

## **Eksplorasi Efek Molekuler Senyawa Kurkumin dan Analog Kurkumin (Pentagamavunon-1) Terhadap Kadar Protein SMN dan Morfologi Mitokondria pada Lini Sel Fibroblas Spinal Muscular Atrophy**

### **INTISARI**

**Latar belakang:** *Spinal Muscular Atrophy* (SMA) merupakan penyakit genetik neuromuskular yang disebabkan oleh defisiensi protein *Survival Motor Neuron* (SMN) akibat delesi gen *SMN1*. Patofisiologi SMA tidak hanya terbatas pada degenerasi neuron motor, tetapi juga melibatkan kelainan pada organel selular, termasuk mitokondria. Kurkumin telah dilaporkan memiliki efek biologis yang relevan dengan patofisiologi SMA, namun keterbatasan bioavailabilitas mendorong pengembangan analog sintetik, seperti Pentagamavunon-1 (PGV-1). Hingga saat ini, efek kurkumin dan PGV-1 secara langsung terhadap kadar protein SMN dan morfologi mitokondria pada model SMA belum dieksplorasi.

**Tujuan:** Mengevaluasi dan membandingkan efek molekuler kurkumin dan PGV-1 terhadap kadar protein SMN dan morfologi mitokondria pada lini sel fibroblas *patient-derived* SMA tipe 1 dan tipe 2.

**Metode:** Lini sel fibroblas diberi perlakuan kurkumin dan PGV-1 selama 48 dan 72 jam, dengan DMSO 0.1% sebagai kontrol. Viabilitas sel dievaluasi menggunakan uji MTT. Kadar protein SMN diukur menggunakan ELISA dan dianalisis menggunakan uji statistik *one-way* ANOVA dan uji *post hoc* Tukey. Morfologi mitokondria diamati melalui imunofluoresens dan dianalisis secara kualitatif terstandar berdasarkan karakteristik fragmentasi dan tubularitas.

**Hasil:** Pada SMA tipe 1, pemberian kurkumin 10 dan 15  $\mu\text{M}$  selama 48 jam meningkatkan kadar protein SMN masing-masing sebesar 1.34 dan 1.47 kali lipat dibanding kontrol. Pada SMA tipe 2, pemberian kurkumin 5  $\mu\text{M}$  selama 72 jam meningkatkan kadar protein SMN hingga 1.75 kali lipat. Sebaliknya, pemberian PGV-1 menurunkan kadar protein SMN. Secara morfologis, fibroblas SMA menunjukkan fragmentasi mitokondria yang nyata. Pemberian kurkumin memperlihatkan kecenderungan perbaikan morfologi mitokondria menuju struktur tubular, sedangkan PGV-1 justru menyebabkan agregasi mitokondria.

**Kesimpulan:** Kurkumin menunjukkan potensi sebagai terapi adjuvan SMA melalui peningkatan kadar protein SMN dan perbaikan morfologi mitokondria, sedangkan PGV-1 tidak menunjukkan efek tersebut. Implementasi pemberian kurkumin dan PGV-1 sebagai terapi adjuvan untuk SMA perlu diambil dengan pertimbangan yang matang.

**Kata kunci:** SMA, Kurkumin, Pentagamavunon-1, Survival Motor Neuron, polifenol.

## **Molecular Effect of Curcumin and Its Analog (Pentagamavunon-1) on SMN Protein Level and Mitochondrial Morphology in Spinal Muscular Atrophy Fibroblast Cell Lines: An Exploratory Study**

### ***ABSTRACT***

**Introduction:** Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder caused by deficiency of the Survival Motor Neuron (SMN) protein due to deletion of the *SMN1* gene. Beyond motor neuron degeneration, SMA pathophysiology also involves cellular organelle dysfunction, including mitochondrial. Curcumin has been reported to exert biological effects relevant to SMA. However, its limited bioavailability has driven the development of synthetic analogues such as Pentagamavunon-1 (PGV-1). To date, the direct effects of curcumin and PGV-1 on SMN protein levels and mitochondrial morphology in SMA models remain unexplored.

**Objective:** To evaluate and compare the molecular effects of curcumin and PGV-1 on SMN protein levels and mitochondrial morphology in patient-derived fibroblast cell lines from SMA type 1 and type 2.

**Methods:** Fibroblast cell lines were treated with curcumin and PGV-1 for 48 and 72 hours, with 0.1% DMSO used as a control. Cell viability was assessed using the MTT assay. SMN protein levels were quantified by ELISA and analyzed using one-way ANOVA followed by Tukey's post hoc test. Mitochondrial morphology was examined by immunofluorescence and analyzed using a standardized qualitative approach based on fragmentation and tubular characteristics.

**Results:** In SMA type 1 fibroblasts, curcumin at 10 and 15  $\mu\text{M}$  for 48 hours increased SMN protein levels by 1.34-fold and 1.47-fold, respectively, compared with controls. In SMA type 2 fibroblasts, curcumin at 5  $\mu\text{M}$  for 72 hours increased SMN protein levels by up to 1.75-fold. In contrast, PGV-1 treatment resulted in a reduction of SMN protein levels. Morphologically, SMA fibroblasts exhibited pronounced mitochondrial fragmentation. Curcumin treatment showed a tendency to improve mitochondrial morphology, whereas PGV-1 induced mitochondrial aggregation.

**Conclusion:** Curcumin demonstrates potential as an adjuvant therapy for SMA by increasing SMN protein levels and improving mitochondrial morphology, whereas PGV-1 does not exhibit similar effects. Therefore, the implementation of curcumin and PGV-1 as adjuvant therapies for SMA should be approached with careful consideration.

**Keywords:** SMA, Curcumin, Pentagamavunon-1, Survival Motor Neuron, polyphenol.