



# Reproductive

## Estrone sulfate

Analyte Information



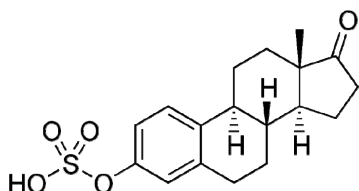


## Estrone sulfate

### Introduction

Estrone sulfate (E1-S) is a sulfate derivative of estrone, and is the most abundant form of circulating estrogens in both men and non-pregnant women<sup>1,2</sup>. It is the aromatized C<sub>18</sub>-steroid with a 3-sulfate group and a 17-ketone. Its chemical name is 1,3,5 (10)-estradien-3-ol-17-one-3-sulfate, its summary formula is C<sub>18</sub>H<sub>22</sub>O<sub>5</sub>S, and its molecular weight is 350.4 Da.

### Fig.1: Structural formula of estrone sulfate



### Biosynthesis

Estrone sulfate is the major metabolite of both estradiol and estrone<sup>2,3</sup>.

Formation of estrone sulfate occurs in various tissues in the body, but primarily in the liver. The reaction requires hydroxysteroid sulfotransferase activity and sulfate ions in the form of an active sulfate, namely phosphoadenosine phosphosulfate (PAPS) (4).

### Metabolism

Estrone sulfate is hydrolyzed to estrone and then converted to various conjugates via sulfonation, glucuronidation and O-methylation. The main site of degradation is the liver, but these reactions may also take place in estrogen target tissues such as the breast, ovary and uterus. The conjugated forms are finally excreted in urine.

Estrone sulfate may also be excreted in urine directly. The direct excretion rate is slow compared to that of the conjugated forms.



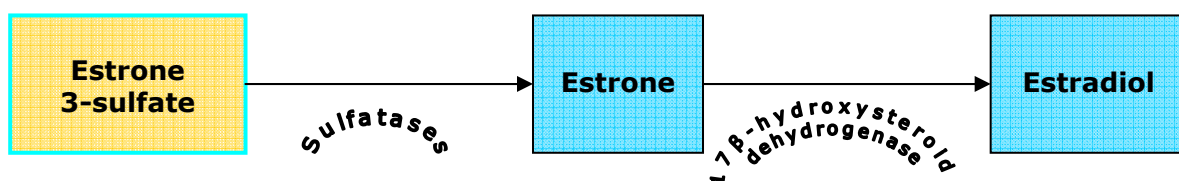
Thus, serum concentrations of estrone sulfate are three to five times higher than that of the corresponding glucuronide, but the opposite is true in urine. This is partly due to albumin's greater affinity for estrone sulfate compared to estrone glucuronide, but also because of estrone glucuronide's higher glomerular filtration rate.

### Physiological Function

Estrone sulfate itself does not have direct estrogenic activity.

Nevertheless, the large pool of circulating estrone sulfate may be viewed as a slowly-metabolized estrogen reservoir<sup>1</sup>. A number of tissues in the body contain sulfatases which can transform the biologically inactive estrone sulfate to estrone by hydrolysis. Estrone can then be further converted to the potent estrogen estradiol by the action of the enzyme 17 $\beta$ -hydroxysteroid dehydrogenase. Thus, it appears that the body maintains a reserve of inactive estrogens which can be readily converted to an active form when necessary.

**Fig.2: Conversion of estrone sulfate to estrone and estradiol**





## Levels

Circulating levels of estrone sulfate are high during fetal life in both sexes, decrease to very low levels within the first few days of life, remain relatively low during childhood, and increase steadily during puberty<sup>4</sup>.

The physiological profile of estrone sulfate in cycling women mirrors that of estrone and estradiol, but on a greater scale in terms of concentration. Concentrations increase several points during pregnancy.

Values decrease significantly after menopause.

They may be affected by oral administration of estrone sulfate in the course of hormone replacement therapy (HRT).

More than 90% of circulating estrone sulfate is bound to albumin.

The following table shows sample reference intervals of estrone sulfate levels taken from the Instructions for Use of Estrone Sulfate RIA kit (Beckman Coulter, cat. No. DSL5400). These are strictly for informational purposes.

For each assay, the relevant reference values are shown in the appropriate instructions for use (IFU).

**Tab. 1: Estrone sulfate levels**

	<b>n</b>	<b>Mean±SD (ng/mL)</b>	<b>Median (ng/mL)</b>	<b>Absolute range (ng/mL)</b>
<b>Normal Males</b>	20	0.96±0.48	0.85	0.16 - 2.01
<b>Females</b>				
Follicular Phase:	20	0.96±0.75	0.80	0.11 - 3.46
Luteal Phase:	25	1.74±1.61	1.34	0.10 - 7.72
<b>Pregnancy</b>				
1st. Trimester:	14	19.47±18.69	12.42	2.78 - 35.30
2nd. Trimester:	17	65.79±84.76	37.30	4.70 - 190.30
3rd. Trimester:	15	104.86±83.86	58.04	20.56 - 325.43
Oral Contraceptive	20	0.74±0.48	0.56	0.11 - 1.95
Postmenopausal (no HRT)	21	0.13±0.14	0.11	ND - 0.56
Postmenopausal (HRT)	22	2.56±2.23	2.01	0.27 - 7.89

*SD* – standard deviation

*ND* – not detectable




## Diagnostic utility


Estrone sulfate serves as an important diagnostic marker in assessing overall individual estrogenicity in pre- or postmenopausal women.

Abnormal values may be found in conditions similar to those characterized by abnormal levels of estrone and estradiol, i.e.:

### Elevated estrone sulfate levels

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- PCOS (polycystic ovary syndrome)
  - androgen-producing tumors
  - estrogen-producing tumors
  - obesity with increased tissue production of E1
  - testicular feminization
  - precocious puberty
  - hyperthyroidism

### Decreased estrone sulfate levels

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- primary ovarian failure
  - Turner syndrome
  - hypopituitarism
  - hypogonadism

## Diagnostic utility – practical applications

Monitoring of hormone replacement therapy in postmenopausal women

Aiding in decisions regarding type, dosage and duration of estrogen treatment, especially in patients with hyperestrogenic conditions

Use as a prognostic marker in prostate cancer



## References

1. Stanczyk F.Z.: Steroid Hormones. in: Mishell DR, Davajan V, Lobo RA (eds.): Infertility Contraception and Reproductive Endocrinology, 3rd. ed. Cambridge, Massachusetts, Blackwell Scientific Publications Inc., 1991, 69
2. Levant S.G., Barnes, R.B.: Pharmacology of estrogen., IN: Lobo RA (ed.): Treatment of the Postmenopausal Woman. New York: Raven Press, 1993, 57
3. Buster J.E.: Estrogen metabolism. IN: Sciarra J.J. (ed.): Endocrinology, Infertility, Genetics, Volume 5. Philadelphia: Harper & Row, 1987
4. Gower D.B.: Catabolism and excretion of steroids. IN: Makin HLG (ed.): Biochemistry of Steroid Hormones. Oxford, England: Blackwell Scientific Publications, 1975, 164
5. Ruder H. R., Loriaux L. and Lipsett M. B.: Estrone sulfate: Production rate and metabolism in man, J. Clin. Invest., 1972, 51(4), 1020