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# ACNE FERRARA 2017

## 14° MEETING di AGGIORNAMENTO su ACNE e DERMATOSI CORRELATE

FERRARA, 24-25 NOVEMBRE 2017

FERRARA FIERE CONGRESSI

# Idratanti e Retinoidi

**Stefano Manfredini, Alessia Bino, Silvia Vertuani**

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ACNEFE-2017, Ferrara, 24 Novembre 2017

# MECCANISMI dell'IDRATAZIONE



## IDRATAZIONE

*Per apporto di acqua  
dall'esterno*

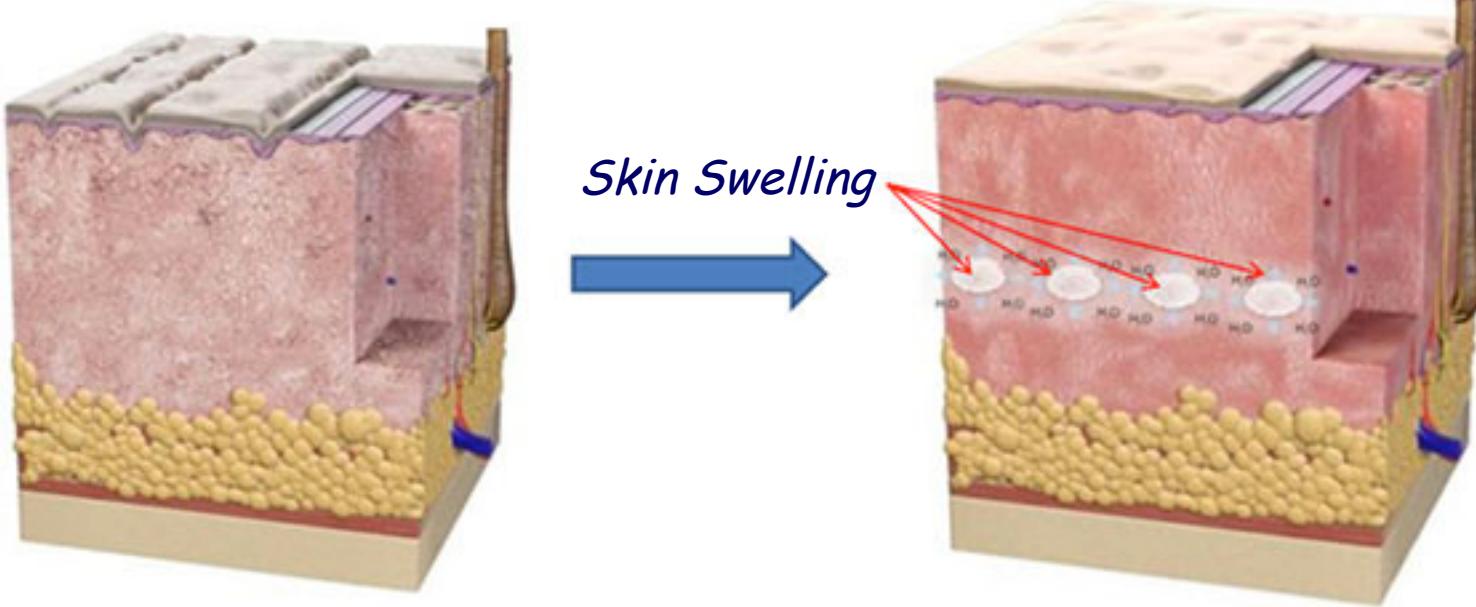
**UMETTANTI**  
(zuccheri e  
polialcoli)

**AQUAPORINE**  
(canali per  
trasporto attivo di  
acqua: glicerina)

Riduzione della  
evaporazione  
(TEWL)

**OLI MINERALI**  
(Paraffine)

## SWELLING



**SC può contenere fino a 5 volte il suo peso di acqua**

Un **PRINCIPIO ATTIVO** farmaceutico e/o cosmetico **può aumentare la propria potenza** di **10 volte** in presenza di SC fortemente idratato a seguito del rigonfiamento dello stesso e **riduzione resistenza** alla diffusione dell'attivo



## Idratare...PRIMA o DOPO?!

Meglio  
durante!!!!



Meglio una formula, contenente il Retinoide, a capacità idratante nota e bilanciata piuttosto che pretrattare o post-trattare con formulazioni umettanti od occlusive

In alternativa, occorre valutare caso per caso in funzione dell'effetto che si vuole ottenere (più o meno forte). L'applicazione dell'idratante deve essere distanziata di 15 minuti.



Sonia Molesini<sup>1</sup>, Federica Urto<sup>2</sup>, Aleksandra Dimitrovska Cvetkovska<sup>2</sup>,  
**Vincenzo Bettoli<sup>3</sup>, Giuseppe Valacchi<sup>4,2</sup>, Alessandra Pecorelli<sup>4,2</sup>,**  
**Stefano Manfredini<sup>2</sup>, Silvia Vertuani<sup>2</sup>**

**Influences of the vehicle in the spreading and release of  
betamethasone**



Journal:	<i>Therapeutic Delivery</i>
Manuscript ID	TDE-2017-0070.R2
Manuscript Type:	Preliminary Communication
Keywords:	lipid-enriched vehicle, betamethasone, topical drug

## Cosa dice la letteratura su idratazione



Journal of Dermatological Treatment

Taylor & Francis  
Taylor & Francis Group

ISSN: 0954-6634 (Print) 1471-1753 (Online) Journal homepage: <http://www.tandfonline.com/loi/ijdt20>

**A double-blinded, randomized, vehicle-controlled study to access skin tolerability and efficacy of an anti-inflammatory moisturizer in treatment of acne with 0.1% adapalene gel**

Leena Chularojanamontri, Papapit Tuchinda, Kanokvalai Kulthanon,  
Supenya Varothai & Waranaree Winayanuwattikun

All patients were randomized into three groups by nQuery program: (i) group A: adapalene gel; (ii) group B: adapalene gel with active formulation containing licochalcone A, L-carnitine and 1,2-decanediol; and (iii) group C: adapalene gel with placebo.



In summary, this study demonstrated that the concomitant usage of moisturizer containing licochalcone A, L-carnitine and 1,2-decanediol in addition to adapalene gel could reduce undesirable effects.

## Cosa dice la letteratura su assorbimento

The percutaneous absorption of topically applied tretinoin and its effect on endogenous concentrations of tretinoin and its metabolites after single doses or long-term use

Louise Latriano, PhD,<sup>a</sup> Georg Tzimas, PhD,<sup>b</sup> Frankie Wong, MS,<sup>c</sup> and Robert J. Wills, PhD<sup>c</sup>  
*Skillman and Raritan, New Jersey, and Thessaloniki, Greece*

**Background:** The percutaneous absorption of topically applied tretinoin cream and emollient cream formulations has not been comprehensively studied.

**Objective:** To assess tretinoin absorption and plasma levels of tretinoin and its metabolites after single and repeated topical tretinoin doses.

**Methods:** In study 1, 28 subjects were equally divided into four treatment groups that received a single dose of tritiated tretinoin in a 0.05% formulation of emollient cream (Renova, Retinova) or cream (Retin-A) alone or after 28 days of repeated nonradioactive doses. In study 2, subjects received single topical doses of tritiated tretinoin cream alone ( $n = 5$ ) or after 1 year of nonradioactive applications ( $n = 4$ ). Plasma, urine, and fecal samples were analyzed to determine absorption; plasma samples in study 1 were also analyzed for concentrations of tretinoin and its metabolites.

**Results:** Percutaneous absorption of tretinoin was approximately 2% after a single dose and after 28 days of daily application. In patients receiving long-term therapy (i.e.,  $>1$  year), absorption averaged 1.1%. Mean plasma concentrations of tretinoin after 28 days of treatment with either tretinoin emollient cream or tretinoin cream were not significantly changed when compared with the corresponding endogenous concentrations before treatment.

**Conclusion:** Minimal percutaneous absorption of tretinoin was obtained after its topical application in cream formulations. Neither single-dose nor long-term treatment with topical tretinoin formulations appeared to affect the endogenous levels of tretinoin or its metabolites. (J Am Acad Dermatol 1997;36:S37-S46.)

## Cosa dice la letteratura su irritazione

DOI: 10.1111/jdv.14410

JEADV

### ORIGINAL ARTICLE

#### Fragility of epidermis: acne and post-procedure lesional skin

G. Fabbrocini,<sup>1</sup> A.B. Rossi,<sup>2,3</sup> M.-D. Thouvenin,<sup>2</sup> C. Peraud,<sup>2</sup> V. Mengaud,<sup>2</sup> A. Bacquey<sup>2</sup>  
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pH = 3,5 !!!!!!

#### Abstract

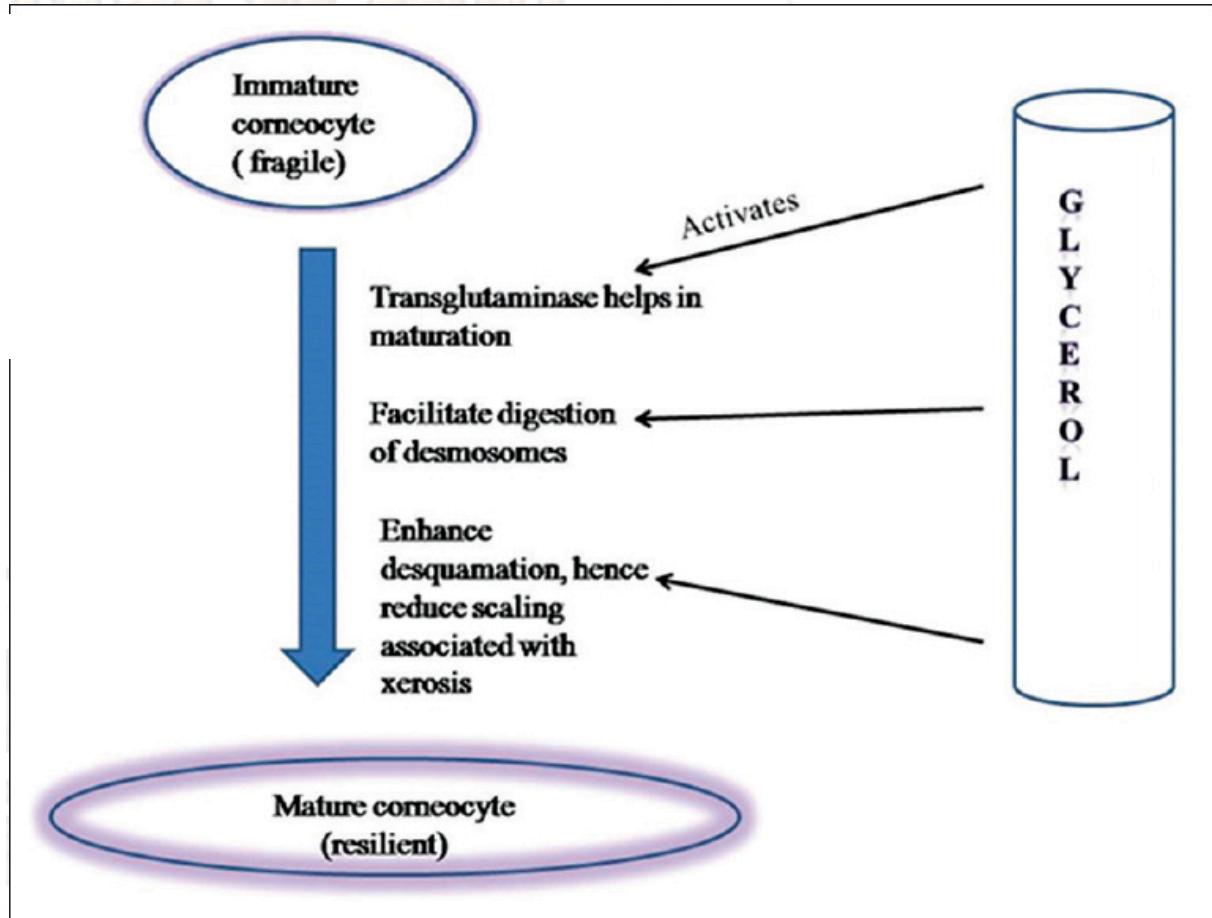
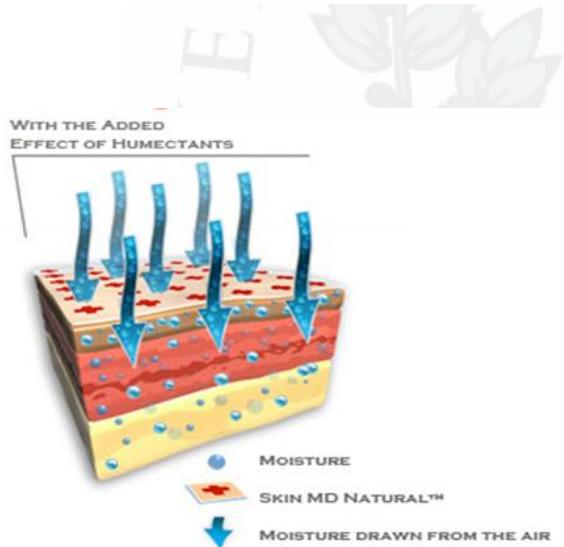
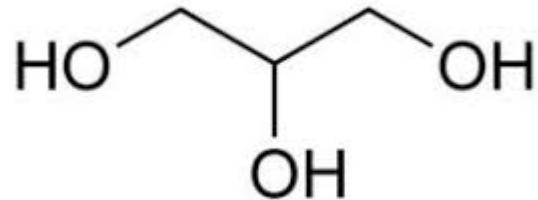
'Fragile skin', or skin with lower resistance to aggressors, can be broadly classified into four causal categories: constitutional (age-dependent or associated with specific vulnerable locations on the body, e.g. eyelids), pathological (related to disease), circumstantial (related to environmental or internal factors, e.g. stress) and iatrogenic (caused by medical interventions or treatments). In this supplement, we focus on the fourth category, the iatrogenic origin of fragile skin and the role that dermo-cosmetics can have in restoring the natural protective function of the skin following treatments for skin diseases and medical interventions. We present epidemiological data on the prevalence of fragile skin in three different geographical regions, and the results of two randomized controlled studies investigating the efficacy and tolerability of dermo-cosmetics in combination with topical acne treatment and following physical skin damage. Overall, we found that prevalence across the three regions (23% in Germany, 41% in UAE, 56% in Taiwan) reflected previous global estimates (24–53%) across skin types, with significant associations found with environmental and lifestyle factors, such as stress, humidity and pollution. The iatrogenic effects of topical acne treatments can result in poor compliance or use of over-the-counter moisturizers, which may reduce treatment efficacy. Dermo-cosmetics were found to aid in restoration of fragile skin caused by the acne topical retinoid treatment adapalene 0.1% gel, by reducing transepidermal water loss and improving skin hydration, as well as reducing the side-effects such as skin irritation that are frequently associated with topical retinoids. Additionally, dermo-cosmetic products were found to accelerate wound closure following skin damage in a laser ablation model and reduced the duration of post-procedural side-effects such as itching and burning.

Received: 28 April 2017; Accepted: 9 June 2017

## IDRATAZIONE ED IRRITAZIONE DA RETINOIDI:

gli idratanti diminuiscono significativamente l'irritazione

## Gli Umettanti

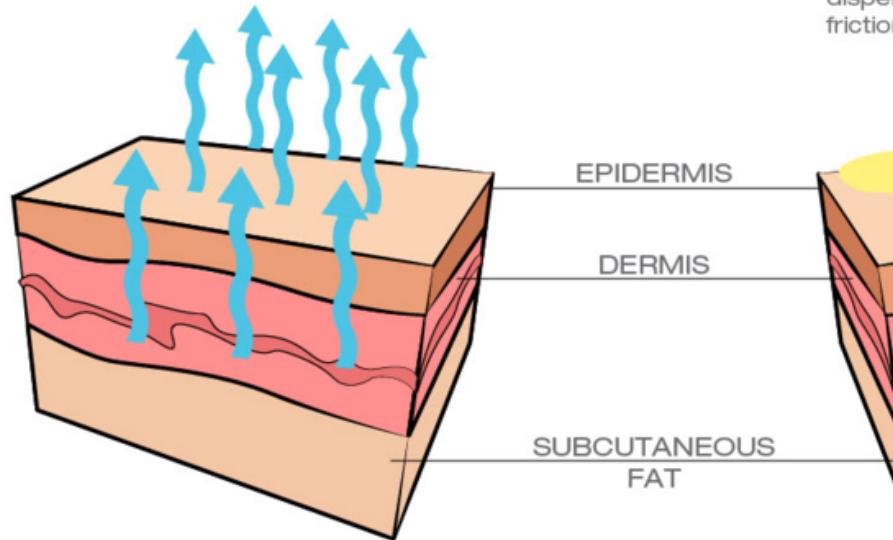


Agiscono trattenendo l'acqua sulla cute,  
la glicerina è il più potente

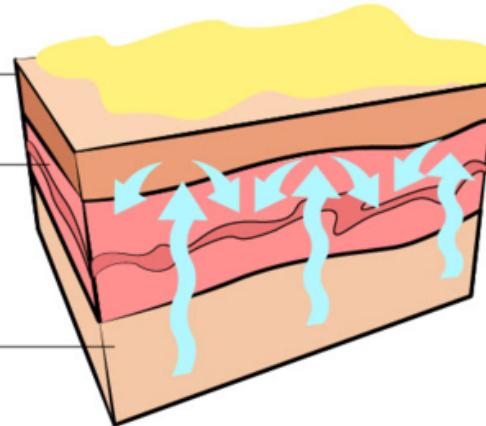
## Riduzione TEWL: filmogeni

Agiscono impedendo l'evaporazione transdermica dell'acqua,  
la vaselina (Petrolatum) è il più efficace

Transepidermal water loss (TEWL) is a normal process of the skin



Lubricants form an occlusive film on the surface of the skin, preventing TEWL. When the lubricant disperses, the hydrated epidermis has an elevated friction level.



# **Idratazione & efficacia**

## **Analisi di Alcuni Prodotti: affinità del retinoide per il veicolo?**

Legenda su ingredienti attivi più significativi per spiegare i concetti presenti nelle formule  
**attivo come umettante / attivo come filmogeno**

### **Crema IDRATANTE (emulsione O/A)**

Aqua, **Cetearyl Isononaoate**, **Isopropyl Miristate**, Glyceryl Stearate, PEG-100 Stearate, **Propylene Glycol**, Butyrospermum Parkii, Prunus Dulcis, Panthenol, Stearic Acid, Sodium PCA, Saccharide Isomerate, **Lanolin Oil**, Equisetum Arvense, Oenothera Biennis, Arginine PCA, Sodium Lactate, PEG-4 ProlineLinoleate, Phospholipids, Sphingolipids, Cholesterol, DEA-Cetyl Phosphate, Superoxide Dismutase, Retinyl Palmitate, Hydrolyzed Wheat Protein, Dimethicone, Phenoxyethanol, Methylparaben, Propylparaben, ImidazolidinylUrea, Parfum, Ethylparaben, Butylparaben, Disodium EDTA, Ascorbyl Palmitate, Hydrogenated Palm Glycerides Citrate.

### **Crema IDRATANTE (emulsione gel O/A)**

Aqua, **Glycerin**, **Petrolatum**, Dicaprylyl Ether, Glyceryl Stearate, Dimethicone, Prunus Amigdalus Dulcis Oil, Cetyl Alcohol, Peg-30 Stearate, Acrylates/C10-30 Alkyl Acrylate Crosspolymer, Benzyl Alcohol, Dimethiconol, Disodium EDTA, Glyceryl Acrylate/Acrylic Acid Copolymer, Methylparaben, Phenoxyethanol, Propylene Glycol, Propylparaben, Sodium Hydroxide, Tocopheryl Acetate

### **Crema IDRATANTE (emulsione O/A)**

AQUA/WATER/EAU, **GLYCERIN**, **MINERAL OIL (PARAFFINUM LIQUIDUM)**, ETHYLHEXYL PALMITATE, DIPROPYLENE GLYCOL, XYLITOL, BIS-PEG/PPG-16/16 PEG/PPG-16/16 DIMETHICONE, SODIUM ACRYLATE/SODIUM ACRYLOYLDIMETHYL TAURATE COPOLYMER, MANNITOL, RHAMNOSE, FRUCTOOLIGOSACCHARIDES, LAMINARIA OCHROLEUCA EXTRACT, GLYCYRRHETINIC ACID, ALLANTOIN, CERAMIDE 3, TOCOPHERYL ACETATE, ISOHEXADECANE, CAPRYLIC/CAPRIC TRIGLYCERIDE, POLYSORBATE 80, DISODIUM EDTA, CETRIMONIUM BROMIDE, GINKGO BILOBA LEAF EXTRACT, DODECYL GALLATE, PROPYLENE GLYCOL, FRAGRANCE (PARFUM).

## Come varia la BIODISPONIBILITÀ?

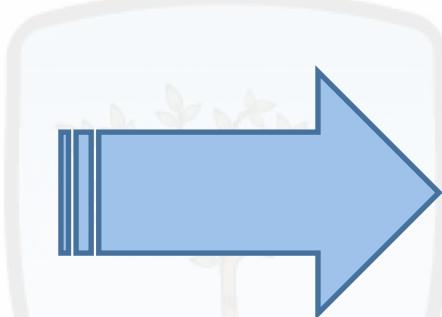
La penetrazione degli attivi attraverso lo strato corneo è un fenomeno complesso e dipende da più variabili:

1. viscosità della formulazione
2. area di applicazione
3. frequenza di applicazione
4. grado di sfregamento sulla pelle (evaporazione veicolo)
5. Spessore della formulazione sulla pelle (percorso maggiore, velocità evaporazione acqua, quantità di ingrediente per unità di superficie)



Cos'è e a cosa serve

## MODELLI MATEMATICI PREDITTIVI

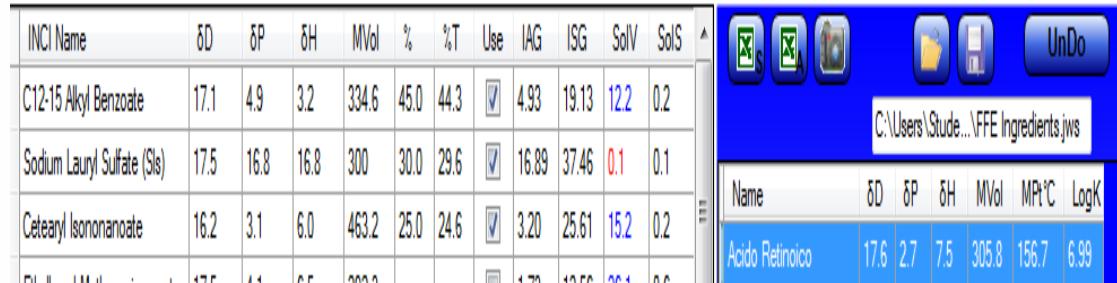


- ✓ Calcolare preventivamente il grado di assorbimento di un attivo al variare degli ingredienti
- ✓ Proporre il tipo di olii e le relative quantità da utilizzare per ottenere un migliore assorbimento per l'attivo scelto
- ✓ Proporre la percentuale di uno o più ingredienti scelti per la formulazione



# SOFTWARE DI MODELLAZIONE

*I software consiglia*



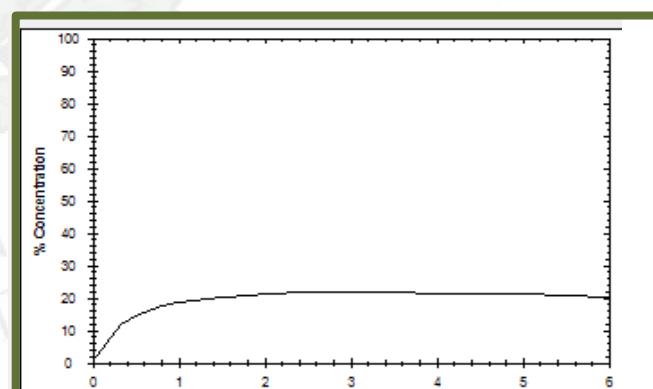
The software interface displays a table of ingredients with their properties and a graph showing the absorption of Retinoic Acid over time.

INCI Name	δD	δP	δH	MVol	%	%T	Use	IAG	ISG	Solv	Sols
C12-15 Alkyl Benzoate	17.1	4.9	3.2	334.6	45.0	44.3	<input checked="" type="checkbox"/>	4.93	19.13	12.2	0.2
Sodium Lauryl Sulfate (Sls)	17.5	16.8	16.8	300	30.0	29.6	<input checked="" type="checkbox"/>	16.89	37.46	0.1	0.1
Cetearyl Isononanoate	16.2	3.1	6.0	463.2	25.0	24.6	<input checked="" type="checkbox"/>	3.20	25.61	15.2	0.2
Retinoic Acid	17.6	2.7	7.5	305.8	156.7	6.99					

Below the table, a smaller window shows a single row for Acido Retinoico:

Name	δD	δP	δH	MVol	MP°C	LogK
Acido Retinoico	17.6	2.7	7.5	305.8	156.7	6.99

A graph on the right shows the percentage concentration of Acido Retinoico over time (0 to 6 hours). The concentration starts at 0%, rises sharply to about 20% by 1 hour, and then levels off at approximately 20% until 6 hours.



Time (hours)	% Concentration
0	0
0.5	10
1	20
2	20
4	20
6	20

-C12-15 Alkyl Benzoate: **45.00%** **EMOLliente**

-Sodium lauryl sulfate: **NA** TA non considerato per il calcolo dell'assorbimento

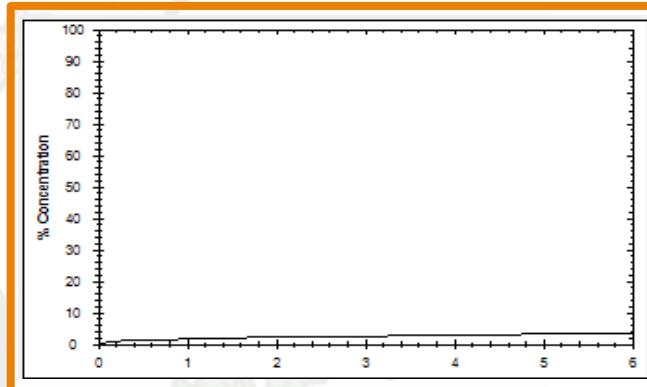
-Cetearyl nonanoate: **25.0 %** **EMOLliente**

***Il 20% di Acido Retinoico viene assorbito dopo 30 minuti dall'applicazione***

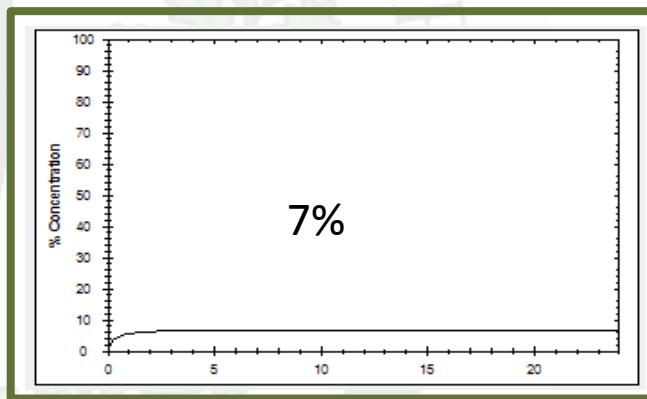
# SOFTWARE DI MODELLAZIONE

Emulsione A/O di 0.5% Acido Retinoico con...

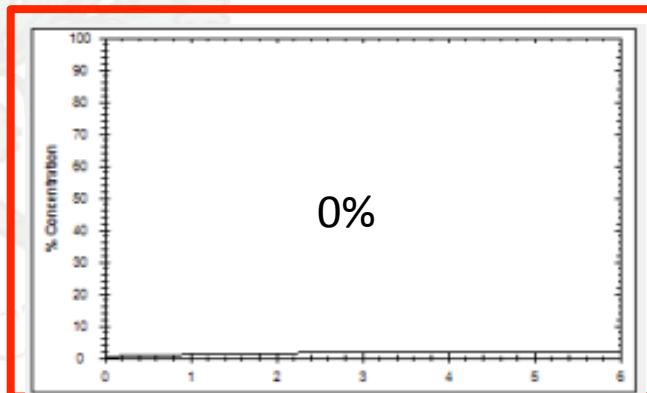
**PETROLATUM**



**ISOPROPYL MIRISTATE**



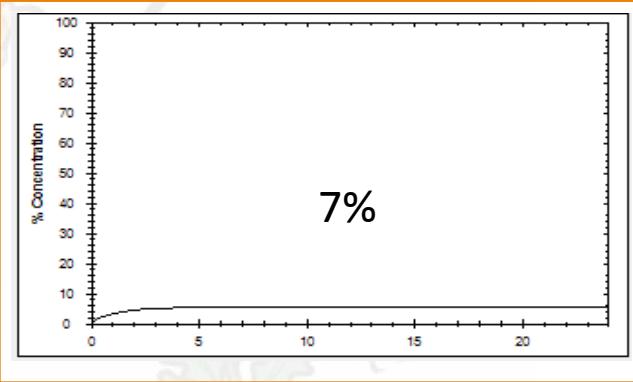
**CYLOHEXASILOXANE**



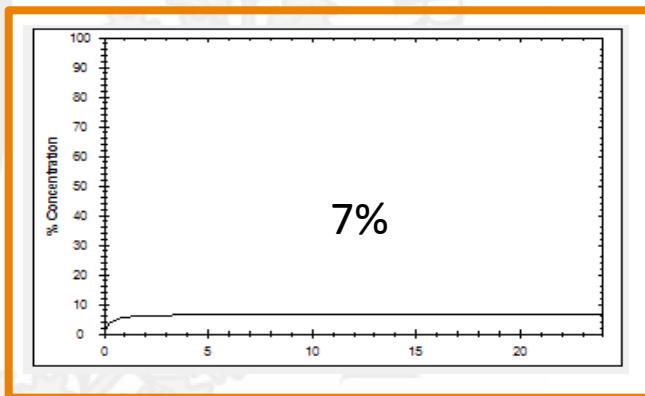
# SOFTWARE DI MODELLAZIONE

Emulsione O/A di 0.5% Acido Retinoico con...

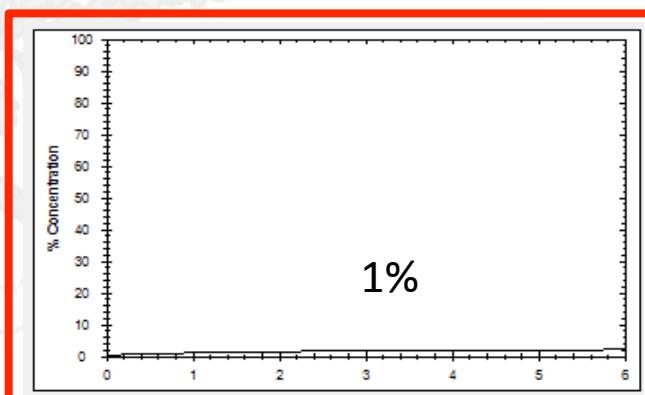
**PETROLATUM**



**ISOPROPYL MIRISTATE**



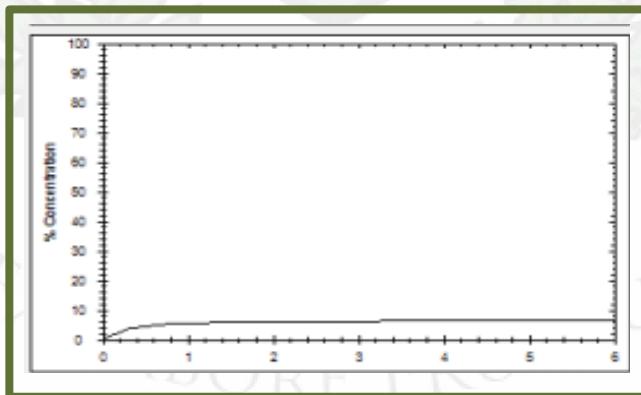
**CYLOHEXASILOXANE**



# SOFTWARE DI MODELLAZIONE

*Il mix dei tre in una emulsione A/O*

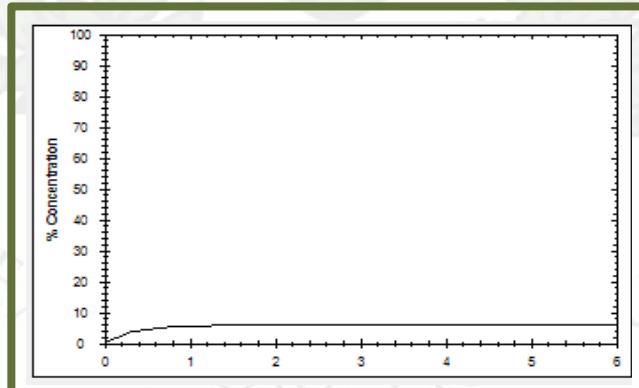
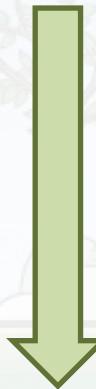
INCI Name	δD	δP	δH	MVol	%	%T	Use	IAG	ISG	Solv	Sols
Isopropyl Myristate	16.2	2.4	3.7	298.6	100.0	39.5	<input checked="" type="checkbox"/>	4.73	21.62	14.7	0.1
Mineral Oil (Light)	16.1	1.8	3.7	424.1	0.0		<input checked="" type="checkbox"/>	4.92	32.90	9.8	0.2
Cyclohexasiloxane	13.1	1.3	0.5	470.6	0.0		<input checked="" type="checkbox"/>	11.49	59.89	0.1	0.2



# SOFTWARE DI MODELLAZIONE

*Il mix dei tre in una emulsione O/A*

INCI Name	δD	δP	δH	MVol	%	%T	Use	IAG	ISG	Solv	Sols
Isopropyl Myristate	16.2	2.4	3.7	298.6	99.0	24.3	<input checked="" type="checkbox"/>	4.73	21.62	14.7	0.1
Cyclohexasiloxane	13.1	1.3	0.5	470.6	1.0	0.2	<input checked="" type="checkbox"/>	11.49	59.89	0.1	0.2
Mineral Oil (Light)	16.1	1.8	3.7	424.1	0.0		<input checked="" type="checkbox"/>	4.92	32.90	9.8	0.2



## Uso di una combinazione di prodotto cosmetico idratante

- Non è consigliato utilizzare una miscela di farmaco retinoido e cosmetico idratante perché altera il veicolo e quindi l'efficacia/tossicologia del retinoido rispetto a quella prevista dal produttore del farmaco
- Il grado di idratazione cutaneo indotta dal cosmetico in pre o post trattamento modifica l'assorbimento del retinoido
- Il grado di idratazione indotta dal cosmetico riduce l'irritazione da retinoido che può essere ridotta anche da ingredienti ancillari presenti nel cosmetico

- Il grado di idratazione dipende da che prodotto cosmetico stiamo usando
- L'assorbimento di un attivo non dipende da un ingrediente ma dal veicolo in toto
- A parità di ingredienti, le percentuali di ogni singolo ingrediente modificano l'assorbimento di un attivo

- **Pretrattare** con un idratante aumenta lo "swelling" e quindi la penetrazione del retinoide
- **Post trattare** con un idratante riduce l'irritazione prodotta dal retinoide e influenza anch'esso assorbimento ma solo in fase successiva.

- Riconoscete qualcuno di questi prodotti?
  - Vi è mai capitato di acquistarne uno?
    - Dove l'avete acquistato?
    - Quanto l'avete pagato?



# PRODOTTI ETNICI

