[BIOINFO 2023]

Unraveling the Protective Mechanisms of Jakyak-gamcho-tang's Phytochemicals Against Muscle Atrophy

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Muscular atrophy, marked by the declining skeletal muscle mass and function, hinders physical performance, affecting patients' quality of life. Currently, there are no established therapeutic interventions for this condition, underscoring the urgent need for effective treatments. Our previous study showed that Jakyak-gamcho-tang (JGT), a decoction of Paeoniae Radix and Glycyrrhizae Radix et Rhizoma, has potential in alleviating muscle atrophy. This study aimed to decipher the protective mechanisms of JGT's phytochemicals confer these muscle-protective effects. We found that the ethanol extract (EJGT) of JGT is more effective than its water extract (WJGT) in protecting C2C12 myotubes from muscle atrophy induced by oxidative stress, palmitic acid, and dexamethasone. From the pathway analysis of the transcriptome data following EJGT and WJGT treatments, we found that EJGT treatment more significantly upregulated genes associated with mitochondria, oxidative phosphorylation, and PGC-1α and ERRα pathways. Network pharmacology analysis of JGT components, taking into account water solubility, revealed distinct molecular mechanisms between EJGT and WJGT. Further, we pinpointed key components that are more prevalent in EJGT, which have muscle-protective effects. Our findings may offer a foundation for developing natural product-based therapeutics targeting muscular atrophy.