S.O.Si.
Società Oftalmologica Siciliana

Hilton Hotel Giardini Naxos

Liposomi nanotecnologici: dimostrazione potere antiossidante in vitro e in vivo

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NEST
NEUROVISUAL SCIENCE TECHNOLOGY

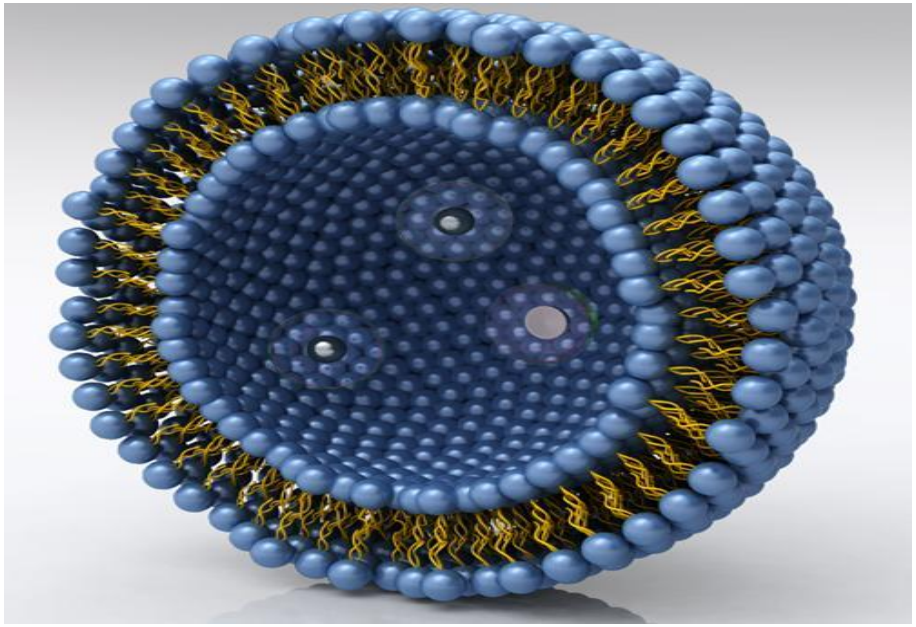
SICILIAE STVDIVM GENERALE · 1434 ·

Cosa sono i liposomi?

Vescicole costituite da doppi strati a struttura lamellare di fosfolipidi , prodotti da lecitina di soia ad alta concentrazione di fosfatidilcolina, fosfatidilinositolo e lisofosfatidilcolina.

STRUTTURA

- Multilamellari
- Diametro tra 500 e 10000 nm
- Struttura a buccia di cipolla



- Unilamellari
- Diametro tra i 25 e 100 nm

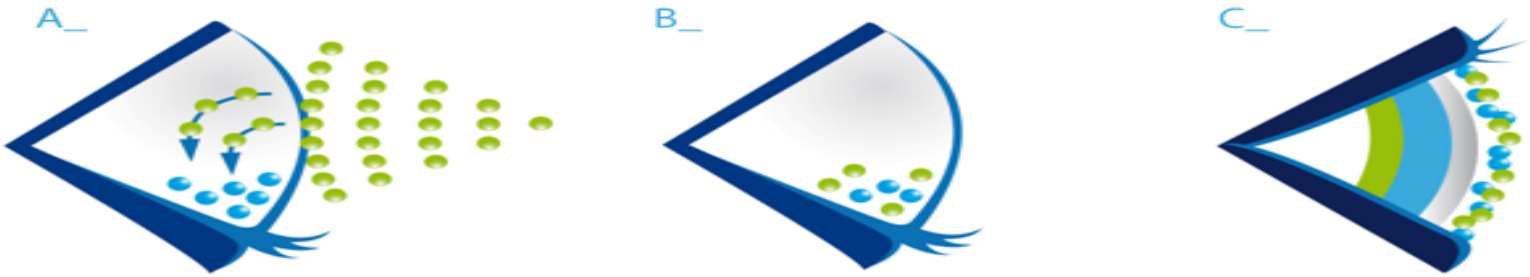
Liposomi nanotecnologici

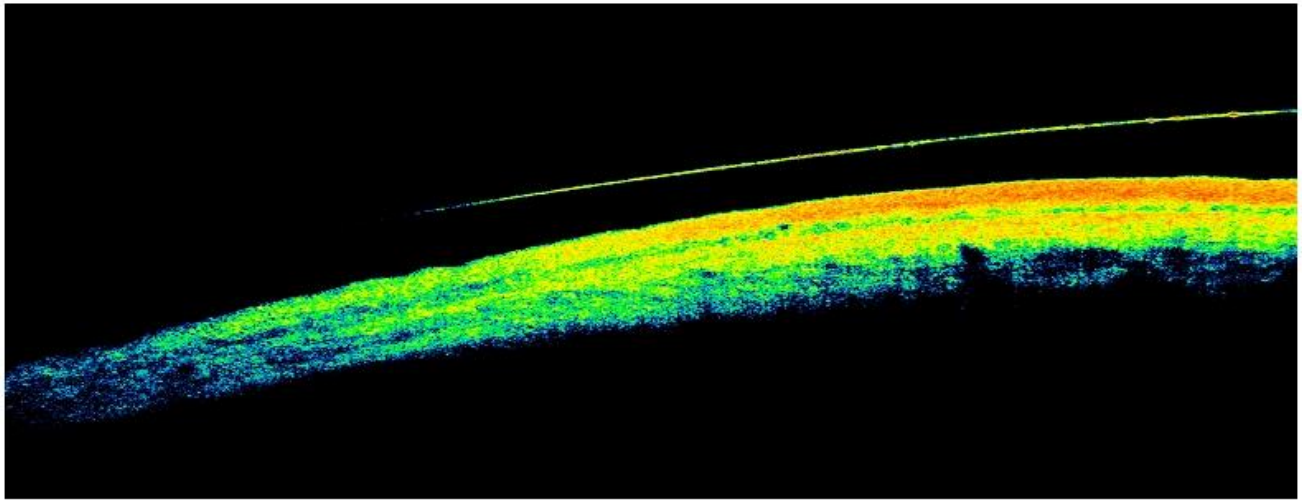
Più piccola è la dimensione dei liposomi e maggiore e più rapido sarà l'assorbimento della sostanza di interesse.

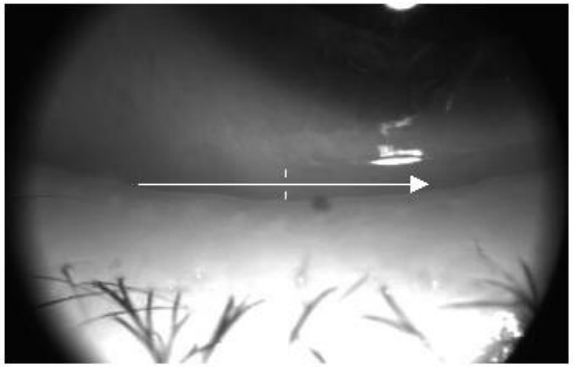
Ad una riduzione delle dimensioni corrisponde infatti un aumento dell'area superficiale disponibile al contatto con l'epitelio

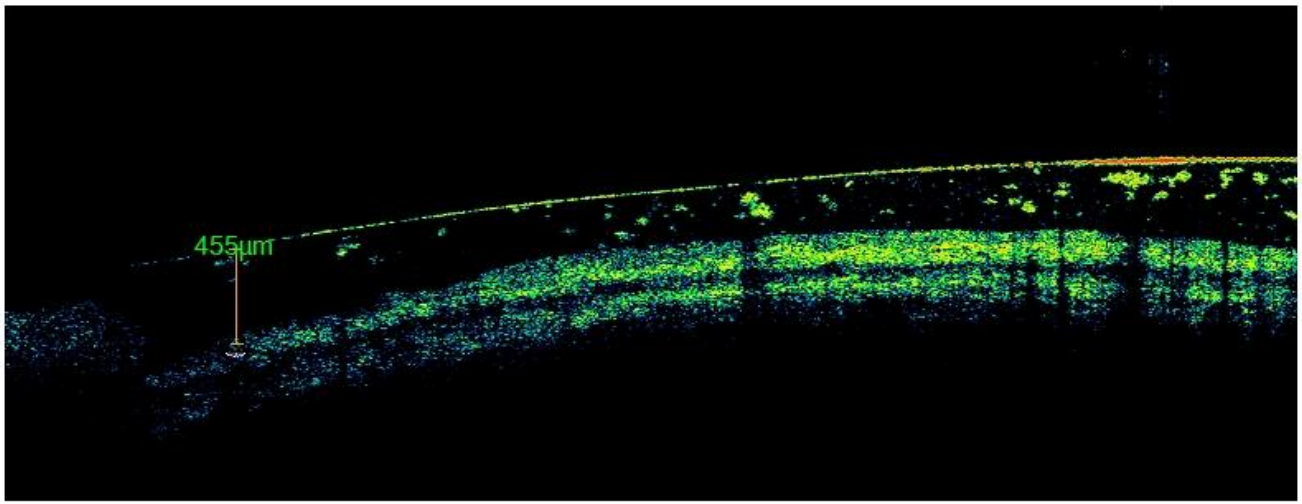
Perché utilizzare i liposomi?

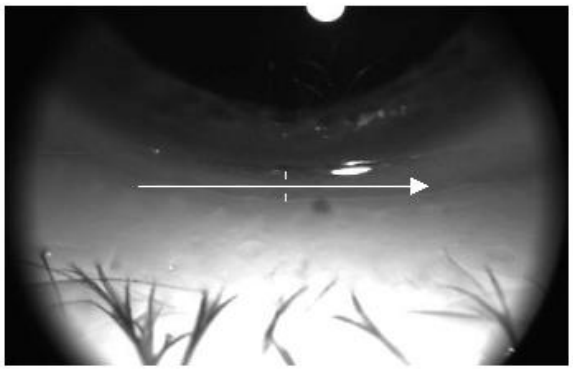
- Sono biodegradabili e biocompatibili
- Uniforme distribuzione del principio attivo
- I componenti attivi sono già solubilizzati
- La componente lipidica migliora la lubrificazione oculare e palpebrale
- Riducono l'evaporazione lacrimale
- Possibilità di caricare principi attivi all'interno (es. aminoacidi, vitamine A ed E)

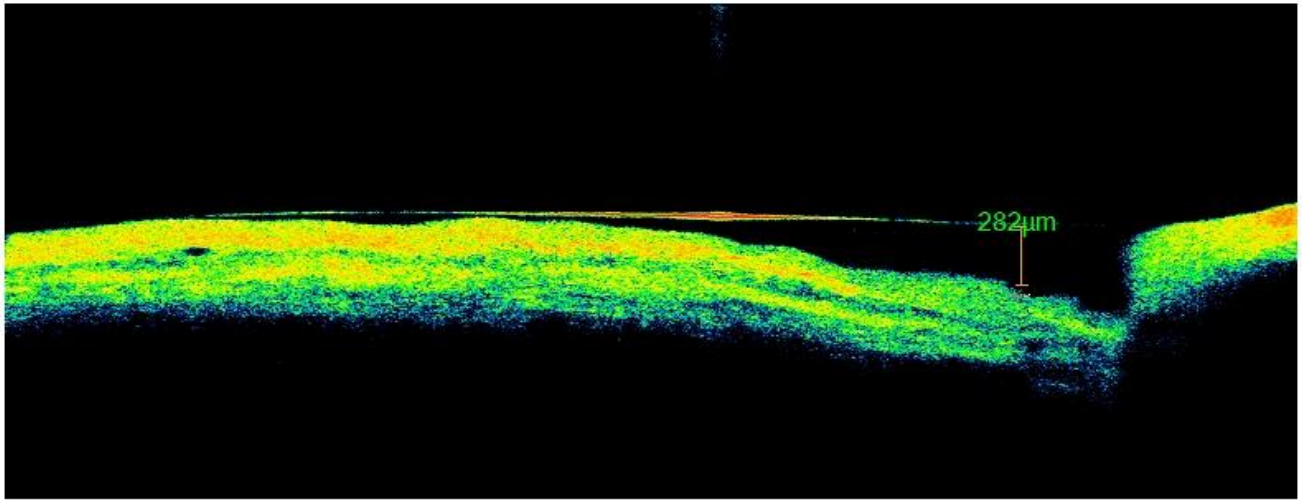


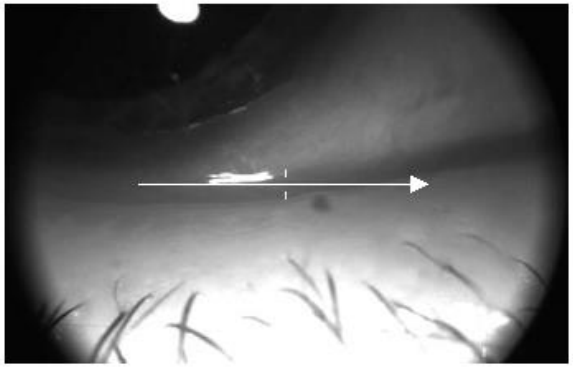


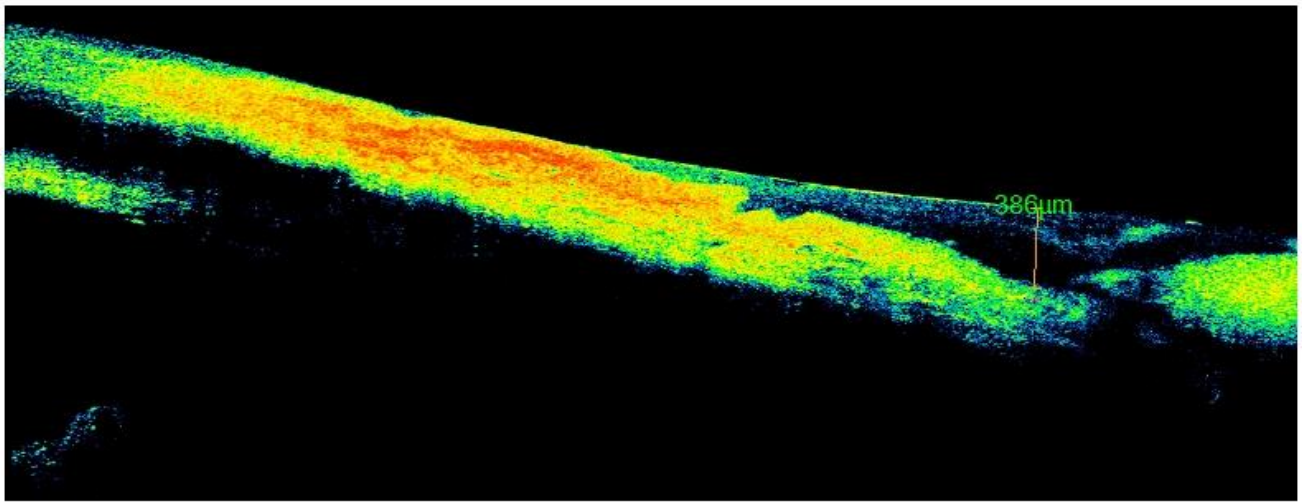


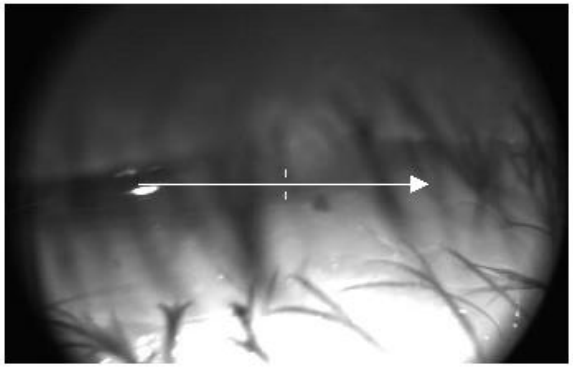

455µm




282µm




386µm

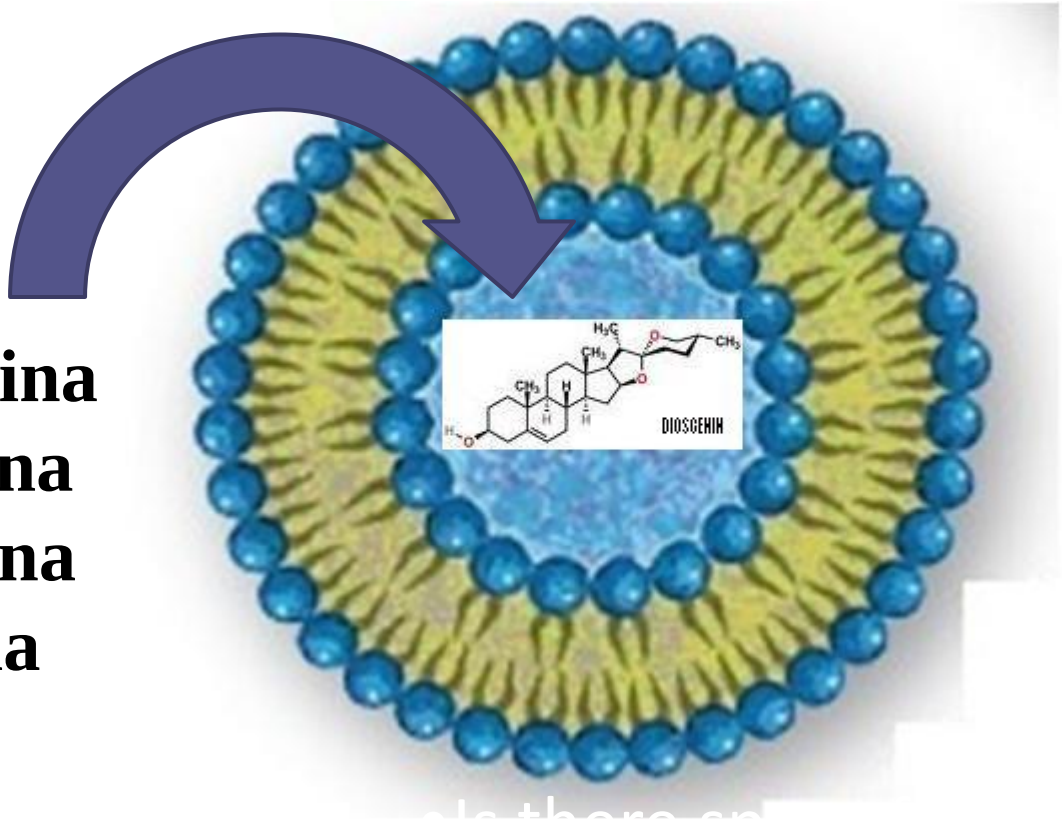


Usi tradizionali delle lacrime artificiali a base di liposomi e vitamine

- Sostituire la componente lipidica delle lacrime e ritardare l'evaporazione del film lacrimale
- La formulazione spray favorisce la normale distribuzione lacrimale con l'ammiccamento
- Sommare l'efficacia antiinfiammatoria di fosfatidilcolina, fosfatidilserina e l'attività antiossidante delle vitamine A ed E.
- Intervento diretto sul margine delle palpebre

VETTORI DI AMINOACIDI

Leucina
Glicina
Prolina
Lisina



Meccanismo anti infiammatorio degli aminoacidi

EQUILIBRIO
OMEOSTASI
CORNEALE

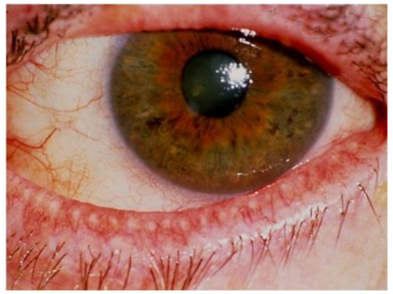
Sindromi da occhio secco nel paziente reumatologico

Malattie reumatologiche

- Sindrome di Sjogren (primaria e secondaria)
- Lupus eritematoso sistemico
- Sclerodermia
- Artrite reumatoide
- Vasculiti
- Connettiviti

Caratteristiche

- Nel 92% grave disfunzione lacrimale **su base lipidica**
- Dry eye iatrogeno
- Esacerbazione delle cause infiammatorie



Meibomian Gland Dysfunction in Patients with Sjögren Syndrome

Jun Shimazaki, MD, Eiki Goto, MD, Masafumi Ono, MD, Shigeto Shimmura, MD, Kazuo Tsubota, MD

Cornea

In Vivo Confocal Microscopy of Meibomian Glands in Sjögren's Syndrome

Edoardo Villani, Silvia Beretta, Michela De Capitani, Daniela Galimberti, Francesco Viola, and Roberto Ratiglia

Tear Evaporation Rates in Sjögren Syndrome and non-Sjögren Dry Eye Patients

EIKI GOTO, YUKIHIRO MATSUMOTO, MIZUKA KAMOI, KOJI ENDO, REIKO ISHIDA, MURAT DOGRU, MINAKO KAIDO, TAKASHI KOJIMA, AND KAZUO TSUBOTA

ARVO
The Association for Research in Vision and Ophthalmology

CONTROL ID: 1905709

TITLE: Investigation of tear osmolarity in systemic sclerosis: relation to disease activity.

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ABSTRACT BODY:

Purpose: To investigate the frequency of dry eye syndrome (DES) by measuring tear osmolarity with TearLab system (TearLab Corp, San Diego, Calif.) in patients with systemic sclerosis (SSc) and the relationship between the severity of DES and SSc disease activity.

Servizio di Immunologia Oculare

Methods: In this cross-sectional prospective study, 44 consecutive patients with SSc were enrolled; this study was performed according to the declaration of Helsinki and was approved by an institutional ethic commission. Twenty-two right eyes of all enrolled patients were examined in this study. Tear osmolarity measurements, tear break-up time (TBUT) test, and Schirmer's tests (type I and II) were performed. SSc disease activity was evaluated according to the disease activity score calculated with modified Rodman Skin Score (mRSS). Skin thickening is assessed on 17 body areas: fingers, hands, forearms, arms, feet, legs and thighs (bilaterally), and the face, chest and abdomen (singly). Each area is scored from 0 to 3, where 0 is normal skin and 3 is severe thickening (range 0 (no thickening) to 51 (severe thickening) in all 17 areas). The patients were divided into 3 groups according to mRSS scores as follows: mild (mRSS ≤ 3.2), moderate (3.2 < mRSS ≤ 5.1), and severe (mRSS > 5.1).

Results: DES was identified in 34 (77.2%) patients with SSc according to the classification of Dry Eye Disease of International Dry Eye Workshop (2007) and tear osmolarity values according to recommendations of the manufacturer with a cutoff value of 308 mOsm/L. There were significant differences among the 3 groups (divided according to the mRSS score) concerning tear osmolarity ($p < 0.001$) and TBUT ($p < 0.05$) scores, whereas there was no significant difference between these groups regarding Schirmer scores ($p > 0.05$). In addition, mRSS values were positively correlated with tear osmolarity values ($r = 0.610$, $p < 0.001$), negatively correlated with Schirmer scores, ($r = -0.231$, $p = 0.045$), and negatively correlated with TBUT scores ($r = -0.325$, $p = 0.007$) among all patients.

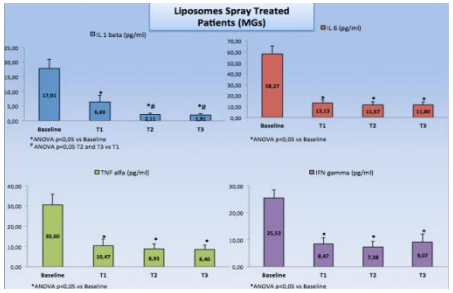
Conclusions: Our study demonstrated a high prevalence of DES in patients with SSc and a relationship between the SSc disease activity and severity of DES by using tear osmolarity measurements with the TearLab system. Therefore, tear osmolarity measurement can not only be added to other classical tests for diagnosing DES but could also be used for assessing the degree of disease activity of SSc.

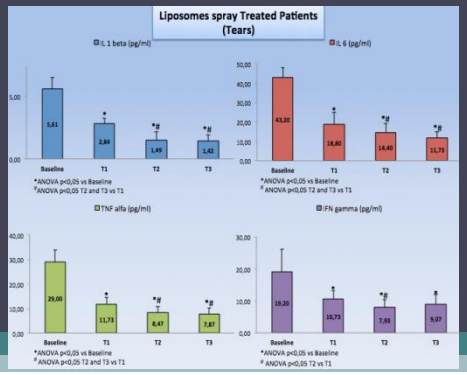
Changes in cytokine profile with liposomes sprayed on the ocular surface and nasal mucosa

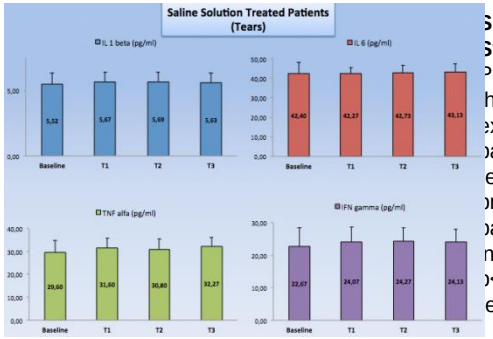
Author Block: *Scollo, Davide[1]; Avitabile, Teresio[1]; Malaguarnera, Giulia[1]; Amato, Roberta[1, 2]; Napolitano, Giuseppe[2]; Marrazzo, Giuseppina[1]; Reibaldi, Michele[1]; Longo, Antonio[1]; Gagliano, Caterina[2].*
INSTITUTIONS (ALL): [1] Eye Clinic, Catania University (Italy); [2] NEST (Neurovisual Science Technology) srl, Catania, Italy

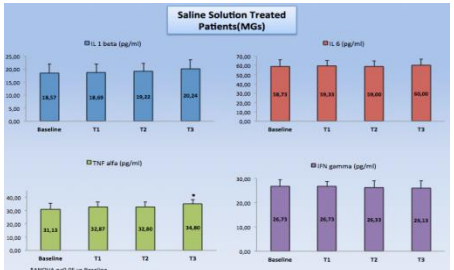
Purpose

Increased levels of several inflammatory cytokines have been correlated with clinical parameters in Dry Eye Desease (DED) [1] and in allergic rhinoconjunctivitis [2]. Tear cytokine levels are already considered as potential markers of inflammation in many ocular diseaes [3]. Pro- and anti-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease were detected [4, 5]. Inflammatory cytokines in the tears of dry eye patients were identified as markers in patients with ocular surface disease [6, 7].
The aim of the present study was to evaluate the effect of sprayed liposomes on signs and symptoms of nasal, pharyngeal and ocular discomfort to measure the levels of inflammatory cytokines in patients with DED and allergies.









Results

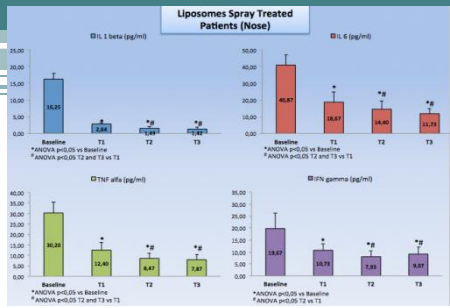
A highly significant reduction was detected in the inflammatory cytokine levels in tears, meibomian glands secretion, and nasal wash of patients treated with the spray liposomes solution in comparison with saline solution controls. Control patients showed elevated levels for most of the tested cytokines. IL-1β was found to be elevated 2.75-fold (P<0.001) at the second week and 3.2 at the end (P<0.001) of treatment in control group with respect to the treatment group with spray liposomes. We also found a significant increase (P<0.01) of inflammatory cell expression in control group after 3 weeks.

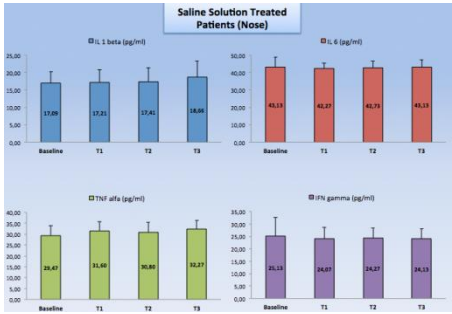
Subjective Assessments Relief of Symptoms

Patients treated with liposomal spray reported that their symptoms disappeared for an extended time period compared to control patients. The question “Did you experience relief of your symptoms when using the preparation" was answered differently by patients of the two groups (T-test for independent samples: T = -3.165; df = 54; p< .01). On average, patients felt the greatest relief when applying the liposomal eye spray.

Clinical advantages

The treatment with liposomes sprayed on eye lid and nasal mucosa show statistically significant clinical advantages: improvement of the examined parameters LIPCOF, BUT, Schirmer, Visual Acuity and inflammation of the lid margin in liposomes spray treated group.





Conclusions

This study showed the ability of spray liposomes loaded with vitamin A and E to modify the pro-inflammatory cytokine profile after their administration on nasal mucosa, eyelid and ocular surface. This effect could be due to the anti-inflammatory mechanism of the vitamins and also to the barrier effect of liposomes on mucosal surfaces.

Nostro studio

- **Scopo del lavoro**

Valutare le modifiche dei segni e dei sintomi di disfunzione lacrimale associata ad alterazione delle ghiandole di Meibomio in soggetti affetti da malattie reumatologiche dopo terapia con liposomi nanotecnologici + vit. A ed E in formulazione spray.

Pazienti

- ✓ Reclutati 16 pazienti con diagnosi accertata di malattia reumatologica e Disfunzione lacrimale severa con Meibomian Gland Disease (MGD)
- ✓ Età: 45,25 ± 7,67 (media ± DS)
- ✓ Genere: 12 donne; 4 uomini
- ✓ Acuità Visiva Corretta: 8,75 ± 1,43 (media ± DS)

Trattamento

- Liposomi nanotecnologici in formulazione spray caricati con vitamina A ed E

Dosaggio

1 nebulizzazione tre volte al dì

Tempi di osservazione

T0 (basale)*

T2 (dopo 15 gg)

T3 (dopo 30 gg)

T4 (dopo 60 gg)

T5 (dopo 90 gg)

A questi intervalli sono stati effettuati:

° Schirmer basale

° T-BUT

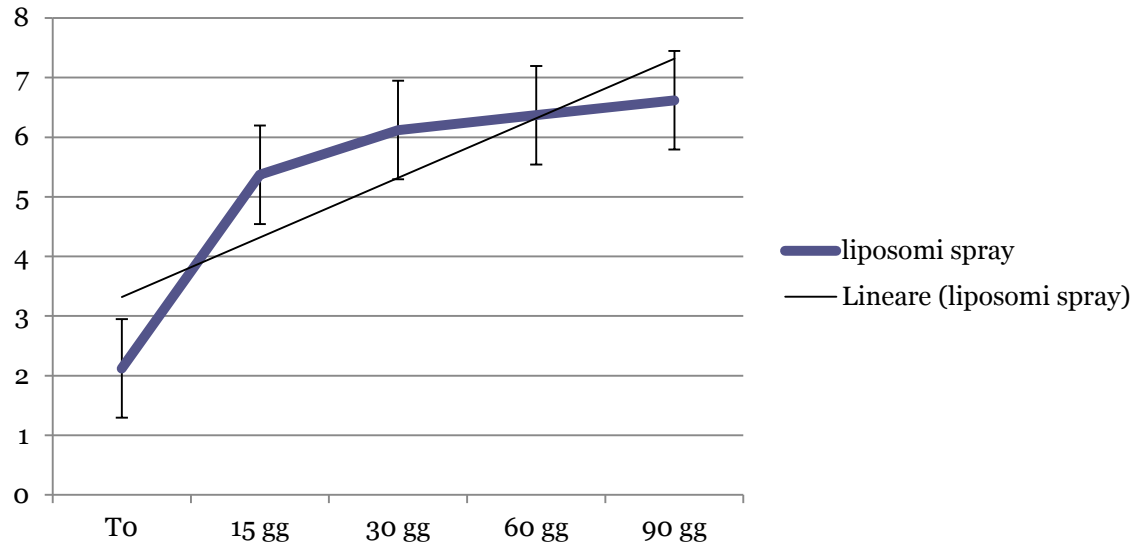
° Lipcof (pieghe congiuntivali)

° Infiammazione del margine palpebrale

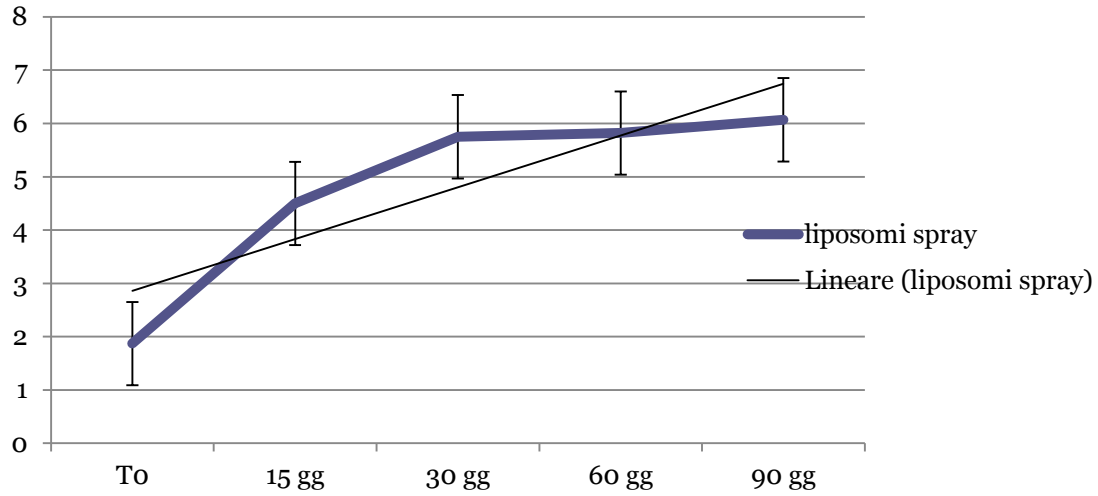
° Osmolarità

° Dryness (sintomi)

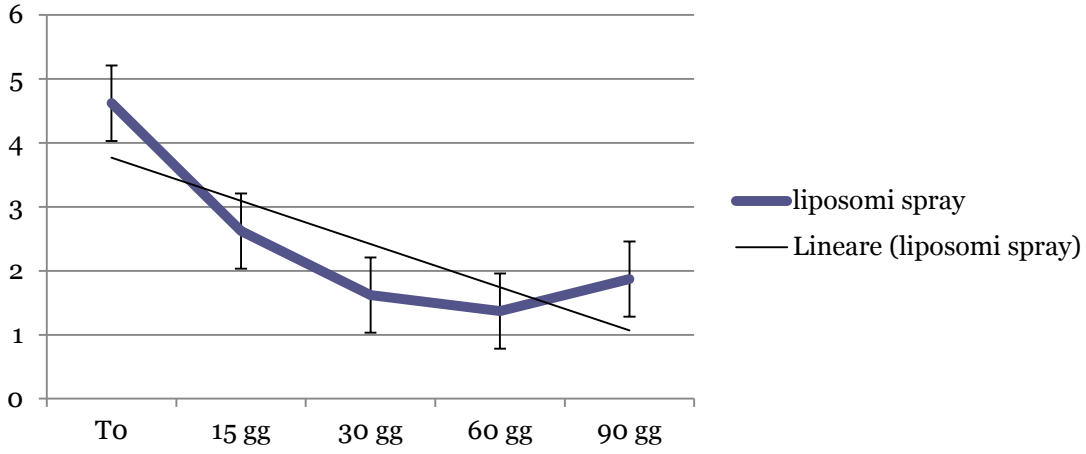
Shirmer Test



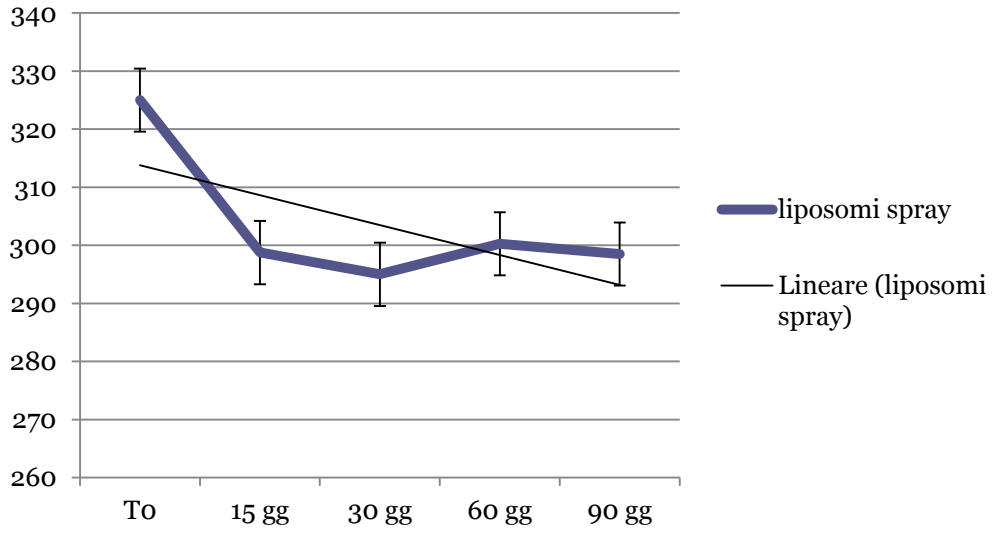
T - BUT



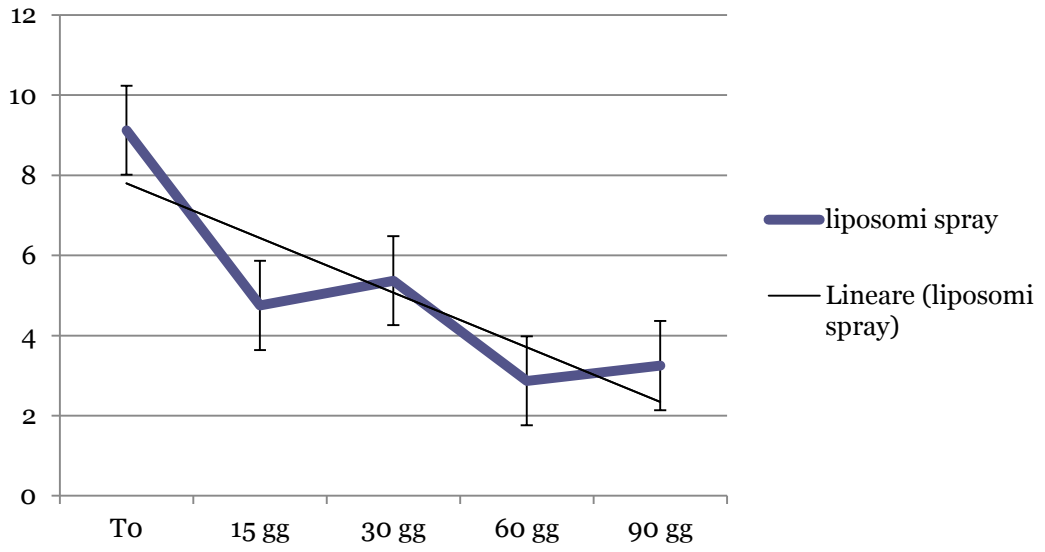
Inflammation



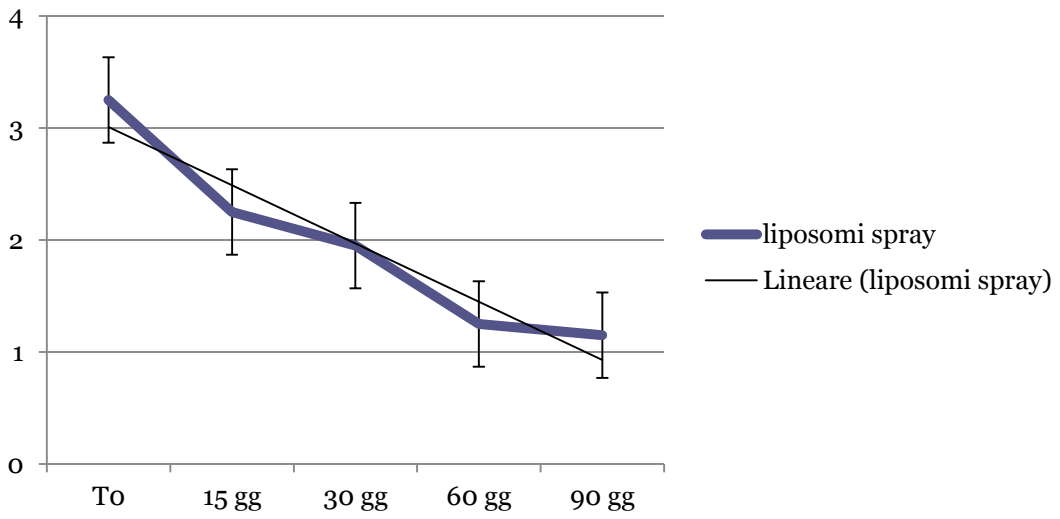
Osmolarity



Dryness



Lipcof



LIPOSOMI NANOTECNOLOGICI IN FORMULAZIONE SPRAY:

- **EFFETTO ANTIINFIAMMATORIO SULLA SUPERFICIE OCULARE E SUL MARGINE PALPEBRALE**

- **SOSTITUTI LIPIDICI LACRIMALI EFFICACI NELLE FORME DI DRY EYE GRAVE IN PAZIENTI AFFETTI DA PATOLOGIE REUMATOLOGICHE**

STUDI IN VITRO

- ANALISI DELLA ESPRESSIONE DI CITOCHINE PROINFIAMMATORIE IN

- CELLULE DEL SISTEMA MONOCITO-MACROFAGICO
- CELLULE EPITELIALI CORNEALI E CONGIUNTIVALI DI CONIGLIO
- CELLULE DA CITOLOGIA CONGIUNTIVALE AD IMPRESSIONE UMANE

- TRATTATE CON
- - LIPOSOMI
- VITAMINA A ed E
- AMINOACIDI (L-PROLINA, L-GLICINA, L-LISINA CLORIDRATO, L-LEUCINA)

Analisi molecolari

- **Estrazione mRNA utilizzando la soluzione TRIzol**
- **Analisi espressione citochine proinfiammatorie (IL-6, IL-1, TNF- ALFA, HMOX-1) mediante RealTime PCR e Western Blot**
- Esame proprietà antinfiammatorie delle vitamine libere, degli aminoacidi e degli stessi incapsulati nei liposomi.

GRAZIE