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Thymosin Beta Advisory

The Racing Medication and Testing Consortium (RMTC) has received questions regarding thymosin β_4, a naturally occurring peptide that is an endogenous substance in the horse. Thymosin β_4 is comprised of multiple smaller peptide chains. One of the chains is named LKKTETQ and it is being synthesized and marketed for use in the horse. These products lack FDA approval and as such there is no information on their safety, efficacy, stability, purity, and potential for adverse reactions.

The N-acetylated LKKTETQ peptide chain is available on a number of websites and is often referred to as TB-500. The marketing materials reviewed claim that TB-500 can build muscle, speed muscle recovery, stop bleeding, increase red blood cells, and decrease inflammation. These claims of effect in the horse are unsubstantiated; the actual effects, to the extent they occur, are unknown. The per-dose cost of these products ranges from $150-300. Dosing regimens have been described as a series of subcutaneous injections of one 2 ml vial once weekly for six weeks then monthly thereafter. There are also descriptions of TB-500 administration the day after an intense workout.

The University of California Davis Kenneth L. Maddy Laboratory has obtained a sampling of TB-500 labeled products. After testing the products, the chemists determined that many of the substances marketed as thymosin β_4 actually do not contain any portion of the thymosin β_4 peptide. Instead, they contain sugars.

However, a few of the samples tested by the Kenneth L. Maddy Laboratory actually did contain the N-acetylated LKKTETQ peptide chain of thymosin β_4. While some of the claims made by the distributors of these products are unsupported in the literature, research studies have shown that this amino acid chain may have some effect in other mammalian species.

Several studies have investigated the effects of introducing thymosin β_4 into animals via injection. [1] Specifically, they have found that the LKKTETQ amino acid sequence may have a role in wound healing. Additionally, this sequence may also be responsible for angiogenesis – the development of blood vessels (not to be confused with erythropoiesis – the development of new red blood cells). It may also be responsible for cross-linking with fibrin at sites of blood coagulation in wound healing.[2] It appears, however, that the anti-inflammatory properties are contained in another amino acid sequence that is not in TB-500-like products. Also, a large portion of administered thymosin β_4 is transported intracellularly where it may be responsible for other, unknown, functions.

[1] Sonse, G., *Biological activities of thymosin β_4 defined by active sites in short peptide sequences*, The FASEB Journal, 24: 2144-2151 (July 2010); Philp, D., *Animal studies with thymosin β_4, a multifunctional tissue repair and regeneration peptide.*

[2] Mannherz, H.G., *The β-Thymosins: intracellular and extracellular activities of a versatile actin binding protein family*, Cell Motility and the Cytoskeleton 66: 839-51 (2009).

The Hong Kong laboratory has developed a test to detect a race-day (or same-day) administration of TB-500.[3] In this study, two horses were administered a single dose of TB-500. Those researchers were able to detect a metabolite of TB-500, unique to the synthetic substance, at 11.3 hours in plasma. However, based upon the dosing regimen described above, a race-day administration would be highly unlikely. Controlling the use of TB 500 cannot be adequately achieved through laboratory analysis alone. Surveillance, premise and vehicle inspections, and document review are key components in deterring the use of this unapproved product.

[3] Ho, E.N., *Doping Control analysis of TB-500, a synthetic version of an active region of thymosin β_4, in equine urine and plasma by liquid chromatography-mass spectrometry*, Journal of Chromatography A, 1265: 57-69 (2012).