

INVESTIGATION OF POTENTIAL ABILITY OF NANOEMULSION FORMULATION, FOR TRANSDERMAL DELIVERY OF DICLOFENAC SODIUM

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Brief Out line.....

- ❑ Formulated micro emulsions using Span 80, olive oil and water at room temperature and 70 °C.
- ❑ Constructed ternary phase diagrams.
- ❑ Measured the particle size of the emulsions formulated using the built-in- scale of a polarized light microscope.
- ❑ pH of the emulsions formulated.
- ❑ Incorporated a model drug, Diclofenac sodium (1% wt/wt) into micro emulsions (79% (wt/wt) of olive oil, 10% (wt/wt) of span 80[®], 10% (wt/wt) of distilled water and 1% (wt/wt)) and studied in-vitro release through a pig skin using Franz diffusion cell.

Emulsion

Emulsion is defined as two immiscible fluids in which one liquid is dispersed as fine droplets in the other. There are different types of emulsions and they are classified depending on.

- ❑ **Size of liquid droplets**
- ❑ **Dispersed phase**
- ❑ **Size of liquid droplets**

Macro



Particle size
0.2 – 50mm

Micro



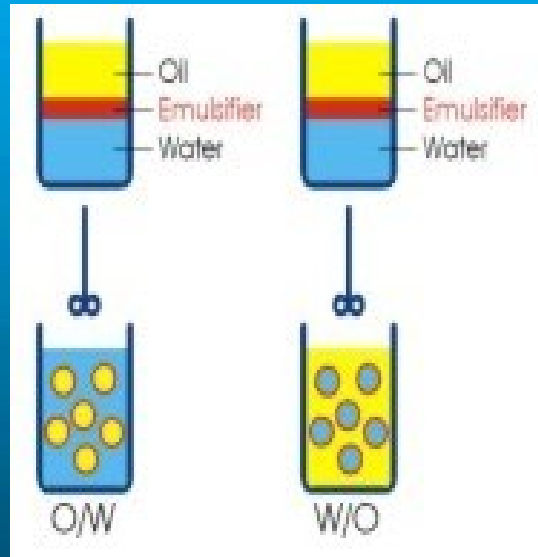
Particle size
0.01- 0.2mm

Nano



Particle size
<0.01 mm

□ Dispersed phase



Oil-in-water emulsion (O/W)

applications requiring a relatively small amount of fatty material as hand, shaving or moisturizing creams.

Water in oil emulsion (W/O)

products are emollient creams and sunscreens.

Micro emulsion

- ❑ Microemulsions are clear, stable, isotropic mixtures of oil, water, and surfactant (S), frequently in combination with a co-surfactant (CoS). Up to date microemulsions have been shown to be able to protect labile drug, control drug release, increase drug solubility, and reduce patient variability.
- ❑ There are many studies on microemulsions as topical drug delivery vehicles, and it has been shown that microemulsion formulations have improved transdermal and dermal delivery properties.

The pharmaceutical sector

□ Advantages

The **high percentage** of emulsifiers causes a very **fast penetration** respectively permeation of the active agents into the skin due to its powerful impact on the skin barrier. This is an advantage especially for the pharmaceutical sector

□ Disadvantages

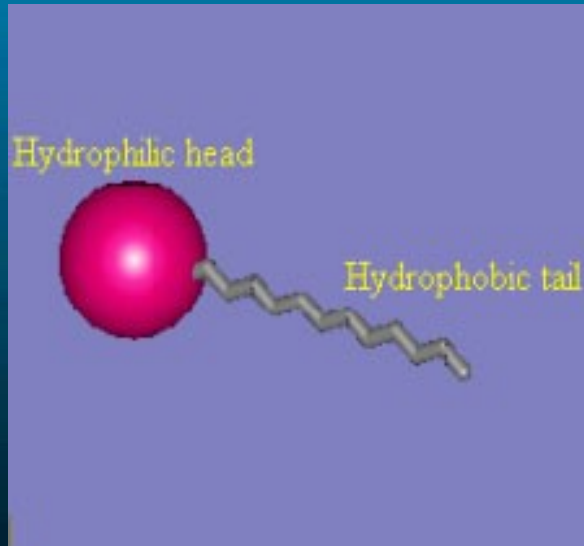
Emulsifiers severely disturb the integrity of the skin barrier layers

The cosmetic sector

In the cosmetic sector micro-emulsions are mostly used in skin cleansing,

Surfactants Reduce Surface Tension

This molecular composition means they have the ability to **reduce the surface tension** when placed into solutions of oil and water.



Surfactants is that they are chemicals which have parts that are both hydrophilic (water loving) and lipophilic (oil loving). In fact, the word “surfactant” is a shortened form of the phrase “**surface active agent.**”

Microemulsion Formulation

Olive oil, surfactants and water

mixed thoroughly in for 30 min

left to equilibrate for 2 weeks

Observed the morphologies

Phase diagram was constructed

Constructed Phase diagrams.

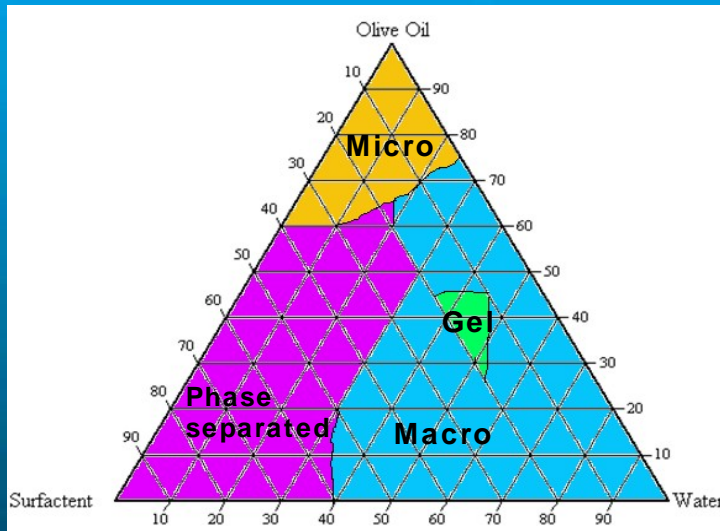


Figure 8: Phase Diagram for the system at room temperature

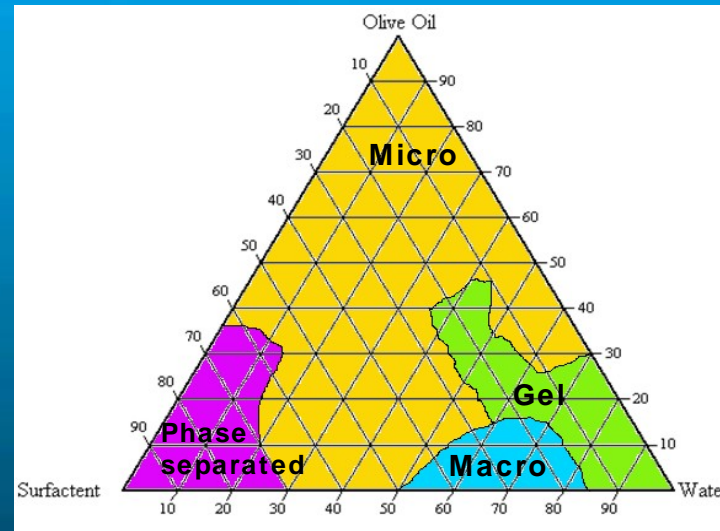


Figure 8: Phase Diagram for the system at 70 °C

Table 1: Compositions of micro emulsions used for further studies

	Oil %	Surfactant %	Water %
Sample - A- Micro (from room temperature)	80	10	10
Sample - B- Micro (from 70 °C)	55	15	30
Sample - C- Micro (from 70 °C)	55	30	15

Study of the variation of the particle size

The variation of the particle size was studied by using the optical micrograph images which were taken by using a polarized light microscope.

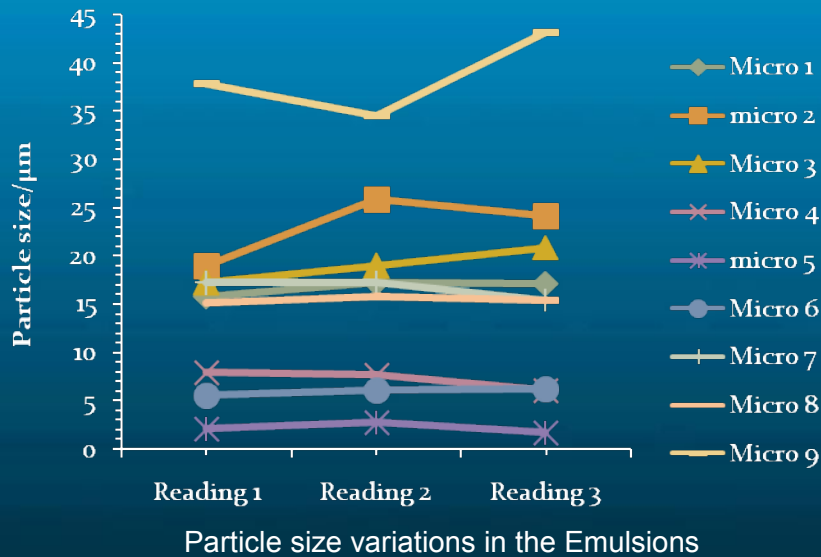


Table 2: Variation of the diameters of the droplets in Emulsions

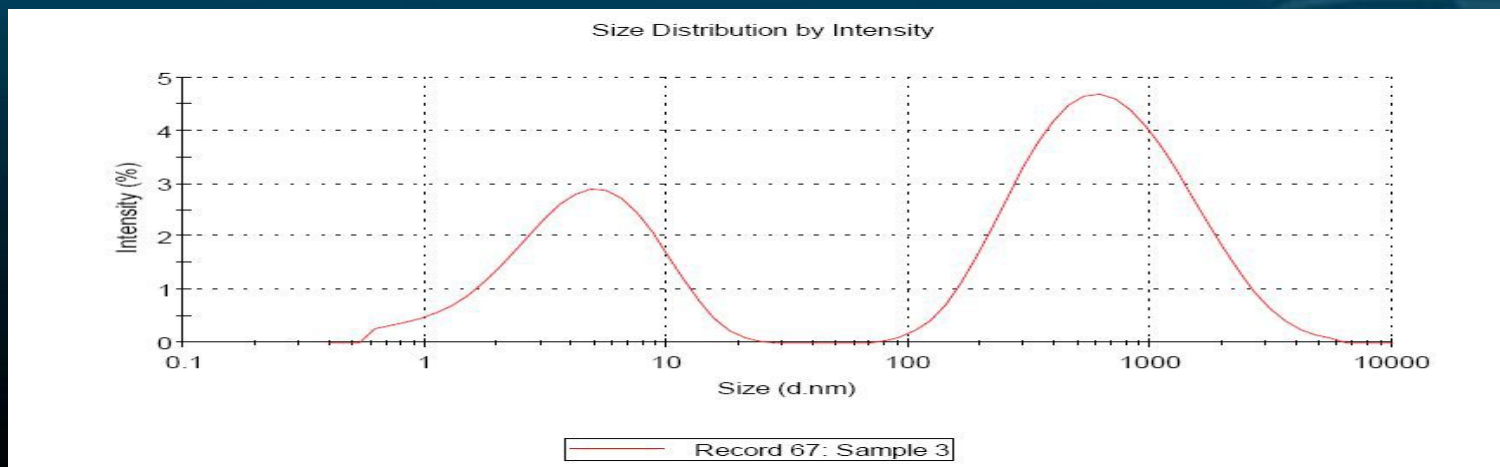
Emulsion no	Particle Size / μm		
	Reading 1	Reading 2	Reading 3
Macro 1	116.94	192.52	177.06
Micro 1	15.85	17.27	17.19
Micro 2	18.99	25.84	24.13
Micro 3	17.27	18.99	20.91
Micro 4	7.96	7.76	6.16
Micro 5	2.13	2.84	1.78
Micro 6	5.61	6.16	6.27
Micro 7	17.27	17.27	15.85
Micro 8	15.17	15.85	15.47
Micro 9	37.86	34.55	43.11

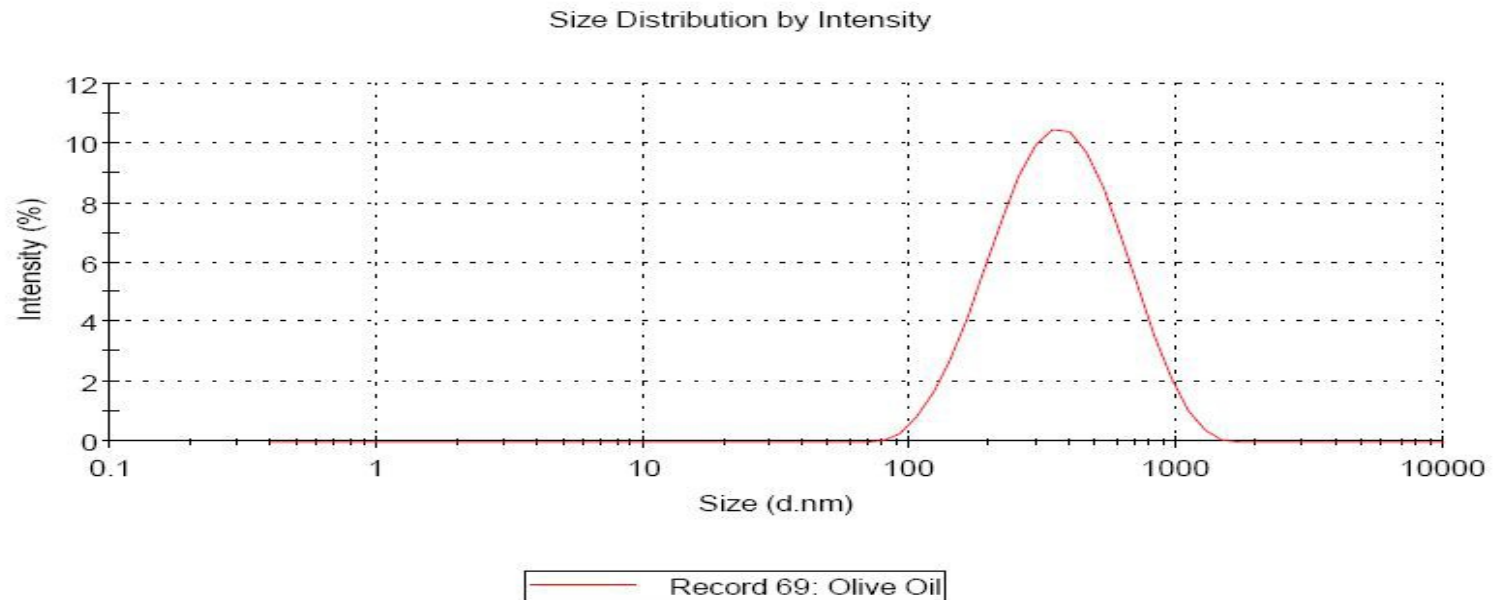
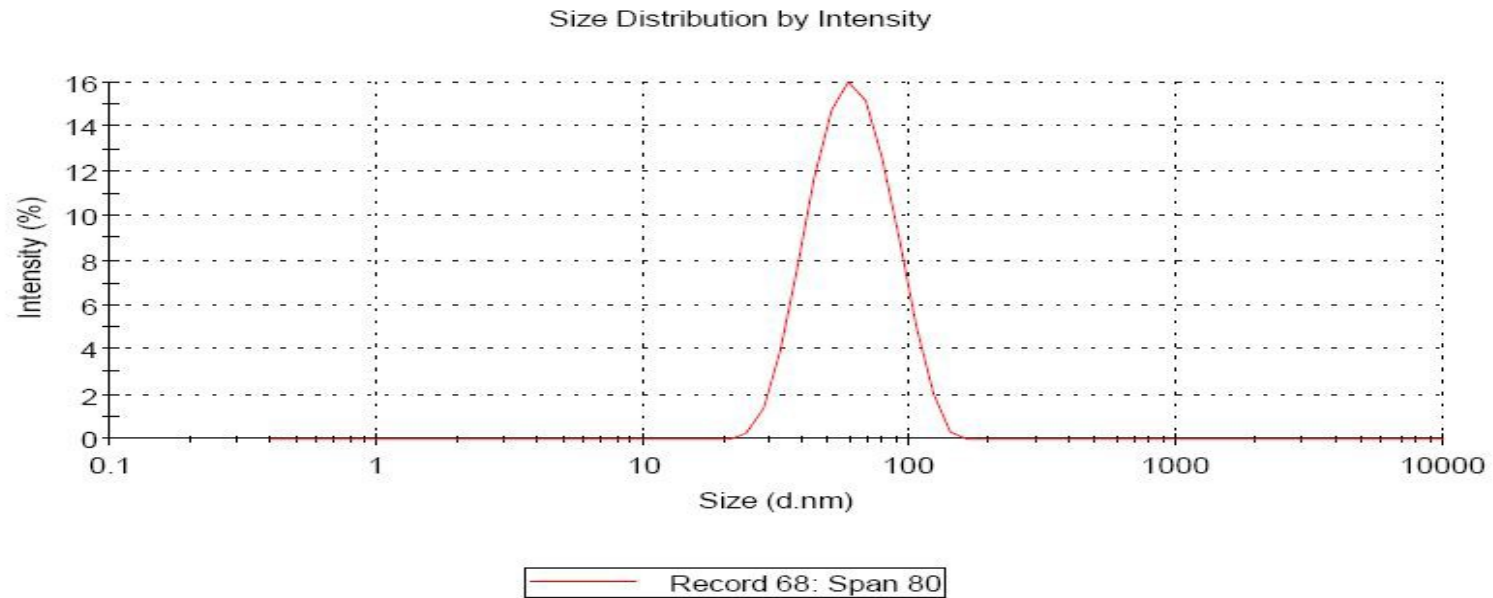
Depending on the observations of particle size, micro emulsions are categorized into four types.

- particle size 35 μm - 45 μm
- particle size 15 μm - 25 μm
- particle size 01 μm - 10 μm
- particle size < 1 μm

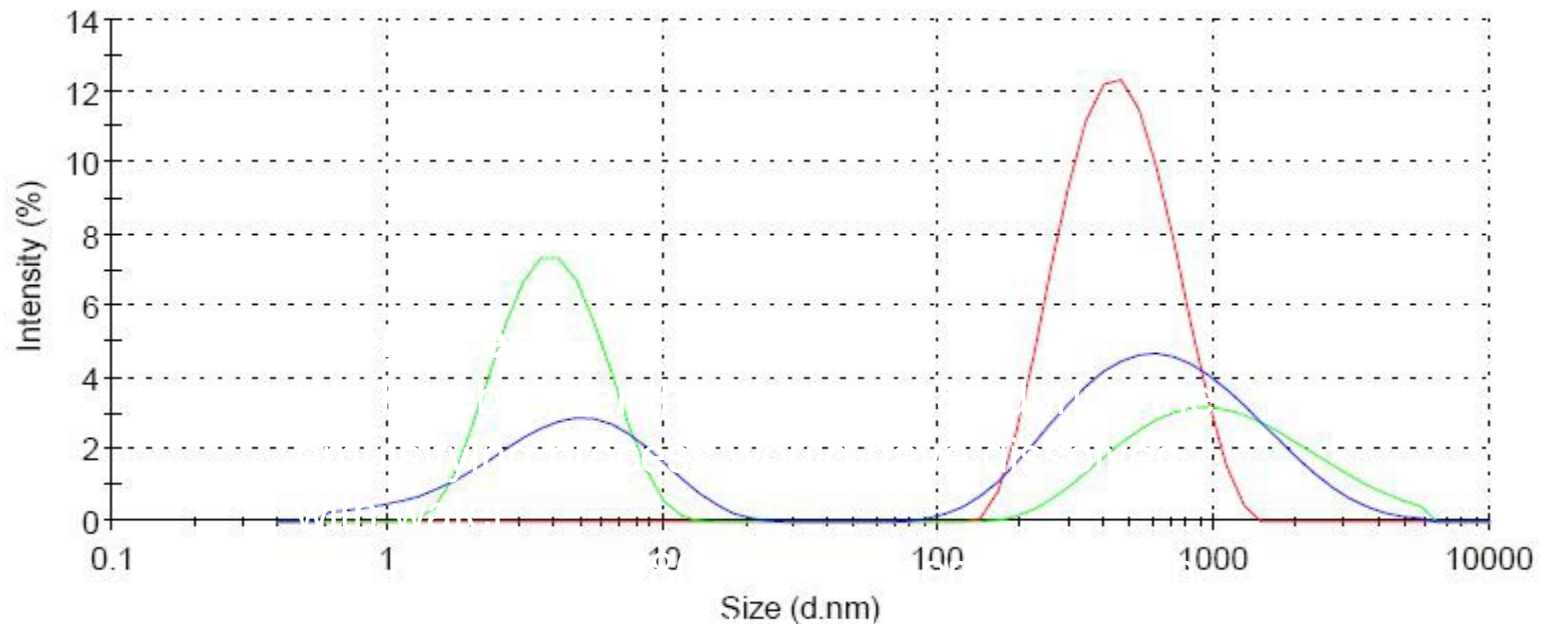
Measure size distribution by Dynamic Light Scattering

Two peaks were observed in the range 4 to 5nm and around 1.0 microns. The peak at 1.0 micron size was for Olive Oil, and the other is that of Emulsion.





Size Distribution by Intensity

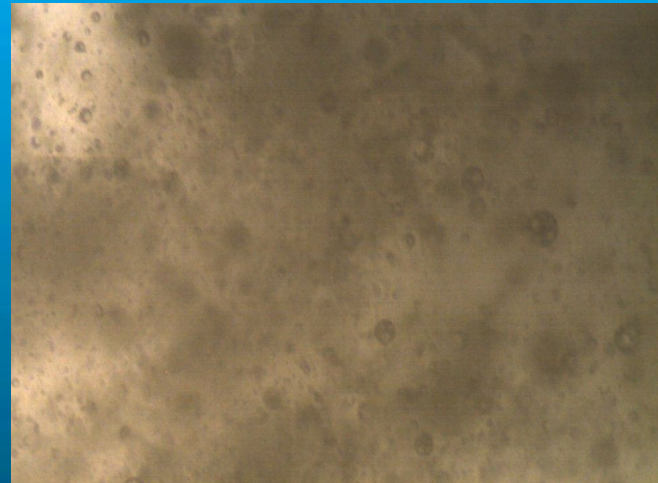
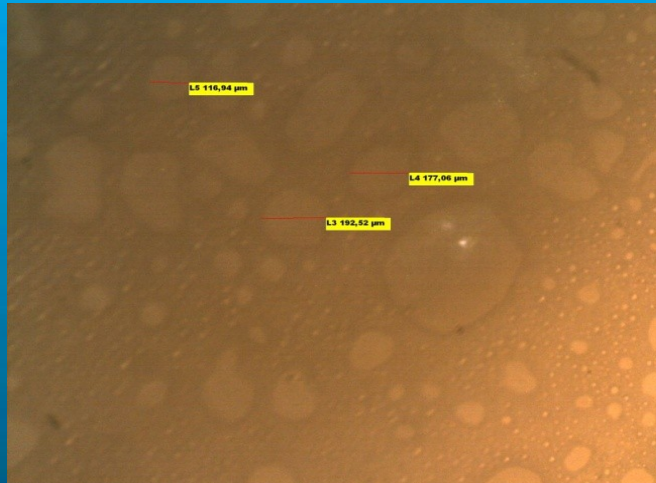


Record 52: Olive Oil Record 66: Composition A Record 67: Sample 3

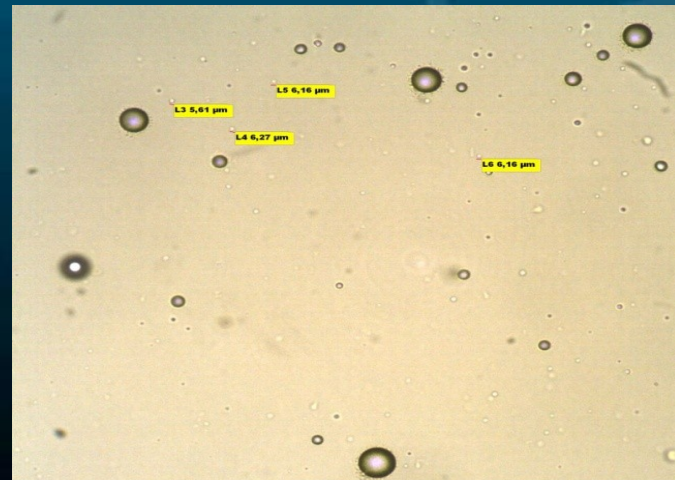
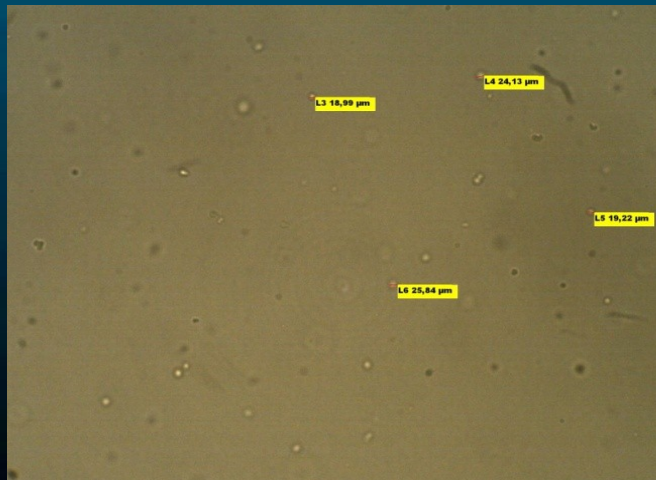
Inferences

We hereby infer that the span 80 during the emulsifying process would have dissolved with water, and hence span 80 is not observed in both the samples, and only emulsion peaks are seen at 5nm.

Macro emulsions

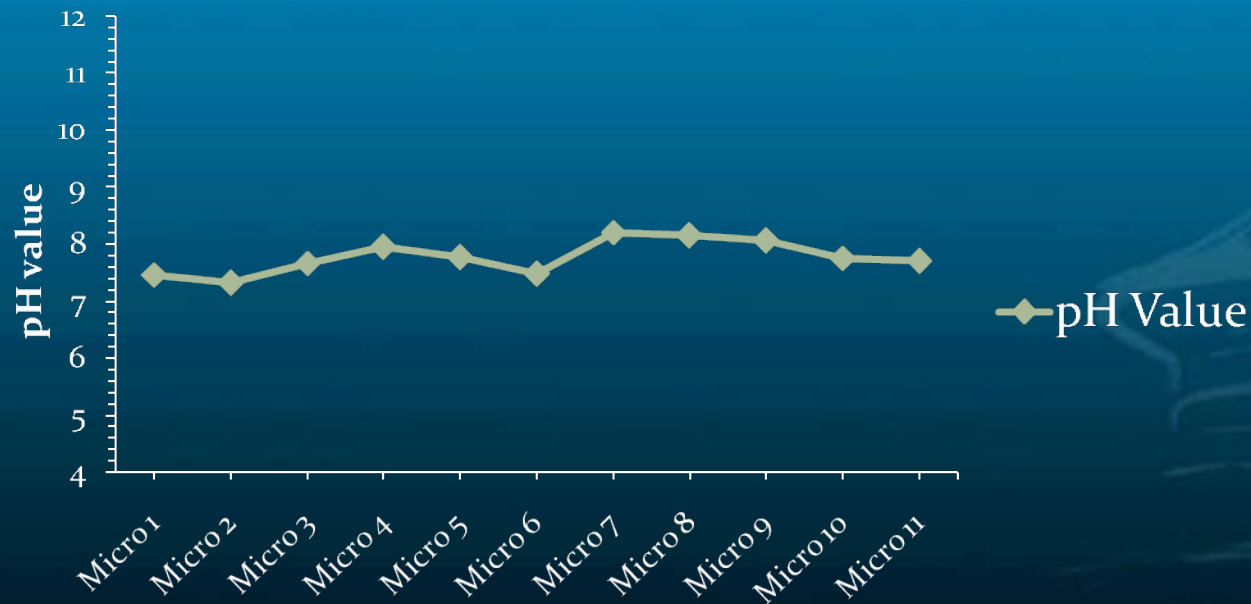


Micro emulsions



Study of pH variation of the emulsions

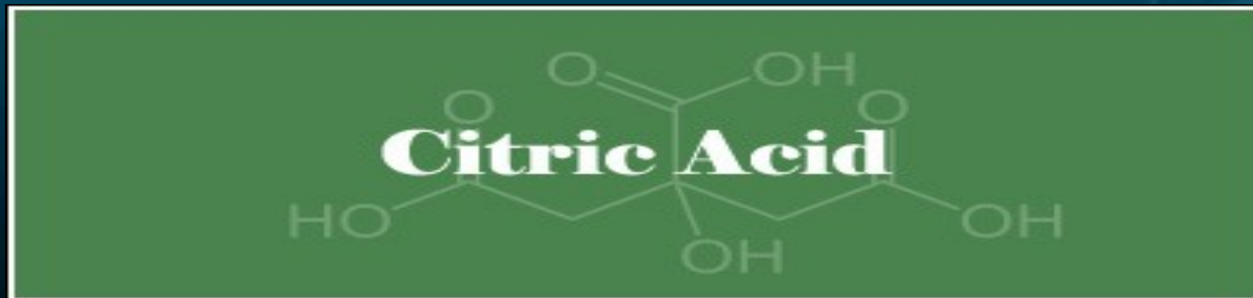
After preparation, the pH values of the emulsions were measured by using a pH meter. The pH values of the emulsions were varied between 7-8



What does pH value 5.5 mean?

The skin's acid protection mantle protects against harmful environmental influences and pathogens. A neutral pH value harms this protective barrier function and can in the worst case even destroy the skin's surface, i.e. lead to dehydration, irritation and allergies. PH neutral - pH value 7- is not the right value to keep skin healthy. Skin exposed to pH neutral products needs several hours in order to regenerate again.

Optimal protection and compatibility with the skin is only achieved with a pH value of 5.5.



What it is?

Citric Acid is an Alpha Hydroxy Acid (AHA). It exists in a variety of fruits and vegetables like lemons, limes, oranges, tangerines and blackberries but can also be made from fermented sugar solutions. At room temperature, it is a white, crystalline powder.

What it does?

Citric Acid is used in cosmetics and personal care products as a preservative and to adjust the pH balance. It is also used to impart a lemon-like fragrance to a product. In addition, Citric Acid, is also said to have antioxidant and toning properties.

Side effects?

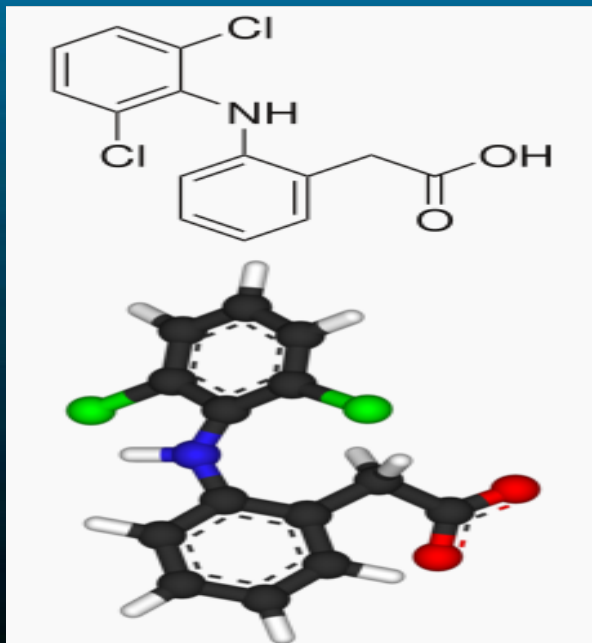
Excessive exposure to Citric Acid can cause **mild skin and eye irritations**. Allergies are rare, but can occur.

In addition, Citric Acid, may increase photosensitivity, so products containing this ingredient should be used in conjunction with a sunscreen.

Diclofenac

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) taken to reduce inflammation and as an analgesic reducing pain in certain conditions.

Derived from its chemical name: 2-(2,6-dichloranilino) phenylacetic acid



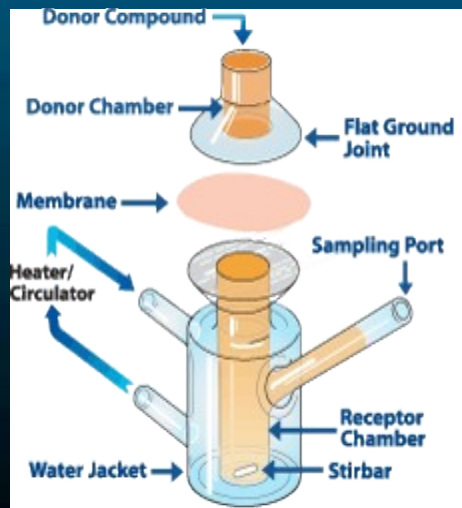
Skin permeation study

The micro emulsion area was identified by constructing pseudo-ternary phase diagrams of water, olive oil and Span 80 system.

Pigs ears brought from slaughter House .

The epidermis of the pig's ear was prepared

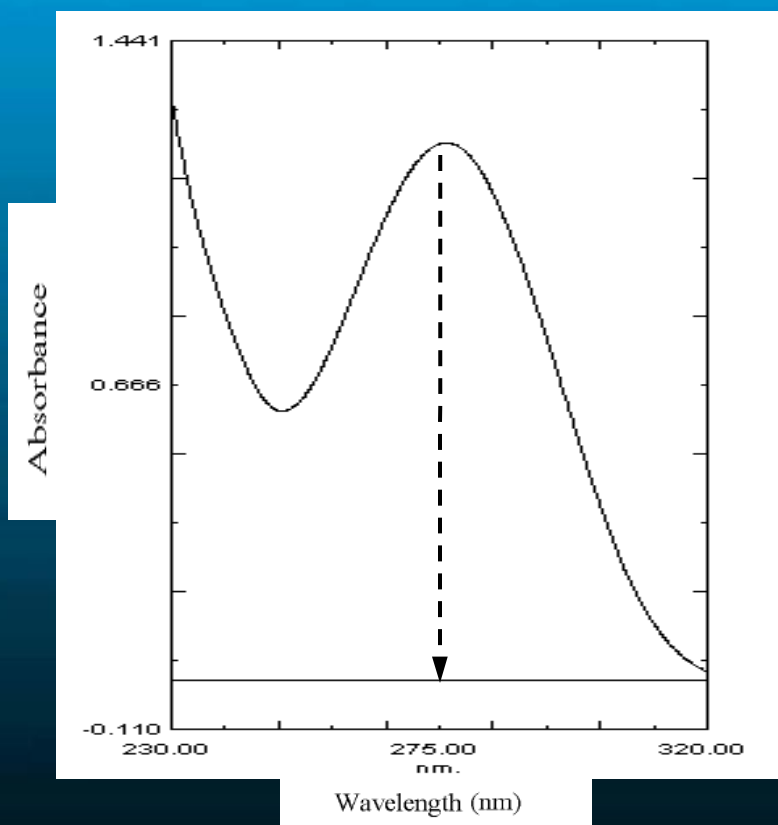
evaluated in pig ear skin using a Franz diffusion cell system



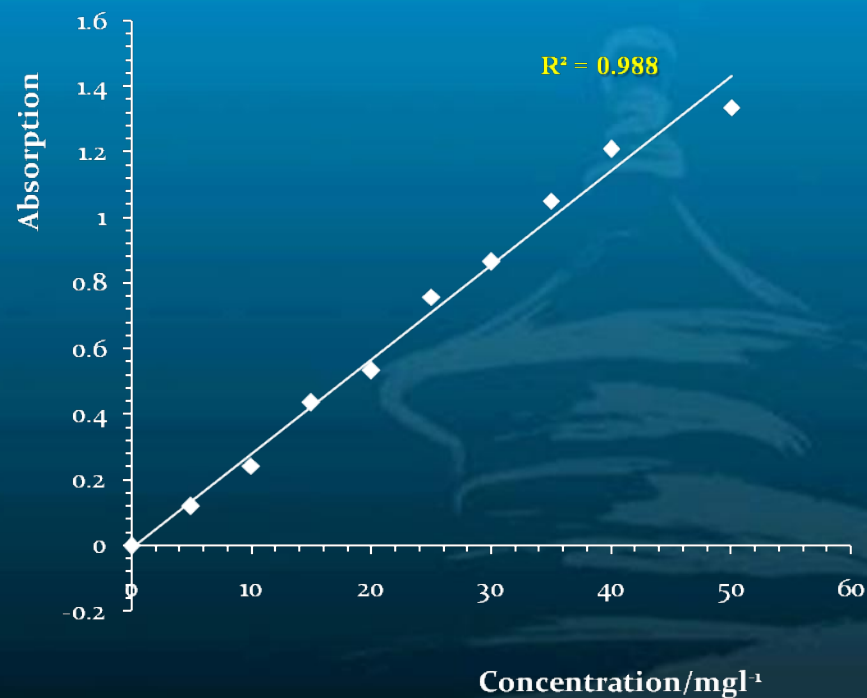
- Flux (J_{ss}) permeability coefficient (K_p) and average permeability of micro emulsion and commercially available cream (Dicloran* Gel) which contains Diclofenac sodium, were calculated

Determination of Diclofenac (Sodium salt) by UV/ Visible Spectroscopy

The absorption spectra was drawn by using UV/ Visible spectrophotometer for 40 mgdm⁻³ standard solution of Diclofenac sodium. λ_{\max} is 276.1 nm

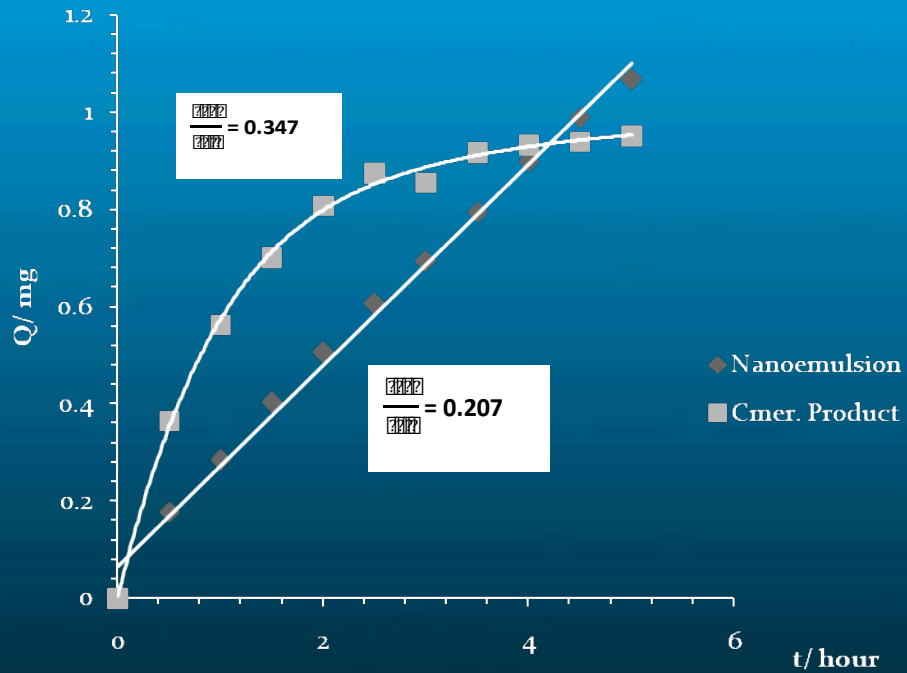


Absorption spectra of the Diclofenac (40 mgdm⁻³).



Calibration curve for Determination of Diclofenac

Calculations



Cumulative mass variations with time for Microemulsion and commercial gel

Table: Variation of Cumulative mass with time

Time/hours	Total mass /mg (Microemulsion)	Total mass /mg (Commercial product)
0.0	0.000	0.000
0.5	0.178	0.366
1.0	0.285	0.564
1.5	0.404	0.701
2.0	0.506	0.808
2.5	0.606	0.876
3.0	0.695	0.856
3.5	0.796	0.918
4.0	0.899	0.934
4.5	0.990	0.941
5.0	1.069	0.953

$$\left. \begin{array}{l} \text{Average Steady state flux (J)} \\ \text{mgh}^{-1}/\text{cm}^2 \end{array} \right\} = \frac{dQ}{dt} * \frac{1}{A}$$

$$\text{Microemulsion} = 5.22 * 10^{-4} \text{ mgmin}^{-1}\text{cm}^{-2}$$

$$\text{Commercial product} = 8.75 * 10^{-4} \text{ mgmin}^{-1}\text{cm}^{-2}$$

$$\text{Permeability (K}_p) = \frac{J}{\Delta C_v}$$

(*By the assumption infinite donor concentration; microemulsion = 12000 ppm, com pro = 37037.04)

$$\begin{aligned} (K_p), \text{ Microemulsion} &= 5.22 * 10^{-4} \text{ mg min}^{-1}\text{cm}^{-2} / (12.00 \text{ mgcm}^{-3}) \\ &= 4.35 * 10^{-5} \text{ cmmin}^{-1} \end{aligned}$$

$$\begin{aligned} (K_p), \text{ Commercial product} &= 8.75 * 10^{-4} \text{ mg min}^{-1}\text{cm}^{-2} / (37.04 \text{ mgcm}^{-3}) \\ &= 2.36 * 10^{-5} \text{ cmmin}^{-1} \end{aligned}$$

$$\text{Total drug percentage penetrate through the skin} = \frac{\text{Receiver concentration}}{\text{Donor concentration}} * 100\%$$

$$\text{Microemulsion} = 44.54 \%$$

$$\text{Commercial product} = 35.30 \%$$

Future planes.....

- Modify the method of formulating emulsions.
- Introduce Drugs (Diclofenac sodium) compounds, antioxidant compounds and study the stability of microemulsions and the release of compounds with time and compare the release with commercially available products.
- Characterization of microemulsions formulated using Particle size analyzer, Polarized microscopy measurements, **DSC** measurements. Etc.
- Study new systems for emulsion formulations using naturally available compounds.

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*Thank
you*