Development of a New Modality of Transdermal Platform Based on Nanofibers for the Delivery of APIs

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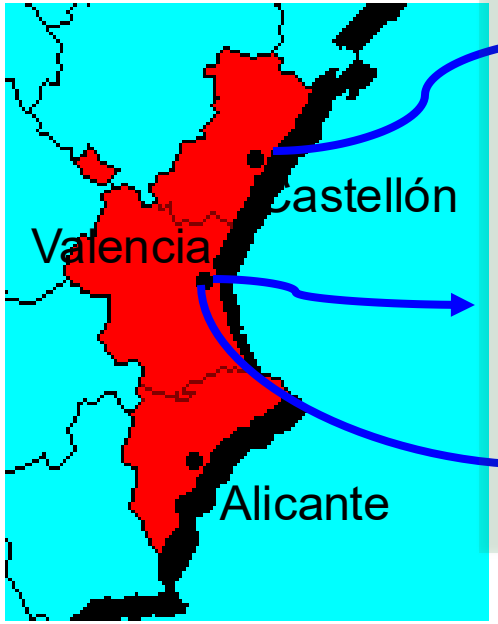
BIONANOPHARMA

CRS 2025
ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

Who and where are we?



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Processing and Mechanical Properties of Nanocomposites

Novel Materials and Nanotechnology

IATA - CSIC, Valencia

UA in Polymers Technology

Fluidnatek® by Bioinicia One Step Ahead

Spinbox by Bioinicia

BIOINICIA

BIONANOPHARMA

BIOINICIA COSMETICS

PROVEIL BY BIOINICIA

About Bioinicia S.L. (CDMO)

Founded by Prof. J.M. Lagaron as a spin-off from the Spanish Council for Scientific Research (CSIC)

- 2009 Contract Development Services
- 2012 Addition of FLUIDNATEK™ electrohydrodynamic processing equipment
- 2016 GMP Pharma Plant (Clinical Trials and Manufacturing)

Headquartered in Valencia, Spain

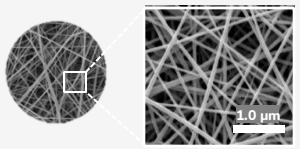
- Equipment manufacturing workshop
- R&D facilities (in cooperation with CSIC)
- Pilot Plant (200 kg capacity)
- 2 Manufacturing plants for Pharma/Biomedical/Cosmetics/PM (up to 40 nanofiber ton capacity)
- **ISO 13485 and GMP Pharma**
- **6 GMP Pharma Clean Rooms and 1 GMP Lab in 2025**
- **20 ton capacity of GMP submicron particles and fibers**

BIONANOPHARMA

Electro-hydrodynamic Processing Principle

- Expose fluids and biofluids to a strong Electric Field
- Migration of electrical charges to the fluid surface
- Competition between surface tension and surface charge which leads to surface deformation into conical shapes
- Breakup of surface tension leading to the emission of an electrically driven liquid jet
- Liquid jet breaks into droplets (electrospray) or fibers (electrospinning) of controlled size and shape
- No heating required

The Only Pharma GMP Approved Facility for Electrospinning and Soon for Electronebulization*



HT sterile eSpinning

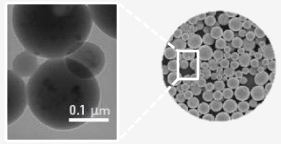
→ Fiber Nonwovens

Administration routes:

- Muco-adhesive buccal, sublingual, transdermal, ophthalmic patches
- Oral Dissolving Film (ODF)
- Subcutaneous inserts
- Wound dressing
- Soft tissue implant
- Filter media for purification of biologics

Diameter range
100nm - 10µm

Installed capacity
Fibers >10 tons/year
Up to OEB 5



HT sterile eSpraying

→ Particles

Administration routes:

- Oral
- Parenteral
- Dry powder inhalation
- Nasal administration
- Long-acting Injectables (LAI)

Diameter range
400nm - 40µm

Installed capacity
Particles >10 tons/year
Up to OEB6

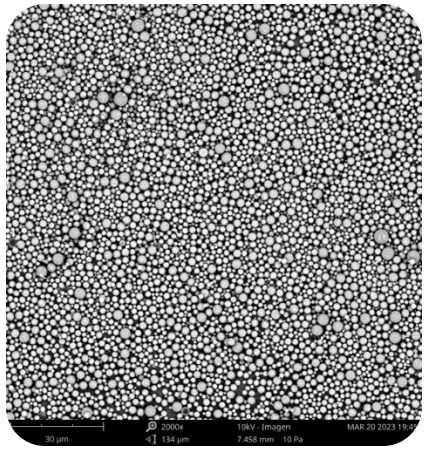
*Electronebulization: Approval expected by October 2025

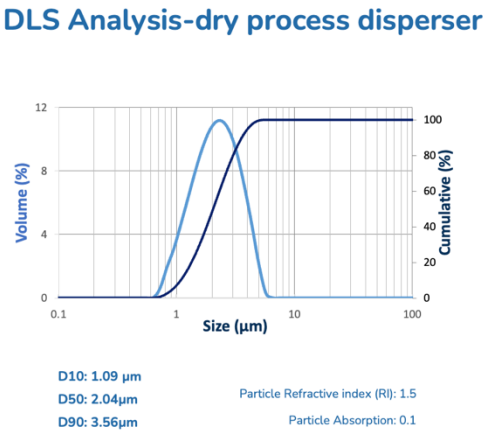
Mild Drying Technology for SC Formulations of mAbs

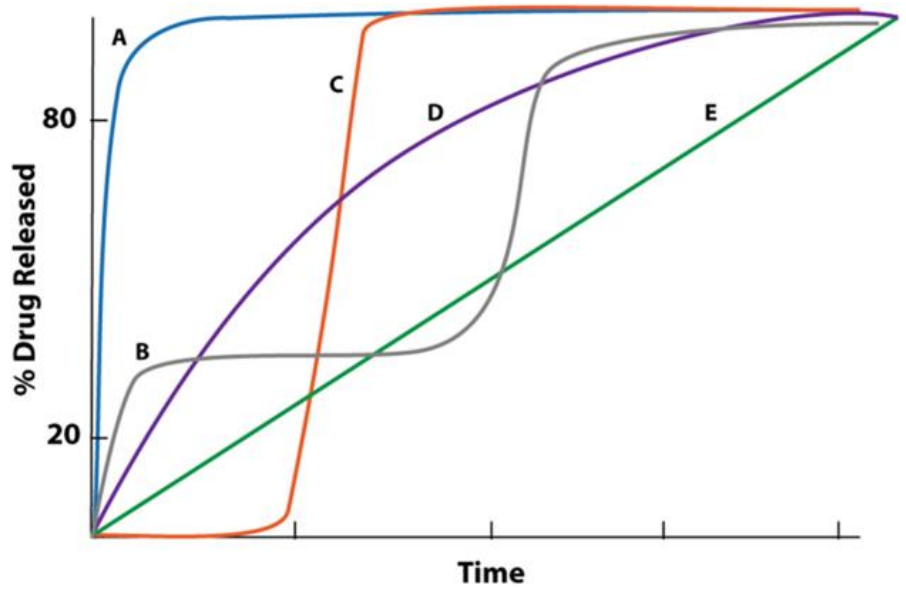
	Spray-drying	Electrospraying
Post-processing bioactivity	Reduced	Retained / Slightly reduced
Process characteristics	Elevated temperaturas	Tolerable high voltage peak Non-thermal process
Ratio API : Excipients	API << Protective excipients	API > ≈ Any excipients
Size distribution	1-100 µm ↓ Homogeneity	+ 50 nm – 20 µm ↑Homogeneity

Controlled release → Long-acting Injectables

- **Controlled release**, e.g. suppression of initial burst release
- **Sustained release** over an extended period
- Bespoke particle size and size distribution
- **Pulsatile release**
- …

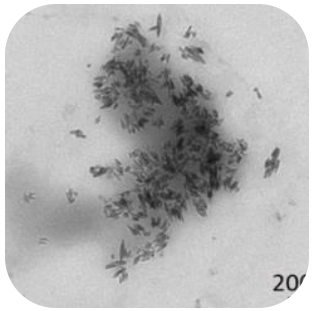


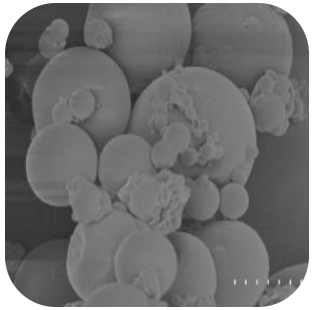




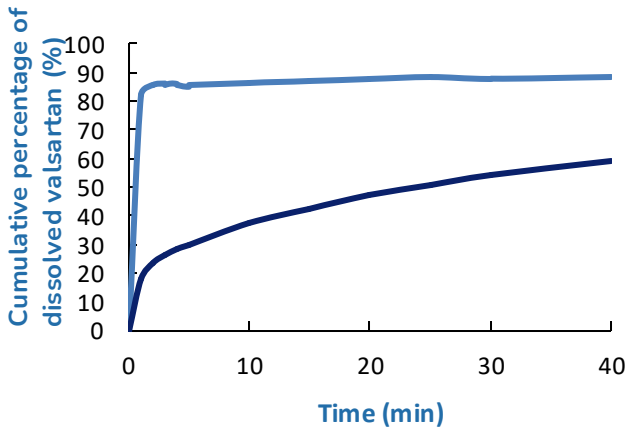
A) Immediate release; B) Pulsatile; C) Delayed Release; D) Extended Release; E) Order Zero

Nano-in-Micro platform for API oral delivery





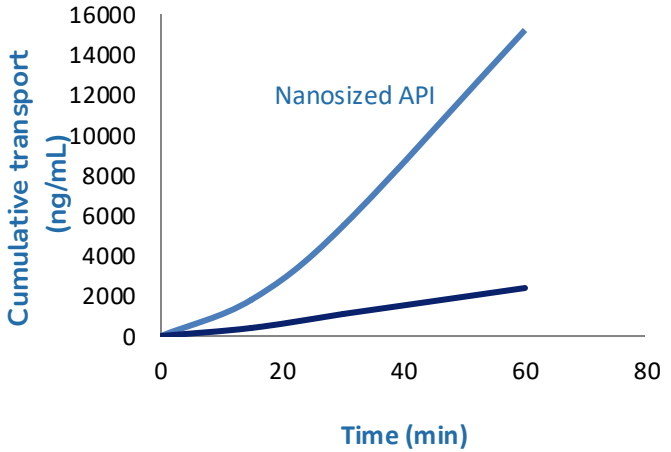
Dissolution rate



Effect of formulation and electrospraying process on dissolution rate

Nanosized valsartan within microparticles leads to near instantaneous dissolution

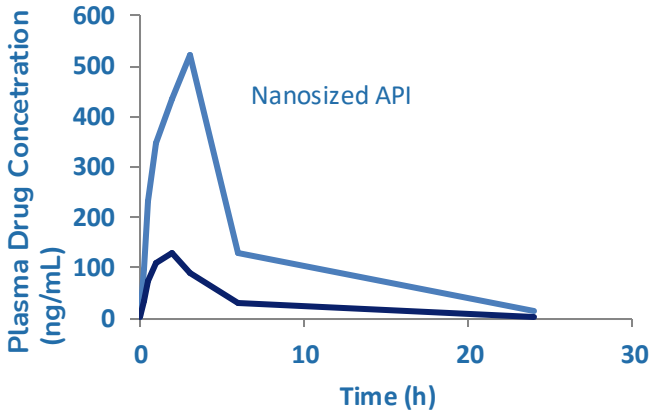
Permeability profile



Effect on permeation across Caco-2 cell membrane

Nanosized valsartan showed over 6x increase in permeability compared with pure API

Plasma concentration

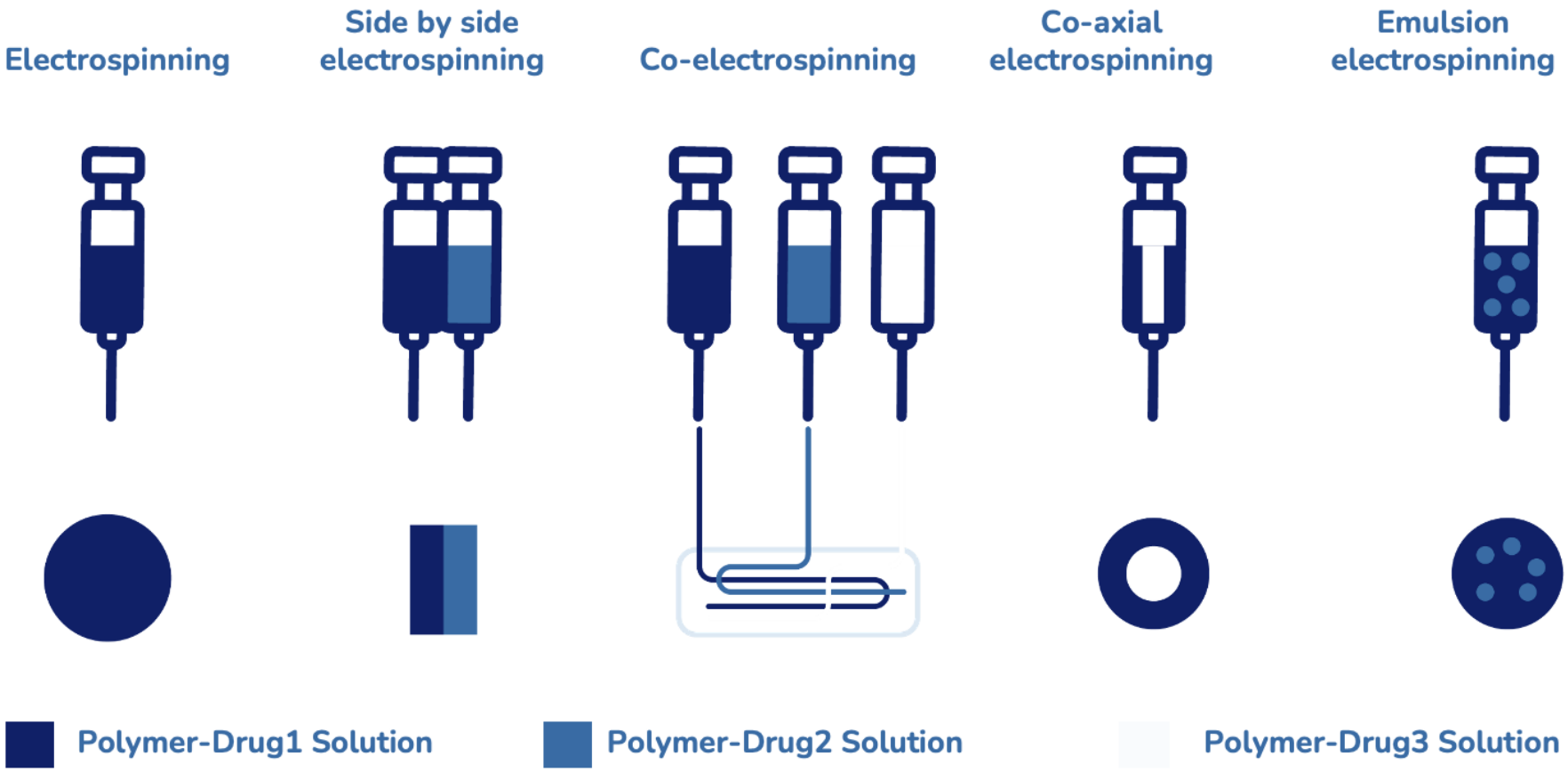


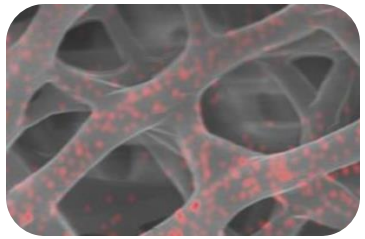
Effect on bioavailability in rats

Nanosized valsartan showed a 4.7x increase in systemic exposure compared with pure API

Mol. Pharmaceutics 2021, 18, 2947−2958
Journal of Drug Delivery Science and Technology 2021, 66, 102780
To be submitted 2025

Electrospinning: Bespoke Controlled Release of APIs





Mucoadhesive patch platforms

- Fiber-based material intimately **conforms to the mucosa/skin**
- Mimics extracellular matrix
- Patch falls off after designated **adhesion time**

Barrier Layer

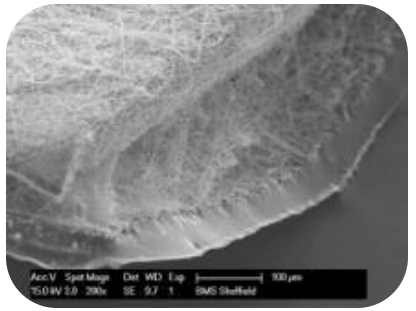
- Facing mouth
- Non-adhesive
- Non-soluble
- Biodegradable

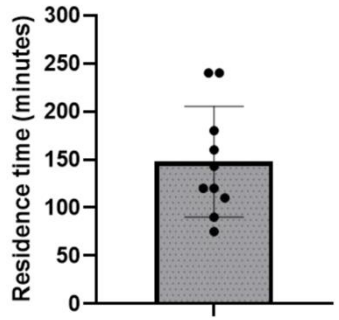
A: Bottom view adhesive/active layers

B: Top view backing layer

Pharmaceutics 2024, 16(2), 220

- **No drug-loss** into mouth – uni-directional delivery towards mucosa
- Controllable adhesion **up to 8 hours** and drug release time
- 100% pharma and food grades **safe** to swallow





Nanomaterials 2022, 12, 438
Biomaterials 2018, 178, 146

Nanofiber Delivery of Cosmetics

4 different shapes avaliable

OLIVE ESSENCE WRINKLE CORRECTOR

BENEFITS

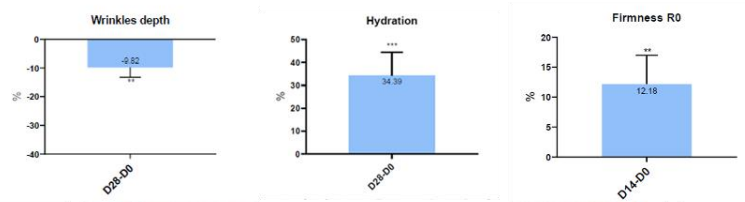
- ✓ Immediate lifting effect
- ✓ Prevents and corrects wrinkles
- ✓ Deeply moisturizes
- ✓ Reinforces skin structure
- ✓ Reverses cellular aging
- ✓ Detoxifying effect

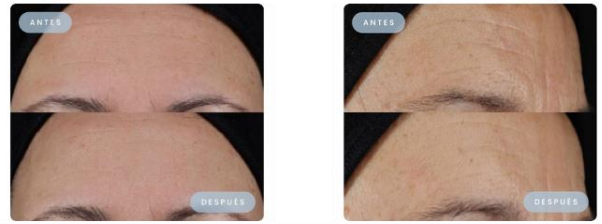
ACTIVES

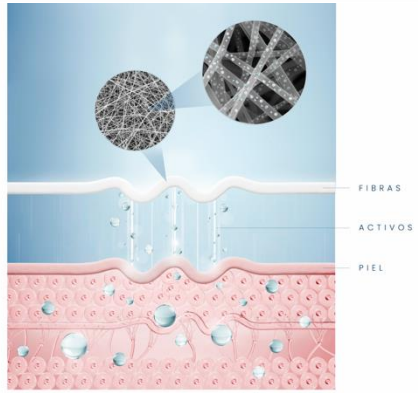
HYDROXYTYROSOL
HYALURONIC ACID (low molecular weight)
PULLULAN
PLANT-BASED ELASTIN

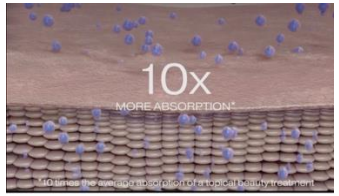
−29%
Wrinkle volume

+34%
Hydration at 28 days









Dry Nanofiber Based Skin Friendly Delivery of Cosmetics

Bioiniciacosmetics.com

Pharma Transdermal Patch Platforms (TDDS)

Advantages of TDDS:

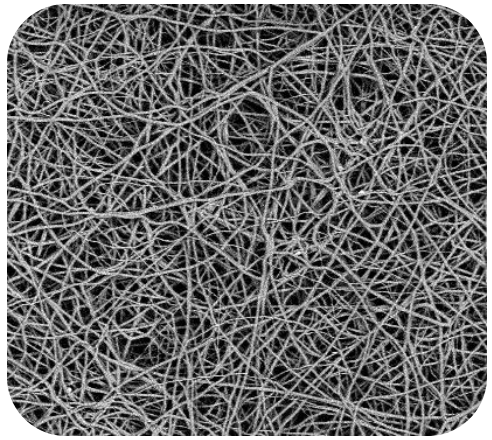
Bypassing first-pass metabolism

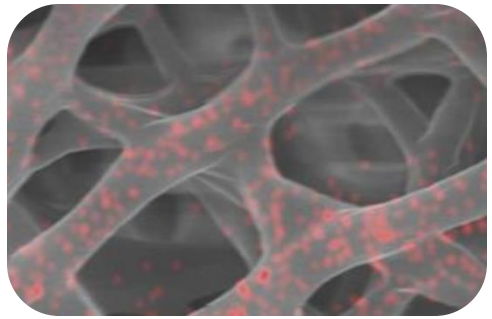
Ease of self-administration

Reduced dosing frequency (QD)

Minimized gastrointestinal side effects

Increased Permeation





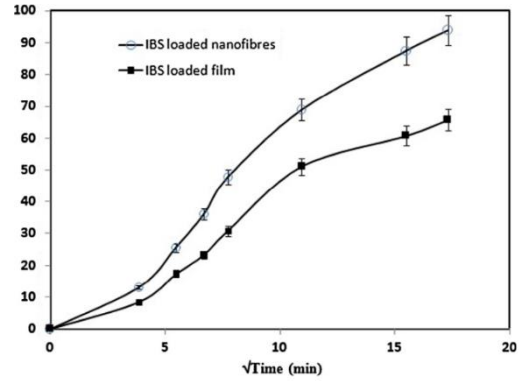
60-90% Porosity
Nanoparticles or ASS of API inside

J. Funct. Biomater. 2022, 13(4), 170
Cosmetics 2020, 7(4), 96
Nanomaterials 2022, 12(3), 438

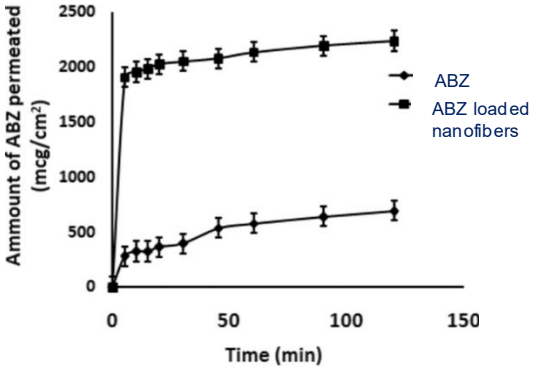
Reduced Patch Size

High API Loading
Controlled thickness
High permeation
Enabling enhancers

Increased Administration



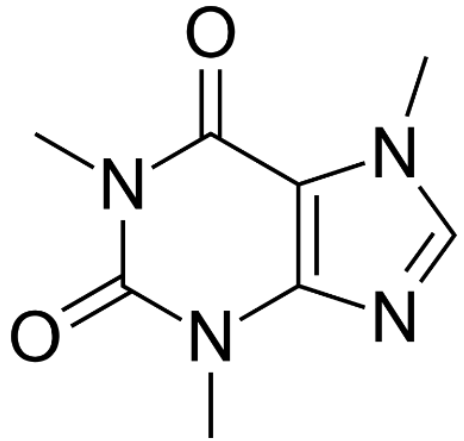
Journal of Advanced Research (2016) 7, 483–489



BioNanoScience (2019) 9:625–636

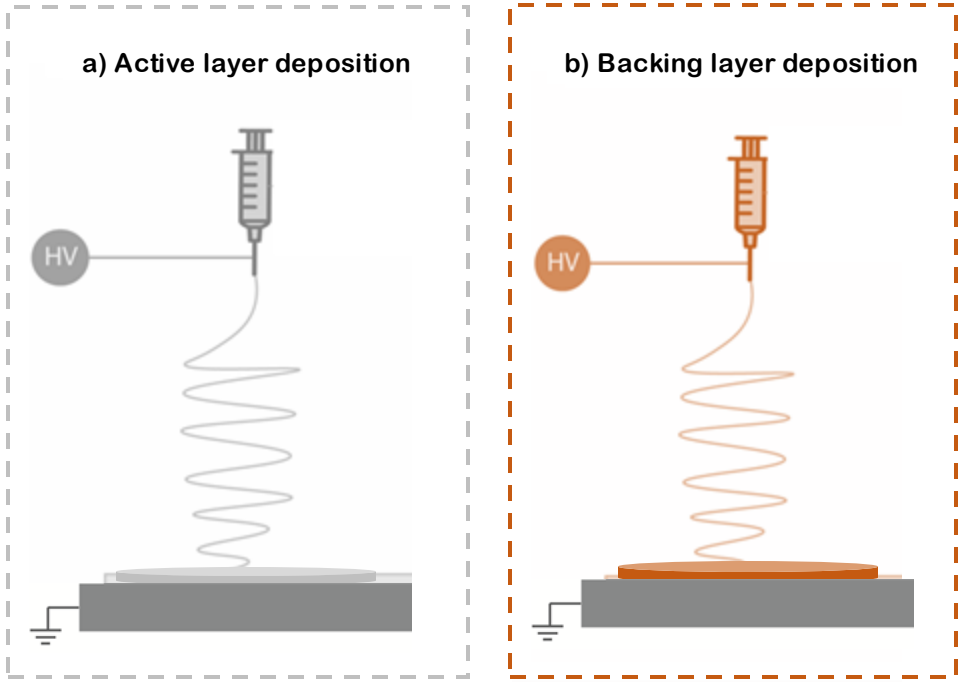
POC: API and Excipients

Caffeine	
Molecular weight (g/mol)	Log P
194.19	-0.07



Excipients	
Name	Use
Polyethylene oxide (PEO, Mw 200kDa)	Fiber Matrix
Polyethylene glycol (PEG, Mw400Da)	Enhancer
Oleic acid (OA)	Enhancer
Propylene glycol (PG)	Enhancer
Eucalyptus Globulus Leaf Oil (Euc)	Enhancer

Bilayer Patch Design

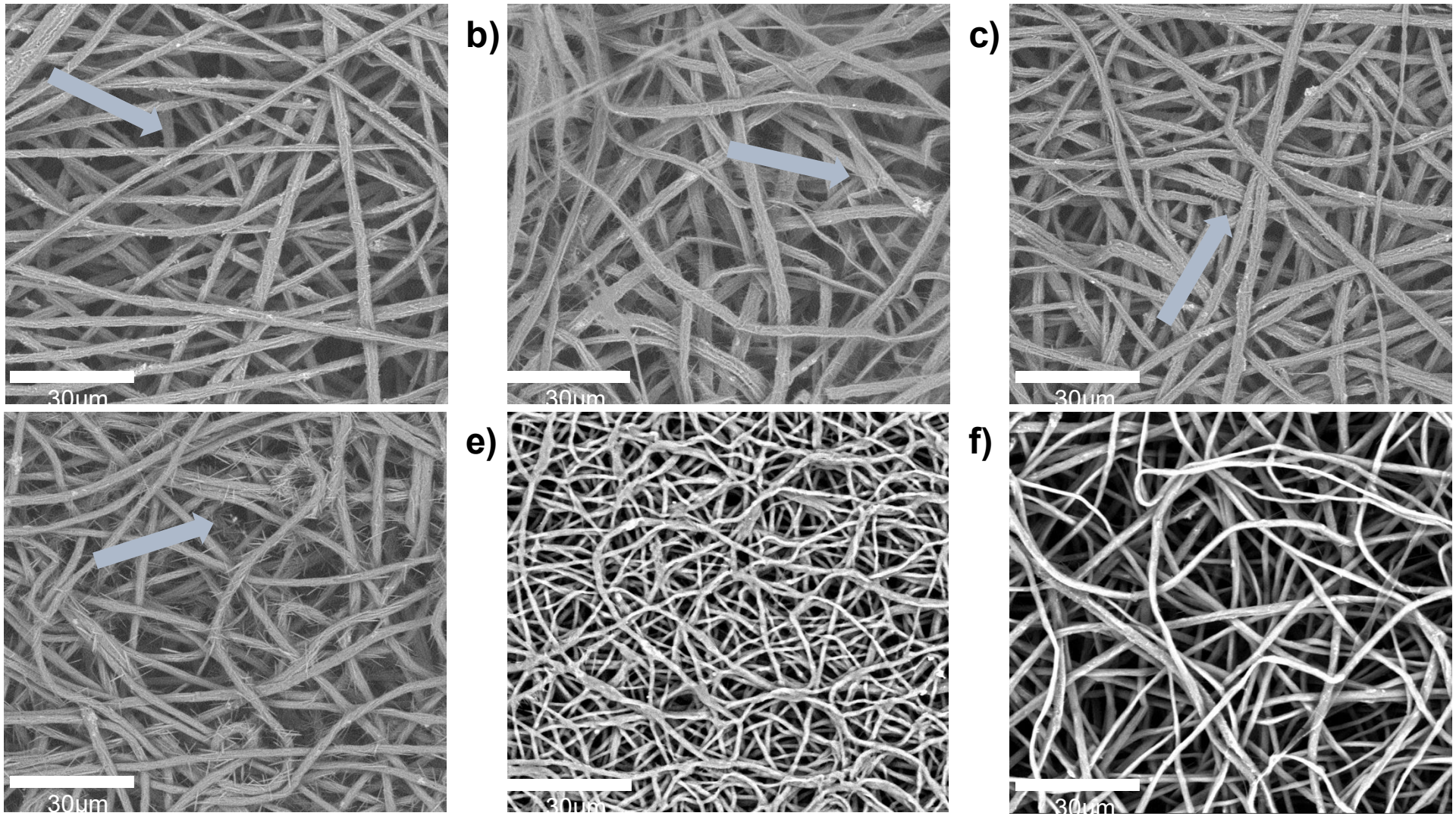


FORMULATIONS

Sample ID	Ratio Polymer/API/Enhancer (w/w)
PEO_CAF	80/20
PEO_CAF_OA	70/20/10
PEO_CAF_PEG	64/20/16
PEO_CAF_PG_OA	56/20/14/10
PEO_CAF_PEG_OA	56/20/14/10
PEO_CAF_PEG_EUC	60/20/15/5

Morphology of the Active Layer by SEM

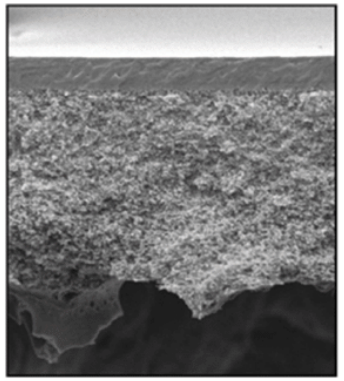
Caffeine needles over fibers



SEM images of PEO/caffeine patches with different enhancers a) without enhancer; b) oleic acid; c) polyethylene glycol; d) propylene glycol and oleic acid; e) polyethylene glycol and oleic acid; and f) polyethylene glycol and eucalyptol.

Permeation Test of the Bilayer

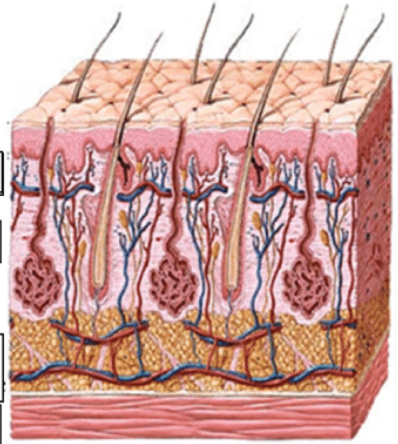
Strat-M Membrane

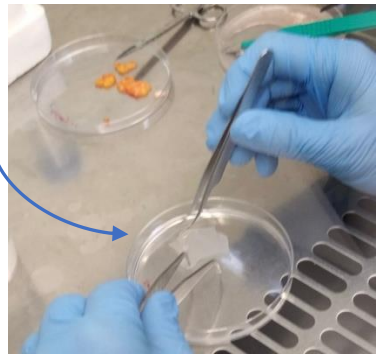


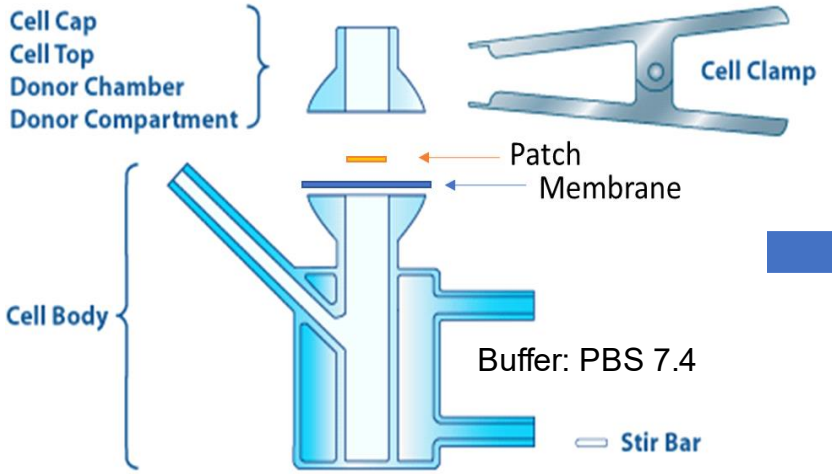
Membrane cross-section

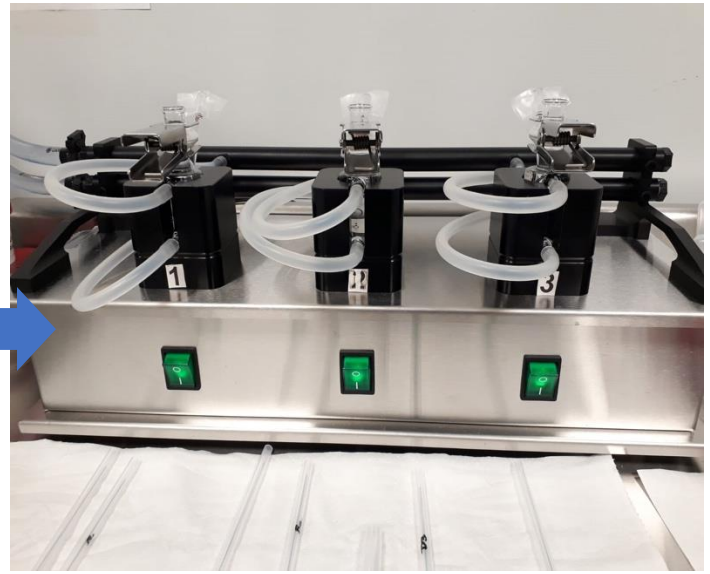
Tight "Skin" layer
Stratum corneum
Polyethersulfone (PES)
Dermis in the skin
PP non-woven fabric support
Subcutaneous fat tissue in the skin

Human Skin

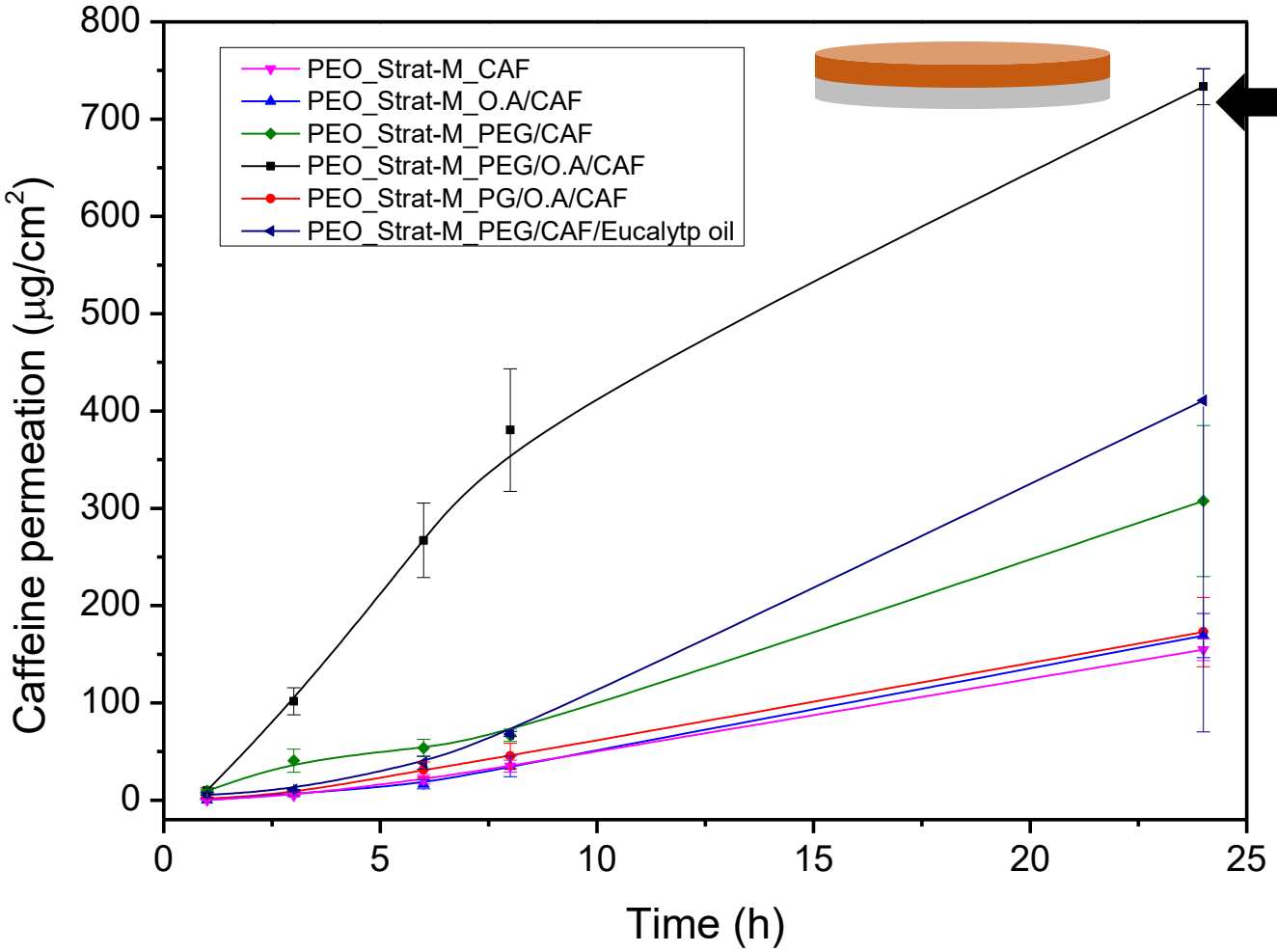








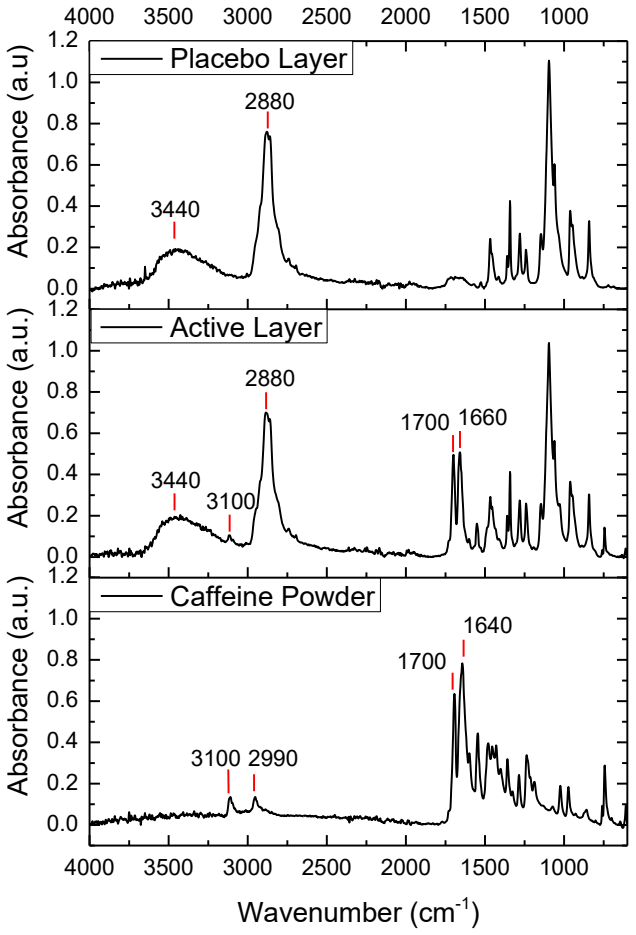
Permeation: Synthetic Strat-M Membrane



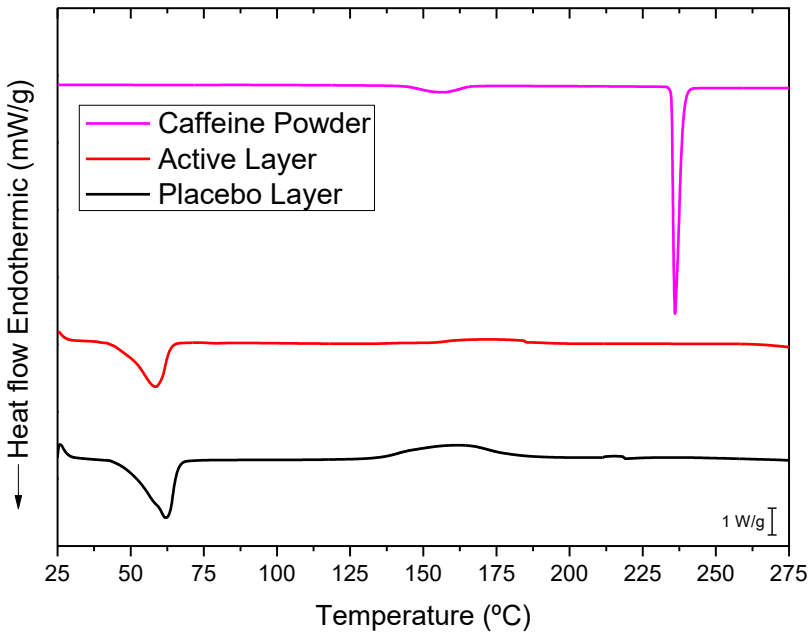
SELECTED FORMULATION	
PEO_CAF_PEG_OA	56/20/14/10

Characterization Selected Active Layer

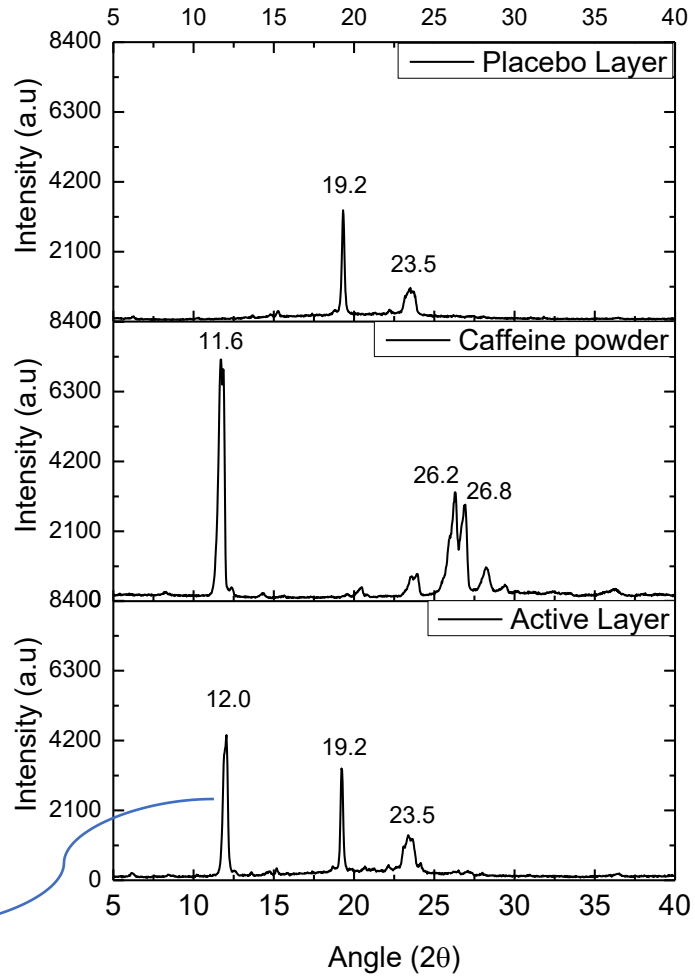
FT-IR



DSC

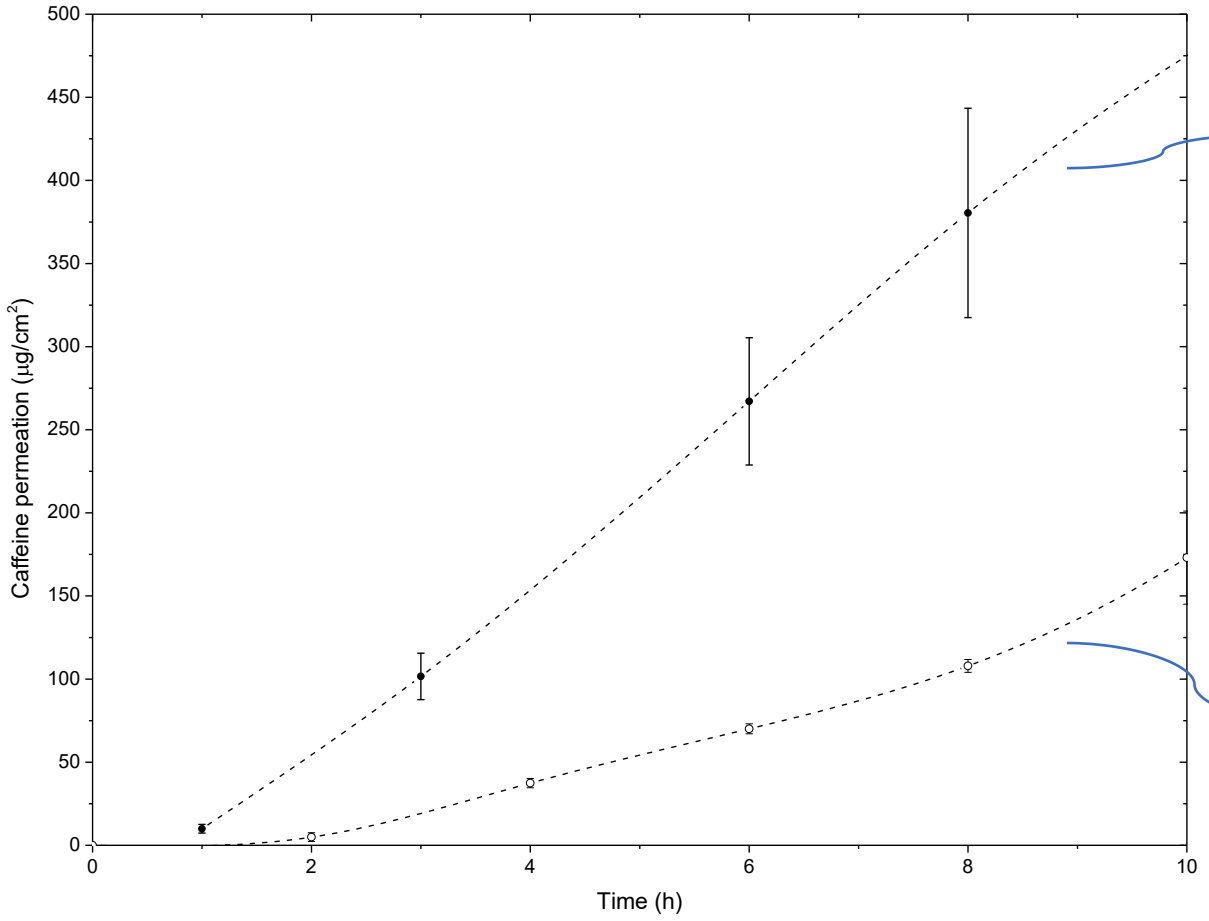


WAXS



Average caffeine nanocrystal sizes of ~25 nm were estimated by WAXS that were not detected by DSC

Permeation: Three Layer vs Bilayer



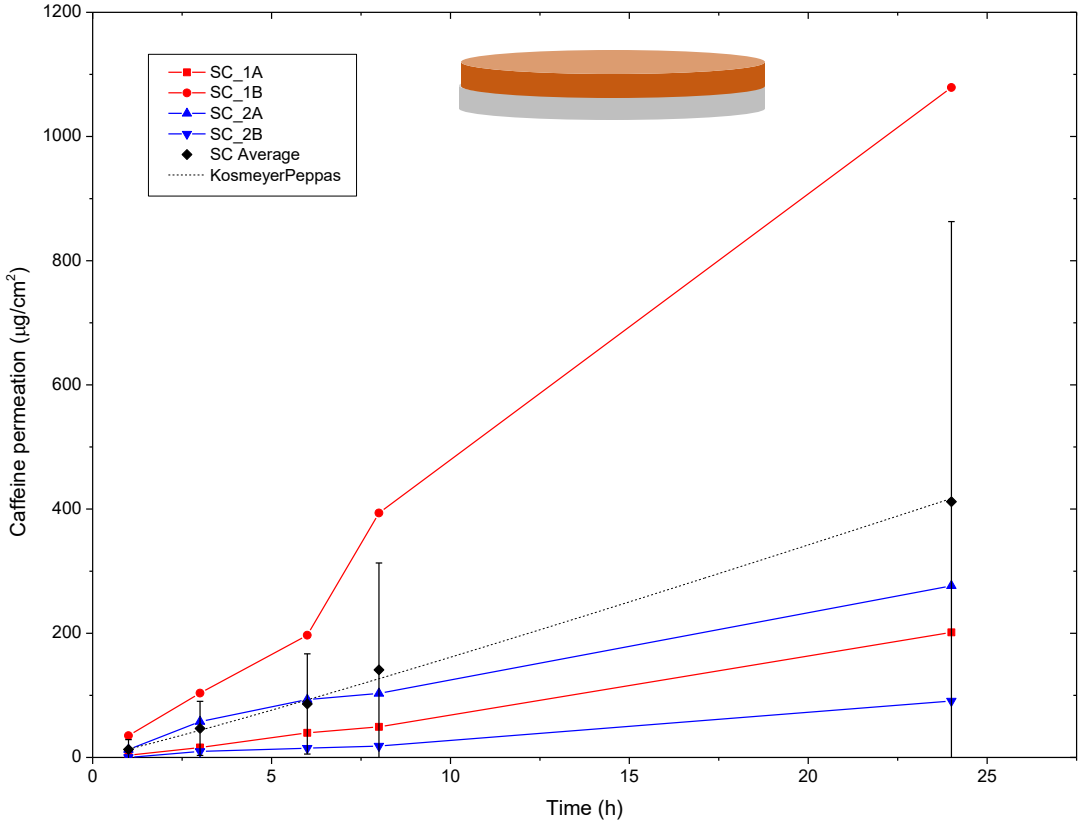
Bilayer patch: Hydrophilic Active Layer

Backing layer
Active/Adhesive layer

Three layer patch: Hydrophobic Active Layer

Backing layer
Active layer
Adhesive Layer

Permeation: Ex-vivo Human Stratum Corneum



Caffeine permeation through ex-vivo human SC specimens of the PEO_CAF_PEG_OA patch. SC-1A and B correspond to SC specimens of the 39-year-old man and SC-2A and B correspond to SC specimens of the 68-year-old woman. SC Average correspond to the average of all specimens and the dotted line correspond to its fitting to the Kosmeyer-Peppas model.

ID	Korsmeyer-Peppas		
	K	n	r^2
PEO_CAF_PEG_OA patch	0.63	1.09	0.96

- The fitting provides an n value (release exponent) slightly higher than 1. When fitting to the Korsmeyer-Peppas model, an n>1 indicates a Super Case II non-Fickian permeation process, dominated by significant swelling, erosion, or hydration effects.
- This behaviour is consistent with the PEO nanofibers undergoing considerable swelling and gelling while adhering and enabling the cross-diffusion of caffeine.
- There is higher variability among specimens in the permeability through the SC, specially at longer testing times.

Main Conclusions

- HT electrospinning offers a very efficient and flexible new modality TDDS technology, even for rather hydrophilic model drugs such as caffeine.

- The use of enhancers is compatible with the technology, in the case here combination of PEG and oleic acid (OA) showed the highest synergistic enhancement of caffeine permeation. The best-performing formulation achieved caffeine permeation rates of 730 μg/cm² after 24 hours in the synthetic membrane.

- Ex vivo SC permeation experiments in Franz cell equipment with low tested areas, i.e. 1 cm^2, showed higher variability than synthetic membranes due to potential statistically relevant morphological features among specimens and possibly membrane degradation after few hours testing.

ACKNOWLEDGEMENTS

CEX2021-001189-S

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