



## Estrogen Detoxification and Neuroendocrinological Activation and Balancing Via Hormonal Yoga

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### Abstract

Estrogen is the major sex hormone formed in both males and females and is responsible for development of reproductive organs as well as secondary sexual characters. In females, its major function is maturation and regulation of ovaries and uterus. Its major forms are Estrone (E<sub>1</sub>), Estradiol (E<sub>2</sub>), and Estriol (E<sub>3</sub>), but E<sub>2</sub> is the most effective form of estrogen and is formed from cholesterol (steroid) ring. Most of the estrogen formed along with other hormones like progesterone is utilized in maintenance of menstrual cycle, uterine health and pregnancy by number of feedback mechanisms. Major detoxification of this chemical messenger occurs in liver by two phase mechanism: hydroxylation and methylation and usually take 2-OH pathway of detoxification which is the safest and the most efficient at molecular levels. This pathway also reduces the chances of formation of estrogen adducts which leads to abrupt DNA processing, mutation, and base exclusion. 4-OH and 16-OH pathways of detoxification is usually neglected but if there is disturbances in feedback mechanisms and estrogen load increases it might leads to blockage of energy channels by overlapping them with steroid hormone. These blocked energy channels can be healed and reopened by yoga and naturopathic interventions along with dietary and lifestyle modifications. Yoga kriyas, asanas, bandhas, mudras and relaxation reactivates and balances hormones by suppressing over-processing or rejuvenating endocrine glands to form more of these chemical messengers, without any synthetic chemicals or invasive interventions.

**Keywords:** Yoga; Estrogen; HPA Axis; Cytochrome-P450 Enzyme Superfamily; Detoxification

### Introduction

Estrogen or Oestrogen is the leading sex hormone formed both in males and females. It predominately controls and helps in development, maturation and regulation of female reproductive organs and secondary sex characters such as formation of breast tissues, pubic hair or thinning of voice [1]. This hormone is formed profoundly by our reproductive organ i.e. Ovaries but glands like adrenal and adipose tissues also produce some amount of it. This hor-

mone regulates not just ovaries and endometrial lining but being a signaling molecule it controls fundamental functions such as, cognitive functions, cardiovascular health, bones and immune system [2]. Our major estrogen is known as 17 $\beta$ -estradiol (E<sub>2</sub>) other types such as Estrone (E<sub>1</sub>) and Estriol (E<sub>3</sub>) are less known and known to have other functions<sup>2</sup>. Estrone is secreted during menopause and Estriol helps in uterine growth during pregnancy.

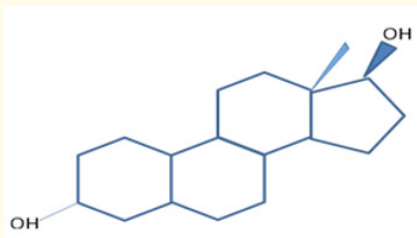


Figure 1: Structure of 17β-Estradiol

Levels of estrogen may vary among individuals of different age and sex. Their fluctuation is pretty common during menstrual cycle and causes mood swings before menstruation commonly called as PMS and hot flushes in menopause as well. Some of the factors that may affect estrogen levels include obesity, extreme dieting, steroid medications and heavy strenuous exercise. High levels of estrogen are usually connected to gain in weight, particularly around waist and hip, causing abrupt waist to hip ratio. Excess of this hormone is also linked some abnormal menstrual problems, such as irregularity in periods, light spotting to heavy bleeding, uterine fibroids or breast tenderness. Some of the signs of excess estrogen are neglected, such as bloating around the belly, cold feet and hands, snoring and difficulty in sleeping, hair loss and headaches decreased sex drive. Per say if neglected it may lead to some severe diseased conditions like cancer of various types, thyroid disease, stroke, blood clots, and even depression [3]. Thus excess hormone must be flushed out of system via estrogen detoxification.

### Estrogen detoxification

The major detoxification of estrogen is done in liver which involves different types of enzymes such as CYP1A1, CYP1B1, CYP19, catechol-*O*-methyltransferase (COMT), Glutathione-*S*-transferase (GST), etc. CYP1A1 catalyzes hydroxylation of E<sub>2</sub> into 2- and 4-hydroxy-estrodial (2-, 4-OH-E<sub>2</sub>) and CYP1B1 helps in hydroxylation of E<sub>2</sub> to catechol estrogens. These catechols if not neutralized by COMT may produce superoxide anion (O<sub>2</sub><sup>-</sup>) and other reactive oxygen species (ROS) which may cause deleterious effects on DNA and E<sub>2</sub>-quinones which are metabolites formed during its metabolism must be inactivated by GST or it may form DNA adducts causing in DNA mutation [4].

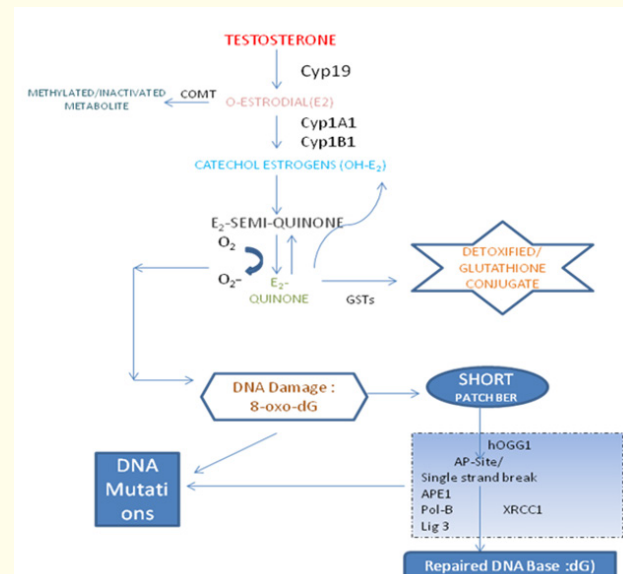


Figure 2: Detoxification series of Estrogen after bio-activation of testosterone by set of enzymes.

Cytochrome P450 super family related enzyme Aromatase catalyzing conversion of testosterone into O-estrodial E<sub>2</sub> and later into catechol E<sub>2</sub> by CYP1A1 (aryl hydrocarbon hydroxylase) and CYP1B1 (monooxygenase of CYP1 family). If these by products are not inactivated by set of enzymes like Glutathione-*S*-transferase (GST) they may lead to DNA damage, such as base pair mutations by superoxide or ROS. These damages are potentially repaired via various mechanisms such base excision repair (BER) or enzyme based (Pol-B) [4].

### Phases of detoxification

Detoxification process works 24x7, it may slow down due to metabolic stress but it doesn't stop. Majority of Estrogen is metabolized in two different phases:

- Phase 1: hydroxylation
- Phase 2: Methylation (detoxification).

In addition to these steps there are three different hydroxylation pathways by which detoxification of estrogen may occur:

### 2-OH (hydroxylation) pathway

This pathway is the leading metabolic pathways when compared to the 4- and 16-hydroxylation pathways. There are set of enzyme super family i.e., cytochrome P-450 enzymes, including CYP1A1 (Aromatase) and CYP1B1 (Monooxygenase). They are enzymes mainly expressed in tissues like breast and liver [5]. These enzymes, along with CYP1A2 (demethylase/oxidoreductase), further catalyze the C-2 hydroxylation of parent estrogen backbone to their respective catechol estrogens E<sub>2</sub> [6]. These secondary metabolites usually have reduced potency as compared to estradiol, and may exhibit both non-estrogenic and anti-estrogenic [7]. At the same time, due to rapid formation of superoxide/anions it has been seen that 2-OH hydroxyestrogens E<sub>2</sub> can damage DNA and cyclic formation of free radicals occurs when COMT is inhibited [8,9].

It is also known as optimal pathway as it leads to lowest risk of forming cancer cells and also 2-OHE1 (2-hydroxyestrone) is considered as good estrogen.



Figure a

Estrone is converted to 2-Hydroxyestrone which is phase one detoxification also known as methylation. In the second step of detoxification (methylation) converts more toxic product, modifies it into a stable and less toxic product which we can be easily be eliminated through the system. 2-OHE1 does not stimulate cell growth and its methylated form (2-MeE1) is cancer protective.

### 4- OH (hydroxylation) pathway

Another set of enzymes controls second p of detoxification. CYP3A4/3A5 both are primary enzymes in the 4-OH hydroxylation of E<sub>2</sub> in liver microsomes [10]. 4-hydroxylated catechol estrogens are potential carcinogenic byproducts of its metabolism as they have the ability to form adducts that further cause DNA damage, this in loop may generate mutations due to oxidative damage and lead towards breast cancer [11].

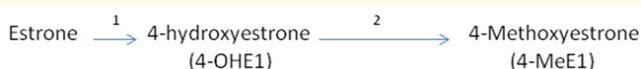


Figure b

This is the most complicated pathway and least possible way to detox estrogen by the system. Estrone from phase 1 is converted to 4-OHE1 later methylated to 4-MeE1. If there is enough methylation 4-MeE1 is easily flushed out of the system or else when later converted to 3,4-Quinones are pro-carcinogenic and leads to cancer by DNA damage.

### 16-OH (hydroxylation) pathway

The most important metabolite of the 16-hydroxylation pathway is 16α-hydroxyestrone. 16α-hydroxyestrone is a potential tumor initiator, which promotes unscheduled DNA synthesis and anchorage independent growth in mouse mammary epithelial cells [11].

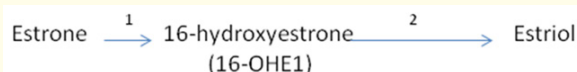
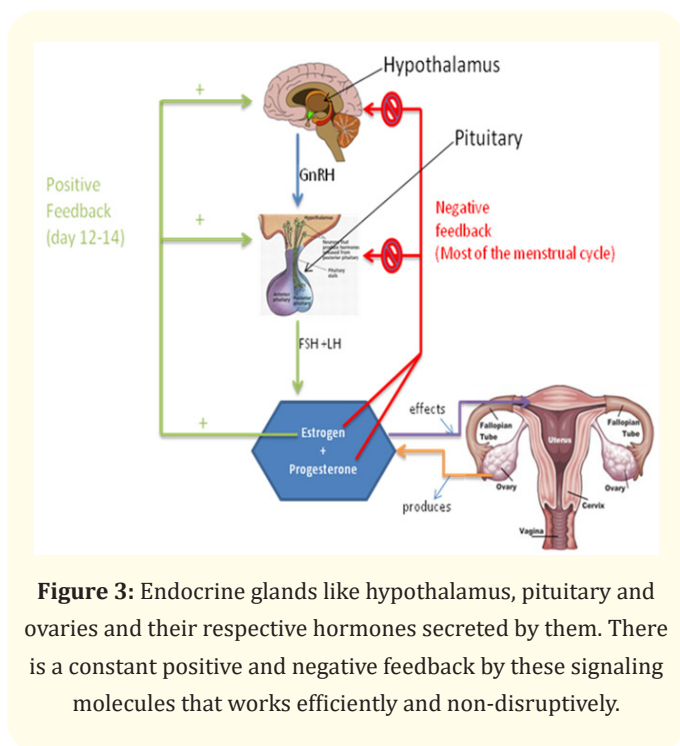


Figure c

Just like other two pathways estrone is converted to 16-hydroxyestrone via hydroxylation but phase 2 in this pathway is reductive and converts into a weaker form of estrogen i.e., estriol [12-14].

### Hormonal Yoga: Therapeutic approach in balancing hormonal influx

Advancements in medicine in past few decades have provided unlimited contraceptive methods. Increase in stress and day to day busy curriculum has become a reason in disturbing hormonal axis. Be it endocrine glands, such as hypothalamus, pituitary, adrenal, pancreas and sex organs or other organs like heart, lungs, etc.; they all are working tirelessly to eliminate toxins and non-avoidable drugs that might enter into our system from diet or environment and accumulate in reservoirs for a prolonged effect that can be deleterious to the body. In text above, we have discussed a single sex hormone Estrogen which if formed in excess have poses adverse effects on our body. There are number of other hormones such as, Gonadotropic releasing hormone, luteinizing and follicle stimulating hormones, cortisol, adipokines, progesterone and testosterone that plays an important role in maintaining harmony to balance HPA axis-Hypothalamus-pituitary-adrenal axis, which altogether control reproductive organs in both male and female.



**Figure 3:** Endocrine glands like hypothalamus, pituitary and ovaries and their respective hormones secreted by them. There is a constant positive and negative feedback by these signaling molecules that works efficiently and non-disruptively.

Treatments like hormonal replacement therapies or oral contraceptive are advised, which confuses feedback mechanism. Fooling our system with synthetic chemicals makes changes which may cause adverse effects at sooner/ later stages, depending upon how well our detoxification mechanism is working. Yoga on the other hand is non-invasive plus no chemical ingestion is needed and safest method of treating hormonal imbalance. Various diseases like hypo/hyperthyroidism, PCOS [15], infertility, early menopause can be easily corrected through yoga and naturopathic interventions [16]. Traditional yoga practices have been proven successful in reducing some of the inflammatory markers like TNF- $\alpha$ , IL-6 and Hs-CRP by enhancing immune system’s own fighting mechanisms [17]. In reducing perceived stress, regulating and activating HPA axis, Yoga is the most beneficial practice as it improves metabolic along with psychological status of the body [18].

Hormonal Yoga is a brief terminology for some exclusive and complex techniques which are governed by some basic rules of Yogic therapy: controlled body movements and breathing. Aiming to gain harmony at various levels should be slow and consistent. Yoga asanas, breathing exercises and other yogic kriyas such as bandhas

(body locks), usually don’t have any negative effect but if these positions are not performed with right technique might cause other complications like swelling, pain or sore muscles. Therefore, these exercises must be performed strictly under guidance. Hormonal yoga session should not overpass an hour and should be a collection of exercises with initial warm up and must end with deep relaxation techniques so that body should recover from injuries if any [19].

**Combination of these exercises must be subjected to the patient’s hormonal status [19]**

- **Breathing exercises:** Bhastrika pranayama (smith’s blower-forceful exhalation), Ujjayi pranayama (winning breath), Kapalabhati pranayama (breath of fire), Surya bhedna pranayama (right nostril breathing), Chandra bhedna pranayama (left nostril breathing), full yogic breath. Rhythmic breathing will activate calm and harmonize energies and stabilize mind and body.
- **Warm up exercises:** Surya namaskara (sun salutation), Khatu pranam (Khatu salutation). Sole purpose of these exercises is they warm up, stretches and releases all the muscles involved during salutation. When we move or bend forward, more blood will move towards head and improve eyesight, activate hypothalamus and pituitary. These positions will improve spine movements which in return regulate our nervous and endocrine systems together.
- **Mudras:** Nasikagra drishti mudra, Khechari mudra, Akashi mudar, Nasagra mudra, Dhyana mudra, Adi mudra. Before doing mudra any body locks or asanas, mudras activates the energy channels and starts rejuvenation by directing its flow in right direction.
- **Bhandana (Body locking):** Jalandhara bandha (throat lock; as by its name and positions, it stimulates thyroid gland), Moola bandha (root lock; mostly focusing on pelvic region it stimulates the nerves around pelvis, thereby activating urogenital tract along with rectum), Uddiyana bandha (abdominal lock; pancreas and adrenal glands are most affected by this lock), Maha bandha (great lock; this lock gives stimulus to entire endocrine system especially on epiphysis. This lock must be done in given order: first Jalandhara, then Uddiyana followed by Maha bandha with deep exhalation).

- **Standing asanas:** Bandha hasta utthanasana (mainly focus shoulders, upper trapezium muscles, stimulates blood circulation towards head and pituitary), Tirkaya tadasana (massage muscles around waist and balance both postural muscles. This posture stimulates circulation towards ovaries and adrenal, it can be more effective if bhastrika pranayama is performed while bending) Kati chakrasana (this posture relaxes both postural and muscles around neck, thereby calming your mind, reduction of mental stress and stimulating thyroid gland), Trikonasana (stretch and relax muscles around both torso and back of twisted leg. This asana improves digestion by stimulating organs of the pelvis and also ovaries), Utthita lolasana (it relaxes back of the thigh muscles. This asana stimulate whole body function as it improves circulation towards head and abdominal cavity, which activates both adrenal and pituitary) Dolasana (works on relaxing thigh muscles, massages organs in abdominal cavity, improves circulation around head and face, specifically stimulates functioning of ovaries and pituitary gland), vayunishkasana (relaxes thighs, knees, shoulder and neck muscles, supports proper circulation in pelvic region and enhances function of ovaries. In combination with other mudras and bandhas it improves function of thyroid gland), Ardha chandrasana (this pose stretches entire spine, activating its energy channels and improves stability by relieving tension around hips and shoulder).
- **Sitting asanas:** Veerasana (relaxes and calm mind, stimulates adrenal and ovaries by increasing circulation towards them), Shashankasana (relaxes spine by releasing any strain/tension, stimulates both ovaries and adrenal glands), Shashank Bhujangasana (functions same as shashankasana, thereby improves uterine health by regulating any irregularities in menses ), Supta vajrasana (this pose is great for improving spinal flexibility and stretches all abdominal muscles which enhances digestion, improves functioning of thyroid gland by stimulating it), Eka padottanasana ( stretches and relaxes thighs and hip muscles, when performed along with bhastrika pranayama it will stimulate adrenal gland and ovaries ), Paschimottasanana (just like eka padottanasana it will improve functioning of adrenal gland, pancreas and ovaries), Chakki chalanasana (this pose relaxes hips and thigh muscles and stimulates ovaries), Nauka sanchalanasana (it gives relief from constipation and also stimulate ovaries), Gatyatmak paschi (it enhances metabolism, relaxes and improves flexibility of thighs and hip joints, improves function of adrenal, ovaries and pancreas), Ardha matsyendrasana (this pose also stimulates function-  
ing of pancreas, ovaries and adrenal glands), Marjariasana (relieves pain/strain in spine along with stimulation of adrenal and ovaries, can perform during painful menstruation for relieving any pain), Vyaghrasana (improves digestion, stimulates adrenal and ovaries), Ushtrasana (relieves constipation and menstrual problems, improves function of thyroid gland), Sirshasana (circulation of blood towards head, stimulates hypothalamus, pituitary, improves mood and cognition, lowers anxiety )
- **Lying asanas:** Supta pawanamuktasana, Jhulana lurhakasana, Naukasana, Bhujangasana, Sarpasana, Ardha shalabhasana, Dhanurasana, Hasta padangushthasana, Kandharasana, Sarvangasana. These asanas should not be repeated more than three times and one shall hold every position for minimum 5-10 seconds. These asanas channelize energy towards a particular organ or muscle to coordinate with the nervous system.
- **Meditation and relaxation:** Om chanting (Om kara, au kara, mm kara), quick or full body relaxation methods should be applied at the end of every session [19]. Without meditation/relaxation methods, no yoga session is ought to be completed. The patient must have exhausted their energy while performing mixture of asanas for an hour or so with intense breathing locking procedures. These relaxation sessions partially focuses on controlled and slow breath, witnessing pain/pleasure around specific organs or muscles, and partially it focus on conserving positive energy and moving negative energies and thoughts from tip of the toe reaching up towards head and releasing them out through nose or mouth. This end session should not be less than 5 minutes can be extended up to 15 minutes, depending upon the need of the patient.

## Conclusion

Human body is a network of energy controlled channels that runs throughout body governed by central nervous system, predominantly controlled as sympathetic and parasympathetic nervous system. Endocrine glands like pineal, hypothalamus, pituitary, thyroid, adrenal, ovaries and testes all are regulated by feedback mechanisms which up/down regulated according to the need of the hour. Hormones are chemical messengers formed by these glands that go into circulation and control functioning of other organs. Disruption in energy channels by blockage might imbalance HPA axis which leads to reduced or increased secretion of hormones or improper detoxification of chemical messengers by liver.

Yoga on the other hand helps in recovering from this disturbance and properly distributes energy into whole body or focusing on few specific organs. Combination of various kriyas, asanas, mudras and relaxation techniques balances out hormones and helps in speedy detoxification. Hormonal yoga is a time consuming process but healing is evident only if accompanied with lifestyle modifications and healthy diet.

### Conflict of Interest

There is no conflict of interest for writing this paper.

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