

# Niacin CRT™

— *Featuring Controlled Release Technology* —

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Niacin, also known as Vitamin B3 or nicotinic acid, is an essential cofactor in many metabolic pathways in the body due to its role in the coenzymes NAD (nicotine-adenine dinucleotide) and NADP (nicotine-adenine dinucleotide phosphate) and in the oxidation-reduction reactions in the mitochondria. In the 1960s niacin was found to inhibit lipolysis in adipocytes (fat cells), leading Butcher et al.<sup>1</sup> to investigate its effect on cyclic AMP. They found that niacin inhibits cyclic AMP production in epinephrine (adrenaline)-exposed adipocytes. Researchers have discovered that HM74A and PUMA-G are the active niacin receptors.<sup>2</sup> These receptors mediate inhibition of adenylyl cyclase in adipocytes and thereby block lipolysis, accounting for the marked reduction of free fatty acids and approximately 30% reduction in triglyceride in fat-fed normal mice supplemented with niacin. In receptor-deficient mice, no reductions in plasma free fatty acid and triglyceride levels were seen.

Niacin's lipid-lowering capabilities were discovered in the 1950's.<sup>3</sup> However, recently niacin has been chosen by many health care practitioners as first-line therapy for hyperlipidemia because of its desirable impact on all lipid fractions—lowers low density lipoproteins (LDL), Lp(a) and triglycerides (TG), raises high density lipoproteins (HDL) and increases ratio of large/small particle LDL. An additional major benefit of niacin therapy is the relatively low toxicity and cost, particularly as compared to other lipid lowering agents.

Researchers from the University of California, Irvine and the Atherosclerosis Research Center recently discovered how niacin improves protective HDL cholesterol levels and therefore helps reduce the risk of heart disease (June 2008; Journal of Lipid Research).<sup>5</sup> The researchers found that a subunit ('beta chain') of the enzyme ATP synthase, the protein that makes the body's energy source ATP, can take up HDL and reduce the levels being eliminated from the body. Specifically, they further found that when human liver HepG2 cells were incubated with niacin, a 27% reduction in the presence of beta chains on the cell surface was observed and a 35% reduction in the uptake of HDL was observed. To put it simply, niacin hinders the liver from removing HDL from the body, thus maintaining high plasma HDL levels.<sup>5</sup>

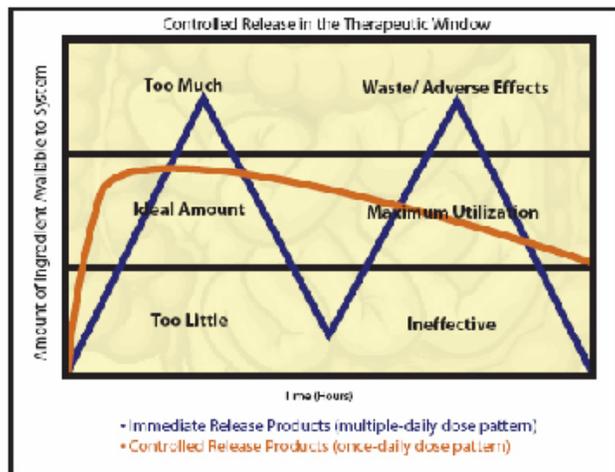
## Controlled Release Technology (CRT)

Until recently, niacin therapy fostered a high incidence of distressing side effects, especially cutaneous flushing, itching and gastrointestinal upset. Studies have reported 16 - 40% intolerance in patients who use immediate release niacin in doses necessary for lipid therapy (1,000-2,000 mg). Controlled Release Technology (developed for pharmaceutical delivery) is also known as steady-state or zero-order release, allowing for a very slow 10-12 hour continuous release of niacin into the body in a very uniform manner. This helps to eliminate the spikes and surges found in older generation sustained release technologies, virtually eliminating unpleasant side effects. This greatly reduces gastrointestinal upset and gut irritation associated with the buildup of localized concentrations of niacin and cutaneous symptoms associated with a rapid rise in blood levels. This technology is designed to deliver measurable amounts of an ingredient to the body at a prescribed rate in a therapeutic window for an extended period of time, ideally allowing for a convenient once-daily dosing rather than having to take morning, noon and night.

Supplement Facts	
Serving Size 1 tablet	
Servings Per Container 60	
Amount Per Serving	% Daily Value
Niacin (as Nicotinic Acid)	500 mg 2500%
Sodium	17 mg 1%
*Daily Value not established.	

**Other Ingredients:** Hydroxypropyl methylcellulose, sodium bicarbonate, pectin, stearic acid (vegetable source).

An example of the therapeutic window (see illustration) helps explain this. When an immediate release product is taken, a highly soluble ingredient may have a burst or spike effect in the bloodstream, in some cases causing unwanted side effects such as uncomfortable skin flushing and itching. As the dosing period lapses, too little of the ingredient may remain, falling below the minimum level deemed necessary to maintain therapeutic value. An effective controlled delivery product is designed to release the ideal amount of the ingredient to maintain a steady state in the body over an extended period of time.



Research presented at the 7th World Congress of Cardiac Rehabilitation and Secondary Prevention (Feb 2000) compared lipid lowering abilities of sustained release niacin vs. lovastatin. Subjects were given either 1500 or 2000 mg/day sustained release niacin or 20-40 mg/day lovastatin. Looking at cost and efficacy, the niacin was determined to be the superior choice for patients with dyslipidemia.<sup>4</sup> Controlled release technology (CRT) is superior to sustained release technology (SRT) and would be expected to yield similar, if not even more impressive, results.

Another true benefit of niacin supplementation is its ability to lower Lp(a). A 1993 study published in the journal *Atherosclerosis* found a 36% reduction in lipoprotein (a) after giving 1 g of niacin, twice daily.<sup>6</sup> Because niacin induces vasodilation, it may be helpful to patients with poor circulation and therefore may be helpful for intermittent claudication or Raynaud's disease.<sup>6</sup>

### How to take Niacin CRT

Niacin CRT™ should be taken at bedtime, as cholesterol synthesis has been shown to be highest in the evening hours. Taking Niacin CRT at bedtime will also help to reduce the incidence and severity of flushing which may occur during early supplementation with niacin. The following dosage titration schedule for Niacin CRT is recommended:

- 1 tablet (500 mg) at bedtime for weeks 1 thru 4;
- 2 tablets (1000 mg) at bedtime for weeks 5 thru 8.
- If necessary after week 8, the dose can be increased by 500 mg every 4 weeks to a maximum of 2000 mg at bedtime or as directed by your health care professional.

Avoid taking with alcohol, hot beverages, or juice as this can accelerate the dissolution of the tablet leading to higher initial levels of niacin.

### Who should not take Niacin CRT

Patients with a history of coronary insufficiency and those on vasodilating drugs should only use niacin under the guidance of a qualified health care provider given the potential for a hypotensive event. Use by patients with known liver disease should probably be avoided, even though no adverse reactions have been reported. Also, if high doses (2 grams or more daily) are being administered, liver enzymes should be monitored every 2-3 months for at least the first six months. In addition, due to its fibrinolytic effect, niacin should be used with caution in conjunction with fibrinolytic and blood thinning drugs. Taking niacin alone may raise homocysteine levels in some individuals.<sup>7</sup> We recommend that any niacin formula be given with adequate amounts of B6, B12 and folic acid, accomplished with the co-use of formulas such as B Supreme, Twice Daily Multi or Homocysteine Supreme. Others requiring increased caution include patients with known history of gallbladder disease, gout or acid-peptic disease.

### References

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7. Desouza C, Keebler M. Drugs affecting homocysteine metabolism: impact on cardiovascular risk. *Drugs*. 2002;62(4):605-16