



10. HRVATSKI KONGRES O GINEKOLOŠKOJ ENDOKRINOLOGIJI,
HUMANIJ REPRODUKCIJI I MENOPAUZI

Johannes Huber: Endocrine estetic and cosmetic in menopause

možete objektivizirati proces starenja na licu

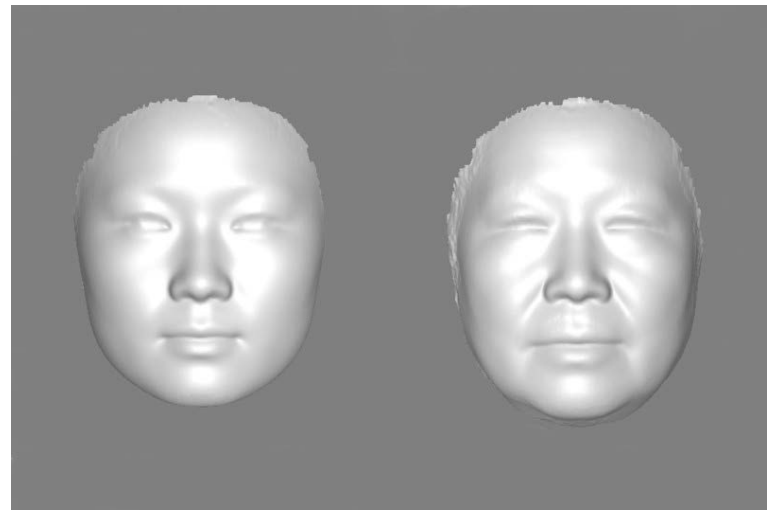
Original Article

Cell Research 25, 574-587 (May 2015) | doi:10.1038/cr.2015.36

Three-dimensional human facial morphologies as robust aging markers

Weiyang Chen, Wei Qian, Gang Wu, Weizhong Chen, Bo Xian, Xingwei Chen, Yaqiang Cao, Christopher D Green, Fanghong Zhao, Kun Tang and Jing-Dong J Han

Aging is associated with many complex diseases. Reliable prediction of the aging process is important for assessing the risks of aging-associated diseases. However, despite intense research, so far there is no reliable aging marker. Here we addressed this problem by examining whether human 3D facial imaging features could be used as reliable aging markers. We collected > 300 3D human facial images and blood profiles well-distributed across ages of 17 to 77 years. By analyzing the morphological profiles, we generated the first comprehensive map of the aging human facial phenome. We identified quantitative facial features, such as eye slopes, highly associated with age. We constructed a robust age predictor and found that on average people of the same chronological age differ by ± 6 years in facial age, with the deviations increasing after age 40. Using this predictor, we identified slow and fast agers that are significantly supported by levels of health indicators. Despite a close relationship between facial morphological features and health indicators in the blood, facial features are more reliable aging biomarkers than blood profiles and can better reflect the general health status than chronological age.

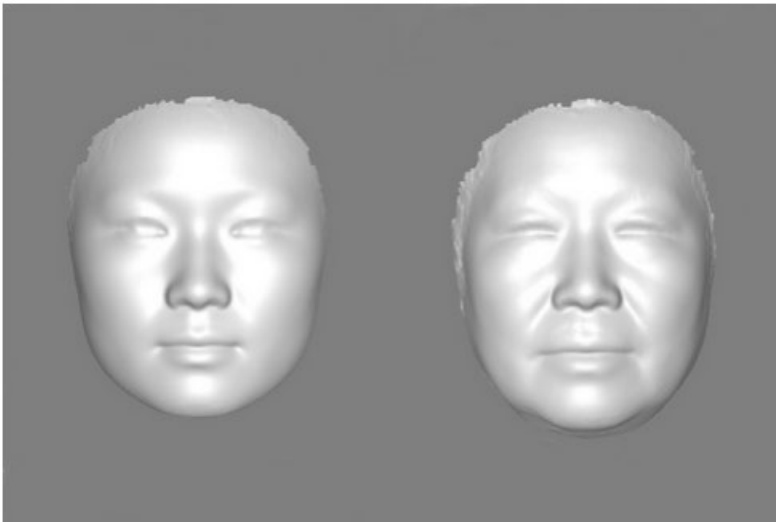


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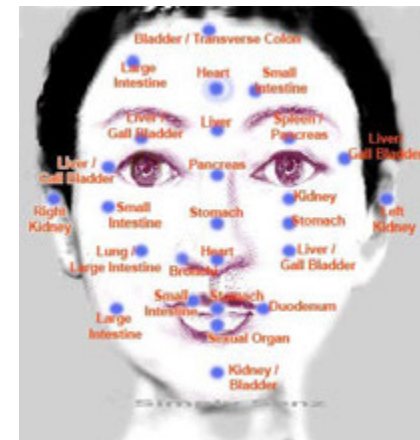
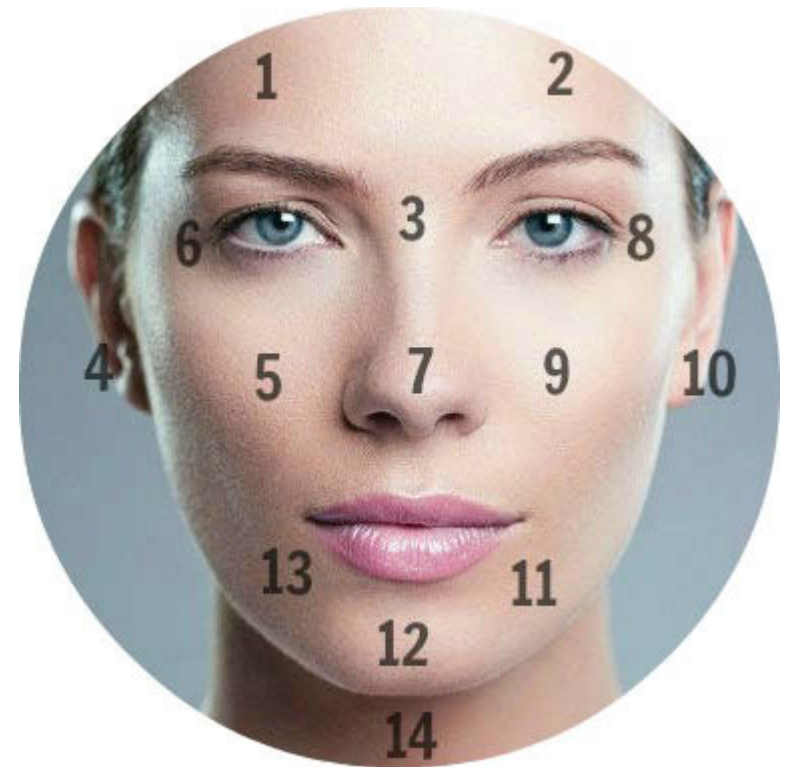
Daily news 31 March 2015

Eek! How your face reveals your body's real age



Composites of the faces of Chinese women aged between 17 and 29, and 60 and 77

(Image: Chen et al., *Cell*, DOI: 10.1016/j.cell.2015.03)



In modern data processing, attempts are being made to discover parameters that will register the process of aging on the face.

razine u serumu estrogena u korelaciji s mladenačkim lice

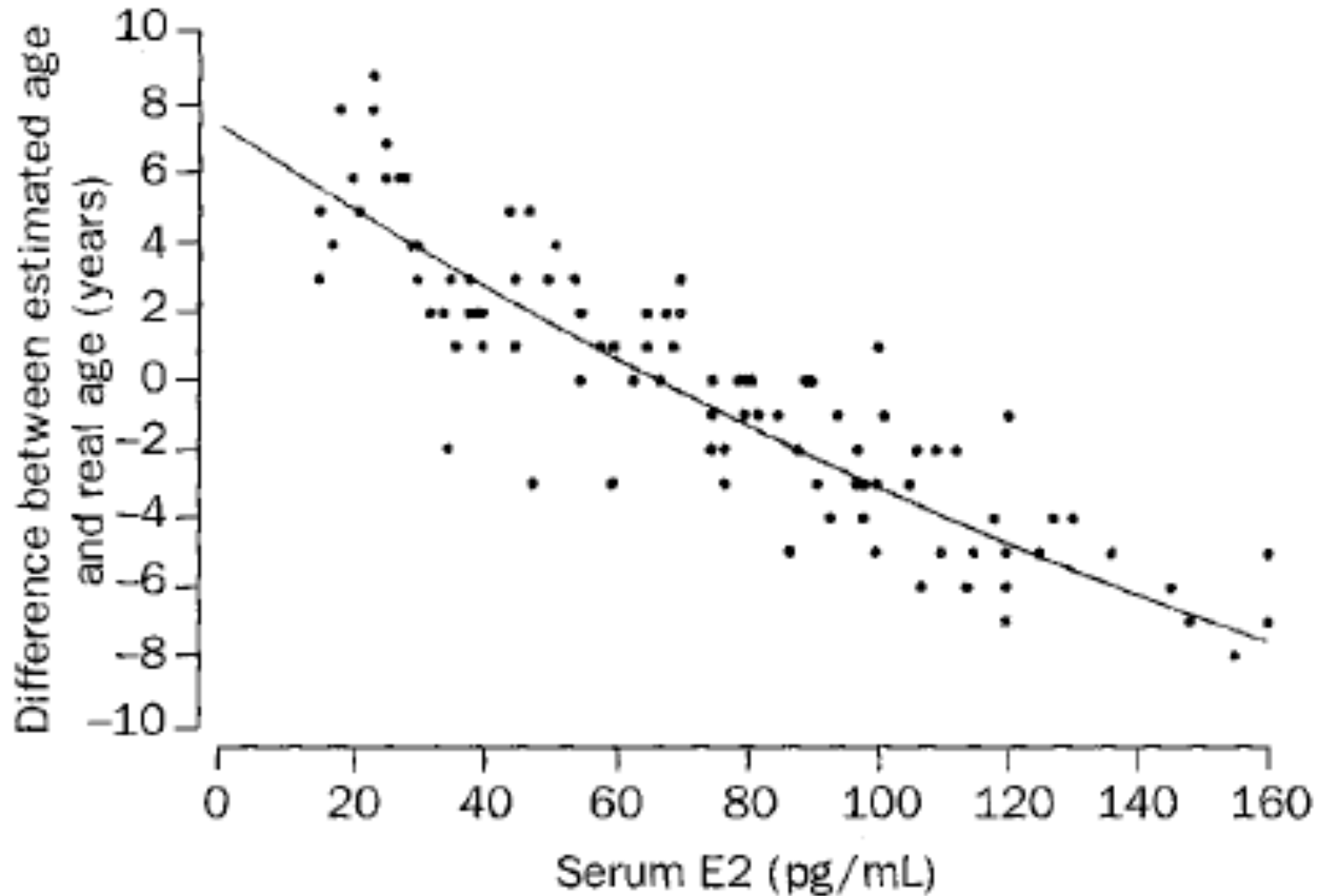
Oestrogen and age estimations of perimenopausal women

Ludwig Wildt, Teresa Sir-Petermann

We estimated the age of perimenopausal women at a first visit and measured the concentrations of oestradiol in serum. The accuracy of estimation of age strongly correlated with oestradiol concentrations: age was overestimated when oestradiol was low and underestimated when oestradiol was high.

The association between oestrogens and sexual attractiveness has been widely discussed in both scientific and popular literature.¹ However, the question how

Estrogen levels correlate with the estimated age of a woman's face.



Solving an age-old problem

Western governments need to rethink their approach to dealing with an ageing population.



publikacije, pokazuje zussmenhang između estrogena i kolagena

Gynecol Endocrinol. 2002 Dec;16(6):431-41

·
Current concepts in aesthetic endocrinology.

Gruber CJ, Wieser F, Gruber IM, Ferlitsch K, Gruber DM, Huber JC.



A prospective, randomized, double-blind, placebo-controlled study on the influence of a hormone replacement therapy on skin aging in postmenopausal women

P.-G. Sator, M. O. Sator*, J. B. Schmidt, H. Nahavandi[†], S. Radakovic, J. C. Huber* and H. Hönigsmann

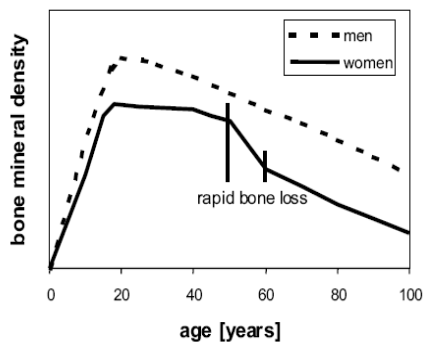
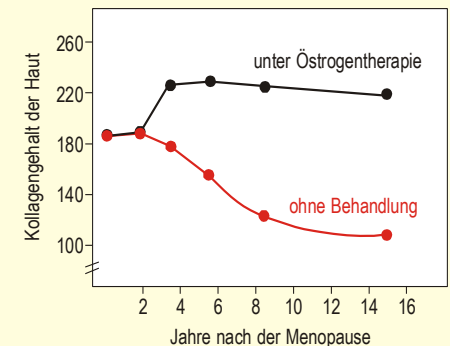


Fig. 1. Bone gain and bone loss in men and women. Adapted from R. Bartl, 2001 [9]



Takoder aktualna estrogen djeluje

Br J Obstet Gynaecol. 1995 Dec;102(12):985-9.

The effect of topical oestradiol on skin collagen of postmenopausal women.

[Varila E](#), [Rantala I](#), [Oikarinen A](#), [Risteli J](#), [Reunala T](#), [Oksanen H](#), [Punnonen R](#).

Ann Chir Gynaecol Suppl. 1987;202:39-41.

Local oestriol treatment improves the structure of elastic fibers in the skin of postmenopausal women.

[Punnonen R](#), [Vaajalahti P](#), [Teisala K](#).

Treatment of menopausal keratoconjunctivitis sicca with topical oestradiol

*Michael O. Sator Registrar, *Elmar A. Joura Consultant/Lecturer, *Thomas Golaszewski Consultant,
*Doris Gruber Registrar, *Peter Frigo Consultant, *Markus Metka Consultant,
†Anton Hommer Consultant, *Johannes C. Huber Professor

*Department of Obstetrics and Gynaecology, Division of Endocrinology and Sterility Treatment, and †Department of Ophthalmology,
University of Vienna, Austria

Objective To investigate the effect of 17β -oestradiol ophthalmic drops in comparison with a traditional tear substitute in postmenopausal women with keratoconjunctivitis sicca.



THE LANCET

Hormonal influences on intraocular pressure

Michael O Sator Doris M Gruber Elmar A Joura

Reprinted from THE LANCET Saturday 14 September 1996
Vol. 348 No. 9029 Pages 761-762



AGEING

Marie-Thérèse Heemels, Senior Editor

Cover illustration

Image courtesy of
B. Yankov/iStockphoto.
Artwork by N. Spencer.

Growing old seems intimately linked with decline. Ageing, the accumulation of damage to molecules, cells and tissues over a lifetime, often leads to frailty and

The number of people aged 60 years and older is growing rapidly worldwide. So keeping the elderly healthy has to be high on the list of priorities. Ageing research is clearly gaining momentum, as the reviews in this Insight testify, bringing hope that at some time in the future we will be able to keep age-related diseases at bay by suppressing ageing itself. As ageing will affect us all sooner or later, we hope that you will find this collection informative and stimulating.

Također hormon trudnoće progesteron ima dermatološkog važnos

Gynecol Endocrinol. 2001 Dec;15 Suppl 6:18-21.

Immunological and dermatological impact of progesterone.

[Huber J](#), [Gruber C](#).

Not only estrogen but also progesterone is important for the skin

Effects and side-effects of 2% progesterone cream on the skin of peri- and postmenopausal women: results from a double-blind, vehicle-controlled, randomized study

G. Holzer, E. Riegler, H. Hönigsmann, S. Farokhnia* and B. Schmidt

Division of Special and Environmental Dermatology, Medical University of Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria

*Pharmacy Department, General Hospital of Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria

Summary

Correspondence

Dr Gregor Holzer.

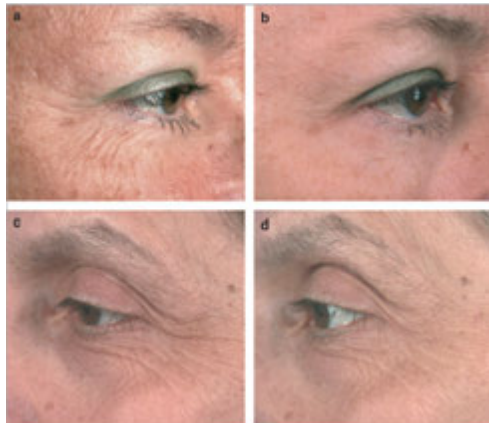
E-mail: gregor.holzer@medunivwien.ac.at

Accepted for publication

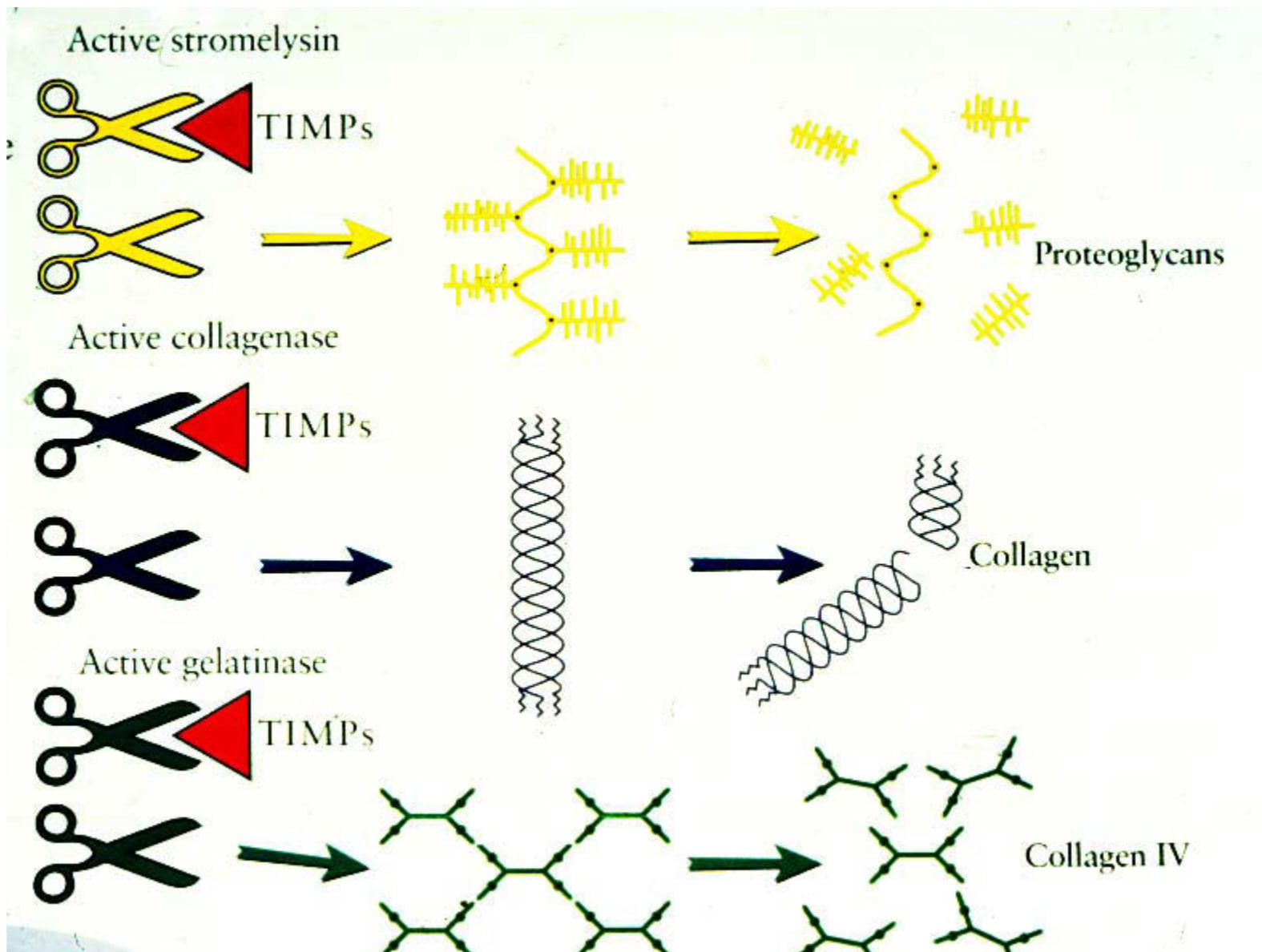
12 January 2005

Background For many years topical progesterone has been prescribed by gynaecologists as an antiageing and skin-firming treatment, without any clinical scientific evidence of its effects, tolerability and safety when applied to skin.

Objectives To evaluate the influence of 2% progesterone cream on function and texture of the skin in peri- and postmenopausal women.



Progesterone does not penetrate the skin easily because it contains 21 carbon atoms



*Estrogen stimulira kolagen struktura
 Progesteron sprječava razgradnju kolagena*

The Nobel Prize in Chemistry 2003



Peter Agre

Prize share: 1/2



Roderick MacKinnon

Prize share: 1/2

The Nobel Prize in Chemistry 2003 was awarded *"for discoveries concerning channels in cell membranes"* jointly with one half to Peter Agre *"for the discovery of water channels"* and with one half to Roderick MacKinnon *"for structural and mechanistic studies of ion channels"*.

Kako mogu kožu za make hormona tijekom

Electroporation as an Efficient Physical Enhancer for Skin Drug Delivery

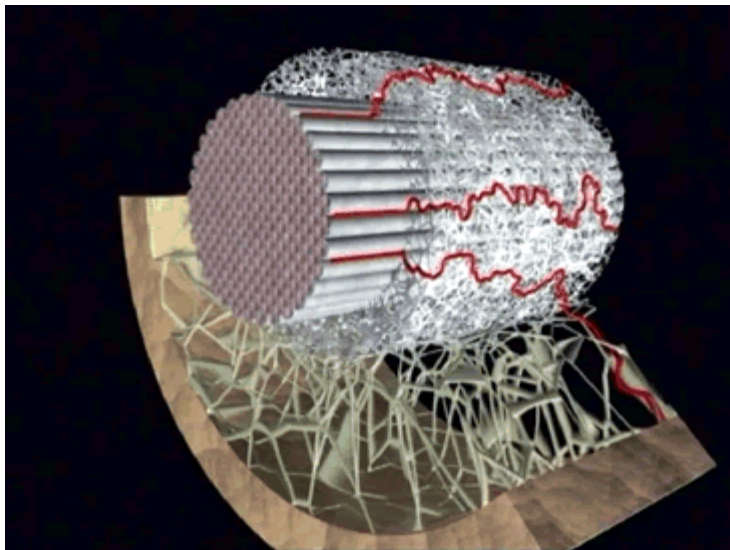
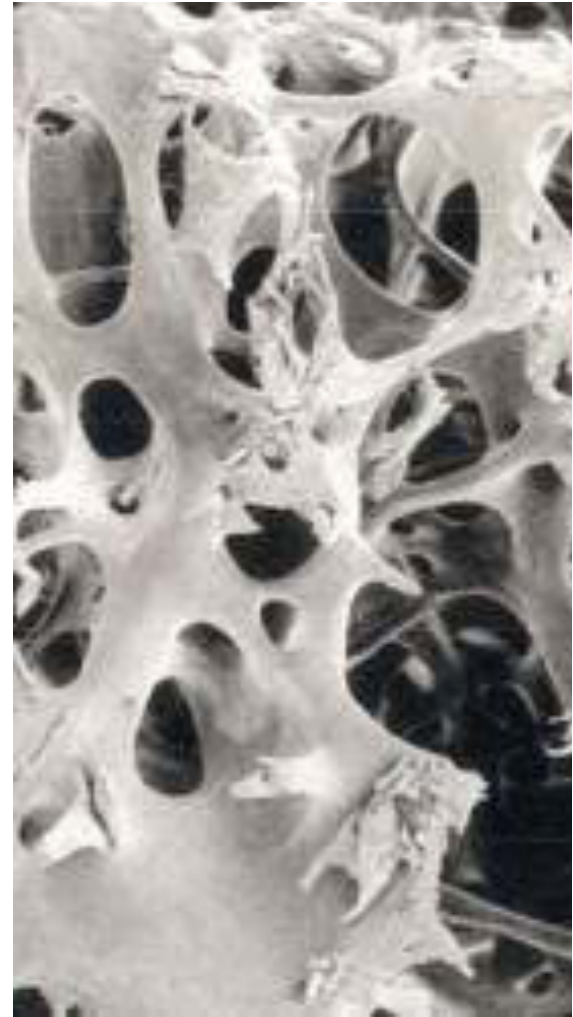
José Juan Escobar-Chávez, PhD, Dalia Bonilla-Martínez, MSc, Martha Angélica Villegas-González, MSc, and Alma Luisa Revilla-Vázquez, PhD

Transdermal drug delivery offers an attractive alternative to the conventional drug delivery methods of oral administration and injection. However, the stratum corneum acts as a barrier that limits the penetration of substances

drugs. The in vivo application of high-voltage pulses is well tolerated, but muscle contractions are usually induced. The electrode and patch design is an important issue to reduce the discomfort of the electrical treatment

***Journal of Clinical Pharmacology,
2009;49:1262-1283***

***© 2009 the American College of Clinical
Pharmacology***



This is important for the treatment of the flabby upper arm, which is caused by weakness of fasciae – similar to the loss of trabeculae in osteoporosis.

Pojas će ovisiti o hormonima

KOSMETISCHE MEDIZIN 2.13 ÜBERSICHTEN | REVIEWS

THE AESTHETIC UPPER ARM:
ON THE ANATOMY AND CLASSIFICATION OF THE LIPODYSMORPHIC UPPER ARM

Der ästhetische Oberarm: Zur Anatomie und Klassifikation des lipodysmorphen Oberarmes

MATTHIAS SANDHOFER¹, PATRICK SCHAUER², FRIEDRICH ANDERHUBER³

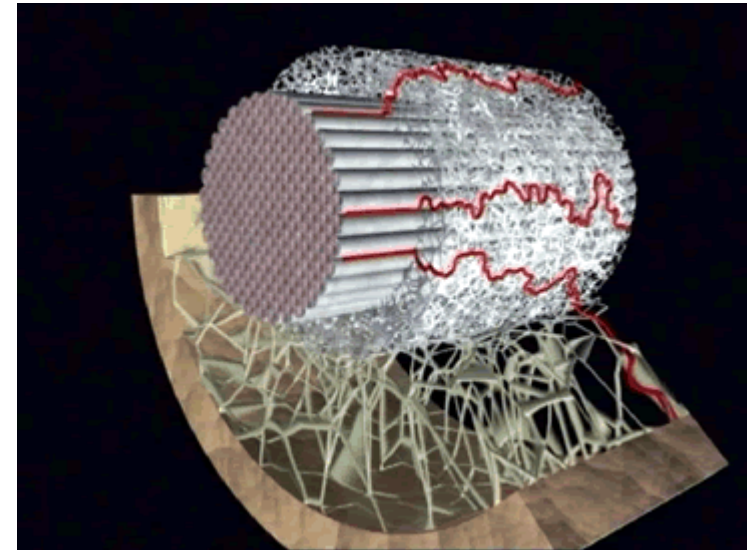
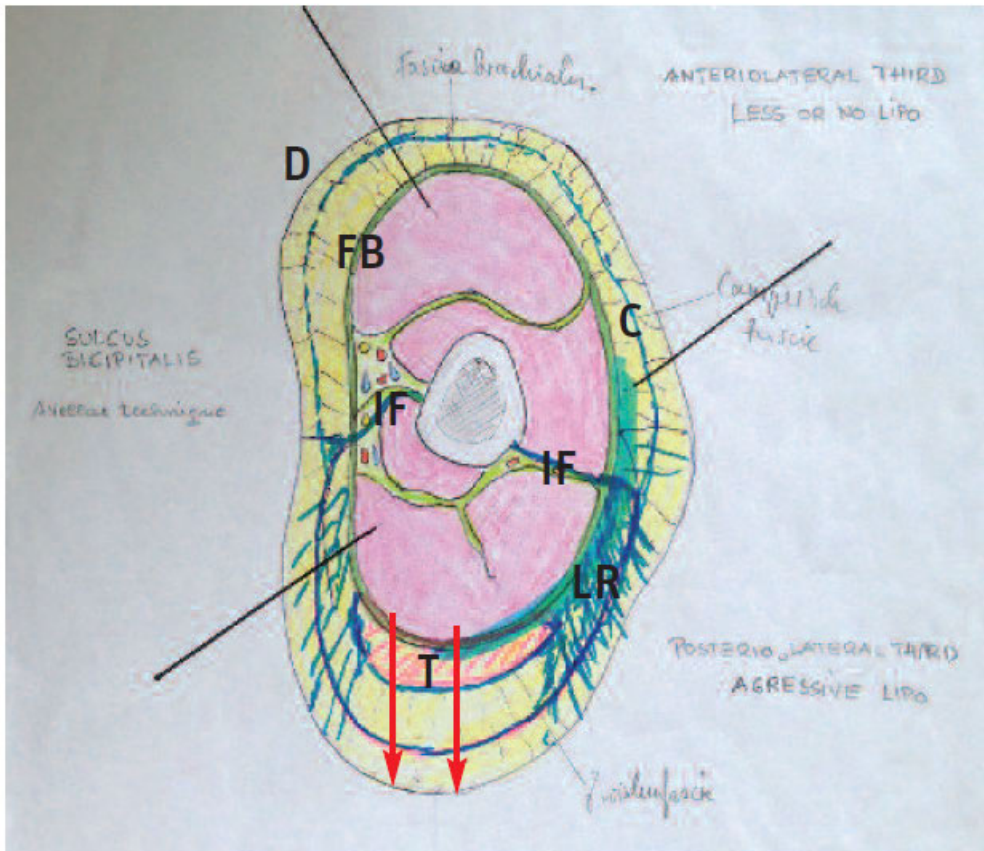


Abb. 14: Auf Grund der von uns durchgeführten Präparationen konnten wir die Dynamik des durchhängenden Oberarmes charakterisieren. Im Vordergrund steht die Muskelatrophie, das Durchhängen der Fascia brachialis (FB) mit ihren vor allem lateral positionierten Retinakula cutis (LR). Auch der über dem „Musculus Triceps“ positionierte Fettkörper (T) ist von diesem Durchhängephänomen betroffen.

A sagging upper arm is caused by weak fasciae.

paratireoidne hormon štiti kosti i pojas



International Journal of Pharmaceutics

Volume 263, Issues 1–2, 16 September 2003, Pages 25–33



Electronically facilitated transdermal delivery of human parathyroid hormone (1–34)

Babu M Medi, Jagdish Singh  

Department of Pharmaceutical Sciences, College of Pharmacy, North Dakota State University, Fargo, ND 58102, USA

Parathormone, which is used for the treatment of osteoporosis, is of interest for the treatment of connective tissue as well.

Thyroid hormones and tendon: current views and future perspectives. Concise review

Francesco Oliva¹

Anna C. Berardi²

Silvia Misiti³

Nicola Maffulli⁴

¹ Department of Orthopaedics and Traumatology, University of Rome "Tor Vergata" School of Medicine, Rome, Italy

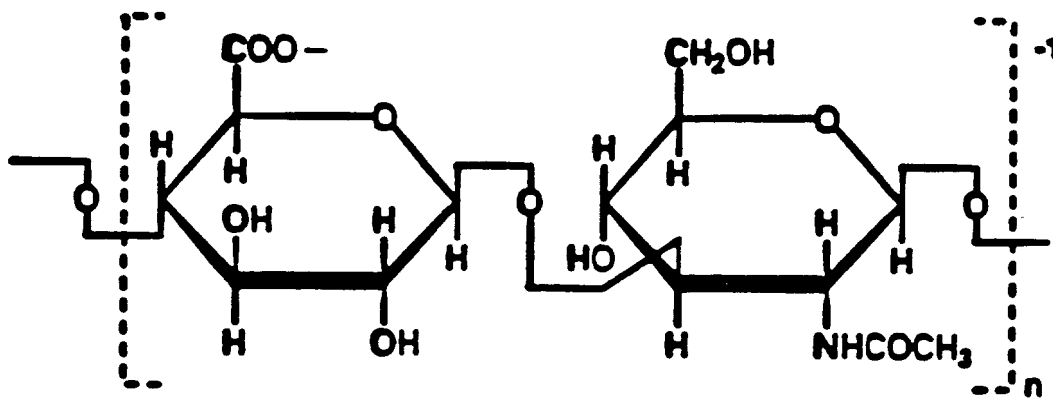
² Department of Transfusion Medicine, Laboratory of Stem Cells, Spirito Santo Hospital, Pescara, Italy

³ Department of Experimental Medicine, Endocrinolo-

role in the development and metabolism of many tissues and organs, and exert profound metabolic effects in adult life, including changes in oxygen consumption, protein, carbohydrate, lipid, and vitamin metabolism¹. The effects of THs are mediated mainly through T3, which regulates gene expression by binding to the TH receptors (TR)- α and - β . TRs belong to a large superfamily of nuclear hormone receptors which includes steroid hormones, retinoic acid, Vitamin D and peroxisomal proliferator receptors (PPARs)². These receptors also bind to enhancer ele-

The thyroid hormone also exerts effects on fasciae and tendons.

Thyroxine is important for both collagen synthesis and matrix metabolism. Hypothyroidism causes accumulation of **glycosaminoglycans** (GAGs) in the extracellular matrix, which may, in turn, predispose to **tendon calcification**. GAGs are involved in the pathogenesis of carpal tunnel syndrome during hypothyroidism



hipotireoza
također utječe
na kožu i
pojas

Tenocytes grew with a doubling time of approximately 49 h. The addition of the THs in the culture medium led to stimulation of cell growth with a reduction of the doubling time. In particular, T3 induced a reduction in doubling time of 27% (36 h) and T4 of 19% (40 h;), with the 10^{-7} M dose.

T3 and T4 play an antiapoptotic action. Hence, to verify whether they counteracted apoptosis in isolated tenocytes, cells were plated and serum deprivation was performed for 48 h to induce apoptosis.

Hormoni štitnjače stimulira tenocytes

Article

Identification and characterization of chondrogenic progenitor cells in the fascia of postnatal skeletal muscle

Guangheng Li^{1,2}, Bo Zheng¹, Laura B. Meszaros^{1,3}, Joseph B. Vella^{1,3}, Arvydas Usas¹, Tomoyuki Matsumoto¹, and Johnny Huard^{1,3,4,*}

1 Stem Cell Research Center, Department of Orthopaedic Surgery, University of Pittsburgh, 450 Technology Drive Suite 206, Pittsburgh, PA 15219, USA

2 Pediatric Cancer Biological Program, Department of Pediatrics, Oregon Health and Science University, Portland, OR 97239, USA

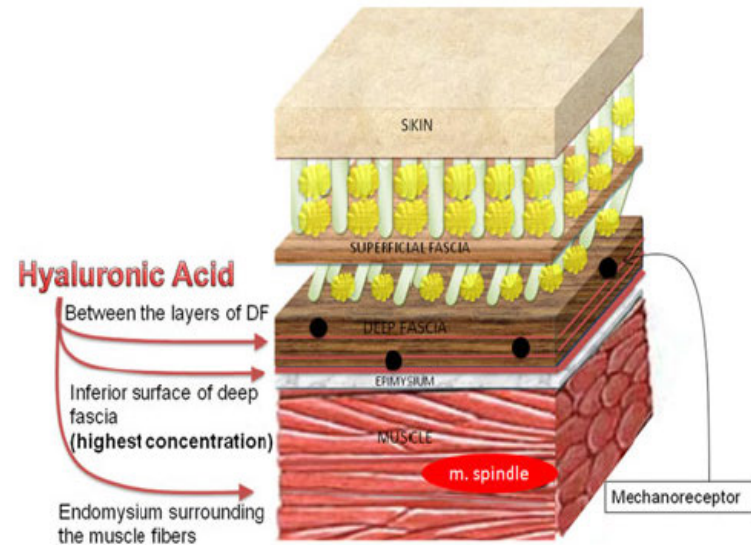
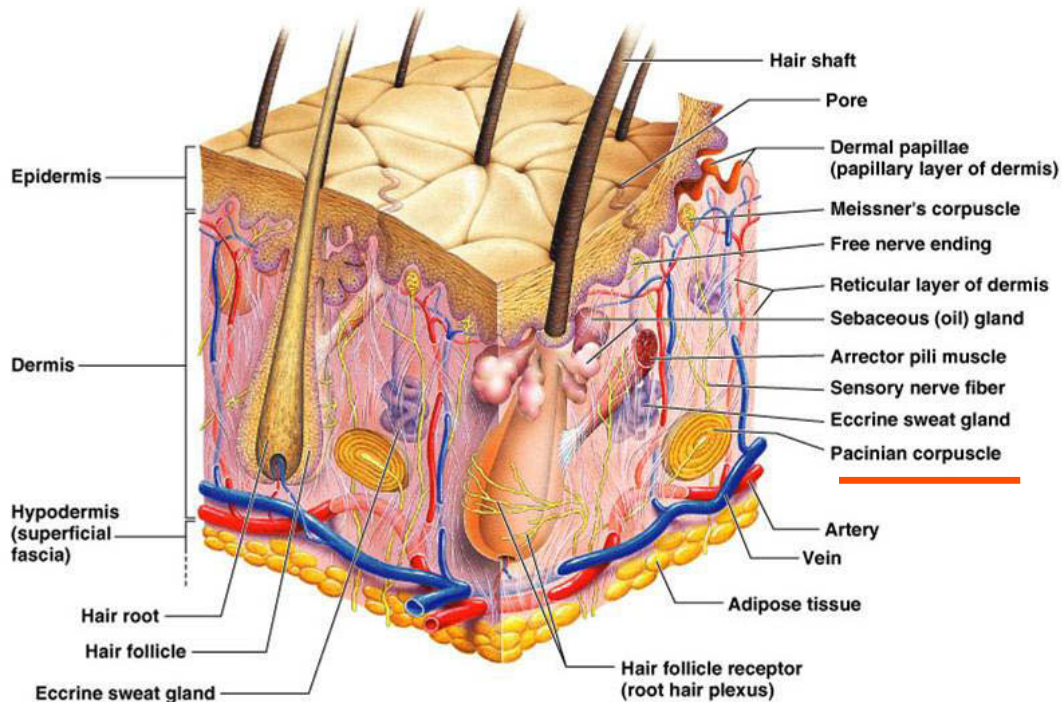
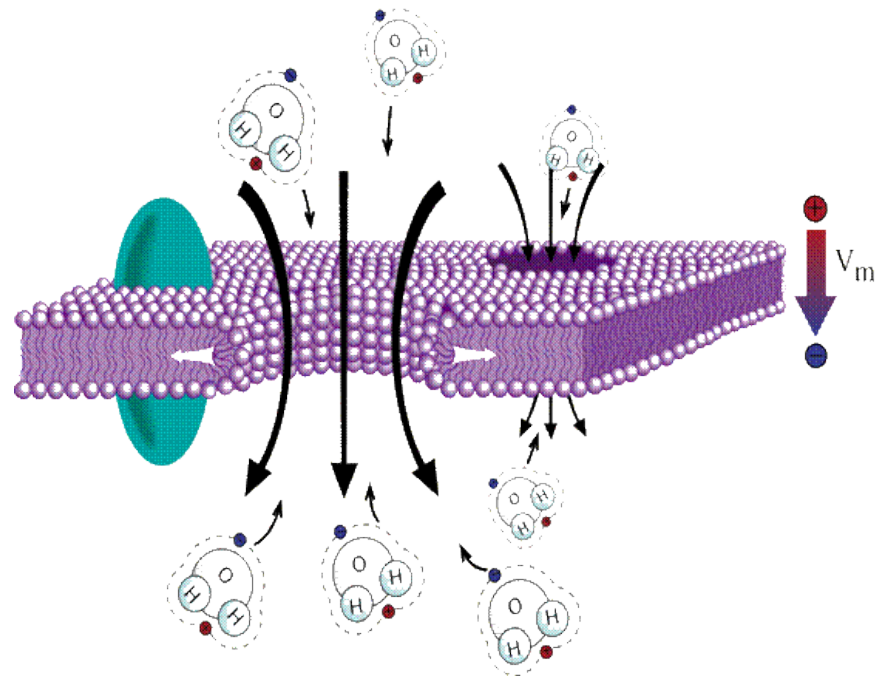
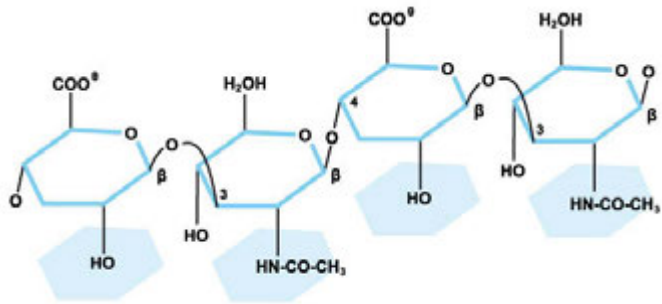
3 Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA 15219, USA

4 Department of Molecular Genetics and Biochemistry, University of Pittsburgh, Pittsburgh, PA 15219, USA

* Correspondence to: Johnny Huard, E-mail: jhuard@pitt.edu

Matične stanice stimuliraju
hormone štitnjače I

hialuronska kiselina može električki podesiti na koži





Journal of Controlled Release

Volume 95, Issue 3, 24 March 2004, Pages 535–546



Electrically assisted skin delivery of liposomal estradiol; phospholipid as damage retardant

Ebtessam A Essa, Michael C Bonner, Brian W Barry , 

Drug Delivery Group, School of Pharmacy, University of Bradford, Richmond Road, Bradford, West Yorkshire, BD7 1DP, UK



Abstract

This work investigated transdermal penetration of a model lipophilic drug (estradiol) through human epidermis from phosphatidylcholine (PC)-based liposomes and saturated aqueous estradiol solution (control). Representative examples of cholate-containing ultradeformable (Transfersomes), non-rigid

Estrogen također može prenijeti elektroporacijom u kožu bolj

Induction of Collagen by Estradiol

Difference Between Sun-Protected and Photodamaged Human Skin In Vivo

Laure Rittié, PhD; Sewon Kang, MD; John J. Voorhees, MD; Gary J. Fisher, PhD

Objective: To evaluate the effectiveness of topical estradiol in stimulating collagen I and III production in naturally aged and photoaged human skin of postmenopausal women and age-matched men.

Design: Vehicle-controlled treatment followed by biochemical and immunohistochemical analyses of skin biopsy specimens.

Setting: Academic referral center.

Participants: Seventy healthy volunteers (40 postmenopausal women with a mean age of 75 years, and 30 men with a mean age of 75 years) with photodamaged skin.

Interventions: Topical application of estradiol, 0.01%, 0.1%, 1%, or 2.5% or vehicle on aged or photoaged skin, with biopsy specimens taken after last treatment.

Main Outcome Measures: De novo synthesis of collagen by quantitative polymerase chain reaction, immunohistochemistry, and enzyme-linked immunosorbent assay.

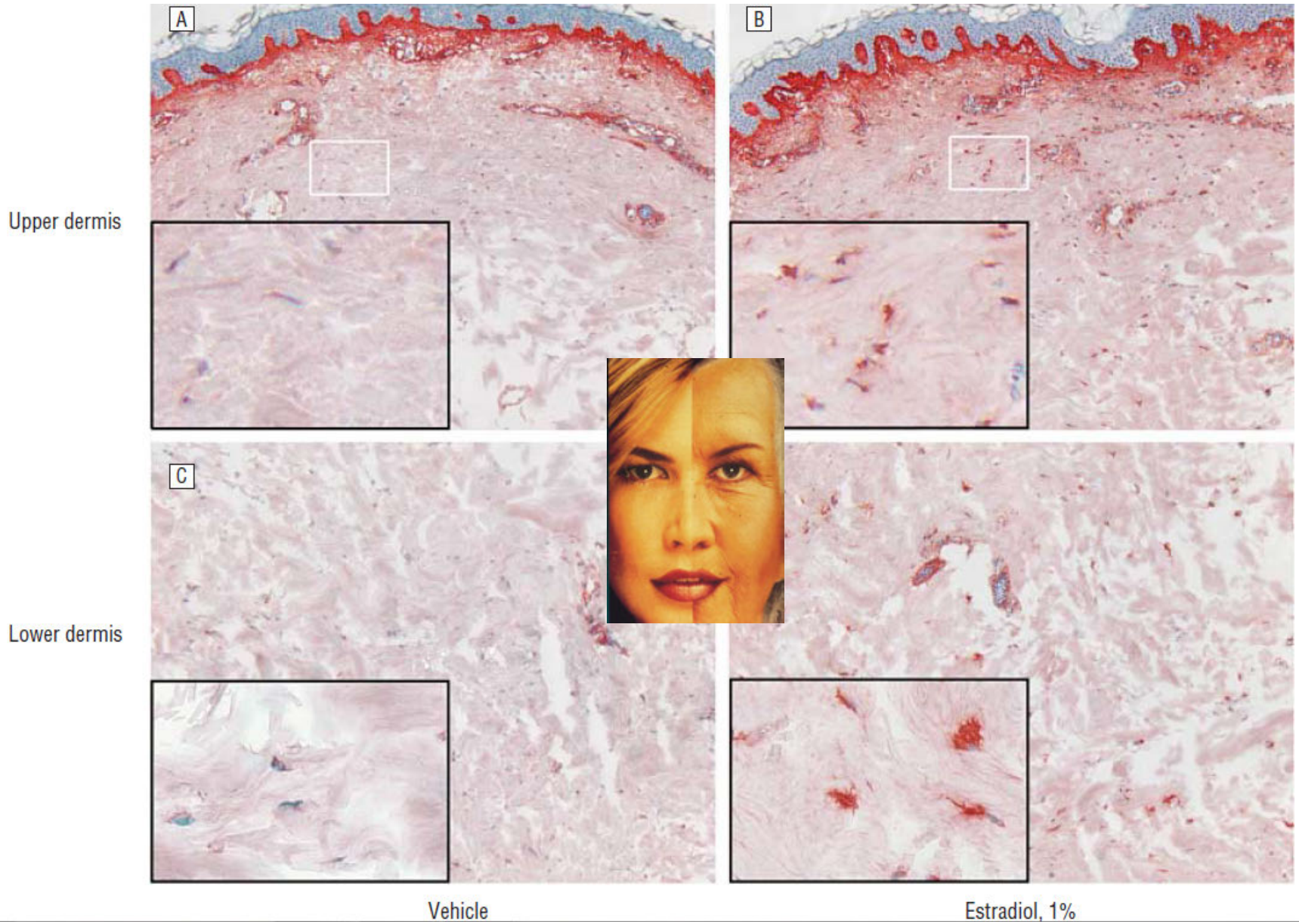
Results: Topical estradiol increased procollagen I and III messenger RNA and collagen I protein levels in sun-

protected aged hip skin in postmenopausal women and, to a lesser extent, in age-matched men. Surprisingly, no significant changes in production were observed in women or men after 2-week estradiol treatment of photoaged forearm or face skin, despite similar expression of estrogen receptors (ER- α , ER- β , and GPR30) in aged and photoaged skin. Estradiol treatment induced the estrogen-responsive gene *GREB1*, indicating that penetration of topical estradiol and genomic response to estrogen were similar in the 3 anatomic sites.

Conclusions: Two-week topical estradiol treatment stimulates collagen production in sun-protected hip skin, but not in photoaged forearm or face skin, in postmenopausal women and age-matched men. These findings suggest that menopause-associated estrogen decline is involved in reduced collagen production in sun-protected skin. Interestingly, alterations induced by long-term sun exposure hinder the ability of topical 2-week estradiol to stimulate collagen production in aged skin.

Trial Registration: clinicaltrials.gov Identifier: NCT00113100

Arch Dermatol. 2008;144(9):1129-1140





ELSEVIER

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb



The effects of topical isoflavones on postmenopausal skin: Double-blind and randomized clinical trial of efficacy

Andrea B. Moraes^a, Mauro A. Haidar^a, José Maria Soares Júnior^{a,*}, Manuel J. Simões^b, Edmund C. Baracat^c, Marisa T. Patriarca^a

Izoflavoni djelovati kroz estrogenskog receptora beta



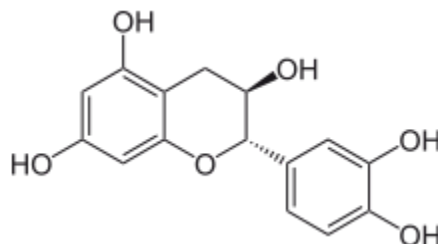
coat of horses *kaput konja*

Transdermal Delivery of Tea Catechins by Electrically Assisted Methods

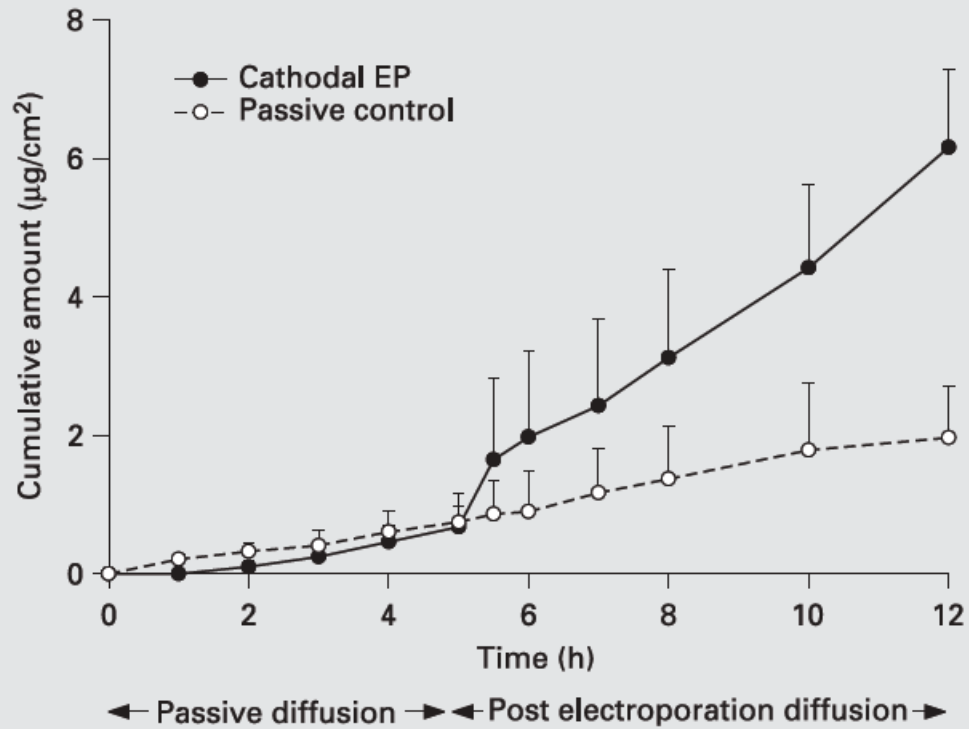
J.-Y. Fang^a C.-F. Hung^b T.-L. Hwang^c W.-W. Wong^a

^aPharmaceutics Laboratory, Graduate Institute of Natural Products, Chang Gung University, Kweishan, Taoyuan;

^bSchool of Medicine, Fu Jen Catholic University, Taipei County, and ^cCell Pharmacology Laboratory, Graduate Institute of Natural Products, Chang Gung University, Kweishan, Taoyuan, Taiwan



The advantage of catechines



Proanthocyanidin: A natural crosslinking reagent for stabilizing collagen matrices

Bo Han, Jason Jaurequi, Bao Wei Tang, Marcel E. Nimni

Tissue Engineering Laboratory, Department of Surgery, Biochemistry and Orthopaedics, Keck School of Medicine, University of Southern California, 2011 Zonal Avenue, HMR-810, Los Angeles, California 90033

Received 21 December 2001; revised 7 June 2002; accepted 19 June 2002

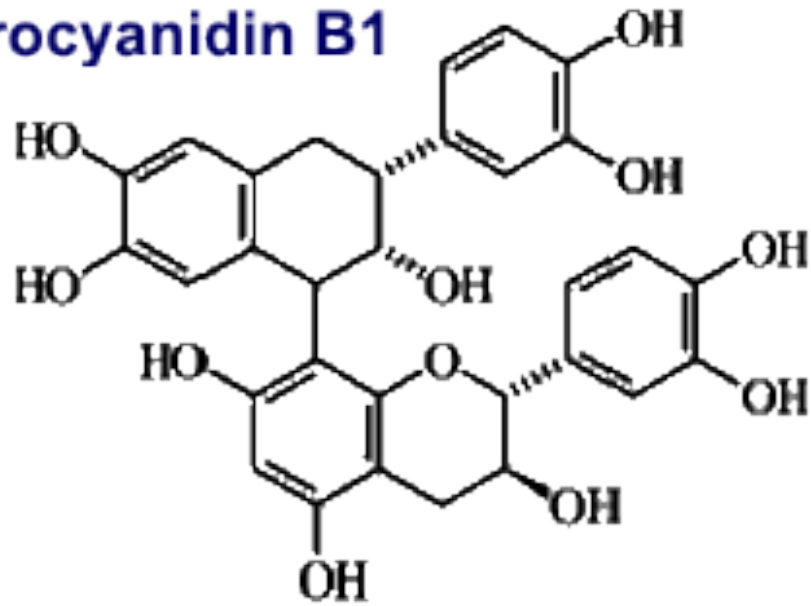
Abstract: While attempting to find a suitable crosslinking reagent for biopolymers, a naturally occurring proanthocyanidin (PA) obtained from grape seeds was selected to fix biological tissues. The cytotoxicity and crosslinking rate, reflected by the *in vitro* and *in vivo* degradation of fixed matrices has been studied. The shrinkage temperature of the fixed bovine pericardium increased from 66 to 86°C. A cytotoxicity assay using fibroblast cultures revealed that PA is ~120 times less toxic than glutaraldehyde (GA), a currently used tissue stabilizer. *In vitro* degradation studies showed that fixed tissue was resistant to digestion by bacterial collagenase. Crosslinks between PA and tissues can be stabilized by decreasing the dielectric constant of the solution during storage. After subcutaneous implantation for periods ranging between 3 and 6 weeks, we found no apparent degradation of the GA- or PA-fixed tissues, whereas fresh tissue controls rapidly disintegrated. Beyond 6 weeks PA crosslinks began to degrade. More fibroblasts migrated and

proliferated inside the PA-fixed implants compared with GA counterparts. Tissues crosslinked with PA manifested an enhanced collagen expression and deposition and did not calcify after implantation. GA, on the other hand, even after thorough rinsing continued to be cytotoxic, inhibited collagen synthesis and encouraged dystrophic calcification. Collagen matrices crosslinked with PA are expected to be of value in the design of matrices that will encourage cell ingrowth and proliferation, which are temporary in nature, and that are intended to regenerate or replace missing tissues, which can delay the biodegradation of collagen. As such they should be of significant value in the emerging field of tissue engineering. © 2003 Wiley Periodicals, Inc. *J Biomed Mater Res* 65A: 118–124, 2003

Key words: collagen; crosslinking; proanthocyanidin; toxicity; degradation



Procyanidin B1

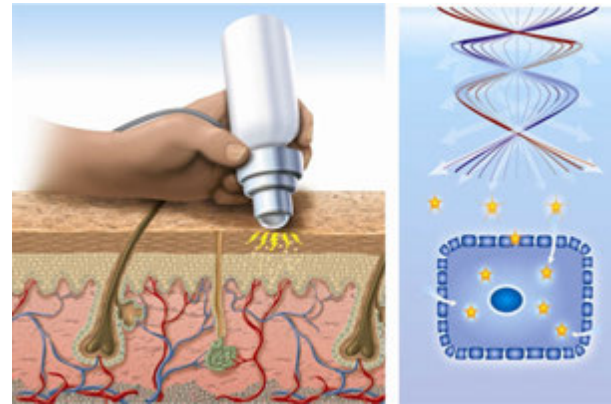


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Preface

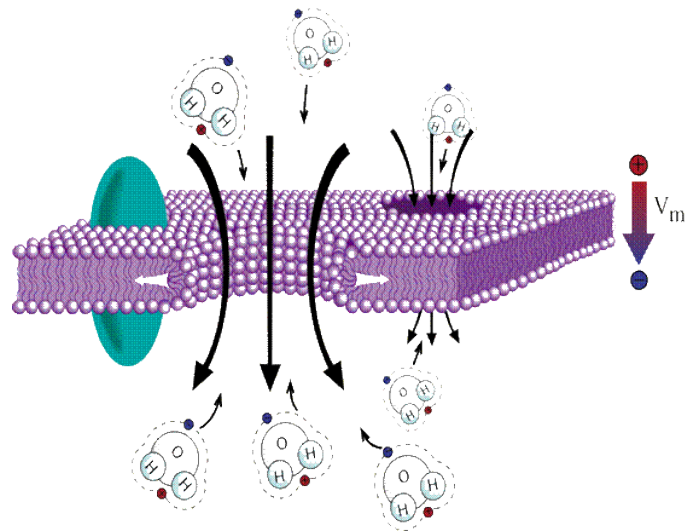
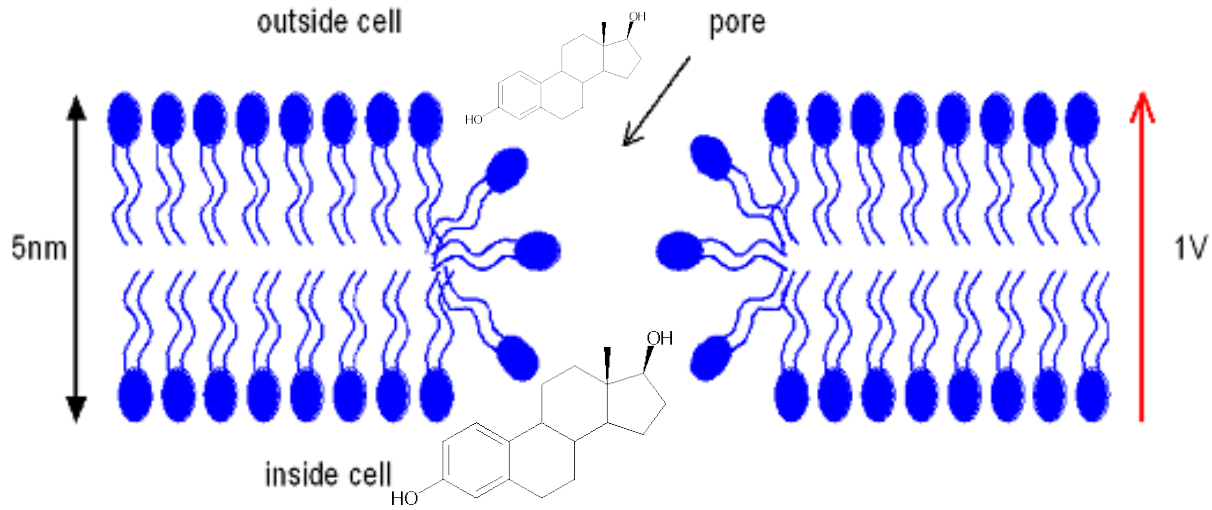
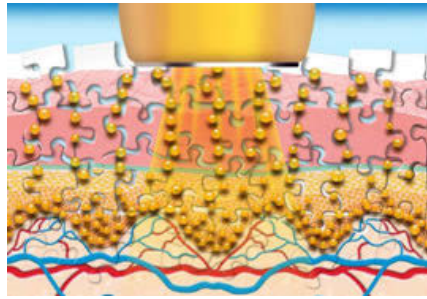
Breaking the skin barrier

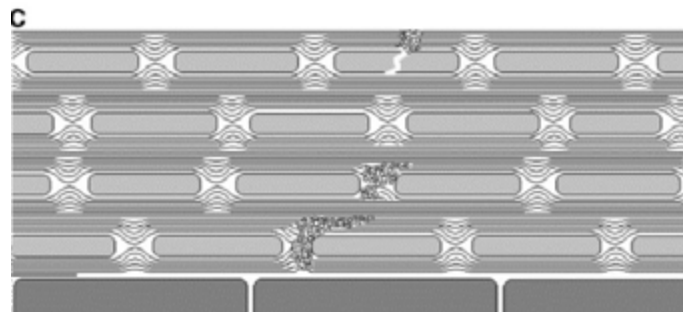
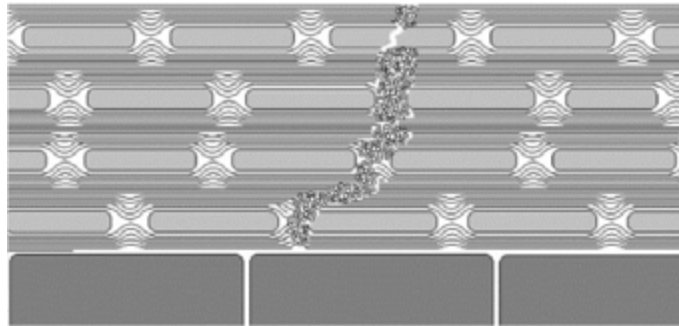
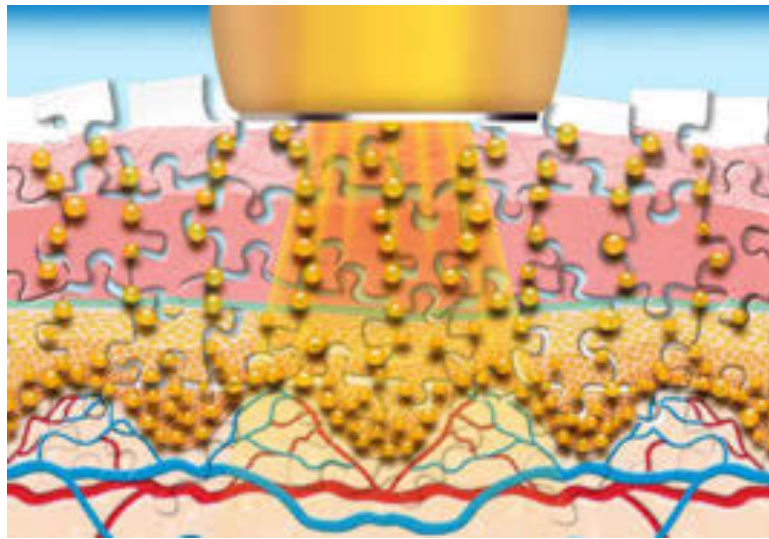
Samir Mitragotri  ((Theme Editor))



The main advantage of the delivery through skin is the possibility of molecules to enter the circulation, avoiding the metabolic processing of the delivered molecules in the liver. **However, the stratum corneum acts as a limiting barrier, therefore only small lipophilic drugs have the ability to penetrate the skin at therapeutic rates by passive diffusion.** Conventional transdermal delivery systems, such as transdermal patches, enable controlled transdermal drug delivery, but are applicable only to small, potent and lipophilic solutes and the transport of drug across the skin is slow with lag times to reach steady-state fluxes in hours

elektroporacija je vrijedan instrument za hormon kozmetike



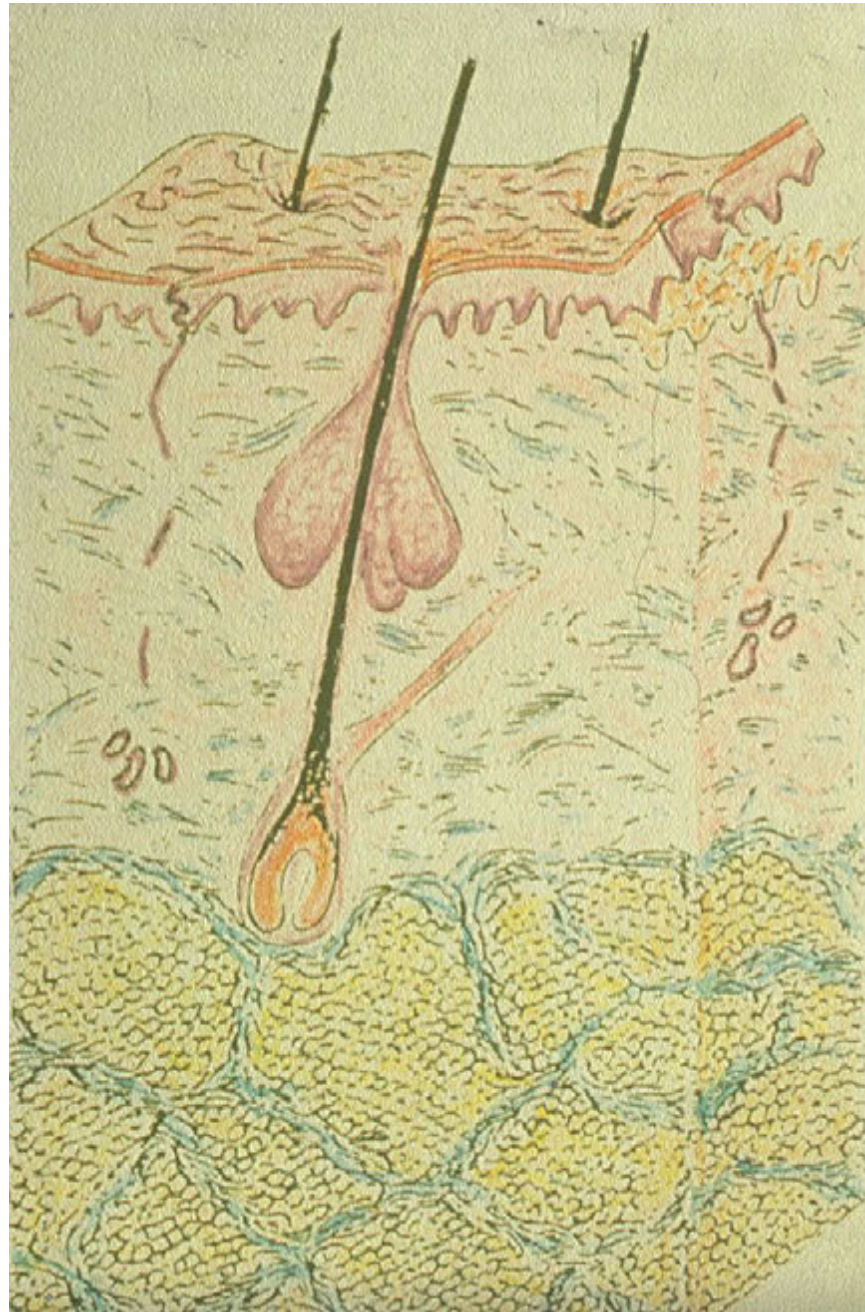


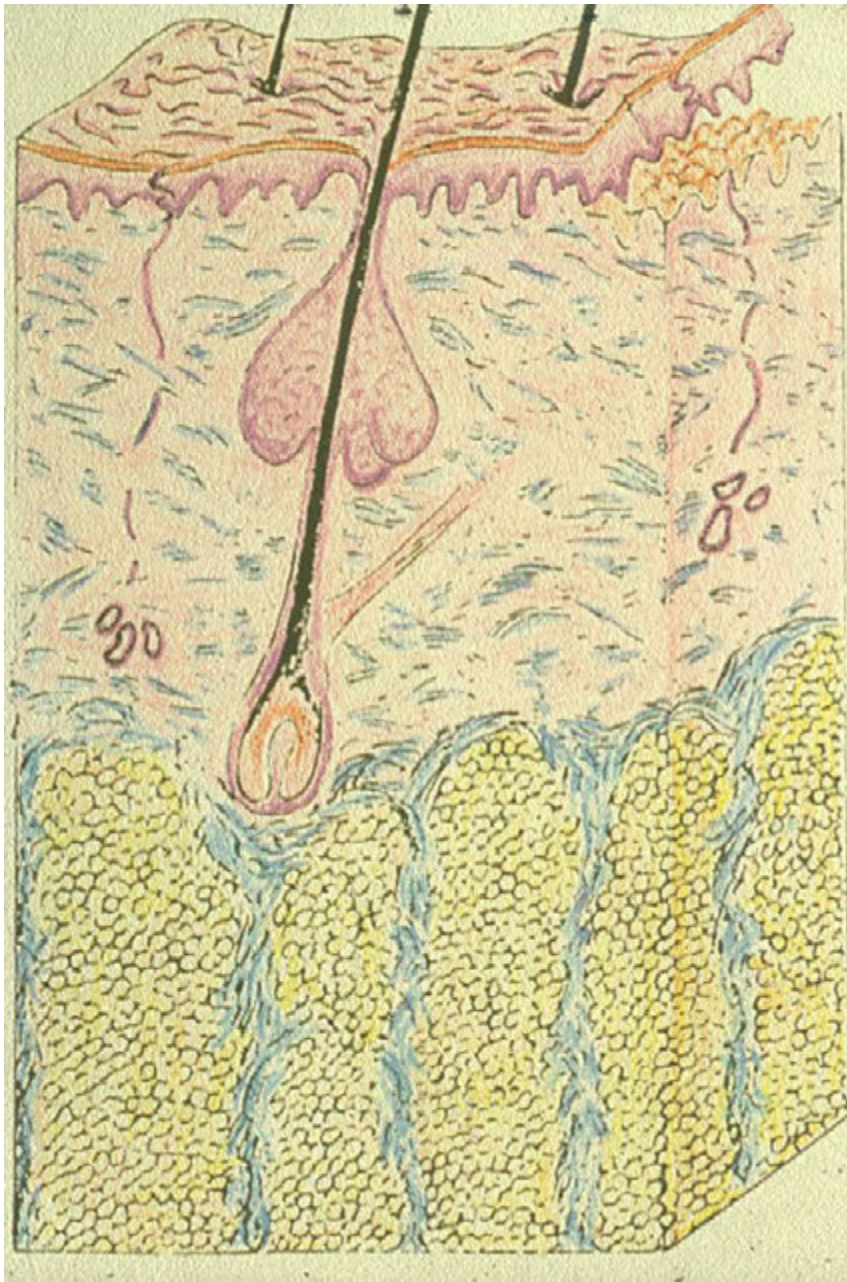
Maturitas 1998 Jun 17;29(3):253-9

Effect of percutaneous androgen replacement therapy on body composition and body weight in postmenopausal women.



**Gruber DM, Sator MO, Kirchengast S, Joura EA,
Huber JC**





The NEW ENGLAND
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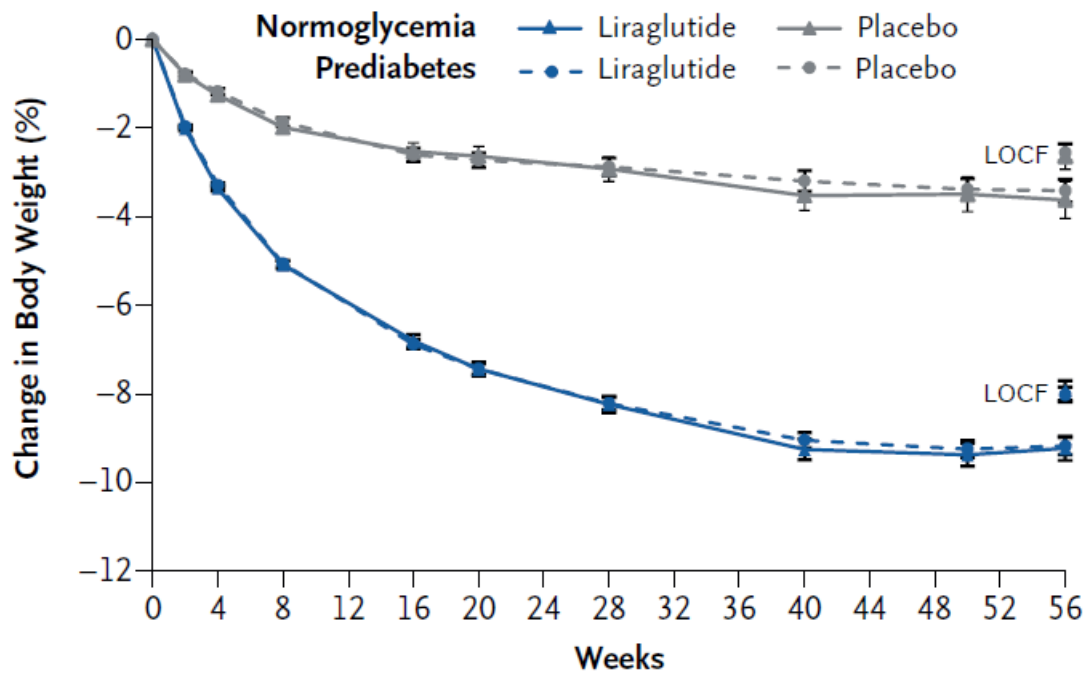
VOL. 373 NO. 1

A Randomized, Controlled Trial of 3.0 mg of Liraglutide
in Weight Management

Xavier Pi-Sunyer, M.D., Arne Astrup, M.D., D.M.Sc., Ken Fujioka, M.D., Frank Greenway, M.D.,
Alfredo Halpern, M.D., Michel Krempf, M.D., Ph.D., David C.W. Lau, M.D., Ph.D., Carel W. le Roux, F.R.C.P., Ph.D.,
Rafael Violante Ortiz, M.D., Christine Bjørn Jensen, M.D., Ph.D., and John P.H. Wilding, D.M.,
for the SCALE Obesity and Prediabetes NN8022-1839 Study Group*

ABSTRACT





B

