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Compare SS 31 to ARA 290

SS-31 (elamipretide) and ARA 290 (cibinetide) are both small therapeutic peptides with mitochondrial and tissue-protective effects, but their mechanisms and preclinical efficacy profiles differ substantially.

Mechanism

- **SS-31**: Binds mitochondrial cardiolipin, stabilizes mitochondrial structure, boosts ATP production, inhibits mitochondrial swelling and ROS generation, and prevents cell death—broadly targeting mitochondrial dysfunction in a variety of tissues.[1]
- **ARA 290**: Mimics a portion of erythropoietin, but lacks EPO's hematopoietic effects. It activates the innate repair receptor (IRR; a β-common receptor/EPO-R heterocomplex). This initiates local anti-inflammatory, anti-apoptotic, and tissue repair responses, especially in neural tissues.[2][3][4]

Preclinical Efficacy Data

Aspect	SS-31 (Elamipretide)	ARA 290 (Cibinetide)
Main Targets	Mitochondria (cardiolipin binding, ATP, ROS, mPTP)	Innate repair receptor (βcR/EPO-R); anti-inflammatory/neuroprotection
Nerve/Neuro	Relieves neuroinflammation and cognitive/memory loss after injury, aging, sepsis; preserves synaptic and mitochondrial integrity [5][1]	Reduces chronic pain, mechanical/cold allodynia in nerve injury models; enhances regeneration and suppresses microglial activation [2][6]
Cardioprotection	Protects against ischemia/reperfusion injury in heart and kidney; improves recovery post-injury and reduces fibrosis [1]	Improves survival, reduces infarct size, and suppresses tissue damage after myocardial infarction and in shock models [2][7]
Metabolic	Improves insulin sensitivity, reduces kidney damage in diabetes models, maintains muscle structure [1]	Improves glucose homeostasis and lipid profiles in diabetic animals; improves corneal nerve density and sensory function [8][4]
Duration	Protection typically seen with repeated daily administration (e.g., 3–5 mg/kg i.p. for days-weeks in mice) [1]	Durable pain relief and tissue protection seen with daily 4 mg/kg s.c. for weeks; functional improvement sometimes lasts up to 20 weeks post-injury [2]

Key Animal Model Results

SS-31:

- Preserves ATP and organ function in renal, cardiac, skeletal muscle, and brain injury models.[1]
- Ameliorates oxidative stress, enhances neurological recovery, and protects against ischemic injury in both acute and chronic models.[5][1]

ARA 290:

- Rapid and dose-dependent relief from neuropathic pain and allodynia in rodent nerve injury models, through βcR/IRR signaling.[6][2]
- Promotes neurite outgrowth, tissue repair, and neuropathy reversal in diabetes and sarcoidosis models.[8][9][4]
- Suppresses spinal microglial activation and reduces pro-inflammatory cytokines, key in pain and neuroinflammation.[2][6]

Distinguishing Features

- **Breadth**: SS-31's effects are broader, covering multiple organ systems tied to mitochondrial dysfunction; ARA 290's greatest strength is neuroprotection, especially pain and small fiber neuropathy, with a clear anti-inflammatory and reparative action.
- **Direct mitochondrial restoration**: SS-31 directly improves mitochondrial bioenergetics; ARA 290 indirectly protects endothelial/neuronal mitochondria via IRR-triggered repair and anti-inflammatory signaling.[6][2][1]
- **Duration and persistence**: ARA 290 provides persistent relief in nerve injury that can outlast treatment; SS-31's actions strongly depend on continued administration.[2][1]

Both peptides display high efficacy in their target models in preclinical studies, but SS-31 is primarily mitochondrial and systemic, while ARA 290 is highly neuro- and tissue-reparative via cytokine modulation and endogenous repair pathways.[4][1][6][2]

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