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The Effect of Schisandra chinensis Extract on Muscle Atrophy: A Systematic Review and Meta-Analysis of Preclinical Studies

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ADMINISTRATIVE INFORMATION

Support - Nonev.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590030

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 September 2025 and was last updated on 8 September 2025.

INTRODUCTION

Review question / Objective The primary objective was to quantitatively evaluate the intervention effects of Schisandra extract on animal models of muscle atrophy, including impacts on muscle structure (e.g., muscle weight, cross-sectional area), function (e.g., grip strength), and oxidative stress markers (e.g., CAT, MDA). This aims to address the evidence gap from dispersed and heterogeneous preclinical studies.

Condition being studied 1、Disease Concept: Muscle atrophy is a pathological condition characterized by progressive loss of skeletal muscle mass and function, involving mechanisms such as protein synthesis inhibition, enhanced degradation (e.g., via ubiquitin-proteasome system), mitochondrial dysfunction, and chronic inflammation.

2、Epidemiology: Globally, sarcopenia (a form of muscle atrophy) affects 10–16% of individuals over 60 years and exceeds 50% in those over 80.

3、Current Intervention Status and Gaps: Existing treatments (e.g., androgens, growth hormones, myostatin inhibitors) show limited efficacy and safety concerns (e.g., immunogenicity, cardiovascular risks). No approved specific drugs are available, highlighting a therapeutic gap.

4、Target Measure and Advantages: Schisandra extract, derived from Schisandra chinensis, offers multi-target potential through its lignans (e.g., schisandrin A/B), with advantages in antioxidant, anti-inflammatory, and protein metabolism modulation, as well as high safety as a natural phytochemical.

METHODS

Participant or population Animal models of muscle atrophy, including rats (n=2 studies), mice (n=8 studies), and fish (n=1 study). No human participants were involved.

Intervention Schisandra extract (crude or standardized) or its primary active lignan monomers (e.g., schisandrin A, schisandrin B,

gomisin G). Administration was primarily oral (10 studies) or intraperitoneal injection (1 study), with varying doses and durations.

Comparator Model control groups, which included vehicle-treated controls (7 studies), untreated controls (3 studies), or sham-operated controls (1 study).

Study designs to be included Randomized controlled trials (RCTs) on animal experiments were included, based on PICOS principles.

Eligibility criteria 1、Inclusion Criteria: Followed PICOS: (i) Animal models of muscle atrophy; (ii) Intervention with Schisandra extract or lignan monomers; (iii) Outcomes such as muscle weight, CSA, grip strength, oxidative stress markers (MDA, SOD, ROS, CAT, GSH), and protein expression (MuRF1, Atrogin1, Myostatin); (iv) Study type: RCTs.

2、Exclusion Criteria: Non-atrophy models; in vitro studies, reviews, case reports, clinical trials, abstracts, editorials, theses, conference papers; studies combining Schisandra with other therapies; studies lacking model control groups; incomplete data or duplicate publications.

3、Additional Criteria: Only final time-point data were used for meta-analysis; if multiple doses or models were present, one representative group was recorded. Disease diagnosis was implicit through the use of established muscle atrophy models (e.g., dexamethasone-induced or disuse atrophy), but specific diagnostic standards were not detailed. Intervention time varied across studies and was not standardized.

Information sources 1、Databases: PubMed, Web of Science, Embase, Cochrane Library, and Ovid.

2、Search Period: From database inception to April 2025.

3、Search Terms: Combined Medical Subject Headings (MeSH) and free-text terms for "Schisandra" (e.g., "schizandra," "Gomisi," "Wuweizi") and "muscle atrophy" (e.g., "Muscular Atrophy," "muscle wasting"). Specific strategies (e.g., for PubMed) are detailed in Supplementary Table 1 (not fully reproduced in the document).

Main outcome(s) 1、Muscle structural indicators: Muscle weight and muscle fiber cross-sectional area (CSA).

2、Functional indicators: Grip strength.

3、Oxidative stress markers: Catalase (CAT) activity, malondialdehyde (MDA) level, superoxide dismutase (SOD) activity, reactive oxygen species (ROS), and glutathione (GSH).

4、Protein expression markers: Myostatin, MuRF1, and Atrogin1.

Quality assessment / Risk of bias analysis Quality was assessed using the SYRCLE risk of bias tool, evaluating 10 domains (e.g., sequence generation, allocation concealment, blinding, incomplete outcome data). Each domain was rated as "low risk," "high risk," or "unclear risk," with a numerical score (max 20): 2 points for low risk, 0 for high risk, and 1 for unclear risk. Included studies scored 9–14, indicating moderate-to-low quality. Major limitations included unclear randomization methods (high risk in 7 studies), lack of allocation concealment (high/unclear risk), and insufficient blinding (high risk in 6 studies).

Strategy of data synthesis Data synthesis involved meta-analysis using RevMan 5.3 software. A random-effects model was applied due to anticipated heterogeneity. Effect sizes were reported as standardized mean differences (SMD) with 95% confidence intervals (CI). Heterogeneity was assessed using I^2 statistics ($I^2 > 50\%$ indicated high heterogeneity, requiring random-effects models). Statistical significance was set at $P < 0.05$. Funnel plots, Egger's, and Begg's tests were planned for publication bias.

Subgroup analysis Subgroup analysis was not performed due to the small sample size (11 studies) and high heterogeneity (I^2 = 80–95%) across outcomes, which limited the ability to explore sources of variability (e.g., animal model type, dosing regimen).

Sensitivity analysis Sensitivity analysis was not conducted, as mentioned in the limitations section. This omission hindered the assessment of result robustness.

Country(ies) involved China.

Keywords Schisandra, muscle atrophy, oxidative stress, meta-analysis, animal models.

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