

The Science of Saliva Testing

Estrogens (estrone, estradiol and estriol), progesterone, testosterone, DHEA-S and cortisol are routinely measured in saliva at ZRT. Why saliva? Steroid hormones in the bloodstream are mostly (95-99%) bound to carrier proteins (hormone-binding globulins, albumin), and in this form they are unavailable to target tissues. Only the unbound fraction freely diffuses into tissues, including the salivary gland. Hormone levels in saliva therefore represent the quantity of the hormone that is currently available to target tissues and actively exerting specific effects on the body. Because of this, salivary hormone levels often relate to specific symptoms of hormone excesses or deficiencies. Research at ZRT has demonstrated clear correlations between salivary hormone levels and reported symptoms. The rationale for and clinical utility of saliva testing is well documented¹⁻¹³.

The very small concentrations of salivary hormones (only 1–5% of the total hormone levels that include protein-bound hormone found in serum) necessitate extremely sensitive assay methods. This is a particular issue for estrogens, which are present in very minute quantities in saliva, especially in older populations such as postmenopausal women. ZRT is unique as the only commercial laboratory using extracted saliva testing for estrogens. Extraction removes contaminants that interfere with the assay and concentrates the sample, significantly improving assay sensitivity compared to the “direct” assay methods available commercially¹⁴. In fact, poor correlations between serum tests and non-extraction salivary estradiol assays have unfortunately led to some skepticism about saliva testing. Also, because of the extremely sensitive assays, it is important to avoid blood contamination of saliva as a result of oral injury, therefore toothbrushing must be avoided before collecting saliva for testing¹⁵. Saliva testing is not appropriate for sublingual hormone users because of direct contamination. Blood spot testing is the preferred option for these patients.

Available Tests

Hormone Trio – E2, Pg, T

Saliva Profile I – E2, Pg, T, DS, Cx1

Saliva Profile II – E2, Pg, T, DS, Cx2

Saliva Profile III – E2, Pg, T, DS, Cx4

Diurnal Cortisol – Cx4

Adrenal Stress Profile – DS, Cx4

Cortisol Awakening Response Profile – DS, Cx6

LCMS Saliva Steroid Profile – E2, E3, E1, EE, PregS, Pg, AlloP, 17OHPg, Adione, T, DHT, D, DS, 7keto, 11DC, C, Cn, Ccn, Ald, Mel, ANZ, FIN, LTZ

Saliva testing measures the amount of hormone available to target tissues – the bioavailable amount. For this reason, saliva testing better relates to specific symptoms of excess or deficiency, and is a good option for monitoring hormone therapy.



Hormone Testing

Non-invasive home test kit

A decorative graphic consisting of several overlapping hexagons of varying sizes, located in the upper right corner of the page.

Conversely, when some hormones, notably progesterone, are administered topically, saliva levels can rise higher than serum levels^{16,17}. This is because progesterone is carried to target tissues including the salivary glands, where there is rapid uptake and release of the hormone into tissues and saliva, leaving very little hormone in the venous blood returning from the tissues¹⁸. Tissue levels of progesterone have been found to be very high after topical progesterone use¹⁹⁻²¹, and a biological response can be demonstrated, e.g., the reduction of endometrial cell proliferation caused by estrogen therapy²². We have recently published a clinical study showing saliva levels of progesterone increased 10-fold while capillary blood spot levels increased 100-fold compared to levels in venous whole blood and venous serum following application of 80 mg progesterone cream or gel²³. This has led us to conclude that when hormones are delivered through the skin or oral or vaginal mucosa, conventional serum hormone tests grossly underestimate hormone delivery to tissues. In contrast, hormone levels in saliva or capillary blood spot better represent tissue hormone uptake.

DHEA-S, the sulfated storage form of DHEA, is measured rather than DHEA because its levels are more stable (DHEA has a much shorter half life in blood) and at ZRT it has been found to correlate very well with reported clinical symptoms. However, as a conjugated hormone that does not diffuse into saliva as rapidly as the unconjugated hormones measured in ZRT's other hormone assays, its passage into saliva is flow rate dependent¹² and therefore flow stimulants such as gum chewing are not advised prior to saliva collection.

Research at ZRT shows good correlations between salivary hormone levels and dosages of hormones given exogenously. Saliva testing is therefore a good option for monitoring hormone therapy and adjusting dosages if necessary.

Advantages

- ▶ Saliva testing, unlike serum tests, measures the bioavailable ("free") levels of steroid hormones, correlating with symptomatology and potential deficiency
- ▶ Samples are collected by the patient at home, allowing convenient timing of collection especially for cortisol, which must be measured at specific times of the day or night
- ▶ Convenience of collection allows frequent sampling, e.g., during a menstrual cycle to determine fertility problems
- ▶ Hormone levels can be assessed during topical hormone supplementation
- ▶ Saliva collection avoids the stress of a blood draw, which can affect levels of cortisol
- ▶ Hormones are stable in saliva at room temperature for up to 2 weeks, allowing for worldwide shipment and convenient mailing of samples for testing
- ▶ Saliva testing is less expensive than conventional serum testing

Clinical Utility

Saliva testing can help providers:

- ▶ Identify hormone imbalances prior to the appearance of symptoms or disease
- ▶ Identify specific hormone imbalances associated with symptoms
- ▶ Establish hormone baselines prior to surgery or beginning therapy
- ▶ Monitor hormone levels while supplementing, allowing for individualized hormone dosing
- ▶ Track patient symptoms and hormone levels using ZRT's comparative history reports provided with follow-up testing

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