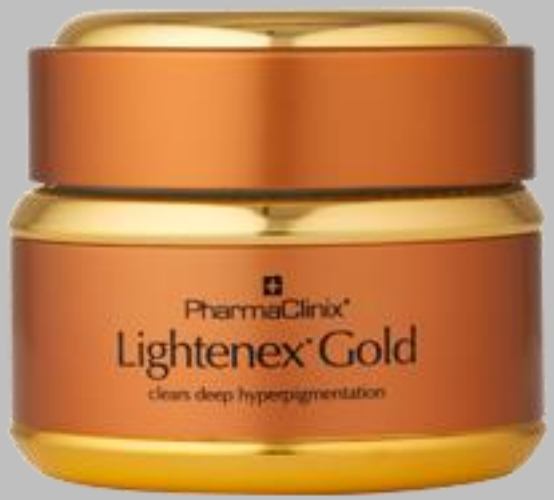
PharmaClinix®
Advanced Cosmeceuticals



- **Fast acting**
- **Complex formulations**
- **Clinically proven ingredients**
- **Economical price**

UK's top selling Professional Skincare

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

PharmaClinix®
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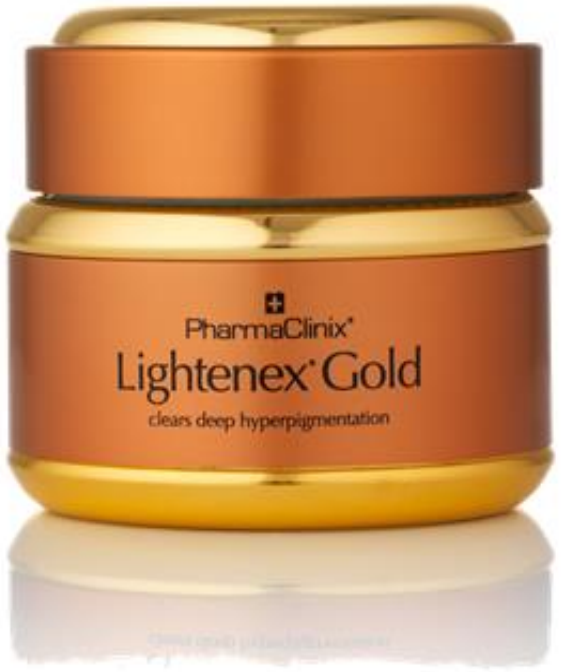
Lightenex® Gold

INGREDIENTS:

- Kojic Dipalmitate 5%
- Phytic acid 5%
- ALPHA ARBUTIN 3%
- BETA ARBUTIN 3%
- MAGNESIUM ASCORBYL PHOSPHATE 10%
- DIOIC ACID 4% (OCTADECENE-DIOIC ACID)
- L-LACTIC ACID 5%
- RETINALDEHYDE 0.25%
- NIACINAMIDE 3%
- N-ACETYL GLUCOSAMINE 3%
- LIQUORICE EXTRACT 3%
- FERULLIC ACID 0.5%+MIXED TOCOPHEROL



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Lightenex® Gold

Kojic Dipalmitate 5%

❖ Stable from f powerful tyrosinase Inhibitor to reduce melanin synthesis.

Long history of use in Skin Lightening

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- Phytic acid Chelates Copper & Iron in skin(makes them unavailable)
- Copper is essential part of the enzyme tyrosinase which makes melanin.
- Gentle exfoliant
- Iron catalyses free Radilcle formation & subsiquent Oxidative damage.

REF-Will Phytic acid replace Hydroquinone.Romulo Mene MD.Plastic Surgeon.Rio De Janiero,Brazil.Third Congress of National Estetic Medicine.Milan,Italy 12 Oct 2001

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Cultured Human Melanoma cells & three dimensional human skin model treated with Alpha Arbutin showed:

- Melanin synthesis reduced by **24%**
- Skin model showed **60%** reduction in Melanin
- Cellular tyrosinase activity significantly reduced.
- Lightenex® Gold has **3%** Alpha Arbutin

REF 1-Pharm Bull.2004 April;27(4):510-4.Inhibitory effects of alpha-arbutin on melanin synthesis in cultured human melanoma cells and a three-dimansional human skin model.Sugimoto K,Nishimura T,Nomura K,Kuriki T.Biochemical Research Laboratory,Ezaki Glico Co Ltd.,4-6-5 Utajima,Nishiyadogawa-ku,Osaka 555-8502,Japan.

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Alpha and Beta Arbutin action on Tyrosinases from Mushroom & Mouse Melanoma showed:

- Beta Arbutin inhibited both Tyrosinases showing non-competitive action.
- Alpha Arbutin only inhibited tyrosinase from mouse melanoma 10 times as strongly as Beta Arbutin showing mixed type inhibition.
- Lightenex® Gold contains both Alpha Arbutin & Beta Arbutins to reversibly & maximally inhibit the enzyme Tyrosinase.

REF 2-Effects of alpha and beta arbutin on activity of Tyrosinases from mushroom and mouse melanoma.Funayama M,Arakawa R,Nishino T,Shin T,Murao S.Biosci Biotechnol Biochem.1995 Jan;59(1):143-4.

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Normal human skin microflora can hydrolyze arbutin to Hydroquinone which shows more potent radical scavanging activity and Tyrosinase inhibition than Arbutin. Lightenex® Gold contains 6% total Arbutin.

REF-3-Hydrolysis of Arbutin to Hydroquinone by human skin Bacteria and its effect on anti-oxidant activity.J Cosmet Dermatol.2008Sept;7(3):189-193.Bang SH,Hans SJ,KimDH.Dept of Life and Nanopharmaceutical Sciences and College of Pharmacy,Kyung Hee University,Seoul,South Korea.

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Dioic Acid (Octadecene-dioc Acid) 4% is present in Lightenex® Gold. This acid is a Di-carboxylic acid (dioic) like Azelaic but is 18 Carbon atoms long instead of 9 carbons like azelaic. It is made from Bio-fermentation of Oleic acid using Yeasts.

An open comparative study of NINETY SIX (96female) Melasma patients in an open, comparative, 12 week study between 1% Dioic Acid & Hydroquinone 2% showed:

- No significant difference between treatments.
- More pruritus with hydroquinone.

REF4-Efficacy of Dioc (Octadecene-dioic acid)compared with Hydroquinone in the treatment of Melasma.Int J Dermatol.2009Aug;48(8):893-5.Tirado-Sanchez A,Santamaria-Roman A,Ponce-Olivera RM.

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- Lightenex® Gold contains 4% Octadecene-dioic acid.
- A twenty patient placebo study on patients of Indian and Pakistani origin given 2% Octadecene-dioic acid over 8 weeks showed
- A significant reduction in melanin ($p<0.025$) measured both by chromameter & mexameter.

REF 5-Inter Jour of Cosmetic Science, Volume 33,issue 3 June,pages 210-221.J M Gillbro, M J Olsson. The Melanogenesis & mechanisms of skin lightening agents, existing & new approaches.

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IN-VITRO STUDIES USING OCTADECENE-DIOIC ACID 2% IN MELANOMA CELLS SHOWS:

- It binds to PPAR -gamma receptors on nuclear membrane of melanocytes to:
- Reduce Tyrosinase mRNA production by 54%
- Reduce Tyrosinase production by 52%
- Reduce melanin synthesis by 46%

REF6-Int Journ of Cosmetic Science-2005,27,123-132.Anew mechanism of action for Skin Whitening agents:binding to PPAR.J W Weichers, A V Rawlings,C Garcia,C Chesne,P Balaguer, J C Nicholas, S Corre & M D Gilbert. Uniqema Skin R&D, Gouda,The Netherlands.A V R Consulting Ltd,26 Shavington way, Northwich, Cheshire, UK.Endocrinologie Moleculaire et Cellulaire des Cancers, Montpelier,France.Lab Genetique et Developpement, CNRS UMR6061,Faculty of Medicine, University of Rennes,1-2 Leon Bernard Avenue,35043 Rennes ,France.

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Lightenex® Gold contains 10% (high strength) Magnesium Ascorbyl Phosphate (MAP).

A Clinical Study using 10% MAP on a total of 34 patients with chloasma or senile freckles showed the lightening effect to be significant on 19 of the 34 patients. In addition 1.6% of the cream remained in the epidermis 48 hours after application.

REF-7.Inhibitory effect of Magnesium ascorbyl phosphate on Melanogenesis in vitro and in vivo. Journal of American Academy of Dermatology.1996 Jan;34(1):29-33.Kameyama K,Sakai C, Kondoh K, Nishiyama S, Tagawa M, MurataT, Ohnuma T, Quigley J, Dorsky A, BucksD, Blanock K. Det of Dermatology, Kitasato University School of Medicine, Sagamihara, Japan.

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- Lactic acid directly suppresses melanin formation by directly inhibiting tyrosinase activity, an effect independent of their acidic nature. Therefore Lactic acid works on Pigmentary lesions not only by accelerating the turnover of the epidermis but also by directly inhibiting melanin formation in Melanocytes.
- Lightenex® Gold contains 5%L-Lactic acid.

REF-8The Inhibitory effect of Lactic acid on melanin synthesis in Melanoma cells.Exo Dermatol.2003;12Suppl2:43-50.Usuki A,Ohashi A,Sato H,Ochiai Y,Ichihashi M,Funasaka Y.Division of Dermatology,Dept of Clinical and Molecular Medicine,Kobe University Graduate School of Medicine,Kobe,Japan.

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Lightenex® Gold contains 0.25% Retinaldehyde.

Reinaldehyde has been shown to improve dyspigmentation by one step conversion to Retinoic acid followed by:

- Increasing epidermal cell turnover-Epidermopoesis.
- Decreases melanosomal transfer of Melanin.
- Stratum corneum changes to affect the permeability barrier to facilitate the penetration of dispigmenting agents in the Epidermis.

REF-9 -Ortonne,JP(2006):Retinoid therapy of Pigmentary disorders.Dermatologic Therapy,19:280-288doi:10.1111/j.15 29-8019. 2006.00085.x

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Lightenex® Gold

Lightenex® Gold contains 3% Niacinamide.

A 138 (one hundred and thirty eight)subject clinical trial using 5% and 2% Niacinamide as well as detailed in-vitro studies showed:

- Niacinamide gave 35-68%inhibition of Melanosome transfer in the co-culture(melanocyte/keratinocyte)model.
- In the clinical studies, Niacinamide significantly decreased Hyperpigmentation and increased skin lightness compared with vehicle alone after 4 weeks of use.

REF9-Hakozaki,T.,Minwalla,L.,Zhuang,J.,ChhoaM.,Matsubara,A.,Miyamoto,K.,GreatensA.,Hillebrand,G., Bissett D,and Boissy,R.(2002),The effect of Niacinamide on reducing cutaneous pigmentation and suppression of Melanosome transfer.British Journal of Dermatology,147:20-31.doi:10.1046/j.1365-2133.2002.04834.x

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Lightenex® Gold contains 3% Niacinamide & 3% N-Acetyl Glucosaminie (NAG). A detailed 10(ten) week double-blind,vehicle controlled , full-face, parrallel group clinical study in101 tested women between 40-60 yrs of age with 101 controls were given 4% Niacinamide & 2%(NAG) showed

- The Niacinamide + NAG combination reduced the appearance of hypermelanization significantly($P<0.05$)

REF 10-Reduction in the appearance of facial hyperpigmentation after use of topical Niacinamide &NAG:results of a randomized double blind vehicle controlled study.British Journal of Dermatology.2010 Feb1;162(2):435-441.Epub2009,Aug8.Kimball AB,Kaczvinsky JR,Li J,Robinson LR,Matts PJ,Berge CA,Miyamoto K,Bissett DL.Harvard Medical School,Boston,M02114,USA.

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NAG alone & NAG + Niacinamide Clinical studies on Hyperpimentation.

Two double blind Placebo controlled clinical studies examined

1) Effect of NAG 2% alone compared to Placebo in 50 Japanese women

Result-NAG was more effective than Placebo

2) Effect of NAG2%+4% Niacinamide against 4%Niacinamide alone in 35 Caucasian women

Result-NAG+Niacinamide was more effective than Niacinamide alone.

REF11- Data presented at 2006 American Academy of Dermatology Meeting.Reduction in the appearance of facial Hyperpigmentation by topical NAG(N-Acetyl Glucosamine).Journal of Cosmetic Dermatology.Volume 6,ISSUE 1,pages 20-26,March 2007.First on line 5/March 2007,DOI:10.1111/j.1473-2165.2007.00295x.D L Bissett,Larry. R.Robinson,Patricia s Raleigh,Jim Li,Gary R Kehn.

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- FERULIC ACID 0.5% + MIXED TOCOPHEROLS 1% are present in Lightenex® Gold.
- Ferulic acid is a hydroxycinnamic acid that has significant anti-oxidant and anti-melanogenic activity.In addition Tocopheryl ferulate is a significant inhibitor of Tyrosinase making it an efficient whitening agent.

ref-12-The depigmenting effect of tocopheryl ferulate on human melanoma cells.Br J Dermatol.1999 Jul;141(1)141(1):20-9.

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- LICORICE EXTRACT 3%-GLABRIDIN.-well used anti - inflammatory and Tyrosinase inhibitor.

REF-GLABRIDIN STUDY ON PHARMACLINIX® CLINICAL TRIALS.

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Start by using Lightenex® Gold once at night. This can be increased to twice a day after one week of using it night.

Indications for Lightenex® Gold

1) Epidermal/Dermal mixed Melasma.
2) Priming of skin for three weeks before intermediate Chemical peel in type3-5 Fitzpatrick skin. Wait for one week before continuing with nightly application of Lightenex® Gold
3) Priming of skin for three weeks before Q=switched for Epidermal /Dermal hyperpigmentation. Lightenex® Gold will assist in rapid removal of epidermal melanin & expose deeper melanin to be targeted with longer wave length laser. In addition it will prevent Post-laser hyperpigmentation.

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In an Independent De-pigmentation study carried out on 50 volunteers of skin types 2-4 for 10 weeks with mixed Dermal/Epidermal hyper-pigmentatation on facial+torso skin showed:

- No adverse reactions such as redness or peeling. Only two subjects abandoned the study because of skin sensitivity causing stinging.
- All subjects felt stinging which is expected with this type of formulation. This stinging lasted only 5 minutes & most volunteers discovered it subsided 4 weeks into the study.
- Measurable Melanin content using Mexameter 18 showed an average reduction of 68% over 10 weeks.

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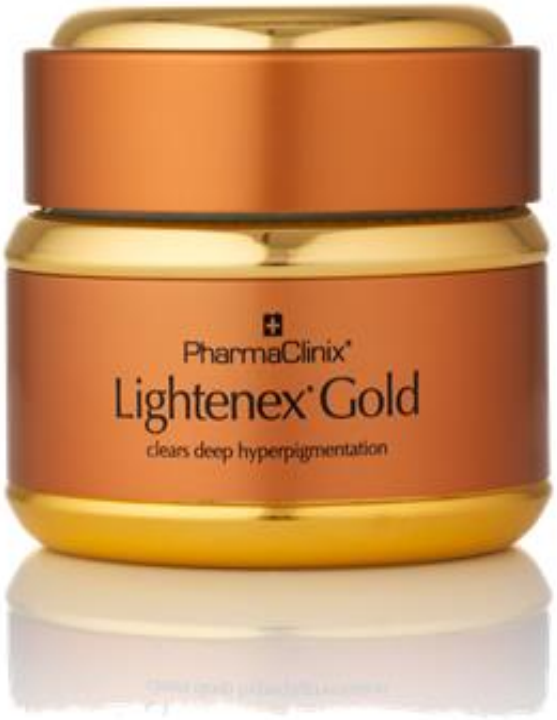

Conclusion

Lightenex® Gold Works

www.pharmaclinix.com