



IMWITOR® 375

NOVEL NANOEMULSION BASED DRUG  
DELIVERY SYSTEMS FOR  
ORAL AND TOPICAL DELIVERY



**IOI OLEOCHEMICAL**

IOI Oleo GmbH  
September, 2024



# CONTENT

## **IMWITOR® 375 – A hidden gem in IOI Oleo`s Portfolio**

- Introduction
- DDSs based on IMWITOR® 375
- Case Studies
- Further information & Summary

## IMWITOR® 375 INTRODUCTION

- **Bioavailability improvement** is a major objective in pharmaceutical and nutraceutical **product development**
- **Scope** of the townhall is to introduce **IMWITOR® 375** as a **safe, powerful** and **versatile** solubilizer for **Pharma** and **Nutraceutical** uses
- **IMWITOR® 375** shows competitive performance in terms of **encapsulation efficacy, solubilization power, penetration depth** and **bioavailability** with e.g. Phospholipids and Polysorbates
- **IMWITOR® 375** addresses a range of **unmet functional needs**
  - **Innovativeness for formulations**
  - **Delivering Bioavailability improvement**
  - **Clean Labelling for Nutraceutical**
  - **Protectability**

**Penetration**

**Encapsulation efficacy**

**Bioavailability improvement**

**Solubilization power**



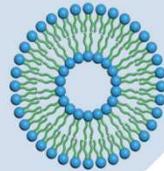
# IMWITOR® 375 BASED DRUG DELIVERY SYSTEMS

## Hydro-Tops®

- **W/O/W Nanoemulsion based on IMWITOR® 375**
- Mono-layered vesicles without PEG based or ethoxylated emulsifiers
- Functional benchmark:  
Similar drug encapsulation to Liposomes

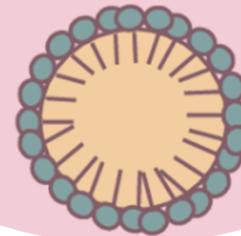


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## Lipo-Tops®:

- **O/W Nanoemulsion based on IMWITOR® 375**
- No need of PEG-based or ethoxylated emulsifiers
- Functional benchmark:  
Nanosomes based on Phospholipids



# HYDRO-TOPS<sup>®</sup>: AT A GLANCE



## W/O/W Nanoemulsion for oral and dermal drug delivery

Proven for hydrophilic, lipophilic, poorly soluble and high-molecular weight APIs

On dermal route fast, deep penetration and sustained release

Alternative technology to PEG, Ethoxylate and/ or phospholipid based solubilization strategies

## Typical Formulation:

- Active Ingredient: upto 12%
- Water-based: > 50 %
- Surfactant: IMWITOR<sup>®</sup> 375
- Co-Surfactants: Ethanol/ Propylene Glycol
- Oil phase: e.g. Ethyl Oleate, Ethyl EPA
- Antioxidant: e.g. Tocopherol

## Particle Morphology:

- Monolayered vesicles
- PSD: 120 - 250  $\mu\text{m}$
- PDI: <0,2

## API Examples:

- Hydrocortisone (0,5 %)
- Finasteride (0,25 %)
- Celastrol (0,5 %)
- Niacinamide (8%)
- Tetrahydrocurcumin (2 %)
- Epigallocatechingallate (2 %) – Greentea Extract

# CASE STUDY ON HYDRO-TOPS® I: PENETRATION OF HYDROCORTISONE



Comparative study of penetration of Hydrocortisone from four different formulations

Encapsulation: 0.5% <sup>3</sup>H-Hydrocortisone

Application: 10 µl/cm<sup>2</sup> human skin

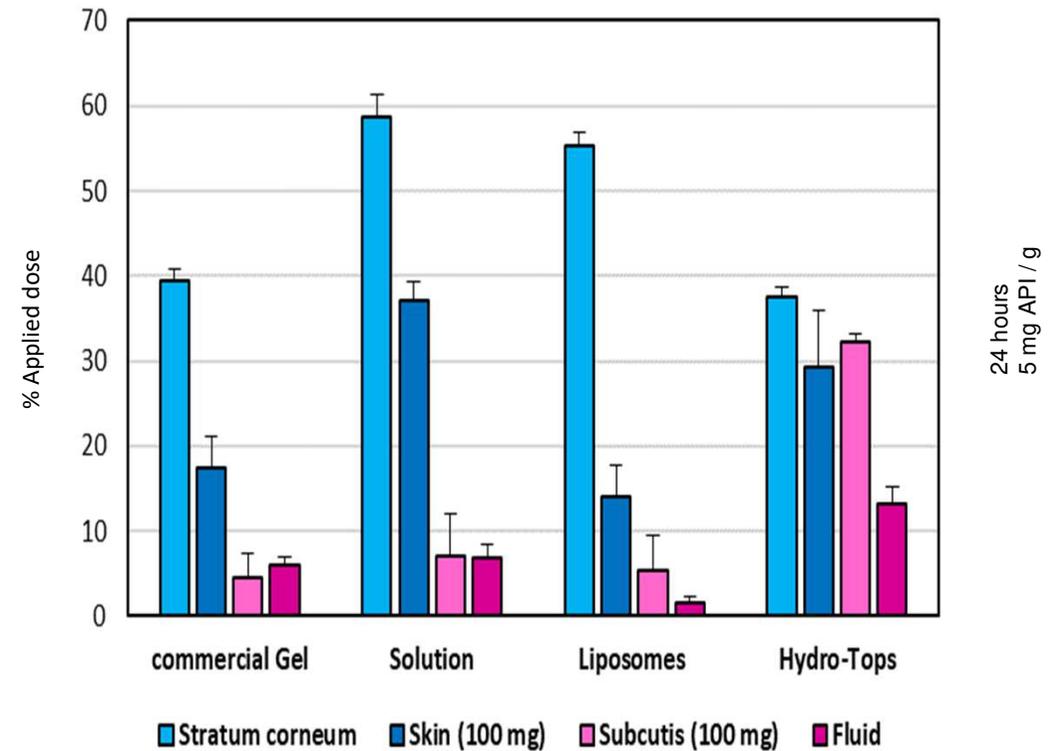
Time: 24 hours

Determination: Radioactivity

Franz Cell testing, ex vivo

Conclusion:

- Highly competitive performance towards overcoming stratum corneum
- Delivery and distribution of high amount of active into deep skin layers



# CASE STUDY ON HYDRO-TOPS® II: EPIGALLOCATECHINEGALLATE DELIVERY



Measurement and comparison of Skin Antioxidative performance of Epigallocatechingallate (EGCG) containing formulations

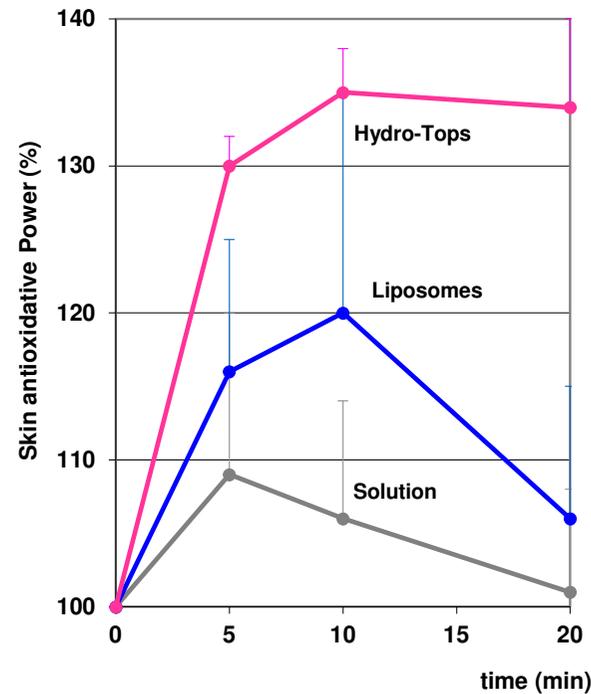
2% Dispersions and 0.2% dispersion in lamellar cream

Encapsulation efficacy comparable with liposomes

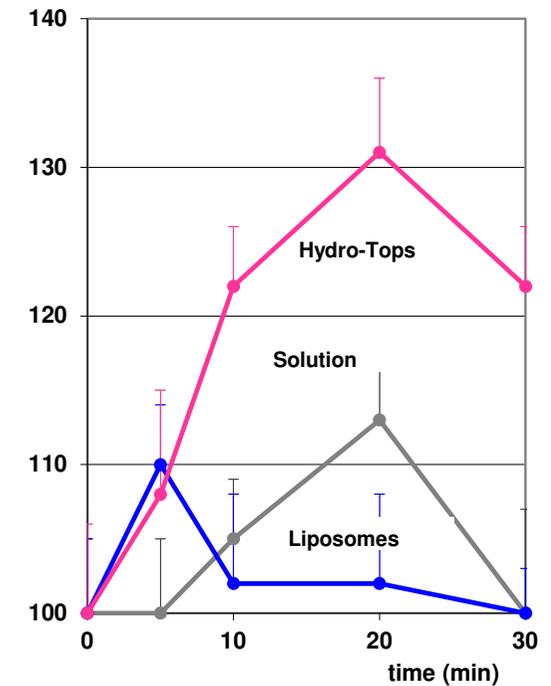
Hydro-Tops® encapsulated active shows highest antioxidative effect in skin measured by ESR

After 20 mins radical scavenging effect of Hydro-Top® encapsulated active found to be higher by factor of more than 2x

Formulated into lamellar cream Hydro-Tops® retain high antioxidative activity, despite dilution effect



Skin antioxidative power of 2% Dispersion of EGCG



Skin oxidative power of lamellar cream loaded with dispersion 0.2% EGCG

# CASE STUDY: EFFECT OF HYDRO-TOPS® BLANK FORMULATION ON SKIN



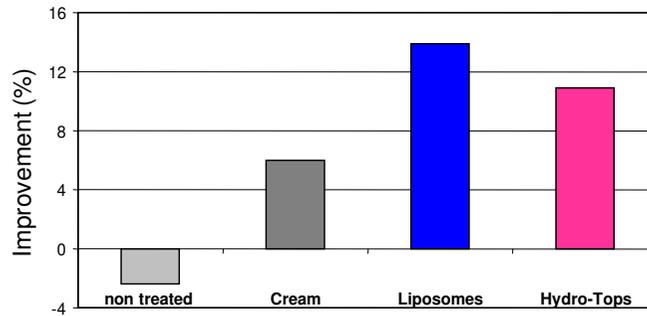
Study of effects on skin of unloaded Hydro-Tops® formulation

Sample Size: n=20

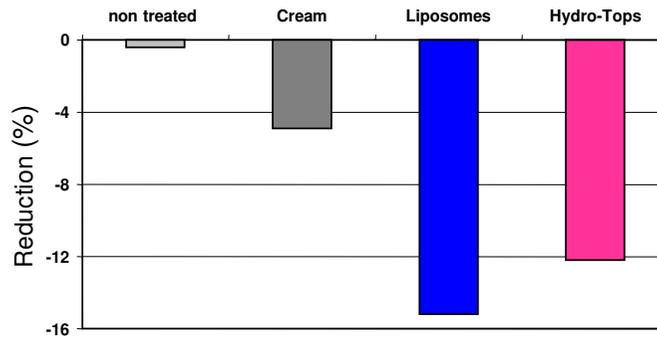
Corneometry & Visioscan camera

Blank W/O/W Hydro-Tops® formulation increase skin moisturization and reduces skin roughness similar to commercially available cream formulations and Liposomes

## Skin Moisturization



## Skin Roughness

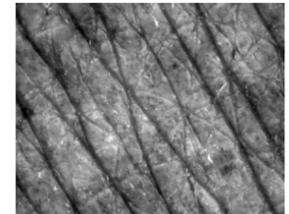
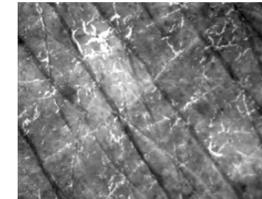


Day 0

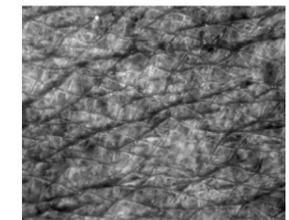
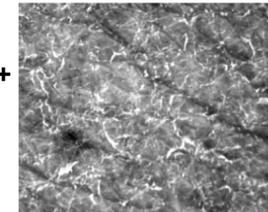
Week 4

RR0

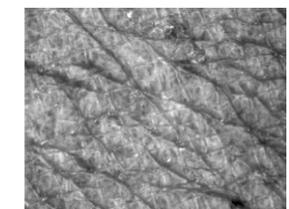
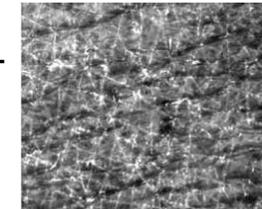
DAC Cream



DAC Cream + Liposomes



DAC Cream + Hydro-Tops



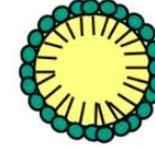
SELS Pictures (Surface evaluation of living skin)

RR0

Dosierung Phospholipid / WOW in DAC

Radsziwill, Robert; 2024-07-24T13:48:49.853

# LIPO-TOPS®: SOLUBILIZATION TECHNOLOGY



## O/W Nanoemulsion for oral and dermal drug delivery

Proven for lipophilic, poorly watersoluble and oily actives

On dermal route fast, deep penetration and sustained release

Alternative technology to PEG, Ethoxylate and/ or phospholipid based solubilization strategies

- Active Ingredient: up to 10%
- Water-based: > 50 %
- Surfactant: IMWITOR® 375
- Co-Surfactants: IMWITOR® 948
- Oil phase: e.g. Ethyl Oleate
- Antioxidant: e.g. Tocopherol

## Typical Formulations:

### Particle Morphology:

- Monolayered vesicles
- PSD: 120 - 250 µm
- PDI: <0,2

### API Examples:

- Boswellin (3% Extract, with 1% AKBA)
- Ibuprofen (0,5 %)
- Tocopherol (10%)
- Cannabidiol (5%)
- Coenzyme Q10 (5%)
- Curcumin C3 Complex (3%)
- Tetrahydrocurcumin (3%) (white)



# CASE STUDY ON LIPO-TOPS® I: IBUPROFEN



Two Ibuprofen containing gels as comparative benchmarks to Lipo-Tops®

Encapsulation: 0.5% <sup>3</sup>H-Ibuprofen in each formulation

Application: 10 µl / cm<sup>2</sup>

Time: 24 hours

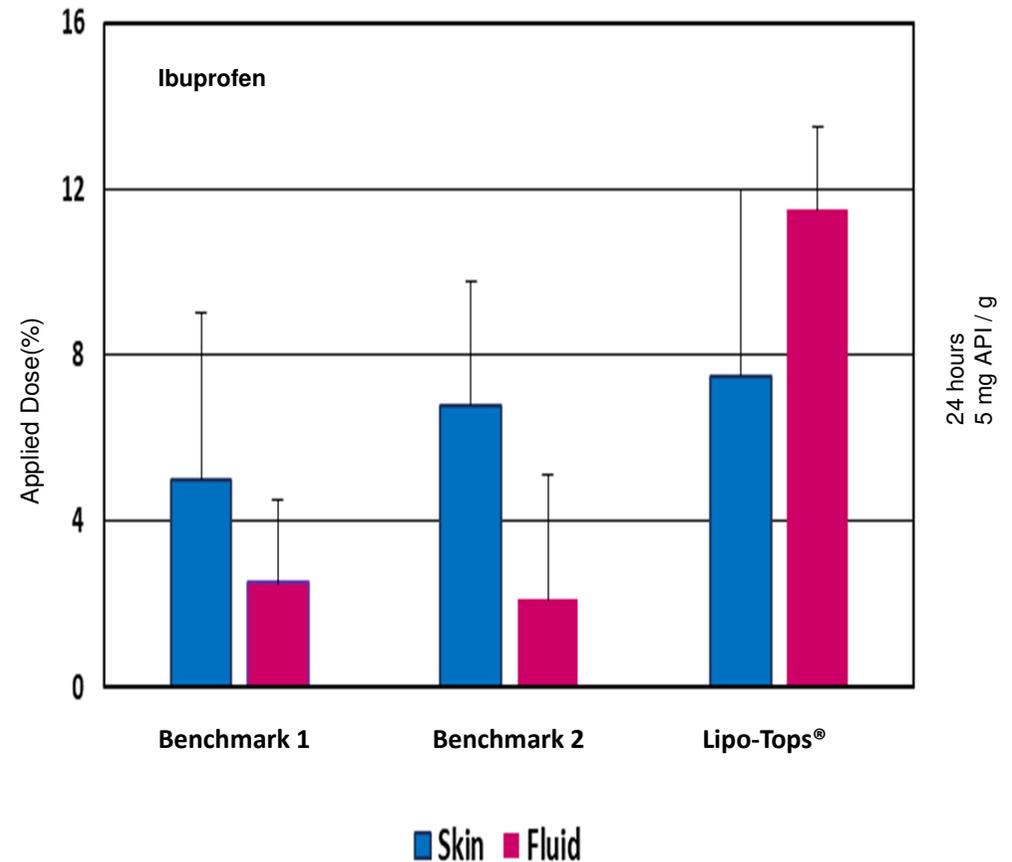
Determination: Radioactivity

Franz Cell testing, ex vivo

Delivery of Ibuprofen into human skin was tested ex vivo from different formulations

Highly competitive performance towards overcoming stratum corneum  
Delivery and distribution of high amount of active into deep skin layers

O/W Nanoemulsion shows highest delivery into skin and fluid, as well as total delivery of applied dose.





## CASE STUDY ON LIPO-TOPS® II: DELIVERY OF TOCOPHEROL



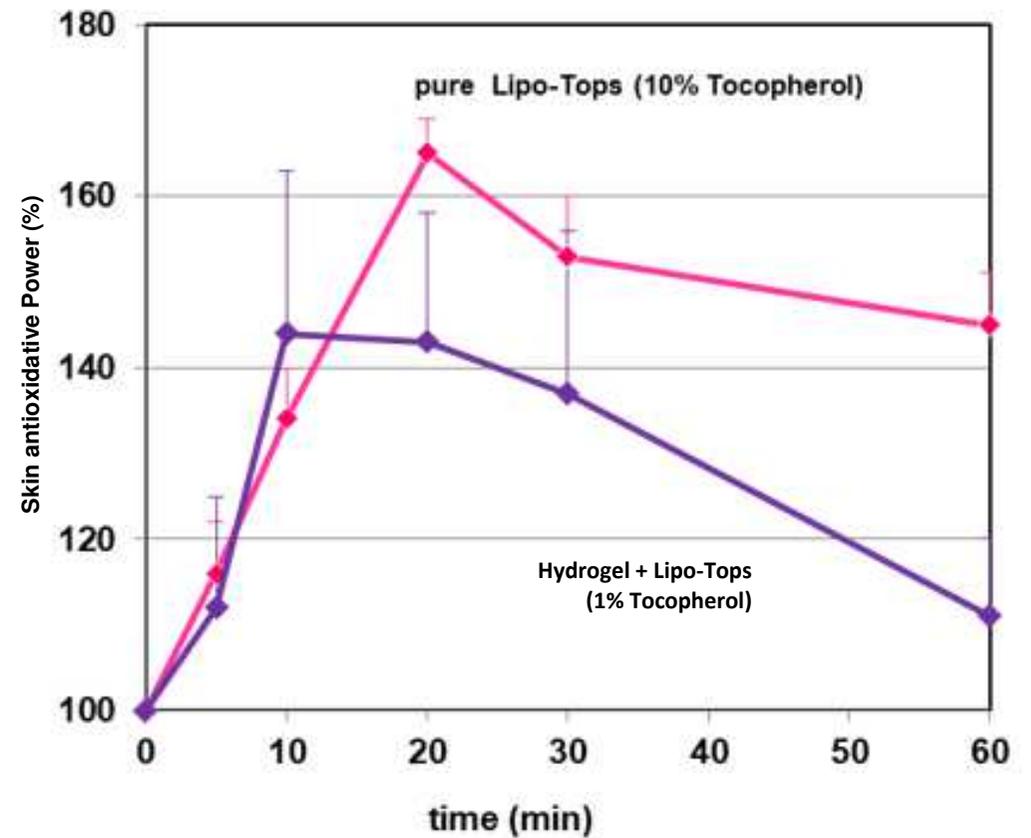
O/W Nanoemulsion with 10% of Tocopherol

Incorporation into Hydrogel to receive 1% active content

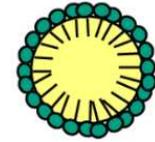
Examination of delivery efficiency via measurement of Skin Antioxidative Power.

Lipo-Tops® offer highly efficient solubilization of Tocopherol

High bioavailability and activity of the antioxidant under skin antioxidative power testing, despite dilution effect



## SOLUBILITY ENHANCEMENT FACTORS – IN LIPO-TOPS®



| Solubility         | Water solubility<br>(lit. based)<br>(mg/ml) | Active load in<br>Lipo-Tops®<br>(mg/ml) | Solubility increase<br>Factor |
|--------------------|---|---|-------------------------------|
| Tetrahydrocurcumin | < 0,01                                      | 30                                      | > 3.000                       |
| AKBA/ Boswellin    | < 0,001                                     | 10                                      | > 10.000                      |
| CBD                | < 0,001                                     | 50                                      | > 50.000                      |
| Q 10               | < 0,001                                     | 50                                      | > 50.000                      |
| Tocopherol         | < 0,0001                                    | 100                                     | > 1.000.000                   |

## KEY INGREDIENT IMWITOR<sup>®</sup> 375: FOR HYDRO-TOPS<sup>®</sup> AND LIPO-TOPS<sup>®</sup>

### Key Features

- Powerful solubilizer with excellent biocompatibility
- Encapsulation of hydrophilic, lipophilic and poorly soluble APIs
- Cold processable
- **Green Chemistry, based on sunflower, sugar beet, sugar cane and rapeseed oil**
- PEG free, vegan and developed to avoid palm oil derivatives

### Precedence of use:

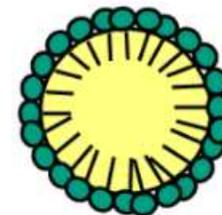
- Pharma, Cosmetics, Food and Nutraceutical
- Oral and topical dosage forms
- Medical Device applications under investigation

### Chemical Description:

- Glyceryl Citrate/Lactate/Linoleate/Oleate
- Ester of mono and diglycerides of unsaturated edible fatty acid with citric acid and lactic acid
- E 472 (b/c)

A unique opportunity for

- New product development
- Line extension
- Relaunch



## ADDITIONAL SUPPORT... AVAILABLE

### Further Case Studies on e.g.

- Finasteride
- Anti-Inflammatory agents e.g. Apigenin, AKBA-Boswellic Acid
- Cellular uptake into Human keratinocytes
- High-molecular weight Actives
- Anti-oxidants combination with cellulosic Hydrogels/Polymeric reservoirs

### Base formulations on:

- Tetrahydrocurcumin
- Boswellin/ Frankincense
- Cannabidiol
- Curcumin

Support on Lab & Large Scale production



**Formulation development and  
technical consultation available –  
Talk to us!**

# INTELLECTUAL PROPERTY ENVIRONMENT

- **Patents and utility models filed for both trademarks for the US and Europe**
- **Cooperation options:**
  - can conduct their own product development
  - can leverage available base formulation under license agreement
  - or have a product developed by IP Holder
- **Opportunity to file own intellectual property on finished products**

# SUMMARY

- **Target industries: Pharma, Nutrition and Medical Devices**
- **Key Arguments / USP:**
  - Market pull, unmet technical needs
  - Alternative technology to Phospholipids and Polysorbates
  - Clean Labelling for Nutraceutical
  - Protectability
- **Various case studies available**
- **Technical and Formulation support**



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# THANK YOU!



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