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Regulation of Erythrocyte Electrophoretic Mobility Using Magnetite Nanoparticles: Prospects of Nanomedicine in Intensive Care and Transfusion Therapy

Belousov AN

Laboratory of Applied Nanotechnology, Kharkiv National Medical University, Ukraine

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Abstract

A decrease in erythrocyte electrophoretic mobility serves as an important diagnostic marker of pathological conditions associated with impaired gas exchange, microcirculation, and tissue trophism, often leading to systemic hypoxia and deterioration of the patient's clinical status. This study investigates the potential of magnetite nanoparticles (MCS-B) to modulate these properties in a targeted and controlled manner. A novel approach is proposed to enhance erythrocyte electrophoretic mobility in patients with toxemia through treatment with magnetite nanoparticles. In vitro experiments demonstrated a statistically significant ($p < 0.001$) increase - nearly threefold - in erythrocyte mobility following exposure to MCS-B, compared to untreated controls. The optimal efficacy was observed at a blood-to-nanoparticle ratio of 2:1.

Furthermore, application of a constant magnetic field with an intensity of 200–250 kA/m for 2-3 minutes resulted in effective removal of residual nanoparticles from blood samples ($p < 0.001$). The results highlight the biocompatibility and clinical potential of this nanomedical approach, which may serve as a basis for new therapeutic strategies in transfusion medicine, critical care, and regenerative therapy. The study addresses a pressing interdisciplinary challenge, bridging hematology, biophysics, and nanotechnology, with implications for both basic science and clinical implementation.

***Corresponding author**: Belousov AN, Laboratory of Applied Nanotechnology, Kharkiv National Medical University, Ukraine.

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Introduction

The electrophoretic mobility of erythrocytes (EPM) is a significant biophysical parameter. It reflects the state of cellular membranes and their surface charge. This indicator provides important information about the functional condition of erythrocytes across a wide range of physiological and pathological states. As a parameter associated with the surface charge of cell membranes, EPM is highly sensitive to changes in membrane composition and structural integrity. Modifications in EPM have been observed in response to oxidative stress, systemic inflammation, oncological diseases, and aging-related processes.

Due to its sensitivity and non-invasiveness, the analysis of erythrocyte electrophoretic mobility represents a promising supplementary approach. It can be applied in clinical diagnostics and biomedical research. For example, EPM assessment may help detect early membrane disturbances in systemic pathologies. It can also be used to monitor therapeutic efficacy and predict disease progression. These capabilities are directly linked to the biophysical and biochemical properties of the erythrocyte membrane. They are also influenced by internal and external environmental factors that determine electrophoretic mobility.

Properties of the Erythrocyte Membrane

- Surface charge and sialic acids. Sialic acids contribute to the negative charge of the membrane. Their loss leads to a decrease in erythrocyte electrophoretic mobility (EPM) [1,2].
- Phospholipid and protein composition. Alterations in the lipid-protein composition, for example during inflammation or diabetes, modify the electrophysiological characteristics of the membrane [3].
- Membrane fluidity and viscosity. These parameters depend on the cholesterol-to-phospholipid ratio. Increased membrane rigidity reduces EPM [4].

Biochemical and Metabolic Factors

- Oxidative stress. Lipid peroxidation and membrane protein damage reduce erythrocyte mobility [5-7].
- pH of the medium. In acidosis, membrane proteins become protonated. This reduces their negative charge and decreases EPM [8,9].

Physiological and Pathological Conditions

- Erythrocyte aging. Aging erythrocytes show decreased sialic acid content and reduced electrophoretic mobility [10].
- Inflammation. Acute-phase proteins, such as fibrinogen and CRP, adsorb onto the membrane. This alters its surface charge [11].
- Anemia, oncological, and autoimmune diseases. These conditions may reduce EPM due to structural and biochemical alterations of the membrane [12-14].

External Factors

- Pharmacological agents. Certain drugs can affect membrane stability and charge [15,16].
- Colloid solutions and procedures. Treatments such as plasmapheresis may temporarily change plasma viscosity and conductivity [16].

Aging and Age-Related Changes

With advancing age, erythrocyte membrane composition and structure are progressively disrupted, including a reduction in sialic acid content. This leads to a decreased negative surface charge and lower electrophoretic mobility (EPM) [17].

Reduced EPM has important functional consequences: it reflects impaired membrane function, slows microcirculation, and diminishes tissue oxygen delivery. Alterations in erythrocyte shape or membrane proteins further compromise capillary flow and oxygenation. As a result, blood viscosity increases and the risk of thrombosis rises, particularly in organs with high metabolic demand, such as the brain and heart. Thus, decreased EPM is not only a laboratory marker of aging but also a pathophysiologically significant factor contributing to microcirculatory dysfunction and tissue hypoxia.

Nanotechnological Modulation of the Biophysical Properties of Erythrocytes: New Horizons

Recent advances in nanotechnology offer new opportunities for modulating the biophysical properties of blood cells, particularly erythrocytes. Of particular interest is the potential for targeted modulation of EPM by nanoparticles, as this parameter reflects the surface charge, structural integrity, and functional state of cell membranes.

An article published in Micro and Nano Systems Let-

ters investigates the effects of pure (ligand-free) magnetite nanoparticles embedded in a sodium chloride matrix on hematological parameters, blood gases, electrolytes, and serum iron. The results demonstrate that such nanoparticles can influence these parameters, which is essential for assessing their biocompatibility and potential impact on erythrocytes [18].

A study published in the Journal of Nanoscience and Nanotechnology explores the interaction between erythrocytes and magnetite nanoparticles. The findings indicate that erythrocytes are capable of internalizing magnetite nanoparticles, which may alter their physicochemical properties and functionality [19].

An article in Toxicology Research examines the hematotoxicity of polyethylene glycol (PEG)-coated magnetite nanoparticles under both in vitro and in vivo conditions. The results reveal that such nanoparticles can exert toxic effects on erythrocytes, which is a critical consideration in the development of nanomaterials for medical applications [20].

Thus, biocompatible nanoparticles - particularly those based on magnetite - are capable of interacting with erythrocyte membranes, modifying their electrostatic and rheological properties. Controlled modulation of erythrocyte electrophoretic mobility by nanoparticles offers the potential to correct hemorheological disorders and optimize microcirculatory function, thereby opening new avenues for nanomedical therapy and treatment monitoring.

The results of the present study highlight the importance of a thorough understanding of the interactions between magnetite nanoparticles and erythrocytes, especially in the context of their application in advanced medical technologies. In this regard, investigating the impact of magnetite nanoparticles on EPM represents a timely and promising direction in the fields of biophysics and nanomedicine.

To date, numerous types of magnetic nanoparticles have been synthesized and are actively employed in clinical practice - for applications ranging from magnetic resonance imaging and targeted drug delivery to magnetic hyperthermia. However, despite their therapeutic potential, these nanoparticles may exert not only modulatory but, in certain cases, cytotoxic effects on blood cells.

Biocompatible magnetite-based nanoparticles were developed in 1995 in Ukraine by Professor Andrey Nikolaevych Belousov, Doctor of Medical Sciences. These formulations - marketed under the proprietary names Micromage-B, MCS-B, and ICNB - represent the first nanotechnology-based medicinal products in the world to be officially registered and approved for clinical use by a national health authority (Ministry of Health of Ukraine, registration granted in 1998).

These nanoscale agents are not cytostatic in nature. Instead, their mechanism of action involves modulation and activation of endogenous physiological processes, including but not limited to:

- immune system stimulation,
- enhancement of antioxidant defense mechanisms,
- activation of phagocytosis,
- facilitation of endogenous detoxification pathways.

The aforementioned nanopreparations have demonstrated clinical safety and efficacy as adjunctive therapies in the management of:

- neurodegenerative diseases,
- autoimmune disorders,
- toxic and post-toxic syndromes,
- malignant tumors.

The invention provides a novel class of magnetically responsive, biologically active nanomaterials with a unique profile of non-cytotoxic systemic modulation, opening new pathways for nanomedical interventions in complex and multifactorial pathologies.

Their mechanism of action is based on controlled sorption of toxins and stabilization of cellular membranes at the nanostructural level [21-23].

Due to their non-toxic nature, these agents are suitable for long-term use in the management of chronic diseases. Their therapeutic activity is not dependent on the genetic profile of the target cell, allowing for broad applicability across diverse pathological conditions [24-27].

Each magnetite nanoparticle represents a subdomain elementary magnet with a size ranging from 6 to 12 nm. When exposed to a constant magnetic field of

300–400 kA/m, not only is the mechanism of selective sorption via magnetophoresis [24] activated, but there is also modulation of cellular metabolic activity and resolution of the "sludge syndrome" phenomenon [26,28]. Collectively, these effects contribute to the activation of sanogenetic mechanisms, induction of hemocorrection, and non-specific stimulation of the body's natural detoxification processes [21].

These findings emphasize the scientific relevance of further investigation into the effects of magnetite nanoparticles on the bioelectrical properties of blood cell membranes in patients with clinical manifestations of toxemia. In this context, particular attention is given to the assessment of erythrocyte electrophoretic mobility as a sensitive biophysical marker of membrane alterations.

The aim of the present study is to develop an innovative nanomedical platform based on biocompatible magnetite nanoparticles capable of restoring erythrocyte electrophoretic mobility (EPM) under conditions of toxemia and hypoxia.

Materials and Methods

Study Material: Erythrocytes obtained from the blood of practically healthy individuals and patients presenting with clinical signs of toxemia. The condition of erythrocytes was assessed in a total of 30 individuals. The sample size (n = 30) was determined a priori based on the expected large effect size (d ≈ 1.2), a significance level of α = 0.05, and a power of 80%, providing sufficient statistical sensitivity to detect differences between groups. All participants were conditionally divided into two groups:

Group I (Donors): 10 practically healthy volunteers (Table 1);

Group II (Main group): 20 patients with clinical manifestations of toxemia who were admitted to the intensive care unit (Table 2).

Table 1: Distribution of donors by age and sex.

Number of Donors (volunteers among practically healthy individuals)	Age (years), sex, number of individuals			
	35-45		45-55	
	M	F	M	F
10	4	1	3	2

Table 2: Distribution of patients in the main group by age, sex, and diagnosis.

Diagnosis	35–45 M	35–45 F	45–55 M	45–55 F	Total (n/%)
Acute gangrenous cholecystitis in gallstone disease	2	2	2	2	8/40%
Chronic hepatitis	2	–	3	–	5/25%
Liver cirrhosis (stage I–II)	–	–	2	–	2/10%
Acute purulent pancreonecrosis with peritonitis	4	–	1	–	5/25%
Total	8	2	8	2	20/100%

Physicochemical Parameters of Magnetite Nanoparticles (Magnetically Controlled Sorbent "MCS-B" Brand).

The magnetically controlled sorbent (MCS-B brand) consists of stabilized magnetite (Fe_3O_4) nanoparticles ranging in size from 6 to 12 nm. The main physicochemical properties of MCS-B are summarized below, as well as in Tables 3-6 and Figures 1, 2:

- Total surface area of the magnetite nanoparticles: Sa = 800–1000 m^2/g
- Saturation magnetization: Is = 2.15 kA/m
- Volume concentration: q = 0.00448
- Viscosity: η = 1.0112 cSt
- Zeta potential: ζ = –19 mV

The small size of the magnetite nanoparticles provides a relatively large specific sorption surface area (Sa = 800-1200 m^2/g). Physicochemical characteristics such as volume concentration (q = 0.00448) and viscosity (η = 1.0112 cSt) allow for rapid and uniform distribution of MCS-B throughout the volume of the blood plasma sample. The saturation magnetization (Is = 2.15 kA/m) not only ensures high polarization capacity of MCS-B but also facilitates its rapid and efficient removal from blood plasma using a low-intensity external constant magnetic field [21].

Table 3: The calculated lattice parameters of the phases.

Phase name	a (Å)	b (Å)	c (Å)	alpha (degree)	beta (degree)	gamma (degree)
magnetite low	8.387836	8.387836	8.387836	90.00	90.00	90.00
magnetite low, syn	5.930687	5.930687	14.705912	90.00	90.00	120.00
Johannsenite	9.891680	9.059276	5.282908	90.00	105.54	90.00

Table 4: Determination of percent composition of the ICNB by X-ray spectrometer ARL OPTIM'X (semi-quantitative analysis).

Compound	Weight%	StdErr	El	Weight%/O2	StdErr	El	Weight%	StdErr
Fe3O4	97.37	0.09	Fe	68.4	0.07	Fe	97.62	0.09
CaO	2.26	0.07	Ca	1.71	0.05	Ca	2.3	0.07
P2O5	0.28	0.027	Px	0.122	0.012	Px	0.157	0.015
MnO	0.255	0.013	Mn	0.198	0.01	Mn	0.278	0.014
SiO2	0.098	0.027	Si	0.046	0.013	Si	0.059	0.016
SO3	0.032	0.013	Sx	0.0126	0.0051	Sx	0.0164	0.0066
Cl	0.028	0.009	Cl	0.028	0.009	Cl	0.038	0.012

Table 5: X-ray analysis of ICNB in X-ray diffractometer Rigaku Ultima IV (CuKα, Kβ filter - Ni), one-coordinate DTeX semiconductor detector.

Phase	Formula	Space group	№ Card Database ICDD
magnetite low	Fe2.886 O4	227 : Fd-3m, choice-2	10861339 (ICDD)
magnetite low, syn	Fe3O4	166 : R-3m, hexagonal	10716766 (ICDD)
Johannsenite	Ca Mn +2 Si2O6	15 : C12/c1, unique-b,cell-1	380413 (ICDD)

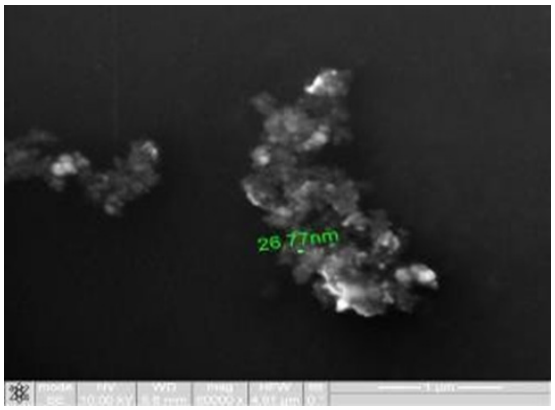


Figure 1: Study of magnetite nanoparticles with use microscope ion-electronic raster-type Quanta 200 3D

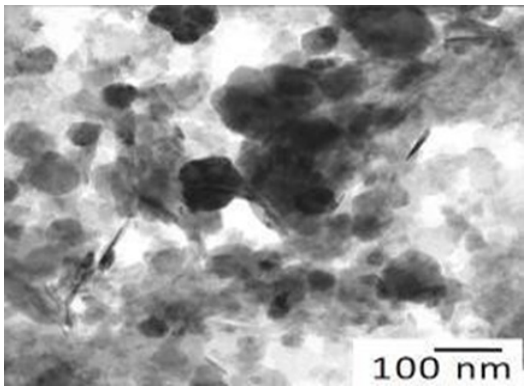


Figure 2: Study of magnetite nanoparticles with use microscope electronic translucent JEM-2100

Table 6: The phases of magnetite of nanoparticles (RIR - method; error 8±3%).

Phases (method of corundum numbers)	Content, %
magnetite low	71
magnetite low, syn (hexagonal)	29

The sorption activity of MCS-B for various substances present in liquid media is presented in Table 7.

Table 7: Some data sorption activity of MCS-B * for a various sort of the substances which are taking place in biological liquid.

Substance	Biological liquid		
	H2O	Plasma of blood	The blood
Phenol	1 mcg	0.05 mcg	0.05 mcg
Albumin		Absent	Absent
Creatinin		Absent	Absent
Urine	Absent	Absent	Absent
Cholesterol		10 mcg	10 mcg
Hormone T3		Absent	Absent
Cu	1.75 mcg	2.5 mcg	1 mcg
Ca	Absent	Absent	Absent
K	Absent	Absent	Absent
Na	Absent	Absent	Absent
Cl	Absent	Absent	Absent
Mg	Absent	Absent	Absent
Zn	10 mcg	Absent	0.75 mcg
NaNO3 (nitrates)	12.5 mcg	10 mcg	Absent
Cr	2 mcg	0.49 mcg	0.5 mcg
Pb	1.17 mcg	0.3 mcg	0,19 mcg
Cd	0.48 mcg	0.68 mcg	1.55 mcg
Ig A	500 mcmol	300 mcmol	250 mcmol
Ig M	200 mcmol	350 mcmol	250 mcmol
Ig G	Absent	200 mcmol	250 mcmol

The note: * - at the rate of 30 mg MCS-B on 1 ml liquids

Method for Investigating Erythrocyte Electrophoretic Mobility and Determining the Optimal Effective Dose of MCS-B.

Electrophoretic mobility was measured using an electrophoresis apparatus according to the methodology described in [29]. The electrical circuit diagram of the electrophoresis setup is shown in Figure 3.

The power source consisted of a rechargeable battery with a voltage of 80-100 V. A Rustrat-type rheostat with a resistance of 4-5 kOhm was used as a potentiometer and connected in series. A voltmeter was connected in parallel to the potentiometer. The current was supplied to the measurement chamber via a commutator that allowed for easy reversal of the current direction.

The current was applied to non-polarizable electrodes. As shown in the figure, copper conductors were immersed in containers filled with a saturated solution of $CuSO_4$. These containers were connected to others containing a 10% KCl solution. The latter were connected to the chamber via agar bridges (siphons). A milliammeter with a measuring range of 50–100 mA was included in the circuit to monitor current intensity. The chamber was placed on the microscope stage, while the non-polarizable electrodes were positioned on a stand on either side of the microscope.

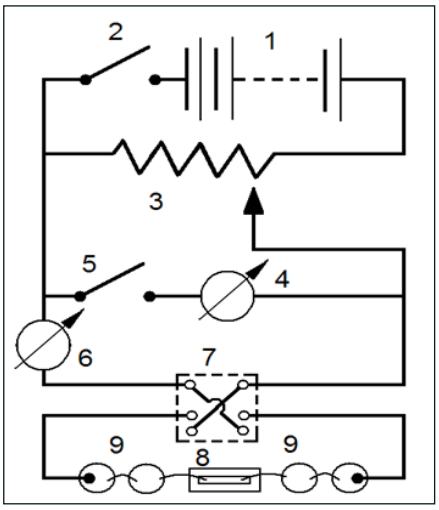


Figure 3: Electrical circuit diagram of the electrophoresis system.

Legend:
1 – battery,
2 – switch,
3 – potentiometer,
4 – voltmeter,
5 – voltmeter activation switch,
6 – milliammeter,
7 – six-pole switch,
8 – chamber,
9 – non-polarizable electrodes.

Procedure and Calculations.

The object of the study was erythrocytes, which were placed into a chamber equipped with non-polarizable electrodes. Cell movement was monitored using a microscope, the eyepiece of which was fitted with a calibrated reticle. The scale calibration of the grid was: 30 divisions = 10 µm.

For each blood sample, two *in vitro* experiments were performed. The first used an untreated blood sample from a patient; the second used the same patient's blood sample treated with magnetite nanoparticles (MCS-B).

A small volume of blood was diluted in an 8% sucrose solution buffered with McIlvaine's citrate buffer to prevent the solution from conducting electric current. The pH of the solution was adjusted to 7.4, matching physiological blood pH to avoid hemolysis.

For each sample, seven measurements of erythrocyte velocity were taken in opposite directions relative to the electric current in order to eliminate the effect of surface tilt. The mean value was then calculated.

Calculations were performed according to the following formulas:

$$\omega = \frac{S}{tE};$$

$$E = \frac{U}{r};$$

$$\omega = \frac{Sr}{tU},$$

where:
ω - electrophoretic mobility (cm/sec·V);
S – distance (in cm) traveled by the particle during time t;
t – time (in seconds);
E – potential gradient, i.e., voltage drop per unit length of the conductor;
U – voltage (in V);
r – distance between the ends of the agar siphons (in

cm).

The study was conducted in vitro in three stages:
Stage I – electrophoretic mobility of erythrocytes from healthy donors;
Stage II – baseline electrophoretic mobility of erythrocytes from patients with toxemia syndrome;
Stage III – electrophoretic mobility of erythrocytes from patients after treatment with magnetite nanoparticles (MCS-B).
The optimal effective dose of MCS-B was determined based on erythrocyte electrophoretic mobility under different volume ratios of blood to MCS-B (3:1, 2:1, 1:1).

Method for Determining the Minimum Magnetic Field Strength Required for Effective Extraction of MCS-B from Blood

MCS-B was introduced *in vitro* into the blood of practically healthy individuals. Using an external constant magnetic field at different field strengths -100-150 kA/m and 200-250 kA/m (measured with a Tesla ammeter F 4354/1; GOST 5.1977-73) - MCS-B was extracted from the blood plasma mixture within 2-3 minutes.

The effectiveness of MCS-B removal from plasma was assessed by determining the concentration of iron (Fe) in plasma *in vitro* [23] at three time points: before MCS-B administration, after MCS-B administration, and after its extraction using permanent magnets with field strengths of 100-150 kA/m and 200-250 kA/m.

All data in this study are presented in International System of Units (SI). The obtained results were statistically analyzed using the method of variational statistics by comparing means with the Student's *t*-test.

Research Results and Discussion

Erythrocyte Electrophoretic Mobility and Its Dose-Dependent Response to Magnetite Nanoparticles (MCS-B).

The **electrophoretic mobility of erythrocytes** serves as an indirect indicator of two fundamental physiological parameters:

1. the **bioelectrical charge of the erythrocyte membrane**, which reflects the functional state and surface potential of red blood cells;
2. the **rheological properties of blood**, particularly the ease with which erythrocytes move through the vascular system under various flow conditions.

Alterations in electrophoretic mobility may therefore signal changes in membrane integrity, surface charge distribution, or systemic hemorheological status - especially under pathological conditions such as toxemia.

In this study, we investigated the **dose-dependent effect of magnetite nanoparticles** on erythrocyte electrophoretic mobility in patients with toxemia. The data, presented in Table 8, illustrate the dynamic response of this parameter following exposure to varying blood-to-MCS ratios.

Table 8: Electrophoretic Mobility of Blood Erythrocytes before and after Treatment with Magnetite Nano-Particles (M±m).

Indicator	Practically Healthy Individuals (n=10)	Patients with Toxemia Syndrome (n=20)			
		Primary Data	Variants of Blood-to-MCS Ratio		
			3:1	2:1	1:1
Electrophoretic mobility of erythrocytes, 10-4cm2/secV	$3.5x10^{-4} \pm 0.2$	1.26x10-4± 0.2 P<0.01	2.70x10-4± 0.2 P<0.05 P1<0.01	3.76x10-4± 0.2 P>0.05 P1<0.001 P2<0.05	3.8x10-4± 0.2 P>0.05 P1<0.001 P2<0.05 P3>0.05

Notes:

1. *P* – probability of differences compared with practically healthy individuals;
2. P_1 – probability of differences after treatment with magnetite nanoparticles compared to baseline values;
3. P_2 – probability of differences compared with the 3:1 blood-to-MCS ratio;
4. P_3 – probability of differences compared with the 2:1 blood-to-MCS ratio.

All values are presented as mean ± standard deviation. Statistical significance was determined using Student's t-test; $P < 0.05$ was considered significant.

All values are presented as mean ± standard deviation. Statistical significance was determined using Student's t-test; $P < 0.05$ was considered significant.

The data presented in Table 8 indicate that, in donors (practically healthy individuals), the erythrocyte electrophoretic mobility (EPM) was $3.5\times10^{-4} \pm 0.2$ cm²/V·sec, whereas in patients with toxemia syndrome (main group), the baseline value was $1.26\times10^{-4} \pm 0.2$ cm²/V·sec.

As a result of blood treatment with magnetite nanoparticles (MCS-B) at a ratio of 3 parts blood to 1 part MCS-B, EPM significantly increased compared to baseline ($p < 0.01$), yet remained significantly different from the normal reference values ($p < 0.05$).

At the ratios of 2:1 and 1:1, the EPM decreased even more significantly compared to baseline values ($p < 0.001$) and no longer differed from the normal range ($p > 0.05$). It should also be noted that no statistically significant difference was found between the 1:1 and 2:1 ratios ($p > 0.05$).

Thus, the optimally effective dose of magnetite nanoparticles for improving erythrocyte electrophoretic mobility is the 2:1 ratio (two parts blood to one part MCS-B). The observed changes provide insight into the potential of magnetite nanoparticles to modulate cell surface charge and improve microcirculatory flow.

The electrophoretic mobility indices of erythrocytes (mean ± standard deviation) in healthy individuals and patients with toxemia before and after treatment with magnetite nanoparticles at different ratios of blood and MCS-B are presented in Figure 4.

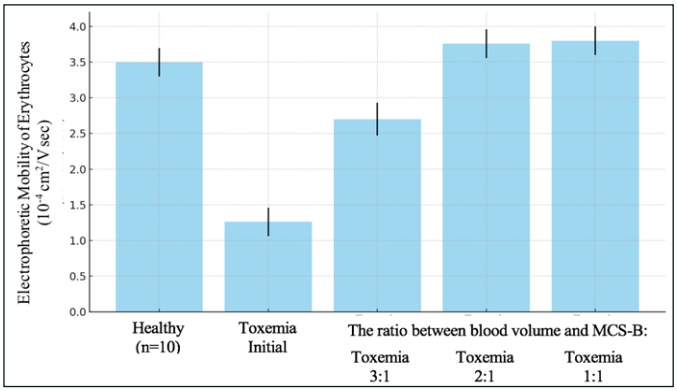
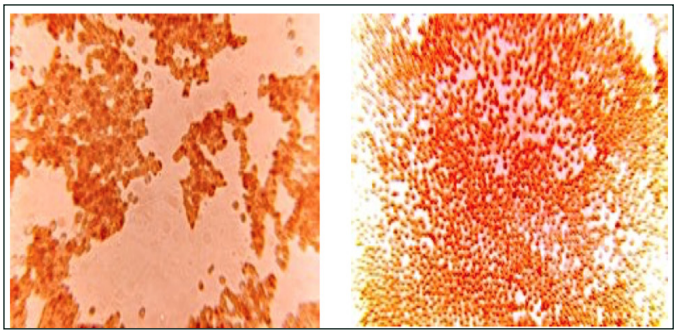


Figure 4: Electrophoretic mobility of erythrocytes at various stages of the experiment (mean ± standard error).



Before After exposure to MCS-B in vitro

Figure 5: Morphological changes in erythrocytes in heparinized blood from a patient with toxemia syndrome before and after in vitro treatment with MCS-B at a 2:1 blood-to-MCS ratio.

Figure 5 illustrates pronounced morphological changes in erythrocytes from heparinized blood of a patient with toxemia syndrome before and after in vitro treatment with the nanodrug MCS-B. Following exposure, a resolution of erythrocyte sludging, restoration of the normal discocyte shape, and an increase in the electronegativity of the cell surface were observed. These findings indicate a reestablishment of erythrocyte dispersion and normalization of blood rheological properties.

From a pathophysiological perspective, such correction of erythrocyte morphology and function contributes to enhanced microcirculation, improved oxygen transport, and a reduction in tissue hypoxia. Furthermore, by restoring blood fluidity and decreasing cellular aggregation, conditions are created for more effective systemic detoxification - a critical therapeutic target in various forms of endogenous intoxication, including sepsis, multiple organ dysfunction syndrome, and severe inflammatory states.

Thus, MCS-B represents a promising agent for pathogenetic therapy in clinical scenarios characterized by impaired hemorheology and compromised oxygen delivery.

Physiological model of the protective mechanisms of MCS-B of MCS-B on erythrocyte membranes in toxemia is based on previously reliably obtained data:

Membrane restoration and detoxification.

Magnetite nanoparticles (MCS-B) effectively adsorb circulating toxins, lipid peroxidation products, and reactive oxygen species [30]. This contributes to the stabilization of the erythrocyte membrane lipid bilayer and the restoration of activity of membrane-associated enzymes such as Na^+/K^+-ATPase [31]. Restoration of the structural and functional integrity of the membrane is essential for the normal function of glycolytic enzymes that support erythrocyte energy metabolism [32].

Reactivation of glycolytic enzymes.

- By correcting ionic balance, pH, and redox potential, glycolytic enzymes regain activity.
- Glycolytic flux increases → more ATP and 1,3-BPG are produced.
- 1,3-BPG is then diverted both to ATP production and to the Rapoport shunt → simultaneous increase in ATP and 2,3-DPG.

Restoration of Metabolic Balance.

- After membrane and redox normalization, erythrocytes can resume adaptive responses to hypoxia or acidosis, increasing 2,3-DPG.
- At the same time, global glycolytic output ensures that ATP levels are restored to physiological range.
- This paradox - concurrent increase of both ATP and 2,3-DPG - is possible only after reversal of toxic suppression.

The combined protective mechanisms of MCS-B action on erythrocyte membranes under conditions of toxemia are summarized in Table 9.

Table 9: Summarizes the integrated protective mechanisms exerted by MCS-B on erythrocyte membranes in

Parameter	Before Treatment (Toxemia)	After Magnetite Exposure
Membrane potential	Disrupted	Restored
Glycolytic activity	Suppressed	Re-activated
ATP	Decreased	Increased
2,3-DPG	Decreased or unstable	Increased
Electrophoretic mobility	Impaired	Restored

The aforementioned mechanisms are supported by previous studies in patients with toxemia, which reliably demonstrated a significant decrease in ATP and 2,3-DPG levels due to a generalized suppression of anaerobic glycolysis in erythrocytes [33,34]. Treatment of blood with magnetite nanoparticles (MCS-B) promotes the effective removal of circulating toxic substances, protects and restores the structural integrity of erythrocyte membranes, and stimulates the activation of key enzymes in the glycolytic pathway [32,35]. This leads to simultaneous restoration of ATP and 2,3-DPG concentrations, which, despite their inverse correlation under physiological conditions, reflects the recovery of metabolic potential and energy homeostasis in the pathological state of toxemia [36,37]. Improvement in cellular energetic status induces modulation of the bioelectrical charge on the erythrocyte outer membrane, contributing to normalization of their electrophoretic mobility, reduction of aggregation, and enhancement of microcirculation.

Determination of Magnetic Field Intensity Capable of Removing Magnetite Nanoparticles (MCS-B) from Blood.

The plasma iron concentrations in practically healthy individuals in vitro at different stages of the study are presented in Table 10.

Table 10: Plasma Fe levels in practically healthy individuals in vitro at different stages of the study (n = 10; M ± m)

Study Stage	Plasma Fe Level (nmol/L, mean ± SD)	p-value
Before MCS-B administration	124.3 ± 25.6	—
After MCS-B administration	656.3 ± 31.3	< 0.001
After exposure to constant magnetic field (2-3 min):		
• 100-150 kA/m	214.3 ± 25.6	< 0.05
• 200-250 kA/m	127.4 ± 24.1	> 0.05

Note: P - significance level of the difference compared to values before MCS-B administration.

As shown in Table 6, exposure of blood plasma from practically healthy individuals to a constant magnetic field with an intensity of 100–150 kA/m for 2-3 minutes resulted in a statistically significant reduction in plasma iron concentration ($p < 0.05$) compared to post-MCS-B administration values. Nevertheless, the iron level remained significantly elevated relative to baseline, suggesting only partial removal of MCS-B from the plasma under these conditions.

Conversely, application of a stronger magnetic field (200-250 kA/m) for the same duration led to a near-complete normalization of plasma iron levels. No statistically significant differences were observed between these post-exposure values and the baseline data ($p > 0.05$), indicating effective elimination of MCS-B from the plasma.

These findings support the hypothesis that magnetically controlled removal of MCS-B is both intensity-dependent and reversible. Specifically, magnetic fields of 200-250 kA/m are capable of achieving highly significant clearance of MCS-B nanoparticles from plasma within 2–3 minutes ($p < 0.001$), confirming the feasibility of external magnetic modulation in regulating the biodistribution of magnetite-based nanomaterials.

Safety and Regulatory Considerations of MCS-B.

This study did not address the toxicity of MCS-B, as it utilized a clinically approved and safe dosage form and a well-established method of administration, both officially approved by the Ministry of Health of Ukraine in 2004. MCS-B, the world's first magnetite nanoparticle-based sorbent, has over 30 years of extensive experimental and clinical studies confirming its safety and efficacy.

However, it should be emphasized that the overall toxicity of nanoparticles depends on numerous physicochemical characteristics (composition, size, coating, dose, route of administration, sorption capacity, polarizing properties, etc.). Accordingly, the regulatory assessment of nanomedicines is based on function, application, and mechanism of action and includes a comprehensive assessment of safety, quality, and efficacy. In each case, MCS-B complies with national and international regulatory standards, ensuring strict control and confirmed biocompatibility.

Conclusion

- A novel method to enhance erythrocyte electrophoretic mobility in patients with toxemia has been proposed for the first time using magnetite nanoparticles (MCS-B).
- In vitro experiments demonstrated that treatment

of blood from patients with toxemia using magnetite nanoparticles resulted in an almost threefold increase ($p < 0.001$) in erythrocyte electrophoretic mobility compared to the control group.

- The optimal effective dose of magnetite nanoparticles for maximal enhancement of erythrocyte mobility was established as a 2:1 ratio (two parts blood to one part MCS-B).
- A constant magnetic field of 200-250 kA/m applied for 2-3 minutes enables highly significant ($p < 0.001$) removal of magnetite nanoparticles from blood.
- The technological innovation of this study lies in the application of controllable nanostructures with defined magnetic and surface properties to modulate the bioelectrical properties of blood cell membranes in a targeted manner.
- This approach has no direct analogues in current clinical practice and may serve as the foundation for novel therapeutic strategies in transfusion medicine, intensive care, and regenerative medicine.

References

1. Durocher JR, Payne RC, Conrad (1975) ME Role of sialic acid in erythrocyte survival Blood 45:11-20.
2. Terayama K (1993) Effects of lead on electrophoretic mobility, membrane sialic acid, deformability and survival of rat erythrocytes. Ind Health 31: 113-126.
3. Gambaro G, Baggio B, Cicerello E, S Mastrosimone, G Marzaro, et al. (1988) Abnormal erythrocyte charge in diabetes mellitus: link with microalbuminuria. Diabetes 37: 745-748.
4. Chabanel A, Flamm M, Sung KL, Lee MM, Schachter D, et al. (1983) Influence of cholesterol content on red cell membrane viscoelasticity and fluidity. Biophys J 44: 171-176.
5. Rifkind J, Nagababu E, Mohanty JG (2014) Red blood cell oxidative stress impairs oxygen delivery and induces red blood cell rigidity and cellular stiffness. Front Physiol 5: 84.
6. Sangeeta Adak, Subhankar Chowdhury, Maitree Bhattacharyya (2008) Dynamic and electrokinetic behavior of erythrocyte membrane in diabetes mellitus and diabetic cardiovascular disease. Biochim Biophys Acta 1780: 108-15.
7. Edwards CJ, Fuller J (1996) Oxidative stress in erythrocytes. Comparative Harmatology International 6: 24-31.
8. Heard DH, Seaman GVF (1960) The influence of pH and ionic strength on the electrokinetic stability of the human erythrocyte membrane. J Gen Physiol. 43: 635-654.
9. Yamaguchi T, Koga M, Fujita Y, Kimoto E (1982) Effects of pH on membrane fluidity of human erythrocytes. J Biochem 91: 1299-304.
10. Mohammad Murtaza Mehdi, Prabhakar Singh, Syed Ibrahim Rizvi (2012) Erythrocyte sialic acid content during aging in humans: correlation with markers of oxidative stress. Dis Markers 32: 179-86.
11. Semenov AV, Gomonova EL, Evgeny A Shirshin, Boris P Yakimov, Petr B Ermolinskiy, et al. (2020) Assessment of fibrinogen macromolecules interaction with red blood cell membrane by means of laser aggregometry, flow cytometry and optical tweezers combined with microfluidics. Biomolecules 10: 1448.
12. Kopczyński Z, Kuźniak J, Thielemann A, Kaczmarek J, Rybczyńska M (1998) The biochemical modification of the erythrocyte membranes from women with ovarian cancer. Br J Cancer78: 466-471.
13. Bosmann HB, Gersten DM, Griggs RC (1976) Arch Neurol 33: 135-8.
14. Rustin MH, Kovacs IB, Sowemimo-Coker SO, Maddison PJ, Kirby JD (1985) Differences in red cell behaviour between patients with Raynaud's phenomenon and systemic sclerosis and patients with Raynaud's disease. Br J Dermatol 113: 265-272.
15. Sangeeta Adak, Subhankar Chowdhury, Maitree Bhattacharyya (2008) Dynamic and electrokinetic behavior of erythrocyte membrane in diabetes mellitus and diabetic cardiovascular disease. Biochim Biophys Acta 1780: 108-115.
16. Daga Ruiza D, Fonseca San Miguelb F, Gonzlez de Molinac FJ, A Úbeda-Iglesias, A Navas Pérez, et al. (2017) Plasmapheresis and other extracorporeal filtration techniques in critical patients. Medicina Intensiva 41: 174-187.
17. Mazzanti L, Rabini RA, Salvolini E, Tesei M, Martarelli D, et al. (1997) Sialic acid, diabetes, and aging: a study on the erythrocyte membrane.

Metabolism 46: 59-61.

18. Lytvyn V, Elena M Vazhnichaya, Daniela E Manno, Yurii A Kurapov, Lucio Calcagnile, et al. (2024) Effect of pure (ligand-free) nanoparticles of magnetite in sodium chloride matrix on hematological indicators, blood gases, electrolytes and serum iron. Micro Nano Syst Lett. https://link.springer.com/article/10.1186/s40486-024-00209-x
19. Soler MA, Báo SN, Alcântara GB, Tibúrcio VH, Paludo GR, et al. (2007) Interaction of erythrocytes with magnetic nanoparticles. J Nanosci Nanotechnol 7: 1069-1071.
20. Ruiz A, Lamiaa M A Ali, PR Cáceres-Vélez, R. Cornudella, M. Gutiérrez et al. (2015) Hematotoxicity of magnetite nanoparticles coated with polyethylene glycol: in vitro and in vivo studies. Toxicol Res 4: 1555-1564.
21. Belousov AN (2004) Extracorporeal hemocorrection using a magnetically controlled sorbent in intensive care of intoxication syndrome in patients with hepatopancreatoduodenal pathology [dissertation abstract]. Dnipro: Dnipropetrovsk State Medical Academy.
22. Belousov AN (2004) Effect of magnetite nanoparticles on cellular metabolism. Visnyk of Problems of Biology and Medicine 2: 34-37.
23. Belousov AN (1998) Obolentsev NI. Experimental study of the sorption activity of a magnetically controlled hemoperfusion sorbent with respect to blood protein complexes. In: Anesthesiology and Intensive Care at the Turn of the 21st Century: Problems, Trends, Prospects. Dnipropetrovsk.
24. Belousov AN (2011) The use of magnetite nanoparticles in applied medicine. Int J Nano Dimens 2: 25-28.
25. Belousov AN (2012) Ultrastructure of hepatic cells in rabbits after injection of nanoparticles MCS-B. In: NSTI Nanotech 2012 Proceedings 3: 258-260.
26. Belousov AN, Belousova EY. Mechanisms cell regulation by nanotechnology preparations (MCSB). Presented at: BioNanotech Conference & Expo 2012; June 18–21, 2012; Santa Clara, CA, USA. Available from: http://www.techconnectworld.com/Biotech2012/sym/nano_medical_sciences.html.
27. Belousov AN, Belousova EYu, Mysyk AV (2025) A clinical case of the successful application of magnetite nanoparticles in the complex treatment of multiple sclerosis. J Nanotech Nanobiotech. Available from: https://scitechjournals.com/articles/a-clinical-case-of-successful-application-of-magnetite-nanoparticles-in-the-complex-treatment-of-multiple-sclerosis.pdf
28. Belousov A, Malygon E, Yavorskiy V, Belousova E (2020) Modernization of the preservative solution for red blood cells by magnetite nanoparticles (ICNB). In: Alexander D, Pogrebnjak A, Pogorielov M, Viter R, editors. Nanomaterials in Biomedical Application and Biosensors (NAP2019). Singapore.
29. Burlakova EV, Kols OR, Krigger YA. (1958) Practicum on General Biophysics. Moscow: "Nauka" 86-98.
30. Belousov AN, Malygon EI, Yavorskiy VV, Belousova EY (2019) Innovative method of nanotechnology to increase the storage time of RBCs due by stabilizing the molecular structure of proteins and lipids of erythrocyte membranes. Biomed J Sci & Tech Res 13: 10079-10088.
31. Belousov AN. (2011) The influence of magnetite nanoparticles (MCS-B) on the hemolysis of erythrocytes. In: NSTI-Nanotech 2011 Conference and Expo Technical Proceedings. Vol. 3. Danvers, MA: CRC Press; p. 484–9. ISBN: 978-1-4398-1783-6. Available from: https://briefs.techconnect.org/wp-content/volumes/Nanotech2011v3/pdf/155.pdf
32. Belousov AN, Malygon EI, Kalynychenko TO, Belousova EY, Yavorskiy VV, et al. (2023) Glycolysis process activation in preserved red blood cells by nanotechnological treatment of resuspending solutions. Regul Mech Biosyst 14: 10-15.
33. Torrance J, Jacobs P, Restrepo A, Eschbach J, Lenfant C, et al. (1970) Intraerythrocytic adaptation to anemia. N Engl J Med 283: 165-9.
34. Mohanty JG, Nagababu E, Rifkind JM (2014) Red blood cell oxidative stress impairs oxygen delivery and induces red blood cell aging. Front Physiol. 28: 5-84.
35. Belousov AN, Malygon EI, Kalynychenko TO, Belousova EY, Yagovdik MV (2024) Nanotechnological innovations: a modern outlook on solv-

ing challenges in erythrocyte preservation during storage. Acta Sci Biotechnol 5: 26-35.

36. Valeri CR, Fortier NL (1970) Red cell 2,3-DPG, ATP, and creatine levels in preserved red cells and in patients with red cell mass deficits or with cardiopulmonary insufficiency. In: Brewer GJ, editor. Red Cell Metabolism and Function. Advances in Experimental Medicine and Biology. Boston (MA): Springer US 289-303.

37. Oski FA, Travis SF, Miller LD (1971) (Delivoria-Papadopoulos M, Cannon E. The in vitro restoration of red cell 2,3-diphosphoglycerate levels in banked blood. Blood 37: 52-8.