

# ВЕСЦІ

## НАЦЫЯНАЛЬНАЯ АКАДЭМІЯ НАВУК БЕЛАРУСІ

СЕРЫЯ ХІМІЧНЫХ НАВУК 2016 № 3

# ИЗВЕСТИЯ

## НАЦИОНАЛЬНОЙ АКАДЕМИИ НАУК БЕЛАРУСИ

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 изопреноидам, 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 стерины, а также многие физиологически активные соединения, в частности стероидные гормоны человека и животных, принадлежат к изопреноидам. 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 изопреноидами: от их распространения в природе, химического синтеза и структурного анализа до молекулярно-биологических, генно-инженерных, экологических и медицинских аспектов.*

*Все аспекты изопреноидов 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

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*This issue is devoted to the 23<sup>rd</sup> 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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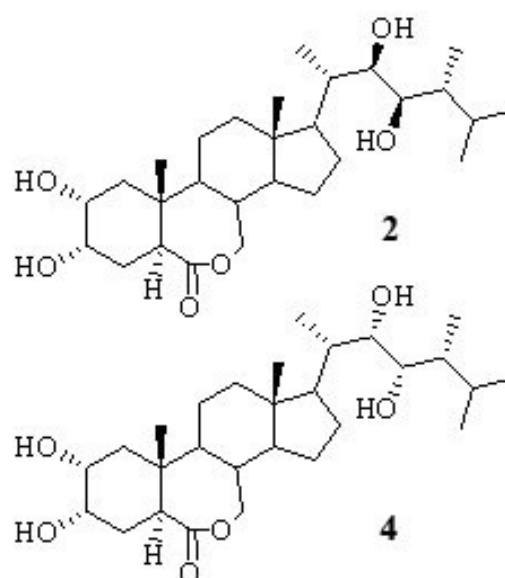
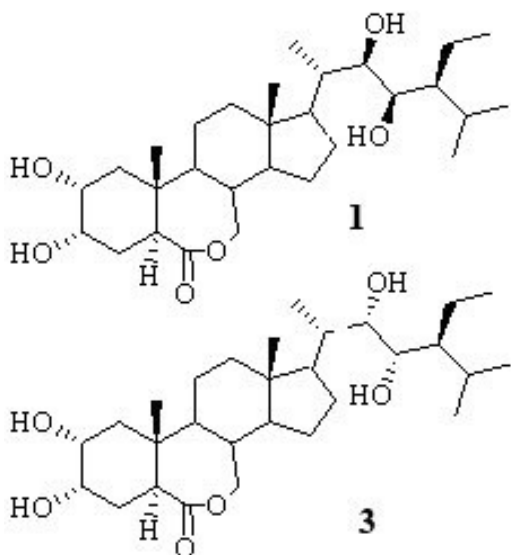
## MOLECULAR MECHANISMS OF ANTIPROLIFERATIVE, CYTOTOXIC AND ANTICANCER EFFECTS OF BRASSINOSTEROIDS

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Brassinosteroids (BS) are group of plant hormones similar to those of animals and humans in both structure and by function: they regulate expression of genes in plants, affect the metabolic processes, cell growth and differentiation. Recently there have been reports of a potential antiproliferative and anticancer activity of brassinosteroids with very low toxicity. The mechanism of action mostly is attributed to the blockade of the cell cycle by changing the expression level of cyclin-dependent protein kinases what leads to apoptosis.

It is proved the participating of monooxygenase systems in the initiation and development of many carcinogenic processes due to the activation of endogenous and exogenous compounds, e.g. estrogen steroids and polycyclic aromatic compounds. However, very little is known about the mechanism by which BS exert their cytotoxic effects. Knowledge of the influence of these compounds on the monooxygenase systems of animal cells is likely to contribute to the explanation of the observed effects.



In this paper, we tried to evaluate the effect of brassinosteroids on monooxygenases ability to ac-

tivate procarcinogens in cell line A549 (lung cancer). Causal relationship between the development



of lung cancer and the change in the activity of cytochrome P-450 under the influence, in particular, components of tobacco smoke in no doubt. Thus, ten times the risk of lung cancer in smokers as compared to nonsmokers associated with the presence of PAHs in tobacco smoke.

To determine the contribution of monooxygenases to the carcinogenic activation we use the reaction of the epoxidation of dihydroxyderivatives of benzo[a]pyrene (B[a]P) (mainly 7,8-dihydroxydihydrobenzo[a]pyrene ((B[a]P-7,8-diol)). This reaction ultimately leads to the formation of two stereoisomeric diepoxydes, of which (+)-anti-7 $\beta$ ,8 $\alpha$ -dihydroxy-9 $\alpha$ ,10 $\alpha$ -epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene ((+)-anti-BPDE) has absolute carcinogenic activity, while the other - no. Since formed diepoxydes are un-

stable and easily hydrolyzed to the tetrol-derivatives, it is possible to determine the formation of an absolute carcinogen. We use four steroid compounds (28-homobrassinolide (1), 24-epibrassinolide (2), (22S,23S)-28-homobrassinolide (3) and (22S,23S)-24-epibrassinolide) (4) that differ in ring and side chain structure.

It was shown that in the A549 cell line the metabolism of B[a]P-7,8-diol is shifted toward the formation of derivatives which indicate the formation of the obligate carcinogen (+)-anti-BPDE. Cultivating of cancer cells in the presence of brassinosteroids changes the activity of monooxygenase system in general, as can be seen on the spending of the substrate, and changes the profile tetrol-derivatives what depends on the structure of BS.

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