Capsinoids in Obesity: A Cardiac Risk?

Leonardo Maciel[1]

Universidade Federal do Rio de Janeiro,[1] *Rio de Janeiro, RJ – Brazil*

Short Editorial related to the article: Treatment with Capsinoids Promotes Impaired Cardiomyocyte Contractility in Obesity without Positively Modulating Metabolic Parameter

Obesity represents one of the greatest public health crises of the 21st century. Its rising prevalence is associated with a broad spectrum of cardiovascular comorbidities, including cardiac remodeling, diastolic dysfunction, and, in more advanced stages, heart failure.[1] In this setting, the search for non-pharmacological weight-control strategies has driven increased consumption of dietary supplements, often without robust scientific support. Among these compounds, capsinoids (Cap) stand out as non-pungent capsaicin analogs extracted from sweet peppers of the genus Capsicum, proposed as potential thermogenic and anti-obesity agents.

The biological plausibility rests on activation of transient receptor potential vanilloid type 1 (TRPV1), a mechanism shared with capsaicin. Meta-analyses in humans have shown that capsaicin and Cap increase energy expenditure and lipid oxidation, particularly in overweight individuals, and may modestly reduce total cholesterol and triglycerides, although effects on LDL, HDL, and glycemic parameters remain inconsistent and supported by low-certainty evidence.[2-5] In the cardiovascular system, capsaicin has exerted favorable effects in models of hypertension, improving cardiac mechanical function via nitric oxide bioavailability.[6] In this context, the study published in this issue of *Arquivos Brasileiros de Cardiologia*[7] offers an original contribution. The authors evaluated the effects of chronic Cap administration (10 mg/kg/day for 8 weeks, by gavage) on metabolic parameters and the contractility of isolated cardiomyocytes in obese Wistar rats. The results challenge expectations: treatment did not reduce adiposity, did not improve glycemic, lipid, or hormonal profiles, and impaired cellular contractile function, with reduced fractional shortening and increased time to 50% peak shortening in the obese group treated with Cap compared with untreated obese animals.[7]

The absence of a metabolic effect is consistent with recent meta-analyses showing that the lipid and glycemic benefits of capsaicin/Cap are small, heterogeneous, and based on few studies, and do not hold up under sensitivity analyses.[4,5] These data reinforce that the widely publicized anti-obesity effect seen in preclinical models does not translate robustly into clinically meaningful metabolic benefit.[3,5] The most striking finding is the deleterious effect on cardiac contractility, the first demonstration that Cap impairs cardiomyocyte contractile function in the context of obesity.[7] Obesity alone already imposes lipotoxicity, oxidative stress, and impaired calcium handling, with reduced SERCA activity and Na^+/Ca^{2+} exchange, culminating in contractile impairment.[8,9] The worsening of this picture with Cap treatment suggests an additive rather than a protective effect.

The mechanism remains speculative, but independent data on capsaicin offer relevant clues. TRPV1 activation raises intracellular calcium in cardiomyocytes and may induce hypertrophy via calmodulin kinase II and MAPK pathways, with reduced SERCA2a observed in models of pressure overload.[10] At higher concentrations, capsaicin also inhibits K^+ currents (IKr, IKs, Ito) and suppresses voltage-gated Na^+ and Ca^{2+} currents in a TRPV1-independent manner, further influencing cardiac electrophysiology.[11] It is plausible that chronic TRPV1 modulation by Cap alters calcium-regulatory proteins, compromising Ca^{2+} availability for contraction, a hypothesis also raised by the authors.[7] Clinically, these findings raise an urgent question about the cardiovascular safety profile of Cap in obese individuals, a population already at elevated cardiovascular risk. The study did not assess in vivo cardiac function, a relevant limitation and a priority for future research.[7] This is an animal model with a specific dose and protocol, which limits direct extrapolation to humans; nonetheless, the internal consistency – absence of metabolic benefit coupled with cellular contractile impairment – strengthens the central message.[7]

In summary, the study[7] demonstrates that chronic capsinoid treatment can impair cardiomyocyte contractility in an experimental model of obesity, without offsetting metabolic benefits.[7] This underscores the need for caution in the indiscriminate recommendation of capsinoid-based thermogenic supplements to obese individuals with increased cardiovascular risk. Future studies should investigate the molecular mechanisms involved, assess in vivo cardiac function, and explore the reversibility and dose dependence of these effects.

Keywords

Obesity; Capsaicin; Myocardial Contraction; Dietary Supplements.

Mailing Addressa: Leonardo Maciel •
Universidade Federal do Rio de Janeiro - Av. Carlos Chagas, 373. Postal Code 21941-901, Rio de Janeiro, RJ – Brazil
E-mail: leonardomaciel@biof.ufrj.br
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