CGPM 2020
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Green optimization of glutaraldehyde vapor-based crosslinking on poly(vinyl alcohol)/cellulose acetate electrospun mats for applications as chronic wound dressings

Chaired by PROF. DR. ANTONIO PIZZI and PROF. DR. FRANK WIESBROCK
polymers MDPI

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Summary

1. Introduction
2. Methodology
3. Results
4. Conclusions

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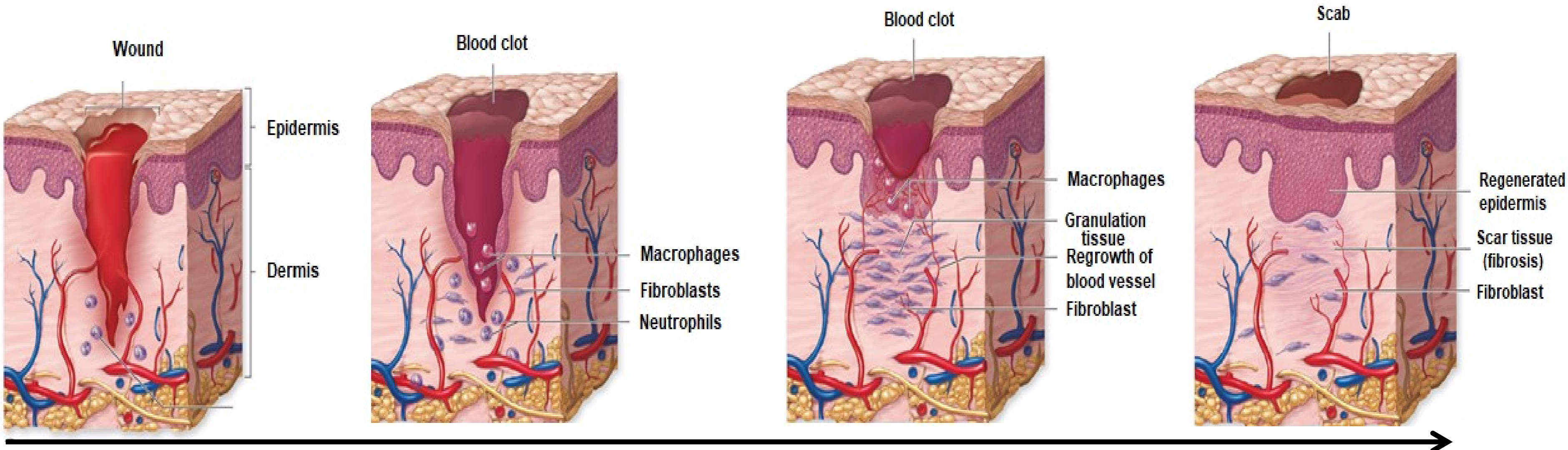
Acute and Chronic Wounds



Hemostasis Phase

Inflammatory Phase

Proliferation Phase

Maturation Phase

ACUTE WOUNDS

Prolongated state

CHRONIC WOUNDS

- defective cell matrix (high levels of proteases, ROS, etc.);
- high bacteria counts;
- moisture imbalance.

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Why engineer new dressings?

Chronic wounds require expensive and time demanding multistep therapies to induce debridement, to fight infection and minimize inflammation.

Films

Not recommended to full thickness, infected or highly exuding wounds

Hydrocolloids

Can cause maceration. Not specified for wounds producing high levels of exudates. Not indicated for infected tissue.

Hydrogels

Not appropriate for wounds with high levels of exudates and infected tissue.

Alginates

May cause dryness and scabbingry.

Limitations

Effective dressings should:

- Allow gaseous exchanges;
- Create a moist environment;
- Be impermeable to microorganisms;
- Remove excess of exudates and prevent desiccation;
- Be non-toxic;
- Provide mechanical protection;
- Be cost-effective;
- Be easy to use.

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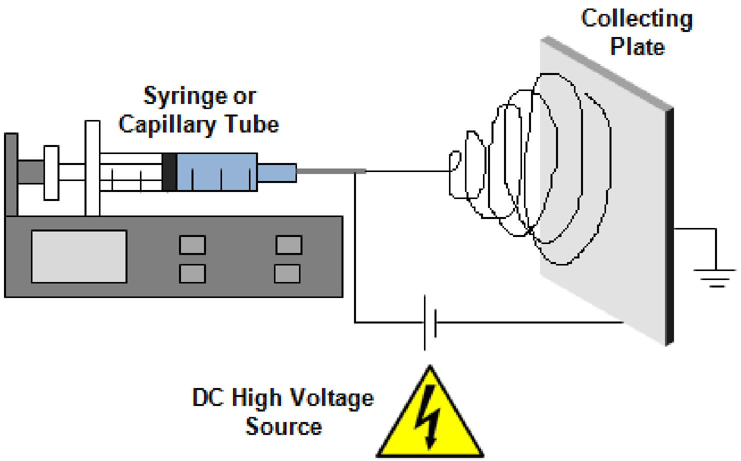
Teixeira, M.A. et al. 2020, Nanomaterials; Hasatsri, S. et al. 2017, Dermatol. Res. Pract.

Electrospinning technique

Principle: A jet of charged fluid of the dissolved or molten polymer is ejected out of a capillary tube after the electric potential overcomes the surface tension (formation of Taylor cone).



- ✓ Simple and low-cost production;
- ✓ Ultrafine fibers (nanoscale diameters);
- ✓ Similar morphologies to the natural extracellular matrix (ECM);
- ✓ Porosity control;
- ✓ Easy processability of both natural and synthetic polymers;
- ✓ Non-woven;
- ✓ Large surface-to-volume ratio;
- ✓ Allows the introduction of additives (e.g. antimicrobial agents).

Dressing Production is influenced by:

Solution parameters (type of polymer, solvent, additives, concentration), **processing conditions** (applied voltage, spinning distance and feed rate), and **surrounding environment** (temperature, humidity and air flow).

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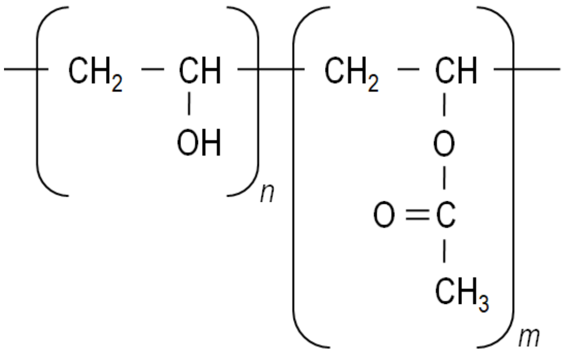
Felgueiras et al. 2017, Colloids Surf. B; Teixeira, et al. 2020, Polym.; Jain, R. et al. 2020, J. Drug Deliv. Sci. Technol.

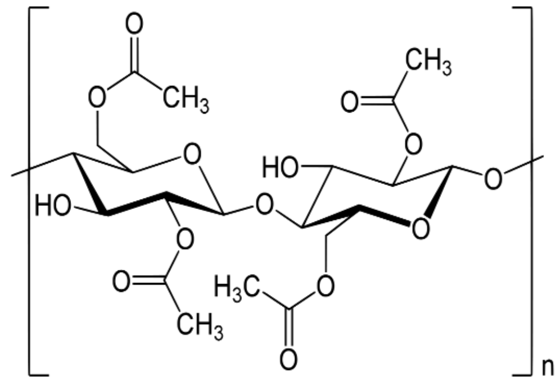
Biodegradable polymers

Poly(vinyl alcohol) (PVA)



- ✓ Food and Drug Administration (FDA)-approved polymer;
- ✓ Biocompatible;
- ✓ Biodegradable;
- ✓ Hydrophilic;
- ✓ Good transparency;
- ✓ Good film forming ability;
- ✓ Thermo-stability and chemical resistance.

Cellulose acetate (CA)



- ✓ Biodegradable;
- ✓ Good mechanical performance;
- ✓ High affinity to other polymers and biomolecules;
- ✓ Good hydrolytic stability;
- ✓ Relative low cost;
- ✓ Excellent chemical resistance;
- ✓ Ability to mimic the ECM to promote cell adhesion.

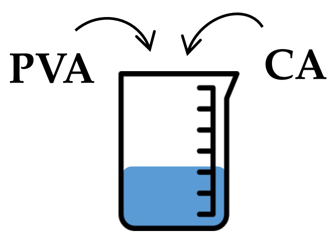
Teixeira, et al. 2020, Polym.; Ma, C. 2012, Thesis; Tayeb, A.H. 2018, Molec.

Methods

Production of meshes

1. Polymeric Solutions

80ºC for 3 h

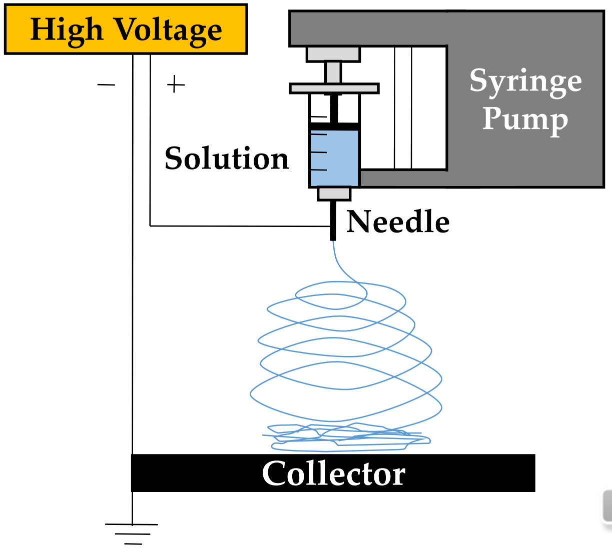


PVA/CA

100/0
90/10
80/20

Concentration: **10% (w/v)**
Solvents: **75/25% (v/v) acetic acid/dH_2O**

2. Eletrospinning



The most stable electrospun nanofibers were reached at:
Voltage: **25 kV**;
Feed rate: **0.8 mL/h**;
Distance between syringe and collector: **18 cm**.

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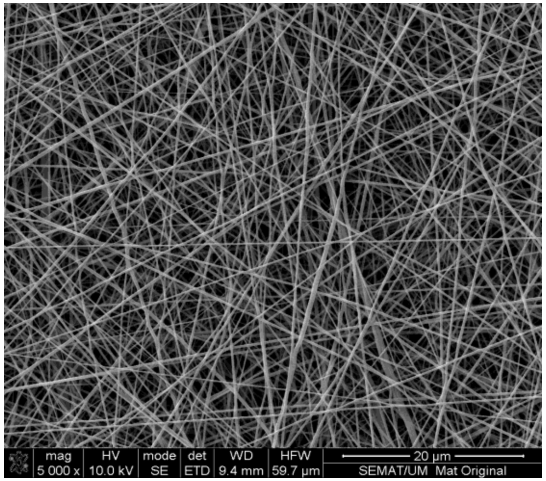
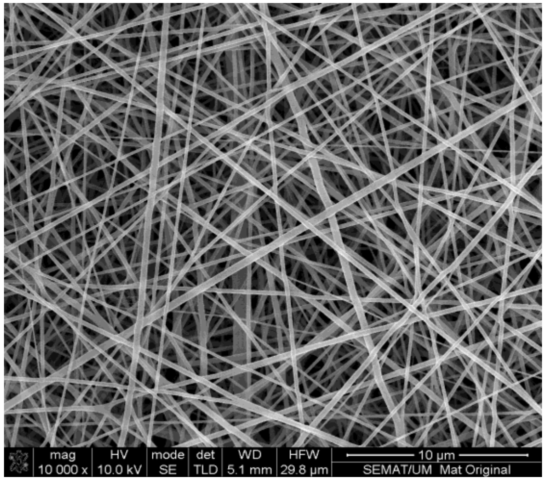
Mats’ Morphology

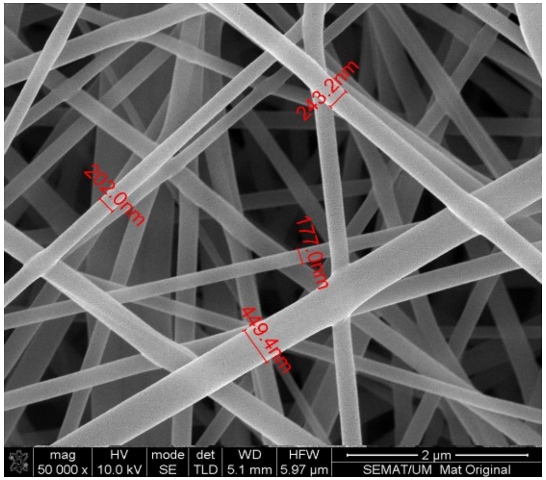
<u>Original Mat</u>: **80/20 PVA/CA; 75/25% (v/v) acetic acid/dH_2O**



Mag 5 000 x



Mag 10 000 x



Mag 50 000 x

Average Fiber Diameter (Arithmetic) **= 194 ± 51 nm**

Data obtained using ImageJ (2 images of Mag 50 000 x – 100 measurements each)

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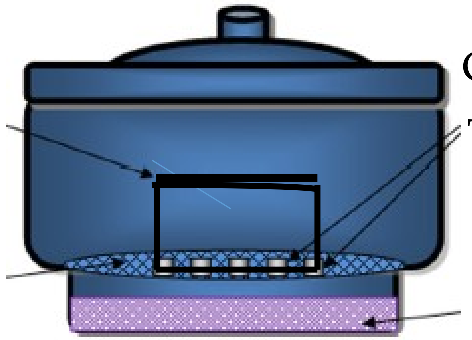
Crosslinking Process

- **1st trial with 80/20 PVA/CA – Starting point:**

Mats were initially dried for 72 h at 40°C



Room temperature
&
60ºC

During 2, 4, 6 and 8 h

Crosslinking accomplished after 6 and 8 h at 60°C.
At 8 h mats became yellowish.

2nd Trial

Temperature: 60ºC
Glutaraldehyde exposure: 7 h
Drying temperature: 60ºC for 24 h

Successful crosslinking

Mats become **yellowish**

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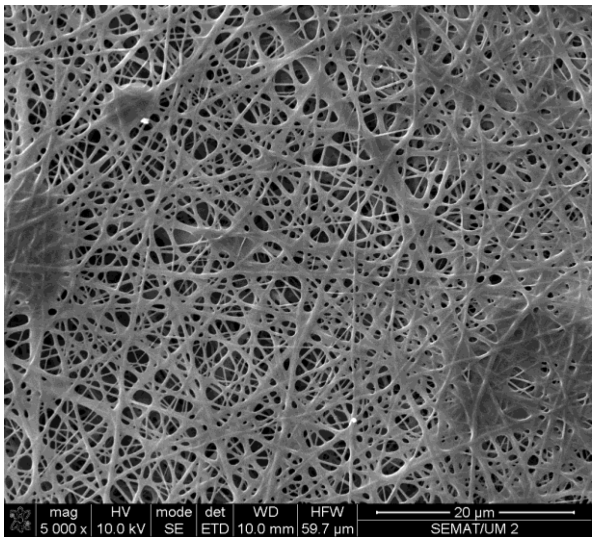
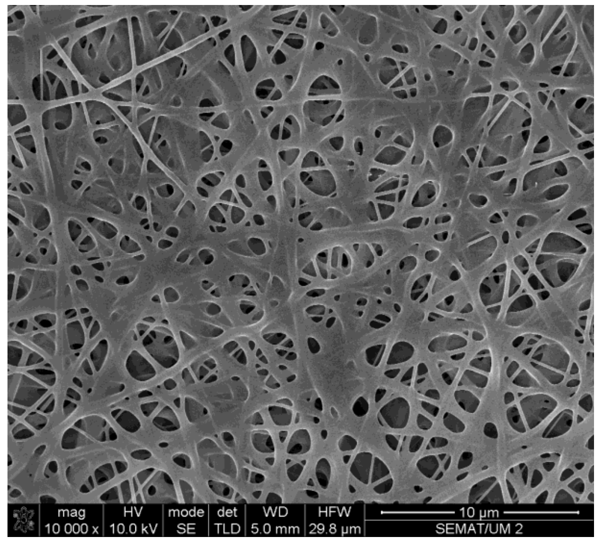
Mats morphology after crosslinking

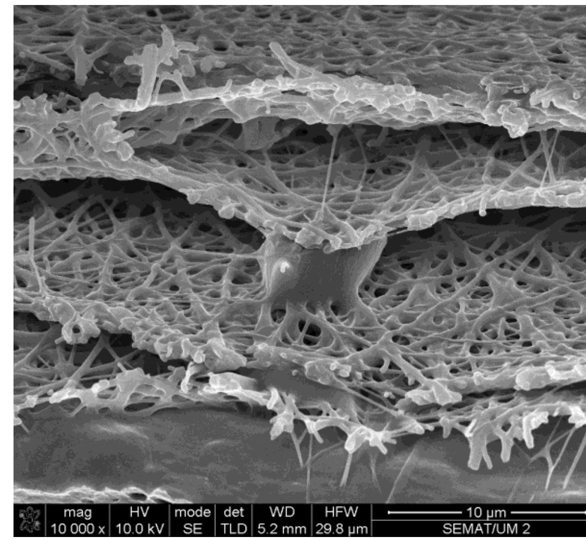
Crosslinking: 60ºC; 7h; 15mL GA (without washings)



Mag 5 000 x



Mag 10 000 x



Mag 10 000 x

Average Fiber Diameter (Arithmetic) **= 343 ± 340 nm**

Data obtained using ImageJ (2 images of Mag 50 000 x – 100 measurements each)

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Crosslinking Process

3rd Trial:

New Conditions:

Temperature: 60ºC
Glutaraldehyde exposure: 7 h
Drying temperature: 45ºC for 24 h

How to prevent the yellow color in the drying process?

Successful crosslinking and drying process

How to remove the glutaraldehyde efficiently?

Sonication	**Orbital shaker**	**0.26M glycine solution**
RT	37ºC at 100 rpm	Orbital shaking at RT during 30 min

SEM **Damaged structure**

15 and 30 minutes (100 ml of dH_2O changed every 5 minutes)

1st: Dry at 45ºC and 40ºC → **2nd:** RT (to avoid the yellow coloration)

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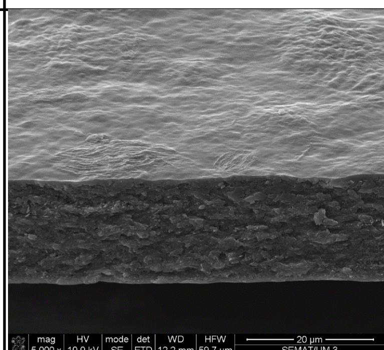
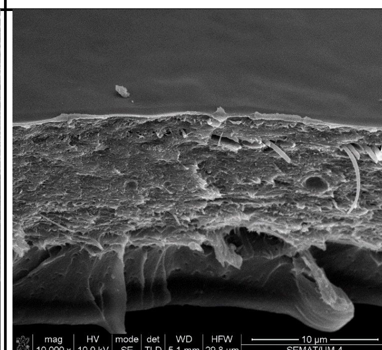
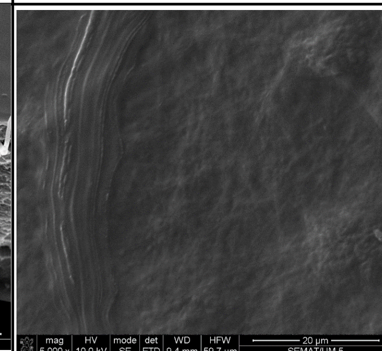
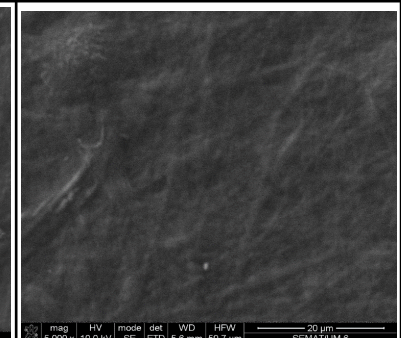
Removal of GA excess

<u>Washings</u>

Process	Sonication	Sonication	Orbital shaker (100 rpm)	Orbital shaker (100 rpm)
Duration (min)*	15	30	15	30
Structure				
Temperature	RT	RT	37°C	37°C

*Every 5 minutes the water changed

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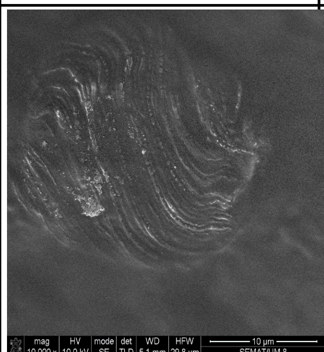
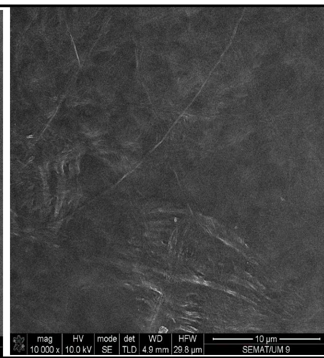
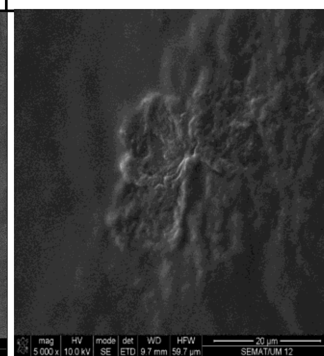
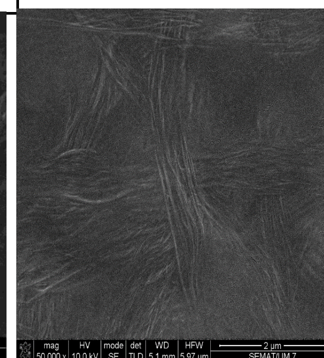
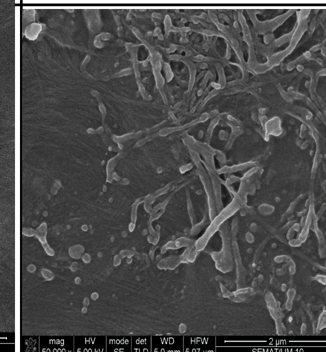
Results and Discussion

Process	Sonication	Orbital shaker (100 rpm)	Orbital shaker (100 rpm)	Orbital shaker (100 rpm)	Orbital shaker (100 rpm)
Duration (min)	30	15	30	30	180
Structure					
Concentration (%)	0.5	0.5	0.5	2.0	0.5
Temperature	RT	37°C	37°C	37°C	37°C

<u>Washings with glycine</u>

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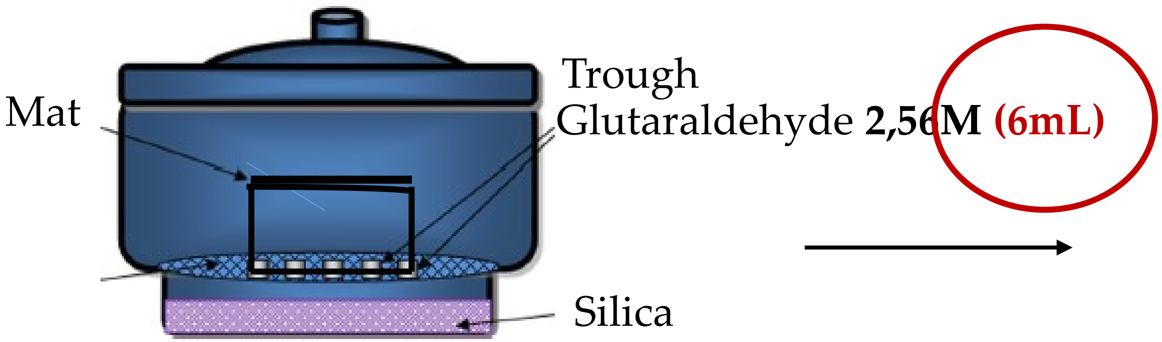
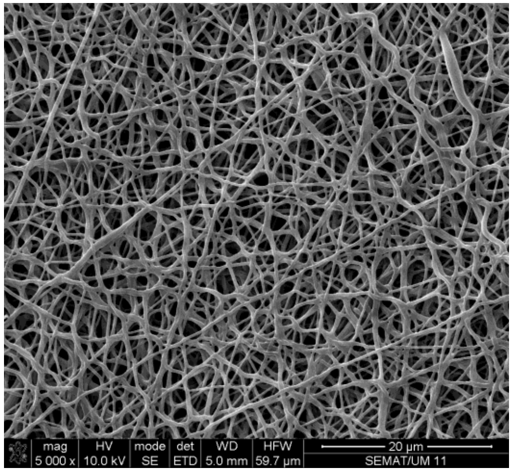
The new crosslinking approach method



60ºC
7h



Successful crosslinking

Without architectural change

Electrospun meshes without compromising their functions

Conclusion

After analyzing and experimenting the various crosslinking and removing excess GA processes, **the amount of GA applied seems to be the simplest and most effective way to attain an effective crosslinking** without harming the structure or turning the surface cytotoxic (due to excess GA).

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Acknowledgments

Thank you for your attention.

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