

Effects of Magnetite Nanoparticles on Erythrocyte Mobility: A Novel Nanotechnology-Based Approach in Intensive Care and Transfusion Medicine

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Received Date: March 17, 2026; **Accepted Date:** March 24, 2026; **Published Date:** March 31, 2026

Citation: Belousov AN, Belousova EYu, (2026), Effects of Magnetite Nanoparticles on Erythrocyte Mobility: A Novel Nanotechnology-Based Approach in Intensive Care and Transfusion Medicine, *J. Biomedical Research and Clinical Reviews*, 12(2); DOI:10.31579/ 2692-9406 /248.

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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.

Key words: erythrocyte electrophoretic mobility; magnetite nanoparticles (MCS-B); nanomedicine; toxemia; regenerative medicine

Introduction

The electrophoretic mobility of erythrocytes (EPM) is a significant biophysical parameter reflecting the state of cellular membranes and their surface charge. This indicator provides important information about the functional condition of erythrocytes across a wide spectrum of physiological and pathological states. As a parameter associated with the surface charge of cell membranes, EPM is highly sensitive to alterations in membrane composition and structural integrity. Modifications in EPM have been documented 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 (EPM) represents a promising supplementary approach both in clinical diagnostics and biomedical research. For example, the assessment of EPM may facilitate the early detection of membrane disturbances in systemic pathologies, as well as the monitoring of therapeutic efficacy and the prediction of disease progression.

These capabilities are directly linked to the biophysical and biochemical properties of the erythrocyte membrane, as well as to internal and external environmental factors that determine their electrophoretic mobility:

1. 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 (e.g., 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].

2. 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, leading to a reduction in their negative charge and, consequently, a decrease in EPM [8,9].

3. Physiological and pathological conditions.

- Erythrocyte aging. The aging of erythrocytes is accompanied by a decrease in sialic acid content and reduced electrophoretic mobility [10].
- Inflammation. Acute-phase proteins (e.g., fibrinogen, CRP) adsorb onto the membrane, altering its surface charge [11].
- Anemia, oncological, and autoimmune diseases. These conditions may reduce EPM through structural and biochemical alterations of the membrane [12-14].

4. External factors.

- Pharmacological agents. Certain drugs affect membrane stability and charge [15,16].
- Colloid solutions and procedures (e.g., plasmapheresis) may temporarily alter plasma viscosity and conductivity [16].

5. Aging and age-related changes.

With advancing age, erythrocyte membrane composition and structure are disrupted, including a reduction in sialic acid content, leading to a decreased negative surface charge and diminished EPM [17]. This parameter may be used to assess biological age and predict age-associated pathologies.

Key factors influencing erythrocyte electrophoretic mobility are illustrated in Figure 1.

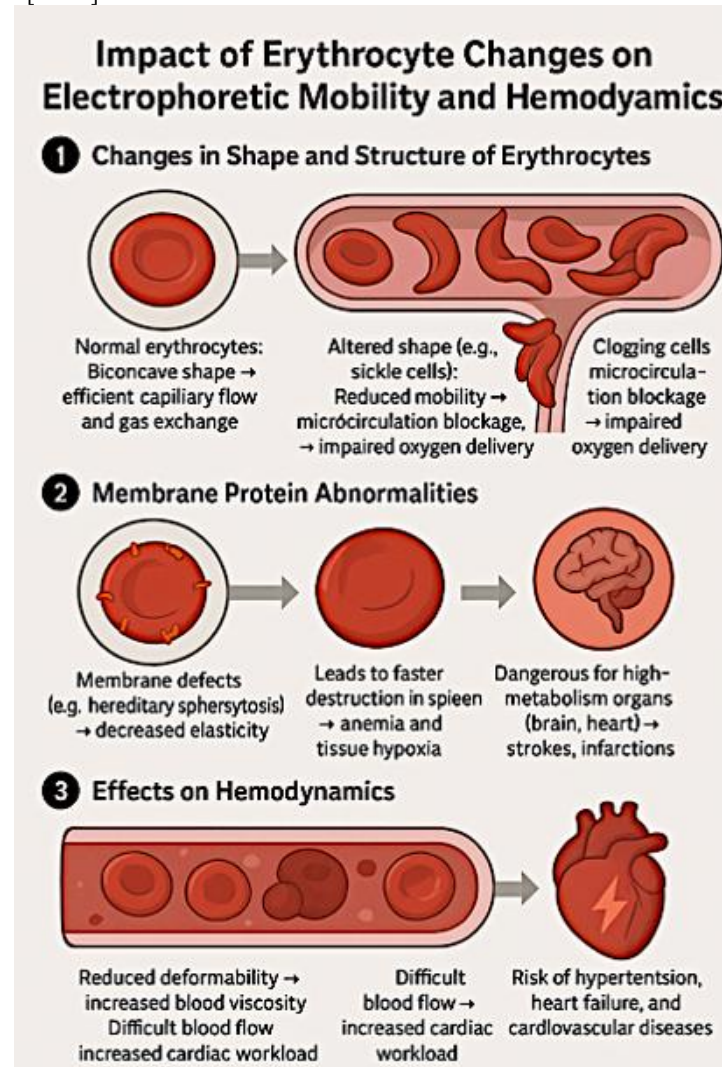


Figure 1: The main factors determining the electrophoretic mobility of erythrocytes.

As shown in Figure 1, alterations in erythrocyte electrophoretic mobility may have significant pathophysiological consequences and be associated with the development of clinically relevant disorders. Electrophoretic mobility of erythrocytes (EPM) is an important indicator reflecting the functional state of the cell membrane and significantly influences microcirculation and tissue gas exchange. Several key factors affect this parameter:

1. Cell Shape and Membrane Integrity.

Under physiological conditions, erythrocytes exhibit a biconcave disc shape that optimizes their hydrodynamic properties, flexibility, and gas exchange efficiency. Alterations in erythrocyte morphology (e.g., in sickle cell anemia) reduce mobility, impairing passage through narrow capillaries. This leads to microvascular occlusion and disrupted oxygen delivery to tissues.

2. Defects in Membrane Proteins.

Mutations or aberrant expression of membrane proteins (as seen in hereditary spherocytosis) compromise erythrocyte elasticity and deformability,

accelerate splenic sequestration, and shorten red blood cell lifespan. These structural abnormalities decrease EPM and contribute to hemolytic anemia and chronic tissue hypoxia.

Impaired electrophoretic mobility of erythrocytes negatively affects systemic hemodynamics by slowing blood flow, increasing blood viscosity, and elevating the risk of thrombosis and venous stasis. Microcirculatory disturbances are particularly detrimental to organs with high metabolic demands (e.g., the brain and heart), potentially resulting in ischemic injuries such as myocardial infarction, stroke, or other acute events.

Thus, reduced erythrocyte electrophoretic mobility serves not only as a laboratory marker but also as a pathophysiologically significant factor contributing to microcirculatory dysfunction, diminished tissue oxygenation, and the development of hypoxic states of varying severity.

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 Letters* 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. 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).

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 1: Distribution of donors by age and sex.

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%

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

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

The magnetically controlled sorbent (MCS-B brand) consists of stabilized magnetite (Fe₃O₄) 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 2 and 3:

- Total surface area of the magnetite nanoparticles: Sa = 800–1000 m²/g
- Saturation magnetization: Is = 2.15 kA/m
- Volume concentration: q = 0.00448

- Viscosity: $\eta = 1.0112$ cSt
- Zeta potential: $\zeta = -19$ mV

The small size of the magnetite nanoparticles provides a relatively large specific sorption surface area (Sa = 800-1200 m²/g). Physicochemical characteristics such as volume concentration (q = 0.00448) and viscosity ($\eta = 1.0112$ 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].

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 3: The calculated lattice parameters of the phases.

Compound	Weight%	StdErr	El	Weight%/ O ₂	StdErr	El	Weight%	StdErr
Fe ₃ O ₄	97.37	0.09	Fe	68.40	0.07	Fe	97.62	0.09
CaO	2.26	0.07	Ca	1.71	0.05	Ca	2.3	0.07
P ₂ O ₅	0.280	0.027	Px	0.122	0.012	Px	0.157	0.015
MnO	0.255	0.013	Mn	0.198	0.010	Mn	0.278	0.014
SiO ₂	0.098	0.027	Si	0.046	0.013	Si	0.059	0.016
SO ₃	0.032	0.013	Sx	0.0126	0.0051	Sx	0.0164	0.0066
Cl	0.0280	0.0090	Cl	0.0280	0.0090	Cl	0.0380	0.012

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

Phase	Formula	Space group	№ Card Database ICDD
magnetite low	Fe _{2.886} O ₄	227: Fd-3m, choice-2	10861339 (ICDD)
magnetite low, syn	Fe ₃ O ₄	166: R-3m, hexagonal	10716766 (ICDD)
Johannsenite	Ca Mn +2 Si ₂ O ₆	15: C12/c1, unique-b, cell-1	380413 (ICDD)

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

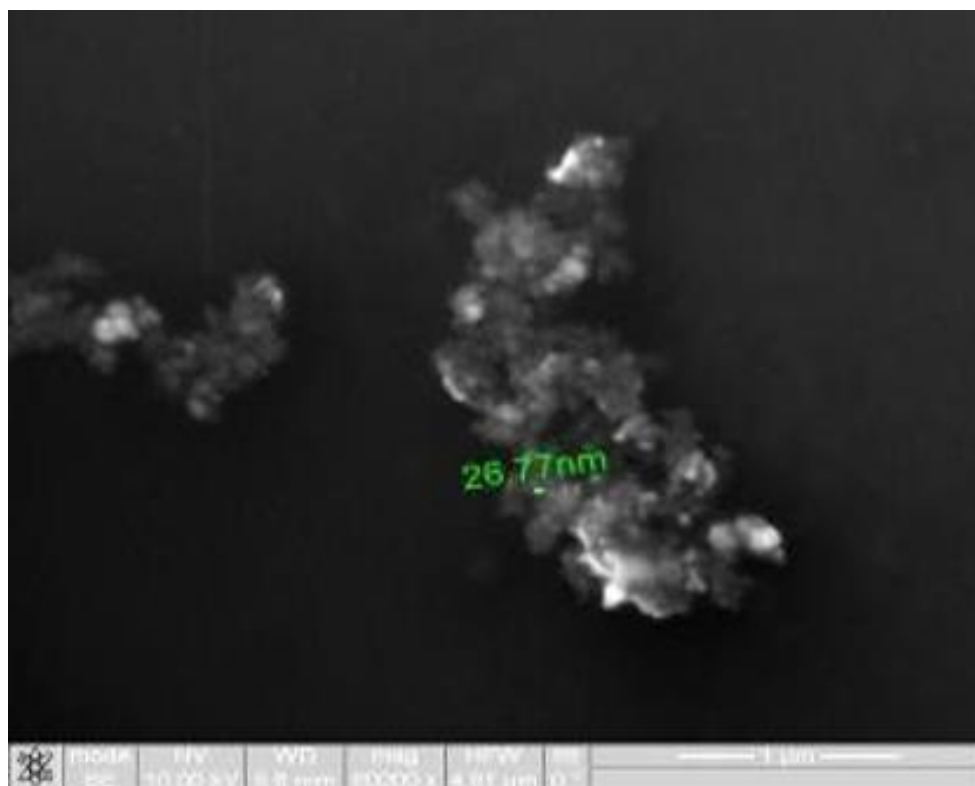


Figure 2: Study of magnetite nanoparticles with use microscope ion-electronic raster-type Quanta 200 3D.

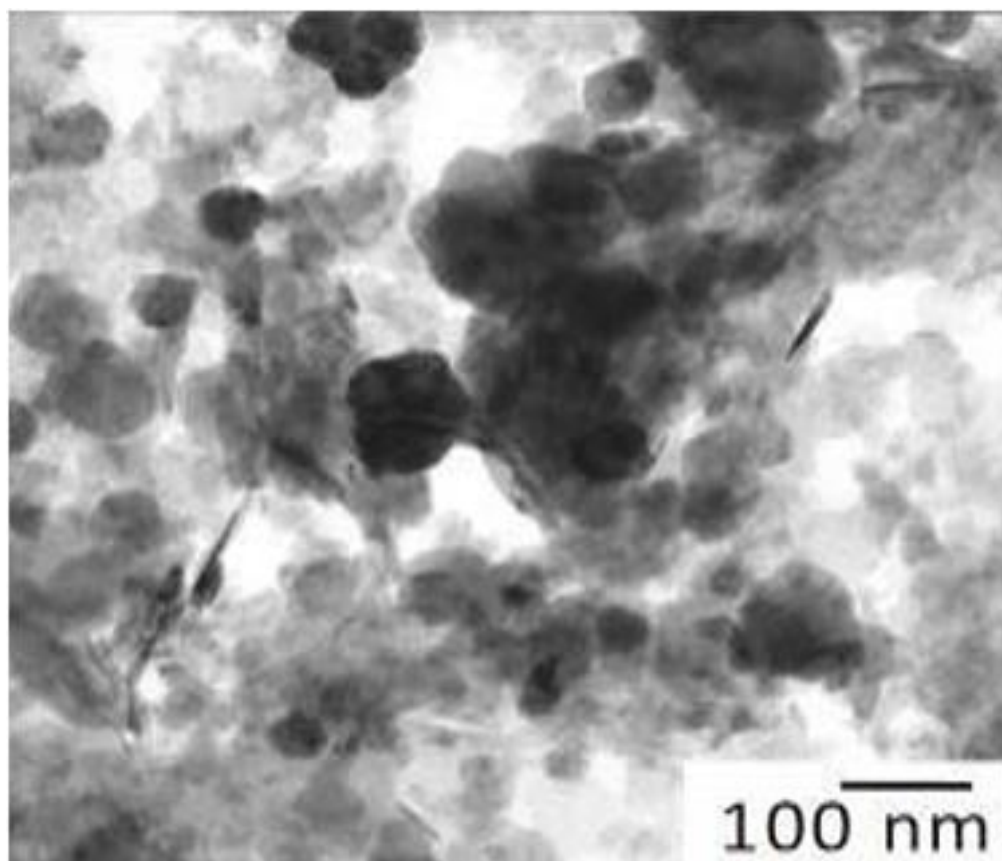


Figure 3: Study of magnetite nanoparticles with use microscope electronic translucent JEM-2100.

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

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

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

Substance	Biological liquid		
	H ₂ O	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 T ₃		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
NaNO ₃ (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

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

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 4.

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 CuSO₄. 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.

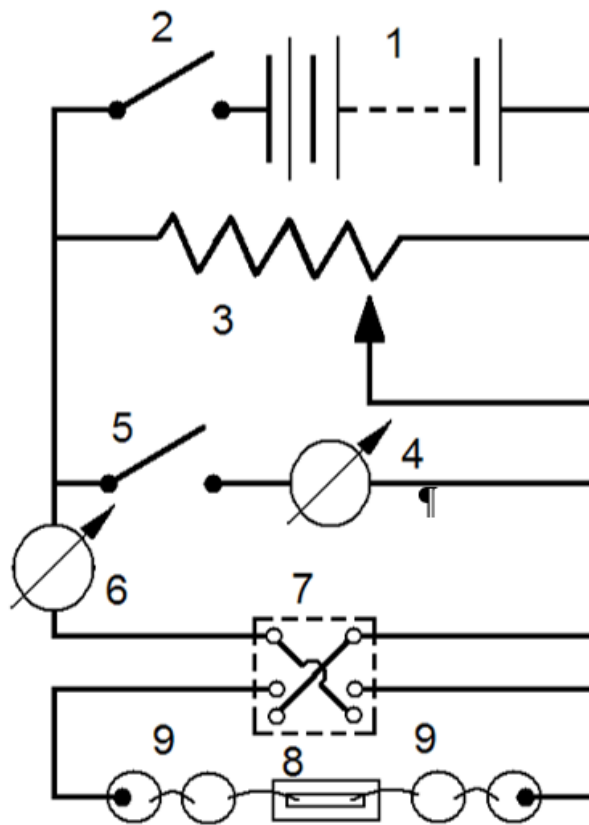


Figure 4: Electrical circuit diagram of the electrophoresis system.

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.

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

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

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

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:

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

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, $10^{-4}\text{cm}^2/\text{secV}$	$3.5 \times 10^{-4} \pm 0.2$	$1.26 \times 10^{-4} \pm 0.2$ $P < 0.01$	$2.70 \times 10^{-4} \pm 0.2$ $P < 0.05$ $P_1 < 0.01$	$3.76 \times 10^{-4} \pm 0.2$ $P > 0.05$ $P_1 < 0.001$ $P_2 < 0.05$	$3.8 \times 10^{-4} \pm 0.2$ $P > 0.05$ $P_1 < 0.001$ $P_2 < 0.05$ $P_3 > 0.05$

Table 8: Electrophoretic mobility of blood erythrocytes before and after treatment with magnetite nanoparticles (M□m).

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 $\pm$ 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 $3.5 \times 10^{-4} \pm 0.2 \text{ cm}^2/\text{V} \cdot \text{sec}$, whereas in patients with toxemia syndrome (main group), the baseline value was $1.26 \times 10^{-4} \pm 0.2 \text{ cm}^2/\text{V} \cdot \text{sec}$. As a result of blood

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.

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 ratio ($p > 0.05$). 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 $\pm$ 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 5.

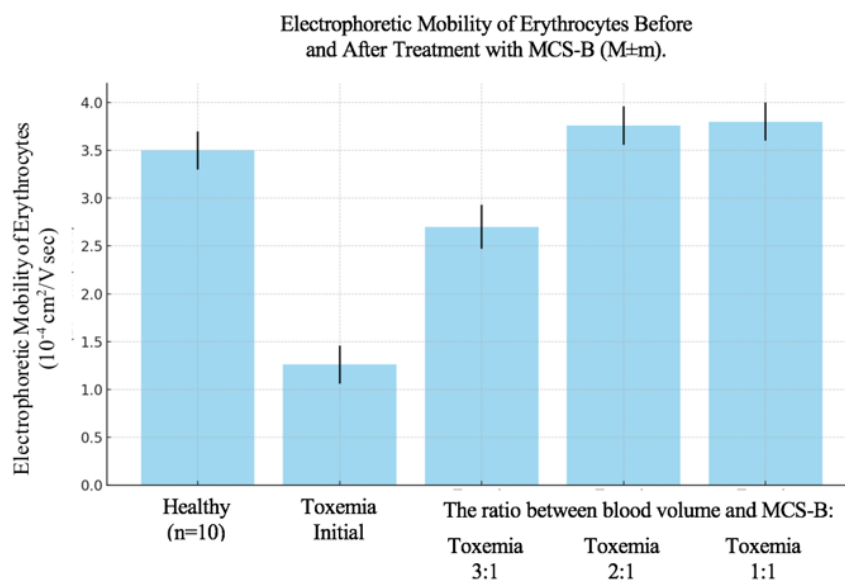


Figure 5: Electrophoretic mobility of erythrocytes at various stages of the experiment (mean $\pm$ standard error).

To visually illustrate the treatment effect, Figure 6 depicts the morphofunctional state of erythrocytes in heparinized blood from a patient with toxemia syndrome, before and after *in vitro* exposure to MCS-B at a blood-to-sorbent ratio of 2:1.

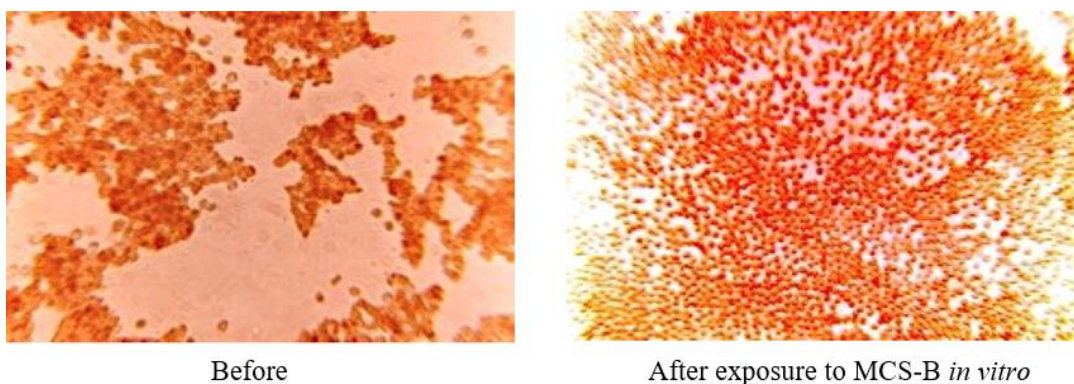


Figure 6: Morphological changes in erythrocytes in heparinized blood from a patient with toxemia syndrome before and after *in vitro* treatment with MCS-B at a 2:1 blood-to-MCS ratio.

Figure 6 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.

Protective mechanisms of MCS-B on erythrocyte membranes under toxemia conditions are attributed to the following factors:

1. 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].

2. Reactivation of glycolytic enzymes.

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

3. 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.

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

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

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.

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

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

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.

Conclusions

1. A novel method to enhance erythrocyte electrophoretic mobility in patients with toxemia has been proposed for the first time using magnetite nanoparticles (MCS-B).
2. 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.
3. 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).

4. 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.
5. 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.
6. 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.

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DOI:[10.31579/2692-9406/248](https://doi.org/10.31579/2692-9406/248)

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