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Azilsartan prevents muscle loss and fast- to slow-twitch muscle fiber shift in natural ageing sarcopenic rats

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Abstract

Sarcopenia is a musculoskeletal disease that reduces muscle mass and strength in older individuals. The study investigates the effects of azilsartan (AZL) on skeletal muscle loss in natural sarcopenic rats. Male Sprague-Dawley rats aged 4–6 months and 18–21 months were selected as young-matched control and natural-aged (sarcopenic) rats, respectively. Rats were allocated into young and old control (YC and OC) and young and old AZL treatment (YT and OT) groups, which received vehicles and AZL (8 mg/kg, orally) for 6 weeks. Rats were then sacrificed after muscle function analysis. Serum and gastrocnemius (GN) muscles were isolated for further endpoints. AZL significantly improved muscle grip strength and antioxidant levels in sarcopenic rats. AZL also restored the levels of insulin, testosterone, and muscle biomarkers such as myostatin and creatinine kinase in sarcopenic rats. Furthermore, AZL treatment improved the cellular and ultrastructure of GN muscle and prevented the shift of type II (glycolytic) myofibers to type I (oxidative) myofibers. The results showed that AZL intervention restored protein synthesis in natural sarcopenic rats by increasing p-Akt-1 and decreasing muscle RING-finger protein-1 and tumor necrosis factor alpha immunoexpressions. In conclusion, the present findings showed that AZL could be an effective intervention in treating age-related muscle impairments.

Key words: azilsartan, gastrocnemius muscle, muscle fiber, natural age, p-Akt, sarcopenia

Introduction

Sarcopenia is a geriatric syndrome that worsens older people's quality of life while impacting various organs and reducing muscular function, strength, and performance (Cruz-Jentoft et al. 2019). The guidelines for sarcopenia were recommended by the European Working Group on Sarcopenia in Older People 2 (EWGSOP) (Cruz-Jentoft et al. 2010) in 2010 and then later on by the Asian Working Group for Sarcopenia (Chen et al. 2020) in 2011, the International Working Group on Sarcopenia (Fielding et al. 2011) in 2011, and the Foundation for the National Institutes of Health (Studenski et al. 2014) in 2014. Further, the EWGSOP revised its guidelines (EWGSOP2), which define sarcopenia as a geriatric syndrome that worsens the quality of life for older people, affecting various organs and reducing muscular function, strength, and performance (Cruz-Jentoft et al. 2019). Recently, the South Asian scientific community, consisting of a group of geriatrics, endocrinology, and general medicine experts from South Asia and neighboring countries, made a consensus document known as the South Asian Working Action Group on Sarcopenia (SWAG-SARCO) (Dhar et al. 2022). Taken together, these guidelines and consensus documents indicate that people are now recognizing sarcopenia as a disease and encouraging its management and treatment.

Sarcopenia has been actively investigated using a range of models, such as Drosophila, *Caenorhabditis elegans*, genetically engineered models (e.g., IL-10(−/−), Sod1(−/−), knockout models), and accelerated aging models like senescence-accelerated prone (SAMP8, SAMP10, SAMP1, and SAMP6) (Xie et al. 2021). Furthermore, tail/hindlimb suspension models, denervation models, and immobilization models in rodents have been utilized extensively in sarcopenia-associated muscle atrophy research (Xie et al. 2021). However, the choice of employing aged rats in the current study as a sarcopenia model is particularly advantageous, given the inherent association between the condition and the aging process.

Several lines of evidence have studied the mechanism of sarcopenia, such as the orchestration between protein synthesis (mammalian target of rapamycin [mTOR],