Development of new materials and structures based on managed physical-chemical factors of local interaction

A L Urakov
Department of General and Clinical Pharmacology, Izhevsk State Medical Academy, Izhevsk, Russia
E-mail: urakoval@live.ru

Abstract. The paper states that assigning certain physical and chemical characteristics to pills and medical drugs solutions can substitute for the development of new drugs (which is essentially equivalent to the creation of new medicines). It is established that the purposeful change of physical and chemical characteristics of the standard ("old") materials (in other words, the known substances) is fundamental for the production of solid and liquid medicines, which allows us to get "new" structures and materials. The paper shows that assigning new physical and chemical properties to "old" materials and their further usage for the production of tablets and solutions from the "old" and well-known medicines can turn even very "old" medicine into very “novel” (moreover, even very fashionable) one with unprecedented (fantastic) pharmacological activity and new mechanisms of action.

1. Introduction
As an example let us consider the evolution of materials and structures of drugs and medical devices introduced into the body. Today they don’t usually analyze the mechanism of drugs action taking into consideration the physical and chemical properties of the powders, tablets, solutions, gases or other objects and forms in which medicines are administered to patients [6,23,24]. Besides, they ignore the change in a medicine physical and chemical properties caused by the fact that it’s not made from the medicines but from excipients [17]. Nevertheless, most of the ready products today often consist of excipients rather than chemical reagents [9].

It is no secret that final pharmaceutical product is completely different from "pure" chemical reagent, which was historically used for examining its toxicity in the beginning [10]. The matter is that "pure" chemical reagent is deliberately made very much "pollute" in the process of tablets, solutions and sprays manufacturing [9,10]. It is deliberately mixed with large amount of excipients and other substances. As a result, the medicine itself often has less than 1% of volume in the resulting mixture or solution which is used to prepare the final pharmaceutical product [10,12,14].

Besides, medicines and medical devices are manufactured by different pharmaceutical companies using different technologies and different starting materials. Therefore, products made by different plants cannot have same physical and chemical properties [10,14,17].

Our results show that these features can be used to distinguish the drugs and medical devices (syringes, probes, catheters, drainage tubes and other devices) between each other in quality and local irritant action on patients’ tissue when administered [20,23]. Moreover, ignoring the role of these factors reduces not only the efficiency and accuracy of diseases prevention, diagnosis and treatment method, but also their safety [5]. Besides, it turned out that it was the local physical and chemical
drugs and medical devices aggressiveness that was the base of their local irritating and damaging
effect on tissue [9,10,16,18]. It is also responsible for the development of medical iatrogenic diseases
[12,19,23,24].

However, solving the local physical and chemical interaction problems for drugs and medical
devices when they are administered to the patient is not only based on their variety and the fact that
they are made of different materials with very unusual physical and chemical properties. The fact that
all human body tissues have different physical and chemical properties, which, in addition, can change
significantly at the period of diseases is also very important. Therefore, the same medicine or medical
device with certain physical and chemical properties (quality indicators) may correspond to physical
and chemical properties of any body tissue in its normal state, and at the same time may not
correspond to it in the health problem situation [13,21]. It may be a friend for one body area and at the
same day an enemy for the others [3,25].

The matter is that the main cause of local irritant actions of drugs and medical devices is the
difference in their physical and chemical properties [12,24].

Which physical and chemical local interactions factors are the most important for the development of
new materials and devices for medical use?

2. Materials and methods

We studied physical and chemical properties of 200 venous blood samples, 300 limbs veins, 300
intravascular catheters which were installed in them and devices used for infusions for 200 patients
who were being treated in Izhevsk Hospitals within the period from March 2008 to October 2014. In
addition, we studied the blood conditions in major vessels and subcutaneous veins in the injection site
and in catheterization area of the wrist veins, forearm and shoulder of 10 corpses of adult patients who
had died in the hospitals. Blood viscosity measurements were performed using a cone-plate viscometer
Brookfield DV-II, coagulation activity of the blood is studied by Lee-White, status of the lumen and
the walls of the veins are studied in vena section, the state of catheter lumen in situ is studied through
visual observations, and with the help of the ultrasonic device Logik Book XP, equipped with linear
transducer 8L [20].

The dynamics of temperature in different parts of the body in 200 patients and in 100 healthy
volunteers was studied using advanced infrared radiation with the help of thermal imager TH91XX
(NEC, USA). Further data processing was performed with Thermography Explorer and Image
Processor software programs. Ambient temperature in the examination room was 24 ± 25°C, the
temperature range in the thermal camera was set as 25 - 36°C. At the examined area we determined
the mean temperature, standard deviation and distribution of isotherms at the thresholds of 34, 32, 30,
29 and 25°C [21].

We studied pus rheology in 100 patients with purulent peritonitis, purulent conjunctivitis and
tuberculosis of the lung and pleura. Pus rheology was studied through visual observations in vivo and in
vitro before and after the introduction of medicines solutions in pus with regard to the interacting
masses volume, their interaction duration, gravity, specific gravity (density), temperature, pH and
osmotic characteristics. Pus was taken for analysis before and 15 minutes after the interaction with
plasma-substituting solutions and antiseptic funds began. Smears were prepared and stained similarly
to blood smears using standard laboratory methods of dyeing with 0.5% Mine-Gryunval paint
prepared with 96° ethyl alcohol, and Romanovsky-Giemsa staining [14].

We have studied the peculiarities of tablets local interaction in the oral cavity, esophagus and
stomach in 10 adult volunteers and 10 conscious piglets. The movement of the tablets in the stomach
cavity was studied using ultrasound. Tablets were administered before and after the introduction of
water and food lumps (white bread) through the mouth and/or stomach probe and/or intestinal probe.
The body position in space was taken into account. Peculiarities of tablets local interaction inside the
stomach were observed in 10 anesthetized cats after cutting the stomach through surgical operations.
For this purpose we have used 0.1 g of ascorbic acid tablets with glucose and/or 0.5 g of calcium
gluconate tablets.
We have identified the most important physical and chemical characteristics of 200 quality medicines produced by pharmaceutical companies in the form of tablets and solution for injection. The medical drugs which were examined belonged to various pharmacological groups. The medicine quality was studied by taking into account the manufacturers and serial number of medicine. To analyze medicine quality we compared quality characteristics values which had been specified by the manufacturer in the medicine passport with the observed ones. Additionally, for the tablets we identified specific deforming hardness in Rockwell units HB (in a Brunel scale).

When evaluating the quality of drugs solutions we were taking into account their osmotic activity and the degree of gas saturation. Osmotic activity of aqueous solutions was defined with cryoscope using vapor-pressure OSMOMAT-030 RS brand osmometer of ANSELMA Industries (Austria) company [10]. The visualization of gas bubbles in carbonated solutions was held in visible spectrum of radiation through visual observation and ultrasound method using “ALOKA SSD-ALPHA 10” ultrasound device and convection sensor with a frequency of 3 to 7 MHz [3,20].

Statistical analysis of the results was performed using the BIOSTAT software program using standard methods.

3. Results
A very important factor is the local temperature of human body tissues. The matter is human body temperature equals 36.6° C only in theory. Our results show that in real life there are no conditions under which the temperature of all body parts would be equal to 36.6° C. The reality is that the temperature of various body parts of different patients can vary ranging from 0 to +42° C. At the same time Arrhenius and Van't Hoff proved that 10° C temperature change can change the chemical reactions flow rate from 2 to 4 times.

Another important factor is the flow and transferability characteristics of the body tissues. The reason is that the human body is constantly changing its position in space, but almost all of its body tissues move insignificantly relatively to each other. Therefore, we assume that a man and his body are relatively mobile, and most of his inside organs and tissues are relatively stationary (stay in one place). At the same time, many of them have moderate and high elasticity. Due to this human body maintains its shape independently of body orientation in space. This is not true for blood, because blood doesn’t have permanent form and doesn’t stay in one place even after person's death and efflux from his body. Therefore, when injected into the skin, subcutaneous fat, skeletal muscle, bone, cerebrospinal fluid, pus and other organs and tissues, these products may remain at the same place for a long time. At the same time, after being injected into blood the products begin immediately to flow with blood, and sometimes are carried far away from the injection point.

Among other important and rather uncertain local interaction physical and chemical factors are its duration, the specific pressure, reduced specific gravity, pH (acidity or alkalinity), concentration, osmotic activity and gas saturation.

In experiments in vitro and clinic observations in vivo the dynamics of the lumen state in subcutaneous veins was studied, as well as rheological properties of blood and pus dense in patients after their interaction with vascular catheters, pleural catheter and plasma-substituting solutions and antiseptics with respect to physical and chemical factors of the local interaction.

It is shown that solutions of medicines are introduced in a body at room temperature (as a rule, at a temperature of +24 - +26°C). However, some solutions may be of lower or higher temperature, as some medicines are deliberately cooled, because they are stored in the refrigerator at a temperature of +4 - +8°C, and some medicines are heated due to ignorance, as there is no temperature control even in the presence of heat sources (solar rays, infrared radiation from incandescent lamps and medical devices). As a result, the intravenous introduction of solutions for injections, executed through the conventional technique often changes the blood temperature inside the veins, which, in turn, changes the temperature of the venous wall and the tissues surrounding it, including the skin in the area of subcutaneous veins projection. We called this phenomenon as “thermo – contrast tissues”, and it
allows us to diagnose the subcutaneous veins localization without x-ray contrast media and without physical contact with the body of the patient due to the capabilities of infrared skin thermography. It turned out that 10% of the patients’ skin above the location of catheter free end in vein is heated and in this place a hyperthermia hotbed is formed, which continues, as a rule, not less than 2 days. In addition, in the vein located under the local hyperthermia hotbed we found the wall surface clot. Moreover, the blood clot is firmly attached to the part of the venous wall, which turns out to be the opposite and close to the open «nozzle» of vascular catheter and which is the least protected by the blood from «pure» drugs (drugs not diluted in blood) irrigation. However, the most amazing is the fact that this part of the venous wall is under the strong influence of heparin, expiring inside of vein from the catheter!

It appeared that 5 - 8 minutes before the local hyperthermia hotbed 0.1 ml of Dopamine solution (2-(3, 4dihydroxyphenyl)-athy lam in4-2(2-aminoethyl)benzen-1,2-diol) or to 2 ml of 2.5% of Chlorpromazine hydrochloride (2-chloro-10[3-(diethilaminopropil)] phenothiazines hydrochloride) was introduced for each patient of this group. At the same time, the experiments revealed some patients in whom the intravenous administration of these drugs did not cause the local hyperthermia hearth appearance. It turned out that at the same time these patients were introduced 200 ml of 4% sodium bicarbonate in vein. In this regard, we measured the acidity of these drugs, and found out that the standard dopamine and 2.5% chlorpromazine hydrochloride solutions are acidic, and the pH is in the range of 4.2 to 4.7. However, after diluting these medicines solutions with 4% sodium bicarbonate solution in a ratio of 1:2 or more, drugs become alkaline and acquire a pH in the range of 7.0 to 8.0.

On the basis of the obtained data the assumption is made that the local aggressiveness sour medications can reduce by combining them with a solution of 4% sodium bicarbonate. To check this assumption we held infrared thermography of 20 patients hands with multiple intravenous introduction of standard solutions dopamine or chlorpromazine hydrochloride accompanied by the introduction of the solution of 4% sodium bicarbonate. It turned out that the immediate intravascular catheters and introduction in veins of the 200 ml 4% sodium bicarbonate solution at room temperature (+24 - +26°C), produced after each dopamine or chlorpromazine hydrochloride injection, allowed to exclude the appearance of local hyperthermia hearth «in vascular catheter course», a clot (thrombus) and clogging of intravascular catheters for 5 days in all 20 patients.

Following this, we conducted similar experiments in vitro with fresh venous blood, fresh blood clots, with cadaveric blood (devoid of the ability to natural coagulation) and with dried blood of patients. The results showed that in vitro fresh blood clots at a temperature of +24, +37 +42°C over 15, 7 and 5 minutes (respectively). In addition, while injecting 1 ml of similar fresh venous or cadaveric blood into 0.1 ml of quality fluids drugs such as dopamine or chlorpromazine hydrochloride, in this blood clots appear immediately. This happens, most likely due to acid coagulation (denaturation) of the plasma proteins, as administered solutions are very acidic. At the same time, the preliminary introduction in fresh blue blood solution of 4% sodium bicarbonate in a ratio of 1:1 or more retains fluid properties of blood at a temperature of +24, +37 +42°C for 30 minutes of observation. The subsequent introduction in 1 ml of this blood 0.1 ml dopamine or chlorpromazine hydrochloride almost completely prevents the coagulation effects on blood.

In addition, it is shown that irrigation fresh blood clots and dried blood spots solution of 4% sodium bicarbonate in comparable volumes dissolves blood clots and softens the dried blood within 1-4 minutes in all studied temperatures. Moreover, it turned out that the ability of a solution of 4% sodium bicarbonate to dissolve blood clots depends on temperature as follows: the higher the temperature of interaction, the higher the efficacy.

However, the results of the experiments have shown that a solution of 4% sodium bicarbonate is not able to completely dissolve all the dried blood, to destroy 100% of residuals spot of blood for 1-4 minutes of interaction even at a temperature of 42°C. In this regard, for the potentiation of hemolytic activity of this solution we decided to add a 3% hydrogen peroxide. The results of experiments show that irrigation residues blood stains solution of 4% sodium bicarbonate and 3% hydrogen peroxide provides practically instant interstitial application only cold «boiling» in the rests of blood stains,
leading in 1-2 seconds to their complete destruction, coupled with the initial brief clarification (change of dark red color of blood on a light red color), quickly changing on the complete and final discoloration of biological mass. These data prove that the solution of 4% sodium bicarbonate is an effective and safe «chemical» anticoagulant and fibrinolysis drug, which can prevent blood clots and blockage of veins and intravascular catheters blood clots when repeated intravenous injections «neutral» and «sour» drugs. To do this, the data of a solution fill needle catheter before introducing them to vein, and then re-filled catheter immediately after removal from the needles and after each entered medication [8].

Our results showed that after injection into a vein of acidic drugs, blood clot can be formed in vein and appearance of the skin of limbs hearth of local hyperthermia above the end of the vascular catheter. However, a quick wash of the area of vein for 3 minutes with a warm solution of 4% sodium bicarbonate eliminates local hyperthermia in the place of location of catheter working end and blockage of veins and catheter blood clots.

It is shown that the rheological properties of thick pus and solutions of antiseptics and substitutes plasma at their local interaction depends mostly on conformity of volume and concentration, density, temperature, alkaline, osmotic and turbulent activity of medicines. The effect of the following factors was studied: gravity, specific gravity, temperature, turbulence, strength, internal pressure, carbonation, pH, osmotic activity, the total concentration of ingredients, the surface activity and the amount of medication.

After placing a thick pus and known plasma substitutes and hygienic liquids in laboratory test tubes in equal amount of samplings at a temperature of 24 or 37 °C pus was always located at the bottom of the tubes and liquids is always located above the pus. In particular, boiled water, tap water, water for injection, solution 0.9% sodium chloride solution, a solution 5% glucose, solution 20% glucose, solution 40% glucose, solution 10% sodium chloride, solution 10% sodium sulfatsil, solution 20% sodium sulfatsil, solution 0.02% furatsilin, solution 0.5% chlorhexidine, solution 70% ethyl alcohol and solution 1% sodium hydrocarbonate were always on top and not mixed with pus during 15 minutes of observation. Therefore rheological properties and other physical and chemical characteristics of pus were not changed. Slight decrease in dense purulent mass viscosity and pus microstructure change during 15 minutes of interaction with these solutions happened only when heated to 42°C.

Then we have defined the indicators for the acidity of water and solutions of antiseptics and plasma substitutes. The obtained results showed that all of them except 4% sodium bicarbonate solution and solutions of 10% and 20% sodium sulfatsil have a pH below 7.0, and so are acidic. In particular, indicators of acidity of tap water, boiled water, water for injection, solution furatsiline 1:500, solution of 3% hydrogen peroxide, solutions 0.9% and 10% of sodium chloride are in the pH range of 5.0-6.0, and the performance of solution acidity of 0.25% novokaine and solutions 5%, 20% and 40% glucose are in the pH range of 2.7 to 4.0 (Table 1).

In the next series of experiments in vitro at a temperature of 24 °C we studied the change of rheology and microstructure of thick pus during 15 minutes after administration into pus water or water solutions of medicines after preliminary artificial amplification of acidification to pH 2.0 or alkalinity to pH 12.0 by introducing them accordingly with hydrochloric acid or sodium hydroxide. Our results showed that only alkalization decreases viscosity and microstructure purulent masses dense.

Along with this, we studied the features of thinning and removal of thick and sticky pus under the influence of water and water solutions of medicines in the conditions of their increased turbulence, which was reached by heating and mechanical wobbled from side to side model cavity (test tube), filled commensurate amounts of pus and one of the investigated solutions. It is shown that the continuous rocking from side to side tubes with interacting environments, namely, with pus and high alkaline liquids (water for injection, solutions 0.9% and 10% sodium chloride, 10% and 20% sulfatsil the sodium, 0.02% furatsilin at pH 12.0), causes continuous reciprocal progressively offset medicated fluid, which is the top layer, with respect to the stationary mass of thick pus, which is the lower layer),
and accelerates the process of pus liquefying on the media separating boundary. Herewith, the shorter
the time interval between the beginning of the interaction and the onset time of removal of the main
pus mass at a temperature of 24°C and 42°C in 4 and 5 times, respectively, compared with the control
(in terms of their physical immobility).

Table 1. Values of pH of the water and of water solutions of modern antiseptic funds and plasma
substitutes

| N  | Liquid medication                        | Manufacture, Series № | pH   |
|----|-----------------------------------------|------------------------|------|
| 1  | Tap water                               |                        | 5.95 ± 0.11* |
| 2  | Drinking water from the kettle          |                        | 6.05 ± 0.07* |
| 3  | Water for injection in vials of 2 ml    | SE “Lividial” Series № 1151205 | 5.02 ± 0.08* |
| 4  | Solution 0.9% sodium chloride for injection, 200 ml | JSC “Calichpharm” Series № 300604 | 5.34 ± 0.04* |
| 5  | Solution 10% sodium chloride for external use 200 ml | Pharmacy № 131 (Izhevsk) | 6.05 ± 0.09* |
| 6  | Solution furacillin 1:5000              | Pharmacy № 131 (Izhevsk) | 5.70 ± 0.10* |
| 7  | Hydrogen peroxide 3% 40 ml              | LLC “БаЧ SCALE-pharmacy” Series № 841101 | 5.45 ± 0.25* |
| 8  | Solution 5% glucose for injection 500 ml | JSC “Biosynthesis” Series № 48102000 | 4.05 ± 0.09* |
| 9  | Solution 20% glucose for injection 500 ml | “Novosibirskpharm” Series № 30703 | 3.50 ± 0.15* |
| 10 | Solution 40% glucose for injection 500 ml | JSC “Dalhimpharm” Series № 210101 | 2.70 ± 0.07* |
| 11 | Solution 0.25% novokaine for injection 500 ml | Pharmacy № 131 (Izhevsk) | 4.05 ± 0.03* |
| 12 | Solution 10% sodium sulfitis 10 ml      | FSUE “Moscow Endocrine Factory” Series № PN 001084/01 | 7.90 ± 0.10* |
| 13 | Solution 20% sodium sulfitis 10 ml      | FSUE “Moscow Endocrine Factory” Series № PN 001084/05 | 8.30 ± 0.15* |
| 14 | Solution 4% sodium bicarbonate 200 ml   | Pharmacy № 131 (Izhevsk) | 8.20 ± 0.09* |

Note: * - P < 0.05, n = 5.

However, it appeared that artificially supported for 30 min increased turbulence of one of the above solutions doesn’t lead to absolutely complete dissolution of the entire mass of pus.

To check the value of high alkalinity activity of the solutions we have studied rheology thick pus under the influence of such famous alkaline drugs as solutions of 4% and 10% sodium bicarbonate (pH 8.0 and 8.0) and solutions of 2.4% and 24% aminofillin (pH 9.0 and 12.0, respectively). Our results showed that after 15 min of interaction of each of these solutions with thick pus, pus completely lost its viscosity and became liquid and very fluid. Solution of 10% sodium bicarbonate has the highest ability to dissolve thick pus.
To check the value of hyperturbulence and hyperthermal activity of the solutions we have studied rheology thick pus under the influence of solution of 4% sodium bicarbonate in conditions of continuous swinging tube containing equal amounts of interacting environments, 24, 37 and 42°C. Found that full pus liquefaction occurred at a temperature of 24 °C for 15 min, at a temperature of +37°C, through of 12.5 min, and at a temperature of 42 °C, 12 min of interaction.

Then we explored a range of specific weight, osmotic and acid activity of purulent masses obtained in patients with purulent peritonitis, purulent pleuritis, purulent conjunctivitis, purulent rhinitis and purulent abscesses. The obtained results showed that all the festering mass is a relatively heavy, isotonic and acidic biomass with a specific gravity within 1.030-1.040 g/cm³, with osmotic activity within 280-300 mOsmol/l of water and acid activity within the pH 5.8-6.2. Following this we defined specific weight of the liquids we used. They all have specific gravity of less than 1.30 g/cm³, except for the solution of 10% sodium chloride and solution 10% sodium bicarbonate. The extensive research has shown that the solutions of sodium bicarbonate in concentrations above 4%, have specific weight, exceeding 1.040 g/cm³ (meaning that they are “heavier” than the “heaviest” pus), pH 8.0 (that is, are alkaline) and osmotic activity above 450 mOsmol/l of water (i.e., are weak hypertonic solutions).

These data allowed to explain why purulent mass sink in water and in solutions with total concentration of ingredients of less than 3%, as well as to suggest that the festering mass will float up. Our studies have confirmed this assumption. Solution 4% of sodium bicarbonate is able to sink in purulent masses under the gravity force implemented in thickness of purulent masses.

Consequently, the high dense, high alkalinity and high osmotic activity, that is inherent in a solution of 4% sodium bicarbonate, ensures a high ability to dilute thick pus. In addition, as it is shown by our results, ability to dissolve thick pus of this solution can be enhanced by high temperature and high turbulence.

It is clear that the maximum permissible hyperthermia can be given a solution to its simple heating up to 42°C, but the maximum high turbulence needed to accelerate the process of liquefaction and dispersion of pus, cannot be achieved by «manual» jiggle the capacity of interacting environments from side to side. Therefore to give a solution the maximum possible turbulence we decided to increase the concentration and the pressure of gases, in particular, due to carbon dioxide similarly carbonated mineral water and due to the hydrogen peroxide. We hypothesized that the high saturation by gas of the solution 4% sodium bicarbonate will have a powerful aggressive action on pus, because warm, heavy, alkaline and high osmotic action of solution is to be able to intensively penetrate into a pus and high saturation solution by gas and rapid formation of bubbles of carbon dioxide within a pus is to be able to blasting it from the inside.

To verify this assumption, we initially added in a solution of 4% sodium bicarbonate carbon dioxide under excessive pressure of 0.2 ATM. Infusion of the solution at a temperature of 42 °C in a test tube with a festering mass withdrawn from the pleural cavity of a patient suffering purulent pleural empyema, led to the rapid formation of purulent foam and for the expulsion of tubes almost all purulent mass. Also intensively formed purulent foam was thrown out of the tube like a geyser. We found that high turbulence and high saturation by gas of warm solution of 4% sodium bicarbonate gave it an ability to effectively and safely dispose of pus out of purulent fistula when pancreatic necrosis.

It also found that high saturation by carbon dioxide of solution 0.9% sodium chloride provides visualization using ultrasound vector direction and speed of movement of streams of a solution into the abdominal cavity is closed when it is flushed with the conditions of purulent peritonitis by identifying and monitoring of the movement of bubbles of carbon dioxide. In addition, it is shown that the visualization of ultrasound move process of gas bubbles in a moving solution of 0.9% sodium chloride in the abdominal cavity allows you to monitor and change the flow of a fluid due to changes in the location of the patient's torso in space together with a cavity. The point is that changing the location of the torso and abdomen in space allows you to change the direction of fluid in the abdominal cavity, necessary to wash better chosen site. The ultrasound provides visualization move the liquid on the change of movement of gas bubbles.
Then instead of the carbon dioxide we added to a solution of 4% sodium bicarbonate 3% hydrogen peroxide. After this activity of dilute pus of this solution has been studied when heated to a temperature of 42°C and introduction in the tube with pus. It turned out that infusion into a test tube with a thick pus equal amount of warm solution of 4% sodium bicarbonate and 3% hydrogen peroxide at a temperature of 42°C leads to 5 min to complete transformation of two interacting environments in one turbid liquid with fluid properties.

In parallel we investigated changes in the state of the blood through visual observation and ultrasound after a single intravenous injection of aqueous isotonic isoalcaline solutions of sodium chloride and sodium bicarbonate, which additionally contains hydrogen peroxide in various concentrations. We determined the ability of hydrogen peroxide to saturate venous blood with oxygen. The formula has been developed and we patented a new quickening tool that represented a hydrogen peroxide solution with osmotic activity 280 mosmol/l of water and pH 7.4. This tool is intended to be injected into the portion of the venous blood, in order to saturate it with oxygen immediately before intravenous injection into the blood stream of the patient and increase the effectiveness of preventing hypoxic damage to the cortex of his brain.

After that we explored the dynamics of color cotton-gauze swabs and skin, soaked venous blood in norm and after injection of solutions of drugs. We investigated decolorizing activity of aqueous solutions of various chemical and medicinal substances with their concentrations in the range of 0.05 - 0.008%, temperatures in the range +20 to +40°C and pH (alkalinity) in the pH range of 6.0 to 8.5. It is revealed that the increase in pH above 7.4 for, or heated above 37°C increases, and the decrease in pH below 7.4, or cooling below 37°C on the contrary reduces the ability of the solutions to discolor bloody tissue. We found that at concentrations less than 0.05%, hydrogen peroxide has the strongest decolorizing effect. We determined the optimal composition of ingredients bleach solution, which formed the basis of medicines called "Bleach bruises".

On the other hand, the physical and chemical characteristics of the tablets also affect the action of drugs when taking them inside. It turned out that the physical and chemical properties of modern tablets significantly differ in their physical and chemical properties of the tissues of the gastrointestinal tract. This difference is the reason that when the local interaction of the tablets have a local physical and chemical effect on the tissues. We found that all the tablets are very heavy (sink in water and gastric juice), many tablets are very solid, slowly decaying, very acidic and/or very salty. However, producers and consumers of drugs are not aware of this!

So today due to the ignorance of doctors and patients many pills damage the enamel of the teeth, established dental designs, localauth and burn the mucous membranes of the oral cavity, esophagus and stomach. A lot of iatrogenic pills cause such damage as medical caries, medication, stomatitis, esophagitis, gastritis and ulcer pyloric stomach.

At the same time, it is shown that the "correct" changes in the physical-chemical properties of the tablets can make them safe. In particular, we invented the "easy" (floating) tablet, which is a thick foam. This pill does not cause an ulcer in the pyloric stomach.

Our data show that the values of specific deforming pressure pills now occupy the range from 0.03 ± 0.0001 Newton/mm² (tablets Xefocam (lornoksikama 4 mg, Nycomed), 160 ± 0.3 Newton/mm² (tablets Ketorol, Dr.Reddy's, India). In other words, all tablets have different hardness. Moreover, the value of specific deforming pressure tablets can distinguish them from one another by 5000 times! That's why when being chewed, some tablets hurt the gums, lips, tongue, teeth, fillings, crowns, dentures, dental implants and braces. In this regard, we proposed to produce only soft tablets, and the value of specific deforming the hardness of the tablets should be included in a legitimate list of monitorable indicators for the quality of medicines.

It was found that rheology of liquid, viscous and dense biological tissues may improve medicines having the following physicochemical characteristics: hypertermia, high alkaline, high turbulence and high saturation by gas. We found that the leaders of improving rheology medicines and biological tissues are sodium bicarbonate, hydrogen peroxide and carbon dioxide, introduced in medicines similar carbonated beverages. The data allowed to develop a new hygienic medicines designed to
liquefy thick purulent masses in patients with pleural empyema, peritonitis, rhinitis, sinusitis, conjunctivitis, tearful stones, osteomyelitis and sulfur tubes. New sanitary preparations are heated to 42°C aqueous solutions 0.5-10% sodium bicarbonate, 0.5%- 3% peroxide of hydrogen and carbon dioxide, which is entered into the solution at a pressure of 0.2 ATM.

A new page in the pharmacology of drugs associated with the presence of gases is opened: it is shown that the tablet is made in the form of a solid foam can float on the surface of the gastric juice, the solution representing the liquid foam can serve as an ultrasound contrast agent and the alkaline solution diluted hydrogen peroxide can whiten bruises in the skin.

4. Conclusion

Thus, the physical and chemical local interaction factors for drugs and medical devices are crucial to many diagnostic and therapeutic procedures outcome. High compliance of physical and chemical properties of pharmaceutical and medical products with the properties of human body tissues, which they are injected into, is the basis of safe medical technologies. Considerable incompatibility of physical and chemical properties of the products with the properties of the tissues in contact is the reason for local irritant, inflammation and even subsequent necrosis. The severity of local damages and their development probability rise together with the increasing difference in factor criteria, interaction period and the local temperature.

It is shown that the physical and chemical characteristics of tablets and solutions of drugs can have a significant impact on the state of the tissues of the human body when the local interaction with them. In particular, sour and hot tablets and solutions can seal, cauterize and "weld" blood proteins, causing thereby denaturing (i.e. chemical) blood clotting, blood clots and blockage of the lumen of the vein and catheter. In turn, alkaline and warm medicines may soften, dilute and dissolve thick pus, blood clots, and dried blood spots. This improves the fluidity of pus and blood and retains for a long period of patency of the blood vessels, vascular catheters, fistulas and probes. On the other hand, cooling not acidic aqueous solutions of drugs can slow down the natural processes of inflammation and blood coagulation. This can cause local bleeding and infection of the injection site. And, finally, the enrichment of tablets and solutions gas up to the formation of these foam (respectively solid or liquid), heating and alkalization gives them their destructive capacity at the local interactions: medications can cause cold interstitial "boiling", "explode" thick and solid clots. The most amazing is that the saturation of medicines with various gases gives them such an incredible pharmacological properties, such as ability to saturate the blood with oxygen and bleach bruises!

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