3D Printing: an emerging technology to revolutionize topical drug delivery

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CONTROLLED RELEASE SOCIETY
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JULY 24-28, 2023 Paris Hotel » Las Vegas, NV, USA
THE FUTURE OF DELIVERY SCIENCE

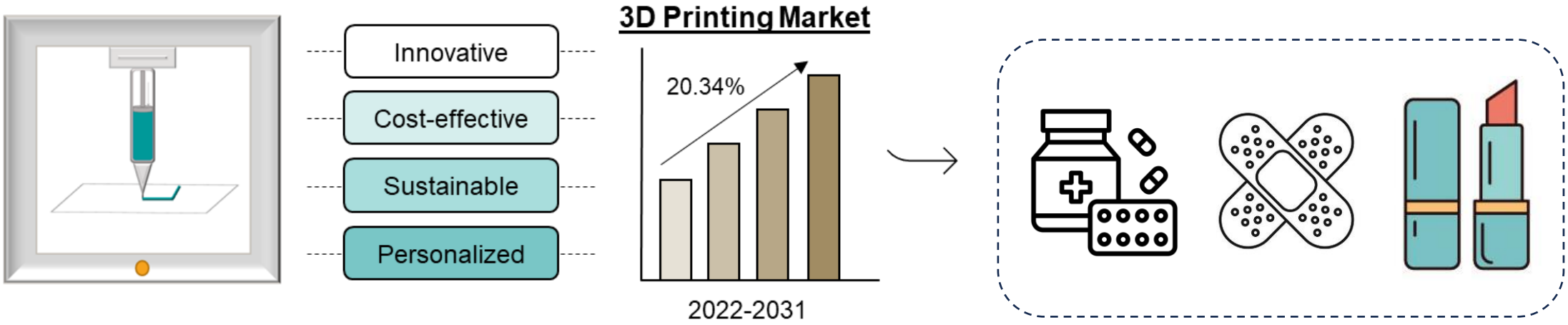
Pharmaceutical Development Lab

Promoting the cooperation between academia and industry

Background

- **3D Printing: concept and application in topical drug delivery systems**

3D Printing: a reality in topical drug delivery systems? It is revolutionizing and disrupting the concepts of one-size-fits-all and one-treatment-fits-all.

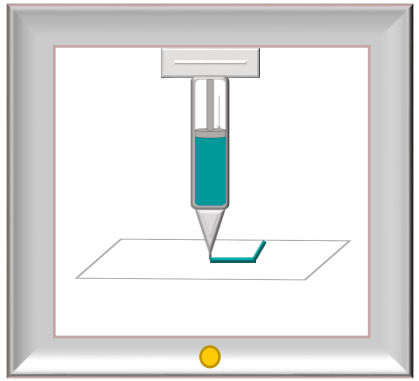


S. Bom, A.M. Martins, H.M. Ribeiro, J. Marto, Int. J. Pharm. 605 (2021) 1–20.
N.P. Kim, J. Kim, M.S. Han, J. Cosmet. Med. 3 (2019) 94–101.

Outline and aims

Printing process optimization

- Development of a 3D Printing tool



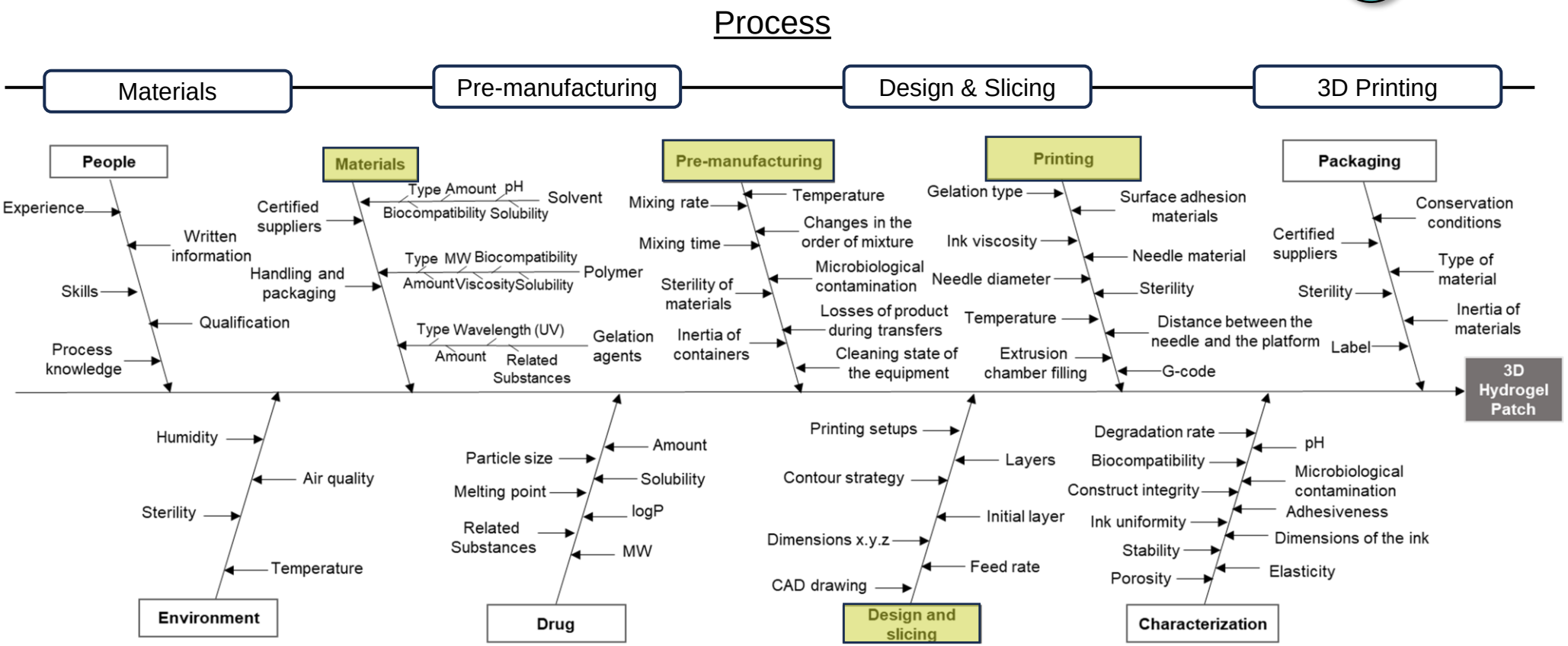
3D patches optimization and characterization

Applications of 3D printing in topical drug delivery systems

3D Printing Optimization

- **What, Why and How optimize the process?**

1 **Risk Analysis**



3D Printing Optimization

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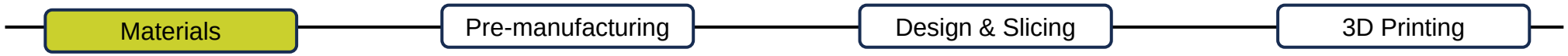

Failure Modes		Raw Materials Attributes				
		Solvent	Polymer	Bioactive or drug		Cells or derivates
		Amount	Amount	Solubility	Amount	Amount
Ink CQAs	Gelation Time	Low	High	Medium	Medium	Medium
	Porosity	Medium	High	Medium	Medium	Medium
	Printing Accuracy	Medium	High	Medium	Medium	Medium
	Printing Fidelity	Medium	High	Medium	Medium	Medium
	Flexibility	Medium	High	Medium	Medium	Medium
	Adhesivenss	Medium	Medium	Medium	Medium	Medium
	Mechanical strenght	Medium	Medium	Medium	Medium	Medium
	Release rate	Medium	Medium	Medium	Medium	Medium

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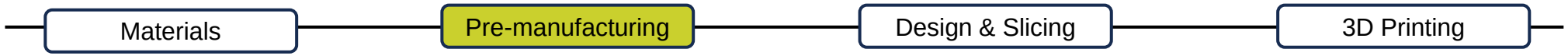

Failure Modes		Process Parameters		
		Pre-manufacturing (Formulation production)		
		Temperature	Mixing rate	Time
Ink CQAs	Gelation Time	Medium	Low	Medium
	Porosity	Medium	Low	Medium
	Printing Accuracy	Medium	Low	Medium
	Printing Fidelity	Medium	Low	Medium
	Flexibility	Low	Medium	Low
	Adhesivenss	Low	Low	Low
	Mechanical strenght	Low	Medium	Medium
	Release rate	Low	Medium	Low

3D Printing Optimization

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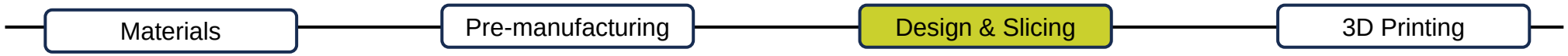

Failure Modes		Process Parameters						
		Design and slicing						
		Line width	Wall line count	Layer Height	Structure	Infill density (%)	Dimensions (x,y,z)	Number of layers
Ink CQAs	Gelation Time	Low	Low	Medium	Medium	Medium	Medium	Medium
	Porosity	Medium	Medium	Medium	Medium	High	High	Medium
	Printing Accuracy	Medium	Medium	Medium	Medium	High	High	Medium
	Printing Fidelity	Medium	Medium	Medium	Medium	High	High	Medium
	Flexibility	Low	Low	Medium	Medium	Medium	Medium	Low
	Adhesivenss	Low	Low	Medium	Medium	Medium	Medium	Low
	Mechanical strenght	Low	Low	Low	Medium	Medium	Low	Medium
	Release rate	Medium	Medium	Medium	Medium	High	Medium	Medium

3D Printing Optimization

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1 Risk Analysis

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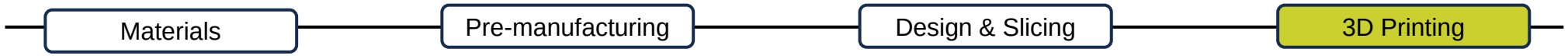
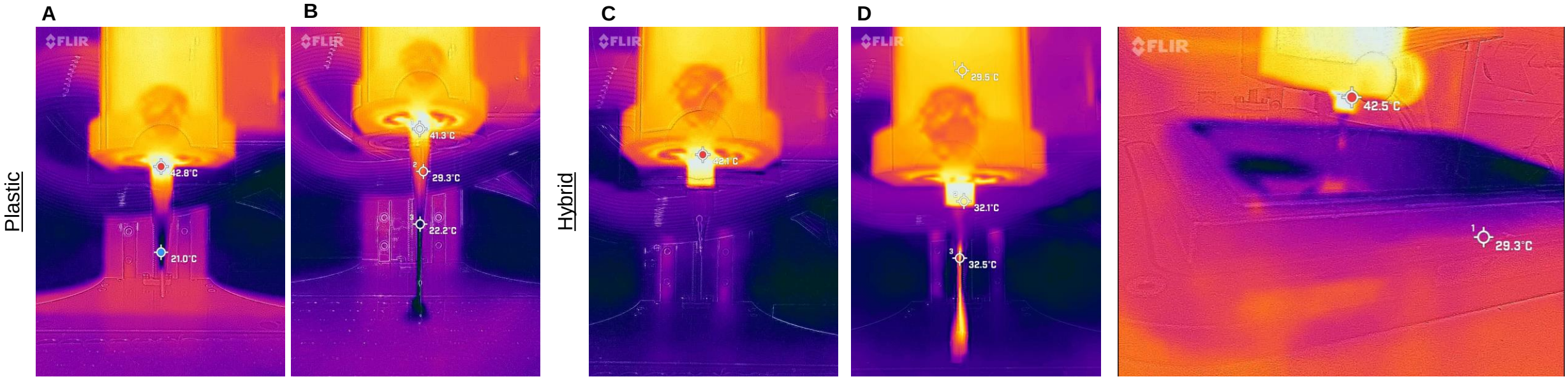


		Process Parameters							
		3D Printing							
	Failure Modes	Printing temperature	Environment temperature	Pressure	Needle material and diameter	Distance between the nozzle and the platform	Ink viscosity	Surface adhesion materials	Extrusion chamber filling
Ink CQAs	Gelation Time	High	High	Low	Low	Low	Low	Low	Low
	Porosity	High	High	High	Medium	Medium	Medium	Medium	Medium
	Printing Accuracy	High	High	High	Medium	Medium	Medium	Medium	Medium
	Printing Fidelity	High	High	High	Medium	Medium	Medium	Medium	Medium
	Flexibility	Low	Low	Low	Low	Low	High	Low	Low
	Adhesivenss	Low	Low	Low	Low	Low	High	Low	Low
	Mechanical strenght	Low	Low	Low	Low	Low	Low	Low	Low
	Release rate	Low	Low	Low	Low	Low	Medium	Low	Low

3D Printing Optimization

- **What, Why and How optimize the process?**

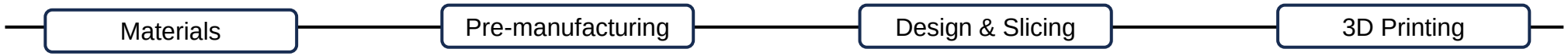


3D Printing Optimization

- **What, Why and How optimize the process?**

1 **Risk Analysis**

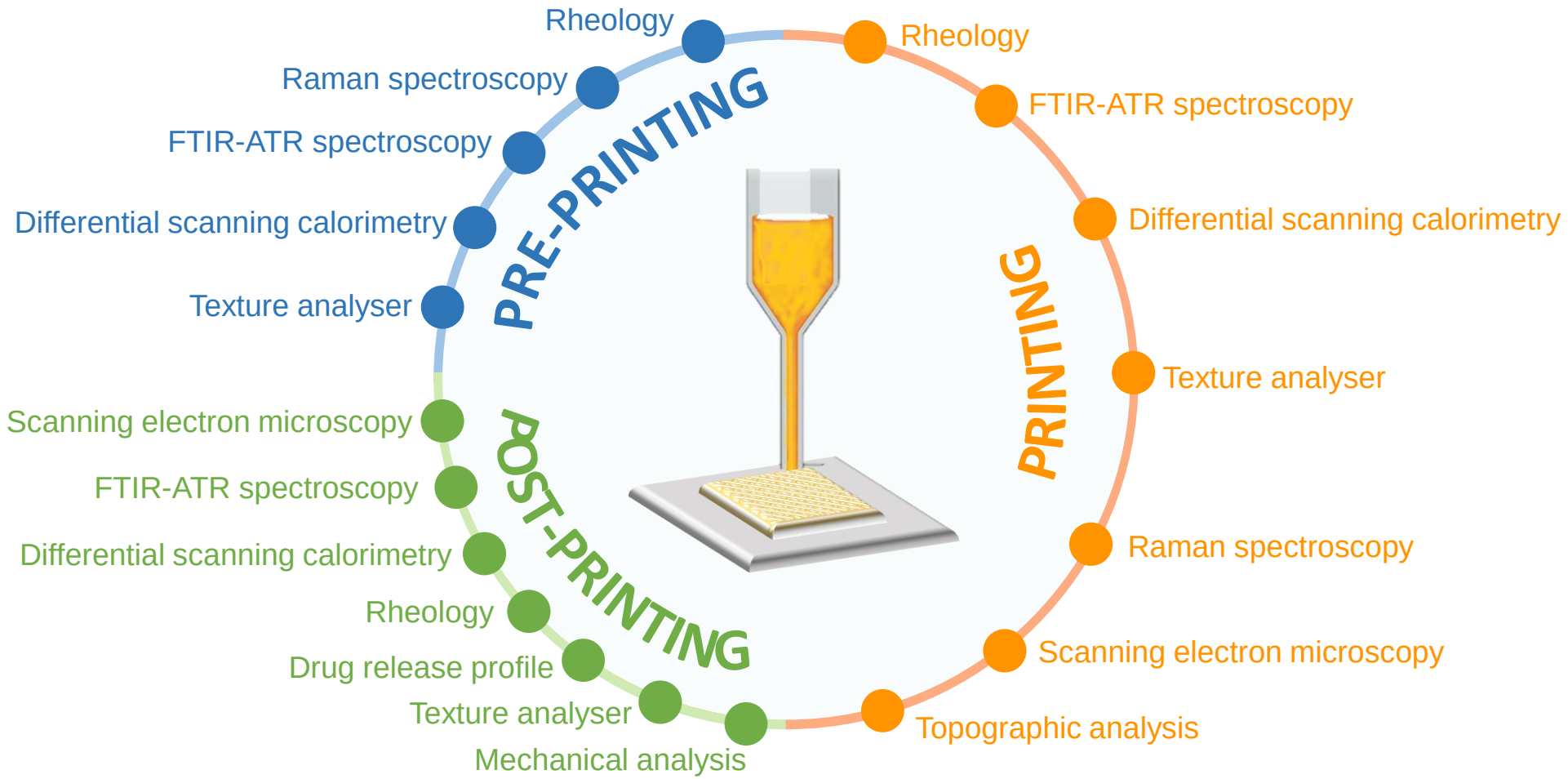
Process



In short, it is fundamental to control the:

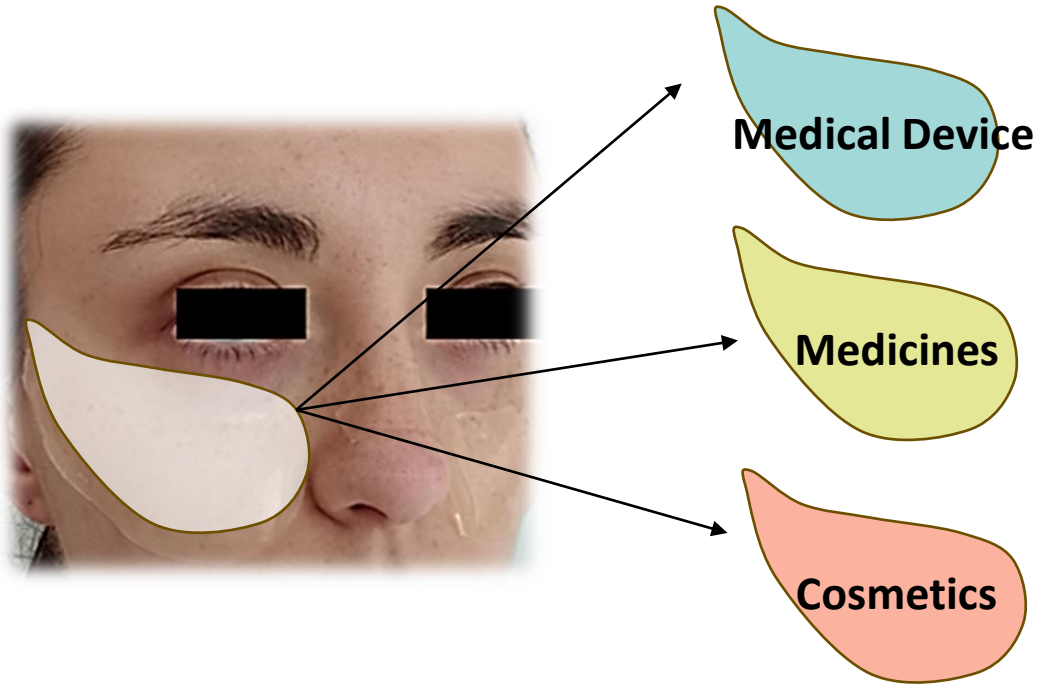
- Polymer amount
- Ink Rheology
- Patch Design
- Printing settings

Characterization

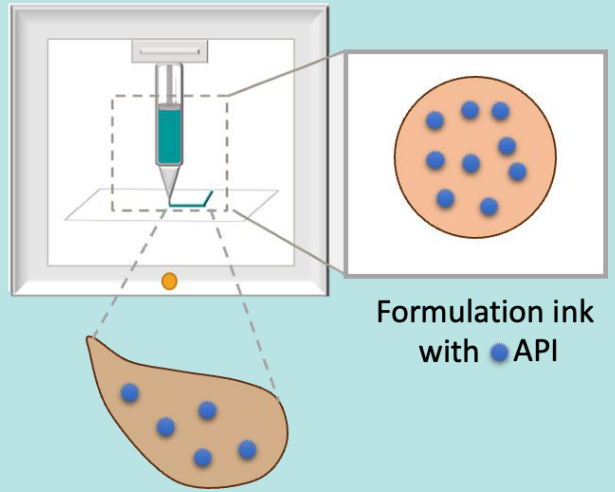


Applications - From a simple formulation to complex structures

From a 3D hydrogel patch, different patches can be followed:



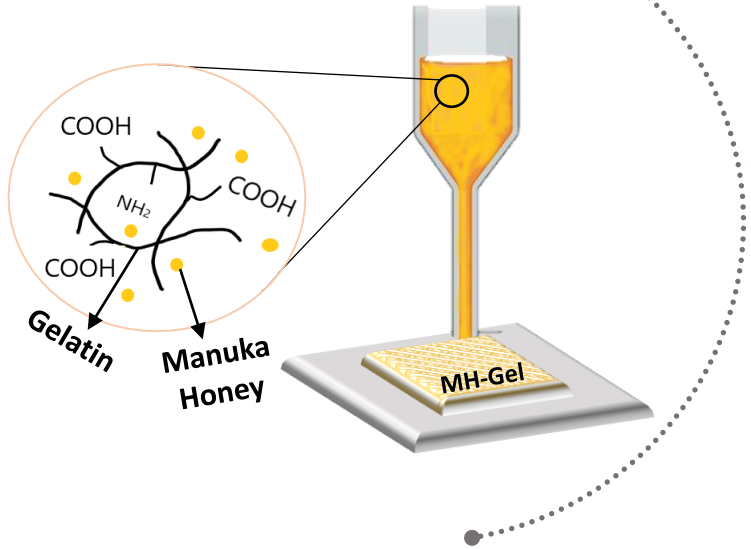
Versatile Formulation can be used in **3D Printing** to create personalized patches for different types of treatments

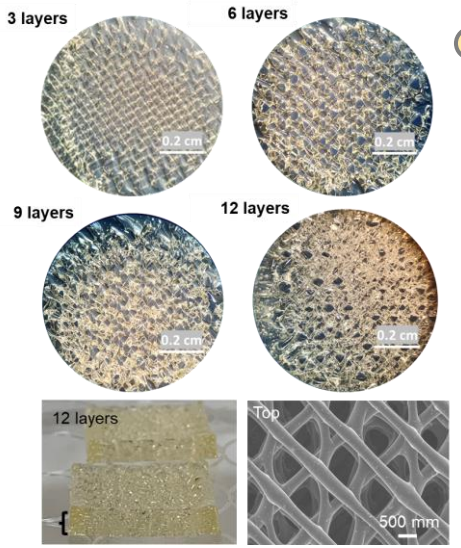


Applications

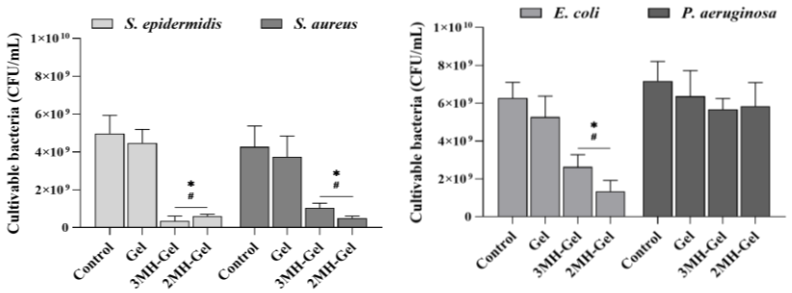
- **Wound healing treatment**

Manuka Honey

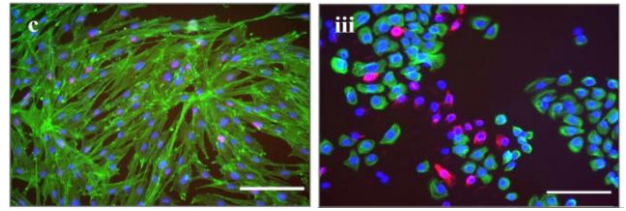




Antibacterial activity



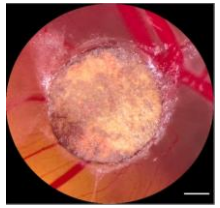
Cytocompatibility



Human dermal fibroblasts

Human epidermal keratinocytes

In vivo Angiogenesis

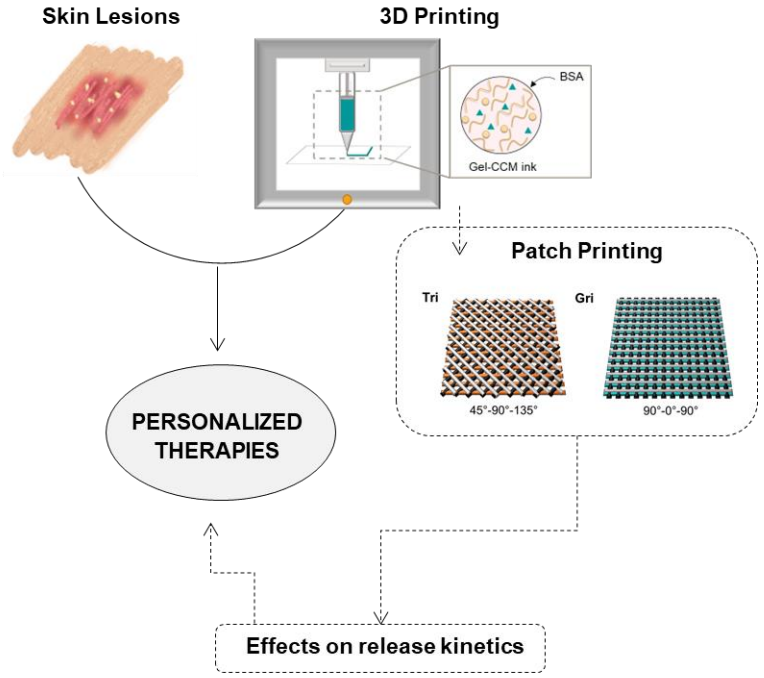


- The 3D Manuka-Gelatin base patches not only have **antibacterial activity** but also **not induce cytotoxicity** against human dermal fibroblasts and human epidermal keratinocytes and did **not induce irritation on HET-CAM tests** and **slightly promoted angiogenesis**.

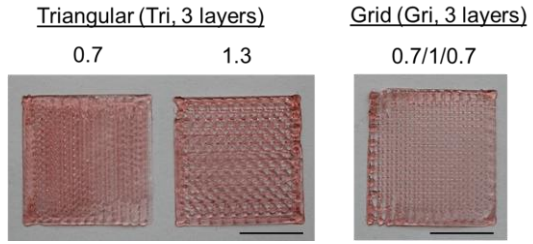
Applications

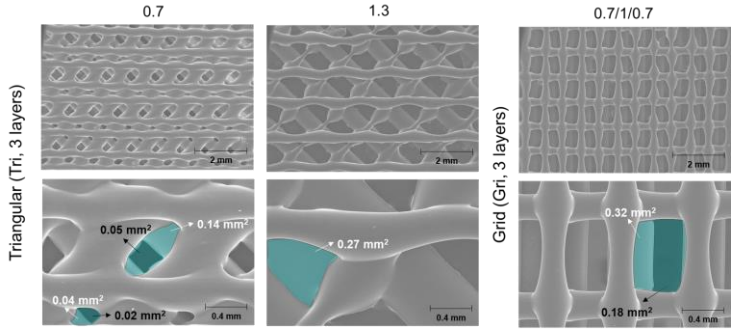
- **Cell-free treatment**

Bovine Serum Albumin (model bioative)

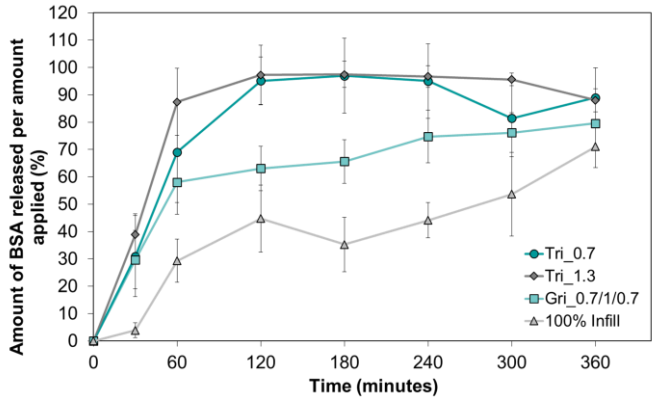


3D Patches Characterization





In vitro release

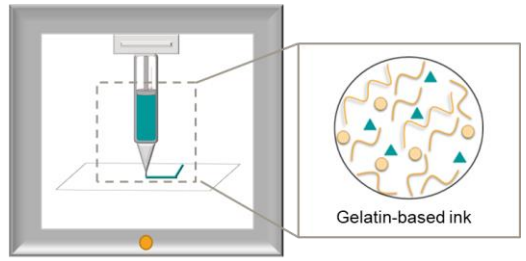


- Insights into **design-dependent release modulation** strategies;
- 3D technology allows rapidly producing patches with different release profiles, depending on the skin's needs.

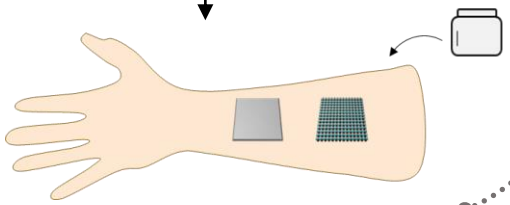
Applications

- **Cosmetic: Moisturizer**

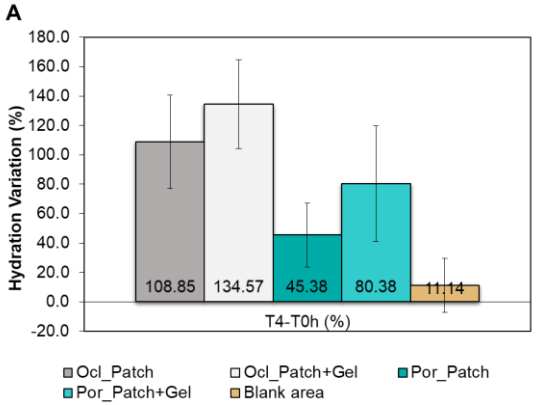
Hydration Efficacy

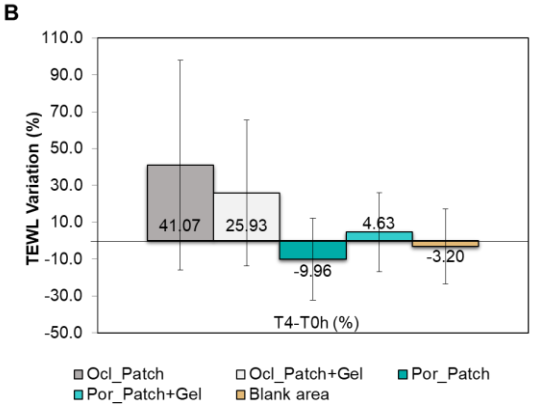


Ocl *vs* Por patches

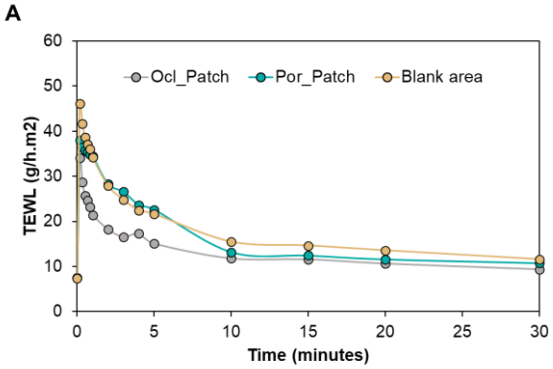


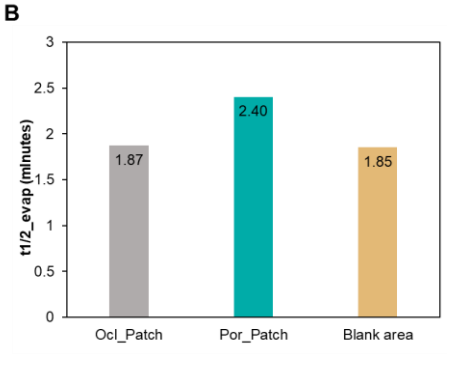
Under no-occlusion (4h)





Under occlusion (24h; plastic occlusion stress test, POST)



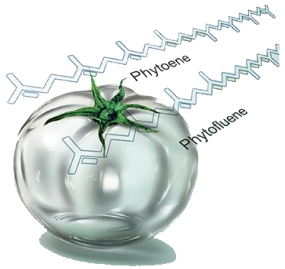


- **Modulate** the hydration rate and control the TEWL by adjusting the skincare mask's internal geometry.

Applications

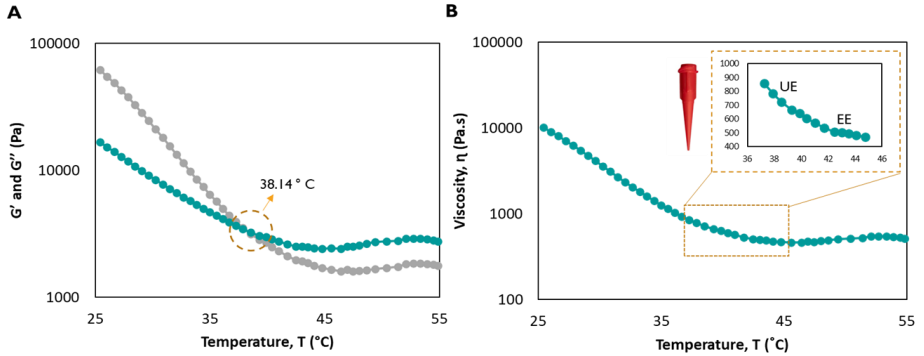
- **Cosmetic: Anti-aging**

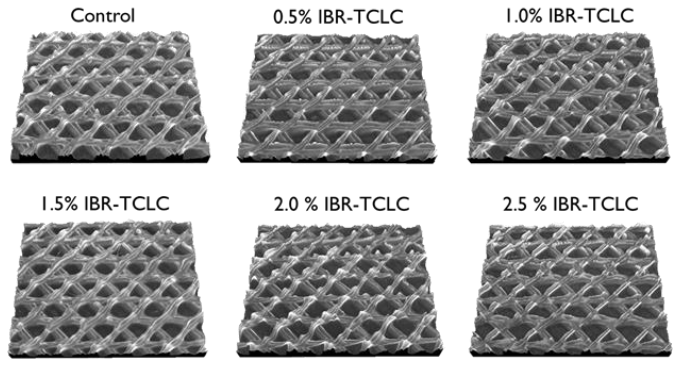
IBR-TCLC



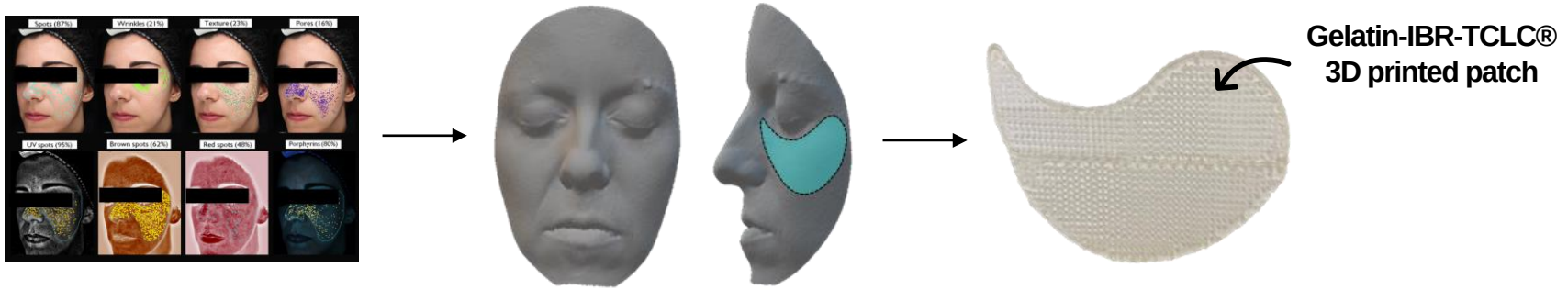
IBR-TCLC® - Purified tomato extract with recognized **antioxidant and anti-aging** properties

Rheological and Topographic analysis





Anti-aging 3D-printed eye patch

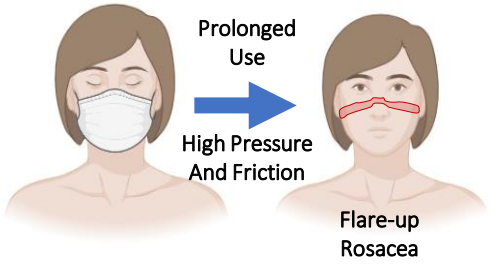


- The adoption of an **adequate printing optimization strategy (from rheology to process settings)** is fundamental to achieve reproducible and high-quality patches that cater the skin needs.

Applications

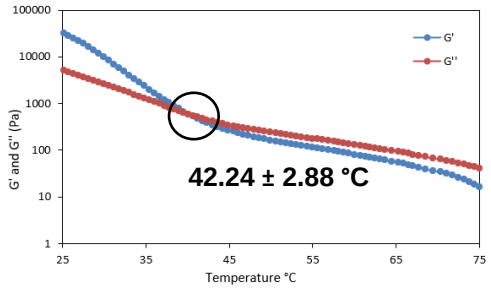
- **Flare-up rosacea treatment**

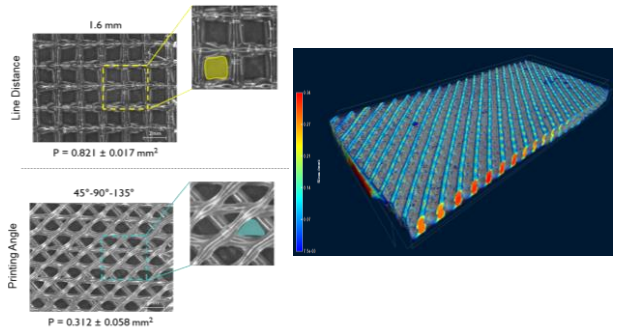
Metronidazole



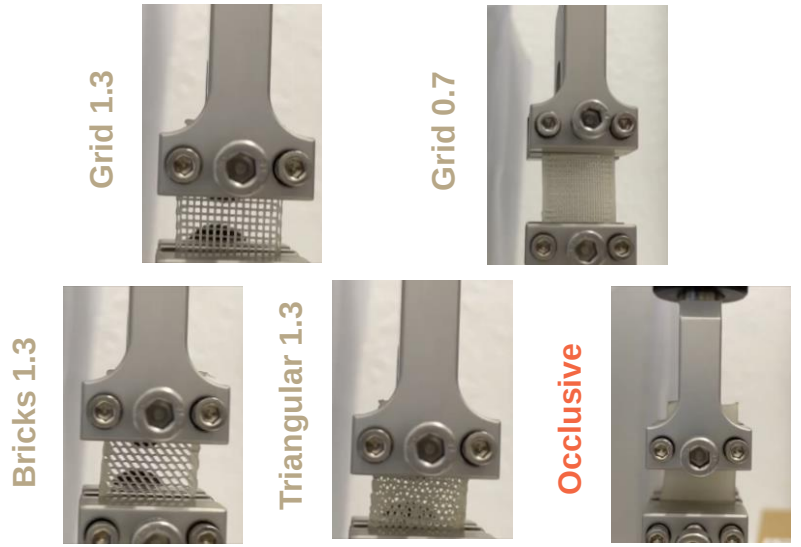
Gelatin-based ink with metronidazole (1%, w/w)

Rheological and Topographic analysis





Influence of internal design and line distance



- The **bricks and triangular** design-patches showed the highest tensile strength, followed by the occlusive and grid ones
- **Decreasing the line distance (1.3 to 0.7)** increased the resistance of patches to breakage in **69.8%.** The **occlusive** ones showed the highest tensile distance (72 mm)

Applications

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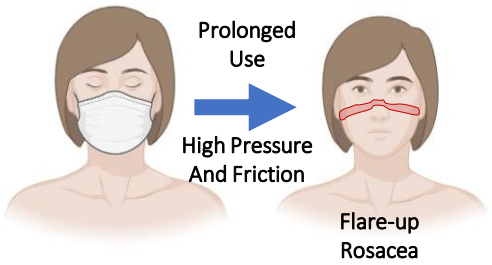
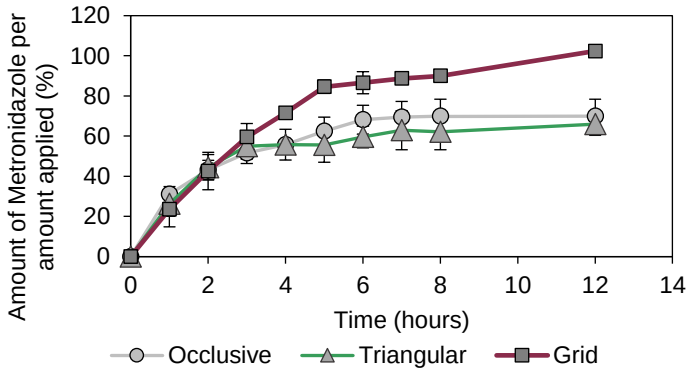
Metronidazole



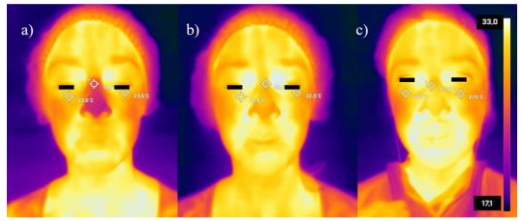
Gelatin-based ink with metronidazole (1%, w/w)

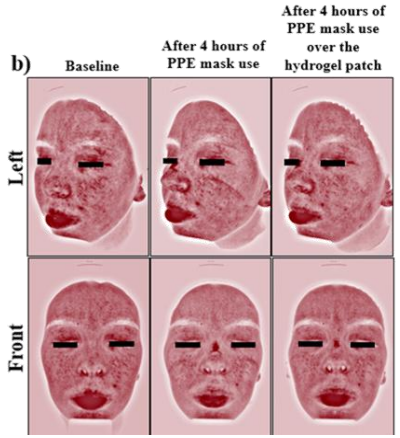
In vitro release Vertical diffusion Franz cells; 32 °C



- Different designs have different forms of release providing personalized treatment

In vivo efficacy





- Facial skin temperature values obtained when the hydrogel patch was placed underneath the mask, from the baseline values. In contrast, increase in skin hydration and attenuation of frontal red areas.

Conclusions and Future Work

Highlights

- Insights into the practicality of using 3DP to modulate the compounds' release by employing straightforward construction design strategies;
- 3D printing technology offers the necessary versatility to quickly modify and adjust the vehicle to the different requirements of various treatments;

Ongoing and Future Work

- Explore *in vivo* the influence of different internal designs on the penetration profile and efficacy;

Questions

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