Silymarin alleviates cisplatin-induced cachexia via modulating tripartite motif containing 63 (TRIM63) and myogenin

Shreya Das, Jyotika, Ritu Pahuja, Sapana Kushwaha[1], Richa Shrivastava

Abstract:

OBJECTIVE: Cachexia is one of the major chemotherapy-induced adverse effects, characterized by gradual depletion of muscle mass. Currently, there is no specific treatment for cachexia. This study aims to evaluate the role of silymarin in attenuating muscle wasting in a model of cisplatin-induced cachexia.

MATERIALS AND METHODS: Female Swiss albino mice were divided into three groups ($n = 6$) and received the treatment according to their group for 7 days: NC (Normal Control, receiving normal saline), CP (Cisplatin, receiving cisplatin 3 mg/kg i.p.) and SY+CP (Silymarin+Cisplatin, receiving silymarin 100 mg/kg orally two hours before cisplatin 3mg/kg i.p). Body weight, muscle weight, tumor necrosis factor alpha (TNF-α), and GSH levels were measured, and muscle histopathological studies were performed.

RESULTS: Silymarin prevented cisplatin-induced damage in the triceps, quadriceps, and gastrocnemius muscles. Cisplatin administration altered tissue architecture and decreased the size and cross-sectional area of all three muscle fibers, which were significantly restored in the silymarin-treated group. Muscle tissue homogenates from the silymarin-treated group exhibited higher levels of reduced glutathione compared to the cisplatin group. The elevated serum TNF-α levels in the cisplatin group were decreased from 183 ± 1.66 pg/mL to 117.40 ± 10.47 pg/mL in the silymarin-treated mice. Tripartite motif-containing 63 (TRIM63), a muscle atrophy marker, was upregulated, and myogenin, a marker of myogenesis, was decreased by cisplatin, and the expression of both markers was reversed upon silymarin treatment.

CONCLUSIONS: Silymarin attenuates cisplatin-induced cachexia through TRIM63 suppression, myogenin restoration, and reduced oxidative and inflammatory stress.

Keywords:

Chemotherapy, muscle wasting, myogenesis, oxidative stress, skeletal muscle