

Ozonía® Dermatological Line

INFORMATION RESERVED FOR MEDICAL AND PARAMEDICAL PERSONNEL

oZonia10® 35 mL



Cream based on 10% of Ozonia 3000®
Creates an unfavorable environment for microbial contamination and stimulates the tissue regeneration process.

oZonia15® 35 mL



Anhydrous lipogel based on 15% of Ozonia 3000®

Protects, hydrates, and soothes delicate, newly formed, hypertrophic, inflamed, itchy, skin. Normalizer for sensitive mucous membranes and skin.

oZoral® 15 mL
GEL ORALE



Hydrogel based on 15% of Ozonia 3000®
Promotes tissue repair of the oral cavity.

TISSUE OZONE THERAPY



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March 2015

Ozonia® Dermatological Line



DERMATOLOGICAL EMULSION (O/W) ADJUVANT FOR THE TREATMENT OF "INJURED" SKIN AND MUCOUS MEMBRANES.

Cream with 10% Ozonia 3000.

Ozonio 10 creates an unfavorable environment for microbial contamination (Tab. 1) and stimulates the tissue regenerative processes.

This makes it useful as a dermo-cosmetic adjuvant for the treatment of "injured" skin. For example, abrasions, excoriation, erosion, disepithelization, skin ulcers following cleaning and debridement, and in the presence of contamination and colonization. Alteration of peristomal skin, dermatological conditions that require deep cleansing, for example, acne, seborrhoeic dermatitis, intertrigo, tinea, etc.; open surgical wounds (post-surgical pilonidal cysts, fistulotomy, Milligan-Morgan hemorrhoidectomy, remaining cavities after surgical closure of stomata, etc.). It promotes the repair of micro lesions and a reduction of inflammation, itching, and pain. It is effectively used in the symptomatic treatment of hemorrhoid disease, and to accelerate the closure of anal fissures.

Ozonio 10 cream does not contain any synthetic fragrances, colors, silicones, or preservatives. Dermatologically and microbiologically tested.

NOT TESTED ON ANIMALS.

Reduction values expressed in % compared to the inoculate

Time (h)	Bacteria				Yeasts	Molds	Protozoa	Fungi
	E.coli	Pse. aeruginosa	Proteus mirabilis	Staph. aureus	Cand. albic.	Asp. niger	Trichom.vag.	Trichophyton m.
2	91,25	93,91	92,94	91,07	86,00	87,50	0,00	0,00
4	90,63	95,65	94,12	96,43	95,0	96,42	36,00	0,00
24	99,83	100,00	99,83	99,93	99,64	99,55	90,00	28,00
48	99,94	100,00	99,94	100,00	99,99	99,99	98,00	94,80
7 days	100,00	100,00	100,00	100,00	100,00	100,00	100,00	99,00
Initial inoculate	1,6X10 ⁶	2,3X10 ⁶	1,7X10 ⁶	2,8X10 ⁶	1,0X10 ⁵	1,2X10 ⁵	1,0X10 ⁵	1,0X10 ⁵

TAB.1

LINEAR REGRESSION REPORT / D-VALUE METHOD

"In vitro" evaluation of the antimicrobial efficacy

Università degli Studi di Ferrara - Department of Experimental and Diagnostic Medicine - Microbiology Division

Ferrara, Italy, June 2010



LIPOGEL HIGHLY SUITABLE FOR "DRY SKIN", AND FOR SKIN AND MUCOUS MEMBRANE HYPERSENSITIVITY AND HYPERACTIVITY.

Lipogel with 15% of Ozonia 3000.

With the same eutrophic and euerdermic effects of Ozonia 10, the fatty structure of Ozonia 15 extends the permanence - interaction with the treated surface, a balanced occlusive action with consequent hydration due to the barrier created against transepidermal water loss, providing emollient soothing protection, for the better care of conditions that explicate in dry skin, xerosis, desquamation, inflammation, fissuring in general, following dyshidrosis, erythema, weakness in factors contributing to epithelium resistance, fragile tissue, delicate tissue, newly formed tissue (peri-wound skin, after burns), hypertrophic and keloid scars, hyper-reactive skin and mucous membranes, impetiginization of injuries from scratching, anal itching, small areas of psoriasis, perianal and perineal dermatitis from fecal and urinary incontinence, atopic dermatitis, palmo-plantar keratoderma. Provides excellent protection and repellency following skin abrasions, laser therapy, and cryotherapy. Ozonia 15 can be used to contribute to debriding eschar, thanks to its emollient effect.

Ozonio 15 Lipogel does not contain petrolatum, paraffin, synthetic fragrances, colors, silicone, or preservatives. Dermatologically and microbiologically tested.

NOT TESTED ON ANIMALS.



ORAL CAVITY PROTECTION AND REPAIR.

Oral gel with 15% Ozonia 3000.

Ozoral has a protective, regenerating effect on oral cavity injuries. It is useful for local treatment of ulcerative and inflammatory conditions of this area (erosion, stomatitis, aphtha, injuries caused by braces, oral surgery, etc.).

Ozoral does not contain petrolatum, colors, silicone, or preservatives. Dermatologically and microbiologically tested.

NOT TESTED ON ANIMALS.

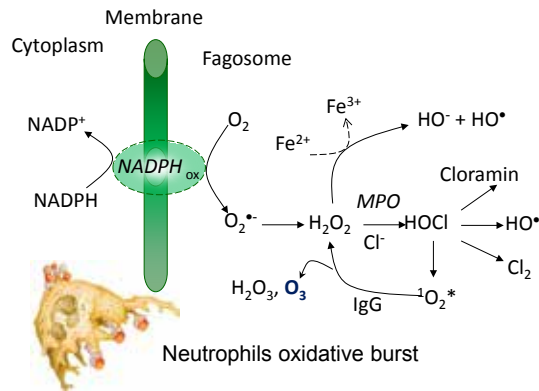
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KNOWLEDGE IN OZONIZED VEGETABLE OILS

Ozonized Sunflower Seed Oil

The Physiology

Antibody-catalyzed ozone generation by human neutrophils
2003. O₃ is present in human physiology !!!!!



Authors demonstrate the physiological presence of an ozone-similar mediator during inflammation, indicating ozone as a new bio-molecule with striking effects which must be considered and studied following new strategies with newly constructed randomized-standardized clinical studies.

Bernard M. Babior et al. PNAS March 18, 2003 100(6): 3031-3034
L. Re, Gregorio Martínez -Sánchez, Emerging therapies: ozone. What the patient should know and how the doctor must act. Ed. Aracne, Roma, Italia 2012. ISBN: 978-88-548-4672-2

The Mechanism

DIRECT OXIDATION (germicide): slowly release of **O₃, formaldehyde, trioxolane** and **lipoperoxides** can destroy by oxidation the infective germs. Involve 1,2,4-trioxolane present in the ozonized oil, when added to the warm exudates film of the ulcer, slowly decomposes generating local oxygen, H₂O₂ as reactive oxygen species (ROS), and a trace of lipid oxidation products (4-HNE). Such a cascade can explain the **prolonged disinfectant action** and stimulation of proliferative activity of fibroblasts and keratinoblasts.

I. Zanardi, S. Burgassi, E. Paccagnini, M. Gentile, V. Bocci, and V. Travagli. What Is the Best Strategy for Enhancing the Effects of Topically Applied Ozonated Oils in Cutaneous Infections? BioMed Research International Volume 2013, Article ID 702949, 6 pages. <http://dx.doi.org/10.1155/2013/702949>

GROW FACTORS RELEASE : O₃ and other oxidized oil components can release grow factor from platelets or from the local tissues (increased expression of PDGF, TGF-β, and VEGF) that act as tissue remodeling factors and stimulating proliferative activity of fibroblasts and keratinoblasts.

G. Valacchi, Y. Lim, G. Belmonte et al., "Ozonated sesame oil enhances cutaneous wound healing in SKH1 mice," Wound Repair and Regeneration, vol. 19, no. 1, pp. 107-115, 2011.
Hee et al. Therapeutic Effects of Topical Application of Ozone on Acute Cutaneous Wound Healing. J Korean Med Sci 2009; 24: 368-74

CYTOTOXICITY: Trioxolane, lipoperoxides and aldehydes are cytotoxic to microorganism; they can inactivate enzymatic pathways by mechanism involved disruption of nuclear mediators.

**Inactivation of proteins,
unsaturated lipid,
peptidoglycans,
DNA, RNA, respiratory
enzymes**



Lysis / death

Nathalia R de Almeida et al. Ozonized vegetable oils and therapeutic properties: A Review. Orbital. The Electronic Journal of Chemistry 2012 4(4): 313-326.

OXIDATIVE PRE-CONDITIONING: local oxidation of tissue by oxidized oil components can stimulate the expression of endogenous antioxidant mechanism (SOD, CAT, GPx) and promote tissue repairation.

Abu-Gharbieh E, Bayoumi FA, Ahmed NG. Alleviation of Antioxidant Defense System by Ozonized Olive Oil in DNBS-Induced Colitis in Rats. Mediators Inflamm. 2014;2014:967205.

Zamora Z, González R, Guanche D, Merino N, Menéndez S, Hernández F, Alonso Y, Schulz S. Ozonized sunflower oil reduces oxidative damage induced by indomethacin in rat gastric mucosa. Inflamm Res. 2008 Jan;57(1):39-43.

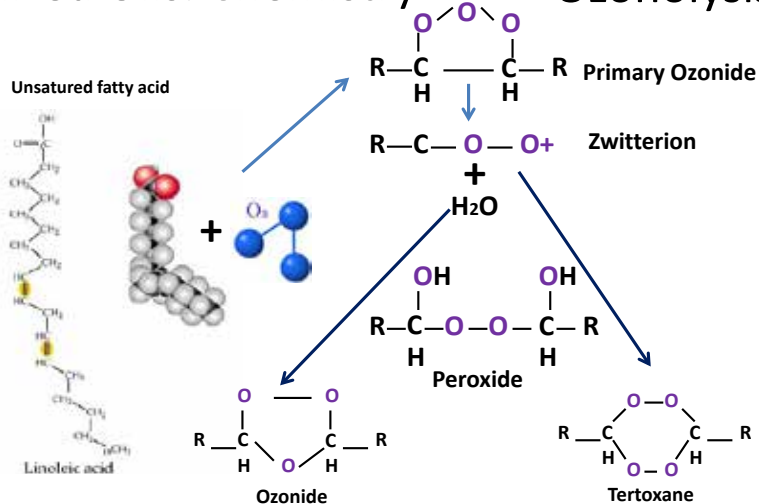
Zamora Rodríguez ZB, González Alvarez R, Guanche D, Merino N, Hernández Rosales F, Menéndez Cepero S, Alonso González Y, Schulz S. Antioxidant mechanism is involved in the gastroprotective effects of ozonized sunflower oil in ethanol-induced ulcers in rats. Mediators Inflamm. 2007;2007:65873.

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KNOWLEDGE IN OZONIZED VEGETABLE OILS

Ozonized Sunflower Seed Oil

Ozonized Oils. Chemistry Ozonolysis



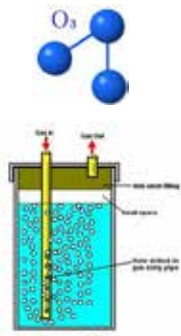
Bailey, P. S.; Ozonation in Organic Chemistry, Volume 1 Olefinic Compounds. New York: Academic Press, 1978.
Criegee, R. Angew. Chem. Int. Ed. 1975, 14, 745.

OZONIA 3000[®]
is the
Ozonized
Sunflower Seed Oil
made by

INNOVARES[®]
in Dermatologia

www.innovares.com

Ozonized oils. How is made?



Ozone generator

Input: O₂
O₂ purity, temperature
O₂ humidity

Pharmaceutical reactor

Control: Raw material quality
Reaction temperature
Reaction time
O₃ flow
O₃ concentration
Stir
Reaction time
Oil viscosity
Flue gases neutralization

Main steps:

Reaction
Reaction Arrest
Quality Control

Standard Operation Procedures according Good Manufacturing Practices. Ozonia 3000[®] Production Cycle 2014. Innovares, Italy.

Iacopo Zanardi, Valter Travagli, Alessandro Gabbrinielli, Luisa Chiasserini, Vello Bocci. Characterisation of sesame oil derivatives as dermatological preparations. Lipids. 2008, 43(9): 877-886

Ozonized oils. Quality Control.

	Method	Ranges Ozonia 3000 [®]
Aspect / Color	Organoleptic	Translucent light yellow
Odor	Organoleptic	Characteristic, acre, no rancid
Solubility	European Pharmacopoeia	Non soluble in water, more soluble in chloroform, ether, petroleum ether and paraffin
Density	European Pharmacopoeia	0.98 ± 0.02 g/mL
Acid Values	European Pharmacopoeia	< 30 mg KOH / 1 g
Peroxide Values	European Pharmacopoeia Modified	3500±300 mEq O ₂ / kg
Iodine Value	European Pharmacopoeia	60.00 ± 20.00 g / 100 g
Viscosity	European Pharmacopoeia	625.00±40 .00 mPa·s

Council of Europe (2010). *European Pharmacopoeia 7th Edition*, Druckerei C. H. Beck, ISBN 978-92-871-9700-2, Nördlingen, Germany. Method: 2.2.5. Relative Density. 2.2.10 Viscosity-Rotating Viscosimeter Method, 2.5.1. Acid Values, 2.5.4. Iodine Value, 2.5.5. Peroxide Value.

Standard Operation Procedures according Good Manufacturing Practices.
Ozonia 3000[®] Production Cycle 2014. Innovares, Italy.

Ozonia3000 is the name of the highly ozonized sunflower seed oil developed and produced in-house by Innovares.

Ozonia3000 constitutes the active ingredient in the formulations of the OZONIA product line (**Ozonia10**, **Ozonia15**, **Ozoral**), carried by various transport structures based on the condition to be treated.

Its active ingredient is expressed by a number of standardized, stabilized peroxides equal to about 3300 meqO₂/kg. The eutrophic, eudermic, and antiseptic effects can be attributed to the high-quality ozonized oil.