NEST

NEUROVISUAL SCIENCE TECHNOLOGY

Caterina Gagliano

# Differenze di genere nella Neutraceutica

S.O.Si. Giardini Naxos 16-18 Aprile 2015

No “sindrome del bikini”

# Crescente interesse per le differenze di genere: perché?

- Sesso (maschio e femmina) e ormoni sessuali (androgeni ed estrogeni) sono importanti per funzioni fisiologiche al di là di quelle pertinenti espressamente alla riproduzione.
- Entrambe le classi di ormoni sessuali sono attive in entrambi i sessi e spesso sono prodotti localmente nel nostro organismo in tessuti extra-gonadici.

# Crescente interesse per la nutraceutica: perché ?

- **Nutraceutica,** termine stato coniato dal Dr. Stephen De Felice nel 1989, è una sincrasi da **"nutrizione" e "farmaceutica"** e si riferisce allo **studio di alimenti che hanno una funzione benefica sulla salute umana**.
- Un nutraceutico è un "alimento-farmaco" ovvero un alimento salutare che associa a componenti nutrizionali selezionati per caratteristiche quali l'alta digeribilità e l'ipoallergenicità, le proprietà curative di principi attivi naturali estratti da piante, di comprovata e riconosciuta efficacia.

# Crescente interesse per la nutraceutica: perché ?

- Valutazione dello stato nutrizionale del soggetto
- Valutazione del fabbisogno energetico/nutrizionale
- Medicina di genere/medicina personalizzata

# Crescente interesse per le differenze di genere: perché?

- Le differenze tra uomo e donna nella fisiologia e nelle patologie oculari sono prevalenti ma conosciamo molto poco per individuare le diverse strategie di trattamento, di prevenzione e di diagnosi determinate da disparità di genere nella salute oculare.
- Numerose malattie oculari e altre condizioni con manifestazioni oculari colpiscono in modo sproporzionato le donne.

**Variazione degli ormoni in base al sesso, età e stato ormonale: ruolo importante nella fisiopatologia dei tessuti oculari ed extraoculari – ogni struttura dell'occhio è sede di recettori degli ormoni steroidei.**

| | *Donna Giovane* | *Donna EP* | *Donna Peri Menopausa* | *Donna Menopausa* | *Gravidanza* | *Uomo giovane* | *Uomo anziano* |
|---|---|---|---|---|---|---|---|
| Estrogeni | N | N | N o ↑ | ↓ ↓ | ↑ | N | N |
| Progestinici | N | N | ↓ | ↓ ↓ | ↑ | N | N |
| Androgeni | N | N | N o ↓ | ↓ | ↑ | N | ↓ |

N = tasso di base ; ↑ o ↓ rispetto al tasso di base ; EP : estro-progestinico.

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# Crescente interesse per le differenze di genere: perché?

- Perché la maggior parte delle ricerche biomediche proviene da studi di popolazioni mixed-gender, o di popolazioni a predominanza maschile.
- Esiste una pressante necessità di ricerche sex and/or gender based a vari punti: dalla ricerca di base a quella clinica.
- Come medici dobbiamo assicurare ai nostri pazienti la migliore cura per le loro esigenze e la cura deve derivare da una ricerca che mostra ciò che è efficace, per chi, e a quali condizioni: "personalized medicine".

Home | Causes of Vision Loss | Prevention and Care | Statistics | Eye Basics | Educational Material | About us

# Women's Eye Health.org

Womens Eye Health.org

## Welcome

## Women's Eye Health Facts:

- 2/3 of blindness and visual impairment occurs in women
- More than 3/4 of visual impairment is estimated to be preventable or correctable
- 1/3 of age-related macular disease and cataract may be due to smoking
- 4/5 of blindness and visual impairment occurs in developing countries
- Women's Eye Health was formed in response to these troubling facts.

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NEST
NEUROVISUAL SCIENCE TECHNOLOGY


**PREVENZIONE DEI DISTURBI NEUROVISIVI NELLA DONNA**
in stato di:
**GRAVIDANZA · MENOPAUSA**
**CONTRACCEZIONE · TERAPIA ORMONALE**

EUROPEAN COMMISSION
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# I Gender Bias

## MIUR: PRIN 2007

Br J Ophthalmol. 2014 Mar;98(3):371-6. doi: 10.1136/bjophthalmol-2012-302705. Epub 2014 Jan 3.

# Low levels of 17-β-oestradiol, oestrone and testosterone correlate with severe evaporative dysfunctional tear syndrome in postmenopausal women: a case-control study.

Gagliano C[1], Caruso S, Napolitano G, Malaguarnera G, Cicinelli MV, Amato R, Reibaldi M, Incarbone G, Bucolo C, Drago F, Avitabile T.

Author information

## Abstract

**AIMS:** To evaluate the role of 17-β-oestradiol, oestrone and total testosterone (TT) deficiency in the pathogenesis of severe evaporative dry eye syndrome (DES), investigating the relationship between tear osmolarity, tear film break-up time (TF-BUT), Schirmer test and serum sex hormones in postmenopausal women.

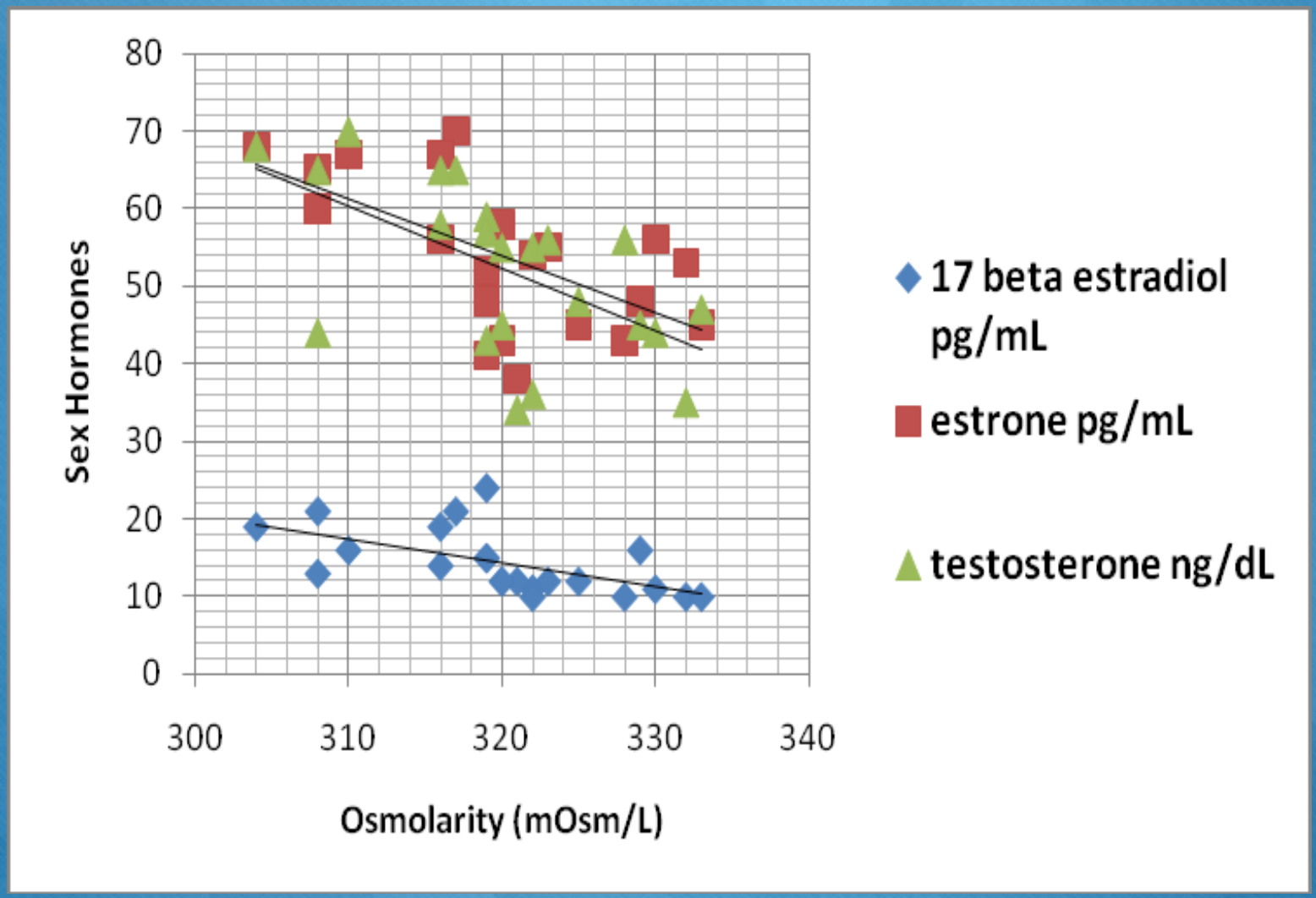
**METHODS:** 44 postmenopausal women were recruited for a case-control study: 22 women with severe evaporative DES (Group A) and 22 without DES (Group B). The tests performed included laboratory blood analysis: fasting plasma profile (17-β-oestradiol, oestrone and TT), glucose level and lipid profile. Detailed eye examinations, including corneal and conjunctival staining, tear osmolarity measurement, tear volume and TF-BUT, were performed. The Ocular Surface Disease Index Questionnaire was also administered.

**RESULTS:** Values of Schirmer test and TF-BUT in Group A were significantly lower in comparison with Group B ($p<0.001$). Serum levels of 17-β-oestradiol, oestrone and TT were significantly lower in Group A compared with Group B ($p<0.05$). In women with severe evaporative DES, the levels of 17-β-oestradiol, oestrone and TT were inversely correlated with the tear film osmolarity ($r=-0.7, -0.88, -0.81$, respectively).

**CONCLUSIONS:** In postmenopausal women with severe evaporative DES, sex hormone levels are lower than control and that tear osmolarity is negatively correlated with sex hormone levels.

**KEYWORDS:** Diagnostic tests/Investigation; Ocular surface; Pharmacology; Tears

# CORRELAZIONE INVERSA TRA LIVELLI EMATICI DEGLI ORMONI SESSUALI ED OSMOLARITA' LACRIMALE



Can J Ophthalmol. 2012 Dec;47(6):489-92. doi: 10.1016/j.jcjo.2012.08.019.

# Effects of phytoestrogen supplementation in postmenopausal women with dry eye syndrome: a randomized clinical trial.

Scuderi G[1], Contestabile MT, Gagliano C, Iacovello D, Scuderi L, Avitabile T.

Author information

## Abstract

**OBJECTIVE:** To evaluate the correlation between tear osmolarity and blood levels of 17-β estradiol, estrone, and testosterone in postmenopausal women with dry eye syndrome, and to assess the efficacy and safety of oral supplementation with phytoestrogens, lipoic acid, and eicosapentaenoic acid in this population.

**DESIGN:** Cross-sectional study including 66 postmenopausal women with dry eye syndrome.

**METHODS:** Sixty-six postmenopausal women with dry eye syndrome were enrolled in a randomized, double-blind, placebo-controlled, crossover study. Patients were divided into 2 groups (groups A and B) and treated, respectively, with phytoestrogen (Bioos, Montegiorgio, Italy) tablets or placebo tablets for 30 days. The 2 treatment periods were separated by a 30-day washout. Patients were examined on days 0 and 30 of each period. Assessments included blood levels of sex hormones, the Schirmer test for tear production, and measurement of tear osmolarity and tear film break-up time.

**RESULTS:** At baseline, all patients had low sex hormone levels, which were correlated with high tear film osmolarity values ($r = -0.59, -0.61, -0.58$, respectively). After 30 days of therapy, the group treated with Lacrisek® (Bioos) had significantly decreased tear osmolarity ($P<0.005$) and significantly increased tear production evaluated with the Schirmer test and tear film break-up time values ($P<0.001$) compared with the placebo-treated group.

**CONCLUSIONS:** Our study confirms that steroid hormones play an important role in ocular surface equilibrium and functions. Consequently, reduced blood levels of these hormones can produce changes at the ocular surface. Phytoestrogen supplementation can significantly improve the signs and symptoms of dry eye syndrome in postmenopausal women.

Curr Eye Res. 2007 Nov;32(11):999-1003.

# Changes in visual evoked potentials during the menstrual cycle in young women.

Avitabile T[1], Longo A, Caruso S, Gagliano C, Amato R, Scollo D, Lopes R, Pulvirenti L, Toto L, Torrisi B, Agnello C.

Author information

## Abstract

**PURPOSE:** Since, during the menstrual cycle, changes in neuronal activity and in auditory, olfactory, and taste thresholds were found, visual evoked potentials were investigated.

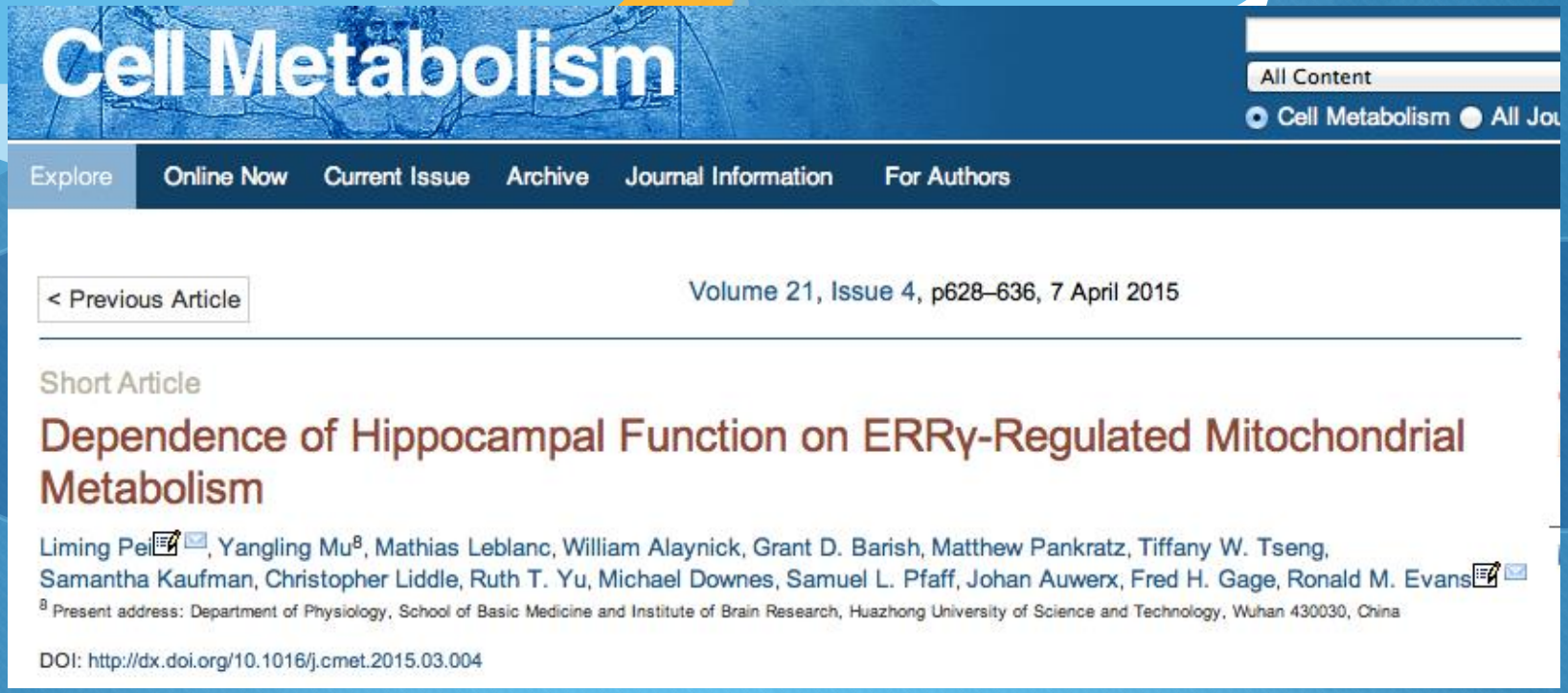
**MATERIALS & METHODS:** In 50 healthy women the latency and the amplitude of P100 wave of pattern reversal visual evoked potentials were measured during the different menstrual phases (follicular, periovular, and luteal), as determined by sonography and serum progesterone level.

**RESULTS:** Compared with the follicular phase, during the luteal phase significant reduction in latency (101.29+/-4.42 vs. 104.76+/-5.02 ms, $P<0.01$) and increase in amplitude (10.44+/-3.15 vs. 8.62+/-3.09 microV, $P<0.05$) were recorded.

**CONCLUSIONS:** Fluctuations in ovarian steroid hormones affect the excitability of the visual system.

# Estrogeni

- SNC
- Plasticità sinaptica
- Sviluppo cervello
- Memoria
- Azione neuroprotettiva (ER-alfa, ER-beta) Amantea et al. Pharmacol. Res. 2005
- Vasodilatazione endotelio-dipendente
- Attività antiinfiammatoria
- Occhio
- ERs retina sensoriale, EP retinico, Cellule ganglionari retiniche, cornea solo in donne pre menopausa (no postmenopausa, no uomini) Ogueta et al. IOVS 1999
- Riduzione fenomeni ischemici e apoptotici (Kaja et al. IOVS 2003)
- Aumento flusso ematico retina e testa del nervo ottico (Deschenes et al IOVS 2010)



Cell Metabolism

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Volume 21, Issue 4, p628–636, 7 April 2015

Short Article

Dependence of Hippocampal Function on ERRγ-Regulated Mitochondrial Metabolism

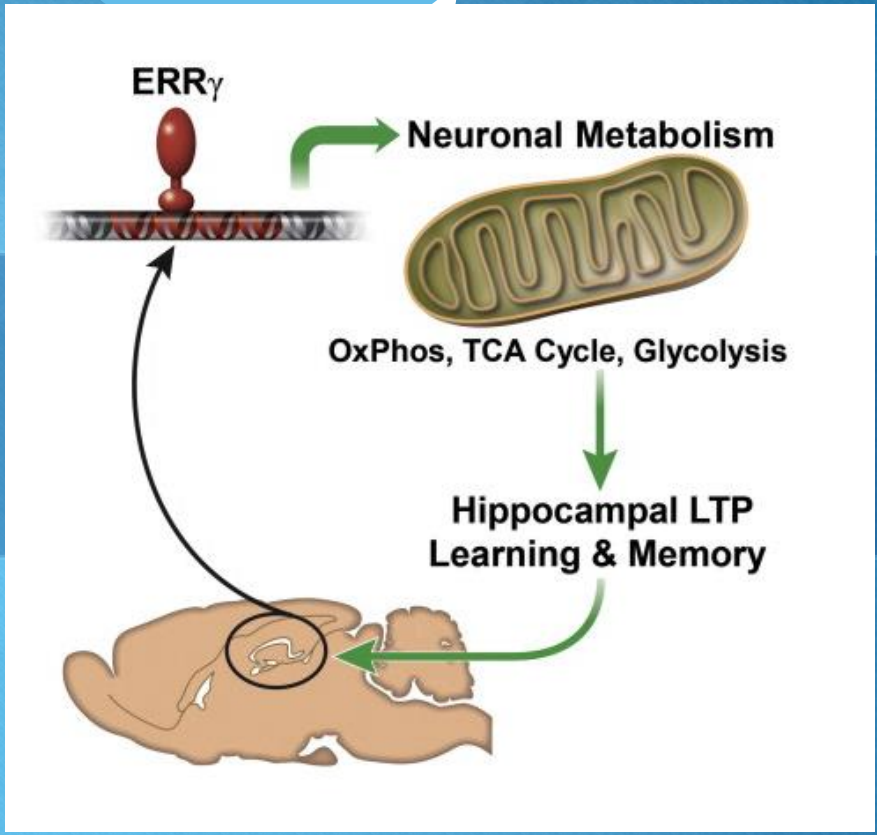
Liming Pei, Yangling Mu[8], Mathias Leblanc, William Alaynick, Grant D. Barish, Matthew Pankratz, Tiffany W. Tseng, Samantha Kaufman, Christopher Liddle, Ruth T. Yu, Michael Downes, Samuel L. Pfaff, Johan Auwerx, Fred H. Gage, Ronald M. Evans

[8] Present address: Department of Physiology, School of Basic Medicine and Institute of Brain Research, Huazhong University of Science and Technology, Wuhan 430030, China

DOI: http://dx.doi.org/10.1016/j.cmet.2015.03.004

**ERR-gamma (*Estrogen-Related Receptor* gamma). Questo gruppo di ricercatori nel 2011 aveva già scoperto che, stimolando l'attività della ERR-gamma nei muscoli di topini sedentari, si produceva un aumento di flusso di ematico che raddoppiava la loro capacità di corsa. Questo effetto è dato dalla capacità che ha la ERR-gamma di 'accendere' tutta una serie di geni a livello del muscolo, la cui funzione è quella di trasformare il grasso in energia.**

**Presenza di questa stessa proteina anche nel cervello ma non se ne conoscevano le funzioni a questo livello; il cervello ricava infatti la sua energia dagli zuccheri, mentre la ERR-gamma si pensava che la facesse produrre solo a partire dai grassi.**



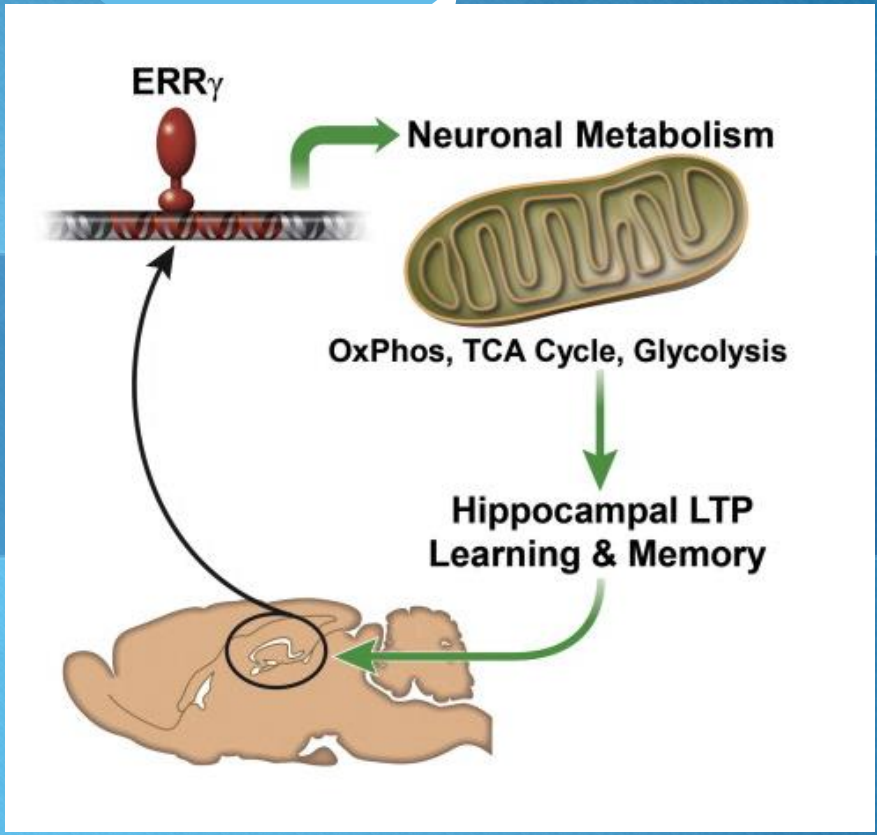

**I neuroni privi di questa proteina non risultavano in grado di fare uno 'scatto' di energia e questo andava a compromettere le loro *performance*.**

**Ottenere un surplus di energia, bruciando più grassi nei muscoli e bruciando più zuccheri nel cervello.**

Area del cervello deputata all'apprendimento e alla memoria che per svolgere questi due compiti così delicati ha bisogno di tanta energia.

Presenza della ERR-gamma ruolo diretto nell'espletamento di questi processi.

Maggiore velocità nell'imparare e memorizzare
Differenze nel metabolismo a livello dell'ippocampo.




Aumentando i livelli di ERR-gamma si potrebbe facilitare l'apprendimento, alla stessa stregua di come nei muscoli questa proteina migliora le *performance*.

# ERs: alfa, beta, gamma

**Effetti cerebrali degli ERgamma: ripercussioni sull'apparato visivo?**

Dalla nostra casistica sugli effetti di nutraceutici abbiamo estrapolato i risultati di uomini e donne sulle performance visive: differenze evidenti!

Unità Operativa Complessa di Oftalmologia

*Direttore: Prof. T. Avitabile*

# Efficacia di una formulazione a base di eleuterococco e vitamine nel contrastare i disturbi astenopeici del videoterminalista

S.O.Si.
Società Oftalmologica Siciliana

XXXIX Congresso

Portorosa Blu Hotel
Furnari (ME)

**Disegno dello studio osservazionale**

Studio aperto, controllato, randomizzato, condotto su 40 pazienti (28 donne, 12 uomini) affetti da astenopia che vengono o meno trattati con Meramirt®.

**Trattamenti**

**Posologia:** Due compresse al giorno, una alla mattina ed una alla sera.

**Metodica:** I pazienti sono stati sottoposti ad una prima visita basale al momento dell'arruolamento (T0) e quindi a visite successive ad 1 e a 3 mesi da T0. Ciascun paziente è stato sottoposto per ciascun tempo di controllo a due visite, una al mattino ed una al pomeriggio, per valutare l'andamento temporale dell'astenopia. Ogni visita, oltre ai normali esami di routine, includeva:

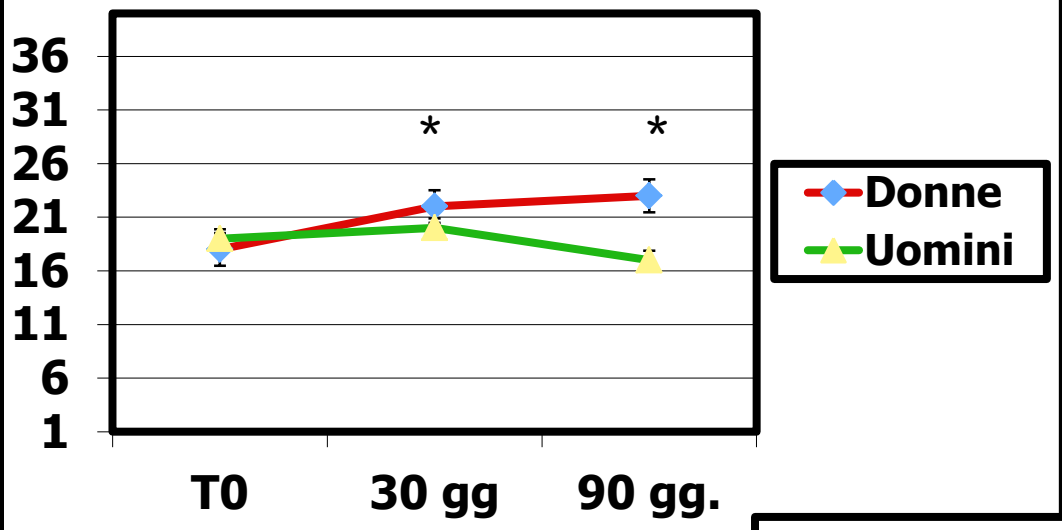
- Acuità Visiva
- Velocità di lettura
- Velocità di scrittura
- Sensibilità al contrasto
- Tempo di recupero dopo abbagliamento
- Questionario

**Valutazione statistica**

La valutazione statistica è stata effettuata con test adeguati al tipo di impostazione sperimentale, alle scale di rilievo dei parametri e alla tipologia dei pazienti inclusi (studio di sottogruppi ecc), con il test ANOVA ed il t-test per dati appaiati.

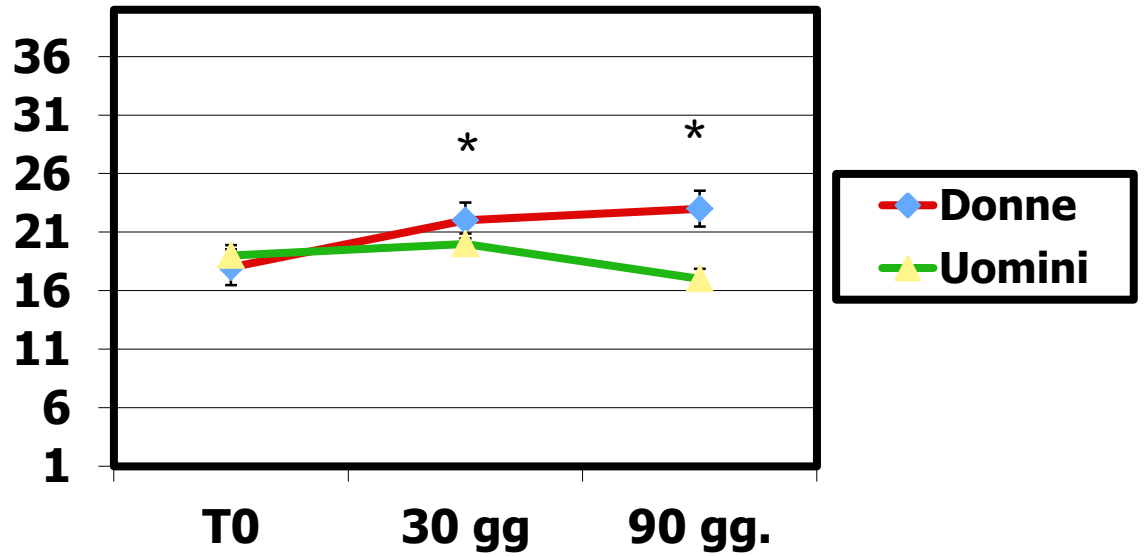
| TEMPI VISITA | | | |
|---|---|---|---|
| **Orario** | **T0 (basale)** | **T1 (1 mese)** | **T2 (3 mesi)** |
| **AM** | velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario | velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario | velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario |
| **PM** | · AV<br>velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario | · AV<br>velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario | · AV<br>velocità di lettura<br>velocità di scrittura<br>visual acuity<br>sensibilità al contrasto<br>tempo di recupero dopo abbagliamento<br>questionario |
| **Note** | Suddivisione dei pazienti al gruppo di Controllo o dei Trattati | | |

## Reading Speed (parole/minuto)

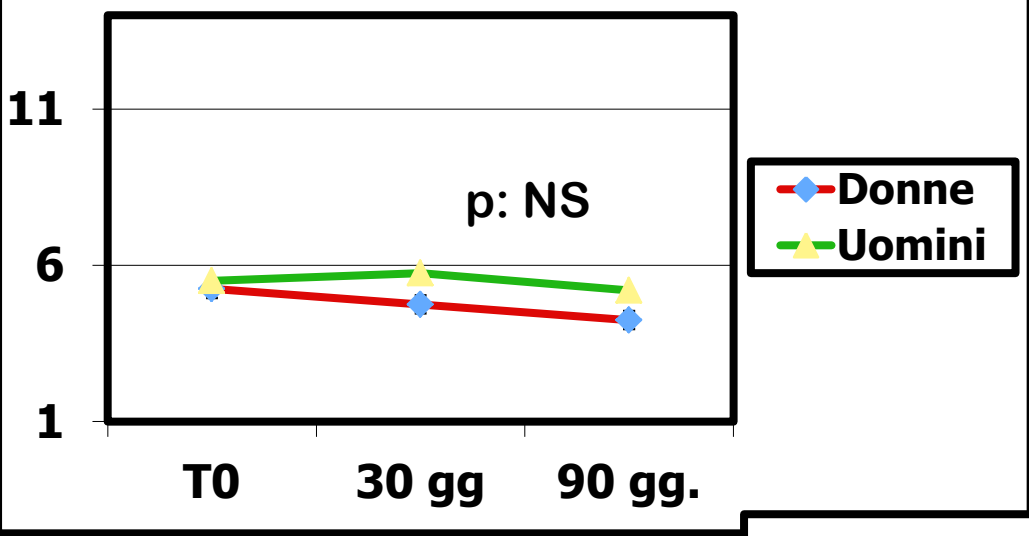



* p<0.05

## Typing Speed (parole/minuto)

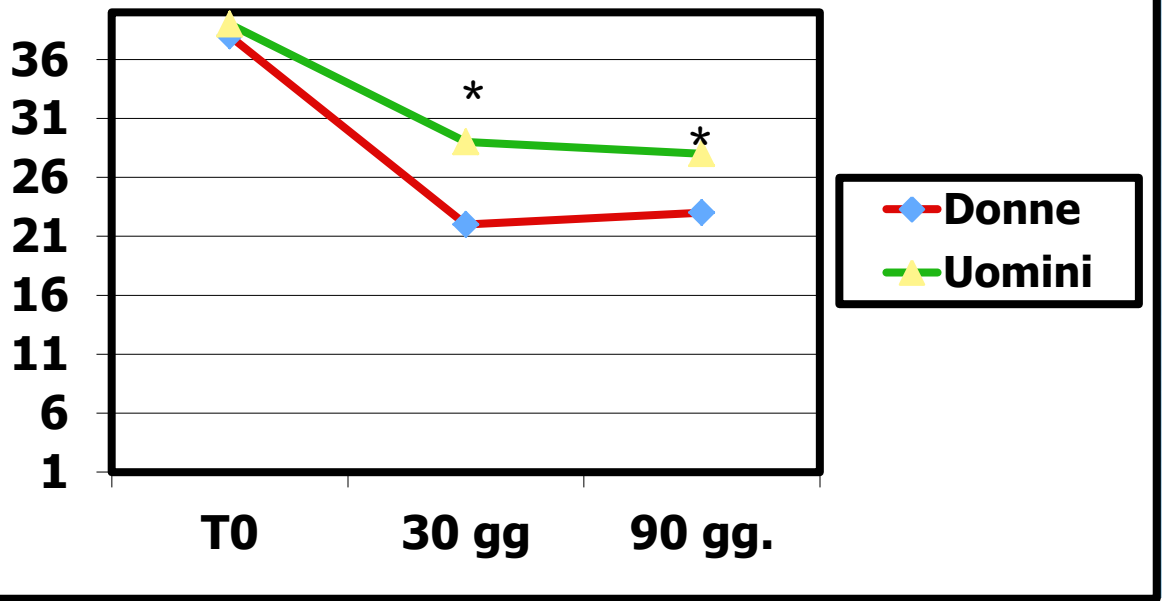


## Sensibilità al contrasto (%)




* p < 0.001

## Tempo di recupero dopo abbagliamento (sec)



# Effects of Black Currant Anthocyanoside Intake on Dark Adaptation and VDT Work-induced Transient Refractive Alteration in Healthy Humans

Hitoshi Nakaishi, MD, DMSC, Hitoshi Matsumoto, MS, Shigeru Tominaga, MS, and Masao Hirayama, PhD

In conclusion, oral intake of BCA brought about a reduction of the dark adaptation threshold and promoted recovery from or served to prevent VDT work-induced transient refractive alteration and subjective symptoms of visual fatigue in healthy subjects. These findings suggest the possibility of prevention of VDT work-induced asthenopia through intake of dietary anthocyanosides. Additional re-

# Eleuterococco

- L'eleuterococco agisce sulle ghiandole surrenali, diminuendo il contenuto intraghiandolare di colesterolo e di vitamina C, aumentando la produzione di ormoni surrenalici.
- Alcuni eleuterosidi si legano ai recettori dei glicocorticoidi, dei progestinici, dei mineralcorticoidi e degli estrogeni (ERRgamma)
- A livello cardiaco, si è osservato un aumento del numero di mitocondri nelle fibrocellule muscolari miocardiche e ciò potrebbe spiegare un aumento della prestazione fisica (i mitocondri sono coinvolti nella produzione di ATP per ossidazione del substrato con l'ossigeno molecolare).

# Gender Disparities in Ocular Inflammatory Disorders

- Ocular inflammatory disorders disproportionately affect women, and the majority of affected women are of childbearing age.
- The role of sex or reproductive hormones has been proposed in many other inflammatory or autoimmune disorders, and findings from non-ocular autoimmune diseases suggest a complex interaction between sex hormones, genetic factors and the immune system.
- However, despite the age and sex bias, factors that influence this disparity are complicated and unclear. This review aims to evaluate the gender disparities in prevalence, incidence and severity of the most common infectious and non-infectious ocular inflammatory disorders.

# Sex-Steroid Imbalance in Females and Dry Eye

- the condition of menopause in aging women may also contribute to DE onset or worsening as a consequence of an overall hormonal imbalance.
- Sex hormones play a key role in ocular surface physiology and they impact differently on ocular surface tissues. Reduced estrogen levels were historically thought to be responsible in age-related DE onset but more recent investigations have reconsidered the role of androgens that are present and exert a protective function on the ocular surface.

# DRY EYE E DONNE

- **Maggiore predisposizione dry eye (Tarumi 1990):**
  - Gravidanza
  - Uso contraccettivi orali
  - Menopausa
  - Terapia sostitutiva (HRT)
- **Maggiore impegno lavorativo ai vdt (Nakazawa 2002)**
- **Sovrastima dei sintomi**

Hormone replacement therapy?
Androgenic influence ?
Estrogenic influence?
Progesterone influence?
All of these?

**ONLY ANDROGENS ?**

*Sullivan Invest Ophthalmol Vis Sci. 2000;41:3732–3742*

**Estrogen receptors in meibomian glands**

***Esmaeli: Ophthalmology.*** **2000;107:180–184**

# There are other important variables:

The ocular surface and Meibomian Glands is an estrogen-dependent unit
(Foulks ’08,Srinivasan ’07,Duarte ’07, Versura ’07)

**Dysfunction of Meibomian glands**

**Disorders of neutral and polar lipid into lipid tear film**

**Instability/imbalance of tear film neads**

new systemic therapies

# Androgen Influence on the Meibomian Gland *David A. Sullivan Invest Ophthalmol Vis Sci. 2000;41:3732–3742*

Schepens Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.

- Meibomian gland is an androgen target organ
- Androgens influence the lipid profile
- 19-nortestosterone treatment modulated the fatty acid profile in the total and neutral lipid fractions of the **rabbit** meibomian gland

# Esmaeli B, Harvey JT, Hewlett B. Immunohistochemical evidence for estrogen receptors in meibomian glands. *Ophthalmology.* 2000;107:180–184

- Our findings demonstrate that sex steroid receptor mRNAs exist in a variety of ocular tissues **(humans)** and suggest that these sites may represent target organs for androgens, estrogens and/or progestins.

Rabbit meibomian gland contributes very little to the tear film lipid layer:The vast majority of lipids on the rabbit's ocular surface originate from other adnexal tissues. This situation contrasts sharply with that in humans, in which the meibomian gland is the primary source of tear film lipids".

**The rabbit does not appear to be an ideal model for determining whether androgen-meibomian gland interactions promote the formation of the tear film lipid layer.**

# La sindrome dell' ovaio policistico (iperandrogenismo) migliora o riduce l' incidenza di disfunzione lacrimale ?

**Assolutamente NO!**

**Al contrario nelle adolescenti iperandrogeniche la disfunzione lacrimale è una costante.**


-Yava G.F. et al.: **Meibomian gland alterations in polycystic ovary syndrome.** Curr Eye Res. 2008 Feb;33(2):133-8. Meibomian gland function and tear film lipid layer affected in cases with PCOS.

-Bonini S. et al.: **Itchy-dry eye associated with polycystic ovary syndrome.** Am J Ophthalmol. 2007 May;143(5):763-771. Epub 2007 Mar 23. Women with PCOS were more likely to have itchy-dry eyes, decreased tear film BUT, and increased goblet cell density.

Testosterone, 17β-estradiol and progesterone exert multiple effects on the lacrimal and meibomian glands. These sex steroid actions are sex-specific and/or opposite.

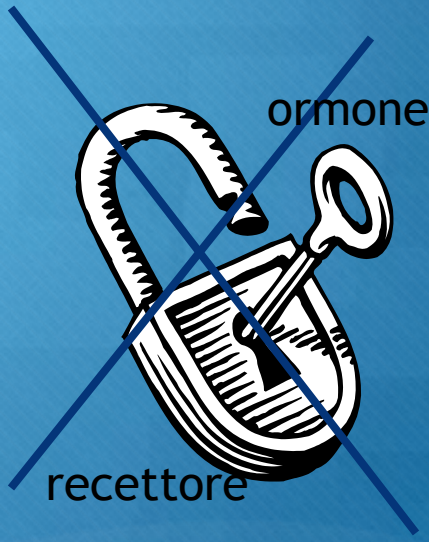
Our analyses did not identify any gene that was uniquely and significantly expressed in female, as compared to male, glands.

These opposing sex steroid effects may play a role in the pathogenesis of dry eye syndrome.

**D.A. Sullivan, R.V. Jensen, T.Suzuki, S.M. Richards Do sex steroids exert sex-specific and/or opposite effects on gene expression in lacrimal and meibomian glands? *Molecular Vision 2009*; *15:1553-1572***

# FITOESTROGENI

## BAGNO ORMONALE




## Modulazione recettoriale

# Receptor modulation

HORMONAL BATH


## PHYTOESTROGENS

**Genistein** → **S**elective **E**strogen **R**eceptor **MODULATOR (SERM)**

**Anti-estrogenic** and **Estrogenic effects** in some tissues

**Androgenic** activity

# -Phytoestrogens

- Because of its differential binding affinity to estrogen receptor (ER) isoforms, genistein is described as a **selective estrogen receptor modulator** (SERM).
- The phytoestrogen induced aromatase activity in the cells; it regulates **aromatase-B** expression in the brain in an ER-dependent manner .

Ye L, Chan MY, Leung LK : Mol Cell Endocrinol. 2009 Apr 10;302(1):73-80

# -Phytoestrogens

- Phytoestrogens have been shown to exert **anti-estrogenic** and estrogenic effects in some tissues

Bandera EV, Williams MG, Sima C, Bayuga S, Pulick K, Wilcox H, Soslow R, Zauber AG, Olson SH Cancer Causes Control. 2009 Apr 8

# -Phytoestrogens

- Phytoestrogens play important role in the maintenance of meibomian gland lipids and overall production or retention of aqueous tears
- May decrease versus enhance prolonged cell death mechanisms, via its estrogenic action, by blocking or promoting Bcl-2 and Bax apoptotic pathways
- Influence of dietary soy isoflavones on certain aspects of brain structure, learning, memory and anxiety along with the brain androgen-metabolizing enzyme, aromatase.
- Produce anxiolytic effects

(Edwin ’02, Lund ’03, Lephart ’03, Trent ’08)

# A controlled Double Masked Clinical Assessment Study of Phytoestrogens, Lipoic Acid and Essential Fatty Acid (EPA) Supplement and Its Effect on Dysfunctional Tear Syndrome

-**Phytoestrogens** (fenugreek 200 mg) :

Diosgenin
Steroidal saponins
alkaloids

-

-**Lipoic Acid (100 mg)**

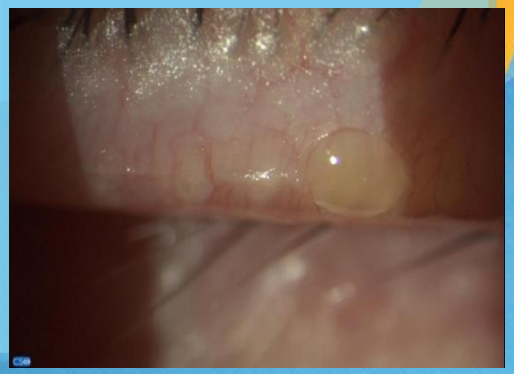
-**EPA (eicosapentanoic acid) (240 mg)**

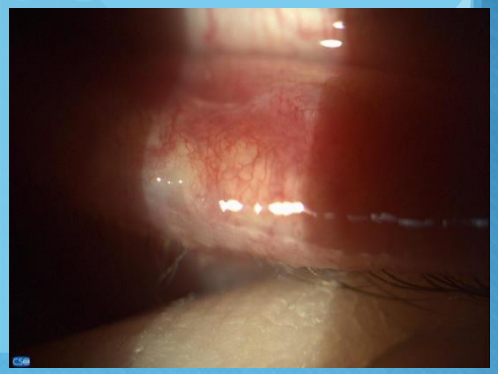
Can J Ophthalmol. 2012 Dec;47(6):489-92. doi: 10.1016/j.jcjo.2012.08.019.

**Effects of phytoestrogen supplementation in postmenopausal women with dry eye syndrome: a randomized clinical trial.**

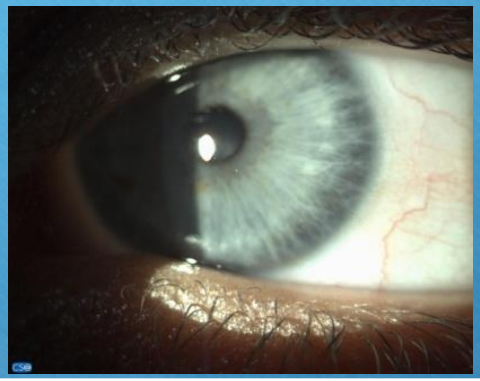
Scuderi G[1], Contestabile MT, Gagliano C, Iacovello D, Scuderi L, Avitabile T.

Author information





- REGULATION OF MG SECRETION
- ANTI-INFLAMMATORY EFFECT ON MG
- EFFECT ON NEUTRAL AND POLAR LIPID INTO TEAR FILM



# Conclusion

**Phytoestrogens** significantly:

1) Decreased tear osmolarity
2) Increased Schirmer values
3) Increased Tear-BUT

**Valid support** in the severe Dysfunctional Tear Syndrome.

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# Effects of phytoestrogen supplementation in postmenopausal women with dry eye syndrome: a randomized clinical trial.

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## Abstract

**OBJECTIVE:** To evaluate the correlation between tear osmolarity and blood levels of 17-β estradiol, estrone, and testosterone in postmenopausal women with dry eye syndrome, and to assess the efficacy and safety of oral supplementation with phytoestrogens, lipoic acid, and eicosapentaenoic acid in this population.

**DESIGN:** Cross-sectional study including 66 postmenopausal women with dry eye syndrome.

**METHODS:** Sixty-six postmenopausal women with dry eye syndrome were enrolled in a randomized, double-blind, placebo-controlled, crossover study. Patients were divided into 2 groups (groups A and B) and treated, respectively, with phytoestrogen (Bioos, Montegiorgio, Italy) tablets or placebo tablets for 30 days. The 2 treatment periods were separated by a 30-day washout. Patients were examined on days 0 and 30 of each period. Assessments included blood levels of sex hormones, the Schirmer test for tear production, and measurement of tear osmolarity and tear film break-up time.

**RESULTS:** At baseline, all patients had low sex hormone levels, which were correlated with high tear film osmolarity values ($r = -0.59, -0.61, -0.58$, respectively). After 30 days of therapy, the group treated with Lacrisek® (Bioos) had significantly decreased tear osmolarity ($P<0.005$) and significantly increased tear production evaluated with the Schirmer test and tear film break-up time values ($P<0.001$) compared with the placebo-treated group.

**CONCLUSIONS:** Our study confirms that steroid hormones play an important role in ocular surface equilibrium and functions. Consequently, reduced blood levels of these hormones can produce changes at the ocular surface. Phytoestrogen supplementation can significantly improve the signs and symptoms of dry eye syndrome in postmenopausal women.

# Nutraceutica dry eye

- Terapia topica: nanoliposomi
- Terapia sistemica: fitoestrogeni

# Gender and Cataract – The Role of Estrogen

- There is evidence from epidemiologic data that cataract is more common in women than men. This is not solely due to a higher rate of cataract extraction in women, as is the case in the western world, but several population-based studies show that females have a higher prevalence of lens opacities, especially cortical.
- Estrogens are known to exert several anti-aging effects that may explain the longer lifespan in women, including metabolically beneficial effects, neuroprotection, preservation of telomeres and anti-oxidative properties

# Gender and Cataract – The Role of Estrogen

- Several investigators have found protection by physiological concentrations of 17β-estradiol against oxidative stress induced by $H_2O_2$ in cultured lens epithelial cells. Although both main types of estrogen receptors, ERα and ERβ, have been demonstrated in lens epithelium, most studies so far indicate that the estrogen-mediated protection in the lens is exerted through non-genomic, i.e. receptor-independent mechanisms, possibly through phosphorylation of extracellular signal-regulated kinase (ERK1/ERK2), a member of the mitogen-activated protein kinase (MAPK)-signaling pathway. Further studies are needed, both epidemiologic as to the role of hormone therapies, and laboratory studies regarding molecular estrogen-mediated mechanisms, in order to comprehend the role of estrogens on cataract formation. (Samsudin et al. Eye 2009)

# Gender Difference in the Pathophysiology and Treatment of Glaucoma

- Depending on the type of glaucoma, hormone therapy, oral contraceptive use and menopausal status have also been associated with glaucoma.
- pregnancy leads to changes in IOP (riduzione per rilassamento del collagene corneo-sclerale dovuto agli estrogeni)
- the treatment of glaucoma must be tailored based on the systemic effects of topical therapeutics on the mother and fetus

# Gender Differences in Ocular Blood Flow

- Although little data is available, estrogen, progesterone and testosterone are most likely important regulators of blood flow in the retina and choroid, because they are key regulators of vascular tone in other organs.
- Estrogen seems to play a protective role since it decreases vascular resistance in large ocular vessels. Some studies indicate that hormone therapy is beneficial for ocular vascular disease in post-menopausal women.

# Effects of Sex and Age on the Normal Retinal and Choroidal Structures on Optical Coherence Tomography

- Macular, retinal layer, and choroidal thickness measured on OCT images in normal eyes showed significant variations by sex and age. **Macular retinal thickness was greater in men than in women,** especially in the center, inner ring, and outer temporal ring areas as defined by the Early Treatment Diabetic Reinopathy Study (ETDRS).

- Moreover, inner retinal thickness decreased with increasing age and choroidal thickness was greater in men than in women and was negatively correlated with age and axial length. These findings provide information that should be considered in analyses of retinal or choroidal thickness in OCT studies of retinal diseases and glaucoma.

# Il segnale estrogenico nella patogenesi dell'AMD

- Pathogenesis of AMD involves constant oxidative stress, chronic inflammation, and increased accumulation of lipofuscin and drusen. Estrogen has both anti-oxidative and anti-inflammatory capacity and it regulates signaling pathways that are involved in the pathogenesis of AMD
- Rallentano la progressione del danno nell'AMD (Vina et al. Free Rad Res 2007)

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# Vitamin D Status and Early Age-Related Macular Degeneration in Postmenopausal Women

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- The relationship between serum 25-hydroxyvitamin D (25(OH)D) concentrations (nmol/L) and the prevalence of early age-related macular degeneration (AMD) was investigated among participants of the Carotenoids in Age-Related Eye Disease Study.
- Among women <75 years, intake of vitamin D from foods and supplements was related to decreased odds of early AMD in multivariate models; no relationship was observed with self-reported time spent in direct sunlight.
- High serum 25(OH)D concentrations may protect against early AMD in women <75 years.

# Grazie per l'attenzione!

**"L'uomo non è il normale della specie umana e la donna non può essere considerata un piccolo uomo!!"**