically active substances, and by chemical standards this is a very short time. The second point is that they are distinguished from other carbon nanoobjects by the fact that they do not have carcinogenic, mutagenic effect, are non-toxic and biocompatible. Our primary experiments with nanodiamonds have shown that. In view of the above we examined the activity of synthesized drugs on the N. As substances on the clean lines of cancer cells (national cancer Institute, Maryland, USA) has been tested casamassina of pirano, bicycloamine, tetrahydropyridine and imidazoles, and tetrahydropyridine. The obtained results show that the activity of substances on H exceeds that without H. However under this. Studies have

ХV МЕЖДУНАРОДНАЯ КОНФЕРЕНЦИЯ СТУДЕНТОВ, АСПИРАНТОВ И МОЛОДЫХ УЧЕНЫХ «ПЕРСПЕКТИВЫ РАЗВИТИЯ ФУНДАМЕНТАЛЬНЫХ НАУК»

shown increased activity of cyano substances "planted" on the nanodiamonds 2-3 times, with multiple simultaneous prolongation of their validity.

Summary. It is shown that tsiansoderzhaschih compounds are cytostatic c activity greater than currently used. Nanodiamonds perfectly fix the above on their surface (6-12%), due to the formation of a large number of hydrogen bonds, while their activity increases

REFFERENCE

- 1. O'Callahan, T. (2011). The prevention agenda. Nature, vol. 471, pp. 2-4.
- 2. Sheverov, V. P., Nasakin, O. E., Davydova, V. V. (2017). The Problem of cancer and carbonitriles. Chuvash state University publishing house, 176 p.
- Meng, L. (2012). Single walled carbon nanotubes as drug delivery vehicles: targeting doxorubicin to tumors. Biomaterials, vol. 33, no. 6, pp. 1689-1698.
- Liu, Z. (2007). Supramolecular chemistry on water-soluble carbon nanotubes for drug loading and delivery. ACS Nano, vol. 1, no. 1, - pp. 50-56.
- 5. Wu, W. (2009). Covalently combining carbon nanotubes with anticancer agent: preparation and antitumor activity. ACS Nano, vol. 3, no. 9, pp. 2740-2750.
- 6. Sobhani, Z. (2011). Increased paclitaxel cytotoxicity against cancer cell lines using a novel functionalized carbon nanotube. International Journal of Nanomedicine, vol. 6, pp. 705-719.
- Das, M. (2013). Augmented anticancer activity of a targeted, intracellularly activatable, theranostic nanomedicine based on fluorescent and radiolabeled, methotrexate-folic acid-multiwalled carbon nanotube conjugate. Molecular pharmaceutics, vol. 10, no. 7, pp. 2543-2557.
- Li, J. (2012). Carbon nanotube bottles for incorporation, release and enhanced cytotoxic effect of cisplatin. Carbon, vol. 50, no. 4, pp. 1625-1634.
- 9. Zhang, X. A. (2012). Comparative study of cellular uptake and cytotoxicity of multi-walled carbon nanotubes, graphene oxide, and nanodiamond. Toxicology Research, vol. 1, no. 1, pp. 62-68.
- Schrand, A. M., Dai, L., Schlager, J. J., Hussain S. M., Osawa, E. (2007). Differential biocompatibility of carbon nanotubes and nanodiamonds. Diamond and Related Materials, vol. 16, no. 12, pp. 2118-2123.

Том 2. Химия

209

Россия, Томск, 24-27 апреля 2018 г.