It is became generally accepted that liposomes are effective drug carriers. Therefore, the question of whether liposomes per se can exhibit their own biological activity will seem strange to someone. Of course, they are not really empty! More precisely, they are not completely empty. The so-called empty liposome, i.e. liposome per se, contains in its cavity the medium in which it was formed. For instance, it could be practically indifferent sodium chloride solution. When we say that some liposomes are empty, we mean that their internal cavity or the membrane does not include any biologically active chemical compounds, such as drugs for pharmacotherapy.

Recently, an international group of scientists [1] in the pages of the Chemical Review journal summed up the results of many years of studies of these amazing formations – liposomes – microscopic capsules (vesicles), which are currently widely used to create drugs around the world. It is well known many years that liposomes are successfully used, first of all, for drug delivery [2] and their self-biological activity has not yet been seriously considered. Since in chemical composition, they are similar to natural cell membranes, able to transport a wide range of medical chemicals (including water-insoluble and toxic ones) and practically do not cause allergic and other adverse reactions.

What qualities of liposomes give them advantages over other drug carriers? First of all, it is an affinity with natural cell membranes in chemical composition. It is known that the lipids that make up the membranes occupy from 20 to 80 percent of their mass. Therefore, with the correct selection of liposome components, this type of pharmacological intervention into the body does not cause negative reactions.

The second important property of liposomes is versatility. Due to their semi-synthetic nature, their sizes, structural characteristics and surface composition, liposomes can be widely varied. This makes it possible to «charge» liposomes to carry a wide range of pharmacologically active substances: antitumor and antimicrobial drugs, hormones, enzymes, vaccines, as well as additional sources of energy for the cell, genetic material.

Thirdly, liposomes disintegrate relatively easily in the body (biodegradation), releasing the delivered substances, but because of their origin, liposomes, themselves devoid of antigenic properties, reliably hide their load from contact with the immune system and, therefore, do not cause protective and allergic reactions of the body.

There is no doubt the thesis that most diseases do not affect the entire body, but individual organs and tissues (although, of course, this does not pass without leaving a trace for other organs and systems). Therefore, the treatment will be faster and more successful if
The drugs are delivered directly to the focus of the disease, i. e., act in a targeted manner. This is especially important in those cases when you have to deal with rather toxic drugs that treat the disease itself well, but at the same time have a bad effect on other body systems. This is the case, for example, in the treatment of cancer.

The creation of the required concentration of medicinal substances in the areas affected by the disease, without affecting the organs and tissues not involved in the pathological process, is not an easy task. After all, medicines, no matter how they were administered, enter the bloodstream and disperse throughout the body more or less evenly. And in order for them to reach the right places («targets»), some kind of carrier is needed that could deliver them there in sufficient quantity. Over the past few years, many attempts have been made to solve this problem, many compounds have been tried, and it turns out that liposomes are the best drug carriers.

Many years ago we first discovered that even empty (i.e., containing no active substances in their internal cavity or membrane) phosphatidylcholine liposomes (PCL), i.e. liposomes per se, have an amazing ability to restore contractile activity of blood vessels impaired under hypoxia [3] and renovate endothelium-dependent vascular relaxation blunted in spontaneously hypertensive rats [4].

Later it was established that liposomes per se possess the ability to normalize endothelium-dependent vascular relaxation damaged after exposure to γ radiation [5]. Finally, it was shown [6] that empty PCL effectively restored Maxi-K channels activity depressed after γ-radiation impact. It was really surprising discovery for us, for which there was no any reliable explanations for long period of time.

The aim of the present work is an attempt to explain why empty liposomes per se have the ability to normalize contractile activity of smooth muscle cells, impaired under the influence of external factors affecting their ionic conductivity and contractile force development.

Methods. Animals and ethical approvals. Mammalian animal studies were performed using adult male Wistar rats in accordance with the recommendations of the European Convention for the protection of Vertebrate Animals used for Experimental and other Scientific Purposes and was approved by the Institutional Animal care and Use Conditions. All experiments were performed on rats housed under controlled environmental conditions (21 °C, 12 h – 12 h light-dark cycle) and free access to water and standard rodent diet.

Contractile recordings. Briefly, experiments were performed on rat portal vein strips and aortal rings obtained immediately after the rats were anesthetized with alpha chloralose, 40 mg/kg plus urethane, 0.4 g/kg b/w., i. p. and sacrificed with cervical dislocation. Then vascular tissues were dissected and prepared with care in order to keep the endothelium intact. Then the preparations were mounted isometrically in a tissue bath between a stationary stainless steel hook and an isometric force transducer (AE 801, SensoNor A/S, Norten, Norway) coupled to a chart recorder (model 202, Cole-Parmer Instrument Company, USA) and were maintained at 37 °C and superfused continuously at a rate of 2 ml/min with standard Krebs-bicarbonate buffer solution. They were allowed to equilibrate for 1 h under resting tension of 400 mg (portal vein) and 3 g (aortas) before experiments commenced.

Electrophysiological studies. Briefly, smooth muscle cells were isolated
from tissues by enzymatic treatment, as described below. Pulmonary artery with diameters of 0.5–1 mm was dissected and was cut into small pieces (1.0 × 1.0 mm) in Ca²⁺-free modified Krebs solution containing (in mM) 120 NaCl, 12 glucose, 10 HEPES, 6 KCl, (pH 7.4). The pieces were digested at 36.5 °C for 20 min in 2 ml Ca²⁺-free modified Krebs solution containing papain (1 mg/ml), dithiothreitol (1 mg/ml), bovine serum albumin (1 mg/ml), then removed and again repeatedly digested at 36.5 °C for 10 min in 2 ml Ca²⁺-free modified Krebs solution containing collagenase type 1A (1 mg/ml), dithiothreitol (1 mg/ml), bovine serum albumin (1 mg/ml) and at the end were washed three times with Ca²⁺-free modified Krebs solution to stop enzymatic digestion.

Ileal SM cells were obtained from two-month-old male mice euthanized by cervical dislocation. Then abdominal cavity was dissected and ileum longitudinal smooth muscle strips were rapidly removed into the normal physiological salt solution (PSS) (in mM) : 120 NaCl, 12 glucose, 10 HEPES, 2.5 CaCl₂, 1.2 MgCl₂, pH adjusted to 7.4 with NaOH. Strips were cut into pieces of 1 mm in length in Ca, Mg-free PSS (in mM: 120 NaCl, 12 glucose, 10 HEPES, 6 KCl, pH 7.4 with NaOH). SM cells were isolated following enzymatic digestion using (in mg/ml): 1 collagenase type 1A, 1 soybean trypsin inhibitor type II-S, 1.5 bovine serum albumin in Ca, Mg-free PSS for 18 min at 36.5 °C. Next, the enzymes were washed out three times by Ca-free PSS. Suspen-
sion was triturated by fire-polished Pasteur pipette, dropped on coverslips with addition of normal PSS at 2:1 ratio and stored in fridge at 5 °C until use within 6-8 hours after cell isolation.

All electrophysiological experiments were carried out at room temperature (about 22–25 °C). Transmembrane currents were recorded using the patch-clamp techniques in the whole-cell or cell-attached configurations using the AxoPatch 200B amplifier and the software pClamp 8 (Molecular Devices, Sunnyvale, CA, USA). Patch pipettes were made from borosilicate glass tubes (external diameter 1.5 mm, internal diameter 0.86 mm; Harvard Apparatus, Hollister, MA, USA) using a micro-electrode puller P-97 (Sutter Instruments, Novato, CA, USA). After filling the pipettes with a pipette solution they had a resistance of 4–5 MΩ.

In the whole-cell mode, patch pipettes were filled with the intracellular solution containing (in mmol/l): KCl 130, MgATP 1, creatine 5, glucose 10, EGTA 0.3, HEPES 10 (pH adjusted to 7.4 with KOH). For single-channel recordings, the pipette solution contained modified Krebs solution while KCl was added (80 mmol/l) to the external solution in order to minimize the resting potential of smooth muscle cells. Unitary currents were recorded at a holding potential of 60 mV. The signal after its analog filtering using the 4th order Bessel filter at 1 kHz was digitized at 10 kHz.

Quercetin-filled phosphatidylcholine liposomes (PCL-Q) preparation. Phosphatidylcholine liposomes were prepared with lipid stock solution in ethanol. Solvent was removed on a rotary evaporator at 35 °C. To prepare PCL-Q, the suspension of lipid and quercetin were dried together in one flask. The weight ratio of quercetin to lipid was 1:50. The solution containing 140 mmol/L NaCl was added to the resultant pellicle and stirred until the lipids were completely emulsified. The suspension was bathed in 40 °C water and sonicated for 1 min using a sonifier (model 300, Fisher). After that, liposomes were frozen at −25 °C and could be stored under argon for 1 week.
The final concentration of filled liposomes in bath solution was 100 µg/mL to lipid content and 3 µg/mL to the active substance, quercetin. The preparation of PCL was the same way as PCL-Q without the quercetin in mixture. The final PCL and PCL-Q were unilamellar vesicles and their diameters were (100 ± 20) nm and (140 ± 30) nm, respectively.

**Preparation of nitric oxide-containing liposomes. Synthesis of nitrosoglutathione (GSNO).**

Briefly, L-glutathione in an amount of 100 mg was dissolved in 2 ml of an aqueous phosphate buffer solution (8 mmol, pH 6.7–7.4). It was cooled to +5 °C and then 20 µl of a hydrochloric acid solution (6 moles) was added, then again cooled to +5 °C. To this solution 0.5 ml of a cooled solution of sodium nitrite (NaNO₂) Xmol) was added. The formation of nitrosoglutathione accompanied by a change in the color of solution to bright red. After that, 20 µl of a cooled solution of sodium hydroxide (6 moles) was added to this solution.

Acetone, cooled to minus 20 °C, was used to precipitate nitrosoglutathione. 10 ml of acetone were added to the resulting solution of nitrosoglutathione, stirred vigorously and centrifuged for 5 minutes at 3000 g at 0 °C. After centrifugation, the supernatant was discarded and the pellet was washed several times with chilled acetone. Next, the precipitate was freeze-dried using a lyophilic MartinChristEpsilon 2D-6 (Germany). About 109 mg of nitrosoglutathione (GSNO) were obtained. Nitrosoglutathione in aqueous solution has spectral absorption peak at a wavelength of 344 nm.

**Preparation of phospholipid liposomes containing cytochrome C inside.** Phosphatidylcholine and dipalmitoylphosphatidylglycerol in a 10:3 ratio were dissolved in the alcohol-chloroform mixture. A film was obtained with the vacuum-evaporator rotor (Buchi, Switzerland), and then washed with a solution of cytochrome C at a concentration of 1.0 mg/ml in phosphate buffer (8 mmol, pH 6.7–7.4). The emulsion was then homogenized on a high-pressure homogenizer (Microfluidics M-110, USA) at a pressure of 600 to 800 bar to obtain a liposomal nanoemulsion with liposomes sizes from 90 to 110 nm (Nano-S, Malvern, UK). Inclusion of cytochrome C into the liposomes was evaluated by HPLC on a Tricorn 200 column (GE, USA) with Sepharose G-25 sorbent (Amersham, Sweden). Inclusion of cytochrome C was not less than 95 %.

**Preparation of the reduced form of liposomal cytochrome C.** To remove atmospheric oxygen, a high purity argon gas was pumped for 30 min through a liposomal emulsion of cytochrome C (100 ml), obtained after homogenization. The aim of this procedure was to prevent nitrous acid formation due to nitric oxide (NO) reaction with oxygen in the aqueous medium. After that, the nitric oxide (NO) obtained in the reaction of nitric acid and metallic copper was fed into the emulsion in an argon flow. The mixture of gases was first passed through a solution of sodium hydroxide to remove the salt-forming oxides. Simultaneously, the liposome emulsion was acidified with nitric acid to pH 6.3–6.5. In this case, the liposomal cytochrome C was transformed into a reduced form (cytC³⁺-NO). The transition indicator was a change in the color of the emulsion from reddish-brown to bright pink, and also spectral absorption peaks at 528 nm and 560 nm. To stabilize the liposomal cytochrome C, 10 mg of nitrosoglutathione was added to the emulsion.

Then, the emulsion was filtered through a hydrophilic membrane (PES) with a pore diameter of 0.2 µm (PALL, Germany), poured over vials and lyophilized on
a lyophilizer (MartinChristEpsilon 2-6D, Germany). For further experimental biological studies work, an emulsion obtained by reconstitution of the lyophilisate with working solutions was used.

**Chemicals.** All reagents and chemicals were obtained from Sigma Chemical (St. Louis, MO, USA), except for the constituents for Lip (NO) preparation which was detailed in [7].

**Data analysis.** Data were analyzed using pClamp 10 (Molecular Devices, Sunnyvale, CA, USA) and OriginPro 9.7 (OriginLab Corporation, Northampton, MA, USA). The «Event Detection – Single Channel Search» algorithm was used to identify channel transitions between closed and open states based on current level crossing 50 % of the maximum amplitude of the open state [8]. For our 1 kHz filter, events that lasted less than 0.32 ms were not taken into account. Mean open and closed dwell times were calculated from thus idealized current traces. Channel open probability was given by Clampfit after completion of the «Single Channel Search» routine.

Activation curves (G-V relationships) were fitted by the Boltzmann equation in the following form:

\[
G = \frac{G_{\text{max}}}{1 + \exp((V - V_{1/2})/k)},
\]

where \(G\) is membrane conductance at membrane potential \(V\), \(G_{\text{max}}\) is its maximal value at strongly depolarized potentials, \(V_{1/2}\) is the potential of half-maximal activation at which \(G = 0.5\ G_{\text{max}}\) and \(k\) is the slope factor.

The current amplitude histograms were approximated by the standard Gaussian equation (normal distribution). The concentration dependences were fitted by the Hill equation:

\[
Y = \frac{Y_{\text{max}}}{1 + ([\text{Lip(NO)}]/EC_{50})^{p}},
\]

where \(Y\) – measured value at a given Lip (NO) concentration, \(Y_{\text{max}}\) – its maximal value, \([\text{Lip(NO)}]\) – molar concentration of Lip(NO); \(EC_{50}\) – concentration at which \(Y = 0.5\ Y_{\text{max}},\ p\) – slope factor.

The results of the statistical processing of the experimental data are presented as means ± the standard error of the mean (n – the number of measurements). Student’s t-test was used for statistical comparison and differences were considered to be statistically significant at \(P < 0.05\).

**Results and discussion.** Below, we present data on the effect of «empty» phosphatidylcholine liposomes on the contractile activity of vascular smooth muscles (thoracic aortas) obtained from rats with genetically determined hypertension (Fig. 1), under conditions of oxygen deficiency (Fig. 2, 3) and under the influence of ionizing radiation (Fig. 4). In all three cases, a clear restoration of the contractile function of the vessels under the influence of liposomes could be clearly observed.

For instance [4], Figure 1 shows that liposomes do not affect the amplitude of acetylcholine relaxation in the thoracic aortas from healthy rats (A). At the same time, they effectively restore endothelium-dependent relaxation damaged in vascular tissues obtained from SHR (B). Figure 2 illustrates an experiments in which ATP- and PCr-filled liposomes were used to make clear the role of high-energy phosphate depletion in hypoxic relaxation of vascular SM [9]. The data obtained indicate that when applied to SM of rat portal vein preconstricted with \(K^+\)-rich solution, phosphocreatin (PCr) – filled liposomes significantly decreased the amplitude of hypoxia-induced vasorelaxation, i. e., in the absence of liposomes filled with PCr, hypoxic relaxation of SM preconstricted with 60 mM KCl has been
revealed to be 60–65 % while in the presence of PCr-filled liposomes it was only about 30 %. The effect of adenosine triphosphate (ATP)-filled liposomes was expressed in a smaller degree. It is interesting that even «empty» liposomes also possess ability to support contractile force of portal vein at hypoxia but this effect was expressed in a lower degree than when they were filled with high energy phosphates.

Figure 3 clearly demonstrates that the addition of PCL to the buffer solution against the background of hypoxia restores the rhythmic contractile activity of rat portal vein smooth muscles and increases the level of isometric tension developed by them [3].

It should be emphasized that it is phosphatidylcholine liposomes that have the most pronounced antihypoxic effect. Sphingomyelin liposomes also
showed antihypoxic effect, but it was expressed to a much lesser extent and cardiolipin liposomes was without any influence on vascular autorhythmic activity (not shown in this figure).

The next Fig. 4 shows the effect of PCL intraperitoneally injected (30 mg/kg) to the rabbits on relaxant responses of thoracic aortas to ACh and therapeutic NO donors. It is clear that PCL almost completely restored ACh-induced relaxation and significantly improved relaxant responses to NO donors when added 1 h after irradiation. But they had no a similar effect being administered 1 h before irradiation. When added directly to the bath solution, PCL (100 µg/ml) restored damaged endothelium-dependent responses to ACh but was without effect on endothelium-independent vascular responses to NO donors. To make the choice of PCL dose we used our previous investigations on vascular smooth muscle from spontaneously hypertensive rats in which its restoring effect was plateaued in a range of 40–100 µg/ml [4]. When administered to the rabbit 1 h after irradiation impact, PCL normalized also the sensitivity of thoracic aorta to authentic NO (aqueous NO solution) that was significantly increased after irradiation. The EC$_{50}$ for healthy and irradiated vascular tissue for NO in vascular tissue before PCL administration were (1.5 ± 0.8) · 10$^{-6}$ M and (2.8 ± 0.8) · 10$^{-7}$ M, respectively (p < 0.05, n = 14). It is important to note that the amplitude of maximal ACh relaxation ($R_{max}$) to NO was without significant difference in both kinds of tissue ($R_{max}$ were (77.8 ± 10.0) % and (87.1 ± 3.9) %, respectively, p > 0.05, n = 14). Under PCL action EC$_{50}$ for irradiated tissue had increased and became very close to normal value – (1.3 ± 0.6) · 10$^{-6}$ M (p > 0.05); $R_{max}$ was (77.6 ± 6.7) % (p > 0.05, n = 12).

It is interesting to note that liposomes are not protective when exposed before irradiation. When administered to animals one hour before exposure to radiation, they did not affect endothelium-dependent and independent vascular reactions. But at the same time, they had a distinct reparative effect if they were prescribed after the end of the radiation exposure.

Figure 5 demonstrates dose-dependent effect of quercetine-filled lipo-
somes and their constituents on BK\textsubscript{Ca} activity in irradiated SM cells of rat thoracic aorta obtained on the 9\textsuperscript{th} and 30\textsuperscript{th} days of post-irradiation. It is clear that on the 9\textsuperscript{th} day of post-irradiation there was no difference in the action of these compounds at the maximal concentrations while a low dose demonstrates a higher activity of PCL-Q as compared to its constituents. In contrast, the maximal repairing effect of PCL-Q, on the 30\textsuperscript{th} day of post-irradiation appears to be higher as compared to Q and so much as the PCL. The therapeutic effectiveness of the compounds investigated can be ranked arranged as the ratio 1.0 : 0.6 : 0.4 for all doses except maximal concentration.

The nature of the interaction of liposomes with cells membrane plays an important role in their advantages over other drug carriers and makes them capable of manifesting their own biological activity. It can take different forms: the simplest one is that liposomes are adsorbed (attached) to the cell surface. The matter may end there, or it may go further: the cell will absorb the liposome (this process of «swallowing» is called endocytosis), and together with it the substances that it delivered will enter the cell. Finally, liposomes can fuse with cell membranes and become part of them. This can change the properties of cell membranes, for example: viscosity and permeability; the amount of electric charge; phospholipid environment of enzymes and ion channels and, accordingly, their activity; changes in the number of channels embedded in membranes (that’s why even the so-called empty liposome can be a biologically active agent!). Thus, thanks to liposomes, a new way of targeting the cell appears, which can be called «membrane engineering», i. e. it becomes possible to modify the cell membrane in a given direction.

There is reason to believe that remodelling of the phospholipid bilayer of the membrane, for example, by polyunsaturated fatty acids, can significantly change the functional activity of ion channels. However, the mechanisms of this phenomenon are still poorly understood [10, 11]. It is known that the Maxi K channel is under double control – the level of membrane potential and intracellular calcium concentration.

Fig. 5. Concentration-dependent effects of quercetin-filled phosphatidylcholine liposomes (PCL-Q), free quercetin (Q) and «empty» PCL on outward currents measured in irradiated aortic SM cells at the end of the pulses to +70 mV. Abscissa – concentration (µg/ml) of active substance. Ordinate – BK\textsubscript{Ca} increment (ΔI) under the treatment with PCL-Q, Q and PCL expressed as a percentage of the initial current, (ΔI = (I\textsubscript{t} – I\textsubscript{0})/I\textsubscript{0}, where I\textsubscript{0} and I\textsubscript{t} – currents before and after the treatment, respectively. The asterisks indicate statistically significant difference for the current values before and after treatment with the drugs investigated (P < 0.05).
Hoshi T. and colleagues [12] showed that docosahexaenoic acid is capable of activating Maxi K at nanomolar concentrations in the absence of stimulation of the potential sensor or calcium binding sites, i.e., its effect on the channel may result from the direct interaction of the channel protein complex and the fatty acid.

There is convincing evidence [13] that TRPV1 channels may be directly activated by lysophosphatidic acid which is a lipid metabolite composed of a phosphate, a glycerol, and a fatty acid. 38 years earlier, when studying the role of fatty acids in molluscs membrane fluidity in the activation of ion channels it has been shown [14] that 2-decanoic acid has strong effect on membrane fluidity and blocks Na channel activity in squid giant axonal membrane.

A little later, in 1987, in the Reports of the Academy of Sciences of USSR was published the work with the participation of Takenaka, in which was hypothesized that the lipid environment of integral channel proteins is important for their specific activity [15]. Their approval was based on the evidence that ouabain-insensitive response to acetylcholine due to activation of sodium and potassium ion channels, are transformed into ouabain-sensitive after the treatment with decylenic acid.

It is well known that though the cell membrane is a protective barrier, it also plays an important role in letting some material and related information through ion channels, integral membrane proteins, that are embedded in the cell membrane. It is becoming increasingly clear that the phospholipid environment can significantly affect channel function. Now new research from the Nobel Prize-winning laboratory [16] earnestly demonstrate convincing evidence that ion channel function is controlled in part by a complex interaction between a channel’s voltage sensor and the cell membrane immediately adjacent to it. They showed that the function of a voltage-dependent K⁺ channel is dependent on the negatively charged phospholipid molecules. When they made some different bilayers with non-phospholipids that were either positively charged, negatively charged, or had no charge at all. They then added Kv channels and tested their function and Kv did not demonstrate function. After that they added phospholipid and the channel function was restored.

Thus, it is becoming clear now that a channel and its surrounding membrane lipids together represent a functional unified unit [17]. Later [18] postulated that the lipids play an important role in the gating of voltage-operated ion channels.

In our control experiments related to studies of liposomal quercetin [7] we observed that «empty» (without quercetin) PCi are able to activate the Maxi-K channels. Simultaneous openings of up to 2 Maxi-K channels were observed, when these were surprisingly activated by empty liposomes (100 µg/ml). Again, single channel conductance remained unchanged as unitary current amplitudes recorded at the same test potential remained constant, while the main effect (clearly evident in Fig. 6) was due to an increase in the frequency of channel openings.

The possible effect of exogenous phospholipids on the function of ionic channel has been observed when studying the effect of liposomal nitric oxide on smooth muscle of pulmonary artery [19].

Figure 7 illustrates an increase in baseline noise in the presence of 10⁻⁵ M Lip (NO) compared to the control (peak...
Widths were (0.212 ± 0.003) and (0.452 ± 0.004), respectively, P < 0.01, which may indicate a certain non-specific effect of Lip (NO) related to membrane destabilization. This effect is most likely to be caused by phospholipids of liposomes after their membrane fusion, and not be due to NO releasing from Lip (NO).

Modulation of the activity of Maxi-K channels, carrying most of the outgoing potassium current, directly affects the level of polarization of the cell membrane and, indirectly, determines the level of activity of voltage-gated calcium channels. The role of ions in the regulation of smooth muscle, as well as contractile responses, is underlined by the observations that phospholipids, in contrast to sugars and proteins, are not active organic molecules.
muscle cell function is difficult to overestimate.

In conclusion, there is reason to believe that, upon embedding into a structure of the cell membrane, liposomes alter the phospholipid environment of the channel, the state of which directly affects the channel ability to be activated. This way the so-called empty phosphatidylcholine liposomes, which do not carry any additional chemical compounds, can exhibit their own biological activity. Obviously, this is due to their ability to influence the phospholipid environment of ion channels and, thereby, change their functional activity.

Why do «empty» liposomes have their own biological activity?

It is well known, that liposomes are successfully used, first of all, in pharmacology and pharmacotherapy, for drug delivery, but their own biological activity cannot be excluded.

The data obtained clearly demonstrate, that even empty (i.e., containing no active substances in their internal cavity or membrane) phosphatidylcholine liposomes (PCL), i.e. liposomes per se, possess an amazing ability to normalize the contractile activity of blood vessels impaired under hypoxia, restore endothelial function at arterial hypertension and diabetes, and even to renovate endothelium-dependent relaxant vascular function damaged after exposure to ionized γ-radiation. It was shown also that liposomes per se effectively restored Maxi-K channels activity damaged following genotoxic oxidative stress induced by γ-radiation.

Thus, empty phosphatidylcholine liposomes have a pronounced intrinsic biological activity regarding vascular tissues. This is a really surprising discovery and these effects may be due to their ability to influence the phospholipid environment of ion channels and, thereby, to modulate ion channel functional activity.

Key words: «empty» liposomes, biological activity, phosphatidylcholine liposomes