

DHEA and DHEAS: An Introduction to Their Function and Measurement

Background

Dehydroepiandrosterone (DHEA) and its sulfated analog (DHEAS) are steroid hormones principally made in the adrenal cortex. DHEAS is the most abundant steroid in humans with serum concentrations 250-500 times higher than DHEA, 100-500 times higher than testosterone, and 1000-10000 times higher than estradiol.(1,2) DHEAS appears to serve primarily as a precursor molecule that is circulated to peripheral tissues throughout the body. In those locations (and in the adrenal cortex) it is desulfated enzymatically to produce DHEA, which is in turn converted into various estrogenic and androgenic compounds. A portion of the DHEA produced locally may also be converted back to the sulfated form.(2) Because the two forms are easily interconverted, it is hard to discuss one without the other, and it is common to refer to them together as DHEA(S).

Circulating levels of DHEA(S) decline after birth until about the age of five, then start to rise a few years before sexual maturation begins. Levels peak around the age of 20 to 30 and then decline to only 20-30% of peak levels by the age of 70 to 80.(2) Lowered levels of DHEA(S) have been associated with critical illness, emotional stress, and a variety of medical conditions, including rheumatic disease,(3) cardiovascular disease,(4) immune system disorders,(5) and osteoporosis.(6) Elevated levels have been observed in connection with obesity and type II diabetes,(7) female hirsutism,(8) and individuals subjected to prolonged physical stress.(2)

DHEA and DHEAS are also synthesized directly in the nervous system, where they appear to help protect against harmful agents.(9,10) Studies are currently exploring relationships between DHEA(S) levels and various areas of neurological function, and at least one paper has suggested that the primary effect of DHEA(S) is in fact neurological, with secondary effects on immune function and growth.(11)

Because of the coincidence between the natural decline of DHEA(S) levels with age and the onset of diseases associated with the aging process, a great deal of research has been directed into an examination of the roles that both hormones play in the body, and to the possibility of supplementing levels to slow or reverse the aging process. Although these studies have reported widespread effects for the hormones, a molecular mechanism of action has not yet been definitively isolated for either DHEA or DHEAS. It remains unclear whether either compound has a physiological role other than serving as a precursor molecule.(12) Recent reviews point out that this lack of understanding about the mode of action of the two hormones, along with problems in the design and analysis of certain studies, have led to discrepancies among the findings.(1,13)

Entry of DHEA and DHEAS into saliva.

DHEA is a neutral steroid, and it passes rapidly from blood into saliva by passive diffusion through the neutral lipid membranes of the salivary cells. Salivary concentrations are about 5% of plasma concentrations.(2) DHEAS, on the other hand, is a charged molecule due to the presence of the sulfate group, and it cannot diffuse through the lipid membranes. Instead, it enters saliva only by squeezing through the tight junctions between cells, and it is too large to do this readily. It is therefore present in relatively small amounts—less than 0.1 % of plasma levels in parotid saliva.(14)

Because of the much higher levels of DHEAS in blood, even the presence of minute quantities of blood or gingival fluid in the saliva can cause false elevation of DHEAS levels. For this reason, some feel that salivary measurement of DHEAS is unreliable.(14) We advise that, if saliva testing for DHEAS is to be valid, subjects must be properly screened for periodontal disease and advised about proper collection procedures that will minimize the risk of blood or gingival contamination. Saliva may also be screened for blood contamination using the Salimetrics Blood Contamination EIA Kit (Cat. No. 1-1302).

Effect of Flow Rate.

Because of the difficulty that DHEAS molecules have moving through the cell membranes of the salivary glands, it is not surprising that, as saliva flow is stimulated, the DHEAS molecules are not able to keep up with the increased flow, and concentrations in saliva drop. Even though this behavior was clearly documented in a seminal paper on saliva testing,(14) some researchers seem unconcerned by it. Our position at Salimetrics is that measurement of DHEAS in saliva requires a correction for saliva flow rate. We advise measuring the length of time needed to collect the desired volume of sample, so as to determine the flow rate. The measured concentration can then be combined with the flow rate to express the results as a function of time, i.e. pg/minute.

Which is preferable: DHEAS or DHEA?

Because of the concern about blood contamination and the need to adjust for flow rate when measuring DHEAS, and a higher serum/saliva correlation for DHEA, Salimetrics originally chose to develop a kit to measure DHEA in saliva. This kit has functioned well, and it has been successfully used by investigators in published research.(15) Since that time, however, some researchers have told us that they prefer to measure DHEAS rather than DHEA, and their work has begun to show some interesting findings. In response to customer requests, therefore, we have decided to add a kit to measure salivary DHEAS. We will continue to manufacture the kit for DHEA, as well, and researchers will be able to choose either kit, depending on their requirements.

References

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