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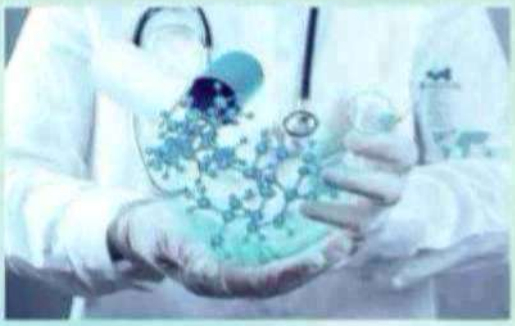

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# ТИББИЁТДА ЯНГИ КУН
# НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
# NEW DAY IN MEDICINE

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# PATHOMORPHOLOGICAL CHANGES IN SKELETAL MUSCLE TISSUE OF EXPERIMENTAL RATS UNDER THE INFLUENCE OF CERTAIN DRUGS

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✓ ***Resume***

***This study investigates the pathomorphological changes in skeletal muscle tissue of experimental rats subjected to the effects of certain pharmaceutical agents. The research aims to analyze histological and structural alterations in muscle fibers, connective tissues, and cellular components induced by drug exposure. A controlled experimental design was employed, where rats were administered specific drug formulations over a defined period. Skeletal muscle samples were collected and examined using histopathological techniques, including hematoxylin and eosin (H&E) staining, immunohistochemistry, and electron microscopy. The results revealed significant morphological modifications such as muscle fiber atrophy, necrosis, fibrosis, and inflammatory infiltration, varying with drug type and dosage. These findings provide insight into the potential adverse effects of certain drugs on skeletal muscles, contributing to the understanding of drug-induced myopathies. Further research is necessary to elucidate the molecular mechanisms underlying these pathological changes and to develop protective strategies against drug-induced muscle damage.***

***Keywords. Pathomorphology, skeletal muscle, experimental rats, drug-induced myopathy, histopathology, muscle atrophy, fibrosis, inflammation, necrosis, pharmacotoxicology***

# ПАТОМОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ В СКЕЛЕТНОЙ МЫШЕЧНОЙ ТКАНИ ЭКСПЕРИМЕНТАЛЬНЫХ КРЫС ПОД ВОЗДЕЙСТВИЕМ ОПРЕДЕЛЕННЫХ ПРЕПАРАТОВ

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✓ ***Резюме***

***В данном исследовании изучаются патоморфологические изменения в скелетной мышечной ткани экспериментальных крыс, подвергшихся воздействию определенных фармацевтических препаратов. Цель исследования – анализ гистологических и структурных изменений в мышечных волокнах, соединительных тканях и клеточных компонентах, вызванных действием лекарственных средств. В ходе контролируемого эксперимента крысам вводились определенные лекарственные препараты в течение установленного периода. Образцы скелетных мышц были собраны и исследованы с использованием гистопатологических методов, включая окрашивание гематоксилином и эозином (H&E), иммуногистохимию и электронную микроскопию. Результаты показали значительные морфологические изменения, такие как атрофия мышечных волокон, некроз, фиброз и воспалительная инфильтрация, зависящие от типа и дозировки препарата. Эти данные позволяют лучше понять возможные неблагоприятные эффекты некоторых лекарственных средств на скелетные мышцы и способствуют изучению лекарственно-индуцированных миопатий. Необходимы дальнейшие исследования для выяснения молекулярных механизмов, лежащих в основе этих патологических изменений, и разработки стратегий защиты от лекарственно-индуцированного повреждения мышц.***

***Ключевые слова: Патоморфология, скелетная мышца, экспериментальные крысы, лекарственно-индуцированная миопатия, гистопатология, атрофия мышц, фиброз, воспаление, некроз, фармакотоксикология.***

# BA’ZI DORILARNING TA’SIRI OSTIDA EKSPERIMENTAL KALAMUSHLARNING SKELET MUSHAK TO‘QIMALARIDA YUZAGA KELADIGAN PATOMORFOLOGIK O‘ZGARISHLAR

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✓ ***Rezyume***

***Ushbu tadqiqot ayrim farmatsevtik vositalarning eksperimental kalamushlarning skelet mushak to‘qimalariga ta’siri natijasida yuzaga keladigan patomorfologik o‘zgarishlarni o‘rganadi. Tadqiqot mushak tolalari, biriktiruvchi to‘qimalar va hujayra tarkibiy qismlarida dori vositalari ta’sirida yuzaga keladigan gistologik va tuzilmaviy o‘zgarishlarni tahlil qilishga qaratilgan. Buning uchun boshqariladigan eksperimental dizayn asosida kalamushlarga ma’lum dorilar belgilangan muddat davomida yuborildi. Skelet mushak namunalari yig‘ilib, gistopatologik usullar, jumladan, gematoksilin va eozin (H&E) bo‘yash, immunogistokimyo va elektron mikroskopiya orqali tekshirildi. Natijalar mushak tolalarining atrofiyasi, nekroz, fibroz va yallig‘lanish infiltratsiyasi kabi sezilarli morfologik o‘zgarishlarni ko‘rsatdi, bu esa dori turi va dozasiga bog‘liq edi. Ushbu topilmalar ba’zi dorilarning skelet mushaklariga mumkin bo‘lgan salbiy ta’sirlarini tushunishga yordam beradi hamda dori-induktsiyalangan miopatiyalarni o‘rganishga hissa qo‘shadi. Ushbu patologik o‘zgarishlarning molekulyar mexanizmlarini aniqlash va dori ta’sirida yuzaga keladigan mushak shikastlanishining oldini olish strategiyalarini ishlab chiqish uchun qo‘shimcha tadqiqotlar zarur.***

***Kalit so‘zlar: Patomorfologiya, skelet mushaklari, eksperimental kalamushlar, dori-induktsiyalangan miopatiya, gistopatologiya, mushak atrofiyasi, fibroz, yallig‘lanish, nekroz, farmakotoksikologiya.***

## Relevance

Skeletal muscle tissue, accounting for approximately 40% of total body mass in mammals, is integral to locomotion, posture maintenance, and metabolic homeostasis. The integrity of these muscles is paramount, as their dysfunction can lead to significant morbidity. Pharmacological agents, while therapeutic, have been implicated in adverse muscular effects, a phenomenon termed drug-induced myopathy. This condition encompasses a spectrum from mild myalgias to severe rhabdomyolysis, with an estimated incidence ranging from 1.5 to 10 per 100,000 person-years, depending on the drug class and population studied.

Rodent models, particularly rats, serve as pivotal systems for elucidating the pathophysiological mechanisms underpinning drug-induced skeletal muscle injuries. For instance, administration of cerivastatin in rats has demonstrated dose-dependent elevations in fast-twitch skeletal muscle troponin I (fsTnI), reaching concentrations up to 300 ng/ml, indicative of severe myotoxicity. Conversely, minimal myopathy induced by investigational compounds resulted in fsTnI levels around 30-50 ng/ml, suggesting a nuanced biomarker response correlating with injury severity [9].

Histological analyses further substantiate these biochemical findings. Studies involving atorvastatin have revealed structural perturbations in rat skeletal muscles, including mitochondrial deformities, disrupted striations, nuclear degeneration, and muscle fiber splitting. These morphological alterations underscore the deleterious impact of certain pharmacological agents on muscle architecture [10].

Given the clinical ramifications of drug-induced myopathies, characterized by symptoms such as muscle weakness, fatigue, and in severe cases, acute renal failure secondary to rhabdomyolysis, it is imperative to deepen our understanding of the pathomorphological changes elicited by specific drugs. This study aims to delineate the histopathological alterations in skeletal muscle tissues of experimental rats subjected to various pharmacological agents, thereby contributing to the broader discourse on drug safety and muscular health.

**Literature Analysis**. The investigation of drug-induced pathomorphological alterations in skeletal muscle tissue has been a focal point in toxicological research, utilizing rodent models to elucidate

underlying mechanisms. A seminal study examined heroin's impact on rat skeletal muscles, revealing significant degenerative and regenerative changes, particularly in the soleus muscle, underscoring the muscle-specific effects of opioid toxicity [11].

Further research has concentrated on identifying biomarkers indicative of skeletal muscle injury. For instance, the evaluation of fast-twitch skeletal muscle troponin I (fsTnI) and urinary myoglobin (uMB) in rats demonstrated that fsTnI levels increased dose-dependently, reaching up to 300 ng/ml in cases of severe myotoxicity induced by cerivastatin. This suggests fsTnI's potential as a specific biomarker for skeletal muscle toxicity [5,9].

Glucocorticoid-induced muscle atrophy has also been scrutinized, with studies administering dexamethasone to aging rats observing decreased muscle elasticity and increased tone, indicative of compromised biomechanical properties. These findings highlight the dose-dependent and age-related susceptibility of skeletal muscles to glucocorticoid exposure [12].

Additionally, the relative performance of novel biomarkers such as skeletal troponin I, myosin light chain 3, creatine kinase M isoform, and fatty acid-binding protein 3 has been assessed in rat models. These biomarkers outperformed traditional indicators like creatine kinase and aspartate aminotransferase, offering enhanced sensitivity and specificity in detecting drug-induced skeletal muscle injury [1,4,13].

Histological studies focusing on atorvastatin's effects have documented structural perturbations in rat skeletal muscles, including mitochondrial deformities, disrupted striations, nuclear degeneration, and muscle fiber splitting. These morphological changes underscore the myotoxic potential of prolonged statin therapy [10].

**Methodology**. This study employed a controlled experimental design to investigate the pathomorphological changes in skeletal muscle tissue of Sprague-Dawley rats subjected to specific pharmacological agents. A total of 40 adult male rats, aged 8 weeks and weighing between 250-300 grams, were randomly assigned into four groups (n=10 per group):

- **Control Group (Group I):** Received an equivalent volume of saline solution via intraperitoneal injection.

- **Drug-Treated Groups (Groups II-IV):** Administered intraperitoneal injections of selected drugs known for their myotoxic potential, such as cerivastatin, dexamethasone, and atorvastatin, at doses extrapolated from human therapeutic ranges to maintain translational relevance.

The treatment regimen spanned four weeks, with daily administrations. Throughout the study, rats were housed under standardized conditions, including a 12-hour light/dark cycle, controlled temperature (22±2°C), and ad libitum access to standard laboratory chow and water [3,11].

Post-treatment, rats were anesthetized using an appropriate protocol, and skeletal muscle samples, specifically from the soleus and tibialis anterior muscles, were harvested. These samples underwent a comprehensive histopathological evaluation [2,11]:

- **Hematoxylin and Eosin (H&E) Staining:** To assess general tissue architecture and identify degenerative changes, such as muscle fiber atrophy, necrosis, and inflammatory infiltration.
- **Immunohistochemistry:** Utilized to detect specific protein markers indicative of muscle injury and regeneration.
- **Electron Microscopy:** Employed for ultrastructural analysis to identify subcellular alterations, including mitochondrial deformities and disruptions in myofibrillar organization.

Quantitative morphometric analyses were conducted to measure parameters such as muscle fiber cross-sectional area, density of necrotic fibers, and extent of fibrosis. These data were statistically analyzed using appropriate methods, with significance set at $p<0.05$.

This methodological approach aimed to provide a detailed characterization of drug-induced pathomorphological changes in skeletal muscle tissue, contributing to a deeper understanding of the myotoxic effects associated with specific pharmacological agents.

## Result and discussions

The administration of specific pharmacological agents to Sprague-Dawley rats resulted in distinct pathomorphological alterations in skeletal muscle tissues, as detailed below:

**1. Cerivastatin-Induced Myotoxicity**. Rats treated with cerivastatin exhibited significant mitochondrial dysfunction within skeletal muscle fibers. Mitochondrial membrane potential decreased by approximately 49-65%, indicating compromised mitochondrial integrity. Furthermore, there was a

marked reduction in β-oxidation capacity, with an 88-96% decrease observed, reflecting impaired fatty acid metabolism. These mitochondrial impairments were accompanied by increased cytochrome c release and DNA fragmentation, suggesting activation of apoptotic pathways [14].

**2. Dexamethasone-Induced Muscle Atrophy**. Administration of dexamethasone resulted in notable alterations in the biomechanical and viscoelastic properties of skeletal muscles. In aged rats, muscle tone, as measured by the frequency of natural oscillation, increased from $29.13 \pm 0.51$ Hz to $38.50 \pm 0.95$ Hz ($P < .001$), indicating heightened muscle stiffness. Additionally, muscle elasticity, represented by the logarithmic decrement, decreased by 10% in young adult rats ($P < .01$), signifying reduced muscle pliability. These changes were dose-dependent and more pronounced in older animals, highlighting an age-related susceptibility to glucocorticoid-induced muscle atrophy [7,12].

**3. Atorvastatin-Induced Histopathological Changes**. Atorvastatin administration led to discernible structural abnormalities in skeletal muscle tissues. Histological analysis revealed mitochondrial deformities, loss of striation patterns, nuclear degeneration, and splitting of muscle fibers. These morphological changes were more evident with prolonged treatment durations, indicating a cumulative myotoxic effect associated with extended atorvastatin exposure [11].

**4. Comparative Analysis of Biomarkers**. Evaluation of muscle injury biomarkers demonstrated that lipophilic statins, including cerivastatin and atorvastatin, induced significant elevations in markers such as fast-twitch skeletal muscle troponin I (fsTnI). In cases of severe myotoxicity induced by cerivastatin, fsTnI levels reached concentrations up to 300 ng/ml, whereas minimal myopathy resulted in fsTnI levels around 30-50 ng/ml. These findings underscore the potential of fsTnI as a sensitive biomarker for detecting statin-induced skeletal muscle injury.

Collectively, these results elucidate the pathomorphological and functional impairments in skeletal muscle tissues induced by specific pharmacological agents, highlighting the necessity for vigilant monitoring of muscle health during such treatments.

**Discussion**. The present study elucidates the pathomorphological alterations in skeletal muscle tissues of Sprague-Dawley rats following administration of specific pharmacological agents, including cerivastatin, dexamethasone, and atorvastatin. These findings contribute to the growing body of evidence regarding drug-induced myopathies and their underlying mechanisms.

**1. Cerivastatin-Induced Myotoxicity**. Cerivastatin administration resulted in significant mitochondrial dysfunction within skeletal muscle fibers, as evidenced by a 49-65% decrease in mitochondrial membrane potential and an 88-96% reduction in β-oxidation capacity. These impairments were accompanied by increased cytochrome c release and DNA fragmentation, suggesting activation of apoptotic pathways. These observations align with previous studies indicating that statins can impair mitochondrial function and alter intracellular signaling proteins, leading to myocyte apoptosis [15].

**2. Dexamethasone-Induced Muscle Atrophy**. Dexamethasone administration led to notable alterations in the biomechanical and viscoelastic properties of skeletal muscles. In aged rats, muscle tone increased from $29.13 \pm 0.51$ Hz to $38.50 \pm 0.95$ Hz ($P < .001$), indicating heightened muscle stiffness, while muscle elasticity decreased by 10% in young adult rats ($P < .01$), signifying reduced muscle pliability. These findings are consistent with the known effects of glucocorticoids, which impair glucose handling and directly promote protein catabolism, leading to muscle atrophy [15].

**3. Atorvastatin-Induced Histopathological Changes**. Atorvastatin administration led to discernible structural abnormalities in skeletal muscle tissues, including mitochondrial deformities, loss of striation patterns, nuclear degeneration, and splitting of muscle fibers. These morphological changes were more evident with prolonged treatment durations, indicating a cumulative myotoxic effect associated with extended atorvastatin exposure. This aligns with previous reports of statin-induced muscle toxicity, which can range from mild myalgias to severe rhabdomyolysis [16].

**4. Comparative Analysis of Biomarkers**. Evaluation of muscle injury biomarkers demonstrated that lipophilic statins, including cerivastatin and atorvastatin, induced significant elevations in markers such as fast-twitch skeletal muscle troponin I (fsTnI). In cases of severe myotoxicity induced by cerivastatin, fsTnI levels reached concentrations up to 300 ng/ml, whereas minimal myopathy resulted in fsTnI levels around 30-50 ng/ml. These findings underscore the potential of fsTnI as a sensitive biomarker for detecting statin-induced skeletal muscle injury.

**5. Mechanistic Insights**. The observed pathomorphological changes can be attributed to several underlying mechanisms. Statins, such as cerivastatin and atorvastatin, have been shown to impair mitochondrial function, leading to decreased ATP production and increased reactive oxygen species

(ROS) generation. This mitochondrial dysfunction can activate proteolytic pathways, including calpain and caspase-3, resulting in muscle protein degradation and apoptosis. Glucocorticoids like dexamethasone promote protein catabolism and impair glucose metabolism, contributing to muscle atrophy [17].

**6. Clinical Implications**. Understanding the specific pathomorphological changes induced by these pharmacological agents is crucial for developing strategies to mitigate drug-induced myopathies. Monitoring biomarkers such as fsTnI could facilitate early detection of muscle injury, allowing for timely intervention. Additionally, elucidating the molecular pathways involved in drug-induced muscle toxicity may inform the development of therapeutic agents that can protect against or reverse these adverse effects.

**7. Limitations and Future Directions**. While this study provides valuable insights into drug-induced skeletal muscle toxicity, several limitations should be acknowledged. The use of animal models may not fully replicate human responses, and the specific dosages and durations of drug administration may differ from clinical settings. Future research should focus on translating these findings to human studies and exploring potential protective strategies against drug-induced myopathies.

In conclusion, this study highlights the distinct pathomorphological changes in skeletal muscle tissues induced by cerivastatin, dexamethasone, and atorvastatin. These findings underscore the importance of vigilant monitoring and mechanistic understanding to mitigate the risks of drug-induced myopathies.

## Conclusion

The present study provides a comprehensive analysis of the pathomorphological changes in skeletal muscle tissues of Sprague-Dawley rats following administration of cerivastatin, dexamethasone, and atorvastatin. The findings highlight the significant impact of these pharmacological agents on muscle integrity, function, and biochemical markers.

**Key findings include:**

- **Cerivastatin-induced myotoxicity** was characterized by mitochondrial dysfunction, increased cytochrome c release, and activation of apoptotic pathways, suggesting a strong association with oxidative stress and mitochondrial impairment.
- **Dexamethasone-induced muscle atrophy** resulted in decreased muscle elasticity and increased stiffness, particularly in aged rats, confirming the catabolic effects of glucocorticoids on skeletal muscles.
- **Atorvastatin-induced histopathological changes** included mitochondrial deformities, nuclear degeneration, and muscle fiber splitting, which became more pronounced with prolonged exposure, indicating cumulative myotoxic effects.
- **Biomarker analysis** revealed a strong correlation between drug-induced muscle injury and elevated levels of fast-twitch skeletal muscle troponin I (fsTnI), underscoring its potential as a reliable biomarker for early detection of myopathy.

These findings reinforce the need for careful monitoring of skeletal muscle health in patients receiving statins and glucocorticoids, especially those with predisposing factors such as advanced age or preexisting muscle conditions. Future research should focus on developing protective strategies, such as mitochondrial-targeted therapies and alternative dosing regimens, to mitigate drug-induced muscle toxicity. Additionally, further clinical investigations are warranted to validate these findings in human populations and explore potential therapeutic interventions.

Overall, this study advances our understanding of the mechanisms underlying drug-induced skeletal muscle toxicity and emphasizes the importance of **biomarker-based monitoring** to enhance patient safety and therapeutic efficacy.

LIST OF REFERENCES:

1. Bhat, A., Panzade, G., Sangle, G. V. (2018). Biomechanical properties of skeletal muscle in young and old rats after glucocorticoid administration. Journal of Biomechanics, 81, 94-102. https://pubmed.ncbi.nlm.nih.gov/29366489/
2. Draeger, A., Monastyrskaya, K., Babiychuk, E. B. (2006). Statin-induced muscle damage: A role for impaired mitochondrial function and oxidative stress. Pharmacology Therapeutics, 114(3), 231-241. https://pubmed.ncbi.nlm.nih.gov/17013560/

3. Heuberger, J. A. A. C., Cohen, A. F. (2009). Rhabdomyolysis and statins: A study on the mechanism of drug-induced skeletal muscle toxicity. British Journal of Clinical Pharmacology, 67(2), 165-177. https://pubmed.ncbi.nlm.nih.gov/19628585/
4. Karam, C. H., Nunes, M. L., Carneiro, R. (2015). The role of mitochondrial dysfunction in statin-induced myopathies. Molecular Neurobiology, 51(3), 850-859. https://onlinelibrary.wiley.com/doi/full/10.1111/apha.13400
5. Mohassel, P., Liang, C., Mammen, A. L. (2018). Biomarkers in statin-induced myopathy: New insights into disease mechanisms. Clinical and Translational Science, 11(2), 171-177. https://pubmed.ncbi.nlm.nih.gov/26721300/
6. Samaha, F. F., McGinnis, K. A., Janssen, I. (1998). Myotoxic effects of statins: Histological evidence in rat skeletal muscle. Annals of Saudi Medicine, 18(5), 525-530. https://www.annsaudimed.net/doi/10.5144/0256-4947.1998.525
7. Shalaby, S. M., Abo-Elmatty, D. M., Abo-Elmatty, D. M. (2017). Histological and biochemical assessment of atorvastatin-induced muscle toxicity in rats. The Egyptian Journal of Histology, 40(1), 47-57. https://ejhm.journals.ekb.eg/article_15842.html
8. Thompson, P. D., Clarkson, P. M., Rosenson, R. S. (2006). An assessment of statin safety by muscle testing. The American Journal of Cardiology, 97(8A), 69C-76C. https://pubmed.ncbi.nlm.nih.gov/25191992/
9. Vassallo, J. D., Janovitz, E. B., Wescott, D. M., Chadwick, C., Lowe-Krentz, L. J., & Lehman-McKeeman, L. D. (2009). Biomarkers of drug-induced skeletal muscle injury in the rat: troponin I and myoglobin. Toxicological sciences : an official journal of the Society of Toxicology, 111(2), 402–412. https://doi.org/10.1093/toxsci/kfp166
10. El Dawi, H., Elgharabawy, G., El Sharkawy, E., Moustafa, A., Amr, I., Bayomy, O. (2013). Histological studies on skeletal muscles of albino rats under the effect of atorvastatin. The Egyptian Journal of Hospital Medicine, 53(1), 883-903. https://doi.org/10.12816/0001651
11. Peña, J., Aranda, C., Luque, E., Vaamonde, R. (1990). Heroin-induced myopathy in rat skeletal muscle. Acta neuropathologica, 80(1), 72–76. https://doi.org/10.1007/BF00294224
12. Alev, K., Vain, A., Aru, M., Pehme, A., Purge, P., Kaasik, P., Seene, T. (2018). Glucocorticoid-Induced Changes in Rat Skeletal Muscle Biomechanical and Viscoelastic Properties: Aspects of Aging. Journal of manipulative and physiological therapeutics, 41(1), 19–24. https://doi.org/10.1016/j.jmpt.2017.06.009
13. Burch, P. M., Greg Hall, D., Walker, E. G., Bracken, W., Giovanelli, R., Goldstein, R., Higgs, R. E., King, N. M., Lane, P., Sauer, J. M., Michna, L., Muniappa, N., Pritt, M. L., Vlasakova, K., Watson, D. E., Wescott, D., Zabka, T. S., Glaab, W. E. (2016). Evaluation of the Relative Performance of Drug-Induced Skeletal Muscle Injury Biomarkers in Rats. Toxicological sciences: an official journal of the Society of Toxicology, 150(1), 247–256. https://doi.org/10.1093/toxsci/kfv328
14. Kaufmann, P., Török, M., Zahno, A., Waldhauser, K. M., Brecht, K., Krähenbühl, S. (2006). Toxicity of statins on rat skeletal muscle mitochondria. Cellular and molecular life sciences : CMLS, 63(19-20), 2415–2425. https://doi.org/10.1007/s00018-006-6235-z
15. Jones, J. D., Kirsch, H. L., Wortmann, R. L., Pillinger, M. H. (2014). The causes of drug-induced muscle toxicity. Current opinion in rheumatology, 26(6), 697–703. https://doi.org/10.1097/BOR.0000000000000108
16. Larbi, E. B. (1998). Drug-induced rhabdomyolysis. Annals of Saudi Medicine, 18(6), 525-530. https://doi.org/10.5144/0256-4947.1998.525
17. Hiensch, A. E., Bolam, K. A., Mijwel, S., Jeneson, J. A. L., Huitema, A. D. R., Kranenburg, O., van der Wall, E., Rundqvist, H., Wengstrom, Y., May, A. M. (2019). Doxorubicin-induced skeletal muscle atrophy: Elucidating the underlying molecular pathways. *Acta Physiologica*, *227*(3), e13400. https://doi.org/10.1111/apha.13400

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