

ABSTRACT

Background: Spinal muscular atrophy (SMA) is caused by loss of *SMN1*, resulting in insufficient survival motor neuron (SMN) protein and progressive motor neuron degeneration. Curcumin has been reported to modulate SMN2-related pathways, but its clinical translation is limited by poor bioavailability; therefore, curcumin analogs such as pentagamavunon-1 (PGV-1) have been proposed as potentially stronger candidates.

Objective: To evaluate the effect of PGV-1 on SMN protein levels in fibroblasts derived from SMA type 1 and SMA type 2 patients, and to assess whether dose and treatment duration influence SMN protein levels.

Methods: This in vitro experimental study used human-derived fibroblast cell lines from SMA type 1 and type 2 patients, with normofibroblasts as reference. PGV-1 was tested at 0.75 μ M, 1.5 μ M, and 2.25 μ M for 48 and 72 hours, with DMSO (0.05%) as vehicle control. Cell viability/cytotoxicity was assessed using MTT. SMN protein concentration was quantified by ELISA. Dose, time, and dose \times time interaction effects were analyzed using two-way ANOVA followed by Tukey post hoc testing ($p < 0.05$).

Results: In both SMA type 1 and type 2 fibroblasts, treatment dose, time, and dose \times time interaction significantly affected measured SMN protein levels ($p < 0.001$). However, across conditions tested, PGV-1 did not restore SMN protein levels toward the normofibroblast reference. In SMA type 1, all PGV-1 groups remained below the negative control at corresponding time points. In SMA type 2, the medium dose showed a higher SMN level than the negative control at 72 hours, but responses were non-linear and not sustained at higher concentrations; the high dose consistently produced the lowest SMN levels alongside more pronounced cytotoxic morphology.

Conclusion: Within the tested concentrations and exposure durations, PGV-1 did not produce a consistent or meaningful increase in SMN protein levels in SMA fibroblasts, and observed changes were influenced by time-dependent effects, non-linear dose dynamics, lack of normalization, and likely cytotoxicity-related confounding.

Keywords: Spinal Muscular Atrophy (SMA), Survival Motor Neuron (SMN), Curcumin analog, Pentagamavunon-1 (PGV-1)