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Form of α-tocopherol affects vitamin E bioavailability in Thoroughbred horses

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Introduction

Vitamin E functions as a biological antioxidant, preventing the oxidation of unsaturated lipid materials within cellular and subcellular membranes by neutralizing production of free radicals. Supplemental vitamin E may be beneficial in horses experiencing oxidative stress such as during parturition and exercise (Hargreaves et al., 2007) and for horses at risk of certain types of neurological diseases (Mayhew et al., 1987; Blythe and Craig, 1993).

Vitamin E can be obtained from natural or synthetic sources, but the chemical structure of each is different. Natural vitamin E is composed of one isomer (d-α-tocopherol [RRR α-tocopherol]), and it is the most bioactive form in human and animal tissue. Synthetic vitamin E is a mixture of eight isomers (dl-α-tocopherol [all-rac-α-tocopherol]), of which only one is identical to the natural isomer. These eight isomers vary greatly in relative biopotency. Synthetic or natural vitamin E is typically added to equine feeds in an esterifed form (α-tocopherol acetate) to prolong shelf life.

To account for differences in biopotency, the relative strengths of different forms of vitamin E are expressed as international units (IU) in which 1 mg of synthetic acetate equals 1 IU, 1 mg of natural acetate equals 1.36 IU, and 1 mg of natural alcohol equals 1.49 IU (Anon, 2000). These conversion factors were developed using laboratory animal models, and they may not be relevant for horses and humans. In fact, studies in humans have suggested that natural-source vitamin E is twice as bioavailable as the synthetic form (Acuff et al., 1998; Burton et al., 1998), and studies in horses have suggested that the relative bioavailability of natural-source vitamin E is greater than synthetic (Pagan et al., 2005; Hargreaves et al., 2007).

The following studies were conducted to determine if synthetic and natural-source vitamin E have similar bioavailabilities when administered at equal IU doses and to determine if water-dispersible forms of vitamin E are more bioavailable than lipid-soluble forms.

Materials and Methods

Two studies were conducted to assess the relative bioavailability of different forms of vitamin E. In study 1, single oral doses of three different forms of vitamin E were evaluated in eight Thoroughbred geldings (age 10.75 ± 2.2 years) during three one-week periods. The forms of vitamin E evaluated included synthetic vitamin E (dl-α-tocopheryl acetate) (SYN)[a], natural-source vitamin E acetate (d-α-tocopheryl acetate) (ACT)[b], and natural-source alcohol (d-α-tocopherol) (ALC)[c]. On the first day of each period, the horses were administered 5000-IU doses of vitamin E top-dressed on 1 kg of unfortified sweet feed at 7:00 AM. Baseline blood serum samples were collected immediately before dosing and at 3, 6, 9, 12, and 24 hours post-dosing.

In study 2, three Thoroughbred geldings (age 5.67 ± 1.2 years) were used in a replicated 3 x 3 Latin square design trial to assess the relative bioavailability of three forms of vitamin E. There were a total of six one-week periods with each horse receiving each form of vitamin E in two separate periods. The vitamin E forms studied were synthetic vitamin E (dl-α-tocopheryl acetate) (SYN)[a], a micellized d-α-tocopherol (Elevate WS)[d], and a d-α-tocopherol (Nano·E)[e] that had been nanodispersed into liposomes. Both of these processes render normally lipid-soluble vitamin E water dispersible. At the beginning of each period the horses received a single 5000-IU dose of one of the vitamin forms top-dressed onto 1 kg of unfortified sweet feed. Baseline blood serum samples were collected immediately before dosing and at 3, 6, 9, 12, 24, 36, and 48 hours post-dosing. Throughout both studies the horses were maintained on an unfortified sweet feed plus grass hay.

Serum α-tocopherol was measured using high-performance liquid chromatography[f], and relative bioavailabilities were calculated from comparisons of magnitudes of responses measured by areas under the concentration versus time curves (AUC) and by comparisons of the peak concentrations of serum vitamin E following each dose. The AUC, baseline, peak, and maximal change from baseline data were analyzed by analysis of variance (ANOVA), and a Tukey-Kramer multiple comparison was used to examine differences between treatments.

Results and Discussion

In study 1, ACT and ALC had a significantly greater AUC than SYN ($P < 0.05$) (Table 1). There was no significant difference in AUC between ACT and ALC. Relative to SYN, the bioavailability of ACT and ALC equaled 197% and 252%, respectively. Time post dosing to peak vitamin E was not different between treatments and averaged 9.2 ± 1.2 (mean ± SE) hours. Although there was a trend towards higher peak levels and maximal change from baseline values for the ACT and ALC treatments compared to SYN, these differences were not significantly different ($P > 0.05$).

Table 1 Response in serum α-tocopherol to 5000-IU doses of synthetic, natural acetate, and natural alcohol forms of vitamin E.

	synthetic[a]	**naturalacetate[b]**	**natural alcohol[c]**
	SYN	**ACT**	**ALC**
n	8	8	8
area under curve (24 hr AUC)	5.9 ± 1.5a	11.6 ± 2.0b	14.9 ± 3.0b
baseline vitamin E(ug/ml)	3.44 ± 1.80a	3.51 ± 0.09a	3.31 ± 0.13a
Peak vitamin E (ug/ml)	3.97 ± 0.08a	4.58 ± 0.39a	4.58 ± 0.39a
Δ vitamin E (ug/ml)	0.52 ±0 .12a	1.07 ± 0.39a	0.93 ± 0.18a

[ab]Means for the same item with the same letter are not different ($P > 0.05$)

In study 2, Elevate WS and Nano·E had a significantly greater AUC than SYN ($P < 0.05$)(Table 2). There was no significant difference in AUC between Elevate WS and Nano·E. Relative to SYN, the bioavailability of Elevate WS and Nano·E equaled 559% and 613%, respectively. Time post dosing to peak vitamin E was not different between
treatments and averaged 12.0 ± 1.4 (mean ± SE) hours. Nano·E had significantly higher peak and maximal change from baseline values compared to SYN ($P < 0.05$).

Table 2 Response in serum α-tocopherol to 5000-IU doses of a synthetic and two water-dispersible forms of vitamin E.

treatment	**Synthetica**	**Elevate WSd**	**Nano·Ee**
n	6	6	6
area under curve (48 hrs)	15.62 ± 3.22a	87.36 ± 25.3b	95.85 ± 25.7b
baseline vitamin E (ug/ml)	3.04 ± .30a	3.00 ± .39a	2.86 ± .42a
Peak vitamin E (ug/ml)	3.63 ± .36a	6.01 ± 1.26ab	6.69 ± 1.39b
Δ vitamin E (ug/ml)	.59 ± .08a	3.00 ± .89ab	3.83 ±1 .15b

[ab]Means for the same item with the same letter are not different ($P > 0.05$)

The results of these studies suggest that natural sources of vitamin E have a greater bioavailability than is accounted for in the current conversion factors of 1.36 and 1.49 used in the feed industry for natural acetate and

alcohol, respectively. These differences should be taken into account when calculating the quantity of supplemental vitamin E required by horses.

Natural-source water-dispersible forms of vitamin E were 5-6 times more bioavailable than synthetic vitamin E acetate, and a 5000-IU dose more than doubled serum vitamin E levels within 12 hr. These forms of vitamin E should be beneficial when a rapid increase in vitamin E is warranted such as during periods of oxidative stress (exercise or parturition) or for horses at risk of certain types of neurological disease.

References

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Footnotes

[a]ROVIMIX E-50 Adsorbate (dl-a-tocopheryl acetate), DSM Nutritional Products AG, Wurmisweg 576, CH-4303 Kaiseraugst, Switzerland

[b]KER Equine Ester™, Kentucky Equine Research, Versailles, KY 40383, USA

[c]NOVATOL™ 5-87 (d-α-tocopherol), Archer Daniels Midland Company, Decatur, IL 62526, USA

[d]Elevate WS®, Kentucky Performance Products LLC, Versailles, KY 40383, USA

[e]Nano·E™, Kentucky Equine Research, Versailles, KY 40383, USA

[f]DCPAH Nutrition, College of Veterinary Medicine, Michigan State University, East Lansing, MI 48824, USA