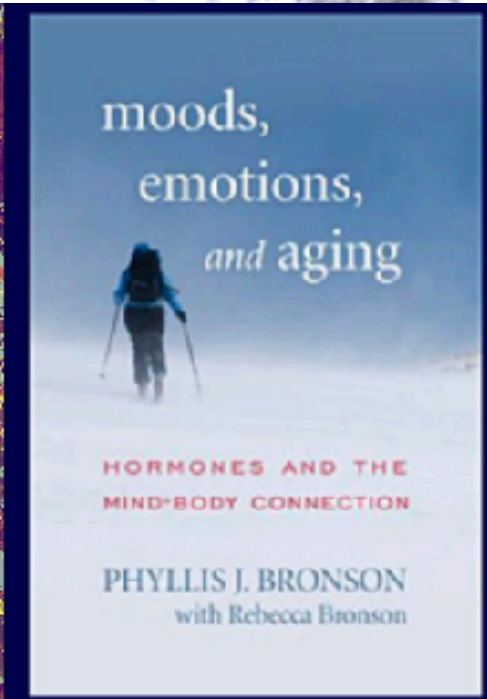


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RELAX

NOTHING IS UNDER CONTROL



Sad Women

- Hot Flashes, anxiety, and panic attacks are hormone deficiency symptoms, relieved with bioidentical hormones. SSRI anti-depressants do not contain estrogen, and their use for estrogen deficiency is an abuse and victimization of women who suffer from estrogen deficiency.
- SSRI drugs should not be used to treat estrogen deficiency symptoms.

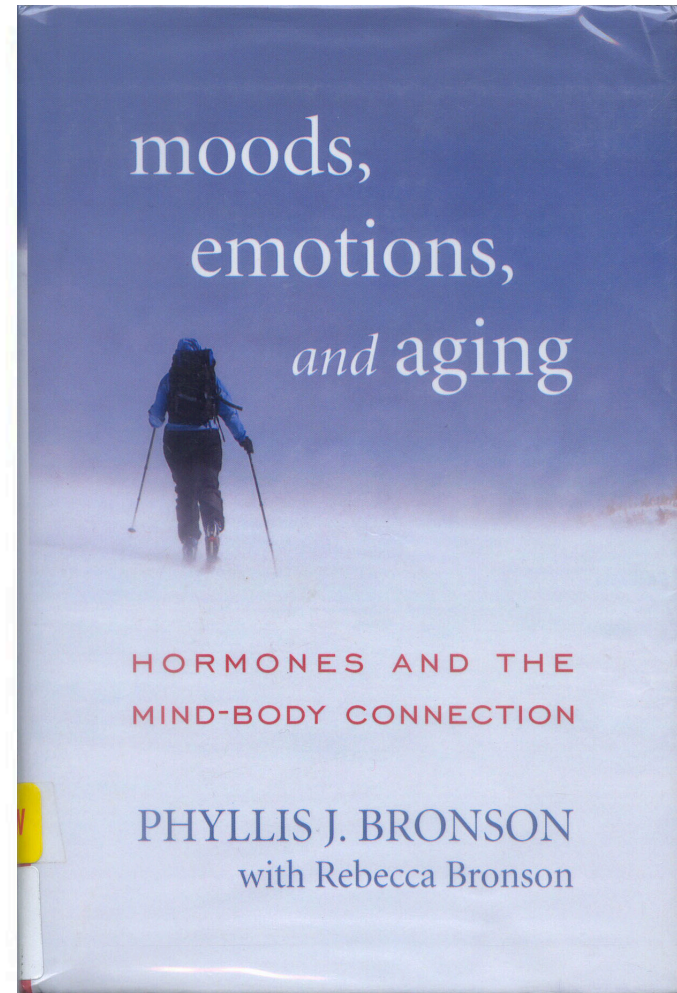
J.Dach, M.D.

Older women need their hormones too

Moods, Emotions, and Aging: Hormones and the Mind-Body Connection
by Phyllis Bronson, PhD

*Book Review by Carol Petersen,
RPh - Women's International Pharmacy*

Dr. Bronson's book could not have been published at a better time. Brisdelle, a version of Paxil or paroxetine, has just been approved by the FDA as a treatment for hot flashes, despite an advisory committee vote of 10-4 against it.





B. Smaller

**"I think the dosage needs adjusting.
I'm not nearly as happy
as the people in the ads."**

Common Signs of Estrogen Deficiency

Insomnia, Difficulty Falling Asleep

Hot flashes

Night sweats

Forgetfulness, Mental Fogginess

Depression

Mood Disturbance

Fatigue, Reduced stamina

Decreased sense of sexuality

Lessened self-image and attention to appearance

Dry eyes, skin, and vagina

Sagging breasts and loss of fullness

Vaginal Dryness, Pain with sexual activity

Weight gain

Menopausal Arthritis, back and joint pain

Headaches and migraines

Gastrointestinal discomfort, bloating

-uzzi reiss

What is the Mechanism of Action of Estrogen in Eliminating Anxiety and Depression?

- Estrogen receptors have been found in the brain, and estrogen increases the expression of an enzyme in the brain called tryptophan hydroxylase-2 (TPH2).
- This enzyme's job is to convert tryptophan to serotonin, an important neurotransmitter responsible for anti-anxiety and calming effect in the brain.

NO on saliva tests because

Gender hormones enter portal blood 3 ways

- 1. Free**
- 2. Loosely bound to Albumin**
- 3. Tightly bound to SHBG**

**All are available to dock at receptors
if bioidentical**

Recent Research

The female uses both weakly bound and free forms of these hormones at receptors. Saliva tests only measure the free, unbound portion of the hormone molecule in serum, so they don't give a complete picture of the available potentially active, or bioavailable, hormone.

I. Vliet

Estriol is safe

- **E3/ Estriol is very safe 80% of naturally occurring estrogen is E3.**
- **Soars 1000X during pregnancy**
- **U.S. Department of Defense conducted major study of 15,000 women. Those with highest estriol during first pregnancy had 58% less breast cancer over next 40 years**

Brain Fatigue

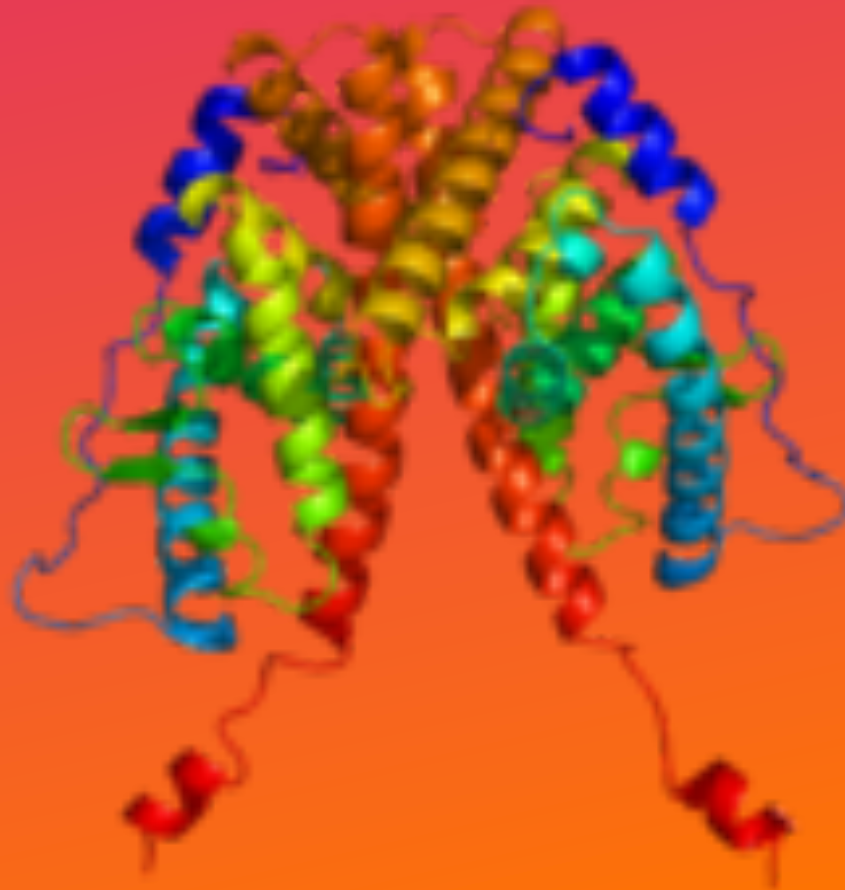
Day-long fatigue -- rising FSH and LH as brain tries in vain to increase falling estradiol. Estrone rises/ estradiol drops and brain fog sets in

Flat affect depression

Recent data shows diminished E2 levels as being primary issue of estrogen depletion at alpha E receptors ($ER\alpha$)

Estrogen Receptor Alpha

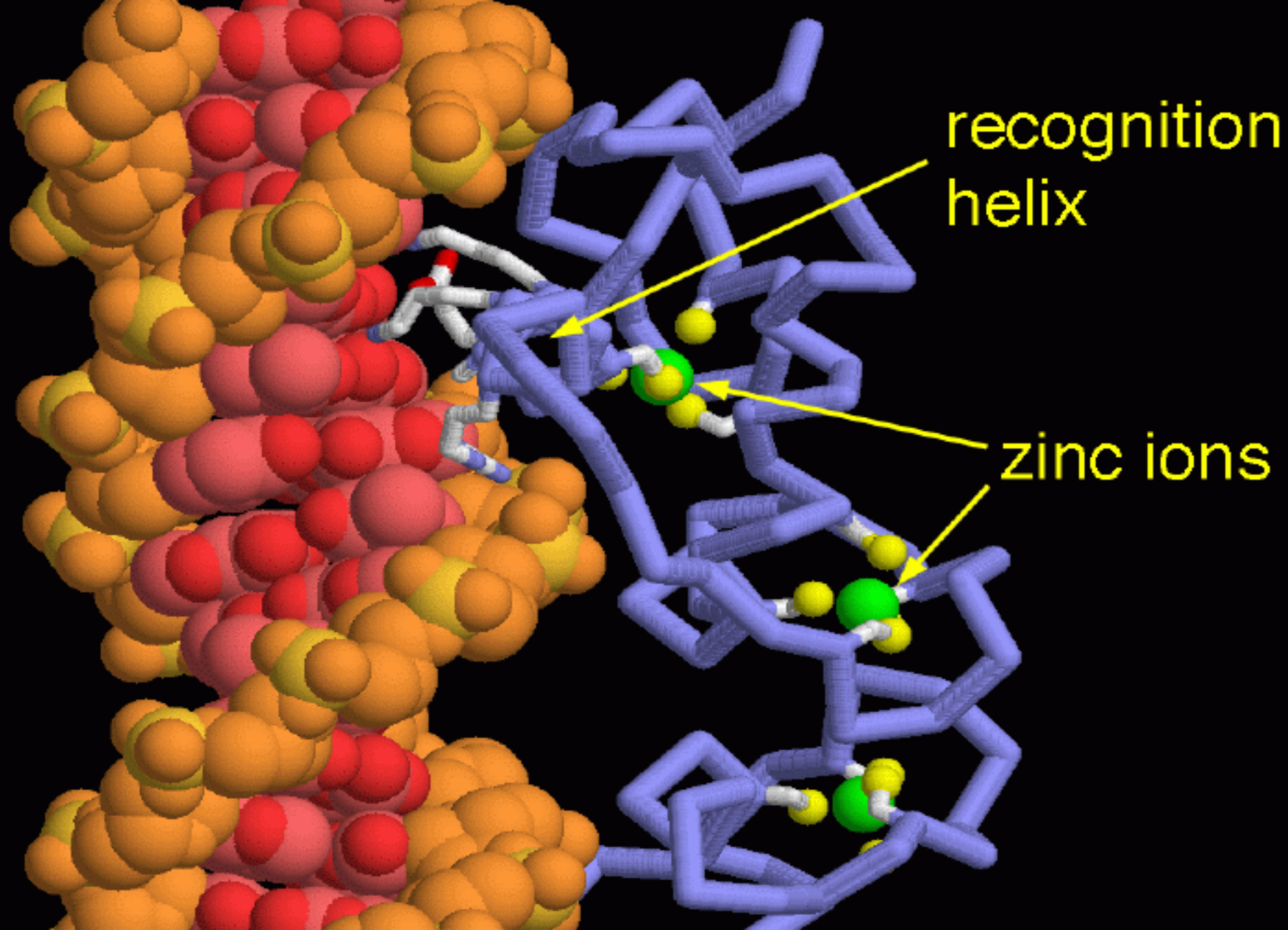
estradiol stimulates both ER alpha
and beta



Soy Phytoestrogens

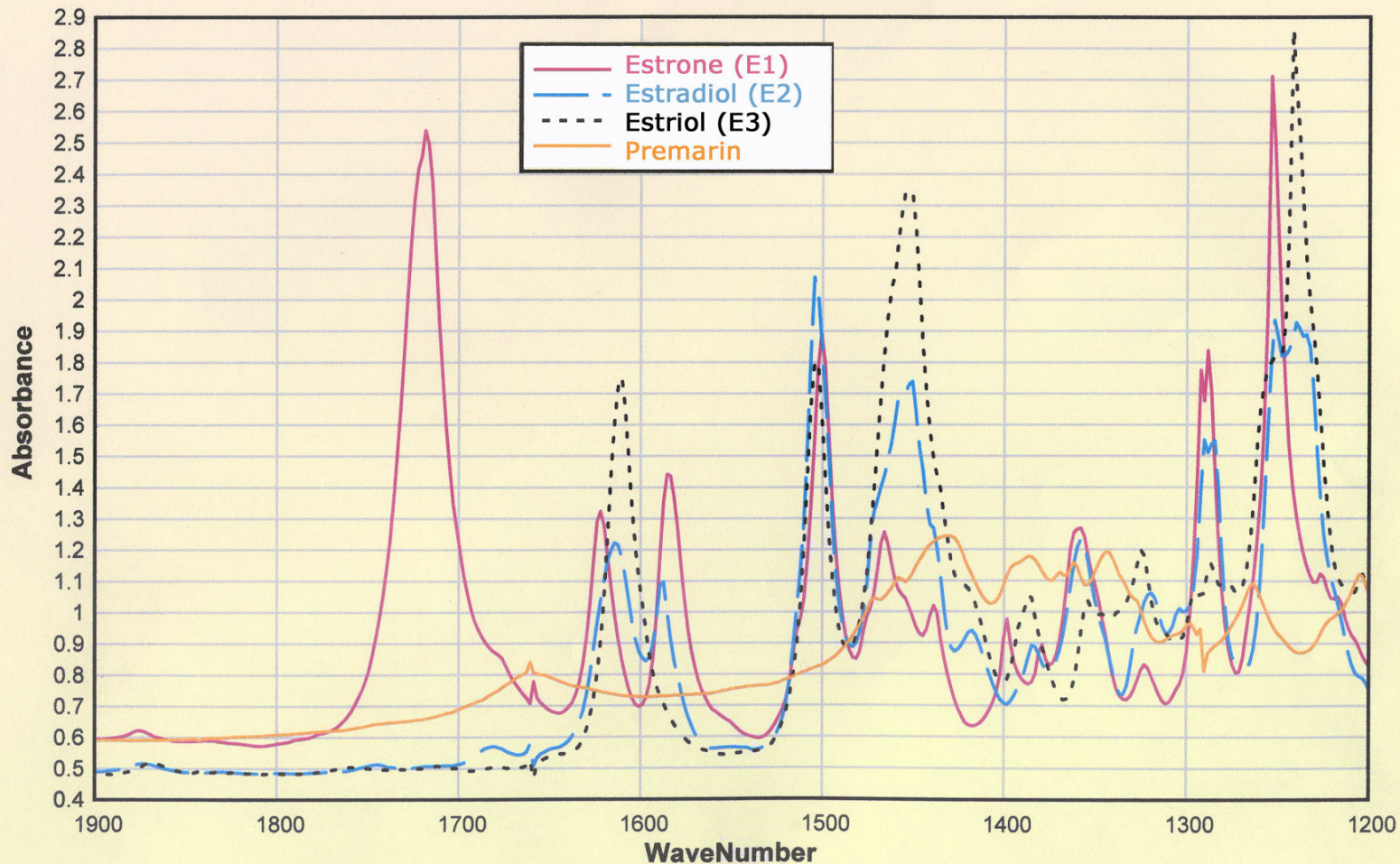
**Very low affinity for Estrogen
receptor-alpha**

High attraction to ER- beta





Estrogen Spectra



- Carbonyl at 1720, unique to estrone
- Aliphatic OH- diminishes naturally in E2
- In presence of PAH greatly diminished OH

16 alpha

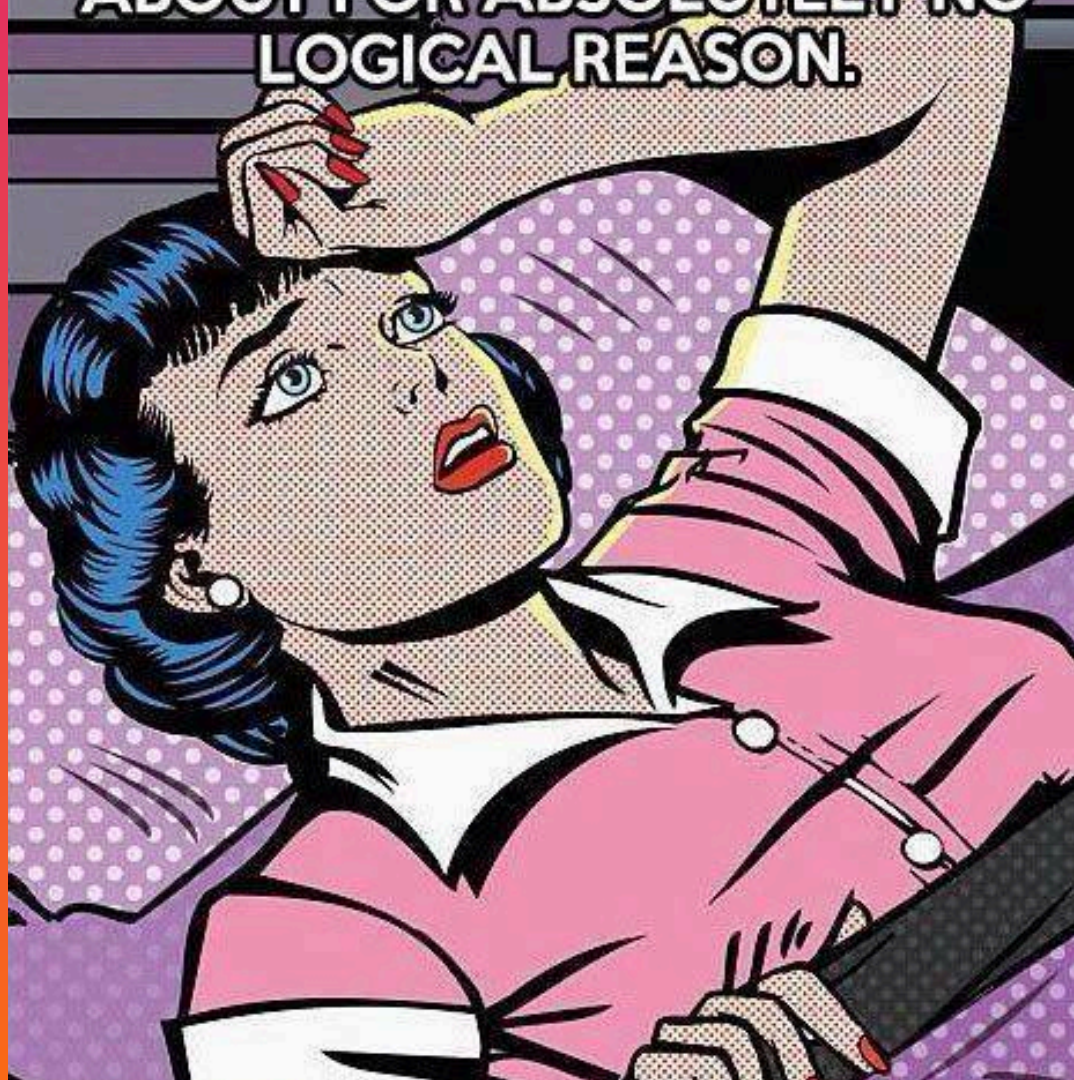
- **16 alpha metabolite of estrone is precursor to relatively inactive estriol: this does not make estriol toxic**
- **Unique spacing of 16 alpha-OH group with proximity to keto group of estrone that lead to negative potent 16 alpha effects**

Calcium, glutamate-induced excitotoxicity

E2/ Neuroprotection

- Loss of Ca^{2+} homeostasis in brain disorders such as stroke, seizures is linked to glutamate excitotoxicity
- Maintenance of intracellular Ca^{2+} is based on E2 mediated neuroprotection

**I'VE GOT 99 PROBLEMS AND 86
OF THEM ARE COMPLETELY
MADE UP SCENARIOS IN MY
HEAD THAT I'M STRESSING
ABOUT FOR ABSOLUTELY NO
LOGICAL REASON.**



Stability of estrogens

The electrode potential of the estrogens do not necessarily reflect their thermodynamic relationship to one another.

The electrode reactions as measured are irreversible, that is kinetically controlled. The current voltage curves which they yield do not necessarily reflect their oxidation/reduction characteristics in physiological systems.

Two doctors from the Cleveland Clinic, one of which has represented pharmaceutical companies that manufacture synthetic hormones, recently published a paper that lambasts any perceived benefits of bioidentical hormones.

The paper, published in December's Cleveland Clinic Journal, states that there is no evidence that bioidentical hormones provide aging benefits, reduce side effects, or present a legitimate option to FDA approved pharmaceutical synthetic hormones.

As to the effectiveness of bioidentical hormone therapy, this was established in a recent study by the University of Texas Health Science Center. The researchers followed 296 women who received bioidentical hormone therapy between 2003 and 2010.

The study found that the women overall experienced a 25% reduction in emotional mood swings and irritability, 22% less anxiety, and a 14% reduction of night sweats.

The researchers concluded that, “This study demonstrates that compounded bioidentical hormone replacement therapy improves mood symptoms.”

A 2009 review of clinical evidence by Kent Holtorf, MD, found that:

- 1) “Patients report greater satisfaction with Hormone replacement therapies that contain progesterone compared with those that contain a synthetic progestin.”**
- 2) Bioidentical hormones have different molecular structures and significantly different metabolic effects from synthetic versions.**
- 3) Clinical research and physiological data has found progesterone not to have the risk for breast cancer associated with synthetic progestins.**

4) Estriol acts differently in the body from estradiol, estrone, and equine hormones. Thus estriol “would be expected to carry less risk for breast cancer,” stated the paper.

5) Progestins from pharmaceutical hormones come with” a variety of negative cardiovascular effects, which may be avoided with progesterone.”

Dr. Holtorf’s paper concluded that bioidentical hormones are linked with reduced risks of breast cancer and heart disease, “and are more efficacious than their synthetic and animal-derived counterparts.

Pharmaceutical Ghostwriting

The article is entitled, “Bioidentical Hormone Therapy: A Review of the Evidence”, by Michael Cirigliano, an Internist at the University of Pennsylvania School of Medicine, published in the Journal of Women’s Health. (2007 Jun;16(5): 600-31.

His conclusion: Not Big Pharma, then not good, **ACKNOWLEDGMENTS:** I received editorial assistance from Eugene R.Tombler, Ph.D., Florencia Schapiro, Ph.D., and Monica Ramchandani, Ph.D., of PharmaWrite,LLC.

Shame: a medical person ghostwriting to support opinions of big pharma

- **Distort the evidence: Cirigliano tries to defend Premarin by saying another pharmaceutical Enjuvia, is synthesized to mimic Premarin for relief of “vaso-motor symptoms”**
- **Pharmawrite concludes that this drug is obtained from plant sources and mimics Premarin- this is not the issue with determining bioidentical status**

News?

**Newsweek is an Infomercial
Masquerading as Medical News**

Newsweek says: "bioidentical hormones are unregulated". This is an outright falsehood. Compounded bioidentical hormones are highly regulated at the state levels.

Opposing effects

Synthetic progestins may also increase the conversion of weaker endogenous estrogens into more potent estrogens, potentially contributing to their carcinogenic effects, which are not apparent with progesterone.

Holtorf

Huge Distinctions

- Progesterone has an opposite effect, stimulating the oxidative isoform of 17-beta-hydroxysteroid dehydrogenase, which
- increases the intracellular conversion of potent estrogens to their less potent counterparts.

Progesterone inhibits

Progesterone inhibits estrogen-stimulated breast epithelial cells.

Progesterone also down-regulates estrogen receptor-1 (ER-1) in the breast, induces breast cancer cell apoptosis, diminishes breast cell mitotic activity.

Holtorf

BRAIN CONNECTION

Estrogen is most important for cognition, but progesterone also serves the brain, decreasing anxiety and mood swings.

Progesterone enhances dendritic activity, so that neuro-inhibitory molecules are more readily up-regulated.

Natural Progesterone from your ovaries or transdermally applied in sufficient quantity affects GABA_A and GABA_C receptors.

BRAIN CONNECTION

Oral Progesterone such as Prometrium or compounded goes through liver first pass, and after being metabolized affects GABA receptors in a more potent BDZ drug like manner.

5-alpha pregnandione is made in upper GI from oral progesterone: this has 12x the potency of Phenobarbital

GABA receptor = FIVE Pentameric subunits

- **Each subunit has M1-M4**
TWO molecules of GABA bond between alpha and beta subunits
- **Neurosteroid- THDOC- increases Cl^- ionic diffusion or electrical migration**

Allopregnanolone

- Allopregnanolone is potent modulator of GABA_A receptor
- Progesterone breaks down into allopregnanolone- in men and women
- Increase in neuronal excitability dependent on upregulation of alpha-4 subunit of GABA_A

S.Smith,Ph.D

γ -Aminobutyric acid (GABA)

GABA depolarizes neurons by opening GABA_A receptor Cl⁻ channel, mimics hydration sphere

SIGNS OF TESTOSTERONE DEFICIENCY

A skier wearing a dark jacket, black pants, and white goggles is standing in a snowy forest. The trees are heavily covered in snow, and the ground is also covered in a thick layer of snow. The skier is holding a red ski pole and is looking towards the camera with a slight smile.

- **The hormone of self- esteem**
- **Lack of energy & stamina**
- **Loss of sense of security and indecisiveness**
- **Decreased sex drive**



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