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Research Article

Magnetically Controlled Nanoplatform for Restoring Hemorheological Function in Systemic Toxemia and Hypoxia

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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.

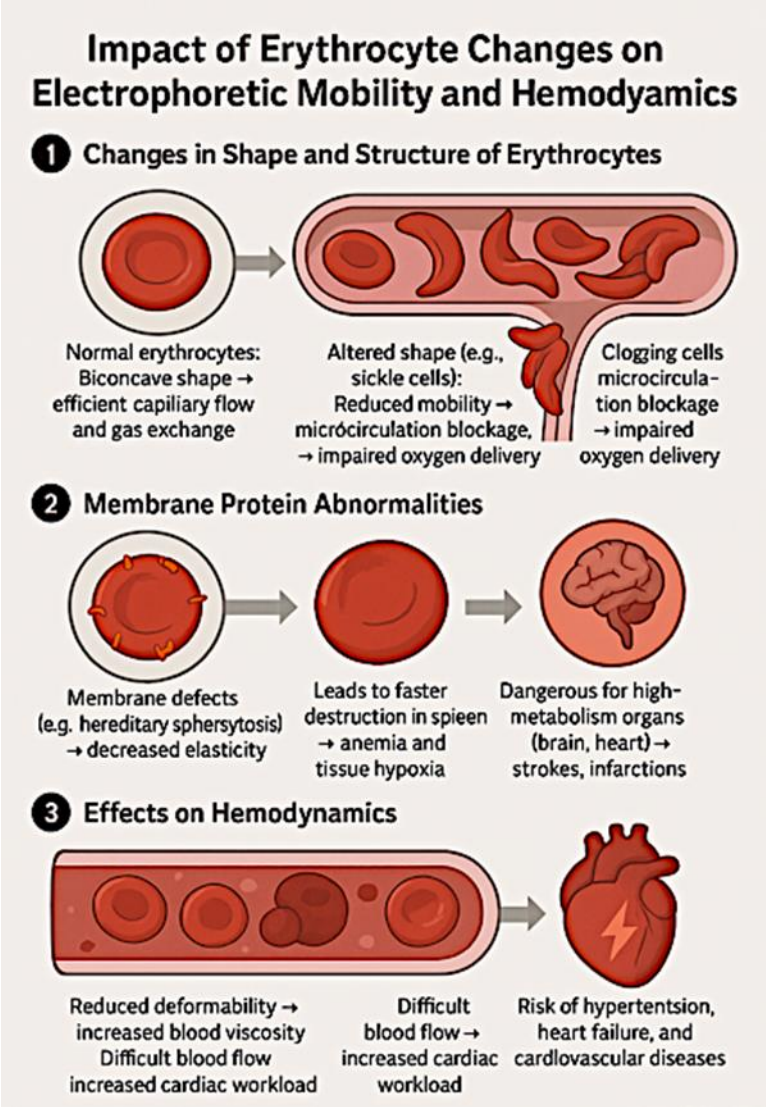


Figure 1: The main factors determining the electrophoretic mobility of erythrocytes**.**

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 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%

Table 1: Distribution of donors by age and sex

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 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: 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 m²/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].

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%	Std Err
Fe_3O_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_2O_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	Fe2.886 O4	227: Fd-3m, choice-2	10861339 (ICDD)
magnetite low, syn	Fe_3O_4	166: R-3m, hexagonal	10716766 (ICDD)
Johannsenite	Ca Mn +2 Si_2O_6	15: C12/c1, unique-b, cell-1	380413 (ICDD)

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

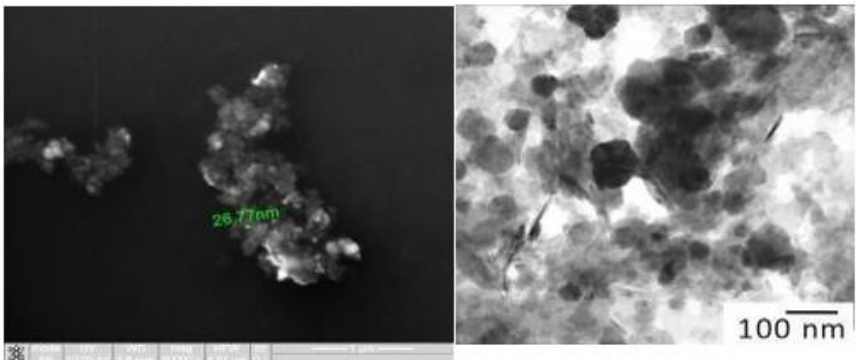


Figure 2: Study of magnetite nanoparticles with use microscope ion-electronic raster-type Quanta 200 3 D

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_2O	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

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

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

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 $CuSO_4$. 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.

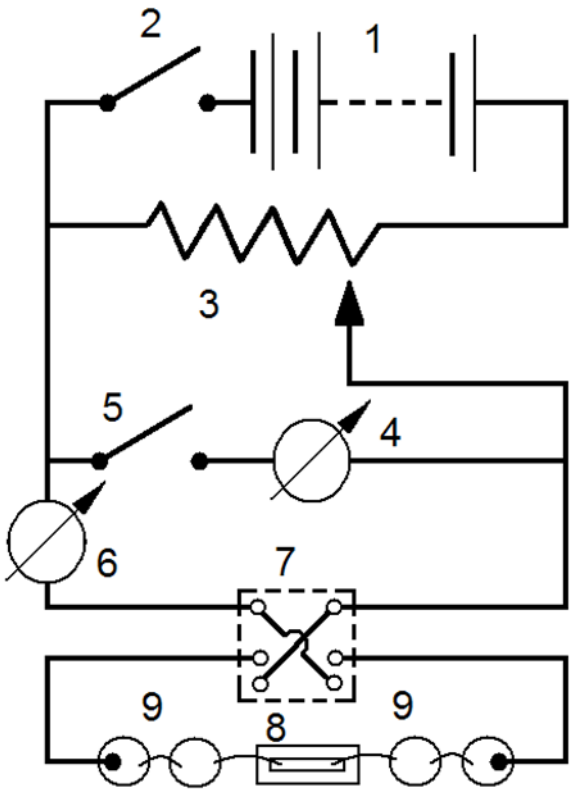


Figure 4: Electrical circuit diagram of the electrophoresis system.

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.

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 secon 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 rati

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, $10^{-4}cm^2/secV$	$3.5x10^{-4}\pm 0.2$	$1.26x10^{-4}\pm 0.2$ $P<0.01$	$2.70x10^{-4}\pm 0.2$ $P<0.05$ $P_1<0.01$	$3.76x10^{-4}\pm 0.2$ $P>0.05$ $P_1<0.001$ $P_2<0.05$	$3.8x10^{-4}\pm 0.2$ $P>0.05$ $P_1<0.001$ $P_2<0.05$ $P_3>0.05$

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 ± 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 3.5×10^{-4} ± 0.2 $cm^2/V\cdot sec$, whereas in patients with toxemia syndrome (main group), the baseline value was 1.26×10^{-4} ± 0.2 $cm^2/V\cdot sec$.

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 ratio ($p > 0.05$).

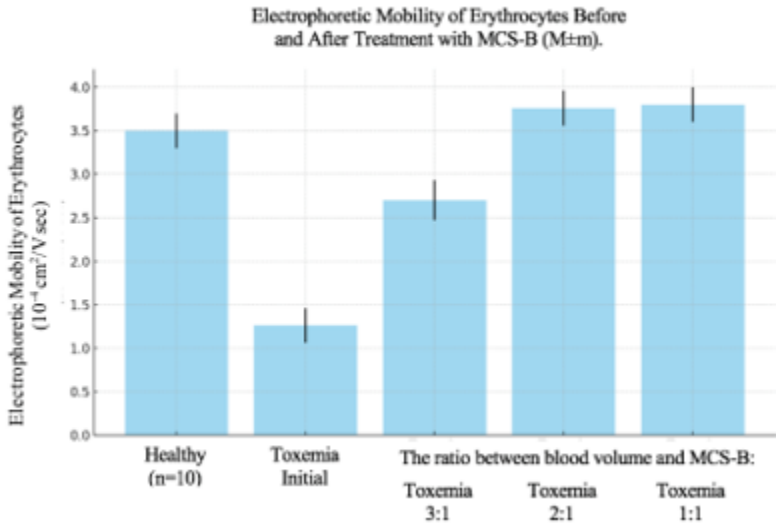
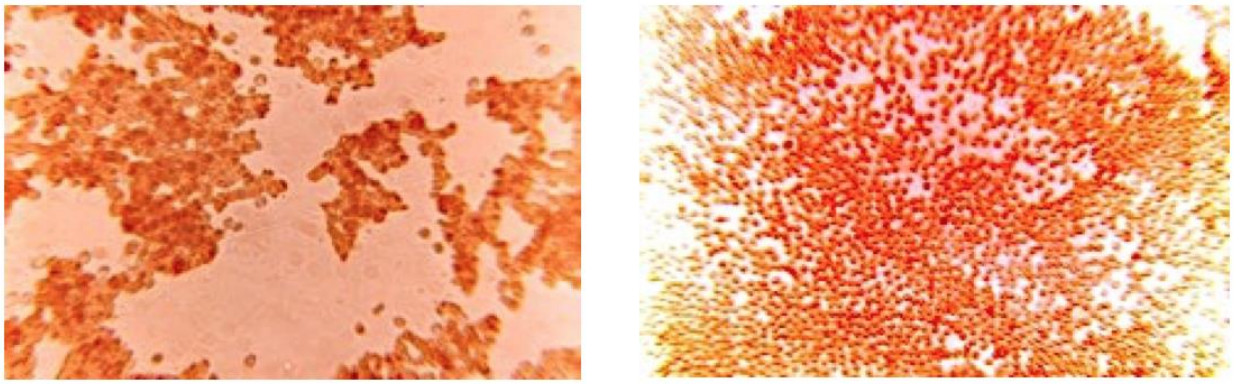


Figure 5: Electrophoretic mobility of erythrocytes at various stages of the experiment (mean ± standard error).

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 5.

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.



Before After exposure to MCS-B *in vitro*

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 in the Context of Toxemia

1. Sorption-Mediated Detoxification

Magnetite nanoparticles (MCS-B) possess a high specific surface area (up to 1200 m^2/g) and demonstrate affinity for endogenous toxic metabolites in blood plasma, including oxidized lipids, free heme, peroxides, phenolic compounds, and misfolded proteins. Upon contact with erythrocyte surfaces, nanoparticles effectively adsorb these molecules, mitigating local oxidative stress and interrupting hemolytic cascades. These effects were confirmed in clinical models of intoxication and systemic inflammation [21,22,30].

2. Membrane-Stabilizing Properties

MCS-B nanoparticles interact with defects in the lipid bilayer, acting as "molecular patches." This restores membrane microviscosity and reduces permeability abnormalities commonly observed under oxidative or inflammatory stress. Additionally, improved transmembrane ion exchange, notably of Ca^{2+} and Na^{+}/K^{+}, promotes cytoskeletal integrity [31]. Ultrastructural analysis supports these findings [25].

3. Modulation of ζ-Potential and Electrophoretic Mobility

Magnetite nanoparticles exhibit a native ζ-potential are –19 mV. Interaction with erythrocyte membranes leads to increased net negative surface charge and enhanced electrostatic repulsion between cells, thereby restoring normal electrophoretic mobility.

4. Antioxidant Activity

Properly stabilized Fe_3O_4 nanoparticles do not provoke Fenton chemistry but instead demonstrate net antioxidant behavior. They catalyze the decomposition of H_2O_2 to water and oxygen, reducing plasma peroxide load and preventing oxidative damage to membrane lipids and proteins. This preserves erythrocyte deformability and mechanical stability [32,33].

The main mechanisms and functional outcomes are presented in Table 9.

Mechanistic Level	Biochemical Effect	Functional Consequence
Sorption	Removal of peroxides, free heme, and LPO	Reduction in erythrocyte aggregation
Membrane stabilization	Recovery of lipid architecture and ion transport	Restoration of cell shape and integrity
ζ-potential modulation	Increase in surface electronegativity	Enhanced electrophoretic mobility
Antioxidant action	Catalysis of peroxide decomposition	Decreased hemolysis and membrane rigidity

Table 9: Summary of Mechanisms and Functional Outcomes

5. Activation of Glycolysis and Energetic Restoration

Erythrocytes rely entirely on anaerobic glycolysis. MCS-B exposure enhances GLUT1-mediated glucose uptake, normalizes intracellular pH and ion gradients, and protects glycolytic enzymes from oxidative inactivation. This leads to improved activity of hexokinase, phosphofructokinase, and pyruvate kinase, along with increased ATP and 2,3-DPG production. These changes support Na^{+}/K^{+}-ATPase activity and shift the oxyhemoglobin dissociation curve to improve tissue oxygenation under hypoxic conditions [31] (Table. 10).

Parameter	Pre-Treatment Status	Post-Treatment with Fe_3O_4 Nanoparticles (MCS-B)
Intracellular ATP	Decreased	Increased
2,3-DPG	Insufficient	Elevated → improved tissue oxygenation
Intracellular pH	Shifted toward acidosis	Normalized
Electrophoretic mobility	Reduced	Restored

Table 10: Functional Summary: Contribution of Glycolytic Activation to Erythrocyte Recovery.

Among the underestimated yet critical effects of biocompatible magnetite nanoparticles on erythrocytes is the stimulation of glycolytic metabolism [33]. This activation leads to an increase in intracellular ATP and 2,3-DPG levels, facilitating the restoration of ion homeostasis, the improvement of erythrocyte morphology, and the enhancement of tissue perfusion via improved oxygen release. Collectively, these mechanisms contribute to the overall normalization of erythrocyte function under oxidative and metabolic stress conditions.

Biochemical mechanisms of erythrocyte energy metabolism stimulation by magnetite nanoparticles during toxemia.

Physiological Background: Glycolysis in Erythrocytes.

Erythrocytes lack mitochondria and derive all of their energy from anaerobic glycolysis. Key points:

•ATP is generated at:

•1,3-bisphosphoglycerate (1,3-BPG) → 3-phosphoglycerate (via phosphoglycerate kinase)

•Phosphoenolpyruvate → pyruvate (via pyruvate kinase)

•2,3-diphosphoglycerate (2,3-DPG) is produced via the Rapoport–Luebering shunt from 1,3-bisphosphoglycerate.

ATP and 2,3-DPG are inversely related under normal conditions - more 2,3-DPG means less ATP and vice versa, since they compete for the same glycolytic intermediate (1,3-BPG).

What Happens During Toxemia.

In toxemia (severe intoxication), the following are typically observed:

•Membrane damage due to oxidative stress and toxic metabolites

•Disruption of ionic gradients and membrane integrity

•Inhibition of key glycolytic enzymes (e.g., aldolase, hexokinase, pyruvate kinase)

•Simultaneous depletion of ATP and 2,3-DPG → This reflects global suppression of glycolysis, not just the balance between ATP and 2,3-DPG

The results of this study highlight several key mechanisms by which MCS-B nanoparticles exert their protective effects on erythrocytes under conditions of toxemia. First, magnetite nanoparticles demonstrate high affinity for circulating toxic compounds, including reactive oxygen species and lipid peroxidation products, thereby reducing systemic oxidative stress. Second, through selective adsorption of surface proteins [26], MCS-B contributes to the structural repair of damaged erythrocyte membranes, restoring their integrity and functional capacity. An important downstream effect of these processes is the reactivation of glycolytic metabolism in erythrocytes - cells that rely exclusively on anaerobic glycolysis for energy production due to the absence of mitochondria. This metabolic restoration results in a simultaneous increase in intracellular ATP and 2,3-diphosphoglycerate (2,3-DPG) levels [34,35]. While these metabolites are typically inversely correlated in healthy cells, their concurrent elevation under pathological conditions reflects a broader recovery of metabolic potential rather than a disruption of physiological balance.

Furthermore, normalization of the erythrocyte energy state leads to modulation of the bioelectrical properties of the cell membrane. This is manifested as restoration of surface charge and electrophoretic mobility, which is critical for reducing erythrocyte aggregation, improving

microcirculatory flow, and potentially mitigating downstream complications of toxemia [36,37].

These findings support the multifaceted role of MCS-B nanoparticles as not only detoxifying agents but also modulators of erythrocyte structure and function. Further studies are warranted to explore their clinical potential in critical care settings involving systemic intoxication and oxidative stress.

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 11.

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.

Table 11: Plasma Fe levels in practically healthy individuals *in vitro* at different stages of the study (n = 10; M ± m)

As shown in Table 11, 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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