Biol. Stud., 2024, 18(4), 37–48 • doi: https://doi.org/10.30970/sbi.1804.791
www.http://publications.lnu.edu.ua/journals/index.php/biology

UDC: 57.013+577.353

C_{60} FULLERENE HELPS RESTORE *MUSCLE SOLEUS* CONTRACTION DYNAMICS AFTER ACHILLOTOMY-INDUCED ATROPHY

Dmytro Nozdrenko, Kateryna Bogutska, Ihor Pampuha, Mykola Petrovsky, Yuriy Prylutskyy

Taras Shevchenko National University of Kyiv, 64 Volodymyrska St., Kyiv 01601, Ukraine

Nozdrenko, D., Bogutska, K., Pampuha, I., Petrovsky, M., & Prylutskyy, Yu. (2024). C_{60} fullerene helps restore *muscle soleus* contraction dynamics after achillotomy-induced atrophy. *Studia Biologica*, 18(4), 37–48. doi:10.30970/sbi.1804.791

Background. The search for new means that would effectively influence the pathological consequences of muscle immobilization is an urgent priority request of modern biomedicine. Previously, the positive effect of water-soluble C_{60} fullerenes, as strong antioxidants, was established on the background of muscle ischemia, mechanical muscle injury, and other muscle dysfunctions. These carbon nanoparticles have been shown to reliably protect muscle tissue from damage caused by oxidative stress.

Materials and Methods. The biomechanical parameters of *muscle soleus* contraction of rats were studied by simulating non-functioning hind limbs using a clinical model – a rupture of the Achilles tendon (achillotomy). Muscle contraction parameters, namely the maximum contraction force and muscle force impulse, were determined on the 15th, 30th, and 45th days after initiation of atrophy using tensometry. As a therapeutic nanoagent, daily oral administration of C_{60} fullerene aqueous solution at a dose of 1 mg/kg was used throughout the experiment.

Results. Previous registration of *muscle soleus* contraction force when applying 1 Hz stimulation lasting 1800 s with three pools revealed a decrease in maximal force responses after 15, 30, and 45 days of atrophy. The 45th day after atrophy is considered to be the limit for the fastest recovery of the muscle after immobilization, the further process takes place over several months. In all the tests performed, the therapeutic administration of water-soluble C_{60} fullerenes (dose 1 mg/kg) an increase in biomechanical parameters was recorded (maximum force of contraction – the change in the form of the “stimulation – force contraction” dependence is a consequence of the development of the pathological process in muscle and the muscle force impulse, which allows

assessing the performance of the muscular system after a long-term immobilization), by approximately 29–49±2 % for the maximum contraction force and by 21–37±2 % for the muscle force impulse compared to the atrophy group for 15, 30 and 45 days.

Conclusions. The obtained results indicate the prospects of using water-soluble C_{60} fullerenes, which can alleviate pathological conditions in the muscular system that arise from skeletal muscle atrophy due to immobilization.

Keywords: *muscle soleus*, atrophy, C_{60} fullerene, biomechanical parameters of muscle contraction

INTRODUCTION

Prolonged immobilization or exposure to weightlessness is recognized to result in a notable reduction in the diameter of muscle fibers and a decline in their force-generating capacity (Thomason & Booth, 1990). The foremost concern lies in the degradation of antigravity skeletal muscles in the hind legs (Ohira *et al*., 2002). The gravity-dependent function of antigravity muscles makes them especially susceptible to weightlessness (unloading), leading to a significant loss of myofibrillar (structural) proteins (Paddon-Jones *et al*., 2006). In terrestrial gravity conditions, the postural muscle (*muscle soleus*), exhibits contractile activity, supporting the animal's weight for most of the day (Hodgson *et al*., 2005). The *muscle soleus* is especially susceptible to insufficient loading caused by space flight, prolonged immobilization, or underutilization. Biomechanical changes in the muscles are mainly linked to a reduction in maximum isometric tension and a decrease in maximum shortening velocity (Tischler & Slentz, 1995; Sayed *et al*., 2023).

Muscle atrophy often occurs due to immobilization, disuse after injury (Ohira *et al*., 2002), poisoning, or chronic disease (Rong *et al*., 2023). In this case, a decrease in muscle contraction force is the most obvious response to atrophy. The force of muscle contraction decreases most significantly during the first two weeks of immobilization. Atrophied muscle is characterized by catabolic metabolism whereby the rate of protein synthesis decreases and the rate of protein breakdown increases (Cao *et al*., 2018). The supply of oxygen to the muscle may be impaired, even though the myoglobin content in the atrophied muscle remains elevated. The amount of connective tissue in the atrophied muscle as well as the surrounding periarticular tissue increases, which can result in heightened muscle stiffness and, ultimately, musculoskeletal degeneration (Rüegg & Glass, 2011; Zuccaro *et al*., 2023). Almost complete recovery is possible, however this phase often lasts much longer than the period of complete immobilization and is accompanied by significant differences in the weight of the restored muscles and the size of the muscle fibers (Appell, 1990; Jørgensen *et al*., 2023).

The search for drugs that effectively influence the pathological consequences of muscle immobilization is an important demand of modern biomedicine. The increase in the number of free radicals in the process of muscle immobilization and the subsequent atrophy plays an important role in determining the level of pathological condition of the muscular system in general (Tidball, 2005). Therefore, special attention is paid to compounds with antioxidant properties (Rüegg & Glass, 2011).

Due to its nanoscale size, high chemical stability, and inherent unique physical properties, the biocompatible C_{60} molecule is of the greatest interest for experimental biological research (Goodarzi *et al*., 2017). In particular, C_{60} fullerenes exhibit a strong reducing ability, readily attaching up to six electrons simultaneously. Due to this, they

and their derivatives act in biological systems as scavengers of free radicals, the overproduction of which leads to many pathologies. This opens up a promising opportunity for utilizing these nanocompounds as powerful antioxidants, with effects surpassing those of the well-known natural antioxidants, such as vitamins C, E, and carotenoids (Eswaran, 2018).

Our previous research on *in vivo* models has shown that the administration of non-toxic (at least at low doses) water-soluble C_{60} fullerenes on the background of muscle ischemia (Nozdrenko *et al*, 2021b), mechanical muscle trauma (Nozdrenko *et al*., 2022), and muscle dysfunctions associated with pesticide poisoning (Nozdrenko *et al*., 2021a) significantly improved the functional activity of skeletal muscles. In addition, these nanostructures can affect the course of the inflammatory process: *in vitro* experiments have shown that C_{60} fullerene derivatives taken up by macrophages cause the release of anti-inflammatory cytokines (Ryan *et al*., 2007). The antihistamine and antioxidant effects of C_{60} fullerenes have been established, which, according to the authors, show promise for their use in treating diseases such as asthma, polyarthritis, heart disease, multiple sclerosis, and atrophic tissue transformations (Grebowski *et al*., 2013). This study aimed to evaluate the potential of C_{60} fullerene, a powerful antioxidant, to improve the contractile dynamics of rat *muscle soleus* following achillotomy-related atrophy.

MATERIALS AND METHODS

To obtain C_{60} fullerene aqueous solution, we used a method based on the transfer of C_{60} molecules from toluene to water, followed by sonication (Scharff *et al*., 2004). The resulting C_{60} fullerene aqueous solution at a maximum concentration of 0.15 mg/mL is a typical nanocolloid (Prilutski *et al*., 1999), which remains stable for 12–18 months at a temperature of +4–25 °C.

The experiments were conducted on 2-month-old male Wistar rats weighing 200±10 g. The study protocol (No. 9, dated September 4, 2023) was approved by the Bioethics Committee of the Institute of Biology and Medicine of Taras Shevchenko National University of Kyiv following the regulations of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, as well as the norms of biomedical ethics under the Law of Ukraine No. 3447-IV of 21.02.2006, Kyiv, „On the Protection of Animals from Cruelty" during biomedical research.

Prior to the commencement of the study, the rats were subjected to Achillotomy, which involved cutting of the Achilles tendon. Seven experimental groups of animals were studied, with 7 animals in each group: control, atrophy after 15, 30, and 45 days, and atrophy+C_{60} after 15, 30, and 45 days. The animals received daily oral administration of C_{60} fullerene aqueous solution (beginning immediately after the initiation of atrophy) and continuing throughout the experiment. It is noteworthy that the way of oral administration of water-soluble C_{60} fullerenes was tested in *in vivo* experiments for their further clinical trials. Importantly, the dosage of water-soluble C_{60} fullerenes at 1 mg/kg was selected as the most optimal when studying their antioxidant effect in other models of muscle pathology (Nozdrenko *et al*., 2021b; 2022) and it was significantly lower than the LD_{50} value of 600 mg/kg when administered orally to rats (Gharbi *et al*., 2005).

Animals were anesthetized by intraperitoneal injection of Nembutal (40 mg/kg). *Muscle soleus* was freed from the surrounding tissues; in the distal share, its tendon part was connected to force measurement sensors. The dynamic properties of muscle contraction were studied using the method of modulated efferent stimulation. To prepare

for the modulated stimulation of efferents in the corresponding segments, the ventral roots were cut directly at the places of their exit from the spinal cord. Stimulation was carried out with electric pulses lasting 2 ms, generated by a pulse generator. Three pools of non-relaxation stimulation with a frequency of 1 Hz and duration of 1800 s each were used, after each pool the relaxation time was 5 min.

The usage of three-component stimulation of *muscle soleus* allowed us to evaluate the level of fatigue processes development in the injured muscle during a prolonged low-frequency stimulation and a standard relaxation period. This approach allows us to evaluate changes in biomechanical parameters of muscle contraction caused by insufficient relaxation period, the increase of which is associated with pathological processes in muscle tissue.

The external load on the muscle was controlled with a system of mechanical stimulators. The force of muscle contraction was measured with strain gauges. The muscle force impulse (area under the force curve), as an indicator of the overall muscle performance at the applied stimulation pools, was calculated numerically using the Origin 9.4 software.

Statistical analysis of the results was done using the methods of variational statistics in Statistica 8.0. Each of the obtained experimental mechanokinetic curves is the result of averaging 10 similar measurements, which were performed from the *muscle soleus* of each animal (n = 7 in each experimental group). To assess the reliability of the detected changes, two-way ANOVA was used, followed by the Bonferroni multiple comparison test. Values of $p < 0.05$ were considered significant.

RESULTS AND DISCUSSION

The study of the impact of immobilization on muscle capillarization in rats has shown that the number of capillaries significantly decreased to 65 % of the normal capillary density (Jozsa *et al*., 1988). An increase in the amount of intramuscular connective tissue was also observed during immobilization, apparently occurring simultaneously with muscle atrophy and loss of muscle capillarity. These factors undoubtedly play a crucial role in the initiation of increased fatigue in active muscles.

Recording of *muscle soleus* contraction force, when applying 1 Hz stimulation lasting 1800 s with three pools, revealed a decrease in the maximum force responses after 15 days of atrophy by 61±3 %, 77±3 %, and 82±3 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared to the control ($p < 0.05$) (**Figs. 1** and **2**).

Under the administration of the C_{60} fullerene aqueous solution, the level of maximum muscle strength increased by 41±2 %, 49±2 %, and 57±2 % at the 1st, 2nd, and 3rd stimulation pools, respectively ($p < 0.05$ compared with the atrophy group). Thus, the C_{60} fullerene therapy is most effective for the prolonged nature of the contractile process, which is in good agreement with previous findings (Vereshchaka *et al*., 2018).

After 30 days of the experiment, the level of maximum effort decreased by 49±2 %, 56±2 %, and 61±3 % of the control values ($p < 0.05$) at the 1st, 2nd, and 3rd stimulation pools, respectively (**Fig. 2**). The use of C_{60} fullerene aqueous solution increased the levels of these indicators by 31±1 %, 39±1 %, and 43±2 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared to the atrophy group ($p < 0.05$).

The 45th day after atrophy is considered to be the limit for the fastest possible muscle recovery after immobilization, with further recovery taking place over several months in rats or years in humans (Tidball & Villalta, 2010). The decrease in the maximum muscle

force generation on day 45 was 32±1 %, 41±2 %, and 49±2 % of the control values ($p < 0.05$) at the 1st, 2nd, and 3rd stimulation pools, respectively (**Fig. 2**). At the same time, the use of C_{60} fullerenes injections increased the level of these indicators by 22±1 %, 29±2 %, and 36±1 % at the 1st, 2nd, and 3rd pools of stimulation, respectively, compared with the atrophy group ($p < 0.05$).

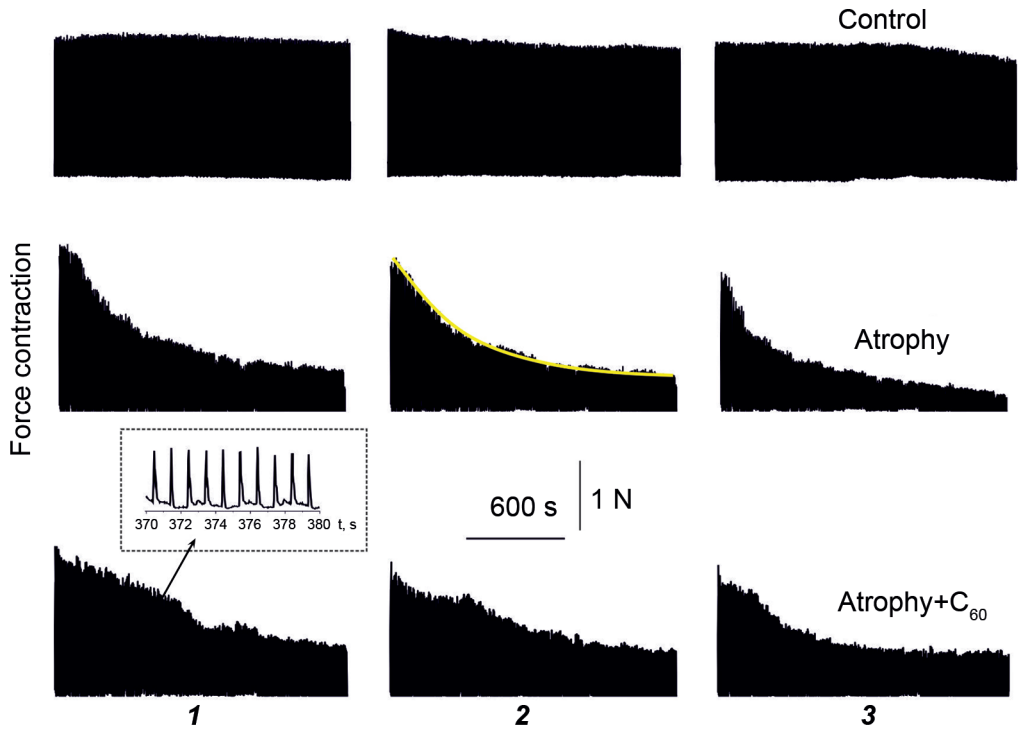

Fig. 1. Contractile force of the rat *muscle soleus* after 15 days of atrophy with three pools of 1 Hz non-relaxing stimulation lasting 1800 s: control, atrophy and atrophy+C_{60} – contraction force of the intact *muscle soleus*, atrophied *muscle soleus* without C_{60} fullerenes and under their administration, respectively; the yellow line indicates changes in maximum contraction forces throughout the entire stimulation period; 1, 2 and 3 – the 1st, 2nd, and 3rd pools of stimulation

The significant differences observed in the severity of muscle fatigue at the 1st, 2nd, and 3rd stimulation pools after 15, 30, and 45 days of atrophy can be explained by the insufficient time of the relaxation period (sufficient in the control) during the development of the studied pathology. The described effect of C_{60} fullerenes can be due to both a decrease in the development of inflammatory processes in muscle tissue and an increase in the force response of an active muscle under their action, which was shown in a previous study (Prylutskyy *et al*., 2017).

The dynamics of muscle contraction is determined by the subtle mechanisms of interaction between motor neuron pools that transmit signals to the muscle, and actin and myosin myofilaments. Changes in the elastic properties of muscle fibers, the structure of tendon elements, and connective tissue determine the shape of the stimulation-force relationship, which is a consequence of the development of a pathological process in the muscle. The analysis of the muscle force impulse allowed us to assess changes in the level of performance of the muscular system after prolonged immobilization (**Fig. 3**).

The impulse of muscle strength on day 15 after atrophy decreased by 59±2 %, 63±3 %, and 75±3 % of the control values ($p < 0.05$) at the 1st, 2nd, and 3rd stimulation pools, respectively. The use of C_{60} fullerene aqueous solution increased this index by 33±1 %, 37±2 %, and 40±2 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared with the atrophy group ($p < 0.05$).

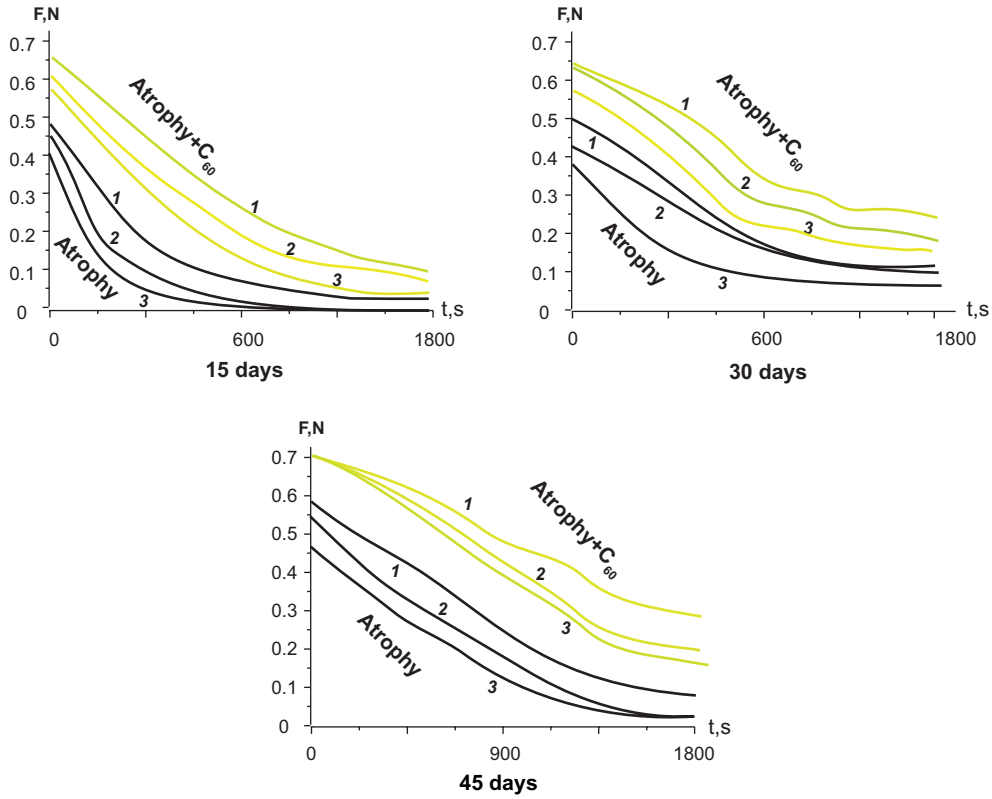

Fig. 2. Curves of maximum force contractions of the rat *muscle soleus* after atrophy with three 1 Hz pools of non-relaxation stimulation lasting 1800 s: atrophy and atrophy+C_{60} – force of contraction of the atrophied *muscle soleus* without C_{60} fullerenes and under their administration, respectively; 1, 2 and 3 – the 1st, 2nd and 3rd pool of stimulation, respectively; 15, 30 and 45 days – the corresponding day after the initiation of atrophy

On day 30 after atrophy, the muscle force impulse decreased by 35±1 %, 45±2 %, and 49±2 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared with the control ($p < 0.05$). The use of water-soluble C_{60} fullerenes showed an increase in these indicators by 21±1 %, 29±1 %, and 31±1 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared with the atrophy group ($p < 0.05$).

After a period of 45 days following the atrophy, the muscle force impulse decreased by 10±1 %, 13±1 %, and 39±2 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared with the control ($p < 0.05$). The positive effect of C_{60} fullerenes was 17±1 %, 19±1 %, and 27±1 % at the 1st, 2nd, and 3rd stimulation pools, respectively, compared to the atrophy group ($p < 0.05$).

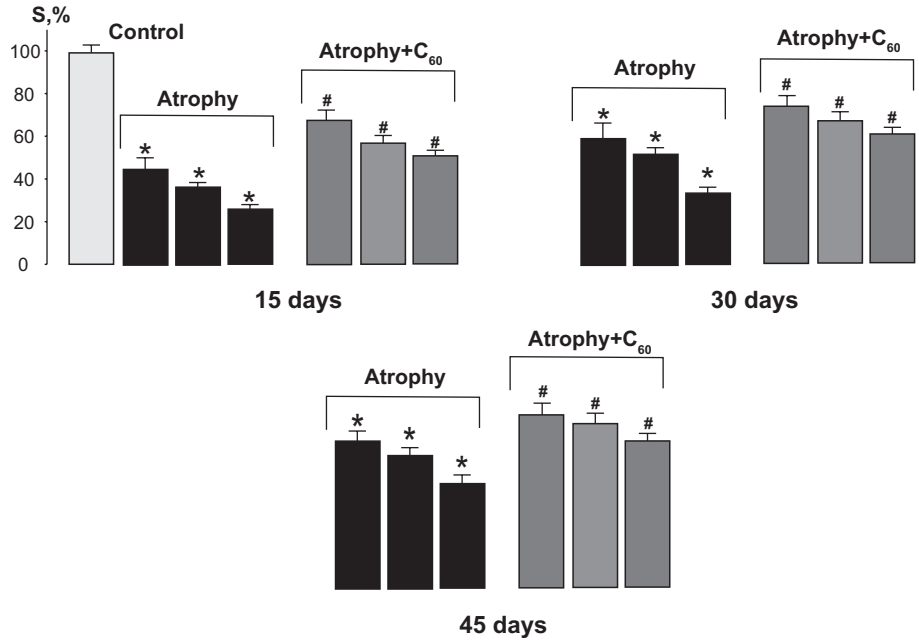

Fig. 3. *Muscle soleus* force impulse (S; relative to the control, taken as 100%) of a rat after atrophy with three 1 Hz pools of non-relaxation stimulation lasting 1800 s: atrophy and atrophy+C_{60} – force of contraction of atrophied *muscle soleus* without and with C_{60} fullerenes, respectively; 1, 2 and 3 – the 1st, 2nd, and 3rd stimulation pools, respectively; 15, 30 and 45 days – the corresponding day after the initiation of atrophy; *p <0.05 compared with the control; #p <0.05 compared with the atrophy group

In conclusion, it should be noted that up to now no effective drugs have been developed to prevent the development of atrophic processes in skeletal muscle during prolonged immobilization. For example, the MG132 proteasome inhibitor is only slightly able to prevent muscle atrophy (Jamart *et al*., 2011). Research (Cozzoli *et al*., 2013) has demonstrated the use of anabolic steroids to counteract muscle atrophy, but their effectiveness remains controversial due to side effects that occur in the cardiac tissue. Recent studies (Yoshihara *et al*., 2022) revealed that losartan, as antagonist of angiotensin II type 1 receptor, is able to partially protect the *muscle soleus* from hindlimb atrophy by reducing TGF-β signaling and inhibiting remodeling. However, for moderate and severe atrophy, the described positive effects do not apply. Finally, as A. Shally and B. McDonagh (2020) showed, oxidative stress, which is a consequence of the development of muscle atrophy after immobilization, plays a key role in the development of this pathology, and its reduction leads to a significant positive therapeutic effect confirmed by the above results on the use of antioxidants C_{60} fullerenes.

CONCLUSIONS

During the experiments lasting 15, 30, and 45 days after modeling muscle atrophy (achillotomy) in rats, an increase in the biomechanical parameters of *muscle soleus* contraction was recorded, namely by about 29–49±2 % for the maximum contraction force and by 21–37±2 % for the muscle force impulse with daily oral administration of

C_{60} fullerene aqueous solution at a dose of 1 mg/kg. Therefore, the use of water-soluble C_{60} fullerene as a therapeutic nanoagent is promising for reducing dystrophic changes in *muscle soleus* caused by prolonged immobilization.

ACKNOWLEDGMENT

The research was supported by the Ministry of Education and Science of Ukraine (project No. 24БП018-02).

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential 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, [D.N.; Y.P.]; methodology, [D.N.; Y.P.]; investigation, [D.N.; K.B.]; writing – original draft preparation, [D.N.; M.P.; Y.P.]; writing – review and editing, [M.P.; Y.P.]; visualization, [D.N.]; supervision, [Y.P.]; project administration, [D.N.; I.P.; Y.P.]; obtaining financing, [D.N.; K.B.; I.P.; Y.P.].

All authors have read and agreed to the published version of the manuscript.

REFERENCES

Appell, H.-J. (1990). Muscular atrophy following immobilization. *Sports Medicine*, 10(1), 42–58. doi:10.2165/00007256-199010010-00005
Crossref ● PubMed ● Google Scholar

Cao, R. Y., Li, J., Dai, Q., Li, Q., & Yang, J. (2018). Muscle atrophy: present and future. In J. Xiao (Ed.), *Muscle atrophy. Advances in experimental medicine and biology* (Vol. 1088, pp. 605–624). Singapore: Springer. doi:10.1007/978-981-13-1435-3_29
Crossref ● PubMed ● Google Scholar

Cozzoli, A., Capogrosso, R. F., Sblendorio, V. T., Dinardo, M. M., Jagerschmidt, C., Namour, F., Camerino, G. M., & De Luca, A. (2013). (2013). GLPG0492, a novel selective androgen receptor modulator, improves muscle performance in the exercised-mdx mouse model of muscular dystrophy. *Pharmacological Research*, 72, 9–24. doi:10.1016/j.phrs.2013.03.003
Crossref ● PubMed ● Google Scholar

Eswaran, S. V. (2018). Water soluble nanocarbon materials: a panacea for all? *Current Science*, 114(9), 1846–1850. doi:10.18520/cs/v114/i09/1846-1850
Crossref ● Google Scholar

Gharbi, N., Pressac, M., Hadchouel, M., Szwarc, H., Wilson, S. R., & Moussa, F. (2005). [60] Fullerene is a powerful antioxidant *in vivo* with no acute or subacute toxicity. *Nano Letters*, 5(12), 2578–2585. doi:10.1021/nl051866b
Crossref ● PubMed ● Google Scholar

Goodarzi, S., Da Ros, T., Conde, J., Sefat, F., & Mozafari, M. (2017). Fullerene: biomedical engineers get to revisit an old friend. *Materials Today*, 20(8), 460–480. doi:10.1016/j.mattod.2017.03.017
Crossref ● Google Scholar

Grebowski, J., Kazmierska, P., & Krokosz, A. (2013). Fullerenols as a new therapeutic approach in nanomedicine. *BioMed Research International*, 2013, 751913–751922. doi:10.1155/2013/751913
Crossref ● PubMed ● PMC ● Google Scholar

Hodgson, J. A., Roy, R. R., Higuchi, N., Monti, R. J., Zhong, H., Grossman, E., & Edgerton V. R. (2005). Does daily activity level determine muscle phenotype? *The Journal of Experimental Biology*, 208(1), 3761–3770. doi:10.1242/jeb.01825
Crossref ● PubMed ● Google Scholar

Jamart, C., Raymackers, J., Li An, G., Deldicque, L., & Francaux, M. (2011). Prevention of muscle disuse atrophy by MG132 proteasome inhibitor. *Muscle Nerve*, 43(5), 708–716. doi:10.1002/mus.21949
Crossref ● PubMed ● Google Scholar

Jørgensen, S. L., Kierkegaard-Brøchner, S., Bohn, M. B., Høgsholt, M., Aagaard, P., & Mechlenburg, I. (2023). Effects of blood-flow restricted exercise versus conventional resistance training in musculoskeletal disorders – a systematic review and meta-analysis. *BMC Sports Science, Medicine and Rehabilitation*, 15(1), 141. doi:10.1186/s13102-023-00750-z
Crossref ● PubMed ● PMC ● Google Scholar

Jozsa, L., Thöring, J., Järvinen, M., Kannus, P., Lehto, M., & Kvist, M. (1988). Quantitative alterations in intramuscular connective tissue following immobilization: an experimental study in the rat calf muscles. *Experimental & Molecular Pathology*, 49(2), 267–278. doi:10.1016/0014-4800(88)90039-1
Crossref ● PubMed ● Google Scholar

Nozdrenko, D., Abramchuk, O., Prylutska, S., Vygovska, O., Soroca, V., Bogutska, K., Khrapatyi, S., Prylutskyy, Y., Scharff, P., & Ritter, U. (2021a). Analysis of biomechanical parameters of *muscle soleus* contraction and blood biochemical parameters in rat with chronic glyphosate intoxication and therapeutic use of C_{60} fullerene. *International Journal of Molecular Sciences*, 22(9), 4977. doi:10.3390/ijms22094977
Crossref ● PubMed ● PMC ● Google Scholar

Nozdrenko, D., Matvienko, T., Vygovska, O., Bogutska, K., Motuziuk, O., Nurishchenko, N., Prylutskyy, Y., Scharff, P., & Ritter, U. (2021b). Protective effect of water-soluble C_{60} fullerene nanoparticles on the ischemia-reperfusion injury of the *muscle soleus* in rats. *International Journal of Molecular Sciences*, 22(13), 6812. doi:10.3390/ijms22136812
Crossref ● PubMed ● PMC ● Google Scholar

Nozdrenko, D., Matvienko, T., Vygovska, O., Soroca, V., Bogutska, K., Zholos, A., Scharff, P., Ritter, U., & Prylutskyy, Y. (2022). Post-traumatic recovery of *muscle soleus* in rats is improved via synergistic effect of C_{60} fullerene and TRPM8 agonist menthol. *Applied Nanoscience*, 12(3), 467–478. doi:10.1007/s13204-021-01703-z
Crossref ● Google Scholar

Ohira, Y., Yoshinaga, T., Nomura, T., Kawano, F., Ishihara, A., Nonaka, I., Roy, R. R., & Edgerton, V. R. (2002). Gravitational unloading effects on muscle fiber size, phenotype and myonuclear number. *Advances in Space Research*, 30(4), 777–781. doi:10.1016/s0273-1177(02)00395-2
Crossref ● PubMed ● Google Scholar

Paddon-Jones, D., Sheffield-Moore, M., Cree, M. G., Hewlings, S. J., Aarsland, A., Wolfe, R. R., & Ferrando, A. A. (2006). Atrophy and impaired muscle protein synthesis during prolonged inactivity and stress. *The Journal of Clinical Endocrinology & Metabolism*, 91(12), 4836–4841. doi:10.1210/jc.2006-0651
Crossref ● PubMed ● Google Scholar

Prilutski, Yu. I., Durov, S. S., Yashchuk, V. N., Ogul'chansky, T. Yu., Pogorelov, V. E., Astashkin, Yu. A., Buzaneva, E. V., Kirghisov, Yu. D., Andrievsky, G. V., & Scharff, P. (1999).

Theoretical predictions and experimental studies of self-organization C_{60} nanoparticles in water solution and on the support. In A. Châtelain, J. M. Bonard (Eds.), *The European Physical Journal D: Atomic, molecular and optical physics* (pp. 341–343). Berlin: Heidelberg. doi:10.1007/978-3-642-88188-6_65
Crossref ● Google Scholar

Prylutskyy, Y. I., Vereshchaka, I. V., Maznychenko, A. V., Bulgakova, N. V., Gonchar, O. O., Kyzyma, O. A., Ritter, U., Scharff, P., Tomiak, T., Nozdrenko, D. M., Mishchenko, I. V., & Kostyukov, A. I. (2017). C_{60} fullerene as promising therapeutic agent for correcting and preventing skeletal muscle fatigue. *Journal of Nanobiotechnology*, 15(1), 8. doi:10.1186/s12951-016-0246-1
Crossref ● PubMed ● PMC ● Google Scholar

Rong, Z., Yang, Z., Zhang, C., Pu, R., Chen, C., Xu, J., & Fei, L. (2023). Bioinformatics analysis of paravertebral muscles atrophy in adult degenerative scoliosis. *Journal of Muscle Research and Cell Motility*, 44(4), 287–297. doi:10.1007/s10974-023-09650-8
Crossref ● PubMed ● PMC ● Google Scholar

Rüegg, M. A., & Glass, D. J. (2011). Molecular mechanisms and treatment options for muscle wasting diseases. *Annual Review of Pharmacology and Toxicology*, 51(1), 373–395. doi:10.1146/annurev-pharmtox-010510-100537
Crossref ● PubMed ● Google Scholar

Ryan, J. J., Bateman, H. R., Stover, A., Gomez, G., Norton, S. K., Zhao, W., Schwartz, L. B., Lenk, R., & Kepley, C. L. (2007). Fullerene nanomaterials inhibit the allergic response. *Journal of Immunology*, 179(1), 665–672. doi:10.4049/jimmunol.179.1.665
Crossref ● PubMed ● Google Scholar

Sayed, R. K. A., Hibbert, J. E., Jorgenson, K. W., & Hornberger, T. A. (2023). The structural adaptations that mediate disuse-induced atrophy of skeletal muscle. *Cells*, 12(24), 2811. doi:10.3390/cells12242811
Crossref ● PubMed ● PMC ● Google Scholar

Scharff, P., Carta-Abelmann, L., Siegmund, C., Matyshevska, O. P., Prylutska, S. V., Koval, T. V., Golub, A. A., Yashchuk, V. M., Kushnir, K. M., & Prylutskyy, Yu. I. (2004). Effect of X-ray and UV irradiation of the C_{60} fullerene aqueous solution on biological samples. *Carbon*, 42(5–6), 1199–1201. doi:10.1016/j.carbon.2003.12.055
Crossref ● Google Scholar

Shally, A., & McDonagh, B. (2020). The redox environment and mitochondrial dysfunction in age-related skeletal muscle atrophy. *Biogerontology*, 21(4), 461–473. doi:10.1007/s10522-020-09879-7
Crossref ● PubMed ● Google Scholar

Thomason, D. B., & Booth, F. W. (1990). Atrophy of the soleus muscle by hindlimb unweighting. *Journal of Applied Physiology*, 68(1), 1–12. doi:10.1152/jappl.1990.68.1.1
Crossref ● PubMed ● Google Scholar

Tidball, J. G. (2005). Inflammatory processes in muscle injury and repair. *American journal of physiology. Regulatory, integrative and comparative physiology*, 288(2), R345–R353. doi:10.1152/ajpregu.00454.2004
Crossref ● PubMed ● Google Scholar

Tidball, J. G., & Villalta S. A. (2010). Regulatory interactions between muscle and the immune system during muscle regeneration. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, 298(5), R1173–R1187. doi:10.1152/ajpregu.00735.2009
Crossref ● PubMed ● PMC ● Google Scholar

Tischler, M. E., & Slentz, M. (1995). Impact of weightlessness on muscle function. *ASGSB Bulletin: Publication of the American Society for Gravitational and Space Biology*, 8(2), 73–81.
Google Scholar

Vereshchaka, I. V., Bulgakova, N. V., Maznychenko, A. V., Gonchar, O. O., Prylutskyy, Yu. I., Ritter, U., Moska, W., Tomiak, T., Nozdrenko, D. M., Mishchenko, I. V., & Kostyukov, A. I. (2018). C_{60} fullerenes diminish the muscle fatigue in rats comparable to *N*-acetylcysteine or β-alanine. *Frontiers in Physiology*, 9, 517. doi:10.3389/fphys.2018.00517
Crossref ● PubMed ● PMC ● Google Scholar

Yoshihara, T., Takaragawa, M., Dobashi, S., & Naito, H. (2022). Losartan treatment attenuates hindlimb unloading-induced atrophy in the *soleus muscle* of female rats via canonical TGF-β signaling. *Journal of Physiological Sciences*, 72, 6. doi:10.1186/s12576-022-00830-8
Crossref ● PubMed ● PMC ● Google Scholar

Zuccaro, E., Marchioretti, C., Pirazzini, M., & Pennuto, M. (2023). Introduction to the special issue "Skeletal muscle atrophy: mechanisms at a cellular level". *Cells*, 12(3), 502. doi:10.3390/cells12030502
Crossref ● PubMed ● PMC ● Google Scholar

C_{60} ФУЛЕРЕН СПРИЯЄ ВІДНОВЛЕННЮ ДИНАМІКИ СКОРОЧЕННЯ *MUSCLE SOLEUS* ПІСЛЯ СПРИЧИНЕНОЇ АХІЛЛОТОМІЄЮ АТРОФІЇ

Дмитро Ноздренко, Катерина Богуцька, Ігор Пампуха, Микола Петровський, Юрій Прилуцький

Київський національній університет імені Тараса Шевченка
вул. Володимирська, 64, Київ 01601, Україна

Обґрунтування. Пошук нових засобів, які дали б змогу ефективно впливати на патологічні наслідки знерухомлення м'язів, є вкрай необхідним запитом сучасної біомедицини. Раніше було встановлено позитивний вплив водного розчину C_{60} фулеренів як потужних антиоксидантів на тлі м'язової ішемії, механічної м'язової травми та деяких інших м'язових дисфункцій, що достовірно захищало м'язову тканину від пошкодження, зумовленого окисним стресом.

Матеріали та методи. Досліджено біомеханічні параметри скорочення *muscle soleus* щурів за імітації нефункціонування задніх кінцівок з використанням клінічної моделі – розриву ахіллового сухожилля (ахіллотомія). Біомеханічні параметри скорочення м'яза, а саме максимальна сила скорочення та імпульс м'язової сили, визначали на 15-ту, 30-ту і 45-ту добу після ініціації атрофії за використання тензометрії. Як терапевтичний наноагент використовували пероральне щоденне введення водного розчину C_{60} фулеренів у дозі 1 мг/кг упродовж експерименту.

Результати. Попередня реєстрація сили скорочення *muscle soleus* під час застосування 1 Гц стимуляції тривалістю 1800 с трьома пулами виявляла зменшення максимальних силових відповідей після 15, 30 та 45 доби атрофії. 45-ту добу після атрофії вважають граничною для максимально швидкого відновлення м'яза після знерухомлення, подальший процес відбувається упродовж кількох місяців. За терапевтичного введення водного розчину C_{60} фулеренів (доза 1 мг/кг) у всіх проведених тестах фіксували зростання біомеханічних параметрів (максимальної сили скорочення – зміна форми залежності "стимуляція–сила скорочення" є наслідком розвитку патологічного процесу у м'язі та імпульсу м'язової сили, який дає змогу оцінити працездатність м'язової системи після тривалого знерухомлення), а саме приблизно на 29–49±2 % для максимальної сили скорочення та на 21–37±2 % для імпульсу м'язової сили, порівняно з групою атрофія упродовж 15, 30 та 45 діб.

Висновки. Отримані результати свідчать про перспективність застосування водного розчину C_{60} фулеренів, здатних зменшувати/коригувати патологічні стани м'язової системи, що виникають за атрофії скелетних м'язів унаслідок їхнього знерухомлення.

***Ключові слова*:** *muscle soleus*, атрофія, C_{60} фулерен, біомеханічні параметри м'язового скорочення

Received / Одержано 31 January, 2024 | Revision / Доопрацьовано 18 July, 2024 | Accepted / Прийнято December, 2024 | Published / Опубліковано December, 2024