

Carnosine Improves Cardiac Function: Treating Heart Failure

- Heart Failure: A serious and costly medical problem.
- Current treatments: There are serious disadvantages associated with current treatments.
- Carnosine: A patented alternative to current therapies.
- Pre-Clinical Data
 - Rat *in vitro* data: In isolated rat hearts carnosine increased cardiac output.
 - Dog heart failure model: Carnosine increases cardiac output in a pacing-induced chronic heart failure model in dogs.
- Human Clinical Data: Carnosine improves cardiac output in healthy human subjects.

Heart Failure: Reduced cardiac output is a serious medical condition arising from congestive heart failure and myocardial infarction, and is often associated with sepsis, and trauma.

- Congestive heart failure affects an estimated 4.6 million Americans. Approximately 400,000 new cases are diagnosed each year.
Direct medical costs: \$10 Billion
- Sepsis is reported to affect 400,000 patients each year and cause 200,000 deaths.
Direct medical cost: \$5-10 Billion.
- As the population ages, the incidence of these conditions is rising.

Current treatments for patients with heart failure with inotropes often have one or more of the following disadvantages:

- Undesirable increases in heart rate and arrhythmias
- Decreased organ blood flow due to vasoconstriction
- Loss of drug responsiveness (down-regulation or resistance)
- Current positive inotropes improve cardiac output, but increase mortality

Carnosine: A Patented Alternative to Current Therapies.

- A commonly available dipeptide composed of the amino acids β -alanine and histidine. (Sold OTC as a nutraceutical.)
- Found in normal heart muscle. Depleted stores of carnosine are associated with diminished cardiac contraction.
- Patent issued (5,512,592) to Wake Forest University for using carnosine to improve cardiac function.

Carnosine has excellent cardiotonic properties, increases calcium, raises heart rate only moderately, but does not cause **vasoconstriction**, **dysrhythmias**, or increase cAMP.

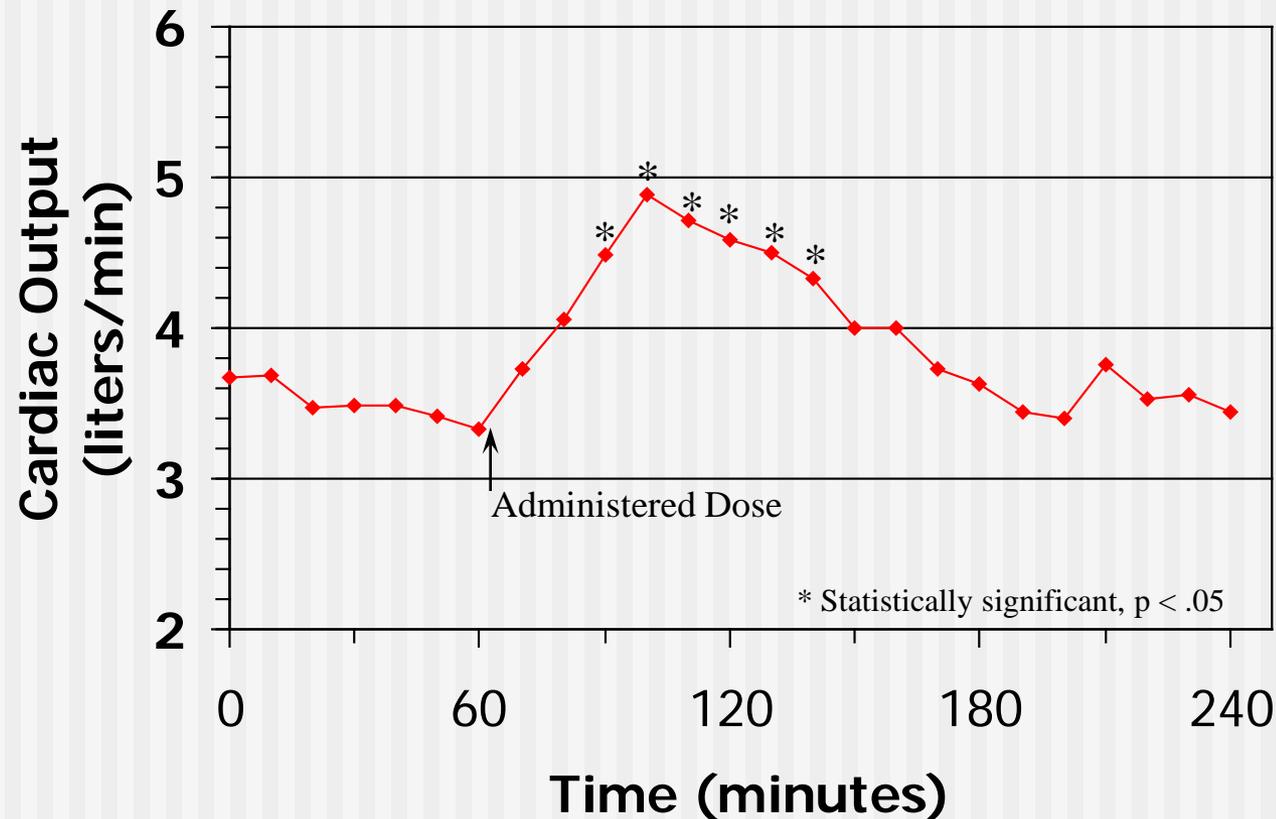
Actions of Cardiotonic Agents

Mechanisms

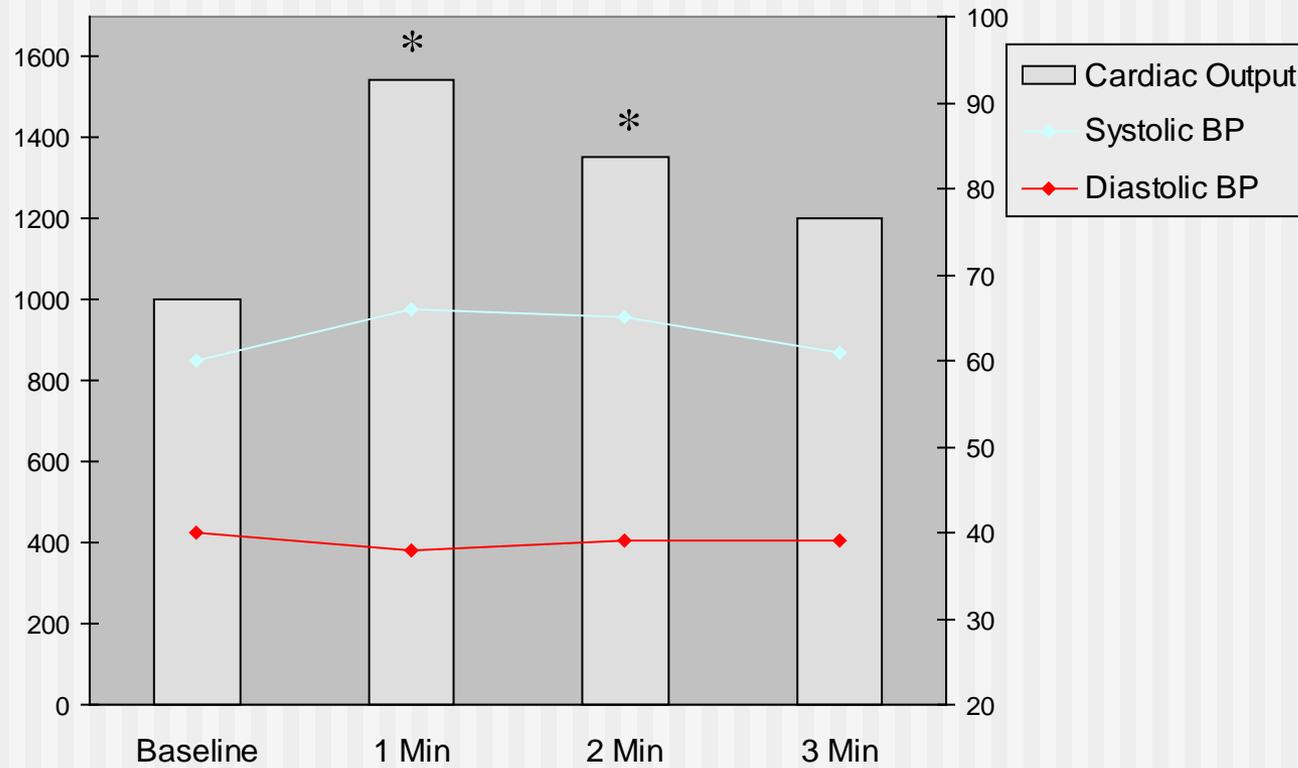
	Cardiac Output	Heart Rate	Dys-rhythmias	Vaso-Constriction	Calcium Sensitization	cAMP
Carnosine	+++	+		-	++	
Isoproterenol	++	+++	+++	-		+++
Epinephrine	++	++	++	++		+++
Dobutamine	++	++	++	-		+++
Dopamine	++	++	++	+		++
Amrinone	+	+	+	-		+
Digoxin			+	-	+	

(+) Increase, (-) Decrease, (Blank) No Effect

In healthy **human subjects**, a single oral dose of carnosine (<300mg/kg) quickly increased cardiac output and the effect lasted approximately one hour.



In Vitro data in isolated rat hearts show the beneficial effects of carnosine. Cardiac output is increased, but blood pressure remains stable.



*p < .05

Dog heart failure model: Carnosine increased cardiac output in a pacing-induced chronic heart failure in dogs.

- Assessed cardiac responses to carnosine after Pacing-induced Congestive Heart Failure (CHF) in dogs (Tachibana et al., 2000).
- Carnosine enhanced the rate of relaxation (thus increasing stroke volume).
- Carnosine enhanced left ventricle contractility.

Conclusions:

- Carnosine increases cardiac output in isolated rat hearts, a dog model of congestive heart failure, and normal human subjects.
- Our preliminary studies indicate that carnosine does not produce detectable unwanted side effects.
- WFU has been issued a patent for the use of carnosine to improve cardiac function.
- Carnosine is a potentially important new oral or i.v. pharmacotherapy for heart patients.

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