



## I WANT TO KNOW

**Q** : I'm looking at your **Total E** product, and it doesn't give the IU values for anything but the alpha-tocopherol. Can you please tell me how many IU there are of all the *other* vitamin E molecules?

**A** : One reason **AOR** doesn't put this information on the **Total E** label is that we're not *allowed* to, legally, in most countries. But even if we were allowed to provide this information, we would still choose to give the amounts of the various E-complex vitamins in milligrams, not IU, because measuring vitamin E molecules IUs is actually very misleading. Your question is therefore important, because it strikes at the heart of the biological activity of vitamin E.

Let's start at the beginning. As you probably know, the IU is not a measure of weight; it's *supposed* to be a measure of "the" *biological activity* of "vitamin E." The trouble is – as you're probably also aware, if you're looking for an advanced E-complex supplement like **Total E** – that "**vitamin E**" has *more than one biological activity* – a fact which is closely related to the fact that there's *more than one vitamin E molecule*. As a result, using one "yardstick" to measure several *different* kinds of biological activity is bound to be misleading.

You'll understand this point better if you look at the similar situation with the B-complex. Different B vitamins do different things, so it isn't reasonable to measure their biological activity in the same way. If we were to measure the activity of one B-vitamin (say, thiamine) using a system of units which was designed to assess the biological activity of another (such as vitamin B<sub>12</sub>), we'd get a pretty warped picture of the balance of the two vitamins present in a B-complex pill: after all, no amount of B<sub>12</sub> is "equivalent" in biological activity to a given amount of thiamin, because B<sub>12</sub> has *none of thiamin's vitamin activity*. One measure of activity cannot take into account the very different functions of the two molecules.

It's a similar story with the various vitamin E molecules. Unlike with

the B vitamins, *all* E-complex vitamins do share *some* functions in common; it's because of these shared properties that the different vitamin E molecules are called "**E vitamers**" rather than being individually labeled as "Vitamin E<sub>1</sub>," "Vitamin E<sub>2</sub>," etc. But on the other hand, there are *other* properties which are held by only *some* of the E vitamers, or which are unique to one, specific E molecule. The problem with the IU, then, is that it measures only one of these functions – namely, what's called "classical" vitamin E activity.

"Classical" vitamin E activity was defined back when alpha-tocopherol was first discovered. Scientists had discovered that pregnant rats fed a fat-free diet would resorb their fetuses, and that the factor present in regular diets that allowed the pregnancies to go to term was highly concentrated in wheat germ oil. Through careful investigation, scientists were able to identify alpha-tocopherol as the mystery molecule.

But scientists then jumped to the conclusion that the prevention of fetal resorption was "the" biological function of vitamin E. In fact, the very word "tocopherol" was coined by combining the Greek words *tokos* ("offspring") and *pheros* ("to bear"): vitamin E, in these early days of research, was considered to be simply the vitamin "to bear offspring." As a result, the IU value – which was *supposed* to be a measure of "the" biological activity of vitamin E – was defined in terms of the "rat fetal resorption assay:" the number of milligrams of a particular vitamin E molecule which are required to allow a rat pregnancy to go to term.<sup>1</sup>

This makes the IU a very important measure of vitamin E activity ... for rat breeders. The problem, of course, is that *people* taking vitamin E supplements are not taking them to avoid fetal resorption – any more than we're taking vitamin C to avoid scurvy, or niacin to avoid pellagra. For the purposes for which health-conscious people want E-complex vitamins, the IU thus gives a very misleading picture of biological activity. The rat fetal resorption assay takes no account of the *different* actions of the various vitamin E molecules. **IU values thus ignore the**

***There's more than one vitamin E molecule, so "vitamin E" has more than one biological activity.***

**tocotrienols' superior antioxidant activity in biological membranes<sup>2</sup> ... and gamma-tocopherol's status as a natural COX-2 inhibitor<sup>3</sup>... and the fact that breast cancer cells in a test tube can be**

**"ordered" to commit cellular "suicide" by tocotrienols and by delta-tocopherol, but not by other tocopherols.<sup>4</sup>**

**The IU also ignores the different ways that the various E-complex molecules are stored in the body.** Alpha-tocopherol is specifically concentrated in sites in the body where it is most required (such as the liver and prostate) by special transport proteins;<sup>4a</sup> on the other hand, tocotrienols are specifically concentrated in the skin.<sup>5</sup> In the case of gamma-tocopherol<sup>6</sup> and gamma tocotrienol,<sup>7</sup> an even greater difference is seen. One of the chief functions of these vitamin E molecules (namely, regulating extracellular fluid) is achieved precisely by *urinating out* the correct amount of their key metabolite (LLU-alpha)!

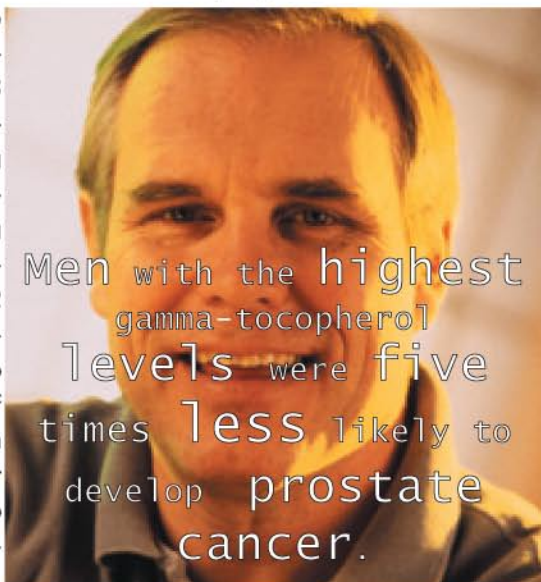
**The effects of interactions among the E vitamers on their**

**biological activities are also misrepresented by the IU.** Measuring alpha-tocopherol's activity in IU ignores the fact that the ability of alpha-tocopherol to protect the body against nitrogen-based free radicals (such as those found in smog) can only manifest itself when gamma-tocopherol is also present: this activity is lost when alpha-tocopherol is present *alone*, no matter how high the "IU" amount.<sup>8</sup> Similarly, the biological activity of gamma-tocotrienol in reducing cholesterol synthesis is reduced when too much alpha-tocopherol is present.<sup>9</sup>

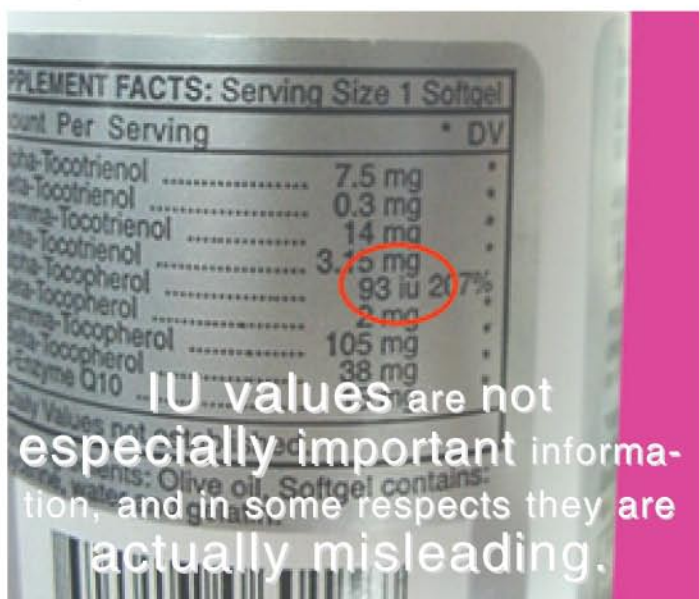
A great example of a synergistic interaction which affects the biological activities of E-complex vitamins was provided in a recent study<sup>10</sup> which found that men whose plasma gamma-tocopherol levels were in the top 20% were an astounding *five times* less likely to develop prostate cancer than men whose levels were in the lowest 20%. And **while there was no significant independent connection found between levels of alpha-tocopherol and risk of prostate cancer, men who had high levels of gamma-tocopherol were at even lower risk if they also had high alpha-tocopherol levels.** In other words, this study suggests that a protective biological activity of alpha-tocopherol against prostate cancer can *only* manifest when it's part of a team with gamma-tocopherol. These functional interactions are not measured by the IU as a measure of "biological activity."

And so on. **AOR** feels that the IU system is so misleading that it would be better if it were simply abandoned. For just this reason, we had originally intended the **Total E** label to give the amounts of *all* of the vitamin E molecules in milligrams only. In the end, however, we decided to give the IU value for alpha-tocopherol, because people are so used to seeing alpha-tocopherol measured this way that making the break would only create confusion. One day, however, when there is greater awareness of the other E-vitamins' unique properties, milligrams may become recognized as the only unbiased way of measuring E-complex vitamins.

Nonetheless, **you can assign IU values to E-complex molecules other than alpha-tocopherol**, using the rat fetal resorption assay. While we aren't allowed to put this information on supplement bottles, IU numbers have been assessed for the various E vitamers. Thus, if you're still interested, it takes 0.66 mg of d-alpha-tocopherol, or 1.3 mg of beta-tocopherol, or 6.7 mg of gamma-tocopherol, or 20 mg of delta-tocopherol,<sup>11</sup> or 2.2 mg of alpha-tocotrienol,<sup>12</sup> to get one IU of "classical" vitamin E activity. To our knowledge, no one has deter-



mined the relative IU value for the other tocotrienols. activity<sup>11</sup>



With all of this as background, we think you'll now understand why we would not choose to list the values for the E vitamers in IU, even if we were allowed to do so. Simply put, **IU values are not especially important information, and in some respects are actually misleading.** But the reasons *why* the IU is a bad measure of biological activity make the question a very important one. Thanks for asking!

#### References

- Bunyan J, McHale D, Green J, Marcinkiewicz S. Forms of vitamin E and their activity. *Br J Nutr.* 1961;15:253-7.
- Serbinova E, Kagan V, Han D, Packer L. Free radical recycling and intramembrane mobility in the antioxidant properties of alpha-tocopherol and alpha-tocotrienol. *Free Radic Biol Med.* 1991;10(5):263-75.
- Jiang Q, Elson-Schwab I, Courtemanche C, Ames BN. Gamma-tocopherol and its major metabolite, in contrast to alpha-tocopherol, inhibit cyclooxygenase activity in macrophages and epithelial cells. *PNAS.* 2000 Oct 10;97(21):11494-9.
- Yu W, Simmons-Menchaca M, Gapor A, Sanders BG, Kline K. Induction of apoptosis in human breast cancer cells by tocopherols and tocotrienols. *Nutr Cancer.* 1999;33(1):26-32.
- Stocker A, Azzi A. Tocopherol-binding proteins: their function and physiological significance. *Antioxid Redox Signal.* 2000 Fall;2(3):397-404.
- Wechter WJ, Kantoci D, Murray ED Jr, D'Amico DC, Jung ME, Wang WH. A new endogenous natriuretic factor: LLU-alpha. *PNAS.* 1996 Jun 11;93(12):6002-7.
- Hattori A, Fukushima T, Yoshimura H, Abe K, Ima K. Production of LLU-alpha following an oral administration of gamma-tocotrienol or gamma-tocopherol to rats *Biol Pharm Bull.* 2000 Nov;23(11):1395-7.
- Christen S, Woodall AA, Shigenaga MK, Southwell-Keely PT, Duncan MW, Ames BN. Gamma-tocopherol traps mutagenic electrophiles such as NO(X) and complements alpha-tocopherol: physiological implications. *PNAS.* 1997 Apr 1;94(7):3217-22.
- Qureshi AA, Pearce BC, Nor RM, Gapor A, Peterson DM, Elson CE. Dietary alpha-tocopherol attenuates the impact of gamma-tocotrienol on hepatic 3-hydroxy-3-methylglutaryl coenzyme A reductase activity in chickens. *J Nutr.* 1996 Feb;126(2):389-94.
- Helzlsouer KJ, Huang HY, Alberg AJ, Hoffman S, Burke A, Norkus EP, Morris JS, Comstock GW. Association between alpha-tocopherol, gamma-tocopherol, selenium, and subsequent prostate cancer. *J Natl Cancer Inst.* 2000 Dec 20;92(24):2018-23.
- Bunyan, McHale, Green, Marcinkiewicz S. Forms of vitamin E and their activity. 1961; *Br J Nutr.* 15:253-7.
- Weimann BJ, Weiser H. Functions of vitamin E in reproduction and in prostacyclin and immunoglobulin synthesis in rats. *Am J Clin Nutr.* 1991 Apr;53(4 Suppl): 1056S-1060S.