ENCAPSULATION EFFICIENCY, INTEGRITY AND IN VITRO SKIN PENETRATION ENHANCEMENT OF DIFFERENT TYPES OF ELASTIC VESICLES

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BACKGROUND

Over the last years, topical drug delivery by vesicular carriers with flexible bilayer system has evoked a considerable interest.

Transfersomes, introduced by Cevc and Blume [1] were the first generation of elastic vesicles. They consist of *phospholipids* and an *edge activator* (single chain surfactant). The vesicles' high deformability allows them to open pores through the skin and are expected to be able to trespass stratum corneum as intact vesicles.

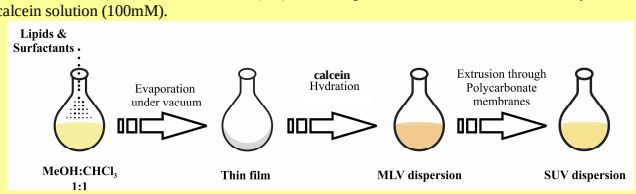
Invasomes (Fahr et al.) [2] are another type of elastic vesicles designed for topical application. They are composed of a mixture of *phospholipids in ethanol* and *terpenes* which are well known to act as penetration enhancers.

PURPOSE OF THE STUDY

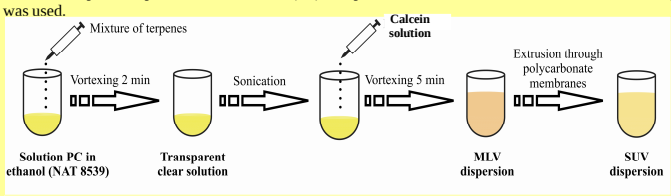
Objective of this study was the investigation of stability and in vitro permeation enhancing effect of two different types of flexible liposomes: Transfersomes and Invasomes.

PREPARATION OF VESICLES

Liposome/Transfersome Preparation: Conventional liposomes and Transfersomes were prepared by the thin film method using purified soybean lecithin (Lipoid S75). Transfersomes contained additionally sodium cholate (SChol) or Tween 80 (Tw) as an edge activator. The thin film was hydrated with a calcein solution (100mM).



Invasome Preparation: Invasomes were prepared by injecting the calcein solution in the ethanolic solution of lipids. As penetration enhancers (PE) a terpene mixture of limonene:citral:cineol=10:45:45) was used.



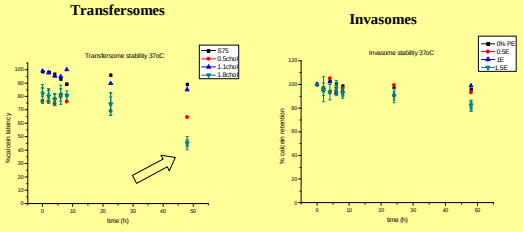
ENCAPSULATION EFFICIENCY (DRUG/LIPID)

Liposomes	D/L drug/lipid
S75	0.045 ± 0.0028
Transfersomes	**D/L**
S75:Schol (0.5%)	0.030 ± 0.0015
S75:Schol (1.1%)	0.021 ± 0.0014
S75:Schol (1.8%)	0.014 ± 0.00026
S75:Tween (0.5%)	0.068 ± 0.0016
S75:Tween (1.1%)	0.062 ± 0.0032
S75:Tween (1.8%)	0.045 ± 0.0044
Invasomes	**D/L**
0% PE	0.021 ± 0.00016
0.5 % PE	0.013 ± 0.00039
1 % PE	0.013 ± 0.00101
1.5 % PE	0.019 ± 0.0026

➢D/L decreases with increase of %surfactant possibly due to increase of vesicle deformability (previous findings-not presented here)

CALCEIN RETENTION

Integrity of vesicles versus time at 37ºC with respect to calcein retention



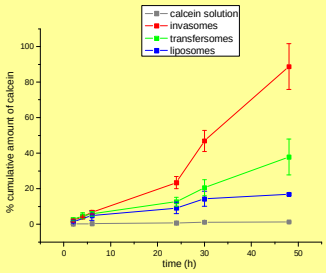
❖Transfersomes are less stable than invasomes at 37°C incubation in terms of calcein retention

IN VITRO PERMEATION STUDY

Calcein-a model hydrophilic drug-was used in order to investigate the permeation of calcein using vesicles through human abdominal skin.

Certain liposome formulations were chosen and tested on the skin for their ability to deliver calcein transdermally.

Samples were incubated on Franz diffusion chambers (3.14 cm^2) occlusively for 48 h at 37 ºC.



Permeation of calcein from different liposome formulations through human skin (n=3)

❖Permeation of liposomes is increased with the following order : Inv>>Tra>con>sol

Table: Permeability coefficient, flux and enhancement ratio

	P (cm/h)	Flux (μg/cm^2*h)	ER
Calcein solution	8.71E-05 ± 1.08E-06	7.59E-03 ± 9.41E-05	-
Liposomes	1.08E-03 ± 4.10E-05	9.41E-03 ± 3.58E-04	**1.24**
Transfersomes	2.46E-03 ± 8.24E-04	1.43E-02 ± 1.15E-03	**1.88**
Invasomes	6.34E-03 ± 9.15E-04	5.49E-02 ± 7.92E-03	**7.23**

➢ Liposomes were able to increase the permeation of calcein through the skin compared to plain drug solution.

➢ Furthermore, Elastic liposomes were more efficient than plain liposomes in delivering calcein and compared to each other Invaseomes were found to be the most effective drug delivery system under the conditions used.

CONCLUSIONS

✓ Encapsulation efficiency of flexible liposomes gradually decreased upon increase of surfactant or terpene mixture.

✓ Flexible liposomes were stable at 37 ºC in terms of calcein retention, but Transfersomes were found to be more unstable compared to Invasomes especially at high surfactant concentration. sfdfg

✓ Permeation experiments have shown that flexible liposomes were able to deliver calcein through the skin more successfully than plain liposomes and that Invasomes in particular were the most successful delivery system.

ACKNOWLEDGMENTS:

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References:

[1] G. Cevc, A. Schätzlein, G. Blume: Journal of Controlled Release 36 (1995):3-16

[2] D.D. Verma, A. Fahr: Journal of Controlled Release 97 (2004):55-66