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Development of New Generation Drugs by Enriching Them with Gases

Aleksandr Urakov [a*], Petr Shabanov [b] and Lubov Lovtsova [c]

[a] Department of General and Clinical Pharmacology, Izhevsk State Medical Academy, Kommunarov Str., 281, 426034, Izhevsk, Russia.
[b] Department of Neuropharmacology, Institute of Experimental Medicine, Acad. Pavlov Str., 12, 197022, Saint Petersburg, Russia.
[c] Department of General and Clinical Pharmacology, Volga Medical Research University, Minin and Pozharsky Str., 10/1, 603005, Nizhny Novgorod, Russia.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AU and PS designed the study and wrote the protocol. Authors AU and LL designed the study, wrote the protocol and the first draft of the manuscript. Authors AU and PS managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Until today, the mechanism of action of drugs is traditionally considered without taking into account the physical-chemical properties of dosage forms. However, at the beginning of the 21st century, there were reports that all drugs contain unaccounted gases that enter drugs from the air and affect the quality of drugs. It is shown that the composition and amount of gases in the dosage forms of all drugs changes their mechanical, physical, chemical and physical-chemical properties and the mechanism of action of drugs, especially when applied topically It is reported that changing the content of gases in drug solutions and tablets allows to regulate their mass, volume, specific gravity, porosity, physico-chemical activity and local action on the routes of drug administration.

**Corresponding author: E-mail: urakoval@live.ru;*

The identification of this pattern allowed to start the production of completely new drugs with a certain gas composition and with a new local pharmacokinetics and a new local pharmacodynamics. The formulations of new drugs in which gas is an auxiliary, formative or main ingredient are given. It is proposed to control the gas composition of medicines as an indicator of their quality and an important factor of their physical-chemical activity. It is proved that the gas in the drug can be not only neutral, but also auxiliary, oppositional, and sometimes the main ingredient. Thus, the control and accounting of the gas contained in drugs will allow the creation of a new generation of drugs in the near future.

Keywords: Development; modernization; reprofiling; drug composition; physical-chemical properties.

1. INTRODUCTION

Initially, the search for new drugs was inseparable from the discovery and study of the chemical properties of new chemical elements and new substances [1]. Historically, a very important role in drugs development was played by the German research doctor Paul Ehrlich. It was he who, in 20st century, was the first to point out the presence of molecular targets for drugs in humans and animals and justified the prospects of directed drug synthesis [2]. However, by now almost all chemical elements have already been discovered. There were a total of 118 of them [3]. In these conditions, the search and development of new drugs are no longer connected only with new chemical elements finding. Therefore, chemical and biochemical synthesis of new compounds and radicals plays a huge role in the creation of new drugs [1,4]. Nevertheless, the concepts of "chemical element" and "substance" remain the main category of chemistry, pharmacy and pharmacology. And no other suggestions have been offered in addition to it and in return for it with the same great value for the process of creating new drugs [5].

In this regard, in the world of pharmacy and pharmacology, as well as in the world of materials science, physics and chemistry, until today, researchers traditionally represent chemical elements (and substances) by their chemical formulas, names and symbols [6]. Usually the material substance itself is also identified with its chemical symbol. In relation to his tradition, all researchers consider each drug from the standpoint of physics, chemistry and physics-chemistry of the original substance, which has become its main active ingredient. Moreover, everyone automatically (without thinking about the legality) replaces the drug with this substance in chemically pure form (namely, with the brand "PFA", that is, pure for analysis) [7].

That is why in textbooks and reference books on medicines, as well as in encyclopedias, reference books and textbooks on chemistry and physics, the characteristics of medicines and chemicals, their physical, chemical, biological activity (including the mechanism of action) are presented in the same way and, very importantly, without connection with changing environmental conditions [6,8]. At the same time, it is believed that each substance under consideration always and everywhere has an ideal high quality and there are completely no impurities in it. In addition, it is understood that this substance is not combined with other active substances, and also it does not represent a certain material object in a certain aggregate state with other physical, chemical and other properties. In particular, it is assumed that this substance is not in atmospheric air and not in water, therefore air and other gases, as well as water, are absent in this substance [9,10].

It follows from this that in encyclopedias, in physical and chemical reference books, as well as in scientific articles, the characteristics of substances and chemical elements, in particular, their properties, are theoretical (illusory) in nature. Frederick Suppe stated this most vividly: "Pure substance is an idealized essence" [11].

2. THE SOURCES OF THE PROBLEM

Since ancient times, real medicines are not chemical reagents, nor chemical formulas and/or their symbols, but certain physical objects that are manufactured by different manufacturers with different quality. It is in this connection that any drug in real conditions always differs from its illusory encyclopedic standard [10]. Natural factors (ambient temperature and local temperature, atmospheric pressure, the composition of the surrounding air, humidity, acidic and osmotic activity of the environment, etc.) have a great influence on the quality of

drugs. The fact is that these factors have an impact on all subjects, not only on drugs [9,10].

Based on the fact that in terrestrial conditions all factors of the natural environment are very variable, all objects, including tablets and solutions of drugs, are subject to changes in this environment. At the same time, their physical and chemical properties initially change. After them, the biological (pharmacological) activity of drugs changes. That is why real drugs in natural conditions always differ significantly from the idealized essence of pure chemical compounds [9,10,12].

According to established practice, the creators of new drugs and the developers of technologies for the production of these drugs have long accepted that there are absolutely no "pure" substances in their hands [13]. The facts are that drug manufacturers deal, at best, with substances that have certain quality indicators (in particular, they have certain mechanical and physical-chemical properties), accepted as a quality standard. At the same time, the Pharmacopoeia states that the same substances, but with different physical-chemical properties, are low-quality substances that should be rejected [6].

It is reported that the change in the physical-chemical properties of drugs does not deprive them of biological activity [14]. Moreover, a purposeful change in the physical-chemical properties of drugs, especially to values that go beyond the physiological in their severity, makes it possible to significantly expand the range of their mechanism of action when applied topically. That being said following pattern appears. If the physical-chemical activity of drugs corresponds to the normal (physiological) values of human body tissues, drugs have a minimal nonspecific local effect. If this activity of drugs differs from the norm in one direction or another, the drugs begin to have a non-specific local mechanism of action in places of local interaction. It has been reported that as the difference in their physicochemical properties increases, drugs consistently begin to have the following pharmacological effects: local irritant effect, denaturing effect and, finally, cauterizing effect [15].

The first report that an artificial change in the physical-chemical properties of real liquid drugs (solutions), carried out by changing their acid (alkaline), osmotic, temperature activity and /or by enriching them with gases, gives drugs a new pharmacological activity and enhances their local effect, appeared in Russia. This pattern was first reported in 2007 [14]. It has been reported that drug quality indicators in solutions and tablets are determined to a large extent by the properties not of their main ingredients, but by the properties of formative substances. The fact is that modern liquid and solid drugs consist of fillers by more than 50%. For example, solutions of most medicines consist of more than 97% water. Therefore, the physical-chemical properties of drug solutions depend mainly on the properties of this water. Moreover, it turned out that due to the changes in the content of carbon dioxide (CO_2) and oxygen gas (O_2) in drug solutions, it is possible to develop new drugs with completely new physical-chemical properties and with a new mechanism of action [16].

One of the first reports was that 0.9% sodium chloride solution, after dissolving CO_2 in it at an excess pressure of 0.2 ATM, acquires the ability of cold boiling under normal atmospheric pressure. This helps the solution to form carbon dioxide bubbles inside itself. It turned out that thanks to these gas bubbles, the solution becomes very well "visible" for ultrasound examination. Therefore, such a solution with intraperitoneal administration provides ultrasound visualization of the process of fluid movement inside the abdominal cavity. This increases the efficiency of washing the abdominal cavity with purulent peritonitis. Therefore, it was proposed to use such a solution with a high gas content in a completely new way, namely, as an original ultrasound contrast agent that improves abdominal flushing in purulent peritonitis by improving visualization of the process of moving the "boiling solution" inside the abdominal cavity [14,16].

Following this, a message appeared that the water quality and properties can be changed by adding hydrogen peroxide to it. Solutions of 0.01-3% hydrogen peroxide have also been reported to change the mechanism of action of many drugs. The fact is that hydrogen peroxide under the action of the enzyme catalase decomposes into water and oxygen gas, which increases the intensity of cold boiling of water. In turn, the enzyme catalase is always present in the blood and in purulent masses. Therefore, the additional introduction of hydrogen peroxide into antiseptic solutions can be used to turn them into drugs that quickly dissolve, loosen and discolor thick

pus, sulfur plugs, blood clots and spots, as well as skin and nail plates in the area of bruises and hematomas [16].

The above results showed that a pure chemical substance or a pure chemical agent is far from a real medicine. Indeed, a laboratory (pharmaceutical) product, despite its name, similar to the name of a chemical substance, is not identical to a perfectly pure substance (chemical reagent) used as the main ingredient of this product. Therefore, it is not entirely correct to use only a chemical formula to designate a laboratory product, especially when this product is a ready-made medicine with certain physical-chemical properties. This problem is not completely new and unusual. For the first time, researchers encountered it when studying the physical-chemical properties and quality of water. Initially, it was established that "water is H_2O". The discovery that water is a compound of hydrogen and oxygen (or, in the terminology of that time, flammable air and dephlogisticated air) showed that water is not an element, but a substance.

This discovery was made in the early 1780s on behalf of no less than four people: Henry Cavendish, Antoine Lavoisier, Gaspard Monge and James Watt [17]. Since then, it has been believed that water is a chemical substance. The chemical formula of water (H_2O) was discovered by A. Humbolt in 1805 [18] (Fig. 1).

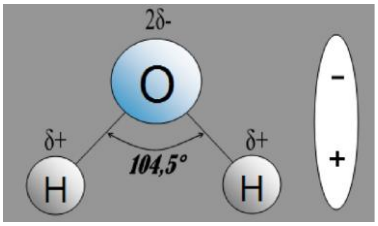

Fig. 1. Schematic representation of the H_2O molecule

Almost 100 years later, at the beginning of the XXI century, scientists managed to deduce the nonlinear geometry of the pyramidal shape of the water molecule, after which 2 more variants of the image of the structure of the water molecule began to be used (Fig. 2).

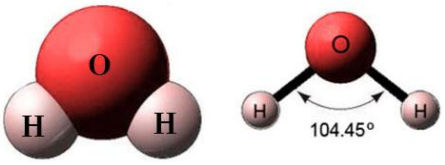

Fig. 2. Stylized schematic representation of the H_2O molecule

Until today, the chemical composition of water is everywhere and unambiguously reduced to the composition of the water molecule [19]. It is considered an axiom that:

- Water (hydrogen oxide) has the chemical formula H_2O;
- A water molecule consists of two hydrogen atoms and one oxygen atom;
- Under normal conditions, it is a transparent liquid that has no color (in a small volume), smell and taste.

It follows from this that everyone has forgotten that water is not only a liquid, but also steam, snow, and ice…(Fig. 3). They forgot that water is not in an airless space.

This is surprising, but the standard list of water quality indicators does not contain a list of gases dissolved in water, and does not provide for the possibility of finding water in different aggregate states, in particular, in the form of gas and ice. At the same time, back in the first chapter of Genesis, Moses wrote: "And God said, Let there be a RAKIYA," that is, "a space" (which in some texts of the Scriptures is translated as "firmament") "in the middle of the water, and let it separate the water from the water. And God created the firmament and separated the water that is under the firmament from the water that is above the firmament. And it became so. And God called the firmament SKAMAIM" (which, according to many scientists, is the same as "ibi aquae" ("There are waters"), but they translate as "Heaven"). "And the evening and morning were the second day. And God said, Let the water gather under heaven (SCHAMAIM) in one place, and let the dry land appear: and it became so. And God called the dry land the Earth, and He called the assembly of waters the seas, etc." [20].

Fig. 3. Spatial structure of water in the state of ice, liquid and gas (steam)

Then God placed various plants and various animals in the water.

Today we know that plants form oxygen that penetrates into the water, and fish consume oxygen from the water. In other words, nature shows us that in natural conditions there is dissolved oxygen gas in the water of rivers, lakes and seas. In addition, nature shows us that water can be solid in the form of snow and ice, and can also be gaseous in the form of steam. All this indicates that the water molecule and its generally accepted symbols do not at all reflect the essence of natural objects made of water, its steam, snow and ice. Sibel Erduran said this most vividly: "H2O is the chemical essence of water, not the essence of water" [21].

This statement confirms several reports. In particular, it is shown that drinking water in all parts of the world has different quality. As a rule, the water is acidic and has a pH below 6.0. But it has been reported that the acidity of the water may differ by 20 times [22]. In addition, the quality of water and concrete made from it at different heights above sea level at different atmospheric pressure values are different. It was reported that in the high-altitude area at low atmospheric pressure, water and concrete contain less air than in the plain area with normal atmospheric pressure [23-28].

Similar data on the effect of the external air pressure on the porosity of aqueous solutions and solids, their specific gravity and volume, were obtained in the field of physical-chemical pharmacy. In particular, it was reported that under conditions of positive atmospheric pressure, almost all material objects, including tablets and drug solutions, contain gases, since air gases easily penetrate them [13]. Vacuum reduces, and excessive external pressure increases the content of gases in water and drug's aqueous solutions.

After it was shown that changes in the content of gases in water and in aqueous solutions of medicines change their physical-chemical properties, in 2015 there was a message about the possibility of developing drugs (and materials) of a new generation by purposefully changing their physico-chemical properties, including changing the composition of gases in them [9]. In fact, this message marked the beginning of a new scientific direction in materials science, which was called "physical-chemical materials science". The prospects of this direction were soon demonstrated by the example of changing the properties of water when the gas content in it changes [29]. It was shown that with a "normal" gas content in drinking water (surrounded by air at an atmospheric pressure of 760 mm Hg), freezing 150 ml of water led to the formation of ice with a volume of 161 cm3. After degassing this drinking water with the help of an average vacuum (at a negative pressure of 10-3 mm Hg), freezing 150 ml of water led to the formation of ice with a volume of 154 cm^3. Then, after artificially increasing the carbon dioxide content in the water due to incubation of water surrounded by carbon dioxide at an excess pressure of 0.2 ATM relative to atmospheric pressure of 760 mm Hg. freezing 150 ml of water led to the formation of ice with a volume of 200 cm^3. Consequently, a decrease in the gas content in water reduces, and an increase in the gas content in water increases the volume of ice formed from this water. The first drug of the new generation was the "Floating tablet", which was like a porous food lump [30].

After that, a new generation of medicines were created from solutions. For this purpose, drug solutions were enriched mainly with carbon dioxide (CO_2) or oxygen gas (O_2) under excessive pressure and/or hydrogen peroxide was added to drug solutions (Fig. 4). The fact is that hydrogen peroxide can decompose under the action of catalase on water and oxygen gas. As a result, several groups of new generation drugs have been developed: bruising bleachers, pus solvents, alkaline bleachers, energy drinks and some other new drugs [14,16,31].

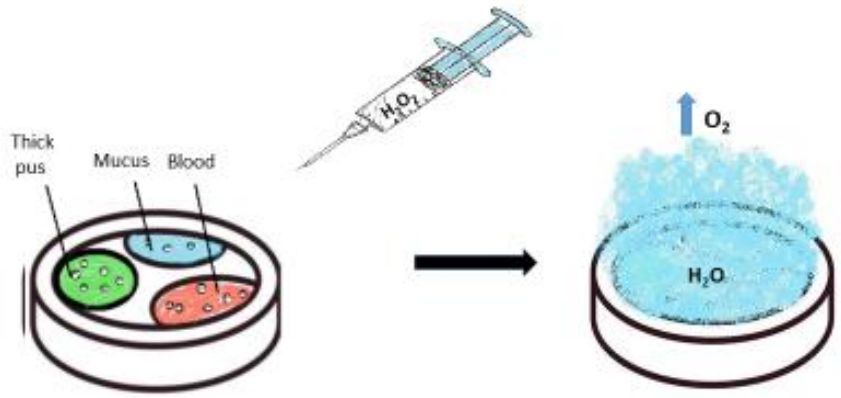

Fig. 4. Scheme of transformation of pus, mucus, and blood, which contain catalase, into a fluffy oxygen foam after administration of an alkaline hydrogen peroxide solution

Most of the new generation drugs are solutions with a pH of 8.4, in which the specified alkalinity is provided by the introduction of sodium bicarbonate.

The following is the composition of some new generation of drug solutions.

1. “Bruise bleacher” (RU Patent No. 2539380, 20.01.2015). It includes 0.01-0.03% hydrogen peroxide and 1.8% sodium bicarbonate [14].
2. “Lympho-subsitute for local maintaining viability of organs and tissues in hypoxia and ischemia” (RU Patent No. 2586292, 10.06.2016). It includes 0.01-0.03% hydrogen peroxide and 0.88% sodium chloride [32].
3. “E. M. Soikher's hyperoxygenated agent for venous oxygen saturation” (RU Patent No. 2538662, 10.01.2015). It includes 0.05-0.29% hydrogen peroxide, 0.10% sodium bicarbonate and 0.85% sodium chloride [33].
4. “Aerated mouthwash” (RU Patent No. 2635992, 17.11.2017). It includes 0.1-0.3% hydrogen peroxide, 0.6% sodium chloride, 0.15% sodium phosphate, 0.05% sodium hydrophosphate, 0.05% lysozyme and helium gas at an overpressure of 0.2 ATM at +8°C [14,16].
5. “Method and means for removal of sulphur plug” (RU Patent No. 2468776, 10.12.2012). It includes 0.3-0.5% hydrogen peroxide and 1.7-2.3% sodium bicarbonate [14].
6. “Bleaching cleanser of dentures” (RU Patent No. 2659952, 04.07.2018). It includes 3 ± 0,3% hydrogen peroxide, 2.0-10.0% sodium bicarbonate and oxygen gas at an overpressure of 0.2 ATM at +8°C [14,16].
7. “Hyper-gassed and hyper-osmotic antiseptic mixture” (RU Patent No. 2331441, 20.08.2008). It includes 2.7 – 3.0% hydrogen peroxide, 0.9- 10.0% sodium chloride and carbon dioxide at an overpressure of 0.2 ATM at +8 °C [14,16].
8. “Agent for increasing resistance to hypoxia” (RU Patent No. 2604129, 10.12.2016). It includes 0.3- 0.5% hydrogen peroxide and oxygen gas at an overpressure of 0.2 ATM at +8 °C [32].
9. “Energy drink” (RU Patent No. 2639493, 21.12.2017). It includes 7.0% glucose, 0.7% ethyl alcohol, 0.3- 0.5% hydrogen peroxide, citric acid until the pH is 4.0 ± 0.5 and oxygen gas under excess pressure 0.2 ATM at + 8 °C [32].
10. “Means for physical endurance increase” (RU Patent No. 2634271, 24.10.2017). It includes 7.0% glucose, 5% hydrogen peroxide and oxygen gas under excess pressure 0.2 ATM at + 8 °C [32].
11. “Bleaching opener of dried blood for wrapping bandages adhered to a wound” (RU Patent No. 2653465, 08.05.2018). It includes 0.75-1% hydrogen peroxide, 1.2% sodium bicarbonate and 0.5% lidocaine hydrochloride [33].
12. “Peeling agent for foot hyperkeratosis” (RU Patent No. 2730451, 24.08.2020). It includes 0.5-20.0% hydrogen peroxide, 3.0-5.0% potassium hydroxide, oxygen gas at an excess pressure of 0.2 ATM at +8 °C. The solution has a pH of 13.0-14.0, osmotic activity of 350-560 mosmol / l and a temperature of +38 - +42°C [14,16].

13. “Gel for children's skin” (RU Patent No. 2713943, 11.02.2020). It includes 0.75-1.0% hydrogen peroxide, 2% lidocaine hydrochloride and cation-active surfactants - in the amount of providing a gel-like consistency at +24 - +26°C [34].
14. “Aerosol for inhalations in obstructive bronchitis” (RU Patent No. 2735502, 03.11.2020). It includes 1.2 sodium bicarbonate, 03-05% hydrogen peroxide and 0.5% lidocaine hydrochloride. The aerosol is prepared from a solution at a pH of 8.5, osmotic activity of 280-300 mosmol/l of water and temperature +41-+55 °C [35].
15. “Aerosol for invasive mechanical ventilation in COVID-19” (RU Patent No. 2742505, 08.02.2021). It includes 2-10% sodium bicarbonate, 03-05% hydrogen peroxide and 0.5% lidocaine hydrochloride. The aerosol is prepared from a solution at a pH of 8.5, osmotic activity of 370-1990 mosmol/l of water and temperature +37-+55°C [35].

During the same period of time other countries also created inventions that contain hydrogen peroxide solutions [36,37]. But these hydrogen peroxide solutions have a pH value of less than 7.0, a temperature below +37°C and do not contain overpressured gas in their composition.

3. DISCUSSION

Thus, over the past 5 years, a dozen and a half new drugs have been developed, which differ from all known drugs in that they are all enriched with gases that are injected into drugs under high pressure, and /or contain a warm alkaline solution of hydrogen peroxide (WAHPS), which, when interacting with the enzyme catalase in this conditions, decomposes into water and oxygen gas [12-14,16,35]. Such drugs, when applied topically, have such local pharmacokinetics and local pharmacodynamics, which significantly distinguishes them from the pharmacokinetics and pharmacodynamics of known drugs [12]. This difference between new drugs and "old" drugs opens up new opportunities in the treatment of many diseases: purulent diseases, wax plugs. vascular catheter thrombosis, ischemia, hypoxia, and respiratory obstruction in COVID-19 [35]. In addition, new drugs allow to discolor the skin in the area of bruises, bloody areas of skin and other tissues, skin and nail plate in the area of the hematoma, to whiten teeth, dental and ceramic products [12,13,14-16,31,32,33,34,35]. Therefore, it is necessary to continue research in this direction in order to get more information about the advantages and disadvantages of drugs enriched with gases both with the help of a WAHPS and/or with the help of overpressure of various gases.

4. CONCLUSION

Thus, water, solutions and tablets of drugs have different gas content. The content and composition of gases in liquid and solid dosage forms depends on the composition of the gases surrounding them and the magnitude of their pressure. Changing the gas content in drugs changes their volume, mass, porosity, specific gravity and other physical, chemical, physical-chemical and mechanical properties, that is, the quality of drugs. In addition, changing the composition and amount of gases in solutions and tablets of drugs allows to change their local pharmacokinetics and local pharmacodynamics. Therefore, the inclusion of certain gases in the composition of liquid and solid drugs is a simple and effective way to modernize drugs. Drugs containing the "right" composition of gases are very beneficial for topical use. In this regard, there is every reason to include certain gases in the formulation of certain drugs. In addition, it is proposed to include the control of gas composition of drugs in the list of controlled indicators of their quality, because the presence and composition of gases in drugs affects the quality of drugs and can determine the local mechanism of action of drugs, especially when they are used topically.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. Metabolites. 2012;2(2): 303-336.
   DOI: 10.3390/metabo2020303.
2. Andrade EL, Bento AF, Cavalli J, at al. Non-clinical studies required for new drug

development - Part I: Early *in silico* and *in vitro* studies, new target discovery and validation, proof of principles and robustness of animal studies. Brazilian Journal of Medical and Biological Research = Revista Brasileira de Pesquisas Medicas e Biologicas. 2016; 49(11):e5644.
Available:https://doi.org/10.1590/1414-431X20165644.

3. Chemical Element. From Wikipedia, the free encyclopedia; 2022.
Available:https://en.wikipedia.org/wiki/Chemical_element.
[Cited 2022 Dec 15]

4. Dahiya K. Drug discovery, development and approval process: Need for an interdisciplinary approach. Drug Discovery - Priory Medical Journals. First Published June 2007.
Available:https://www.priory.com/pharmacy/Drug_Discovery.htm
[Cited 2022 Dec 15].

5. Chellan P, Sadler PJ. The elements of life and medicines. Philos Trans A Math Phys Eng Sci. 2015;373(2037):20140182.
DOI: 10.1098/rsta.2014.0182.

6. United States Pharmacopeia 36 and National Formulary 31. 2013;(3 Vol Set). [Cited 2022 Dec 01].

7. Egorova KS, Ananikov AV. Toxicity of metal compounds: Knowledge and Myths. Organometallics. 2017;36(21):4071–4090. DOI: 10.1021/acs.organomet.7b00605.

8. Jeevanandam J, Barhoum A, Chan YS, et al. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol. 2018;9:1050-1074.
DOI: 10.3762/bjnano.9.98.

9. Urakov AL. The change of physical-chemical factors of the local interaction with the human body as the basis for the creation of materials with new properties. Epitőanyag – Journal of Silicate Based and Composite Materials. 2015;67(1):2–6.
Available:http://dx.doi.org/10.14382/epitoanyag-jsbcm.2015.1

10. Urakov AL. Development of new materials and structures based on managed physical-chemical factors of local interaction. IOP Conf. Ser.: Mater. Sci. Eng. 2016;123:012008.
DOI: 10.1088/1757-899X/123/1/012008.

11. Suppe F. The semantic conception of theories and scientific realism. Urbana: University of Illinois press; 1989. Available:https://philpapers.org/rec/SUPTSC.
[Cited 2022 Dec 15].

12. Urakov AL, Urakova NA., Stolyarenko AP. How to turn an old medicine into a new medicine. J. Bio. Innov. 2020;9(5): 774-777.
Available:https://doi.org/10.46344/JBINO.

13. Urakov A, Alies M, Urakova N, et al. The change in the quality and properties of new materials by changing the content of gas in them. The 5-th International Conference on Competitive Materials and Technology Processes (Miskolc-Lillafured, Hungary, October 8-12, 2018). Book of Abstracts. 2018;49-50.

14. Urakov A, Urakova N, Reshetnikov A. Oxygen alkaline dental's cleaners from tooth plaque, food debris, stains of blood and pus: A narrative review of the history of inventions. Journal of International Society of Preventive & Community Dentistry. 2019;9(5):427-433.
DOI: 10.4103/jispcd.JISPCD_296_19.

15. Urakov A, Urakova N. Osmotic activity of drugs is an important factor of their local action at their Injection site: What we don't use to prevent post-injection abscesses. Journal of Pharmaceutical Research International. 2021;33(59B):647-650.
DOI: 10.9734/jpri/2021/v33i59B34428.

16. Urakov AL. Creation of "necessary" mixtures of baking soda, hydrogen peroxide and warm water as a strategy for modernization bleaching cleaners of ceramic. Epitőanyag – Journal of Silicate Based and Composite Materials. 2020;72 (1):30-35.
DOI:10.14382/epitoanyag-jsbcm.2020.6.

17. Elements and Atoms: Chapter 6. Water is not an element: Lavoisier.
Available:https://web.lemoyne.edu/~giunta/EA/LAVEAUann.HTML.
[Cited 2022 Dec 15].

18. Vigasin AA. Molecular structure and chemical properties of atmospheric water. Types and Properties of Water. Encyclopedia of Life Support Systems. 2020;I.

Available:https://www.eolss.net/ebooklib/cart.aspx.

[Cited 2022 Dec 15].

19. Eisenberg D, Kauzmann W. The structure and properties of water. New York, Oxford: Oxford University Press; 2005.
20. Guericke OV. The Firmament and the waters above it, according to the sacred Scriptures. International Archives of the History of Ideas Archives internationales d'histoire des idées. Springer. 2022; Chapter 28.

Available:https://link.springer.com/chapter/10.1007/978-94-011-2010-4_32#enumeration.

[Cited 2022 Dec 15].

21. Erduran S. Applying the philosophical concept of reduction to the chemistry of water: implications for chemical education. Sci Educ. 2005;14:161–171.

Available:https://doi.org/10.1007/s11191-005-0687-7.

22. Cappellesso VG, dos Santos Petry N, Dal Molin DCC, et al. Use of crystalline waterproofing to reduce capillary porosity in concrete. J Build Rehabil. 2016; 1:9.
Available:https://doi.org/10.1007/s41024-016-0012-7.
23. Mielenz RC, Wolkodoff VE, Backstrom JE, et al. Origin, evolution and effects of the air void system in concrete. Part 1-entrained air in unhardened concrete. ACI Structural Journal. 1958; 55:95–121.

Available:https://trid.trb.org/view/95722.

24. Shi Y, Yang H, Zhou S, et al. Effect of atmospheric pressure on performance of AEA and air entraining concrete. Advances in Materials Science and Engineering; 2018.
Available:https://doi.org/10.1155/2018/6528412.
[Cited 2022 Dec 17].
25. Zhu CH, Xie YJ, Zhang Y, et al. The effect of air pressure of environment on concrete's air-containing. Concrete. 2004; 4:9-10.
26. Luo Z, Fu Z, Li X. Effect of atmospheric pressure on air content and air void parameters of concrete. Magazine of Concrete Research. 2015;67(8):1-10.

DOI: 10.1680/macr.14.00256.

27. Li Y, Wang Z, Wang L. The Influence of Atmospheric Pressure on Air Content and Pore Structure of Air-entrained Concrete. Journal of Wuhan University of Technology-Mater Sci Ed. 2019;34(6): 1365-1370.

DOI: 10.1007/s11595-019-2200-1.

28. Huo J, Wang Z, Chen H, He R. Impacts of Low Atmospheric Pressure on Properties of Cement Concrete in Plateau Areas: A Literature Review. Materials (Basel). 2019; 12(9):1384.

DOI: 10.3390/ma12091384.

29. Borosnyói A. Message from the editors. Epitőanyag – Journal of Silicate Based and Composite Materials. 2015;67(1):6.

Available:http://dx.doi.org/10.14382/epitoanyag-jsbcm.2015.1.

30. Urakov A, Urakova N, Reshetnikov A, et al. About what is happening in the stomach after swallowing human river pebbles, gravel, chalk, clay and tablets drugs. Epitőanyag – Journal of Silicate Based and Composite Materials. 2016;68(4):110-113. Available:http://dx.doi.org/10.14382/epitoanyag-jsbcm.2016.19.
31. Urakov AL. Development of new materials and structures based on managed physical-chemical factors of local interaction. IOP Conf. Ser.: Mater. Sci. Eng. 2016;123(115):010083.

DOI:10.1088/1757-899X/123/1/012008.

32. Gurevich K, Urakov A, Fisher E, et al. Alkaline hydrogen peroxide solution is an expectorant, pyolytic, mucolytic, hemolytic, and bleaching drug for treating purulent diseases, hematomas and bruising. Journal of Pharmaceutical Research International. 2022;34(30B):13-20.

DOI: 10.9734/jpri/2022/v34i30B36073.

33. Urakov A, Urakova N, Nikolenko V, et al. Current and emerging methods for treatment of hemoglobin related cutaneous discoloration: A literature review. Heliyon. 2021;7(1):e059542.
Available:https://doi.org/10.1016/j.heliyon.2021.e05954.
34. Urakov AL, Urakova NA, Stolyarenko AP. Development of children's gel from nettle burn. Adv. Biores. 2020;11(5):150-156.

DOI: 10.15515/abr.0976-4585.11.5.150156.

35. Shabanov PD, Fisher EL, Urakov AL. Hydrogen peroxide formulations and

methods of their use for blood oxygen saturation. Journal of Medical Pharmaceutical and Allied Science. 2022;11(6):5489–5493.

DOI: 10.55522/jmpas.V11I6.4604.

36. Reed P, Reed W. US Patent. US 20040101571; 2004.

37. Beger B, Botta MA, Brown MB, et al. AU Patent. AU 2015249841; 2020.

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