УДК 338.012

ПРОФИЛАКТИКА ОНКОЛОГИЧЕСКИХ ЗАБОЛЕВАНИЙ С ИСПОЛЬЗОВАНИЕМ ДИАРИЛИОДИОННЫХ СОЛЕЙ С OXONE® В КАЧЕСТВЕ ОКСИДАНТА: ИННОВАЦИОННЫЙ МЕТОД ПОВЫШЕНИЯ СОЦИАЛЬНОГО БЛАГОПОЛУЧИЯ

Барышева Г.А., Егорова М.С., Шмидт А.Э., Богачев А.И.

Национальный исследовательский Томский политехнический университет

Информация о статье
Принята 01 января 2018 г.

Ключевые слова: социальное благополучие, инновации, здоровье, профилактика рака

DOI: 10.26730/2587-5574-2018-1-4-15

Аннотация.
Инновационная технология передовой диагностики рака основана на внедрении новейших продуктов химии в сферу здравоохранения. Одним из способов снижения вредного воздействия рака в результате антропогенного загрязнения на социальное благополучие населения является внедрение передовых диагностических технологий с использованием солей иодния. Механизм внедрения технологии использования диарилиодионных солей с Oxone® в качестве оксиданта в здравоохранении основан на следующих достижениях современной химии. Поливалентные соединения йода (III) стали особенно популярными в последние годы из-за возможности их использования в качестве предшественника в синтезе трассеров для позитронно-эмиссионной томографии (ПЭТ). Инновационная технология, направленная на снижение токсичности, увеличение фактора окружающей среды, снижение стоимости синтетического материала и увеличение изменчивости конечных продуктов, может способствовать решению некоторых проблем, связанных с трассировщиками для позитронно-эмиссионной томографии. Основными потенциальными заказчиками изготовленных солей диариодониума могут быть небольшие исследовательские лаборатории, специализирующиеся на изучении полимерных материалов, а также медицинских учреждений, где проводятся доклинические и клинические исследования трассиров для позитронно-эмиссионной томографии.

CANCER PREVENTION USING A DIARYLIODONIUM SALTS SYNTHESIS WITH OXONE® AS OXIDANT: INNOVATIVE METHOD OF IMPROVING SOCIAL WELLBEING

Galina A. Barysheva, Maria S. Egorov, Andrey E. Bogachev, Andrey I. Shmidt

National Research Tomsk Polytechnic University

Article info
Received January 01, 2018

Keywords:
social wellbeing, innovations, health, cancer prevention

Abstract.
The innovative technology of advanced diagnosis of cancer is based on the implementation of the latest products of chemistry into the sphere of public health services. One of the ways of reducing harmful effects of cancer as a consequence of anthropogenic pollution on social wellbeing of the population is the introduction of advanced diagnostic technologies using iodonium salts. The mechanism of implementing the technology of using diaryliodonium salts with Oxone® as an oxidant in public health care is based on the following achievements of modern chemistry. Polyvalent iodine compounds (III) has become especially popular in recent years due to the possibility of their use as a precursor in the synthesis of tracers for positron-and-emission tomography (PET). An innovative technique, focused on reducing toxicity, increasing environmental factor, reducing the cost of synthesis, and increasing the variability of final products, can contribute to solving some problems associated with the tracers for positron emission tomography. Main potential customers of produced diaryliodonium salts may be small research laboratories spe-

ISSN 2587-5574

cialising in studying polymeric materials, as well as medical facilities, where preclinical and clinical studies of tracers for positron-and-emission tomography are carried out.

1 Introduction / Введение

It is impossible to consider the modern discourse of social wellbeing to be complete due to the absence of a single paradigm that integrates objective factors of its dynamics and the subjective perception of the totality accessible tangible and intangible values by the individual. Up to now philosophers, sociologists, economists, medical researchers can not accurately match human wellbeing with various forms of life - material, human, spiritual and social. Therefore, the economic analysis does not allow achieving the required identity of factors, criteria, evaluations of individual and social significance of the various wellbeing forms. As a consequence, it is difficult to search for consistent and effective ways of its extension, both at the individual and society level.

This significantly improves the relevance of inter-subject social wellbeing studies, becoming of its diversified methodology, and opens up the prospect for a new discourse -continuous wellbeing, based on the convergence of advanced trends of various branches in modern science.

Modern methodology of social wellbeing tends to the economic and sociological research. Accordingly, new technological possibilities and innovations in the medicine field, bio-chemistry, and microbiology opening the access to the new values for the public are considered statically, without taking into account the future opportunities. Within the framework of the existing methodology it is difficult to identify the specific factors of continuous wellbeing that accompanies a person throughout his life, as during this period the availability of the achievements of progress and their distribution radically expands in society.

1.1. Study context

Therefore, the key issue in understanding of the continuous wellbeing nature is: "Can prosperity entirely be measured by tangible achievements over the lifetime period?" This issue has become particularly relevant in the last two decades, when the breakthrough innovations have accelerated the pace of progress and shortened the period of economic cycles. As a result the increased markets' entropy leads to asymmetry of social wellbeing criteria, shifts emphasis from possession of material goods towards individuals' access to information technology, the latest achievements in medicine and health care, social exchange.

Institutional environment of formation of continuous social wellbeing throughout a person's life is also undergoing major changes. Along with protection from the destructive consequences of external shocks associated with the risks of inflation, devaluation, cyclical downturn and unemployment social protection mechanisms generated by the state are increasingly focused on stimulating technological innovation.

These technological innovations, being developed on the converged basis, will determine the boundaries of controllability of chaotic forms of social reality in the near future. The main factors of social wellbeing continuity in the works of most scholars are high performance of professional career, allowing "save for a comfortable old age", as well as a high level of social benefits (pensions, disability benefits, maternity leave). However, the volatility of economic dynamics and the cyclical nature of the market economy do not allow us to guarantee the sustainable wellbeing for 50-60 or more years - the period from the start of working activity until the end of a person's life in the developed countries. On the contrary the innovative technologies that determine the health conditions of every human and society in general are developing progressively and with acceleration.

The increase of innovation technological factor of continuous social wellbeing is also stipulated by the cyclical nature of material goods consumption and its high dependence on the institutional maturity of a society. In such circumstances, the main vector of the convergence of innovative technologies determining the continuous wellbeing is health preservation and provision of longevity in the process of reducing mortality from dangerous diseases previously considered to be difficultly recoverable and even cureless. The synchronicity of material benefits provision and preservation of health, positive emotional attitude in the face of increasing instability in the economic system becomes the main measurable instrument of continuous social wellbeing.

1.2. Theoretical framework

This work is situated within the body of research on the continuous social wellbeing. In general human wellbeing is determined, above all, by three fundamental factors: material wellbeing, health and safety. In such multicomponent structure the following indicators can be identified:

- financial or material wellness (income, housing conditions, the share of spending on health preservation and cultural development);
- physical wellness (health, wellbeing, personal safety):
- wellness of social relations (interpersonal relations, participation in social life, satisfaction from social status and social roles);
- emotional wellness (positive functioning of individual, mental health, stress, beliefs and convictions);
- professional wellness (professional competences, productivity, professional satisfaction). Professionally prosperous people perceive the job as a favorite occupation that helps them to realize their strengths and to achieve their goal.

These objective and subjective indicators of social wellbeing are closely connected, forming its level for particular social groups, regions, nations and for all humanity. These objective (external for the individual) and subjective (perceived by him) factors of social wellbeing are linked by his most important parameter - health.

It is the health as an indicator of the physical human wellbeing and the nation as a whole that leads us to a new level of its understanding - continuous.

We believe that continuous social wellbeing of a person is based on society's wellbeing, but is determined by personal assessment of his wellbeing and satisfaction of life in comparison with his own living conditions in the past or living conditions of other people. And this, in turn, is impossible without the preservation of health of a specific individual and society as a whole, throughout a person's life. Preservation of health as a key factor of the continuous wellbeing should be considered in several aspects:

- as a basis of a comfortable life, which forms the overall physical and emotional wellness;
- as a key factor of employment or entrepreneurial activity, necessary for the creation of material and professional wellness;
- as a necessary condition of the continuous wellbeing - saving at a high level the basic life parameters throughout the life, as well as its extension to the maximum possible period. After the termination of employment or business activity it is human health which starts to determine his wellness of social relations.

Thus, we see that health is a factor combining the separate types of wellbeing into its continuous form. However, in modern society, step by step transformed into a post-industrial one, dilemma of financial and professional wellness on the one hand, and physical and mental wellness on the other hand, gradually finds the solution in the process of automation and robotics of hazardous industries, the development of "green" industries. However, it is possible to form the true continuous wellbeing only on the basis of the convergence of industrial, social, economic, medical technologies. The starting point of convergence may become a common goal of their development - continuous access to the health protection technologies, prevention, early diagnosis and effective treatment of dangerous diseases for the whole society.

2 Methodology / Методология

As interdisciplinary category, based on the philosophical, economic, sociological, medical aspects of understanding of various spheres of life, social wellbeing is considered ambiguously and often eclectic by the scientists. A number of researchers analyzing wellbeing emphasize the provision of individuals with wealth and maintenance of social and economic stability of society [1-2]. Other authors give priority to the perception by the individual, community, and even a certain nation of objective living conditions [3-9].

The problem of continuous social wellbeing was closely studied by the authors who observe it as a set of external conditions, economic opportunity, personal values and professional skills making it possible to receive certain benefits over the lifetime period [10-12]. Some researches connect continuous wellbeing with the "lifetime employment" in Japanese corporations [13], others – with the social paternalism in the socialist countries as an attempt to approve the continuous wellbeing [14].

ISSN 2587-5574

Taking into account the opinion of these authors, we consider the social wellbeing as a space of human existence, which is stipulated by the actual performance of his physical condition, social and economic development of society, the current level of goods consumption and availability of health care technologies and a positive emotional state. Long-term, not limited by active labor or entrepreneurial activity, stay in such a space we consider to be continuous wellbeing.

One of the most important aspects of forming continuous social wellbeing is the fight against dangerous diseases such as cancer, especially in the diagnosis level. Cancer causes many fatalities in old industrial regions in Russia (like Tomsk, Kemerovo regions [15] that influences badly not only on the well-being itself, but on the labour force [16-17]).

With regard to the growth of continuous wellbeing, the internal organs cancer diagnostics must become available for the screening of the whole population. It requires multiple cost reduction of nuclear medicine which, along with the transplantation, remains one of the most expensive areas of modern medicine.

If periodically carried out investments in the renewal of nuclear medicine equipment are sufficiently distant in time from each other and are carried out by the government health care funds, the need to purchase expensive reagents always exists. It significantly reduces access to modern diagnostics for the masses. Therefore, to reduce the cost of these reagents the innovative technologies for cancer diagnostics are required. Their mass availability can be reached with the new technologies of diaryliodonium salts synthesis.

However, existing methods for preparing substituted diaryliodonium salts are rather expensive. In some cases, they require carrying out the process in an inert gas [18] and more expensive reagents, such as aryl tributil stannane and a Koser reagent [19]. Meanwhile, the effective application of diaryliodonium salts as a precursor for the synthesis of a nucleophilic radiotracer [18F] F-DOPA exists for the diagnostics of Parkinson's disease and neuroendocrine tumors [20].

It is known that diaryliodonium salts with tosylate and bromide counter ion are excellent precursors for the synthesis of salts with other counter ions: triflate, hexafluorophosphate, etc. These reagents in turn allow the introduction of 18F isotope in the amino acids to form the marked analogues of L-tyrosine – the perspective radiopharmaceutical reagent for the diagnosis of brain tumors [21], 2-fluoro-2-deoxy-D-glucose – another radiopharmaceutical reagent for detection of accumulations of tumor cells [22], obtaining radioligands for imaging the central benzodiazepine receptors [23], providing laboratory tests and radioimmunoassay.

Thus, the methodology of using the diaryliodonium salts synthesis as an innovative method of improving social wellbeing comprises advanced studies of the tendencies of society dynamics and the development of affordable "medicine of the future".

2.1. Analysis

Despite the importance of the "material" wellbeing, we believe it to be "non-continuous", as it lasts as long as its two main conditions are fulfilled.

The first condition of «non-continuous» social wellbeing is to achieve a certain level of material and professional wellness.

The second condition is the existence of an individual satisfactory state of physical and mental health, sufficient for successful business or labor.

Therefore, as soon as one of these conditions is violated, mainly due to the human aging, «non-continuous» wellbeing can be lost. It is no accident that basis of social wellbeing of society as a whole is considered to be the standard of living, stipulated by the indicators of per capita income and the minimum subsistence level, the concept of life quality determined by the health and sanitary conditions of the population’s life, the probability of receiving qualified medical assistance and the provision of social security.

At the same time, millions of people constantly face the choice of working in harmful and stressful environment and the preservation of health for many years. Accordingly, there is no unity in the research of economists and social scientists devoted to the dilemma between the building-up the material wellness and keeping health (they both, as it was mentioned above, are the basic of continuous wellbeing).

Thus, the proponents of "welfarism" [24] point out that the pursuit of maximum material wealth has some kind of affect, under the influence of which a person for some time can forget his desire for continuous wellbeing and neglect some threats for his health or put up with severe stress. Momentary happiness from the growth of material wellness is a sign of «non-continuous» wellbeing in case people

have been deliberately neglecting their health preservation for many years. This can be illustrated by the following examples. People often think that a new car will make them happy, but after two weeks its utility growth is reduced. They think that overtime work and extra money will bring them happiness, but it turns out that feeling unwell and destroyed family relationships have much more intensive and long-term negative impact on their wellbeing.

In turn, the supporters of the liberal model of wellbeing assessment offer to take into account people' own preferences in the analysis of various factors of social wellbeing [25-26]. This depreciates the role of health in achieving continuous wellbeing and increases the role of other factors, mainly, professional and material (for example, the possibility of getting life rent). This also can explain fairly high stress level, diseases of the cardiovascular system and mental disorders in the most prosperous social groups in modern technologically advanced countries - managers of financial companies and banks, IT developers, politicians.

At the same time, a gradual change in attitude towards health as a key factor of the continuous wellbeing illustrates «Easterlin's paradox» [27]. It consists in the fact that in the developed countries the average level of wellbeing, subjectively evaluated by a large number of respondents, is relatively insensitive to changes in income. That is, people are increasingly aware that they tend to material achievements that have little impact on social wellbeing, in particular continuous.

However, in an effort to bring their wellbeing in line with modern standards, people increasingly appreciate a lifetime opportunity to lead an active life - to travel, to communicate and to have an effective control over their health.

The lifetime health preservation problem makes people look widely at the essence of health. In addition to stress reduction, avoidance of harmful working conditions, the risk of injury and accidents, continuous wellbeing involves reducing the risk of chronic and fatal diseases leading to premature mortality. Special attention is deserved by the disease that is sufficiently independent on the level of material and professional wellness, in particular, cancer.

It sharpens the problem of "embedding" the modern health technologies associated with early diagnosis of such diseases into the continuous wellbeing model. We note that the feature of present stage of technological changes is convergence of basic technologies, which is called NBIC-convergence. NBIC is an acronym for the following types of technologies: N -nano; B -bio; I -info; C - cogno. With regard to the continuous wellbeing, it means the connection of medical, chemical and economic (marketing, investment) technologies within a new industry - medicine of continuous wellbeing.

3 Results / Результаты

A key role in the technological basis of medicine of continuous wellbeing we give to chemistry and biotechnologies, which, together with nano-technology, are one of the most important and the fastest "horizontal" technological areas. The intensive development of biotechnologies is stipulated by not only the success of chemistry and molecular biology, but also the crisis of traditional technologies (especially against the background of new trends in medicine and ecology), the need to increase the length of active life, to preserve physical wellness throughout life, to maintain healthy nation's gene pool. The presence of serious scientific groundwork and experimental development in the field of continuous wellbeing medicine technologies will make it possible in the coming years to expand significantly the scope of preventive detection of life-threatening diseases, to develop affordable drugs and diagnostic systems, to involve the broad masses of population in the process of the physical wellness extension for many years. Except this direct effect on the process of achieving the continuous wellbeing, the convergence of NBIC technologies will also provide the achievement of a number of goals, indirectly determining the conditions for long-term conservation of the various forms of human wellbeing:

- counter the spread of various types of human and animal diseases;
- producing chemicals for broad application in medicine from renewable raw materials intended to replace more expensive drugs and to provide new products with unique properties;
- conversion into a routine preventive diagnosis of dangerous diseases.

Distribution of NBIC-convergence in the field of medical continuous wellbeing changes the question about the value of the development and implementation of innovative chemical and biochemical technologies into mass production. If referring to «non-continuous» wellbeing new drugs and tools of diagnosis of chronic and deadly diseases have individual value, than when applied to the continuous wellbeing they are valuable for the whole society. Therefore, proclamation of continuous wellbeing as

ISSN 2587-5574

the imperative of social-and-economic development of modern society will undoubtedly require a significant price reduction of the diagnosis and treatment of diseases affecting people with different levels of material and professional wellbeing.

Among serious diseases that require complex diagnosis and expensive treatment we can name cancer. Therefore, we see prospective early introduction into mass production the chemical compounds intended for innovative early diagnosis and prevention of cancer. The main application area of such technologies is nuclear medicine as a highly promising sphere of long-term and continuous improvement of physical wellness in reducing chronic and fatal illnesses. The current development of the global nuclear medicine is characterized by the following features:

1. The increased volume of radionuclide production for medical purposes (as for the last decade the annual increase of output was up to 10%).
2. An increasing number of users (more than 100 specialized nuclear medicine facilities are functioning in the world; in the coming years it is expected to increase their number in 2 times).
3. Higher-than-anticipated growth of consumption of the therapeutic radionuclide production.
4. Extension of the areas of diagnostic test applications.
5. Increased requirements to the technologies of radionuclides production (economic cost-effectiveness and environmental safety).

The global market of radionuclide production for medical purpose has a strong annual growth tendency up to 15%. This trend will continue during the next 15-20 years. Growth in production of diagnostic products and equipment is provided both by expanding the areas of their application and by the development of innovative technologies in this field greatly reducing the cost of their mass application.

One of these compounds used in nuclear medicine for cancer diagnostics are diaryliodonium salts. They are stable compounds known since 1894, when the first diaryliodonium salts were synthesized in the action of strong mineral acids on aryl odozocarboxylates. The structure of diaryliodonium salts can be represented by two aryl rings, bound with electron-positive iodine atom with any of the proto ion (Fig. 1).

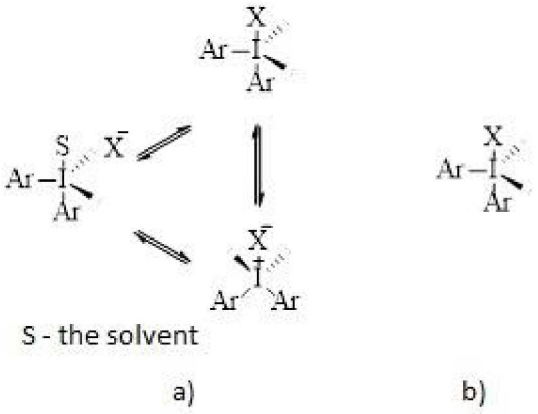

Figure 1 – The structure of diaryliodonium salts in the solution (a) and in the solid state (b)

The study of the structure of diaryliodonium salts showed that for the solid state the angle between bonds $Ar^1–I–Ar^2$ is about 90°, and there is a double bond between iodine atom and anion.

Anion in the composition of the diaryliodonium salts influences on their solubility and reactivity. It was found that diaryliodonium salts with halogen atoms usually have moderate solubility, while the triflates, tosylates and tetrafluoroborates are better soluble. When the diaryliodonium salts include anions with stronger coordinating ability, they are less soluble in organic solvents, while anions from less strong coordinating ability usually tend to increase the solubility of the salts. Therefore it is desirable to use weakly coordinating anions for synthesis of diaryliodonium salts such as triflates, tosylates tetrafluoroborate, hexafluorophosphate instead of halogens. For the purpose of cheapening the synthesis of diaryliodonium salts in the context of expanding coverage of cancer screening it is important that using halogenide-anions is problematic due to their strong nucleophilic nature.

Innovative technological "bridge" connecting the synthesis of diaryliodonium salts with the formation of the continuous wellbeing within the advanced diagnosis of dangerous diseases is presented as

a positron emission tomography (PET). It is modern and very sensitive diagnostic method used in oncology, cardiology, neurology and in other areas of modern clinic medicine. For the implementation of PET radio-tracers are required [28].

Today, in the world PET practice ^{18}F-marked compounds are mostly used. This is connected with the time of the half-life of the isotope ^{18}F (109.8 minutes) which is sufficient for the diagnosis (Holden 2004). One of the most promising trends in the technology of ^{18}F- containing radiopharmaceutical compounds synthesis is using multivalent iodine (MIC) compounds. Introduction of ^{18}F atoms in organic compounds can be carried out by nucleophilic substitution in the MIC-iodonium salts and by their subsequent decomposition in the presence of fluoride anion (Fig.2).

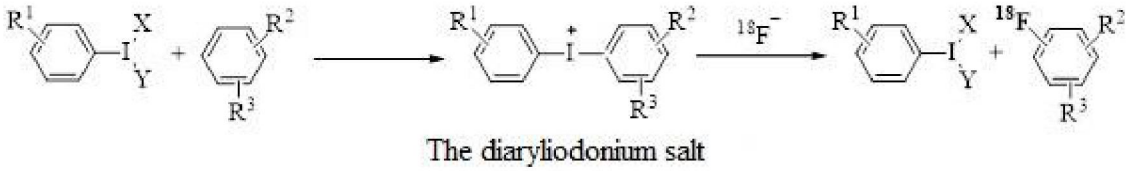

Figure 2 - The diaryliodonium salt synthesis process

The main advantage of this approach is that the reaction time is usually no more than 30 minutes, which is very important for the short-lived isotope ^{18}F. The simplest method of obtaining a preparation for PET diagnostic [^{18}F] DAA1106 is based on the above described principle of iodonium salts' attack [29]. There is also the possibility of performing the fluorine-promoted reaction of ligand exchange in diaryliodonium salts in deuterated acetonitrile and benzol, thanks to which diaryliodonium salts with triflate, hexafluorophosphate and fluoride counter ion were obtained [30]. In addition, there was the analysis of reaction's regioselectivity made by thermal decomposition of obtained asymmetric diaryliodonium salts.

Preparation of the radiotracer ^{18}F-DOPA from diaryliodonium halides is conducted by the method of "cold" fluorination with fluoride tetramethylammonium using such solvents as acetonitrile, DMSO (dimethylsulphoxide), dimethyl phthalate, toluene. We also recommend using "hot" fluorination in the hot cell using azeotropically dried salt [^{18}F]KF•Kryptofix 222•K_2CO_3 as a fluorinating reagent in the solvent system "acetonitrile – DMSO". A convenient method of synthesis of 4- [^{18}F] fluorobenzene is based on the use of 4.4'-diaryliodonium salt as the precursor. Subsequently, 4- [^{18}F] fluorobenzene was involved in the reaction of the cross combination for Sonogoshire / Stille for a number of radiotracers obtaining. We also emphasize the possibility of nucleophilic radiofluorination of diaryliodonium salts to produce meta-substituted [^{18}F] hydrofluoric ethers for the purpose of further synthesis of mGluR5 - radioligand for visualization of pathological changes in the brain.

In its turn, the aromatic radiofluorination of diaryliodonium tosylates allows to obtain [^{18}F] flumazenil with high radiochemical output. [18F]-marked flumazenil is an important radiopharmaceutical compound for evaluation of the concentration of the central benzodiazepine receptors in the brain. We note that the stability and reactivity of the tosylate precursor plays a key role in increasing the output of the fluorinated product. And this is what determines the volume of the synthesis of oxidants, an increase of which allows covering the largest possible number of people with modern diagnostics of dangerous diseases - PET.

The main area of appliance of salts under consideration is PET (positron emission tomography). PET has rather large range of applications. In oncology, PET is used for the detection of malignant tumors and assessment of cancer incidence and the presence of distant metastases (it's worth noting that it is more sensitive than CT and magnetic resonance tomography). In cardiology it is used for determining the blood flow state on the coronary arteries and for detection of ischemic heart disease, in neurological - for detection of functional changes in the brain vascular diseases, dementias, and also for the differential diagnosis of focal lesions.

All this seems very important for the development of continuous wellbeing as an innovative technology of improving its most important component - physical wellness. Therefore, for us it is important that along with me- medical organizations potential consumers of this product can be small research laboratories specializing in research in the field of polymer materials and developing innovative mass screening technology.

ISSN 2587-5574

It is known that the formation of diaryliodonium salts includes several steps. The first step is the oxidation of iodine-containing substrate to iodine compound (III) followed by coupling with the arene or aryl halide by electrophilic aromatic substitution mechanism. The final step is to obtain diaryliodonium salt by introduction of counter ion – water solutions – toluene sulfonic acid and potassium bromide (Merritt and Olofsson 2009).

Methods of synthesis of diaryliodonium using sulfuric acid immobilized on the silica gelsurface:

In a round bottom flask (25 ml) 204 mg (1 mmol) of iodobenzene and 3 ml of acetonitrile are added. Further, while stirring, 430 mg (1.46 mmol) Oxone® and 300 mg of sulfuric acid impregnated silica gel are added. Then 920 mg (9 mmol) of sulfuric acid is slowly added by dropping while cooling. Iodobenzene conversion is monitored by TLC method (the system "hexane - ethyl acetate 3: 1"). After 5 hours of complete iodobenzene conversion, 1.1 mmol of arene (ArH) is added dropwise to the reaction mixture. Then silica gel is filtered on a glass filter and 1.5 mmol of p – toluenesulphonic acid in the case of tosylates or potassium bromide in case of bromides are added to the stock solution in 2 ml of water. In the case of the tosylate the solvent's distilling off is required. The resulting oily precipitate is washed with hexane and diethyl ether mixture (3: 1). In case of bromides after adding potassium bromide the precipitation is observed, which is filtered and washed with water and hexane (Fig. 3):

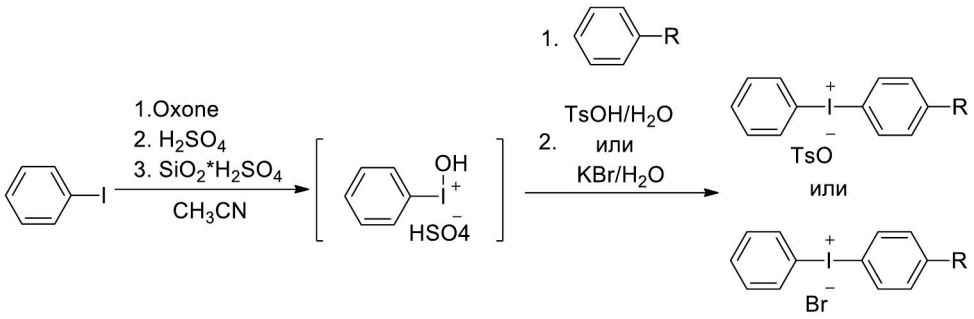

Figure 3 - Sedimentation after adding of potassium bromide

These products can be offered to the technological complexes for medical radionuclides and radiopharmaceuticals reagents production, as well as to diversified medical centers of preclinical and clinical research, to biochemical and biotechnological laboratories. Therefore, we propose a process for preparing asymmetric substituted diaryliodonium and tosylate salts with a bromide counter ion without isolation of intermediates, with the use of it available iodobenzene substrate and oxidation systems based on the relatively inexpensive reagents – Oxone® - H_2SO_4 и Oxone® - H_2SO_4- $SiO_2 \times H_2SO_4$. The outputs produced by this way are substantially similar to the outputs of the same substances produced with the help of previously developed techniques. In research we observed a number of principles of "green chemistry" [31]:

1. Produced compounds - diaryliodonium salts – have minimal toxicity and respectively do not harm the environment.

2. Synthesis reaction of the products is carried out in a minimal amount of solvent;

3. The number of auxiliary stages of receiving the desired product is minimized; the only additional operation is to clean the product from unreacted reactants;

4. The substances and their physical state are selected in such a way in order to limit the possibility of unforeseen accidents, including leaks, explosions and fires;

5 Analytical control in real time mode is used (TLC).

6. Environmentally friendly oxidant Oxone® and silica - reagent, which may be reused after regeneration, are used.

Polyvalent iodine reagents have been widely used as environmentally friendly oxidants in organic synthesis, mainly because of low toxicity, availability, ease of use, efficiency and stability in the air and moisture resistance. Thus, these compounds are an excellent alternative to heavy metals such as lead (IV), thallium (III) and copper (II). However, in the existing methods of diaryliodonium salts synthesis more toxic oxidants such as m-chloroperoxybenzoic acid are dominating or obtaining the respective salts. This article contains a description of the method of producing diaryliodonium salts (DuPont company) using Oxone® as an oxidant. Today in the world PET practice 18F-marked compounds are widely

spread, which is connected with the lifetime of 18F isotope sufficient for diagnostics. Using these compounds requires some special conditions like the accessibility of precursor, minimal time (less than an hour) and safe methods of synthesis. So the most promising way of production 18F-containing drugs is to use polyvalent iodine compounds.

Researches in the field of knowledge-intensive, innovative technologies, such as the production of radiofarm components of diagnostic purpose are crucial to social-and-economic development. The ultimate goal of the work within the development of radioisotope output is the production of import-substituting domestic isotope products for medical purposes. There is a huge potential need in increasing the efficiency of the production of substrates with a radioisotope traces; one of the directions is to provide the greatest selectivity when entering radioisotope traces into organic molecules.

4 Discussion and conclusion / Обсуждение и заключение

Creating of low-cost effective methods for the introduction of radioisotope traces in organic substratum will allow receiving domestic radio ligands for PET studies and further commercialization of the results of this work could give appreciable social-and-economic effects, including a significant increase in continuous wellbeing. The most expected results of cancer prevention using a diaryliodonium salts synthesis include the following:

1. The dramatic decline in the mortality from cardiac and cancer diseases, which accounts for the largest number of deaths among Russian population;
2. Improving the lives and health of the population due to better and earlier diagnosis, this will allow carrying out treatment of patients more efficiently;
3. Improve the ability to work and increase the employable period of the population;
4. The use of the existing and the development of scientific potential of domestic scientists and developers;
5. Creation of hundreds additional jobs for scientists, engineers and technical staff;
6. The development of import substitution industries;
7. Increasing the export potential of domestic producers.

In summary, we emphasize the important role of the convergence of innovative technologies in the fields of medicine and biochemistry in the formation of the continuous social wellbeing. This continuousness means a lifelong access to both material goods and the latest technologies, preservation of health and prevention of dangerous diseases. Even today, these technologies are becoming the dominant component of the continuous wellbeing, determining its standards in developed countries and directly affecting the consumption of high-tech goods. New diagnostic tools, vaccines and medicinal drugs can be obtained with the help of convergent medical and biotechnologies.

The peculiarity of the development of convergent biomedical technologies in the XXI century is not only in their rapid growth in the applied aspect, but also rapid expansion in human daily life. But for the continuous social wellbeing the development of innovative technologies gives another, more significantly prolonged, effect. It is an exceptional opportunity for sustainable development of the society in which the growth of economic activity of people will be accompanied by the extension of their physical wellbeing in the process of preventive diagnosis and disposal from dangerous diseases.

Today, economic and technological barriers in fight with one of these diseases - cancer - are the complication and high cost of the complex diagnostics and therapy. A breakthrough in the field of formation of the continuous wellbeing in cancer control is improving the availability of the latest achievements of nuclear medicine. One of the promising directions of this process we can see in using diaryliodonium salts synthesis with Oxone® as oxidant. The development of the available means of modern cancer diagnosis in the near future will allow socializing new technologies and generating new impulses to satisfy the growing needs in maintaining a prosperous life, expanding the boundaries of human happiness.

Список источников

1. Bartel A.P., Lichtenberg F. Technical Change, Learning, and Wages // National Bureau of Economic Research. Working Paper. – 1991. – vol. 4. – pp. 2732.

2. Rahn W., Brehm J. Individual-Level Evidence for the Causes and Consequences of Social Capital // American Journal of Political Sciences. – 1997. – Vol. 41. – pp. 999-1023.

ISSN 2587-5574

3. Diener E. Guidelines for national indicators of subjective well-being and ill-being // Social Indicators Network News. – 2005. – Vol. – pp.4-6.

4. Berkman L., Glass T., Brissette I., Seeman T. From social integration to health: Durkheim in the new millennium // Social Science and Medicine. – 2000. -Vol. 51.6. – pp. 843-857.

5. Melchior M., Niedhammer I., Berkman L., Goldberg M. Do psychosocial work factors and social relations exert independent effects on sickness absence? A six year prospective study of the GAZEL cohort // Epidemiol Community Health. – 2003. – Vol. 57(4). – pp.285–293.

6. Kahneman D., Riis J. Living and thinking about it: Two perspectives on life. In: Huppert F., N. Baylis, B. Kaverne (Eds.) The science of well-being. Oxford University Press, Oxford, 2005.

7. Alatartseva E., Barysheva G. What is Well-Being In The Modern Society: Objective View // The European Proceedings of Social & Behavioural Sciences. – 2016. – Vol. VII (February). – pp. 375-384.

8. Zhironkin S., Gasanov M., Zhironkina O. The Analysis of Social Wellbeing Indicators in the Context of Russian Economy Structural Changes // The European Proceedings of Social & Behavioural Sciences. – 2016. – Vol. VII (February). – pp. 124-131.

9. Zhironkin S., Guzyr V. Social Responsibility of Business – an Important Factor of Continued Wellbeing // The European Proceedings of Social & Behavioural Sciences. – 2016. Vol. VII. – pp. 160–166.

10. Gasanov M.A., Zhironkin S.A. Neo-industrial Base of Network Social Prosperity in the Russian Economy // Procedia - Social and Behavioral Sciences. – 2015. – Vol. 166. – pp. 97–102.

11. Fields G.S., Yoo G. Falling Labor Income Inequality in Korea's Economic Growth: Patterns and Underlying Causes // Review of Income and Wealth. – 2000. – Series 46, vol. 2. – pp. 139-159.

12. Gallup G.H., Hill E. The secrets of long life. New York, Geis Associates. Random House, 1960.

13. Koshiro, K. Lifetime employment in Japan: three models of the concept. Foreign Labor Developments // Bureau of Labor Statistics. – 2012. – Vol. 23. – pp.44-53.

14. Coons C. Weber M. Paternalism: Theory and Practice. Cambridge, Cambridge University Press, 2013.

15. Прокудина М.Д., Нуфер Л.П. Статистический анализ уровня смертности в Кемеровской области // Экономика и предпринимательство. – 2016. – № 1-2 (66-2). – С. 411-414.

16. Прокудина М.Д. Статистический анализ, оценка и прогнозирование занятости населения кемеровского региона: Дисс. канд. экон. наук. – Москва, 2006.

17. Каленов О.Е. Эволюция социального и экономического развития северных территорий России // Экономика знаний: теория и практика. – 2017. – №2. – С.39-48.

18. Bielawski M., Olofsson B. High-yielding one-pot synthesis of diaryliodonium triflates from arenes and iodine or aryl iodides // Chemical Communications. – 2007. – Vol. 73(6). – pp. 2521.

19. Pike V.W., Butt F., Shah A., Widdowson D.A. Facile synthesis of substituted diaryliodonium tosylates by treatment of aryltributylstannanes with Koser's reagent // Journal of the Chemical Society, Perkin Transactions. – 1999. – Vol. 1. – pp. 245–248.

20. Edwards R., Westwell A.D., Daniels S., Wirth T. Convenient Synthesis of Diaryliodonium Salts for the Production of [18F]F-DOPA // European Journal of Organic Chemistry. – 2015. – Vol. 21. – pp. 625–630.

21. Stegmayr C., Schöneck M., Oliveir D. Reproducibility of O-(2-18F-fluoroethyl)-L-tyrosine uptake kinetics in brain tumors and influence of corticoid therapy: an experimental study in rat gliomas // European Journal of Nuclear Medicine and Molecular Imaging. – 2016. – Vol. 43. – pp. 1115–1123.

22. Kinoshita H., Yamakado H., Kitano T. Diagnostic utility of FDG-PET in neurolymphomatosis: report of five cases // Journal of Neurology. – 2016. – Vol. 2. – pp. 1–8.

23. Telu S., Chun J.-H., Simeon F.G., Lu S., Pike V.W. Syntheses of mGluR5 PET radioligands through the radiofluorination of diaryliodonium tosylates // Organic and Biomolecular Chemistry. – 2011. – Vol. 9. – pp. 6629.

24. Burns J.H. Happiness and utility: Jeremy Bentham's equation // Utilitas. – 2005. – Vol. 17. – pp. 46–61.

25. Sen A. Commodities and Capabilities. Amsterdam, Elsevier, 1985.

26. Clark A.E., Oswald, A.J. A Simple Statistical Method for Measuring How Life Events Affect Happiness // International Journal of Epidemiology. – 2002. – Vol. 31(6). – pp. 1139–1144.

27. Easterlin R. A. Will Raising the Incomes of All Increase the Happiness of All? // Journal of Economic Behavior and Organization. – 1995. – Vol. 27(1). – pp. 35–47.

28. Ametamey S.M., Honer M., Schubiger P.A. Molecular Imaging with PET // Chemistry Review. – 2008. – Vol. 108(5). – pp. 1501–1516.

29. Zhang M.-R., Kumata. K., Suzuki K. A practical route for synthesizing a PET ligand containing [18F]fluorobenzene using reaction of diphenyliodonium salt with [18F]F- // Tetrahedron Letters. – 2007. Vol. 48. – pp. 8632–8634.

30. Wang B., Cerny R.L. Fluoride-promoted ligand exchange in diaryliodonium salts // Journal of Fluorine Chemistry. – 2010. – Vol. 131. – pp. 1113–1121.

31. Anastas P.T., Kirchhoff M.M. Origins, current status, and future challenges of green chemistry // Accounts of Chemical Research. – 2002. – Vol. 22. –686- 694.

References

1. Bartel A.P., Lichtenberg F. Technical Change, Learning, and Wages. National Bureau of Economic Research. Working Paper. 1991. Vol. 4. pp. 2732.

2. Rahn W., Brehm J. Individual-Level Evidence for the Causes and Consequences of Social Capital. American Journal of Political Sciences. 1997. Vol. 41. pp. 999-1023.

3. Diener E. Guidelines for national indicators of subjective well-being and ill-being. Social Indicators Network News. 2005. Vol. pp.4-6.

4. Berkman L., Glass T., Brissette I., Seeman T. From social integration to health: Durkheim in the new millennium. Social Science and Medicine. 2000. Vol. 51.6. pp. 843-857.

5. Melchior M., Niedhammer I., Berkman L., Goldberg M. Do psychosocial work factors and social relations exert independent effects on sickness absence? A six year prospective study of the GAZEL cohort. Epidemiol Community Health. 2003. Vol. 57(4). pp.285–293.

6. Kahneman D., Riis J. Living and thinking about it: Two perspectives on life. In: Huppert F., N. Baylis, B. Kaverne (Eds.) The science of well-being. Oxford University Press, Oxford, 2005.

7. Alatartseva E., Barysheva G. What is Well-Being In The Modern Society: Objective View in The European Proceedings of Social & Behavioural Sciences, Vol. VII (February), 2016, pp. 375-384.

8. Zhironkin S., Gasanov M., Zhironkina O. The Analysis of Social Wellbeing Indicators in the Context of Russian Economy Structural Changes. The European Proceedings of Social & Behavioural Sciences. 2016. Vol. VII (February). pp. 124-131.

9. Zhironkin S., Guzyr V. Social Responsibility of Business – an Important Factor of Continued Wellbeing. The European Proceedings of Social & Behavioural Sciences. 2016. Vol. VII. pp. 160–166.

10. Gasanov M.A., Zhironkin S.A. Neo-industrial Base of Network Social Prosperity in the Russian Economy. Procedia - Social and Behavioral Sciences. 2015. Vol. 166. pp. 97–102.

11. Fields G.S., Yoo G. Falling Labor Income Inequality in Korea's Economic Growth: Patterns and Underlying Causes. Review of Income and Wealth. 2000. Series 46, vol. 2. pp. 139-159.

12. Gallup G.H., Hill E. The secrets of long life. Geis Associates – Random House, New York, 1960.

13. Koshiro K. Lifetime employment in Japan: three models of the concept. Foreign Labor Developments. Bureau of Labor Statistics. 2012. Vol. 23. pp.44-53.

14. Coons C. Weber M. Paternalism: Theory and Practice. Cambridge University Press, Cambridge, 2013. 634 p.

15. Prokudina M.D., Nufer L.P. Statisticheskij analiz urovnja smertnosti v kemerovskoj oblasti [Mortality statistics in Kemerovo Region]. Jekonomika i predprinimatel'stvo = Economics and business. 2016. Vol. 1-2 (66-2). pp. 411-414.

16. Prokudina M.D. Statisticheskij analiz, ocenka i prognozirovanie zanjatosti naselenija kemerovskogo regiona [Statistic analysis, estimation and prediction of employment in Kemerovo Region]. Candidate of Science Thesis, Moscow, 2006.

17. Kalenov O.E. Jevoljucija social'nogo i jekonomicheskogo razvitija severnyh territorij Rossii [Evolution of socio-and-economic development of the Russian northern lands]. Jekonomika znanij: teorija i praktika = Knowledge economy: theory and practice. 2017. Vol 2. pp.39-48.

18. Bielawski M., Olofsson B. High-yielding one-pot synthesis of diaryliodonium triflates from arenes and iodine or aryl iodides. Chemical Communications. 2007. Vol. 73(6). pp. 2521.

19. Pike V.W., Butt F., Shah A., Widdowson D.A. Facile synthesis of substituted diaryliodonium tosylates by treatment of aryltributylstannanes with Koser's reagent. Journal of the Chemical Society, Perkin Transactions. 1999. Vol. 1. pp. 245–248.

20. Edwards R., Westwell A.D., Daniels S., Wirth T. Convenient Synthesis of Diaryliodonium Salts for the Production of [18F]F-DOPA. European Journal of Organic Chemistry. 2015. Vol. 21, pp. 625–630.

21. Stegmayr C., Schöneck M., Oliveir D. Reproducibility of O-(2-18F-fluoroethyl)-L-tyrosine uptake kinetics in brain tumors and influence of corticoid therapy: an experimental study in rat gliomas. European Journal of Nuclear Medicine and Molecular Imaging. 2016. Vol. 43. pp. 1115–1123.

22. Kinoshita H., Yamakado H., Kitano T. Diagnostic utility of FDG-PET in neurolymphomatosis: report of five cases. *Journal of Neurology.* 2016. Vol. 2. pp. 1–8.

23. Telu S., Chun J.-H., Simeon F.G., Lu S., Pike V.W. Syntheses of mGluR5 PET radioligands through the radiofluorination of diaryliodonium tosylates. Organic and Biomolecular Chemistry. 2011. Vol. 9. pp. 6629.

24. Burns J.H. Happiness and utility: Jeremy Bentham's equation. Utilitas. 2005. Vol. 17. pp. 46–61.

25. Sen A. Commodities and Capabilities. Amsterdam: Elsevier, 1985.

26. Clark A.E., Oswald, A.J. A Simple Statistical Method for Measuring How Life Events Affect Happiness. International Journal of Epidemiology, 2002. Vol. 31(6). pp. 1139–1144.

27. Easterlin R. A. Will Raising the Incomes of All Increase the Happiness of All? Journal of Economic Behavior and Organization. 1995. Vol. 27(1). pp. 35–47.

28. Ametamey S.M., Honer M., Schubiger P.A. Molecular Imaging with PET. Chemistry Review. 2008 Vol. 108(5). pp. 1501–1516.

29. Zhang M.-R., Kumata. K., Suzuki K. A practical route for synthesizing a PET ligand containing [18F]fluorobenzene using reaction of diphenyliodonium salt with [18F]F-. Tetrahedron Letters. 2007. Vol. 48. pp. 8632–8634.

ISSN 2587-5574

30. Wang B., Cerny R.L. Fluoride-promoted ligand exchange in diaryliodonium salts. Journal of Fluorine Chemistry. 2010. Vol. 131. pp. 1113–1121.

31. Anastas P.T., Kirchhoff M.M. Origins, current status, and future challenges of green chemistry. Accounts of Chemical Research. 2002. Vol. 22. 686- 694.

Авторы

Барышева Галина Анзельмовна, доктор экономических наук, профессор школы инженерного предпринимательства, Национальный исследовательский Томский политехнический университет, 634050 Томск, пр. Ленина, 30, e-mail: ganb@tpu.ru

Егорова Мария Сергеевна, Отделение социально-гуманитарных наук, ассистент, Национальный исследовательский Томский политехнический университет, 634050 Томск, пр. Ленина, 30, e-mail: egorovams@tpu.ru

Шмидт Андрей Эдуардович, Магистрант, Национальный исследовательский Томский политехнический университет, 634050 Томск, пр. Ленина, 30.

Богачев Андрей Игоревич, Магистрант, Национальный исследовательский Томский политехнический университет, 634050 Томск, пр. Ленина, 30.

Authors

Galiva A. Barysheva, Doctor of Sc. (Economics), Engineering entrepreneurship school, National Research Tomsk Polytechnic University, 30 Lenin Av., 634050, Tomsk, Russian Federation, e-mail: ganb@tpu.ru

Maria S. Egorova, assistant, Department of social-and-humanitarian sciences, National Research Tomsk Polytechnic University, 30 Lenin Av., 634050, Tomsk, Russian Federation, e-mail: egorovams@tpu.ru

Andrey Shmidt, Master's Degree Student, National Research Tomsk Polytechnic University, 30 Lenin Av., 634050, Tomsk, Russian Federation

Andrey I. Bogachev, Master's Degree Student, National Research Tomsk Polytechnic University, 30 Lenin Av., 634050, Tomsk, Russian Federation

Библиографическое описание статьи

Барышева Г. А. Профилактика онкологических заболеваний с использованием диарилиодионных солей с Oxone® в качестве оксиданта: инновационный метод повышения социального благополучия / Г. А. Барышева, М. С. Егорова, А. Э. Шмидт, А. И. Богачев // Экономика и управление инновациями — 2018. —№ 1 (4). — С. 4–15.

Reference to article

Barysheva G.A., Egorov M.S., Bogachev A.E., Shmidt A.I. Cancer prevention using a diaryliodonium salts synthesis with Oxone® as oxidant: innovative method of improving social wellbeing. Economics And Innovation Management, 2018, no. 1 (4), pp. 4-15.