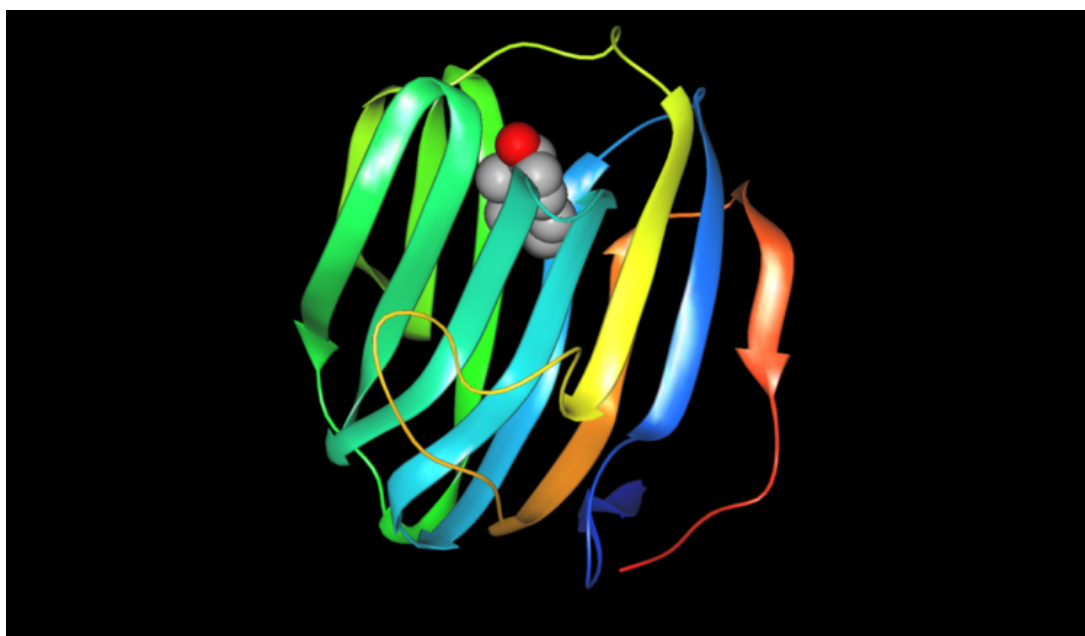


Hormone-Binding Proteins

[See online here](#)

Proteins that bind to hormones and carry them to target tissues to produce a desired effect are called hormone-binding proteins (HBPs). There are four major types of HBPs depending on the type of hormone they carry. These include sex hormone-binding globulin (SHBG), thyroid-binding globulin (TBG), cortisol-binding globulin (CBG), and steroid hormone-binding protein (serum albumin).



Hormone-Binding Proteins

HBPs regulate the **amount of hormone** reaching the target cells. They also regulate the **non-protein-bound, or free, circulating active steroid hormones**, which are considered the primary gatekeepers of steroid action.

Albumin has limited specificity and affinity for steroids. **SHBG** and **CBG**, unlike albumin, have a higher affinity for steroids and control access to the target tissues. SHBG binds with **androgens** and **estrogens**, whereas CBG binds with **glucocorticoids** and **progesterone**. Both of these binding proteins are **glycoproteins**, but they are structurally different.

Plasma SHBG and CBG levels vary based on their production in the [liver](#); they also vary with age, development, and different physiologic or pathophysiologic conditions. Various pathologies are associated with disturbed production of SHBG and CBG and their abilities to bind hormones.

Binding protein	Hormone
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SHBG	Estrogen, Testosterone
CBG	Cortisol
Neurophysins	Vasopressin, Oxytocin
TBG	Thyroid hormone
IGFBP	Insulin-like growth factors
VDBP	Calcitriol

Sex Hormone-Binding Globulin – SHBG

SHBG is produced mainly in the liver and in small amounts in the brain, testes, uterus, and placenta. This binding protein carries the following:

- Dihydrotestosterone
- [Testosterone](#)
- Estradiol/estrone

Dihydroepiandrosterone (**DHEA**) and **androstenedione** are almost completely bound to albumin, but their affinity for SHBG is 4 to 5 times greater. SHBG is bound to biologically active androgens and estrogens. Levels of SHBG vary throughout life, depending on hormonal and metabolic factors. More of the protein is bound in men than in women because men have more androgens. Other steroid hormones, such as progesterone, cortisol, and other corticosteroids, are bound to CBG (transcortin).

Conditions that cause an increase in production

In some **conditions**, the production of SHBG is increased. These include:

- Increased growth factors
- Increased estrogen
- [Hyperthyroidism](#)
- Pregnancy
- [Anorexia nervosa](#)

Drugs: Various drugs also increase the production of these proteins. Such drugs are:

- Estrogens
- Soy isoflavones (licorice)
- Synthetic progestins
- Glucocorticoids
- Growth hormone
- Phenytoin

Conditions that cause a decrease in production

In some conditions, the production of SHBG is decreased. Such conditions cause increased levels of androgens in the blood or increased CBG (transcortin) levels. These include

- [Polycystic ovary syndrome](#)
- [Diabetes](#)
- [Hypothyroidism](#)
- Obesity
- Cushing's syndrome

- Acromegaly

Drugs: Various drugs also decrease the production of these proteins. In this group fall

- Exemestane
- [Testosterone](#)
- Anabolic steroids

Thyroid-Binding Globulin (TBG)

TBG is formed in the [liver](#) and released into circulation to bind reversibly to the **thyroid hormones**, primarily T3 and T4. TBG has the greatest affinity for T4, and its affinity for various forms of thyroid hormones varies: T4 > T3 > T1/T2.

The normal levels of TBG in circulation are 1.1-2.1 mg/dL. An increase in this level leads to an increase in the total T4 and T3 levels but not an increase in free hormone activity. Newborns have relatively very high levels of TBG.

Conditions that cause an increase in production

- Acute intermittent porphyria
- [HIV](#)
- [Severe liver disease](#)
- [Hypothyroidism](#)
- Pregnancy (normal)

Drugs:

- Estrogens, circulating thyroid/free T3 + T4, tamoxifen
- Heroin
- Mitotane
- Methadone
- Fluorouracil
- Phenothiazines

Conditions that cause decrease in production

- [Kidney failure](#)
- Acute illness
- Acromegaly
- [Hyperthyroidism](#)
- Malnutrition

Drugs:

- Testosterone
- Valproic acid
- Phenytoin
- Slow-release nicotinic acid
- Anabolic steroids
- Glucocorticoids (Prednisone)

Corticosteroid-Binding Globulin (CBG) (or transcortin)

CBG, also called transcortin, is an alpha-globulin encoded by the *SERPINA6* gene and secreted by the liver. It carries various hormones at different levels:

- 75% of cortisol
- 78% of corticosterone
- 17% of aldosterone
- 18% of [progesterone](#)

Other hormones carried by CBG include 4% of testosterone and **11-deoxycorticosterone** (DOC), which is an aldosterone precursor. It is the **main determinant of circulating plasma cortisol levels** in humans. CBG has maximum affinity for cortisol, carrying more than 90% of this steroid hormone. CBG levels are higher before puberty, during pregnancy, and after use of estrogen as medication.

Production is decreased in the following conditions

In some conditions, the production of CBG is decreased. These include:

- Hypoproteinemia
- [Cushing's syndrome](#)
- Corticoid treatment
- Some cases of vitamin B12 deficiency
- Septic shock

Drugs: Various drugs also decrease the production of CBG. These include androgens.

Serum Albumin

Serum albumin is produced in the liver. It is one of the most abundant proteins in the blood. It binds nonspecifically with **steroid hormones** and **other small lipophilic molecules**:

- Thyroid hormones
- Fat-soluble hormones
- Fatty acids in the liver
- Unconjugated bilirubin
- Various minerals

Albumin binds to all of the steroid hormones with the same affinity. Still, 99% of albumin binding sites remain open. Albumin concentration decreases with **age**.

In some conditions, production of albumin is increased. These include:

- [Dehydration](#)
- Congestive heart failure
- Poor protein utilization
- Glucocorticoid excess (adrenal overproduction of cortisol, tumor)

Drugs: Various drugs also increase the production of albumin. These include:

- Anabolic steroids
- Androgens

- Growth hormone
- Insulin

In some conditions, the production of albumin is decreased. These include:

- Kidney disease like nephrotic syndrome
- Liver Disease like cirrhosis
- Pregnancy
- Severe malnutrition
- Conditions of decreased nutrients:
 - [Crohn's disease](#)
 - Low protein diet
 - Tropical sprue
 - [Whipple's disease](#)
 - Insufficient anabolic hormone (DHEA, growth hormone, testosterone)

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Notes