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CHANGES IN SPONTANEOUS CONTRACTILE ACTIVITY OF SMOOTH MUSCLES IN THE GASTROINTESTINAL TRACT OF RATS UNDER LONG-TERM INTAKE OF A MIXTURE OF POLYPROPYLENE NANOPARTICLES AND MICROPARTICLES

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Background. Plastic is the most common pollutant in the environment. In natural conditions, plastic undergoes mechanical and photochemical degradation, forming micro- and nanoparticles that are accumulated by living organisms. Regular intake of plastic micro- and nanoparticles (MNP) in the gastrointestinal tract (GIT) leads to the development of inflammatory processes in the alimentary canal walls and disrupts intestinal microbiota. However, the contractile activity of smooth muscles in the GIT under these conditions is yet to be studied.

The aim of the study was to investigate the spontaneous contractile activity of circular smooth muscles of the *antrum* and *caecum* of rats under long-term peroral intake of MNP of one of the most common plastic pollutants for the environment, polypropylene (PP).

Materials and Methods. The suspension of polypropylene particles was prepared using disposable dishes by Roursgaard's method with slight modifications. The determination of the average hydrodynamic diameter of PP particles in the aqueous suspension involved the method of dynamic light scattering. The animals in the experimental group received the PP suspension in their drinking water (at a daily dose of 2.5 mg/kg) for 6 weeks. The tenzometric experiments were conducted in the isometric mode of

registration, using isolated circular smooth muscle preparations from the *antrum* and *caecum* of rats. The spontaneous contractions were analyzed by mechanokinetic analysis with the estimation of force, time, velocity, and impulse parameters.

Results. The polypropylene suspension contained particles of up to 4 μm, 34.1 % of which were < 1 μm. Long-term peroral intake of PP into the organism was accompanied by the impairment of the spontaneous contractile activity of smooth muscles in the *antrum* and *caecum*: a decrease in the frequency and modulation of mechanokinetic parameters of some contractions. In case of the *antrum* muscles, there was an increase in force and velocity parameters, time parameters were below the control ones, while the impulse parameters remained unchanged. Under the effect of PP, the mechanokinetic parameters of contractions in the *caecum* demonstrated the following changes: there was a considerable increase in force parameters for the amplitude and phase of contraction, as well as all the time and impulse parameters, whereas velocity parameters were considerably decreased.

Conclusions. Prolonged intake of polypropylene MNP into the organism causes changes in the frequency of spontaneous smooth muscles contractions, likely due to impaired functioning of pacemaker cells; whereas changes in amplitude parameters are likely due to MNP's action on smooth muscle cells.

Keywords: mixture of nano- and microplastics, polypropylene, smooth muscles, *antrum*, *caecum*, spontaneous contractions, mechanokinetic parameters

INTRODUCTION

Due to their unique physical properties, plastics are universal materials in modern industry, so, despite environmental pollution and hazards for human health, their production is increasing every year, reaching over 350 million tons per year (Wieland *et al.*, 2022; Donisi *et al.*, 2024; Zurub *et al.*, 2024). Since plastics are quite durable, often have a very short lifespan, and are not adequately recycled, they end up in the environment in huge quantities, currently being the main pollutant of ecosystems. In particular, about 8 million tons of plastic rubbish enter the global ocean every year (Bora *et al.*, 2024).

In conditions of the environment, plastics undergo mechanical and photochemical degradation, forming micro- and nanoparticles. It should be noted that in the global production volume of plastics, there is clear prevalence of thermoplastic materials (polyethylene, polypropylene, polyvinyl chloride, polystyrene, polycarbonate, polyethylene terephthalate, etc.), which, in addition to the polymer base itself, also contain additives (chlorine, phthalates, bisphenols, brominated flame retardants, etc.), the release of which during the degradation of plastics poses an additional threat (Wieland *et al.*, 2022; Donisi *et al.*, 2024). The most common environmental pollutants, particularly in soils and water bodies, are thermoplastics such as polyethylene (PE), polystyrene (PS), and polypropylene (PP) (Sadri & Thompson, 2014; Zurub *et al.*, 2024).

At present, the terminology, used to classify plastic particles of different sizes, is as follows: microplastic (MP) – particles of > 1 μm and < 5 mm; nanoplastic (NP) – particles of 1 nm – 1 μm (as per another, less common classification, 1–100 nm); in case of a mixture of micro- and nanoplastic, the term micro-nano-plastics (MNP) is used (Zhu *et al.*, 2023; Pradel *et al.*, 2023; Dube & Okuthe, 2023; Zurub *et al.*, 2024). In terms of forms, MNPs are classified into fragments, fibers, granules, spheres, films, foams, leaves, etc. (Kiran *et al.*, 2022). Depending on their origin, plastic particles are classified into primary

(intentionally produced) and secondary (formed during the degradation of larger plastic fragments under light, mechanical, or microbial effects) (da Silva Brito *et al.*, 2022).

Every year, over 50 thousand (according to other data, over 200 thousand) particles of plastic penetrate a human organism (Yang *et al.*, 2023; Bora *et al.*, 2024; Chi *et al.*, 2025). Mostly, the intake occurs via the gastrointestinal tract ($4.88 \cdot 10^5 – 5.77 \cdot 10^5$, and according to other data – over 140 thousand MP particles) and the respiratory system ($0.21 \cdot 10^5 – 2.51 \cdot 10^5$ MP particles) (Yang *et al.*, 2023). The first route predominates, since considerable amounts of this pollutant are present in drinking water, food products, and medical and personal hygiene products (pharmaceutical containers, toothpaste, exfoliants, etc.) (Gopinath *et al.*, 2022; Yang *et al.*, 2023; Donisi *et al.*, 2024; Bora *et al.*, 2024). In the recent decade, nanoplastics have been viewed as promising nanocarriers for targeted delivery of medical preparations, including those for antitumor therapy (Sun *et al.*, 2018; Yu *et al.*, 2021).

A great amount of data has already been accumulated about the penetration of MNP inside the organism and the toxic effects caused by these particles. When MNP particles enter the GIT, a protein crown composed of predominantly low-molecular-weight proteins forms around them, facilitating their diffusion through the mucin layer (Paul *et al.*, 2020). NP may be capable of being absorbed by gastric endothelial cells; at least, a simulation using human gastric adenocarcinoma cells demonstrated that particles of 100 nm can be endocytosed and activate the expression of genes encoding proinflammatory cytokines (Forte *et al.*, 2017). MNP particles are mostly translocated via the intestinal wall. Plastic fragments of < 2.5 mm are endocytosized in small intestine by microfold cells of Peyer's patches and then distributed in tissues (including bone marrow, liver, kidneys, and spleen); larger particles (5–10 μm) are absorbed by specialized cells, for instance, macrophages, and were identified in internal organs (for instance, in liver) (Jani *et al.*, 1990; Simon *et al.*, 1997; Paul *et al.*, 2020). The *in vivo* study using mice demonstrated high absorption of large MP (5 and 20 μm) following peroral application at doses of 0.01, 0.1, and 0.5 a day; permanent concentrations were observed 14 days after the beginning of the experiment (Deng *et al.*, 2017). At present, researchers believe that generally the bioavailability of MNP particles is under 10% (Jin *et al.*, 2019).

A relevant specificity of regular and long-term intake of MNP in the GIT is the induction of inflammatory processes due to intestinal microbiota disruption, impaired intestinal barrier ("leaking" gut), pathological changes in the metabolism of bile acids and other metabolic processes (Jin *et al.*, 2019; Fackelmann & Sommer, 2019; Paul *et al.*, 2020; da Silva Brito *et al.*, 2022; Chi *et al.*, 2025). In the case of a systematic MNP input, pathological changes are induced in intestinal walls, leading to a decrease in the efficiency of the intestinal barrier and thus higher permeability of digestive tract walls for MNP (Bora *et al.*, 2024; Bao *et al.*, 2025). Also, as demonstrated under the *in vivo* effect, MNP particles penetrate tissues and organs, causing the disruption of the reproductive function in both male and female animals (Jeon *et al.*, 2024; Zhao *et al.*, 2025), remodeling of vascular walls and apoptosis of smooth muscle cells in them, mediated by the damage of mitochondria (Zhang *et al.*, 2024; Xie *et al.*, 2024; Persiani *et al.*, 2025). In addition, MNP particles are capable of direct penetration to brain structures via the hematoencephalitic barrier and can exert an indirect effect on peripheral links (Shan *et al.*, 2022; Kopatz *et al.*, 2023; Wu *et al.*, 2025).

Although the effects and mechanisms of MNP-induced inflammation in the intestinal wall and the impairment of the microbiome are well studied, there are no data on the

contractile activity of smooth muscles in the GIT under these pathological conditions. Therefore, the aim of the study was to investigate the spontaneous contractile activity of circular smooth muscles of the *antrum* and *caecum* of rats under long-term peroral intake of MNP of one of the most common plastic pollutants for the environment, polypropylene.

MATERIALS AND METHODS

Preparation of polypropylene particles and their characterization. The suspension of polypropylene particles was prepared using disposable dishes (composition – polypropylene, 100 %) by Roursgaard's method with slight modifications (Roursgaard *et al.*, 2022). At first, plastic dishes were mechanically cut with medical scissors into fragments of up to 5 mm. Then, plastic fragments were added to distilled water, cooled to 4 °C, in a 1:1 ratio, and their mechanical homogenization was performed using a laboratory homogenizer IKA A11 (IKA-Werke GmbH & Co. KG, Germany) for 30 min. After processing with the homogenizer, the plastic fragments were filtered through a sieve with pores of 50 μm, and the weight of microparticles in the suspension was determined. To prevent aggregation, the polypropylene particle suspension was sonicated for at least 10 min before use; as shown by dynamic light scattering, this is sufficient to ensure that the hydrodynamic particle diameter distribution is stable for at least 3 days.

To determine the average hydrodynamic diameter of polypropylene particles in the aqueous suspension, the method of dynamic light scattering with the laser correlation spectrometer "ZetaSizer–3" (Malvern Instruments, Great Britain), equipped with He-Ne laser LGN-111 (P = 25 mW, λ = 633 nm; the measuring range of the device is from 1 nm to 20 μm) was used. The registration and statistical processing of the laser irradiation, dissipated from aqueous (n = 1.33) suspension of the particles, were conducted five times in the course of 60 s at the temperature of +22 °C under the dissipation angle of 90°. The obtained results of the measurements were processed using PCS-Size servicing software, version 1.61.

Protocol for working with animals. The studies were conducted using Wistar rats, which were kept on a standard diet and under standard conditions: temperature of 20 ± 2 °C, relative air humidity of 50–70 %, and a light:darkness ratio of 12:12 h. All the manipulations with the animals were conducted according to the International Convention for the Protection of Animals and the Law of Ukraine "On Protection of Animals from Cruelty" (the Minutes of the Bioethics Commission of Taras Shevchenko National University of Kyiv No.8 dated December 26, 2024). The animals were euthanized by hypoxia, induced by carbon dioxide (CO_2).

The experimental protocols (Jin *et al.*, 2019; Li *et al.*, 2020) were accepted as the basis for the study design. The study used 16 female rats (aged 8 weeks), which were randomly divided into two groups: control (6 animals) and experimental (10 animals). The animals were weighed three times a week to control the dose of microplastics. All the animals had free access to food and water; the animals in the experimental group received the PP suspension in their drinking water (at a dose of 2.5 mg/kg, every day) for 6 weeks. The dose was defined using the estimate of daily water use by adult rats in the amount of 12.0 mL per 100 g of weight (in "Techniques in the Behavioral and Neural Sciences", 1994), which corresponded to the average value of the MP input into the human organism (Senathirajah *et al.*, 2021). Prior to adding the suspension of particles to the drinking water, it was processed with ultrasound for 20 min.

Immediately after euthanasia, the *antrum* and *caecum* of the animals were extracted, thoroughly washed with large volumes of the Krebs solution, cleansed from the mucosa, and used for smooth muscle preparations.

The study of the contractile activity of the GIT smooth muscles. The tenzometric experiments were conducted using the preparations (the average size of 2×10 mm) of circular smooth muscles of the *antrum* and *caecum*. The muscle preparations were placed into the working chamber (the volume of 2 mL) with the flowing Krebs solution (the flow rate of 8 mL/min), thermostated at 37 °C. The preparation was passively tensed at the rate of 10 mN and left for at least 1 h until the occurrence of spontaneous contractions with constant frequency and amplitude characteristics. The contractile activity was studied in the isometric mode using the force-sensing device. The signals were registered with an analogue-to-digital transformer.

Krebs solution that was used in the experiments (mM): 120.4 NaCl; 5.9 KCl; 15.5 $NaHCO_3$; 1.2 NaH_2PO_4; 1.2 $MgCl_2$; 2.5 $CaCl_2$; 11.5 glucose; pH 7.4.

The mechanokinetic analysis of spontaneous contractions. The contractions of the *antrum* and *caecum* preparations were analyzed using the method of multiparameter mechanokinetic analysis (Kosterin *et al*., 2021). The analysis of the complete profile of single spontaneous contractions involved their primary linearization within the coordinates, where f and t – instant values of force and time at the level of the contraction cycle (indices C and R indicate the phases of contraction and relaxation, respectively), Δt – arbitrary fixed time interval (which varied within 5–8 s). A fragment of a single spontaneous contraction from the beginning of the increase in the force to its maximal value F_{max} (at a time moment τ_0) was considered to be a contraction phase, and a part of a spontaneous contraction from F_{max} till the force returned to the initial level was considered the relaxation phase. The linearization charts were used to determine the characteristic constants k and n, which were further used to calculate the parameters: force (F_{max}, as well as F_C and F_R – force values at the inflexion points of the mechanogram at the level of contraction and relaxation phases), time (τ_0, as well as τ_C and τ_R – time values at the inflexion points of the mechanogram at the level of contraction and relaxation phases), velocity (V_C and V_R – maximal velocities of the contraction and relaxation phases, respectively, which occur at the inflexion points) and impulse (I_{max}, I_C and I_R – force impulses at the level of the amplitude and maximal velocities of contraction and relaxation, respectively).

Statistical analysis. MS Excel and Origin 2021 were used to estimate mechanokinetic parameters and conduct statistical analysis. The samples were checked in terms of belonging to normally distributed general populations according to the Shapiro–Wilk test. The homogeneity of dispersions was checked using Fisher's criterion. The paired version of the *t*-test for independent groups of data with equal or unequal variances was used to determine the significant differences between the mean values of samplings.

The analysis of data approximation while using the mechanokinetic analysis method by the linear function was performed using Fisher's test; determination coefficients (R^2) were at least 0.96 in all cases.

The data were exhibited as a mean ± standard error of the mean (SE). The differences were considered statistically significant at $p < 0.05$, n – number of experiments.

RESULTS AND DISCUSSION

The characterization of the suspension of polypropylene particles. The dynamic light scattering method demonstrated that the aqueous suspension of polypropylene microparticles had an average hydrodynamic diameter of 1.4 μm and a particle distribution width of 1.63 μm. The particles were distributed in the range of 446 nm (4.4 %) – 4.02 μm (1.5 %), and their largest amount (44.2 %) had the average diameter of 1.34 μm (**Fig. 1**).

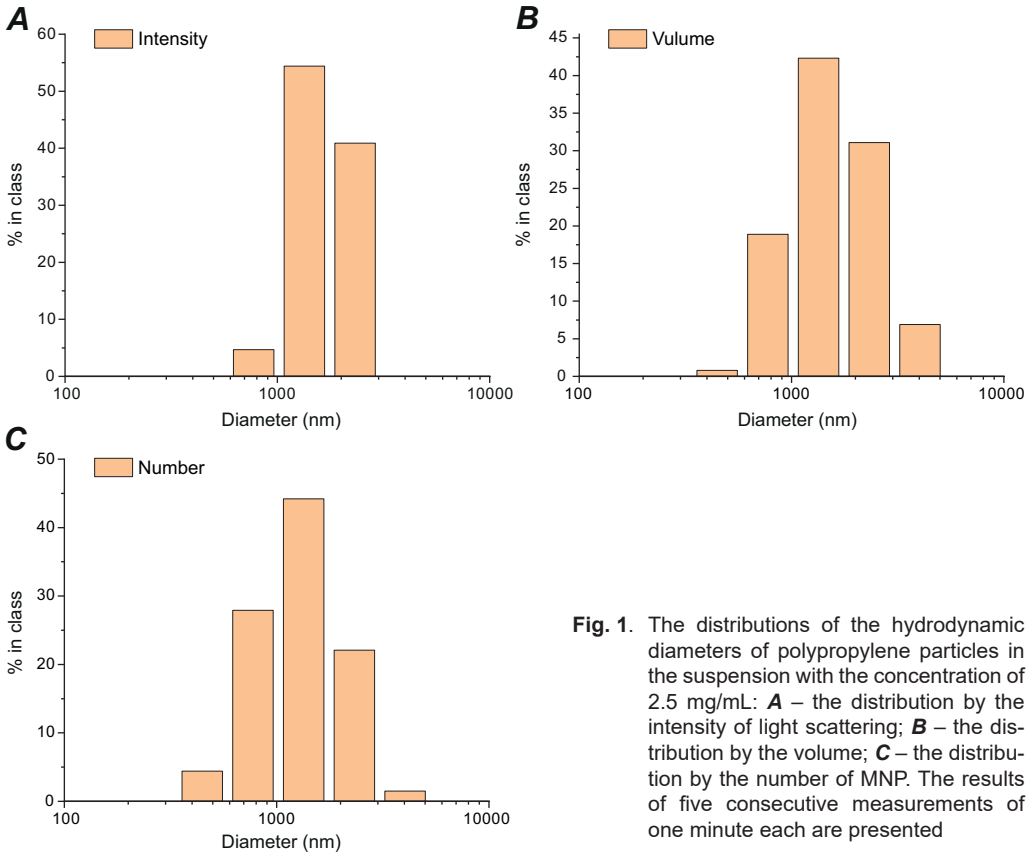

Fig. 1. The distributions of the hydrodynamic diameters of polypropylene particles in the suspension with the concentration of 2.5 mg/mL: ***A*** – the distribution by the intensity of light scattering; ***B*** – the distribution by the volume; ***C*** – the distribution by the number of MNP. The results of five consecutive measurements of one minute each are presented

Since a rather large amount of particles (4.4 %) in the suspension had an average size of 446 nm, this fraction was studied separately. To analyze small particles, the initial suspension was passed through a syringe filter with a 600 nm pore diameter, and the obtained fraction of the suspension was analyzed by the method of dynamic light scattering. According to histograms of particle distribution by intensity and volume, the fraction had some amount of particles of larger size (**Fig. 2*A*** and ***B***), which could have been caused by partial damage of the filter during the filtration, yet this contamination was minimal, since it did not impact the histogram of the particle distribution by amounts (**Fig. 2*C***). The low-size fraction contained the largest amount of particles of 44.5 nm (44.5 %), as well as 20.3 % particles of 20.3 nm and 28.7 % particles of 34.8 nm. A mixture of polypropylene micro- and nanoparticles was also used in the study.

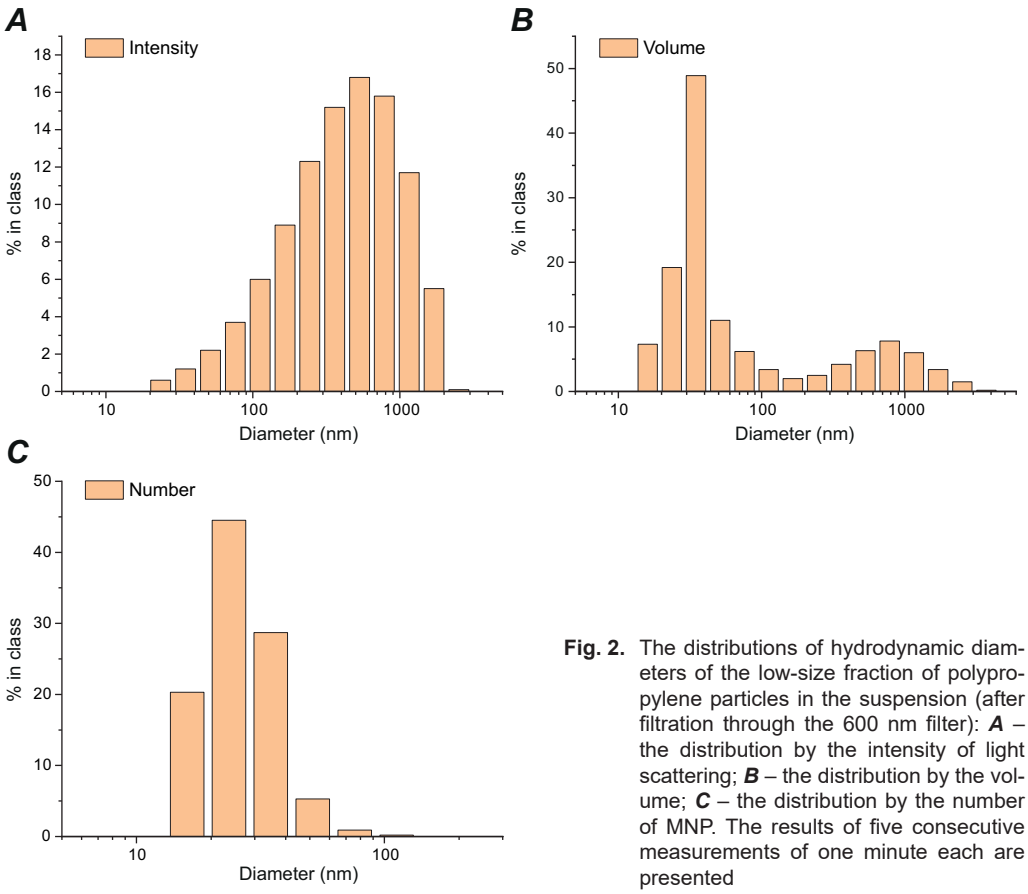

Fig. 2. The distributions of hydrodynamic diameters of the low-size fraction of polypropylene particles in the suspension (after filtration through the 600 nm filter): ***A*** – the distribution by the intensity of light scattering; ***B*** – the distribution by the volume; ***C*** – the distribution by the number of MNP. The results of five consecutive measurements of one minute each are presented

Thus, since in the PP suspension, the particles of < 1 μm (29.7 % particles were of 773.1 nm and 4.4 % – 446.0 nm) constituted about one-third of the total number, we used the MNP suspension in the *in vivo* study.

The modulation of spontaneous contractions in the antrum of rats in response to the suspension of polypropylene particles. In case of the control animals, the circular smooth muscles of the *antrum* generated spontaneous contractions with the overall frequency of 14.5 ± 0.9 contractions/10 min (n = 6). These contractions consisted of two subgroups: low frequency ones with high amplitude (with the average frequency of 0.65 ± 0.12 contractions in 10 min and the average amplitude of 11.1 ± 0.45 mN) and high frequency ones with low amplitude (with the average frequency of 1.1 ± 0.14 contractions in 10 min and the average amplitude of 3.33 ± 1.01 mN) (**Fig. 3*A***).

After long-term peroral use of the aqueous MNP suspension of PP, smooth muscles of the *antrum* generated spontaneous contractions with a decreased overall frequency, which on average was 8.3 ± 0.6 contractions in 10 min (n = 10, p < 0.05) (**Fig. 3*B***). The decrease in the overall frequency occurred due to the drop in the frequencies of both fractions of spontaneous contractions, although the frequency of low amplitude contractions changed to a higher degree, the amplitude of low frequency contractions increased

considerably too, whereas that of high frequency contractions decreased. Thus, two fractions of contractions were observed in these conditions: with the average amplitude of 15.1 ± 0.79 mN and frequency of 0.7 contractions in 10 min, and 1.45 ± 0.18 mN and 0.52 ± 0.11 contractions in 10 min.

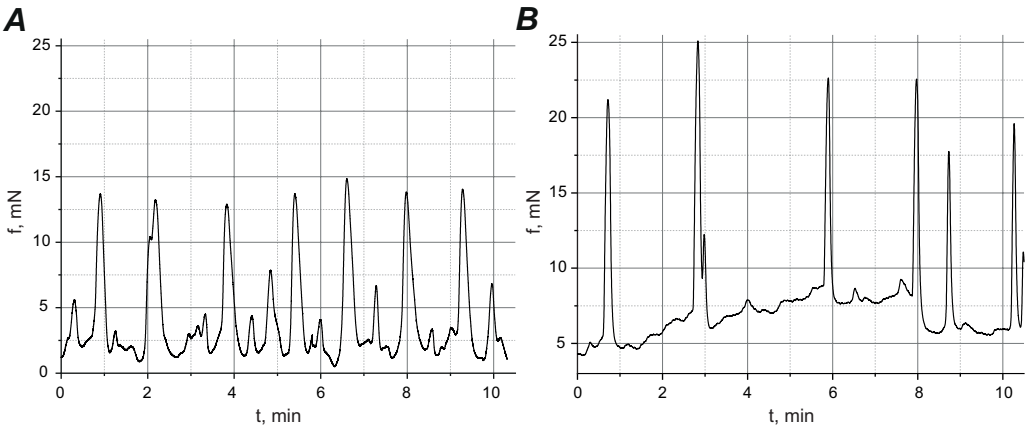

Fig. 3. The typical mechanograms of spontaneous contractions of circular smooth muscles of the *antrum* of rats in the control (***A***) and under long-term peroral intake of polypropylene MNP into the organism (in the daily dose of 2.5 mg/kg for 6 weeks) (***B***)

Since it was important to determine whether some characteristics of contraction-relaxation cycles change under the effect of PP, which would indicate the impact of this xenobiotic on the processes of Ca^{2+} ion translocation in myocytes, further on, high amplitude contractions were analyzed by multiparameter mechanokinetic analysis (Kosterin *et al.*, 2021). It was found that in case of the *antrum* muscle preparations, obtained from the animals that drank the aqueous suspension of PP MNP, there was a change in most parameters of some contraction-relaxation cycles. For instance, all the force parameters demonstrated a significant increase: amplitude (F_{max}) on average to 139.3 ± 5.1 % ($p < 0.001$, n = 10); indices of the force at the mechanogram inflexion points at the level of phases of contraction (F_C) and relaxation (F_R), respectively, up to 140.6 ± 5.2 % and 145.3 ± 4.6 % (in both cases $p < 0.001$, n = 10) (**Fig. 4*A***). Also, under the effect of PP, there was a similar decrease in the parameters of the time of reaching the amplitude (τ_0), the mechanogram inflexion points at the level of phases of contraction and relaxation (τ_C and τ_R), respectively: 60.8 ± 3.4 %, 55.6 ± 2.3 % and 62.6 ± 4.2 %, respectively (in all cases $p < 0.01$–0.001, n = 10) (**Fig. 4*B***). Also, there was a two-fold increase in the parameters of maximal velocities at the level of phases of contraction (V_C) and relaxation (V_R): 228.5 ± 6.3 % and 220.5 ± 8.1 % (in both cases $p < 0.001$, n = 10) (**Fig. 4*C***). The only group of mechanokinetic parameters that did not incur any changes due to PP MNP was the impulse parameters (**Fig. 4*D***). However, the absence of changes in the impulse parameters may be explained by the fact that mathematically, the force impulse parameters are calculated as a force integral equation, generated by the muscle within a certain period of time. Since in this case, against the background of the increase in force, time parameters decreased, this combination eliminated any evident changes in impulse parameters I_{max}, I_C and I_R.

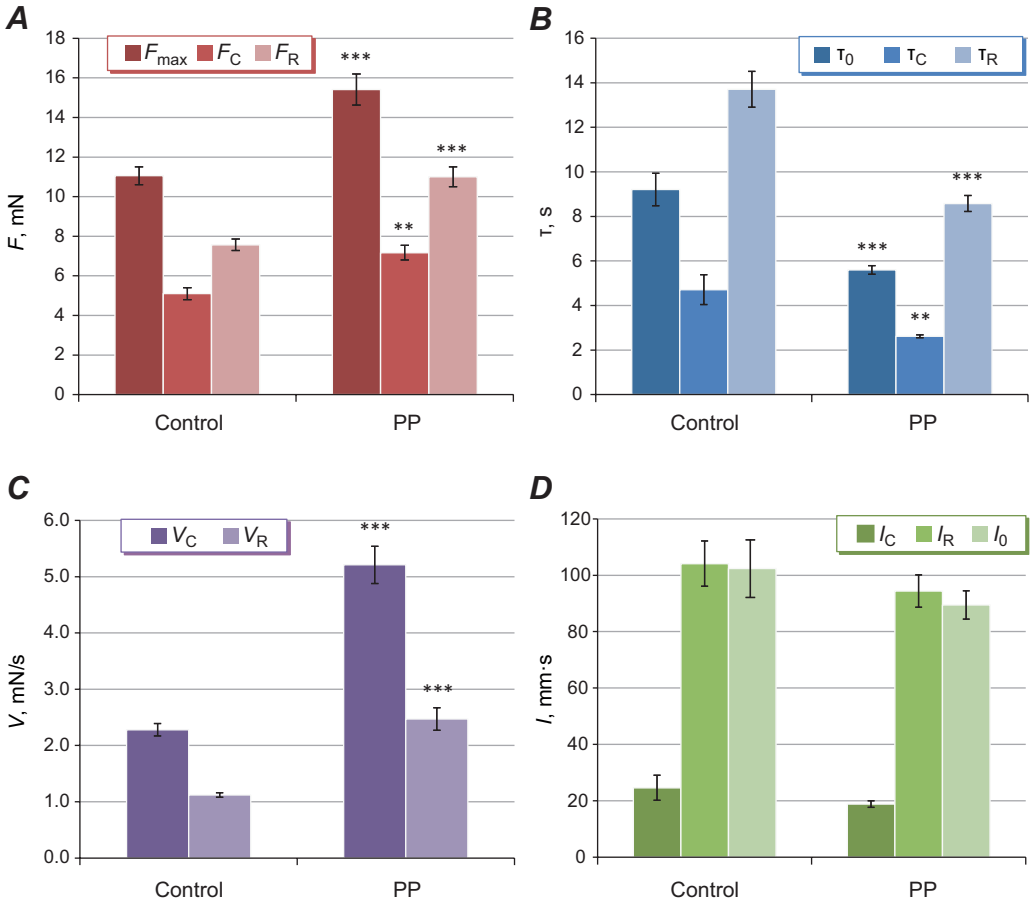

Fig. 4. The summary of mechanokinetic parameters of spontaneous contractile activity of circular smooth muscles of the *antrum* of rats in the control (***A***) and under long-term peroral intake of polypropylene MNP into the organism (in the daily dose of 2.5 mg/kg for 6 weeks): ***A*** – force parameters (F_{max}, F_C, and F_R); ***B*** – time parameters (τ_0, τ_C, and τ_R); ***C*** – velocity parameters (V_C, and V_R); ***D*** – impulse parameters (I_0, I_C, and I_R). n = 6–10; ** – p < 0.01, *** – p < 0.001 significant regarding the control

The modulation of spontaneous contractions in the caecum of rats in response to the suspension of polypropylene particles. Since a considerable translocation of xenobiotics occurs via the intestinal walls, further on, we investigated the spontaneous contractile activity of the circular smooth muscles of the *caecum* of rats that received the MNP suspension for a long time. In the control, the circular smooth muscles of the *caecum* were characterized by spontaneous contractions with the overall frequency of 49.8 ± 4.2 contractions in 10 min (n = 6). These contractions consisted of two fractions: low frequency contractions with a high amplitude (with the average frequency of 12.8 ± 2.2 contractions in 10 min and the average amplitude of 12.5 ± 0.41 mN) and high frequency ones with a low amplitude (with the average frequency of 41.5 ± 3.1 contractions in 10 min and the average amplitude of 1.88 ± 0.32 mN) (**Fig. 5*A***).

Similarly to the smooth muscles in the *antrum*, a long-term intake of polypropylene MNP into the organism was accompanied by considerable changes in the spontaneous

activity of the *caecum* muscles. For instance, due to the effect of this xenobiotic, the overall frequency of spontaneous contractions decreased considerably on average to 12.8 ± 3.7 contractions in 10 min (n = 10). It should be noted that under these conditions, low-frequency contractions mostly overlapped with the high-frequency ones, resulting in the disruption to the trends for some contractions (**Fig. 5*B*** and ***C***).

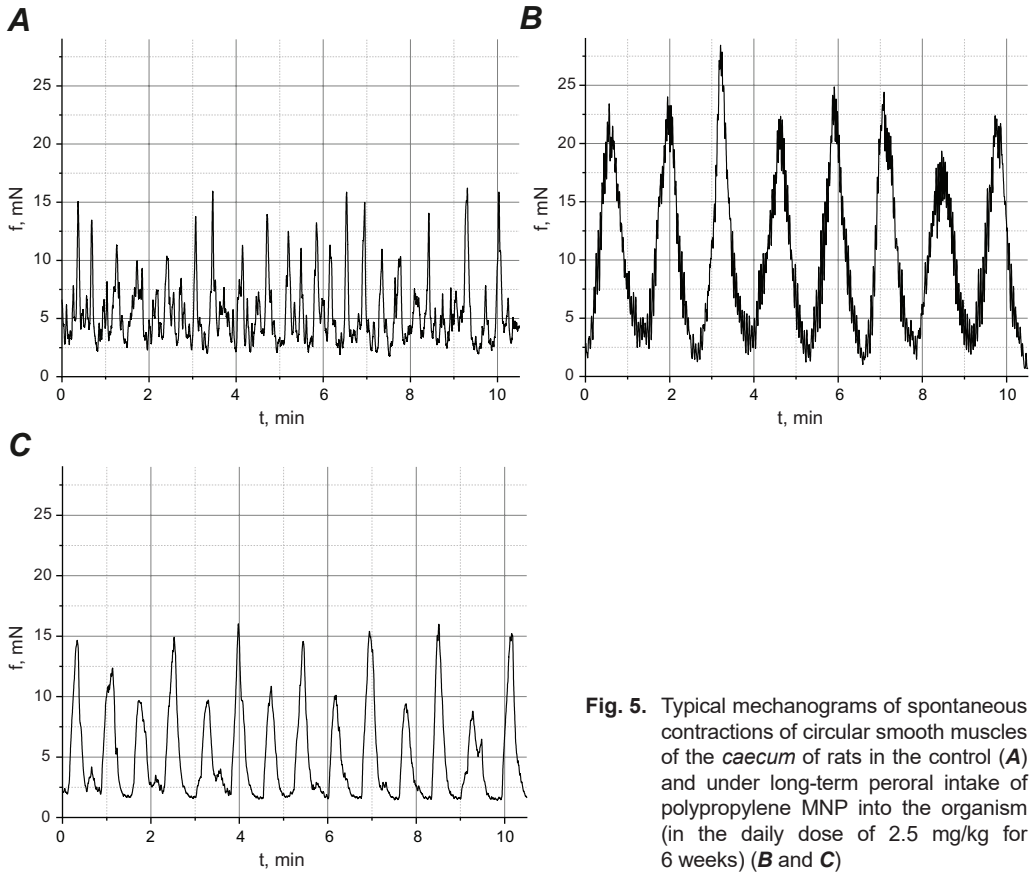

Fig. 5. Typical mechanograms of spontaneous contractions of circular smooth muscles of the *caecum* of rats in the control (***A***) and under long-term peroral intake of polypropylene MNP into the organism (in the daily dose of 2.5 mg/kg for 6 weeks) (***B*** and ***C***)

Further, the high-amplitude contractions were analyzed using multiparameter mechanokinetic analysis. It was determined that under the effect of PP, there was a considerable increase in the force parameters F_{max} and F_C (on average up to 144.6 ± 8.0 and 147.9 ± 7.8 %, respectively, in both cases $p < 0.05$, n = 10) and all the time parameters (τ_0 to 362.0 ± 12.9 %, τ_C to 265.4 ± 16.6 % and τ_R to 393.5 ± 12.5 %, in all cases $p < 0.05$, n = 10) (**Fig. 6*A*** and ***B***). A considerable increase in time and velocity parameters reflected on the increase in the impulse parameters of spontaneous contractions, which depended on them: I_0 to 567.6 ± 17.9 %, I_C to 397.6 ± 23.5 %, and I_R to 624.9 ± 17.0 %, in all cases $p < 0.05$, n = 10) (**Fig. 6*C***).

Also, due to a considerable disruption in the trend for single spontaneous contractions under the effect of PP, there was a considerable decrease in both velocity parameters V_C and V_R, amounting to 38.9 ± 7.8 % and 30.0 ± 6.4 %, respectively (in both cases $p < 0.001$, n = 10) (**Fig. 6*D***).

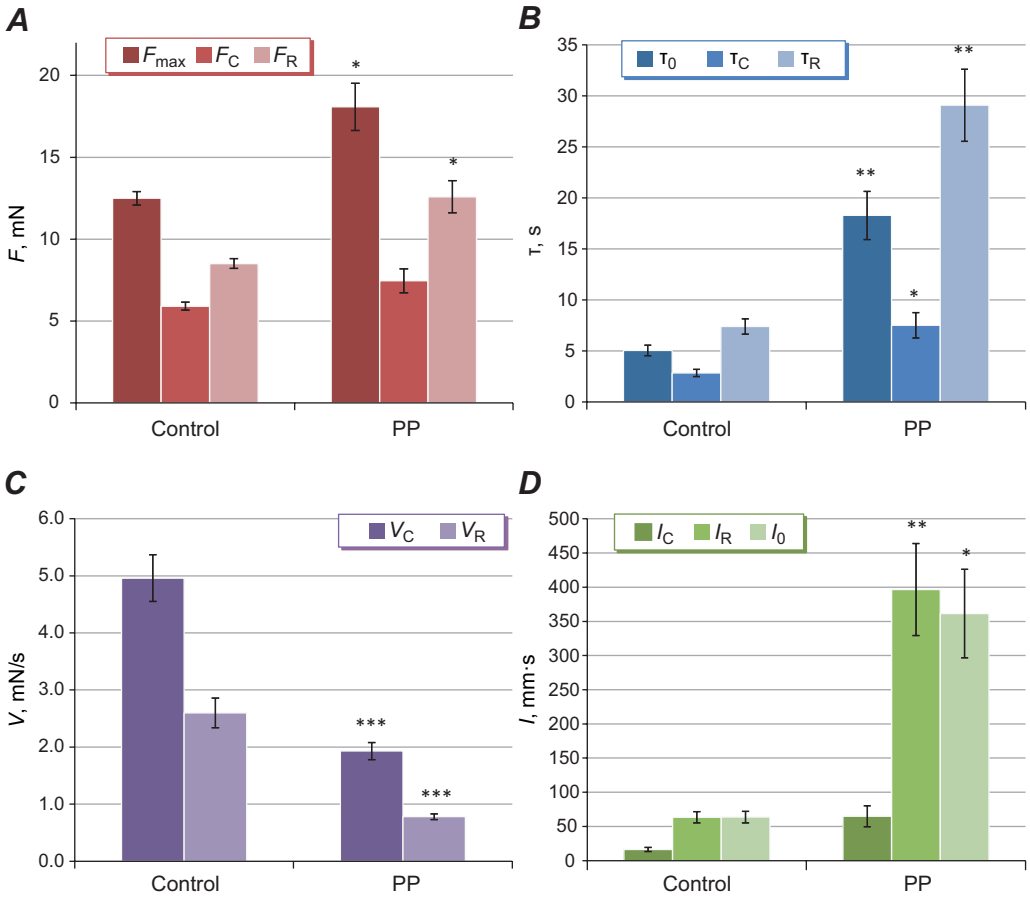

Fig. 6. The summary of mechanokinetic parameters of spontaneous contractile activity of circular smooth muscles of the *caecum* of rats in the control (***A***) and under long-term peroral intake of polypropylene MNP into the organism (in the daily dose of 2.5 mg/kg for 6 weeks): ***A*** – force parameters (F_{max}, F_C, and F_R); ***B*** – time parameters (τ_0, τ_C, and τ_R); ***C*** – velocity parameters (V_C, and V_R); ***D*** – impulse parameters (I_0, I_C, and I_R). n = 6–10; * – $p < 0.05$, ** – $p < 0.01$, *** – $p < 0.001$ significant regarding the control

Therefore, a long-term effect of polypropylene MNP on the organism caused a considerable disruption in the rhythmic activity of smooth muscles of the gastrointestinal tract of rats; these changes were especially evident in the *caecum*. We can speculate about the tissue mechanisms of this disruption. It is known that spontaneous contractions of smooth muscles of the digestive tract are induced by pacemaker cells – interstitial cells of Cajal, which exist in at least seven types, and the presence of some ICC types is different for different GIT parts, each of them inducing contractions with a different frequency (Hwang *et al.*, 2025; Di Natale *et al.*, 2025). ICC-SM pacemakers are present in the walls of the *antrum* and *caecum* – they are located under the circular layer of smooth muscle cells and contact with the submucosa layer of the wall; while ICC-MY are located next to the Auerbach's plexus ganglia between the longitudinal and circular layers of myocytes. According to the data reported by Smith *et al.* (1987), the ICC-MY subpopulation cells generate a low-amplitude rhythm of muscle depolarization,

while ICC-SM – a high-amplitude one. Thus, the frequency of spontaneous contractions in the digestive tract muscles is determined by the functioning of ICC. The force of contractions is determined by the processes of activation of the contraction apparatus in working myocytes. These processes can be divided into those directly dependent on the concentration of Ca^{2+} ions in the myoplasm, and Ca^{2+}-independent processes of sensitization of proteins of the contraction apparatus. The latter are mostly conditioned by the inhibition of the activity of the phosphatase of light chains of myosin by inhibitory phosphorylation with RhoA-dependent kinases CPI-17 and ROCK (Mahavadi *et al.*, 2017). The general mechanism, by which microplastics cause the disruption in the functioning of tissues and organs, is the inflammation induction. It is known that one of the consequences of inflammation in smooth muscle tissues is the induction of oxidative stress in cells (Liu *et al.*, 2025). The increase in spontaneous contractions under oxidative stress, as shown in the example with smooth muscles of the *antrum* and the urinary bladder, is the hyperactivation of Rho-kinase (Al-Shboul & Mustafa, 2015) and inhibition of K^+-current via Ca^{2+}-activated K^+-channels of low conductivity (Wang *et al.*, 2018). Similar changes in force, time, and velocity parameters, detected by the mechanokinetic analysis, also indicate the absence of specific changes in the functioning of the systems of passive (when the parameters of the contraction phase and amplitude are sensitive) and active (when the parameters of the relaxation phase are sensitive) transportation of ions in myocytes under the effect of the polypropylene particles (Kosterin *et al.*, 2021).

Therefore, since the volume of industrial use of plastic, its environmental pollution, and its entry into organisms remain at a very high level, and also do not currently have prospects for a quick solution, the study of violations of the functioning of physiological systems under *in vivo* exposure is of high relevance. This work is the first to analyze violations of the motility of the digestive tract under conditions of a regular long-term peroral intake of the polypropylene MNP. The results presented in the work are important for understanding the mechanisms of motor dysfunction under the action of this xenobiotic, and can also be useful for developing a strategy for therapeutic normalization of this dysfunction.

CONCLUSIONS

Long-term intake of polypropylene MNP into the organism causes a change in the frequency of spontaneous contractions of smooth muscles, which is likely due to impaired ICC functioning. Since, in these conditions, there is a change in the amplitude parameters of contractile activity, it is possible to predict changes in the processes of activation of smooth muscle cell contractions, which may be due to the increase in sensitization of contraction proteins.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: the authors declare that they have no conflict of interest.

Human Rights: this article does not contain any studies with human subjects performed by any of the authors.

Animal Studies: all international, national and institutional guidelines for the care and use of laboratory animals were followed.

AUTHOR CONTRIBUTIONS

Conceptualization, [O.T.; M.S.]; methodology, [M.S.; O.T.; A.C.; V.M.; A.S.; O.S.; S.M.; O.A.; K.S.]; research, [M.S.; O.T.; A.C.]; resources, [M.S.; O.T.; A.C.; V.M.; A.S.; O.S.; S.M.; O.A.; K.S.]; data processing, [M.S.; O.T.; A.C.]; writing – preparation of the original project, [M.S.; O.T.]; writing – review and editing, [M.S.; O.T.; A.C.; V.M.; A.S.; O.S.; S.M.; O.A.; K.S.]; visualization, [M.S.; O.T.]; supervision, [O.T.]; project management, [O.T.]; funding search, [–].

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ЗМІНИ СПОНТАННОЇ СКОРОЧУВАЛЬНОЇ АКТИВНОСТІ ГЛАДЕНЬКИХ М'ЯЗІВ ШЛУНКОВО-КИШКОВОГО ТРАКТУ ЩУРІВ ЗА ТРИВАЛОГО НАДХОДЖЕННЯ В ОРГАНІЗМ СУМІШІ НАНО- І МІКРОЧАСТИНОК ПОЛІПРОПІЛЕНУ

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Обґрунтування. Пластик є найбільш поширеним забруднювачем навколишнього середовища. У природних умовах пластик піддається механічній і фотохімічній деструкції, формуючи мікро- та наночастинки, які асимілюються живими організмами. Регулярне надходження суміші нано- і мікрочастинок пластику (МНП) у шлунково-кишковий тракт (ШКТ) спричиняє розвиток запальних процесів у стінках травного каналу та порушення кишкової мікробіоти. Однак залишається недослідженою скорочувальна активність гладеньких м'язів ШКТ за таких умов.

Метою роботи було дослідити спонтанну скорочувальну активність кільцевих гладеньких м'язів шлунку і товстого кишечника щурів за тривалого перорального вживання МНП одного з найбільш поширених пластикових забруднювачів навколишнього середовища – поліпропілену (ПП).

Матеріали і методи. Суспензію частинок поліпропілену готували з одноразового посуду за методом Roursgaard з незначними модифікаціями. Визначення середнього гідродинамічного діаметра частинок ПП у водній суспензії здійснено методом динамічного розсіювання світла. Тварини експериментальної групи упродовж 6 тижнів отримували суспензію ПП у питній воді (в дозі 2,5 мг/кг щодобово). Тензометричні досліди проводили в ізометричному режимі реєстрації на ізольованих препаратах кільцевих гладеньких м'язів антрального відділу шлунку (*antrum*) і сліпої кишки (*caecum*) щурів. Спонтанні скорочення аналізували методом механокінетичного аналізу із розрахунком силових, часових, швидкісних та імпульсних параметрів.

Результати. Суспензія поліпропілену містила частинки до 4 мкм, із них 34,1% частинок мали розмір <1 мкм. Тривале пероральне надходження в організм ПП супроводжувалося порушенням спонтанної скорочувальної активності гладеньких м'язів antrum і caecum: зниженням частоти і модуляції механокінетичних параметрів окремих скорочень. У випадку м'язів *antrum* суттєво зростали силові та швидкісні параметри; часові параметри були нижчими за контрольні; імпульсні параметри залишалися без змін. Механокінетичні параметри спонтанних скорочень caecum за дії ПП зазнавали таких змін: значно зростали силові параметри амплітуди і фази скорочення, всі часові й імпульсні параметри, тоді як швидкісні параметри були суттєво знижені.

Висновок. Тривале надходження в організм МНП поліпропілену спричиняє зміну частоти спонтанних скорочень гладеньких м'язів, ймовірно, внаслідок порушення функціонування пейсмейкерних клітин, а зміну амплітудних параметрів – ймовірно, внаслідок дії на гладеньком'язові клітини.

Ключові слова: суміш нано- і мікропластику, поліпропілен, гладенькі м'язи, антральний відділ шлунку, сліпа кишка, спонтанні скорочення, механокінетичні параметри

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