

ВЕСЦІ

НАЦЫЯНАЛЬНАЯ АКАДЭМІЯ НАВУК БЕЛАРУСІ

СЕРЫЯ ХІМІЧНЫХ НАВУК 2016 № 3

ИЗВЕСТИЯ

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СЕРИЯ ХИМИЧЕСКИХ НАУК 2016 № 3

ЗАСНАВАЛЬНІК – НАЦЫЯНАЛЬНАЯ АКАДЭМІЯ НАВУК БЕЛАРУСІ

Часопіс выдаецца са студзеня 1965 г.

Выходзіць чатыры разы ў год

Настоящий номер журнала включает материалы 23-й Конференции по изопrenoидам, которая состоится в Минске 4–7 сентября 2016 г. Тематика конференции охватывает различные аспекты исследований этой большой группы природных соединений, молекулы которых построены из C5-изопреновых элементов, связанных различным образом друг с другом. Ряд витаминов, феромонов, аллелопатинов, рецепторных сенсоров, ключевых элементов структуры клетки таких как стероиды, а также многие физиологически активные соединения, в частности стероидные гормоны человека и животных, принадлежат к изопrenoидам. Они отвечают за размножение, половую дифференциацию, развитие, адаптацию, регуляцию минерального и белкового метаболизма, нервной активности и пищеварительной системы, т. е., по существу, за все важнейшие функции живого организма. Отличительной особенностью конференции является разнообразие тем, связанных с изопrenoидами: от их распространения в природе, химического синтеза и структурного анализа до молекулярно-биологических, генно-инженерных, экологических и медицинских аспектов.

Все аспекты изопrenoидов рассматриваются специалистами из разных областей в ходе общих дискуссий, которые предлагают широкое видение предмета, что особенно важно для молодых ученых, позволяя оценить текущее состояние и перспективы изучения и практического использования этой группы природных соединений – основы лекарств, агропрепаратов и биотехнологий для настоящего и будущего.

Данный номер журнала отражает содержание более 80 докладов, представленных на конференции (авторский стиль и орфография тезисов сохранены).

PROCEEDINGS

OF THE NATIONAL ACADEMY OF SCIENCES OF BELARUS

CHEMICAL SERIES 2016 N 3

FOUNDER IS THE NATIONAL ACADEMY OF SCIENCES OF BELARUS

The Journal is published since January, 1965

The Journal is issued four times a year

This issue is devoted to the 23rd Conference on Isoprenoids, which takes place in Minsk on September 4-7, 2016. The subject of the Conference is a widespread large group of natural compounds whose molecules consist of C5 isoprene units connected to each other in various ways. A number of vitamins, pheromones, allelopathins, receptor sensors as well as sterols, the key elements of cell structure, and many other physiologically active natural compounds, such as e.g. steroidal hormones of humans and animals, belong to isoprenoids. They are responsible for the reproduction, sexual differentiation, development, adaptation, regulation of mineral and protein metabolism, nervous activity, digestive system, i.e. virtually all the vitally important functions of a living organism. An attractive feature of the Conference is a variety of isoprenoid-related topics: from their search in natural sources, chemical synthesis and structural analysis to molecular biological, genetic engineering, ecological, and medicinal aspects.

All topics are considered by the specialists from different fields during common discussions offering a broad vision of a subject that is especially important for young scientists for imaging the current state and perspectives of natural products chemistry – a basement of efficient medications, ecologically friendly agrochemicals and biotechnologies for modern time and for future.

The current issue contains more than 80 abstracts of papers presented at the Conference (the author's style and spelling retained).

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EFFECTS OF 24-EPIBRASSINOLIDE, 28 HOMOCASTASTERONE AND THEIR SYNTHETIC DERIVATIVES ON THE VIABILITY OF CANCER CELL LINE A549 (LUNG CARCINOMA) AND ELUCIDATION OF THE MECHANISM OF THEIR ACTION

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It is known that the treatment of cancer with classical chemotherapeutics, for example, doxorubicin, is facing a number of challenges, some of which are the side effects of their action on the body. Therefore, it becomes necessary to search for new compounds that reduce the viability of cancer cells and at the same time not having effects on normal cells. Such compounds may have a vegetable origin - brassinosteroids. Brassinosteroids have been recognized to be an integral part of the plant hormonal system.¹ Among various biological activities of brassinosteroids, the most significant one is the ability to increase plant resistance to unfavourable biotic and abiotic environmental factors. Of particular interest are numerous reports describing their anticancer properties, especially in respect of hormone-dependent cancer cell line.^{2,3} However, very little is known about the

mechanism by which they exert their cytotoxic effects.

In this work with the help of flow cytometry the effect of two natural brassinosteroids: 24-epibrassinolide, 28-homocastasterone and two their synthetic derivatives (22*S*,23*S*)-24-epibrassinolide, (22*S*,23*S*)-28-homocastasterone (Fig. 1) on the viability of hormone-independent cancer cell line A549 (lung carcinoma) was evaluated.⁴ To determine the level of reactive oxygen species (ROS) was used fluorescent label 2',7'-dichlorodihydrofluorescein diacetate, and for determining the level of apoptosis and cell cycle - the intercalating dye ethidium bromide.

It has been shown that synthetic analogues of brassinosteroids increase ROS level 3-5 times, and they are more effective in reducing the viability of A549 cells, as compared to natural (Fig. 2b).

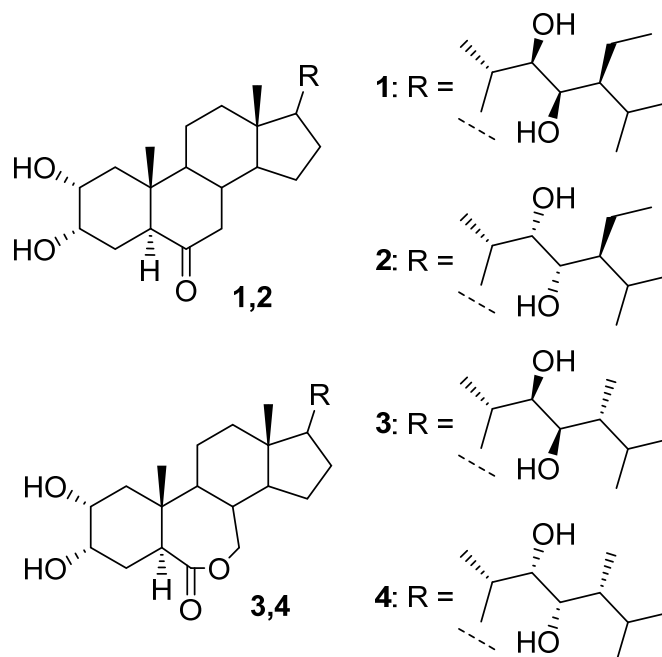


Fig. 1 Structures of evaluated brassinosteroids: 1 - 28-homocastasterone, 2 - (22*S*,23*S*)-28-homocastasterone, 3 - 24-epibrassinolide, 4 - (22*S*,23*S*)-24-epibrassinolide.

IC₅₀ for (22S,23S)-24-epibrassinolide, (22S,23S)-28-homocastasterone was 100 and 130 μ M, respectively (Fig. 2a). With regard to cell cycle, % S-phase under the effect of brassinosteroids reduced in some extent, but the greatest inhibition was ob-

served under the influence of 24-epibrassinolide-28% as compared with control -44%. At the same time, both natural compounds caused a doubling level of apoptosis compared with the control.

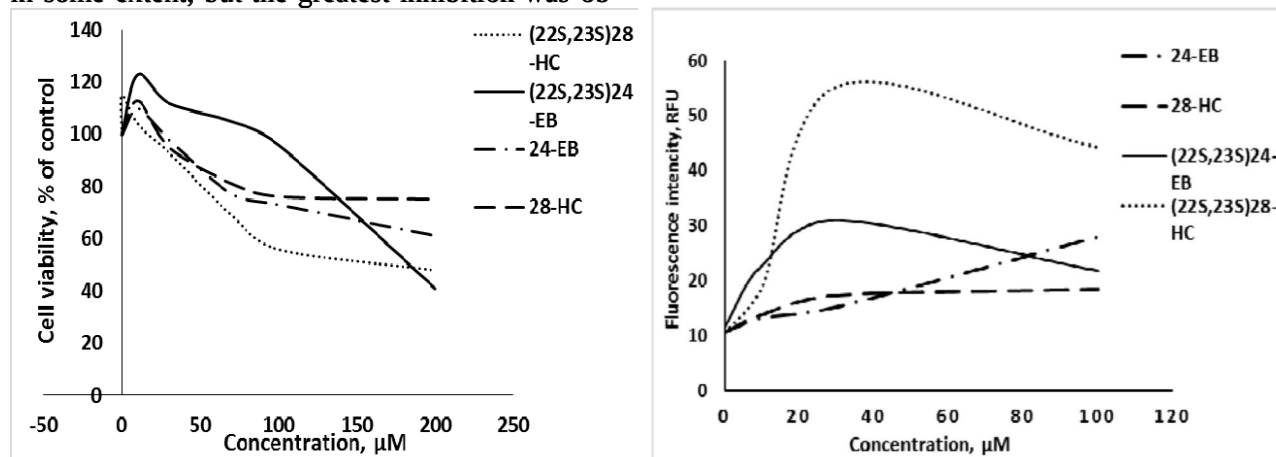


Fig. 2 – Influence of brassinosteroids on a.) cell viability; b.) intrinsic level of ROS.

For investigating possible mechanism of cell death caused by test compounds, a series of experiments using ethidium bromide (Et-Br) was conducted. It is known that ethidium bromide has intense fluo-

rescence upon binding to DNA. In the first series of experiments it was described effect on cellular ROS levels permeability.

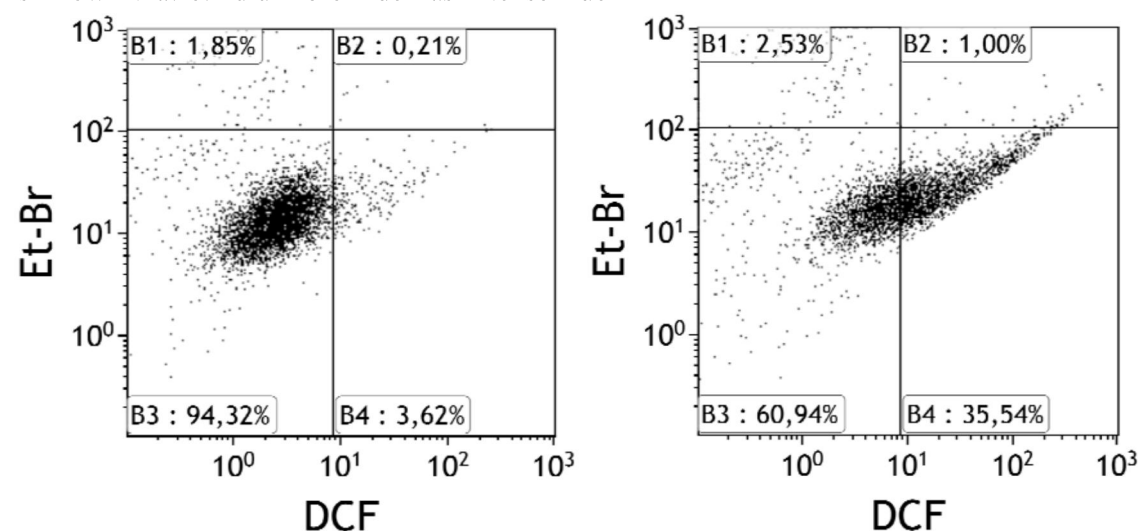


Fig. 3 - Comparison of cell death and intracellular ROS in cancer cell lines A549: 1-control; 2-10 μ M (22S,23S)-28-homocastasterone.

As follows from Fig. 3, with the addition of synthetic (22S,23S)-28-homocastasterone there is a direct correlation between the intensity of the luminescence of cells caused by exposure to ethidium bromide (y-axis) and the level of reactive oxygen species (x-axis). This is due to the fact, that the increase in the level of ROS causes progressive

disruption of the cell membrane permeability Et-Br, which is a sign of necrosis.

Thus, the tested compounds can be considered as potential antitumor agents. However, their mechanism of action is different: 24-epibrassinolide and 28-homocastasterone cause cell cycle arrest and apoptosis, which was previously shown on hor-

mone-dependent MCF-7 cell line.³ The action of the synthetic brassinosteroids may be associated with an increased intracellular level of ROS damage to cell membranes, which can lead to cell necrosis.

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