Solvents of pus-medicines with physical-chemical aggressive action

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Abstract. In laboratory and clinical conditions was studied rheology of pus and sulfuric tubes after their interaction with aqueous solutions of drugs from different pharmacological groups. It is shown that solutions of almost all medicines can influence or not influence on their rheology, because local action is determined not by the name, dose or route of administration of medicines. It is established that only physical-chemical properties of fluids and physical-chemical factors of their interaction with dense pus can give them the ability to dissolve or thickening pus. We found that deliberate change physical-chemical properties of medicines solutions from various pharmacological groups, namely, raising the temperature to +42°C, increasing the alkalinity above pH 8.1 and aeration as for example by introducing carbon dioxide under pressure of 0.2 ATM, or by introducing hydrogen peroxide in 0.5 - 3%, turning them into solvents of pus, ear wax and sulfuric tubes. Discovered that solutions of drugs with such physical-chemical activity may turn thick pus and solid sulfur tube in a homogeneous liquid after a few minutes after injecting them into these biological mass.

1. Introduction

It is no secret that any infection is dangerous the appearance of pus, it becomes a source of germs and the cause of the destruction of healthy tissue in the body of a diseased person. The germs multiply very rapidly, so the suppurative focus is growing very rapidly. In this regard, for effective treatment of purulent diseases need as soon as possible to save the patient from pus. While it is best to remove all the pus out, then it is advisable to wash with an antiseptic solution, disinfectant or cauterizing agents. Quick completion of this task in the clinic is possible only at a superficial or outer location of the purulent focuses. However, when the location of the purulent focus in the body cavities in the depth of the soft and hard tissues cannot quickly remove the pus out, because the pus is sticky and viscous. In such situations, the pus cannot be removed using surgical tools, because it is dangerous to the health of the patient, and with medication, because special solvents pus not developed [18].

Previously, we reported that the nature of the local action of drugs on tissues of our body is determined primarily by physical-chemical factors of the interaction [9,13,15]. It was shown that the conformity of the physical-chemical properties of drugs and physical-chemical properties of tissues prevent local irritating action of the drugs and vice versa [20]. The larger the difference between medicines and tissues from each other on the physical-chemical properties, the stronger change their

aggregate condition in the local interaction [21]. In this case, we were able to identify physical-chemical factors, that determine the state of aggregation and the rheology of thick pus [1, 10, 17].

What physical and chemical properties of drugs are most important for turning the drugs in solvents of pus ?

To date, there is no doubt that one of the most important factors for physical and chemical dissolution thick pus is the local hyperthermia [1, 5, 17]. 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 in hospital can vary ranging from +24 to +42° C [20]. 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) [10, 12, 13,]. However, some medicines 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) [20]. 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 [7].

It is shown, that very important factor for the rheology of blood and pus is alkalinity [1, 16, 18]. Very important factor for physical move of the biological mass is gravity [3, 4, 6, 19]. 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, but pus and cerumen are relatively stationary inside his body and these products may remain at the same place for a long time for two reasons. First, due to the high friction, and secondly, due to the high viscosity.

In addition, it is assumed that other important factors for medical dissolution of pus can be duration of local action of drugs and its gas saturation [2, 4, 8, 10, 11, 12].

2. Materials and methods

We studied pus rheology in 10 patients with tuberculous empyema, in 5 patients with purulent peritonitis and in 10 patients with hearing loss. Pus rheology was studied through visual observations in vivo and in vitro before and after the introduction solutions of medicines in pus with regard to the volume of interacting masses, the duration of their interaction, gravity, specific gravity (density), local temperature, pH and osmotic activities. Pus was taken for analysis before and after 15 minutes after the start of its interaction with solutions of medicines began.

We have identified the most important physical and chemical characteristics about 200 quality medicines produced by pharmaceutical companies in the form “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, we identified osmotic activity with cryoscope using vapor-pressure OSMOMAT-030 RS brand osmometer of ANSELMA Industries (Austria) company. Behind them we controlled acidy (alkalinity) of solutions and purulent masses defined with strips of the universal indicator paper company Lachema.

When evaluating the quality of drugs solutions we were taking into account their osmotic activity and the degree of gas saturation. The visualization of gas bubbles in aerated solutions was held in visible spectrum of radiation through visual observation on the eyes and ultrasound method using an ultrasound device “ALOKA SSD-ALPHA 10” using convection sensor with a frequency of 3 to 7 MHz [3, 19].

An additional the dynamics of temperature in different parts of the body in 25 patients was studied using advanced infrared radiation with the help of thermal imager TH91XX (NEC, USA). All patients were being treated in Izhevsk Hospitals within the period from March 2008 to October 2015. 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.

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

3. Results

Purulent mass, extracted from the pleural cavity of patients with pleural empyema, had the consistency of opaque, shapeless, thick, viscous and sticky mass of yellow-grey. Then the purulent mass is then maintained this state after placing them in transparent laboratory glass vials at room temperature. The test tubes during the study were table stands motionless in a vertical position with the bottom down. Purulent mass flowed down the walls of the tubes to the bottom and was in the bottom of the tubes still.

Sulfuric tubes, extracted from patients ears with hearing loss, had the form of a solid and opaque flagellum gray-brown in color with rounded ends. Then sulfuric tubes maintained this state at room temperature after placing them in Petri dishes.

The results showed that the careful infusion to purulent masses and sulfur tubes of known aqueous solutions at comparable volumes at a temperature of +24 or +37° C did not lead to the dissolution of pus and cerumen in the last 15 minutes of observation. Moreover, the studied biological mass always remains unchanged at the bottom of the dish, and injected fluid does not mix with them and remained transparent. Moreover, between biological mass and the fluids remained clear border of separation of environments and biological mass always sank when lowering them inside the well-known liquids and never surfaced to the top. In particular, during 15 minutes of interaction at a temperature of +24° C boiled water, tap water, water for injection, a solution of 0.9% sodium chloride solution 5% glucose solution 20% glucose solution 40% glucose solution 10% sodium chloride, 10% solution sulfatsila-sodium, a solution of 20% sulfatsila-sodium, a solution of 0.02% furatsilina solution of 0.5% chlorhexidine, 70% solution of ethyl alcohol, and solutions of 4% sodium bicarbonate was not mixed with pus and with sulfuric jams. Therefore, the rheological properties and other physico-chemical characteristics of pus and sulfur tubes, and their shape and state of aggregation remained unchanged.

A slight decrease in the viscosity of thick purulent masses after 15 minutes of interaction with fluids was observed only when the increase temperature 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 solution of 4% sodium bicarbonate 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 of furatsiline 1:500, solution of 3% hydrogen peroxide, solutions of 0.9% and 10% of sodium chloride are the pH range of 5.0 - 6.0, and the performance of the acidity of solution 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 of thick pus throught 15 minutes after administration in pus water or water solutions of medicines after preliminary artificial amplification acidification to pH 2.0 or alkalinity to pH 12,0 by introducing them accordingly hydrochloric acid or sodium hydroxide. Our results showed that only alkalization decreases viscosity purulent masses.

So, after 15 minutes after infusion to thick purulent mass of an equal volume one of the following “hyperacid” liquids (they all have a pH 2.0) - water for injection or water solution of one of the following means: solution of 0.9% or 10% sodium chloride, solution of 10% or 20% sulfatsil sodium, solution of 0,02% furatsilin or 0.5% chlorhexidine, purulent masses remain practically unchanged: thick, sticky and viscous. At the same time, 15 minutes after infusion to thick purulent mass of an equal volume one of these liquids with a pH value of 12.0 thick and sticky pus turns into a liquid with a good fluidity.

Table 1. Values of acidity (alkalinity) of some antiseptics and plasma substitutes

No.	Liquid medication	Manufacture, Series No.	Values of acidity (alkalinity) (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 " Lvivdialect" Series No. 1151205	5,02 ± 0,08*
4	Sol. 0.9% Sodium chloride for injection 200 ml	JSC «Galichpharm» Series No. 300604	5,34 ± 0,04*
5	Sol. 10% Sodium chloride for external use 200 ml	Pharmacy No. 131 (Izhevsk)	6,05 ± 0,09*
6	Sol. Furatsillin 1:5000 500 ml	Pharmacy No. 131 (Izhevsk)	5,70 ± 0,10*
7	Hydrogen peroxide 3% 40 ml	LLC «Ватхэм-pharmacy» Series No. 841101	5,45 ± 0,25*
8	Sol. 5% Glucose for injection 500 ml	JSC «Biosynthesis» Series No. 48102000	4,05 ± 0,09*
9	Sol. 20% Glucose for injection 500 ml	«Novosibirskpharm» Series No 30703	3,50 ± 0,15*
10	Sol. 40% Glucose for injection 500 ml	JSC «Dalhimpharm» Series No. 210101	2,70 ± 0,07*
11	Sol. 0,25% Novokaine for injection 500 ml	Pharmacy No. 131 (Izhevsk)	4,05 ± 0,03*
12	Sol. 10% Sodium sulfatsil 10 ml	FSUE «Moscow endocrine factory» Series No. PN 001084/01	7,90 ± 0,10*
13	Sol. 20% Sodium sulfatsil 10 ml	FSUE «Moscow endocrine factory» Series No. PN 001084/05	8.30 ± 0.15*
14	Sol. 4% Sodium bicarbonate 200 ml	Pharmacy No. 131 (Izhevsk)	8,20 ± 0,09*

Note: * - $P < 0,05$, $n = 5$.

In parallel, we studied the features of dissolution of thick and sticky pus and sulfuric tubes under the influence of water and water solutions of medicines in the conditions of increased their 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 with liquids with high alkalinity (water for injection, solutions of 0.9% and 10% sodium chloride, solution of 10% and 20% sulfatsil sodium, solution of 0,02% furatsilin at pH 12,0), causes continuous reciprocal progressively offset fluid, which is the top layer, with respect to the stationary mass of thick

pus and sulfuric tubes, which is the lower layer, and accelerates the process of liquefying of pus and cerumens on the dividing line between interacting environments.

However, it appeared that artificially supported for 30 min increased turbulence all of the above fluids don't lead to absolutely complete dissolution of pus and sulfuric tube.

On the basis of obtained results it was concluded that the above fluid does not possess the ability to effectively dissolve thick pus and cerumen impactions. At the same time, such physical and chemical factors of their local interaction, as hyperthermia, high alkalinity and high turbulence may underlie the nonspecific ability of drugs to dissolve the thick solid pus and cerumen impactions.

We checked the validity of these assumptions. For this was studied the dynamics of aggregation state thick pus at a temperature of 24°C after infusion solutions of 4% and 10% sodium bicarbonate (pH 8.1 and pH 8.3, respectively) or solutions of 2.4% and 24% aminophylline (pH 9.0 and pH to 12.0, respectively). Our results showed that solutions of sodium bicarbonate and solution of aminophylline good dissolve thick pus. The results showed, that 15 minutes after the introduction of these solutions into test tubes with thick pus thick pus were completely dissolved and transformed into a homogeneous liquid.

After that, we investigated the role of high turbulence and temperature of the drugs solutions to dissolve thick. To this end, the dynamics was studied the state of aggregation of thick pus after the transfer to it of an equal volume solution of 4% sodium bicarbonate at a temperature of +24, +37 or +42°C under continuous rocking of the tubes. The results showed that complete dissolution of pus occurred at a temperature of +24, +37 and +42° C, respectively after 15, 12.5 and 12 minutes. Therefore, high turbulence and temperature solutions and turn them into solvents of thick pus.

Consequently, moderate and high alkalinity, high turbulent and thermal activity of drugs solutions gives them a reasonable physical-chemical aggressiveness, therefore, is able to turn them into solvents of thick pus.

Then, we were define the value of specific gravity, osmotic and acid activity of purulent masses, obtained in patients with purulent peritonitis, purulent pleurisy, purulent conjunctivitis, purulent rhinitis and purulent abscess. It was found that the pus has a value of specific gravity in the range of 1.030 - 1.040 g/cm^3, has osmotic activity within 280 - 300 mOsmol/l of water and has an acid activity in the range of pH 5.8 - 6.2.

After this was determined the specific weight of liquids is known, which the traditional use for sanitation of purulent cavities. The results showed that they all have a specific gravity less than 1.30 g/cm^3. In other words, the specific weight of the sanitizing solutions was less than the specific weight of purulent masses. These data allowed us to explain why the pus is always drowning in these solutions, and solutions are always over flowing with pus and do not penetrate inside it.

The extensive research has shown that the solutions of sodium bicarbonate in concentrations above 4%, have specific weight, exceeding 1.040 g/cm^3 (meaning that they are more «heavy» than the «heaviest» pus), pH 8.1- 8.2 (that is, are alkaline) and osmotic activity above 450 mOsmol/l of water (i.e. are weak hypertonic solutions).

These data suggest that solutions of sodium bicarbonate at a concentration of above 4% will be able to sink into the festering mass under the action of gravity. It was also assumed that such "heavy" solutions can be implemented on top of the thick purulent masses and it's possible that they can dissolve the thick pus, because they are alkaline buffers. In order to increase the ability of solution of 4% sodium bicarbonate to dissolve thick pus, we decided to heat the solution and give it the activity is 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 of the maximum possible turbulence 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 test this hypothesis, we initially injected carbon dioxide under excessive pressure of 0.2 ATM in a solution of 4% sodium bicarbonate and then heated carbonated solution to a temperature of +42°C. After that entered a warm carbonated solution into a test tube, in which there was pus. It turned out that this solution immediately entered a turbulent interaction with pus and turned it into a festering foam. The foam was expelled outward from the tube almost in its entirety. The process of foam formation and its ejection from the tube out was very intense and resembled a Geyser.

Then we found that high turbulence and high saturation by gas of warm solution of 4% sodium bicarbonate gives him ability to effectively and safely disposed of pus out of purulent fistula when pancreatic necrosis [2, 4, 10, 16].

Similar results were obtained with sulfuric jams. It turned out that the injection of aerated and warm solution of 4% sodium bicarbonate inside the sulfuric tube also quickly destroys the tube. Sulfuric tube begins to increase in size due to the formation within it of a plurality of gas bubbles. In fact, sulfuric tube begins to foam. However, it breaks into several small pieces, which soon also begin to foam, so very quickly all sulfuric tube is falling apart and turns into a foam dirty-brown color [].

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 shown by our results, ability to dissolve thick pus of this solution can be enhanced by high temperature and high turbulence.

Following this, it was decided to study the rheology solution of 0.9% sodium chloride and peculiarities of its interaction with pus in peritonitis after introduced the gas carbon dioxide excessive pressure of 0.2 ATM and heated solution to a temperature of +42°C. The results showed the unexpected benefit of sanitizing activity aerated solution of 0.9% sodium chloride solution. The fact that this solution formed gas bubbles, provide a visualization of the vector flow of fluid in the peritoneal cavity using ultrasound. 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 [3, 19].

Therefore, the formation of gas bubbles in solutions of sanitizing agents can enhance their ability to dissolve (or destroy) the pus, as the formation of gas bubbles in liquids creates conditions cold "boiling".

The data obtained by us testify that we are in half-step beyond the creation of a completely new group of drugs - solvents of pus. In this regard, we continued the research. The intuition prompted that to complete the formation of the basic physicochemical properties of new drugs is not enough antiseptic with a more reliable and a proven ability cold boiling. The analysis of known funds have allowed us to choose for these purposes, the hydrogen peroxide.

Then a solution of 4% sodium bicarbonate we added hydrogen peroxide in a concentration of 3%, and then heated the solution to a temperature of +42°C. Studies have shown that this solution possesses all the properties necessary for medicinal means - solvents of pus. The results showed that the infusion in a test tube with thick pus equal number of solution of 4% sodium bicarbonate and 3% hydrogen peroxide at a temperature of 42°C leads to the fact that all the pus is dissolved and after 5 minutes, turns into a turbid liquid. Thus the solution additionally has antiseptic and deodorizing activity.

Thus, it was found that medicines having the following physicochemical characteristics: high temperature, high alkaline, high turbulence and high ability to lead liquid in a state of cold boiling, may improve rheology of liquid, viscous and dense biological tissues. Leader of improvement of

rheological properties of thick pus is a solution of sodium bicarbonate and hydrogen peroxide, which additionally contains carbon dioxide under excess pressure of 0.2 ATM like food, fizzy drinks.

The mechanism action of drugs of this group on the pus boils down to the fact that under the influence of alkaline drugs activity hydrolysis of proteins and saponification of fats in the festering mass. It dilutes the colloidal intercellular environment in the pus and facilitates the penetration of drugs inside the pus. The medicines liquefy the pus by increasing its temperature. In other words, the hot solutions heated pus, and therefore it melts (melt). And, finally, the drugs have the potential to cause interstitial cold boiling, that is, to form gas bubbles within the purulent masses. This is the reason that drugs make the pus into the foam. In this case, the gas bubbles can occur due to the fact that the gas can be inside solvents of pus under high pressure, or oxygen gas can emerge from the hydrogen peroxide by the enzyme catalase, which is always available in the purulent masses.

Today we can announce that the data has allowed us to develop several new hygienic preparations for the dissolution of thick purulent masses in purulent diseases, such as empyema, peritonitis, rhinitis, sinusitis, conjunctivitis, osteomyelitis, otitis and hearing loss with occlusion of the auditory canal of a sulfuric stopper [2, 3, 4, 5, 6, 8, 14].

Here are the recipes of several solvents of pus.

1. **Means for liquefaction the thick and sticky pus** (RUS Patent No. 2360685):
   - Hydrogen peroxide is 2,7 – 3,3 %
   - Sodium hydrogen carbonate 5,0 – 10,0 %
   - Water for injections The rest

   This means is designed to dissolve very thick and sticky pus and to remove it like a geyser from cavities and tracts.
2. **Hiper fizzy and hyperosmotic antiseptic** (RUS Patent No. 2331441):
   - Hydrogen peroxide is 2,7 – 3,0 %
   - Sodium chloride 0,9 - 10.0 %
   - Carbon dioxide to create excess pressure of 0.2 ATM. at $+8^0$ C
   - Water for injections The rest

   This tool is used to dissolve thick purulent masses and removing them like a geyser from the cavities and sinus tracts.
3. **Powerful solution for epibulbar instillations** (RUS Patent No. 2452478):
   - Hydrogen peroxide 0,55 – 1,0 %
   - Sodium bicarbonate of 1.0 – 1.5 %
   - Lidocaine hydrochloride 0,5 – 1,0 %
   - Water for injections The rest

   The tool is intended for rehabilitation of the organ of vision and skin purulent conjunctivitis, the gluing of the eyelids and the lacrimal accumulation of stones.
4. **Remedy for fistula sanitation in infected pancreonecrosis** (RUS Patent No. 2455010):
   - Sodium chloride 0,9 %
   - Sodium gidrofosfat 0,142 %
   - Sodium dihydrogen phosphate 0,120 %
   - Water for injections The rest

   This tool is intended for repeated and prolonged rehabilitation fistulas in necrotizing pancreatitis.
5. **Means for removal of cerumen** (RUS Patent No. 2468776):
   - Hydrogen peroxide 0.3 - 0.5 %
   - Sodium bicarbonate 1.7 - 2.3 %
   - Water for injections The rest

   This means is designed to dissolve and remove the ear tube of their external auditory canal during hearing loss.

It should be noted that the strongest solvent and the destroyer of pus can be safely applied only for the rehabilitation of open purulent wounds, because the drug is very quickly embedded in pus and rapidly turns it into foam. Pus begins to foam right before your eyes and the volume of foam increases several times. So the strongest solvent of pus cannot be inserted into the deaf purulent cavity.

4. Conclusion

It is shown that the physical-chemical characteristics of the solutions of drugs can have a significant influence on the rheological properties of pus under local interaction with him. Found that aqueous solutions with a high temperature, alkaline, relatively heavy, hyperosmotic activity and hiper aeration capable of dissolving thick purulent masse.

There is every reason to believe that we have developed a new group of medicines, which was called "Solvents of pus". Drugs - solvents of pus differ from all other preparations that are heated to +42° C aqueous solutions 0.5-10% sodium bicarbonate and 0.5-3,0% of hydrogen peroxide, which is potentially ready to cold boiling. The most powerful drug in this group is the carbonated solvent pus, which contains carbon dioxide at a gauge pressure of 0.2 ATM.

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