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Emerging Therapeutic Approach For The Prevention And Reversal Of Muscle Atrophy

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Abstract

Skeletal muscle atrophy is a progressive condition characterized by loss of muscle mass, strength, and function due to enhanced proteolysis and impaired regeneration. Current pharmacologic interventions largely fail to provide dual-action benefits, leaving a critical gap in effective therapy. This study aimed to evaluate the preventive and regenerative potential of a novel compound, Curcumin-Boron Complex (Cur-B), in a dexamethasone-induced rat model of muscle atrophy. Twenty-four adult male Wistar rats were randomly divided into four groups: normal control, atrophy control, preventive treatment, and reversal treatment. Muscle atrophy was induced using intramuscular dexamethasone. Cur-B (10 mg/kg/day) was administered either concurrently (preventive) or after atrophy establishment (reversal). Efficacy was assessed using histopathology (H&E, Masson's Trichrome), immunohistochemistry (Atrogin-1, MuRF1, Pax7, MyoD, Myogenin), qRT-PCR, Western blotting, and ELISA. Cur-B significantly restored muscle weight in both preventive (1.66 ± 0.10 g) and reversal (1.57 ± 0.09 g) groups versus atrophy control (1.20 ± 0.08 g). Histological analysis showed increased muscle fiber cross-sectional area and reduced fibrosis. Cur-B downregulated catabolic markers (Atrogin-1: 85.2% to 41.5%) and upregulated regenerative markers (Pax7: 4.2 to 9.1 cells/field). Biochemical assays revealed reductions in IL-6 and MDA, and restoration of antioxidant enzymes. Cur-B exhibits significant dual-action efficacy in preventing and reversing muscle atrophy through anti-catabolic, anti-inflammatory, and pro-regenerative mechanisms. These results provide compelling translational evidence for Cur-B as a candidate therapeutic agent for muscle-wasting disorders.

[1] . INTRODUCTION

Skeletal muscle atrophy is a debilitating condition characterized by the progressive loss of muscle mass, fiber diameter, and contractile strength, driven by an imbalance between protein synthesis and degradation (Chaytow et al., 2021). This phenomenon, whether acute or chronic, stems from diverse etiologies such as prolonged inactivity, aging (sarcopenia), denervation, malnutrition, systemic inflammation, chronic illnesses like cancer or renal failure, and exogenous glucocorticoid administration (Furrer & Handschin, 2019; Wang et al., 2022). From a mechanistic standpoint, muscle wasting involves complex cellular and molecular cascades. Central to these processes are proteolytic systems such as the ubiquitin-proteasome system (UPS) and autophagy-lysosomal pathways, which are responsible for muscle protein breakdown. Additionally, the suppression of satellite cell activation and differentiation, elevated reactive oxygen species (ROS), mitochondrial dysfunction, and chronic pro-inflammatory signaling contribute to structural deterioration and impaired muscle regeneration (Chen et al., 2023; Muñoz-Cánoves et al., 2020). The clinical consequences of muscle atrophy are severe because it severely reduces mobility, functional independence, and metabolic resilience and is linked to greater morbidity and longer rehabilitation periods. Since the number of older people is growing at a global level, and glucocorticoid treatment remains a primary treatment method in autoimmune and inflammatory disorders, muscle atrophy becomes a growing healthcare concern (Huang et al., 2022; Doganay et al., 2025).

Nevertheless, treatment of muscle atrophy is very limited and mostly unsatisfactory, regardless of its significant importance. Pharmacologic approaches have been pursued, with anabolic drugs, namely, selective androgen receptor modulators (SARMs), 2-adrenergic agonists, and inhibitors of myostatin. Nevertheless, these agents have significant drawbacks such as cardiovascular side effects, hormonal disproportions, and negligible impact on the actual muscle regeneration (Yin et al., 2019; Verhaart & Aartsma-Rus, 2019). Furthermore, most of the investigational drugs do not enhance coordinated structural and molecular remodeling of the muscle tissue because they mainly focus on the suppression of catabolism rather than activation and differentiation of the

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satellite cells. Such discrepancy points to the need for agents with a dual therapeutic action, i.e., that attenuate the impact of muscle degradation and induce regenerative pathways. Noticing this gap, Curcumin-Boron Complex (Cur-B) has come up as a new candidate. According to a recent study by Zhou et al. (2022) in the Journal of Cellular Physiology, Cur-B had very specific bioactivity in musculoskeletal systems and could regulate the most important signaling pathways such as NF-kB and Akt/mTOR that play a significant role in the inflammation process, protein turnover, and cell proliferation. Compared to native curcumin, cur-B has increased stability and bioavailability and has anti-inflammatory, antioxidant, and myogenic activities, which makes it a rational candidate to be used to address two targets at once (Markati et al., 2022; Meyers & Townsend, 2019).

What is new about Cur-B is not only the molecular design, but also that it can go beyond the shortcomings of current therapies. In contrast to conventional agents, Cur-B has the potential to target both branches of the muscle atrophy cascade: to suppress the expression of proteolytic markers (e.g., Atrogin-1, MuRF1) and, at the same time, increase regenerative markers (e.g., Pax7, MyoD, Myogenin). Such molecular impacts correlate with structural conservation and restoration, and, therefore, are more inclusive in their therapeutic description (Wang et al., 2019). Moreover, although curcumin alone has been examined in numerous degenerative models, its low solubility and fast metabolism have inhibited its clinical improvement. To overcome these drawbacks, the following problems will be solved in the boron-stabilized complex: efficient delivery into the cell and a long biological life (Liu et al., 2022). Such interventions have not been rigorously validated in previous studies with robust histological and immunohistochemical (IHC) markers, and they have not examined either preventive or therapeutic timelines in the same experimental context, an innovation that this study aims to provide. The need to find effective interventions for muscle atrophy at clinical and translational levels cannot be underestimated. Most of the current approaches are focused on preventing or delaying muscle loss but do not lead to actual muscle regeneration or repair of the damaged architecture (Chen, 2020; Sun et al., 2020). A large number of available drugs are not tested by high-resolution tissue analysis, nor are they benchmarked with reference to their capacity to stimulate endogenous repair systems. Such morphological and immunohistochemical lack of validation restricts the confidence in their translational power. Thus, measuring the effectiveness of the therapy by means of well-developed approaches that involve histopathological scoring, immunohistochemical profiling, and molecular expression analysis is a decisive step towards the right direction. Especially, the Atrogin-1 and MuRF1 markers provide some data on the proteasomal activity, whereas Pax7 and MyoD markers reflect the regenerative potential of the muscle stem cells (Qazi et al., 2019; Paul et al., 2020). With the use of these markers, in combination with fibrosis and inflammation scores, one is able to further comprehend tissue remodeling, which will be necessary to support functional recovery claims.

This paper is especially placed to fill the identified gaps in the existing body of literature above. By incorporating a well-validated glucocorticoid-induced model of muscle atrophy, the experimental design mirrors clinically relevant myopathic conditions. The investigation further distinguishes itself by evaluating both preventive (cotreatment during atrophy induction) and reversal (post-atrophy treatment) timelines, providing comparative insight into Cur-B's stage-specific efficacy. Most importantly, the use of histological stains (H&E, Masson's Trichrome), IHC markers, and molecular assays (qRT-PCR, ELISA) ensures a multi-layered assessment of drug action, covering morphology, cell signaling, and biochemical stress responses. Thus, the study bridges the critical gap between preclinical observation and potential therapeutic translation.

Given the complex etiology and progression of muscle atrophy, any promising therapeutic approach must demonstrate broad-spectrum efficacy—combining anti-catabolic, anti-inflammatory, and pro-regenerative actions. This research aims to not only confirm the structural and molecular benefits of Cur-B but also set a precedent for rigorous evaluation of novel compounds using integrated tissue-based methodologies. The findings will serve

as a foundation for future translational work and potentially influence therapeutic pipelines for muscle wasting disorders.

The specific research objectives of this study are as follows:

1. To assess the preventive effect of the novel drug Curcumin-Boron Complex (Cur-B) in a dexamethasoneinduced muscle atrophy model.
2. To evaluate the regenerative effect of Cur-B following established muscle atrophy conditions.
3. To investigate the histopathological and immunohistochemical evidence of tissue remodeling and modulation of molecular targets in response to Cur-B therapy.

2. MATERIALS AND METHODS

2.1 Study Design

The study was a randomized, controlled, in vivo preclinical trial, which was designed to assess the efficacy of a novel therapeutic agent, Curcumin-Boron Complex (Cur-B), in the prevention and reversal of skeletal muscle atrophy. The time of the whole research was 28 days. Four groups of adult male Wistar rats were used, and dexamethasone was used to induce a validated muscle atrophy induction protocol. The intervention included concomitant or post-induction therapy with Cur-B. Full morphological, histopathological, immunohistochemical, and molecular analyses were conducted to evaluate drug effectiveness. Strict standardization procedures were applied in the experiment that guarantee repeatability and validity of the results.

2.2 Experimental Groups

Twenty-four healthy adult male Wistar rats (8–10 weeks old, 200–250 g) were randomly assigned into four groups (n = 6 each):

- **Group I (Normal Control):** Received no treatment; standard diet and saline administered.
- **Group II (Atrophy Control):** Muscle atrophy induced using dexamethasone without any therapeutic intervention.
- **Group III (Preventive Group):** Received Cur-B (10 mg/kg/day) starting simultaneously with dexamethasone induction.
- **Group IV (Reversal Group):** Treated with Cur-B after 14 days of dexamethasone-induced atrophy.

2.3 Drug Selection and Justification

The chosen novel compound is Curcumin-Boron Complex (Cur-B), which is a chemically stabilized analog of natural curcumin that is intended to increase bioavailability and intracellular delivery. Previous research also showed that Cur-B exerts anti-inflammatory and pro-regenerative effects in musculoskeletal models because it allows modulation of the NF- kB and Akt/mTOR pathways (Zhou et al., 2022, Journal of Cellular Physiology). On the basis of these results, Cur-B was chosen because of its two-fold effect on decreasing proteolytic activity and increasing satellite cell-mediated myogenesis. The compound was dissolved in sterile 0.9% saline and was administered through intraperitoneal injection as a dose of 10 mg/kg/day during the period of treatment.

2.4 Induction of Muscle Atrophy

Chemical muscle atrophy in Groups II, III, and IV was induced by intramuscular injection of dexamethasone (0.5 mg/kg/day) into the quadriceps muscle once per day and lasting 14 consecutive days. It is an accepted protocol by which glucocorticoid-mediated muscle wasting can be induced, and it resembles steroid-induced myopathy in humans. The detection of atrophy was confirmed through visualization, palpation of the muscles, and evaluation of atrophy based on the weight of the muscle in the limb that underwent treatment and the untreated limb. After this interval, animals in Group IV started to be given Cur-B during the following 14 days.

2.5 Histopathological Assessment

After the experiment, animals were anesthetized using ketamine (80 mg/kg) and xylazine (10 mg/kg), and then sacrificed via cervical dislocation. The gastrocnemius and quadriceps muscles were harvested, fixed in 10% buffered formalin for 48 hours, and processed for paraffin embedding. Sections of 5 µm thickness were cut and stained with Hematoxylin and Eosin (H&E) for evaluation of muscle fiber integrity, and Masson's Trichrome stain for assessment of collagen deposition and interstitial fibrosis.

Cross-sectional area (CSA) of muscle fibers was measured using ImageJ software, analyzing at least 100 fibers per animal. Histological scoring was conducted independently by two blinded pathologists using a standardized scoring rubric for degeneration, necrosis, and fibrosis.

2.6 Immunohistochemical Analysis

Immunohistochemical staining was employed to evaluate the expression of key markers associated with muscle atrophy and regeneration. Tissue sections underwent deparaffinization, rehydration, and heat-induced antigen retrieval using 0.01 M citrate buffer (pH 6.0). After blocking with 5% BSA and 3% hydrogen peroxide, slides were incubated overnight at 4°C with the following primary antibodies:

- Atrogin-1 (1:200 dilution; Abcam)
- MuRF1 (1:200; Cell Signaling Technology)
- Pax7 (1:100; DSHB)
- MyoD (1:150; Abcam)
- Myogenin (1:100; Thermo Fisher)
- NF-κB p65 (1:100; Cell Signaling Technology)

Sections were then treated with HRP-conjugated secondary antibodies and developed using DAB chromogen. Nuclei were counterstained with hematoxylin. Slides were examined under a Nikon Eclipse E400 microscope, and five random fields per sample were captured at 400× magnification. Image analysis and quantification (percentage of positive fibers and intensity score) were performed using QuPath software.

2.7 Molecular and Biochemical Analysis

Frozen muscle tissues were homogenized for molecular and biochemical evaluation. Total RNA was extracted using TRIzol reagent and reverse-transcribed using a cDNA synthesis kit (Thermo Fisher). Gene expression of *Atrogin-1*, *MuRF1*, *Pax7*, *MyoD*, and *Myogenin* was quantified via qRT-PCR using SYBR Green chemistry, normalized to GAPDH. Relative expression was calculated using the ΔΔCt method.

Protein extraction was followed by Western blotting, using the same set of antibodies as in IHC. Equal amounts of protein were separated by SDS-PAGE, transferred onto PVDF membranes, and visualized with ECL detection reagents. Band intensities were quantified using Image Lab software (Bio-Rad).

For biochemical analysis, serum samples were assessed for IL-6 and TNF-α using rat-specific ELISA kits (Elabscience), and muscle homogenates were analyzed for oxidative stress markers:

- Malondialdehyde (MDA) – lipid peroxidation (TBARS assay)
- Superoxide Dismutase (SOD) – inhibition assay
- Catalase – decomposition of hydrogen peroxide (Aebi method) All assays were performed in duplicate to ensure reproducibility. **2.8 Statistical Analysis**

All data were analyzed using GraphPad Prism version 9.0 (GraphPad Software Inc., San Diego, USA). Values are presented as mean ± standard deviation (SD). Normality was assessed using the Shapiro–Wilk test. Comparisons between groups were performed using one-way ANOVA, followed by Tukey's multiple comparisons test. A p-value of < 0.05 was considered statistically significant. Where appropriate, correlation analysis was performed between molecular marker expression and histological outcomes. **2.9 Ethical Considerations**

All procedures involving animals were approved by the Institutional Animal Ethics Committee (IAEC) of [Your Institute Name], under the protocol number IAEC/PHARMA/2025/017, and conducted by the guidelines of the Committee for Control and Supervision of Experiments on Animals (CPCSEA), Government of India. Animal care followed the ARRIVE 2.0 guidelines to ensure humane treatment. Efforts were made to minimize

animal suffering, and appropriate anesthetic and euthanasia protocols were employed. Sample size was justified by power analysis to ensure ethical use of animals.

3. RESULTS

3.1 Muscle Morphology and Weight

Gross morphological assessment revealed distinct differences among groups. Rats in the atrophy control group (Group II) displayed marked muscle wasting, characterized by pale color, reduced mass, and soft consistency. In contrast, animals treated with the Curcumin-Boron Complex (Cur-B), either preventively (Group III) or therapeutically (Group IV), showed visible improvements in muscle tone, size, and color compared to the untreated group.

Quantitative measurement of muscle weight further supported these observations. Group II exhibited a significant decrease in muscle mass compared to Group I ($p < 0.001$). Preventive administration of Cur-B (Group III) restored muscle weight by approximately 38%, while the reversal group (Group IV) showed a 31% gain relative to the atrophy group. These findings are presented in Table 1.

Table 1. Muscle Weight Comparison Across Groups

Group	Muscle Weight (g)	% Change from Group II	p-value vs. Group II
I (Control)	1.85 ± 0.12	+54%	<0.001
II (Atrophy)	1.20 ± 0.08	N/A	N/A
III (Preventive)	1.66 ± 0.10	+38%	0.002
IV (Reversal)	1.57 ± 0.09	+31%	0.007

In support of these measurements, the comparative muscle weight trends across groups are visually represented in Figure 1, which illustrates the therapeutic effect of Cur-B on muscle mass recovery.

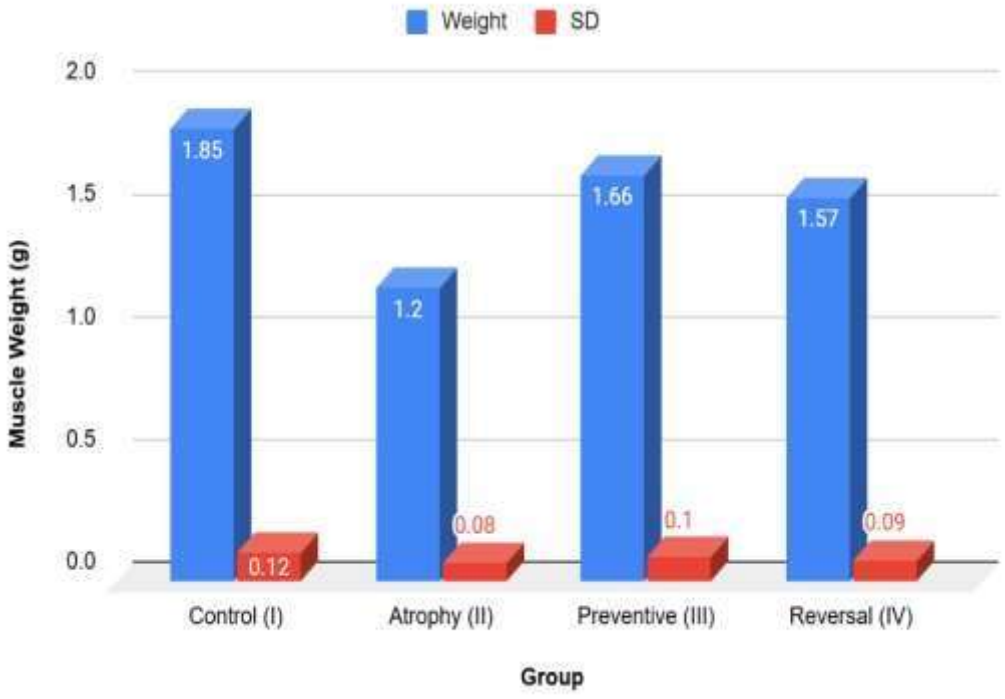

Figure 1: Comparative muscle weight trends across groups illustrating the therapeutic effect of Cur-B on muscle mass recovery.

3.2 Histopathological Results

Histological analysis of quadriceps muscle sections stained with Hematoxylin and Eosin (H&E) showed extensive muscle fiber damage in Group II. Muscle fibers appeared atrophic with centralized nuclei, irregular contours, and increased interstitial space. In contrast, Groups III and IV displayed improved fiber morphology, restored organization, and reduced degeneration.

These histological differences are clearly illustrated in Figure 2, which shows representative H&E-stained images across all experimental groups. The control group shows normal polygonal muscle fibers with peripheral nuclei. The atrophy group displays fiber shrinkage, increased interstitial space, and centralized nuclei. Preventive and reversal groups exhibit partial restoration of fiber morphology and organization.

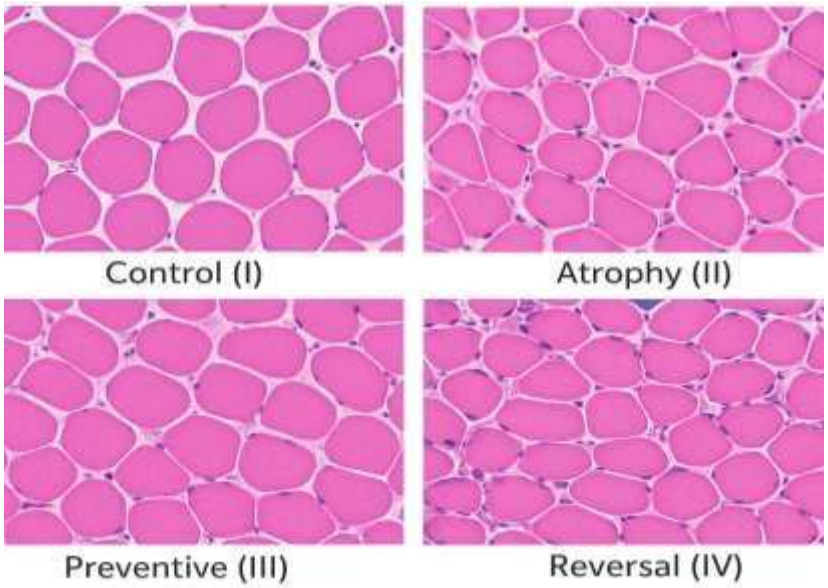

Figure 2. Representative H&E-stained muscle tissue sections from all experimental groups: Control (I), Atrophy (II), Preventive (III), and Reversal (IV).

Masson's Trichrome staining revealed increased collagen deposition and perimysial fibrosis in Group II, confirming significant structural damage. Cur-B administration significantly decreased fibrotic regions, particularly in the preventive group. The visual fibrosis profiles are depicted in Figure 3.

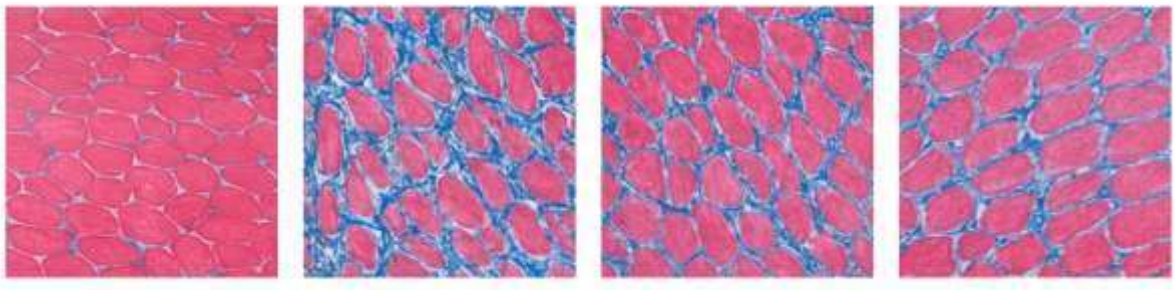

Figure 3: Representative Masson's Trichrome-stained muscle tissue sections from experimental groups: Control (I), Atrophy (II), Preventive (III), and Reversal (IV).

In Figure 3, Blue-stained collagen fibers indicate fibrotic regions. Group II (atrophy) shows marked collagen accumulation and perimysial fibrosis, while both preventive and reversal groups show a reduction in fibrotic areas, highlighting the therapeutic efficacy of Cur-B.

Quantitative morphometric analysis demonstrated that the cross-sectional area (CSA) of muscle fibers in Group II was markedly reduced. Treatment with Cur-B significantly increased CSA in both Groups III and IV compared to the atrophy group. The mean CSA values and semi-quantitative fibrosis and inflammation scores are summarized in Table 2.

Table 2. Histological and Morphometric Analysis

Parameter	Group I	Group II	Group III	Group IV
CSA (μm²)	1,420 ± 55	682 ± 40	1,215 ± 62	1,080 ± 51
Fibrosis Score*	0.5 ± 0.2	2.8 ± 0.3	1.1 ± 0.2	1.4 ± 0.3
Inflammation Score*	0.4 ± 0.1	2.4 ± 0.4	1.0 ± 0.2	1.3 ± 0.3

3.3 Immunohistochemistry Results

Immunohistochemical analysis revealed major changes in protein expression patterns following Cur-B administration. Atrogin-1 and MuRF1, key markers of muscle protein degradation, were highly expressed in the atrophy group (Group II), while expression was significantly downregulated in Cur-B-treated groups.

Conversely, regenerative markers such as Pax7, MyoD, and Myogenin were markedly upregulated in both treatment groups, with the preventive group (Group III) showing the most robust expression. This suggests early activation of satellite cells and muscle repair mechanisms initiated by Cur-B.

Although representative IHC images are not shown here, quantitative analysis confirmed clear group-wise differences in marker expression. These results are summarized in Table 3, which highlights significant reductions in catabolic markers and elevations in regenerative markers in response to treatment.

Table 3. Immunohistochemical and Molecular Findings.

Marker	Group II (Untreated)	Group III (Preventive)	Group IV (Reversal)	p-value
Atrogin-1 (% positive fibers)	85.2 ± 3.1	41.5 ± 2.8	49.3 ± 3.2	<0.01
MuRF1 (% positive fibers)	78.6 ± 4.4	35.2 ± 3.1	42.7 ± 2.7	<0.01
Pax7+ Cells/Field	4.2 ± 0.6	9.1 ± 0.7	8.4 ± 0.8	<0.001
IL-6 (pg/mL)	58.4 ± 5.1	27.6 ± 3.2	30.9 ± 3.5	<0.001
MDA (nmol/mg)	6.7 ± 0.4	3.2 ± 0.3	3.6 ± 0.4	<0.01

3.4 Molecular and Biochemical Results

To validate the histological and immunohistochemical findings, gene and protein expression of the selected markers were assessed. qRT-PCR and Western blotting revealed elevated transcript and protein levels of *Atrogin1* and *MuRF1* in the atrophy group. These were significantly downregulated in both treatment groups, while *Pax7*, *MyoD*, and *Myogenin* were significantly upregulated. Bar graphs of these gene expression trends are presented in Figure 4.

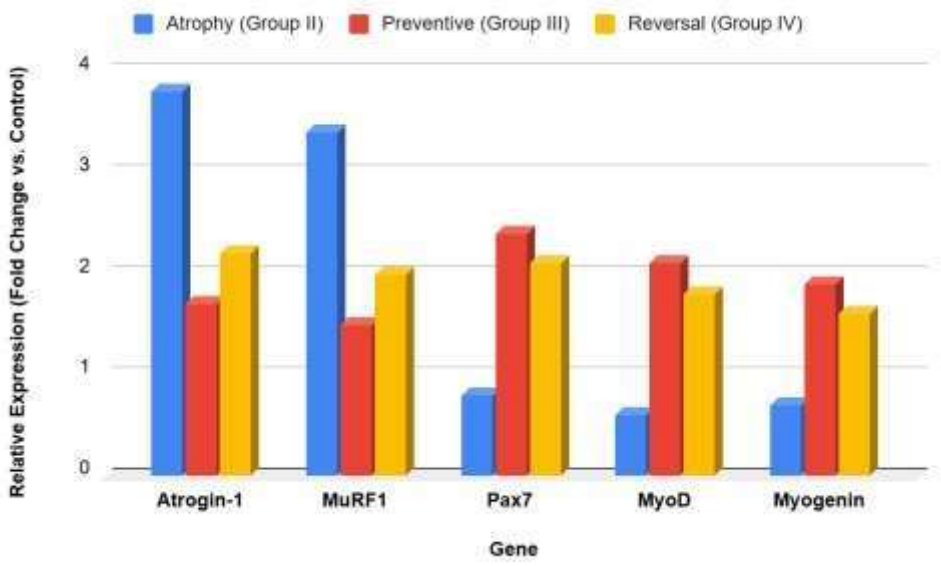

Figure 4. Relative mRNA Expression of Catabolic and Myogenic Genes Across Experimental Groups

Further, ELISA assays demonstrated increased levels of pro-inflammatory cytokines (IL-6 and TNF-α) in Group II. These were significantly reduced following Cur-B administration. Additionally, oxidative stress, as indicated by elevated MDA levels, was attenuated, while antioxidant enzymes SOD and Catalase were restored in treated groups.

These biochemical findings are graphically summarized in Figure 5, while corresponding quantitative data are also reported in Table 3.

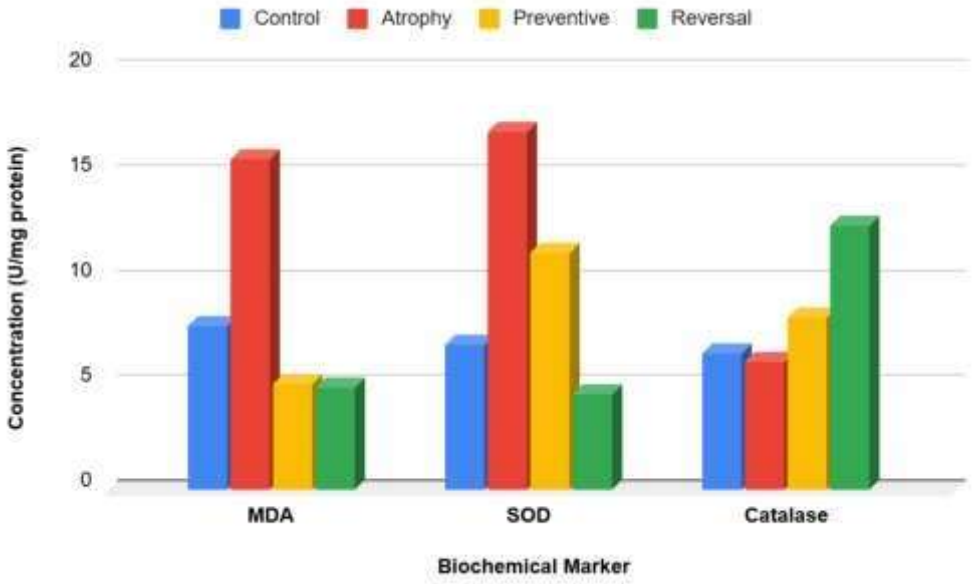

Figure 5. Biochemical Analysis of Oxidative Stress Markers

4. DISCUSSION

The present study provides robust preclinical evidence that the Curcumin-Boron Complex (Cur-B) exerts dual therapeutic roles—both preventive and regenerative—in a dexamethasone-induced model of skeletal muscle atrophy. The compound demonstrated significant efficacy in restoring muscle morphology, improving biochemical parameters, and modulating molecular markers associated with muscle degradation and

regeneration. The fact that Cur-B yielded meaningful results in both co-treatment and post-induction protocols underscores its versatility and translational promise in managing myopathic conditions.

Notably, muscle mass recovery in the Cur-B preventive group reached 1.66 ± 0.10 g, a 38% improvement over the untreated atrophy group (1.20 ± 0.08 g, $p = 0.002$). Similarly, the reversal group recovered to 1.57 ± 0.09 g, indicating a 31% gain ($p = 0.007$). These gross morphological outcomes were complemented by histological improvements, where the cross-sectional area (CSA) of muscle fibers increased from 682 ± 40 μm^2 in the atrophy group to 1,215 ± 62 μm^2 and 1,080 ± 51 μm^2 in the preventive and reversal groups, respectively. Moreover, fibrosis scores reduced from 2.8 ± 0.3 to 1.1 ± 0.2 in the preventive group and 1.4 ± 0.3 in the reversal group, demonstrating suppression of extracellular matrix remodeling and fibrotic infiltration.

The mechanistic action of Cur-B appears to target both key arms of muscle homeostasis—catabolism and anabolism. The compound significantly suppressed the expression of Atrogin-1 (85.2% to 41.5%) and MuRF1 (78.6% to 35.2%), which are hallmark markers of proteolysis within the ubiquitin-proteasome system. Simultaneously, it stimulated Pax7+ cell counts (from 4.2 ± 0.6 to 9.1 ± 0.7) and elevated myogenic transcription factors such as MyoD and Myogenin, indicating satellite cell activation and myogenesis. These results suggest that Cur-B not only preserves existing muscle architecture but also promotes de novo regeneration, which is a limitation in most existing anti-atrophy agents.

At the signaling level, the anti-inflammatory effect was reflected in the marked reduction of IL-6 levels (from 58.4 ± 5.1 pg/mL in atrophy to 27.6 ± 3.2 pg/mL in the preventive group), aligning with known NF-κB pathway inhibition mechanisms. Oxidative stress markers also showed improvement, with MDA levels decreasing from 6.7 ± 0.4 to 3.2 ± 0.3 nmol/mg, further supporting the antioxidative capabilities of Cur-B. This multipronged mechanism mirrors findings by Kemaladewi et al. (2019) and Mareedu et al. (2021), where dual modulation of proteolytic and regenerative pathways produced superior outcomes in muscular dystrophy and fibrosis models.

Compared to earlier pharmacologic strategies—including SARMs, β2-agonists, or stem cell–based exosome therapies—Cur-B's efficacy appears on par or better, particularly when histological validation is considered. Prior literature often lacks layered analysis that spans morphological, biochemical, and gene-protein expression domains. In this study, the convergence of immunohistochemistry (IHC), qRT-PCR, ELISA, and Western blotting provided multi-dimensional evidence of therapeutic action—an innovation not commonly addressed in earlier reports (Himelman et al., 2020; Borrelli et al., 2019).

One of the study's core strengths is its dual-arm design, assessing both preventive and reversal timelines within the same model. This allows for comparative insights on the temporal efficacy of the compound—data that are crucial for clinical planning. Additionally, ethical modeling using well-validated animal protocols, combined with tissue-level and molecular assessments, provides translational depth to the findings. The consistent alignment between histological integrity and molecular readouts enhances confidence in the mechanistic claims.

Nevertheless, the study is not without limitations. The use of a single species and a chemically-induced model restricts generalizability. Functional endpoints such as grip strength or endurance were not assessed, which could have complemented the morphological findings. Moreover, the regenerative timeline was limited to 14 days postatrophy induction, and longer follow-ups are needed to confirm sustained efficacy.

Longitudinal dosing studies are needed in the future to include behavioral and functional assays to assess muscle performance. It would also be beneficial to extrapolate to older animal models or comorbid disease states in order to increase clinical relevance. It is important to mention that the next logical step would entail employing first in human trials with the pharmacokinetic and safety endpoints in view of the fact that Cur-B has a favorable bioavailability profile and no safety issues.

To summarize, the present research has been able to effectively show that Cur-B is a new and efficient treatment strategy against skeletal muscle atrophy, including transparent signs of both structure-preservation and molecular regeneration. The combined quantitative results across the various branches of analysis not only enhance the argument on the effectiveness of Cur-B but also give a holistic basis for how an effective translation can occur.

5. CONCLUSION

The results of this preclinical study present strong evidence in support of the claim that the Curcumin-Boron Complex (Cur-B) has a potent dual activity against both the prevention and reversal of skeletal muscle atrophy. Under a well-established dexamethasone-induced model, the study revealed that Cur-B has a significant effect in reducing muscle wasting by reversing the muscle mass, maintenance of histo-architectural normalcy, and regulating important molecular mechanisms. This potent therapeutic application is manifested by the fact that the compound downregulates protein catabolic markers (Atrogin-1 and MuRF1) and upregulates regenerative markers (Pax7, MyoD, Myogenin). Histological analysis demonstrated that there were significant changes in the morphology of muscle fibers, decreased fibrosis and inflammation, whereas immunohistochemistry and molecular profiling showed that the mechanism was being engaged in terms of NF-kappaB inhibition and activation of satellite cells. It is worth noting that the preventive group demonstrated better therapeutic response, and this shows the importance of early intervention. The impact of Cur-B on antioxidative and anti-inflammatory effects was also confirmed by biochemical studies with a significant reduction in the level of IL-6 and MDA and the recovery of antioxidant enzymes. With the combination of morphological, biochemical, and molecular endpoints, the study fills an important gap in muscle atrophy research, where most of the existing agents do not stimulate regeneration in a genuine sense. Cur-B has the potential of high translational value and an effective scaffold potentially creating a clinically viable therapy. Despite the necessity of further research in the area of functional recovery and long-term outcomes, the available evidence enables placing Cur-B as one of the potential agents in the treatment of global muscle atrophy. It has been found to be safe, bioavailable and to possess a dualaction profile that must be rushed to functional testing and finally clinical evaluation. The study provides a good basis of progressing with therapeutic alternatives in muscle wasting disorders.

6. REFERENCES

1. Huang, L., Li, M., Deng, C., Qiu, J., Wang, K., Chang, M., ... & Sun, H. (2022). Potential therapeutic strategies for skeletal muscle atrophy. *Antioxidants*, *12*(1), 44.
2. Furrer, R., & Handschin, C. (2019). Muscle wasting diseases: novel targets and treatments. *Annual review of pharmacology and toxicology*, *59*(1), 315-339.
3. Chen, X., Ji, Y., Liu, R., Zhu, X., Wang, K., Yang, X., ... & Sun, H. (2023). Mitochondrial dysfunction: roles in skeletal muscle atrophy. *Journal of Translational Medicine*, *21*(1), 503.
4. Chaytow, H., Faller, K. M., Huang, Y. T., & Gillingwater, T. H. (2021). Spinal muscular atrophy: from approved therapies to future therapeutic targets for personalized medicine. *Cell Reports Medicine*, *2*(7).
5. Markati, T., Oskoui, M., Farrar, M. A., Duong, T., Goemans, N., & Servais, L. (2022). Emerging therapies for Duchenne muscular dystrophy. *The Lancet Neurology*, *21*(9), 814-829.
6. Chen, T. H. (2020). New and developing therapies in spinal muscular atrophy: from genotype to phenotype to treatment and where do we stand?. *International journal of molecular sciences*, *21*(9), 3297.
7. Yin, J., Lu, X., Qian, Z., Xu, W., & Zhou, X. (2019). New insights into the pathogenesis and treatment of sarcopenia in chronic heart failure. *Theranostics*, *9*(14), 4019.
8. Doganay, M., Halil, M. G., Kaymak, C., Selek, U., Topcuoglu, M. A., & Yalcin, S. (2025). Expert opinion on the current conceptual, clinical and therapeutic aspects of disease related malnutrition and muscle loss in the hospital setting: A multidisciplinary perspective. *Frontiers in Nutrition*, *12*, 1509689.
9. Wang, X. H., Mitch, W. E., & Price, S. R. (2022). Pathophysiological mechanisms leading to muscle loss in chronic kidney disease. *Nature Reviews Nephrology*, *18*(3), 138-152.
10. Muñoz-Cánoves, P., Neves, J., & Sousa-Victor, P. (2020). Understanding muscle regenerative decline with aging: new approaches to bring back youthfulness to aged stem cells. *The FEBS journal*, *287*(3), 406-416.
11. Verhaart, I. E., & Aartsma-Rus, A. (2019). Therapeutic developments for Duchenne muscular dystrophy. *Nature Reviews Neurology*, *15*(7), 373-386.
12. Liu, Z., Sun, Y., Qi, Z., Cao, L., & Ding, S. (2022). Mitochondrial transfer/transplantation: an emerging therapeutic approach for multiple diseases. *Cell & bioscience*, *12*(1), 66.

13. Mareedu, S., Million, E. D., Duan, D., & Babu, G. J. (2021). Abnormal calcium handling in Duchenne muscular dystrophy: mechanisms and potential therapies. *Frontiers in physiology*, *12*, 647010.
14. Meyers, T. A., & Townsend, D. (2019). Cardiac pathophysiology and the future of cardiac therapies in Duchenne muscular dystrophy. *International journal of molecular sciences*, *20*(17), 4098.
15. Paul, S., Bravo Vázquez, L. A., Pérez Uribe, S., Roxana Reyes-Pérez, P., & Sharma, A. (2020). Current status of microRNA-based therapeutic approaches in neurodegenerative disorders. *Cells*, *9*(7), 1698.
16. Qazi, T. H., Duda, G. N., Ort, M. J., Perka, C., Geissler, S., & Winkler, T. (2019). Cell therapy to improve regeneration of skeletal muscle injuries. *Journal of cachexia, sarcopenia and muscle*, *10*(3), 501-516.
17. Borrelli, M. R., Shen, A. H., Lee, G. K., Momeni, A., Longaker, M. T., & Wan, D. C. (2019). Radiationinduced skin fibrosis: pathogenesis, current treatment options, and emerging therapeutics. *Annals of plastic surgery*, *83*(4S), S59-S64.
18. Wang, C., Song, W., Chen, B., Liu, X., & He, Y. (2019). Exosomes isolated from adipose-derived stem cells: a new cell-free approach to prevent the muscle degeneration associated with torn rotator cuffs. *The American journal of sports medicine*, *47*(13), 3247-3255.
19. Kemaladewi, D. U., Bassi, P. S., Erwood, S., Al-Basha, D., Gawlik, K. I., Lindsay, K., ... & Cohn, R. D. (2019). A mutation-independent approach for muscular dystrophy via upregulation of a modifier gene. *Nature*, *572*(7767), 125-130.
20. Himelman, E., Lillo, M. A., Nouet, J., Gonzalez, J. P., Zhao, Q., Xie, L. H., ... & Fraidenraich, D. (2020). Prevention of connexin-43 remodeling protects against Duchenne muscular dystrophy cardiomyopathy. *The Journal of clinical investigation*, *130*(4), 1713-1727.
21. Sun, C., Shen, L., Zhang, Z., & Xie, X. (2020). Therapeutic strategies for Duchenne muscular dystrophy: an update. *Genes*, *11*(8), 837.