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# Hypersensitivity to lipoic acid

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## KEY WORDS

*Lipoic acid; allergy; hypersensitivity; mast cells; tryptase.*

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## Doi

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To the Editor,

though we daily deal with adverse reactions to almost any kind of allergen, sometimes our job can still be surprising. We examined a 44-year-old woman with autoimmune hypothyroidism and essential hypertension, who was regularly taking Eutirox<sup>®</sup> and Triatec HCT<sup>®</sup> tablets (**table I**). A recent immediate (< 60'), diffuse, self-limiting (about 2-3 hours) urticarial rash after the intake of Destior R+<sup>®</sup> (Sintactica, Italy) stood out in her allergological history. Destior R+<sup>®</sup> is an antioxidant-multivitamin product containing lipoic acid (LA, 600 mg), thiamine, pyridoxine, DL-alpha-tocopheryl acetate, lysine, lactose, carboxymethylcellulose (50 mg) (1) microcrystalline cellulose, stearate, and talc. Planning the diagnostic path, we decided to bypass the skin tests phase because of the moderate features of the adverse event and the low/uncertain sensitivity and predictive values expected. During a first challenge test (DPT) with Destior R+<sup>®</sup>, about 25 minutes after completing the whole dose, the patient developed another widespread urticarial reaction, without other complaints; complete resolution was obtained with prompt administration of antihistamines and steroids. Serum tryptase was elevated at 5.3 mcg/L, compared to a baseline of 1.8 mcg/L. Since we couldn't acquire pure components of Destior R+<sup>®</sup> except carboxymethylcellulose, we decided to surrogate them with commercially available products. DPTs with pure carboxymethylcellulose (80 mg; Roquette, France), thiamine (100 mg; Benerva<sup>®</sup>, Teofarma, Italy), pyridoxine (100 mg; Benadon<sup>®</sup>, Bayer, Germany), DL-alpha-tocopheryl acetate (100 mg; Evion<sup>®</sup>, Dompé,

Italy) were performed uneventfully; conversely, our patient reacted to LA (670 mg; Tiobec<sup>®</sup>, Laborest, Italy) developing another urticarial rash, easily controlled again without the need for epinephrine administration; serum tryptase was 4.2 mcg/L.

Lipoic acid, also known as thioctic acid, is a medium-chain fatty acid derived from caprylic (octanoic) acid by addition of two sulphur atoms to form a five-membered ring (**figure 1**) (2). Small amounts of LA are found in various foods. It acts principally as an antioxidant, and its R (alpha) enantiomer has been proposed for the treatment of several conditions (3).

We couldn't find cases of generalized immediate reactions to LA or orally administered vitamin B1/B6/E in the scientific literature (PubMed, Google Scholar, Web of Knowledge). Allergic reactions to lipoic acid have previously been rarely described, mainly of the delayed type, both as local contact dermatitis (4, 5), and in one case as a delayed skin rash due to the consumption of another LA oral supplement (6); recently, a case of contact urticaria to LA has also been reported (7). Until now, systemic immediate reactions to LA were only generically supposed (8) or just self-reported without any evidence (9). Here, challenge tests led to the diagnosis of systemic immediate hypersensitivity to LA, showing

**Figure 1** - Lipoic acid



**Table I** - Components of the aforementioned products.

Product	Producer	Components
Eutirox®	Merck	Thyroxine; corn starch, citric acid, carboxymethylcellulose, gelatine, stearate, mannitol
Triatec HCT®	Sanofi	Ramipril, hydrochlorothiazide; hydroxypropyl methylcellulose, corn starch, microcrystalline cellulose, stearyl fumarate
Destior R+®	Sintactica	Lipoic acid 600 mg, vitamin B1 as thiamine 1.1 mg, vitamin B6 as pyridoxine 1.4 mg, vitamin E as DL-alpha-tochopheryl acetate 24 mg; lysine, lactose, carboxymethylcellulose, microcrystalline cellulose, stearate, talc
Benerva®	Teofarma	Thiamine 100 mg, talc, povidone K90, stearate, methacrylate/ethyl acrylate copolymer, macrogol 6000, carboxymethylcellulose
Benadon®	Bayer	Pyridoxine 100 mg, povidone K90, talc, stearate, methacrylate/ethyl acrylate copolymer, macrogol 6000, carboxymethylcellulose
Evion®	Dompé	DL- $\alpha$ -tochopheryl acetate 100 mg, sucrose, isomalt, corn starch, skimmed milk, talc, arabic gum, orange flavour, titanium dioxide, red iron oxide, stearate
Tiobec®	Laborest	Alpha-lipoic acid 800 mg, microcrystalline cellulose, dicalcium phosphate, silicon dioxide, talc, stearate, carboxymethylcellulose, glyceryl behenate, hydroxy-propyl methylcellulose, polyvinylpyrrolidone, shellac, microcrystalline cellulose, stearic acid, fatty acids mono- and acetate diglycerides, titanium dioxide

once again their essential role in our clinical practice. A further DPT with pure LA was not performed because of ethical concerns: indeed, the clinical picture was clearly indicative of hypersensitivity to LA, being LA the only relevant antigen contained in any product which caused our patient an immediate urticarial reaction and not contained in the tolerated products. The rise of serum tryptase levels after LA intake suggests that the reactions occurred through mast cell activation (10).

In the end, we learnt that in case of strong suspicion of an allergic reaction to a LA-containing product, hypersensitivity to LA must also be considered among the possible causes.

We report that ethical approval not necessary; written informed consent for anonymous disclosure was obtained.

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None.

### Contributions

FM: conceptualization, investigation, methodology, project administration, visualization, writing - original draft, writing - review & editing. AC: resources, supervision, writing - review & editing.

### Conflict of interests

The authors declare that they have no conflict of interests.

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