

# Dangers of OTC Herbal Supplements: Dilated Cardiomyopathy after Ingestion of TRIAC (triiodothyroacetic acid, Tiratricol)

D Marks

## Citation

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## Abstract

Cardiomyopathy associated with hyperthyroidism is a serious and potentially lethal condition. We describe a patient who developed a dilated cardiomyopathy (DCM) after consuming an over-the-counter (OTC) supplement containing triiodothyroacetic acid. With early diagnosis and treatment by removal of the source, cardiomyopathy may be reversible, as in this patient's case. The dangers of use of OTC medications, and problems and assumptions associated with FDA monitoring and removal from the market of harmful substances are discussed.

The author accepted no support for preparing this abstract, although the case initially was analyzed as part of a compensated expert consultation for litigation.

## INTRODUCTION

Tricana, containing triiodothyroacetic acid, was sold as an OTC herbal supplement preparation, and promoted for potential beneficial metabolic effects, including weight loss and energy enhancement. Tricana was withdrawn from the market in 2000 by the FDA<sub>1</sub> when Tricana use was associated with various adverse effects, including heart attacks and strokes. Symptoms associated with ingestion of Triac included many of those typical of hyperthyroidism: insomnia, nervousness, sweating, and diarrhea. This report describes the case of a reversible dilated cardiomyopathy in a woman who used Tricana.

## METHODS

The basis of this case report was a thorough review of the medical records, an interview with the patient, and a search of the current medical literature. A determination of causal relatedness between the consumption of Tricana and the development of DCM was made using universally accepted algorithms, as described<sub>2</sub>.

## REPORT OF A CASE

The patient was a female in her late 40s with a past medical history significant primarily for an episode of post-partum thrombophlebitis while in her early 20s. She also had mild

hypertension and mild hypercholesterolemia, both controlled without pharmacologic therapy. She denied smoking, alcohol use, or illicit drug consumption. There was no family history of premature coronary disease.

The patient used the nutritional supplement Tricana, which contained TRIAC (tiratricol, triiodothyroacetic acid) for approximately 16 days, as an attempt to achieve weight loss. The patient also consumed two doses of a weight-loss supplement called Adipokinetix (ephedra with caffeine) on a single day during the same time period. Adipokinetix was discontinued after the first two doses because of anxiety, which had resolved by the next day.

The patient presented to her primary care physician after 16 days of use of Tricana with a two-week history of acute panic-like attacks, shortness of breath, sweating, and tachycardia. BP 140/90, HR 110, weight 150 lbs, 61 inches height. EKG showed sinus tachycardia with T wave inversion. Thyroid function tests – thyroxine and TSH were normal. T3 level was not measured. An echocardiogram showed severe dilated cardiomyopathy with generalized hypokinesis of all ventricular segments. The ejection fraction was estimated at 15-20%, with a trivial degree of tricuspid regurgitation. A chest radiogram revealed an area of infiltrate at the left lung base. A perfusion lung scan was normal.

Cardiac Catheterization gave a picture consistent with idiopathic cardiomyopathy, with severe biventricular failure

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and an ejection fraction in the 15-20% range. Left ventricular end diastolic pressure was elevated, but right side pressure had stabilized. No evidence of significant coronary artery disease was noted. A cardiac biopsy showed focal myocyte hypertrophy and mild fibrosis. No changes of ischemia and no inflammatory infiltrate were seen, with only a mild increase in collagen. The changes were consistent with the clinical picture of congestive cardiomyopathy of metabolic origin.

The patient's symptoms rapidly improved once the Tricana supplement was discontinued. A repeat echocardiogram performed two months after discontinuation showed a cardiac ejection fraction of 62%, but with concentric LVH and some residual tricuspid regurgitation. A repeat echocardiogram at 1 year showed an LV EF of 64%, mild concentric LVH, mild left apical enlargement and mild tricuspid regurgitation.

### DISCUSSION

Tricana was an over-the-counter (OTC) commercial product that was promoted as a dietary supplement before the FDA ordered its withdrawal<sub>1</sub> in the summer of 2000. The active ingredient of Tricana was TRIAC, or triiodoacetic acid, also known as tiratricol. TRIAC is a naturally-occurring acetic acid analogue of T3, believed to be derived primarily from extra-thyroidal metabolism of T3. It is also thought that some TRIAC originates from extra thyroidal 5'-monodeiodination of tetrac, the acetic acid analogue of thyroxine<sub>3</sub>. While only 1-2% of T4 is normally metabolized to T3, about 15% of T3 is normally metabolized by conversion to TRIAC<sub>3,4,5,6</sub>.

### DETERMINATION OF CAUSAL RELATEDNESS

Standard rules of causation<sub>2</sub> were employed to determine the degree of relatedness of development of DCM to consumption of Tricana. DCM was not present in this patient before the use of Tricana, and DCM developed within a reasonable time of consumption, as explained by the kinetics and toxicology of triiodothyroacetic acid. Thyrotoxicosis is an established cause of DCM. No concurrent illnesses or medications were present which could present similarly. The DCM reversed over a period of a few months after discontinuation of the triiodothyroacetic acid supplement.

### ABSENCE OF A REASONABLE ALTERNATIVE EXPLANATION

while attempting to establish causation in this specific case,

a list of alternative etiologies to this reversible dcm was considered:

**Figure 1**

Causes of DCM	Application to this case
Post-myocardial infarction	no history of MI or angina syndromes
Alcoholic	negative history
Infectious	negative history
Inflammatory	negative history
Autoimmune: $\beta$ 1-adrenergic autoantibodies	negative history
Mitral Regurgitation	negative echocardiogram
Hereditary	negative family history
Hemochromatosis	no findings of iron overload, and also was reversible
Heavy Metals: Cobalt, Lead, Mercury	negative history and labs
Tachycardia Induced, including <b>Hyperthyroidism</b> , atrial fibrillation, pacemakers	<b>PRESENT</b>
Drug Induced	no history of use of offending agents, other than Tricana
Muscular Dystrophies	no physical findings
Deficiencies: Thiamine, Selenium, Carnitine	no supportive syndromes
Physiologic dilation in very well-conditioned athletes	patient was not a well-conditioned athlete

From the above list, it can be seen that only Tricana exposure, and the resultant clinical hyperthyroidism, can explain the transient development of DCM in this patient. Further, the reversible nature of the DCM shortly after discontinuation of the offending agent – a challenge dechallenge response – supports further the identification of Tricana as the cause. The medical literature was supportive of a causal relatedness<sub>7,8,9</sub>, as was the patient's treating cardiologist.

On review of medical literature on Medline published since 1966, no other cases of cardiomyopathy associated with TRIAC were found. TRIAC's potency as a thyroid hormone has been associated with a number of major clinical symptoms characteristic of the hyperthyroid states. In addition to an increased rate of untoward cardiac events and strokes, TRIAC usage in humans has been associated with abnormal thyroid function tests, debilitating diarrhea, exhaustion, major weight loss, insomnia, nervousness, and excessive sweating<sub>1</sub>.

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When patients present with DCM or myocarditis in the absence of known etiologies, a careful medical history should be obtained to elicit symptoms of hypothyroidism, and the presence of elevated blood levels of T3, T4 and TSH should be investigated.

OTC products are available for purchase by the consumer without requiring a prescription. There is a misconception by the public that, because of their unrestricted availability, OTC products are inherently safe. The public apparently is also trusting that statements on OTC products concerning claimed efficacy and safety must be truthful. Herbal supplements, while sounding safe and innocuous, have the potential to cause significant injury. A recent example is the development of strokes, heart disease and hypertension after consumption of OTC products containing ephedra. Manufacturers must inform the public, in easy to understand language, of the potential for OTC products to cause harm.

Just as it had been recognized that thyroid hormone ingestion is not a safe method of promoting weight loss, the FDA recognized<sup>1</sup> in August 2000 that TRIAC-containing products promoted for weight loss were inherently unsafe. The FDA ordered the withdrawal of all TRIAC-containing products. Some of these included, in addition to Triax, Metabolic Hormone Analogue, such products as Triax Metabolic Accelerator, Tria-Cutz, Thyroid Simulator, Sci-Fi-Tri Cuts Dietary Supplement Capsules, and T-Cuts. In the case of the Triax preparation, the FDA estimated that the recommended dose of that preparation provided the equivalent of 10 times as much thyroid hormone effect as would be derived from a full replacement dose of thyroxine in an individual lacking a functioning thyroid gland.

Many reports in the literature have associated dilated cardiomyopathy with clinical hyperthyroidism<sup>7,8,9</sup>, although to our knowledge, this is the first association of DCM with TRIAC. Mechanistically, TSH receptors have been identified in the human myocardium<sup>10,11</sup>. It is thus important to include hyperthyroidism in the differential diagnosis of dilated cardiomyopathy, because thyrotoxicosis-associated cardiomyopathy may reverse significantly with treatment of the thyrotoxicosis alone.

It is interesting to note that the patient's conventional thyroid functions tests were completely normal in spite of a severe clinical thyrotoxicosis. This is almost certainly a reflection of the acute nature of this TRIAC thyrotoxicosis. The hypothalamic pituitary-thyroid axis can take several months

to adjust to acute perturbations in thyroid hormone levels<sup>12,13</sup>. There simply may not have been enough time elapsed in this unfortunate patient for the effects of the TRIAC-induced thyrotoxicosis to cause a suppression of TSH, and then, sequentially, of T4 levels. Had she taken the TRIAC supplement for several months, she almost certainly would have demonstrated markedly-suppressed levels of both TSH and T4.

### **SUMMARY**

The diagnosis of DCM secondary to thyrotoxicosis should be considered in any patient with a DCM of unknown etiology. Although thyrotoxicosis is most commonly due to Graves' disease, exogenous sources of thyroid hormone, including therapeutic doses and non-prescription "nutritional supplements", must also be considered in the differential diagnosis. A high degree of clinical suspicion is required to make a prompt and correct diagnosis.

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**Author Information**

**Donald H. Marks, M.D., Ph.D.**

Department of Medicine, Cooper Green Mercy Hospital