Cardiovascular Treatment

VCU Innovation Gateway
Office of the Vice President for Research and Innovation

Pulmonary Fibrosis Treatment

Enhanced action of melatonin-curcumin hybrid compound

Pulmonary fibrosis (PF) is a rare but devastating lung disease that causes scar tissue formation and associated loss of normal respiratory function and death within 2-3 years of onset. Tumor growth factor-beta 1 (TGF-β1) is thought to be the master switch driving the series of events that lead to the disease phenotype, however approved drugs to treat the anti-oxidative and anti-inflammatory symptoms have shown only moderate effects. Additionally, these formulations have low bioavailability in oral delivery forms, cause several local and systemic adverse effects, and can have an annual cost of up to $100,000 to patients. There is a large need to identify molecules that effectively treat all aspects of the disease's progression and can be delivered directly to the lungs.

The technology

Researchers at VCU have developed a hybrid molecule of melatonin and curcumin originally intended for neurodegenerative disorders, but have found it to pertain anti-fibrotic activities. The hybrid molecule has been shown to be a potent inhibitor against induced proliferation of (1) lung fibroblasts, (2) fibroblast-to-myoblast differentiation, (3) deposition of extracellular matrix, collagen and (4) alveolar EMT, and (5) radical scavenging anti-oxidative activities. It is also able to maintain a stimulatory activity of the collagen-degrading enzyme, cathepsin K. These effects display higher potency over melatonin or curcumin alone, their admixture, or of the FDA-approved drug pirfenidone in vitro. Even in vivo results in a PF rat model indicate remarkable intervention activities, attenuating dense fibrosis and honeycomb development in the airspace, impairment of treadmill exercise endurance, and induction of collagen deposition (Figure 1). Finally, the hybrid melatonin-curcumin molecule is intended for inhalation for local delivery and treatment of PF, thereby reducing the overall effective dose, negative side effects, and overall patient cost.

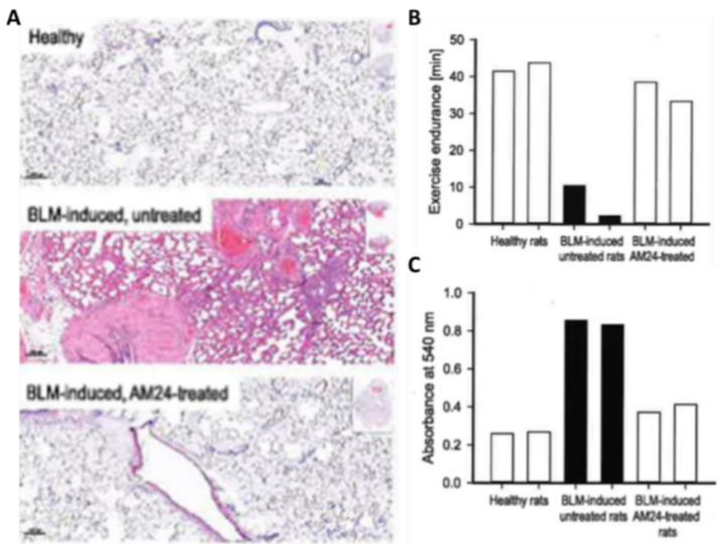

Figure 1. Effects of melatonin-curcumin hybrid molecule (AM24) on bleomycin (BLM) induced PF rat model. H&E staining of lung tissue with attenuated development of dense fibrosis and honeycomb (A). Attenuated impairment of treadmill exercise endurance in BLM-induced PF rat (B). Attenuated induction of lung collagen deposition in BLM-induced PF rat (C).

Benefits

- Multi-inhibitory activities on PF of melatonin-curcumin hybrid molecule
- Reduction in PF symptom development and progression
- Inhaled dosage form local treatment and reduced system toxicity

Applications

- Treatment of PF in inhaled dosage form
- Treatment potential of hybrid molecule on other forms of fibrotic disease

Patent status:
Patent pending: U.S. and foreign rights are available.

License status:
This technology is available for licensing to industry for further development and commercialization.

Category:
Biomedical

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