Encapsulation of the colorant, acid red 51 (C.I. 45430) in lipid microparticles : effect on photodegradation

***S. Scalia*[1], *A. Dozzo*[1], *G. Scarcella*[2]**

[1]Dept. of Life Science and Biotechnology, University of Ferrara (Italy)

[2]G.Fracastoro Hospital, Verona (Italy)

UNIVERSITÀ DEGLI STUDI DI FERRARA

- EX LABORE FRUCTUS -

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Tattoo inks composition

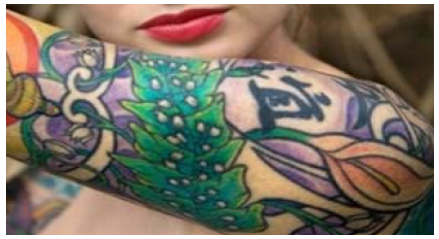
COUNCIL OF EUROPE CONSEIL DE L'EUROPE
Committee of Ministers
Comité des Ministres

Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up. (ResAP-2003-2)

"Tattooing is a practice whereby a permanent skin marking or design is administered by intradermal injection of products consisting of colorants and auxiliary ingredients" .

"A permanent make-up (PMU) consists of colorants and auxiliary ingredients which are injected intradermal for the purposes of enhancing the contours of the face".

PMU also used to hide pathological conditions, camouflage of scars, vitiligo, alopecia, breast cancer surgery



Tattoos: potential health problems

→ **Bacterial contamination**

→ **Long term exposure to the injected chemicals, their impurities and degradation products**

✔ **No specific legislation on tattoo colorants**

✔ **Several pigments present in tattoos are not authorized in cosmetics**

- ***Simunovic et al.,*** Complications of decorative tattoos: recognition and management. *Am J Clin Dermatol*, 15, 525 (2014)
- ***Laux et al.,*** A medical-toxicological view of tattooing. *Lancet* , 387, 395-402 (2016)
- ***Piccini et al.,*** Safety of tattoos and permanent make-up. *JRC. EUR 27528 EN* (2015)
- ***Piccini et al.,*** Safety of tattoos and PMU . Final report *JRC . EUR 27947 EN* (2016)

Photochemical behaviour of tattoo pigments

- ✔ **Several pigments have been reported to decompose following irradiation with a solar simulator generating toxic products**
- ✔ **Laser irradiation of tattoo pigments has been shown to give rise to toxic products**
- ✔ **Photo-decomposition of tattoo pigments by exposure to solar or laser light has been demonstrated also in vivo (hairless mice)**

It is essential to enhance the stability of tattoo pigments under solar or laser irradiation

- ***Cui et al.,*** Photodecomposition of pigment yello *74.Phochem Photobiol* , 175 (2004).
- ***Vasold et al.,*** Tattoo Pigments are cleaved by laser light.. *Phochem Photobiol* , 185 (2004).
- ***Engel et al.,*** Tattooing of the skin result in transportation … *Experimental Dermatology*, 54 (2010)
- ***Carlsen and Serup,*** *Photosensitvity and photodynamic ...J. Europ Acad Dermatol and Venerol*, 231 (2014).

Photochemical behaviour of tattoo pigments

✔ **Microencapsulation as possible strategy to improve the characteristics properties of tattoo pigments**

Our Approach

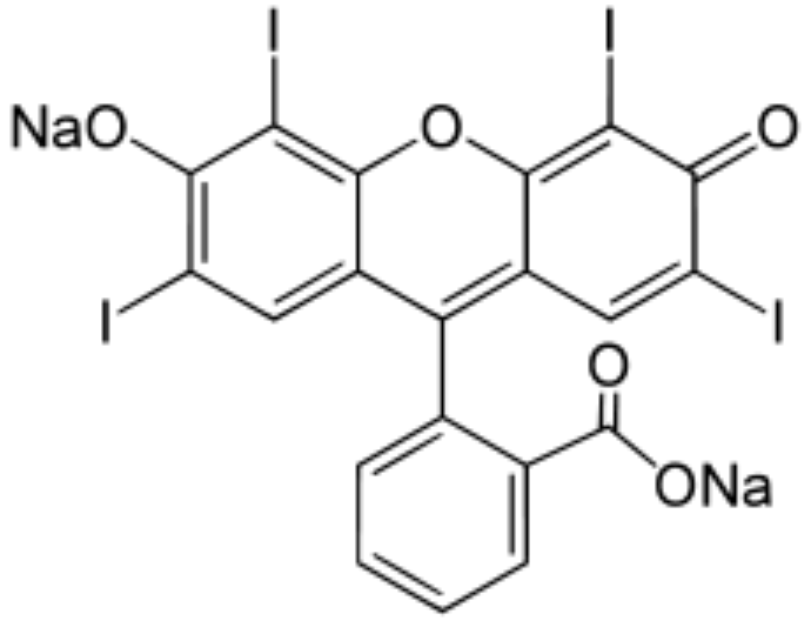
Lipid microparticles

- ***Klitzman B, Koger KE*** , inventors. Tattoo inks. USA patent 6, 013,122. Jan 11(2000)

- ***Laux et al.,*** A medical-toxicological view of tattooing. *Lancet* , 387, 395 (2016)

Photochemical behaviour of tattoo pigments

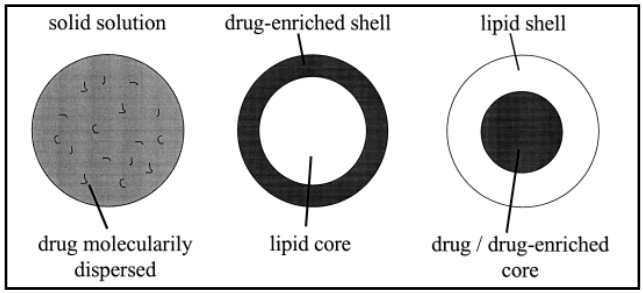
Pigment selected : C.I. 45430 (acid red 51) – EEC n. E127 ; FD&C Red 3 .



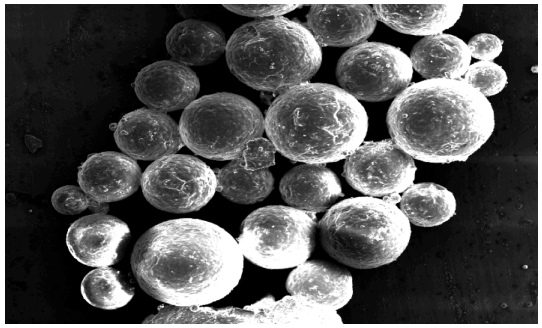
- ***Piccini et al.,*** Safety of tattoos and permanent make-up. *JRC. EUR* 27528 EN (2015)
- ***European Commission - Scientific Committee on Consumer Safety*** – Opinion on CI 45430 (Eythrosine) -22-06-2010

Why lipid microparticles

- ✓ Biocompatible (regulatorily accepted excipients, GRAS)
- ✓ Safety, tolerability
- ✓ Easy industrial-scale production, relatively low costs
- ✓ Protection of labile compounds
- ✓ Proper size for reduced diffusion and penetration through membranes (toxicity concerns related to nanoparticles)



Incorporation mechanisms in lipid microparticles

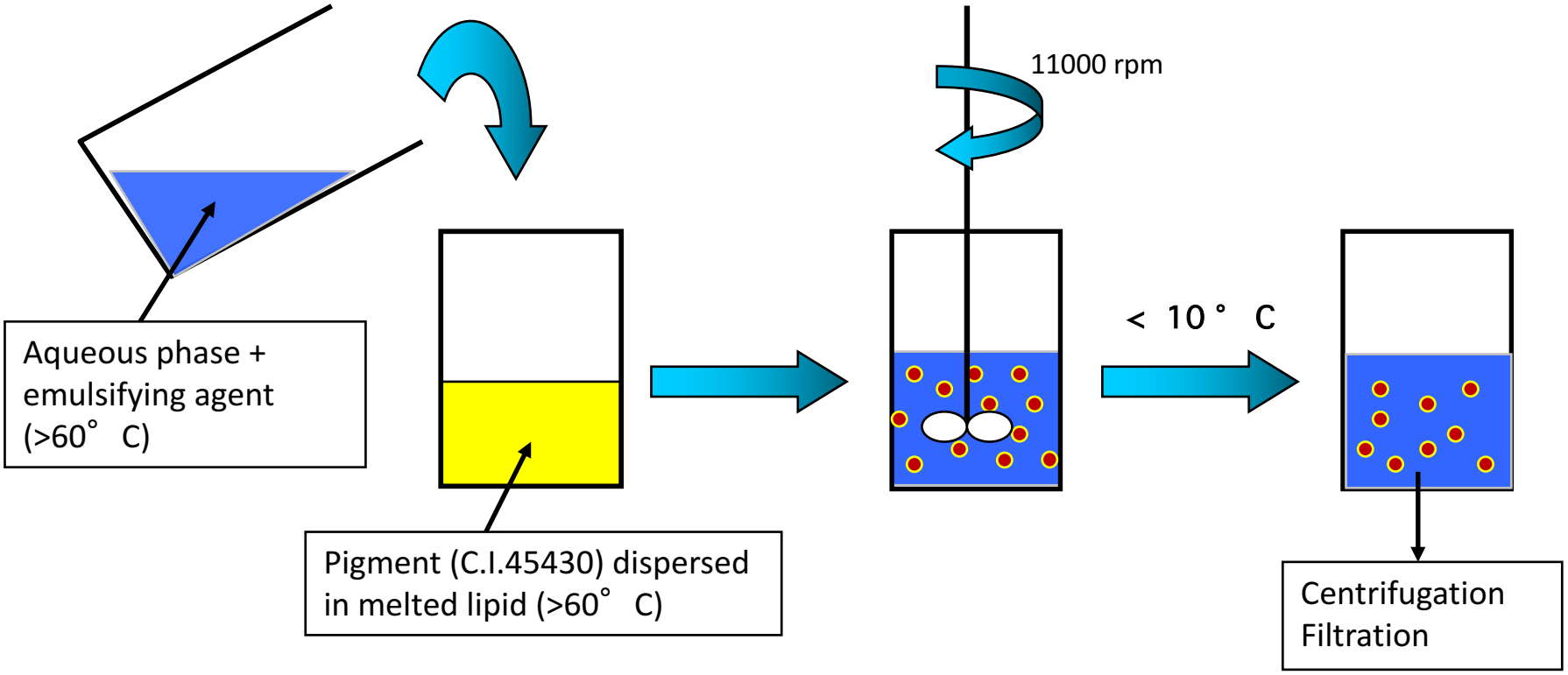


Scanning electron microscopy (SEM) image of lipid microparticles

Scalia S, Traini D, Young P. Solid lipid microparticles as an approach to drug delivery, *Exp. Opin Drug Deliv*, 583-599 (2015)

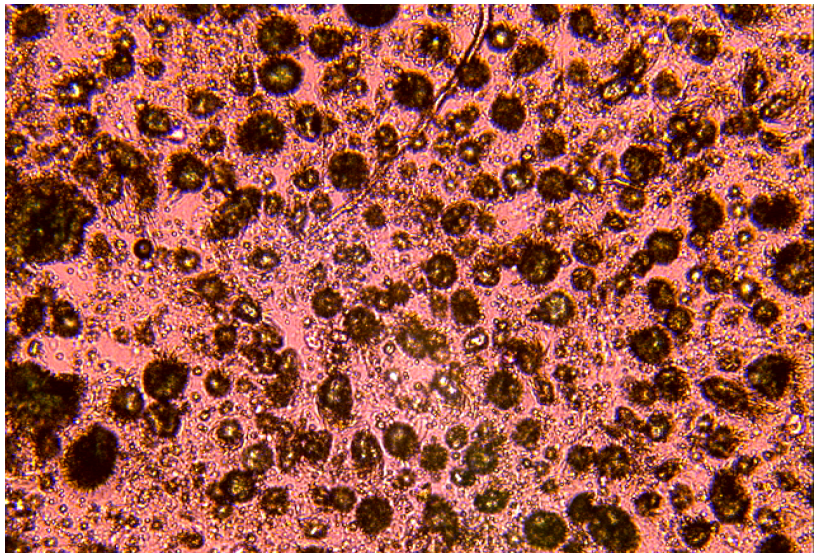
Lipid microparticles preparation

Melt emulsification technique – organic solvent-free methodology



✔ **Lipids examined** : tristearin, stearyl alcohol, cetyl palmitate, carnauba wax
✔ **Emulsifier** : phosphatidylcholine

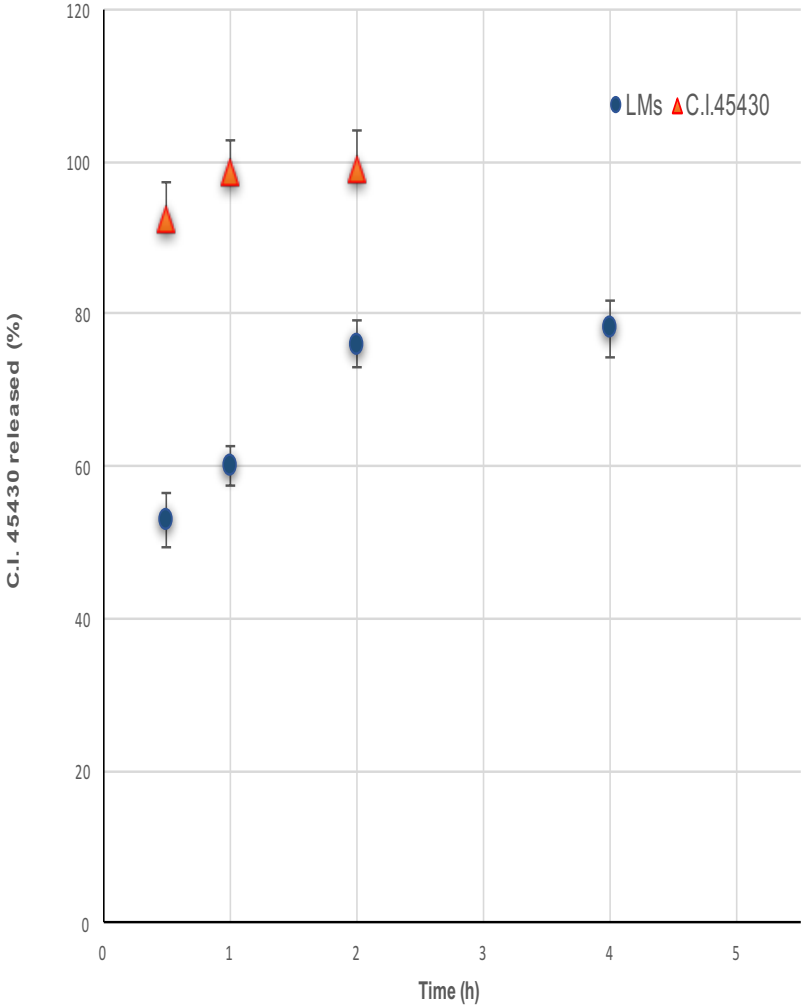
Microparticle characterization



Optical microscopy image of stearyl alcohol lipid microparticles containing CI 45430

→ **Particle size :**
19.4 ± 5.2 μm

→ **C.I. 45430 loading:**
5.6 ± 0.6 % (w/w)



C.I. 45430 dissolution and release profiles from stearyl alcohol lipid microparticles (LMs)

Photodegradation studies

✔ Samples dispersed in water or rat tail collagen

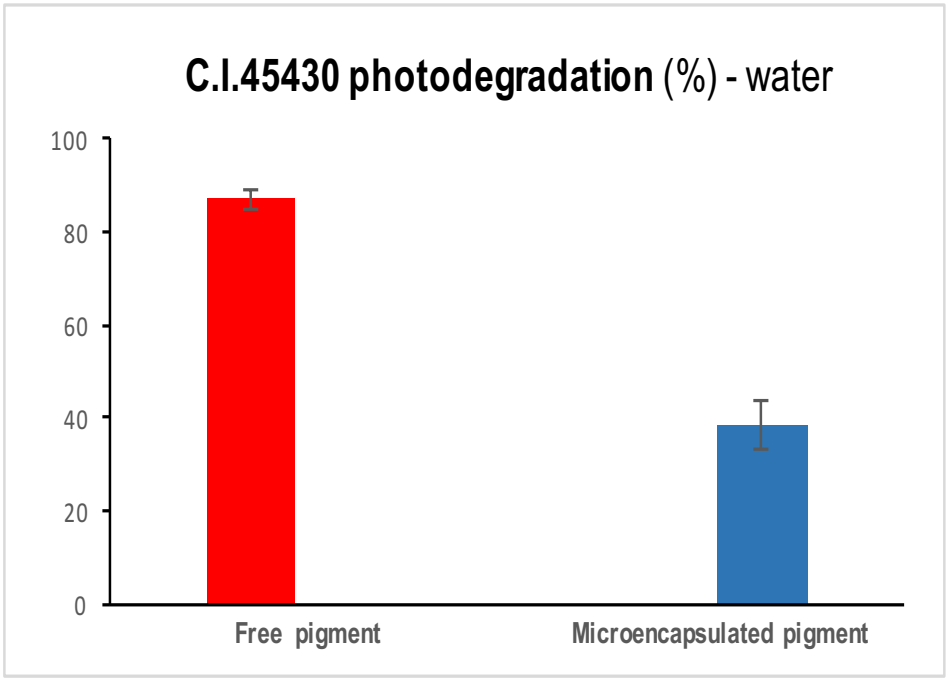
✔ Irradiation performed with a solar simulator (Suntest CPS+)

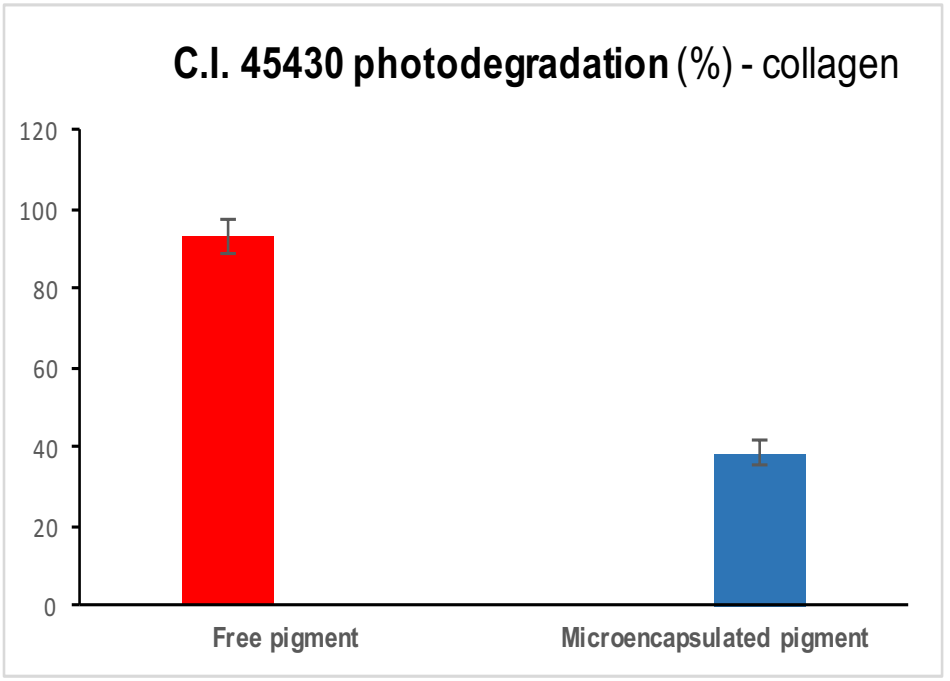
at 500 W/m^2 for 1 h

✔ Extent of degradation measured by high-performance liquid Chromatography (HPLC) after sample extraction

Photodegradation studies

✔ Samples dispersed in water or rat tail collagen





✔A 58-60 % reduction of C.I. 45430 photodegradation was achieved by the lipid microparticles

Ongoing projects

✔ **Study on free- and microencapsulated-pigment exposed to laser radiation**

Parameter	PicoWay	RevLite
Wavelengths	1064, 785, 532 nm	1064, 532, (585, 650) nm
Max Energy	1064nm - 400 mJ 785nm - 100mJ 532nm - 200 mJ	1064 nm - 1.6 J 532 nm – 500 mJ 585 nm – 300 mJ 650 nm – 150 mJ
Pulse width	450 ps / 300ps / 375 ps	10 ns
Peak Power (Max E / PW)	0.9 GW @ 1064nm 0.33 GW @ 785nm 0.5 GW @ 532nm	0.16 GW @ 1064 nm 0.07 GW @ 532 nm 0.06 GW @ 585 nm 0.04 GW @650 nm
Max Fluence	1064 nm – 12.5J/cm^2 785nm – 3.25J/cm2 532 nm – 6.25J/cm^2	1064 nm – 12 J/cm2 532 nm - 5 J/cm2 585 nm - 10 J/cm2 650 nm - 6.5 J/cm2
Spot Sizes	2-10 mm (1064nm& 532nm) 2-4 (785nm)	1064 nm – 3 to 8 mm 532 nm – 2 to 6 mm 585 nm - 2 to 3 mm 650 nm - 2 to 3 mm
Max Rep Rate	10 Hz @ 1064 & 532 nm 5Hz @ 785nm	10 Hz @ 1064 & 532 nm 1 Hz @ 585 nm 1 Hz @ 650 nm

Ongoing projects

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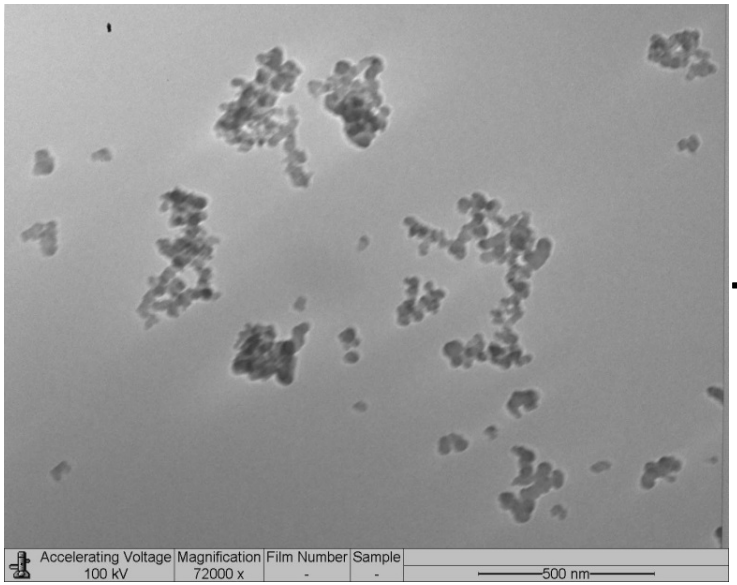
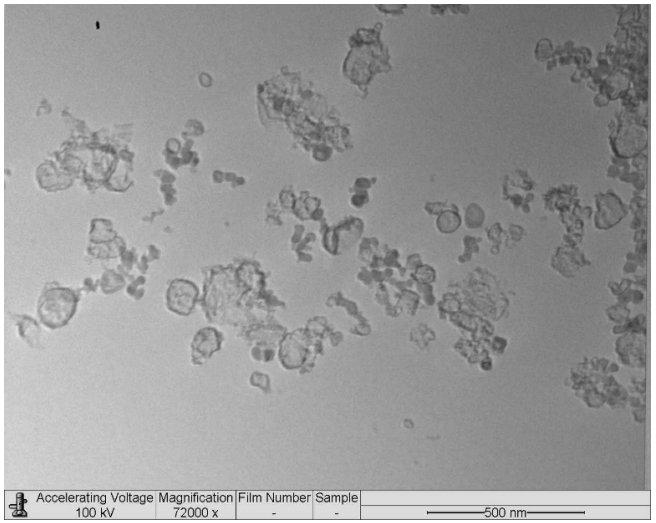
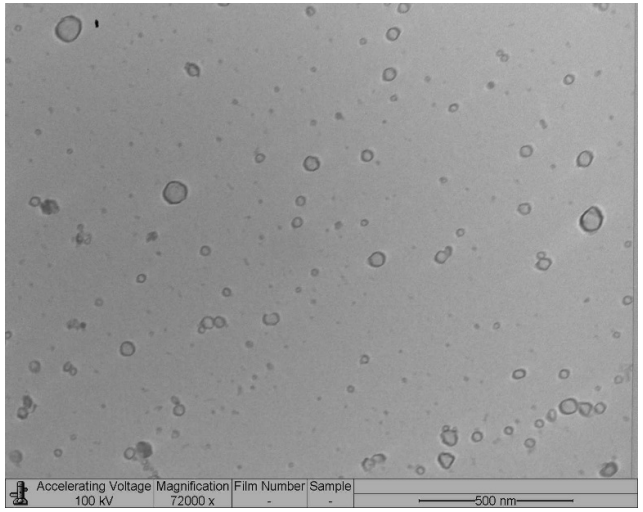
Untreated Control Sample



50 ns



450 ps



Conclusions

- Lipid microparticles may provide a useful approach to enhance the photostability of tattoo pigments, thereby reducing potential toxicological effects.
- Limitations : (i) differences between the irradiation medium used and the dermis and (ii) direct exposure of the pigment to the simulated solar radiation.
- In vivo evaluation of the microparticle formulation should be performed.
- Different materials for the microparticle preparation and other pigments should be examined

→ **Still a long way to go…**

- ***Laux et al.,*** A medical-toxicological view of tattooing. *Lancet* , 395 (2016)