

PharmaClinix[®]
Advanced Cosmeceuticals



**FAST ACTING
COMPLEX FORMULATIONS
CLINICALLY PROVEN INGREDIENTS**



UK's top selling Professional Skincare

PharmaClinix Ltd, Unit 3 Issigonis House, Cowley Road, London, W3 7UN, UK

ANTI-AGEX® SERUM

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INGREDIENTS:

L-ASCORBYL ACID - 5%

ASCORBYL TETRAISOPALMITATE (LIPOPHILIC) - 5%

RETINALDEHYDE (HIGH STRENGTH RETINOID) - 0.5%

NIACINAMIDE - 4%

FERULIC ACID 2%

HYALURONIC ACID -5%

MATRIXYL SYNTHÉ'6 - 2%

SALICYLIC ACID - 2%

GREEN TEA EXTRACT – 2%

MIXED TOCOPHEROLS – 2%



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5% L-Ascorbyl Acid

- Double blind randomised placebo controlled trial over six months using 5% L-Ascorbyl Acid under "Declaration of Helsinki" code of clinical trials allowed showed statistically significant improvement in:
 - Hydration
 - Roughness
 - Small wrinkles
 - Brown spots
 - Improved elastin fibres
 - Reduce deep furrows
 - Electron Microscopy - Reduced elastin damage, well organised collagen.
 - Less melanin in Keratinocytes

Ref 1: Exp Derma 2003 June; 12(3): 237-234

Topical Ascorbic Acid on Photo aged skin: clinical topographical and ultra structural evaluation: double blind study with Vs Placebo. Humbert PG, Haftek M, et al. Dept of Dermatology, Hospital Saint Jacques, University of Frauche-Coute, Besaucon, Frauce.

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(ATIP) Ascorbyl Tetraisopalmitate - 5%

Very stable non-irritating vitamin C with rapid absorption into skin. In Vitro study anti-oxidant activity shows ATIP to be more active in a Lipid system.

(Plasma Membranes)

In Vivo ATIP showed increase Stratum Corneum moisture content when tested on the forearm.

Ref 2: In Vitro anti-oxidant activity and In Vivo efficacy of topical formulations containing Vitamin C and its derivatives studied by non-invasive methods. Skin Research & Technology Volume 13, Issue 3, Page 376-380 Aug 2008 Patricia MBG, Maia Campos et al

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Anti Agex® Serum has 0.5% Retinaldehyde (RAL) - High Strength

- RAL is converted by one step to retinoic acid. (RA)
- RAL highly Lipophylic easily absorbed into skin (80% in Epidermis, 20% in Dermis)
- Enhanced epidermal cell turnover and reduced contact time between Keratinocytes and Melanocytes reduces hyper-pigmentation. (Increased Epidermopoesis)
- Reduces fine lines and wrinkles by increasing water holding capacity of epidermis and increased GAG (Ground Substance) production.
- Increased collagen synthesis in dermis.
- reduces enzymes that breakdown collagen (Collagenases).

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Retinaldehyde the best retinoid - 0.5%

Retinaldehyde has the best scientific evidence supporting its efficacy in reducing the signs of symptoms of ageing.

Ref 3:

Journal of Clinical Aesthetic Dermatology 2010 Feb, 3(2) : 22-41

How much do we really know about our favourite cosmeceutical ingredients?

Jacqueline Levin DO, Saira B. Morin DO, James Q. Del Rosso DO



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Retinaldehyde the best retinoid - 0.5% Cont..

125 patient study:

40 on 0.05% retinoic acid (RA)

40 on 0.05% retinaldehyde (RAL)

45 in vehicle group (placebo)

Tested at 18 & 44 weeks, result: significant wrinkle & rough skin reduction was observed with both RAL & RA. RAL was better tolerated, RA caused more irritation.

Ref 4.

JAM Academy Dermatology 1998 Dec; 39(6):960 – 965

Profilometric evaluation of Photo damage after topical RAL & RA treatment.

Creidi P, Vienne MP et al Department of Functional Dermatology Besauchon, France

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Retinaldehyde (RAL) - 0.05%

Prospective one year instrument study on 40 patients who applied 0.05% RAL showed:

- Significantly increased epidermal thickness of the temple, compared to the control
- Significantly increase cutaneous elasticity

Ref 5:

Dermatol 1999; 199 Supplement: 37-41 Efficacy of topical 0.05% Retinaldehyde in skin aging by Ultra Sound Rheological techniques
Dirdollou S, Vienne MP, Alibert M et al Jeau Louis Alibert Center Pierre Fabre Research Institutue, Toulouse, France

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Retinaldehyde (RAL) - 0.05%

Retinoid Biological activity measured by:

- a) increase of cellular retinoic acid binding protein type 2 (CRABP2) mRNA & Protein
- b) rank order for cRAB was RA > RAL > 9cisRetinoic Acid > Retinol > Beta- Carotene

Volunteers treated for 1-3 months with 0.5% 0.1% & 0.05% RAL showed dose dependant increase in:

- epidermal thickness
- keratine 14 immunal reactivity
- ki 67 positive cells
- involucrin
- transglutaminase
- fillaggrin immunal reactivity

Conclusion - Topical RAL has dose dependant biological activity and well tolerated up to 0.5%

Ref 6: Journal of Investigative Dermatology (1994) 103, 770-774, 1523-1747, 1241-2861 Topical Retinaldehyde on Human Skin: Biologic Effects & Tolerance Jeau Hulaire Saurat et al. Department of Dermatology, University Hospital, Geneva, Switzerland

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Niacinamide 4% (Nicotinamide)

- a) Important pre-cursor in co-factors Niacinamide Adeenosine Dinucleotide (NAD) & its phosphate derivatives NADP.

- b) These co-factors and their reduced forms (NADH & NADPH) serve as reduction oxidation co-enzymes in 40 cellular reactions.

Ref 7:

Namazi , MR Nicotinamide as a potential addition to the anti atopic dermatitis therapy,
International Immunol Pharmacology 2004 issue No4 709-712



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Niacinamide 4% (Nicotinamide)

- Niacinamide has proven to be easily absorbed from the skin.
- Niacinamide application causes significant increase in skin NAD.

Ref 8:

Feldmann RJ, Maibachhi

Absorption of some organic compounds through the skin in man. Journal of Investigative Dermatology (1970) 54: 399-404

Ref 9: Franz TJ. Percut Absorption

Journal of Investigative Dermatology (1975); 64: 190-195

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Niacinamide 4% (Nicotinamide)

Niacinamide increases the anti-oxidant capacity of skin after topical use by increasing reduced forms NADH & NADPH.

Niacinamide reduces epidermal hyper pigmentation by inhibiting melanosome transfer from melanocyte to keratinocytes.

REF14- Hakozaki. T. et. al.

**The effect of Niacinamide on reducing cutaneous pigmentation & suppression of melanosom transfer
British Journal of Dermatology (2002); 305: 260-268**

Ref 10: Baumaun L. Less known Botanical Cosemeceuticals, Dermatology Therapeutics 2007; 20 330-342

Ref 11: Shindo Y, Witt E, Hau D et al

**Enzymic & non-enzymic antioxidants in epidermis & dermis of human skin.
Journal of Investigative Dermatology (1994) 102: 122-124**

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Niacinamide 4% (Nicotinamide)

- 2% Niacinamide improved barrier function of skin by increasing skin ceramide and other lipids.
- In Vivo reduced transepidermal water loss (TEWL) and increase in stratum corneum moisture (SC)
- Increase NADP levels --> Keratinocyte differentiation --> increase Keratin 1 --> thicker stratum corneum --> increase skin barrier --> increase hydration retention of stratum corenum.

Ref 12: Tanno, Ota Y, Kitamuran, et al. Nicotinamide increase biosynthesis of seramides aswell as other stratum corneum lipids too improve epidermal permeability. British Journal of Dermatology (2000); 143: 524-531

Ref 13: Ertel KD, Berge CA, et al.

New facial moisturiser technology increase exfoliation without compromising barrier function presented at the 58th Annual meeting of the American Academy of Dermatology (2000); San Francisco, USA

Ref 14: Gerring. Nicotinic Acid/Niacinamide and the Skin Journal of Cosmetic Dermatology (2004); 3: 88-93

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Niacinamide 4% clinical studies

1) 18 Japanese women treated in a split face study over 8 weeks with 5% Niacinamide showed significant lightening of Hyper-pigmentation on the treated side compared with the vehicle alone.

2) 120 Japanese women treated with SPF 15 cream with or without 2% Niacinamide showed lightening of the skin in the Niacinamide group AT 4&6 WEEKS

REF-15.Tarno O,Ota Y et al.Br J Dermatol.2000;143:524-531.

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Niacinamide 4%

- 1) Long term 2.5% Niacinamide can correct the skin surface damage from ageing.
- 2) 3.5% Niacinamide can reduce skin roughness by 14.8% over 4 weeks.
- 3) Gold standard Study by Bissett et al in a randomized, double-blind, split face, placebo controlled trial 50 white females with photo damage applied Niacinamide 55 for 12 weeks showed:
 - reduced fine lines & wrinkles.
 - reduced pigmentation
 - reduced red blotches
 - reduced sallow skin.

Ref 15 Matts PJ, Soleneck ND. Predicting visual perception of human skin texture with multi-angle reflectance. Presented at The 59th Annual Meeting of the American Academy of Dermatology; 2001 Washington Ref 16 Bissett DL, Miyamoto K, Topical Niacin reduces yellowing, wrinkling, red blotchiness, hyperpigmented spots in ageing facial skin. International Journal of Cosmetic Science 2004; 26: 231-238

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Hylauronic Acid - 5%

- a) Hylauronic Acid freely penetrates the human skin in healthy volunteers & may be used as a vehicle to carry other ingredients deep into the human dermis
- b) Ageing skin loses Hylauronic acid until non is present age 60, skin moisture level reduces with loss of elasticity causing lines and wrinkles. Water causes a rise in extra cellular fluid giving smooth moist skin.

Ref 17 Absorbtion Hylauronoun applied to the surface of intact skin. Department of Biochemistry and molecular Biology, Monash University, Melbourne, Victoria, Australia The Journal of Investigative Dermatology (1999) 113(5): 740-746 Brown T, et. al.

Ref 18 International Journal of Dermatology (1994) Feb 33 (2): 199-22, Hyaluronic acid in Cutaneous Intrinsic Ageing, GHERSETICHI, LOTTI T, CAMPANILE G, GRAPPONE C, DINI G, Department of Dermatology, University of Florence, Italy

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Matrixyl® Synthe 6 - 2% (PALMITOYL-LYSL-DIOXYMETHINOYL-LYSINE)

Dioxy Tripeptide Palmitoyl Ester (Sederma) This is a Metrikine-Mimetic Peptide, this is a cytokine like chemical that stimulates skin Matrix production.

In Vivo test using 2% in 25 females showed applying twice a day for two months anti wrinkle effect on the four head:

- reduced volume of main wrinkle: - -31% (P = 0.05)
- reduction in skin roughness:- -28% (P < 0.05)
- reduction in depth of wrinkle:- -16.3% (P < 0.05)

In Vitro test showed:

- Increase in collagen 1,3 & 5
- Increase of Laminin-5, Fibronecting & Hyluronic Acid (Ground Substance)

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Matrixyl® Synthe 6 - 2% (PALMITOYL-LYSL-DIOXYMETHINOYL-LYSINE)

Dioxy Tripeptide Palmitoyl Ester (Sederma)

Anti Wrinkle effect on crow's feet using fringe projection or imprinting on 25 women showed:

- Decrease of surface area of deep wrinkles (-28.5%)
- Decrease in the volume of main wrinkle (-21%)
- Decrease in mean depth of wrinkle (-15%)
- Decrease in visible cutaneous roughness (-12.6%)
- Opening of the wrinkle (-8.5%)



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Ferulic Acid 2%

When combined with Vitamin C and E showed:

- increase stability of C & E
- double photo protection
- inhibits cell death
- reduce DNA damage
- pure low molecular weight and easily absorbed into skin

Ref 19

Journal of Investigative Dermatology (2005) October 125(4): 826-832

Ferulic Acid stabilises a solution of Vitamin C & E and doubles its photo protection of skin

Lin FH et al Duke University, Medical Centre, Durham, North Carolina, 27710, USA



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Ferulic Acid 2%

Ferulic Acid a hydroxy cinnamic acid in-vitro antioxidant action:

- strong super oxide and hydroxyl radical scavenging ability
- significantly inhibits melanin synthesis
- reduces damage to collagen fibres
- reduces abnormal elastin
- reduces epidermal hyperplasia in UV radiated skin

Ferulic Acid at PH 3 or 7.2 effectively penetrates the Stratum Corneum. In healthy human ferulic acid proved to afford a significant protection to the skin against UVB induced erythema.

Ref 20 - Journal of Agricultural Food Chem. (2007) May 16; 55(10): 3920-5 EPUB 2007 March 31

Ref 21 - Journal of Nutritional Bio-Chemistry (2012) May; 23(5): 443-51 Stanforth V, et.al.

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Green Tea Extract - 2%

Polyphenols in green tea have:

- Anti-oxidant, anti-inflammatory, anti-carcinogenic properties
- In healthy human skin, inhibits UVB induced erythema oxidative stress and inflammatory leucocytes

Topical green tea extract applied to healthy volunteers skin after simulated solar radiation prevents oxidative damage to DNA and Langerhans cells.

Ref 22 - Current Drug Targets Immune Endocr Metabol Disorder: 2003 Sep; 3(3): 234-242 Skin photo protection by green tea: Antioxidant & immunal modularity effects. Katiyar SK, Department of Dermatology University of Alabama, Birmingham, AL35294, USA

Ref 23 - Experimental dermatology (2009) June; 18(6): 522-6 Topical application of green tea extract provides photo protection camouse MM et. Al. Department of Dermatology, Unversity Hospitals, Case Medical Center, Cleveland, ohio 44106, USA

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Green Tea Extract - 2%

Green tea extract applied on human skin after solar radiation:

- significantly prevented depletion of anti-oxidant enzymes glutathione peroxidase & catalase resulting in higher glutathione levels.
- significant prevention of Lipid & protein per-oxidation

Ref 24

Carcinogenesis: (2003) May ; 24(5) 927-936, Vayalil PK

Department of Dermatology University of Alabama, Birmingham, 1670 University Blvd, Volker Hall, 5535293, USA

Treatment of Green Tea Polyphenols in Hydrophilic Cream prevents UVB oxidation of Lipids, proteins, anti-oxidant enzymes.

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Salicylic Acid -2%

When applied on the mid back region of volunteers for 3.5 weeks & radiated with solar lamps showed:

- less erythema
- less DNA damage
- less sun burn cell formation

10% glycolic acid increased sensitivity to the sun

Ref 25 Journal of Dermatological Science (2009) July; 55(1): 10-7

The effects of topically applied glycolic acid & salicylic acid on UV radiation induced erythema, DNA damage & in sunburn cell formation in human skin. Korn Hauser A.

Centre for food safety & nutrition, US FDA, College Park, MD 20740, USA

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Tocopherols - 2%

- Primary function as a cell membrane anti-oxidant
- Strong inhibitor of lipid per oxidation
- Reducing cell death
- Oral vitamin E is in-effective in preventing photo damage



Ref 26 - Machin L. Editor Vitamin E: A comprehensive Treatise. New York Marcel Dekker' 1980

Ref 27 - Wafers H, Siers H. The protection by Ascorbate & Glutathione against microsomal lipid Peroxidation is dependent on vitamin E. Eur J Biochem (1988); 174(2) 353-7

Ref 28 - Kagan V, Witt E, et al. UV Induced generation of Vitamin E radicals & their recycling
Free radical Research Communication 1992; 16(1): 51-64

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Indications of Use

- Primary night maintenance serum for ALL SKIN TYPES sensitive or resistant.
- Perfect priming serum for dermarolling, microderm-abrasion, laser or peels
- Post peels, abrasion & rolling or laser rejuvenation
- Excellent long term safety and tolerance profiles



Conclusion



**Anti Agex® Serum
*Works***

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