Safety Concerns Behind DEB Coating Technology

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The Competitors

Company	DCB Name	Drug formulation
Aachen Resonance GmbH (distributed by Biotronik AG in UK, Switzerland, Benelux, Italy and Ireland).	ELUTAX®	Formulated with a matrix of pure Paclitaxel
B. Braun Melsungen AG	SeQuent® Please	Paclitaxel with ioporimde formulation (Paccocath® technology)
Bayer AG (MEDRAD, Inc.)	CotavanceTM with Paccocath® coating technology	Paclitaxel with ioporimde formulation (Paccocath® technology)
Caliber Therapeutics, Inc.	TADD (Targeted Angioplasty Drug Delivery)	Rapalog-based with unknown formulation
Cook Group, Inc.	Advance® 18PTX®	Paclitaxel with unknown additive-based formulation
Eurocor AG	DIOR®	Paclitaxel without any formulation. (Opto Circuits Ltd. also developing rapamycin-based technology)
Invatec s.r.l.	IN.PACT™ Amphirion	Paclitaxel with FreePac™ hydrophilic formulation
Lutonix, Inc.	Unknown	Paclitaxel with unknown formulation

Shellac Utilization

Usage:

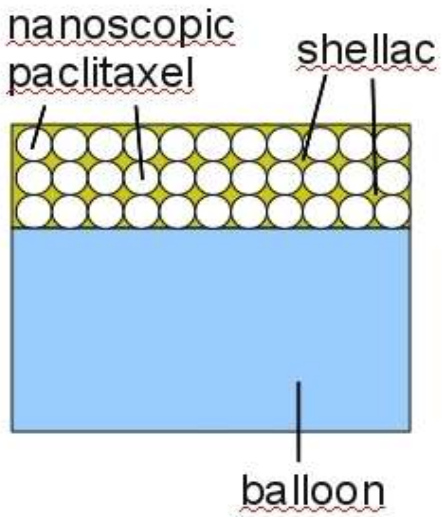
- Politur
- Food additive (E904)
- Pharma
- Cosmetics

Technology

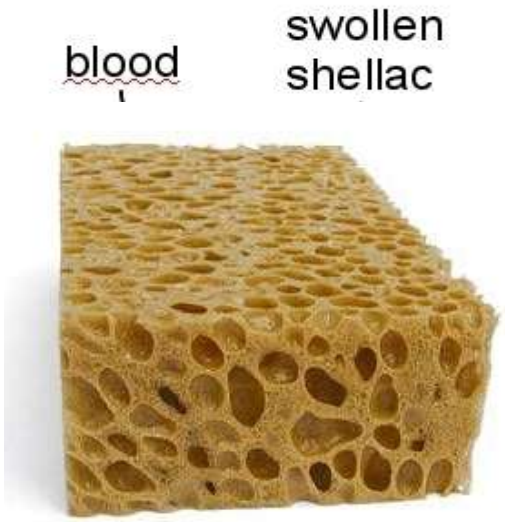
Shellac

(Ph.Eur. 4.8)

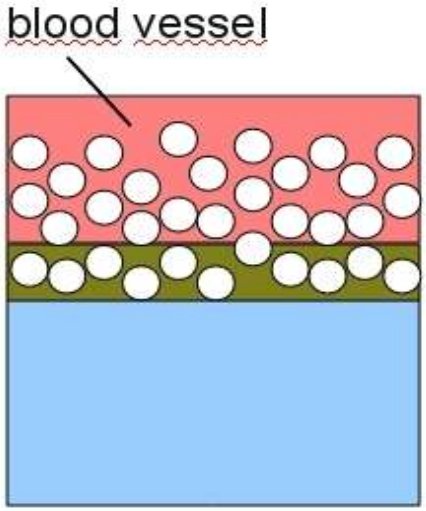
Shellac is not a polymer



coated balloon

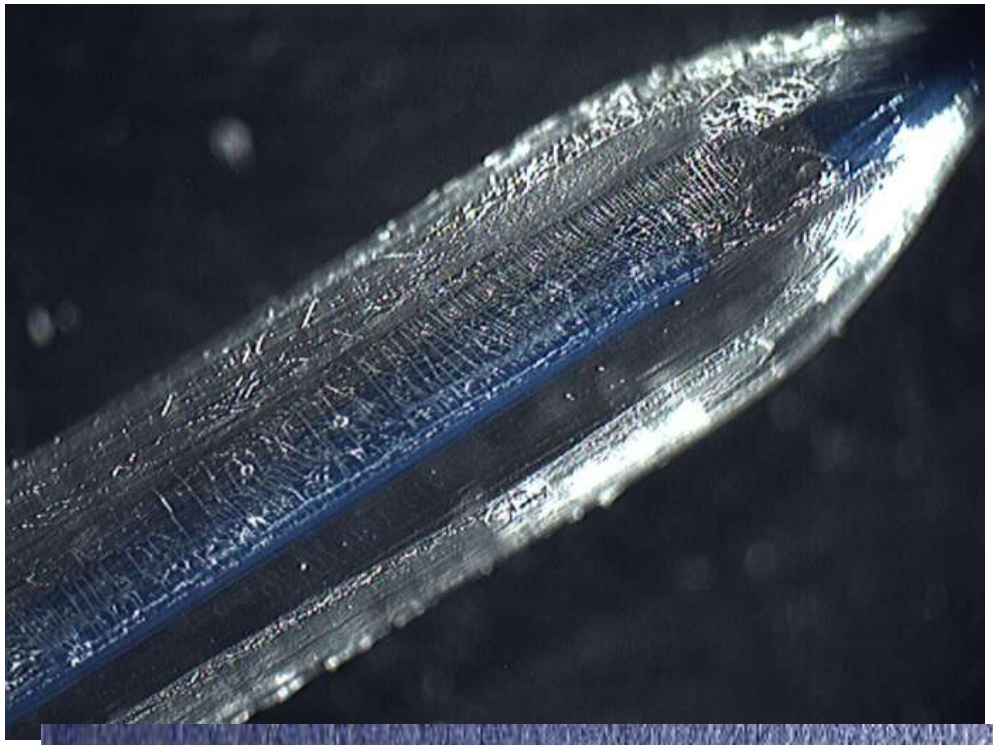


in contact with blood



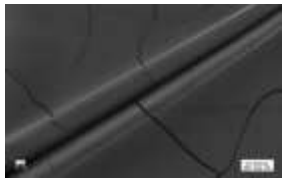
inflating

Shellac: How Does it Look?



Compared to competitive products Shellac gives balloon a shiny appearance

Micropipetting technology



Micropipetting ensures the most homogeneous and controllable method of coating application

- Coating layer by layer

- Micropipetting allows coating solution to go into pockets under folds

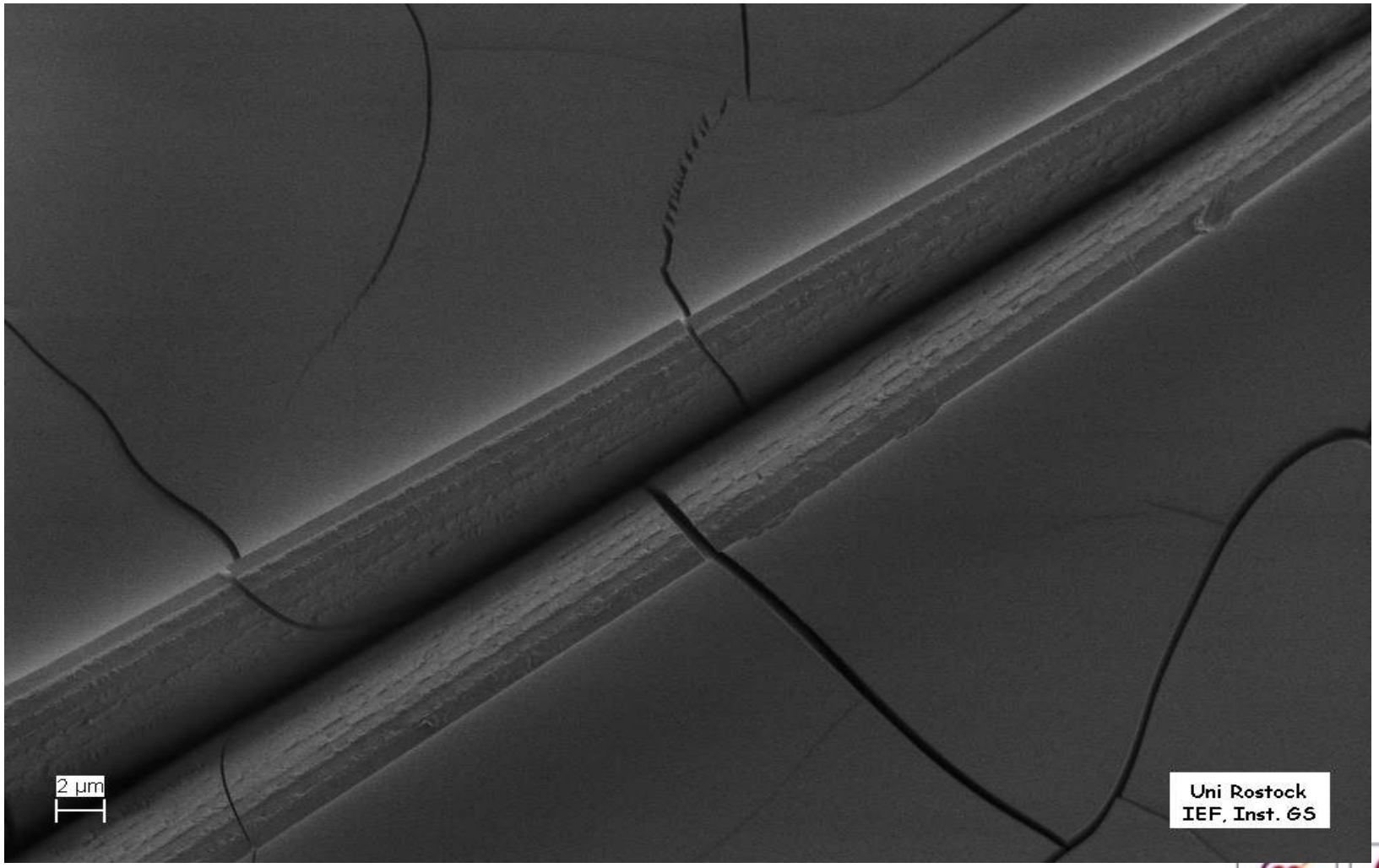
- No-thickening by layer coating
- Only 6 µm layer thickness

Advantages of the micropipetting technology

- 100% dose control
- Homogeneous coating over length and diameter
- Reproducibility of appearance, dosage, homogeneity
- Balanced adherence and drug transport properties

Requirement	Dose control	Reproducibility	Homogeneity	Effect
Spray coating	Poor	Good	**Very good**	Mid
Dip coating	Very poor	Poor	Poor	Very low
Micropipetting	**Very good**	**Very good**	**Very good**	**High**

Coating surface: non-crystallin

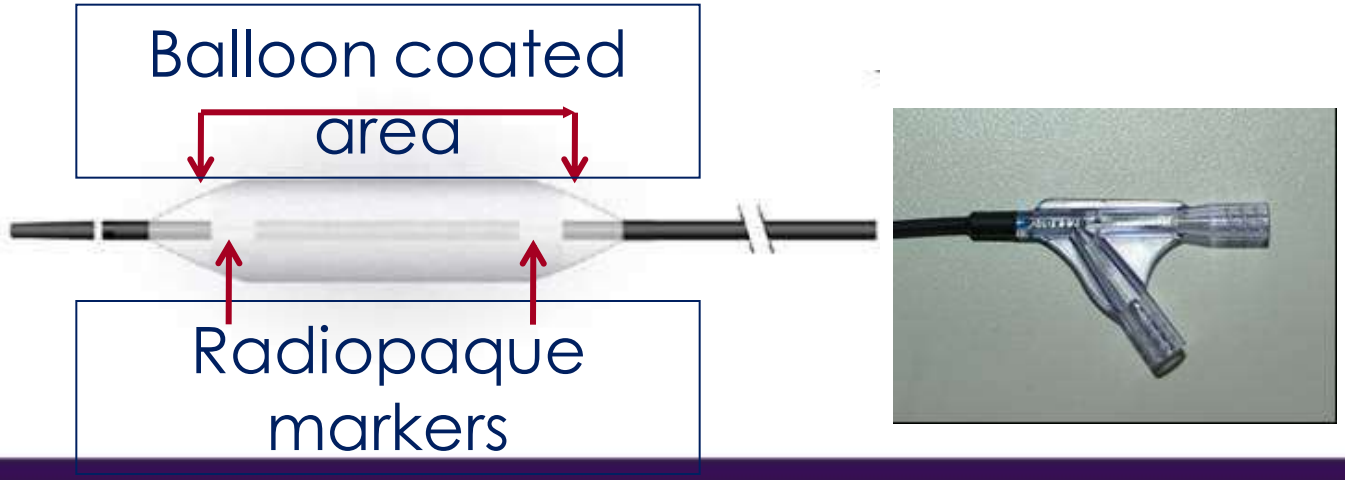


Coating Location

- The active coating on the balloon is placed onto the cylindrical portion of the balloon and extends into the tapered part of the balloon

- Coating extends slightly outside the margins of the markers

- This ensure proper treatment of drug to the entire region that is touched by the balloon inflation



Experimentel design

- Shellac coating was performed by spraying a commercially available shellac suspension on glass and polished titanium alloy discs

- Investigated cell types: Human dermal EC (HDMEC) and humane smooth muscle cell (HSMC)

- Exposition with extraction product and direct contact

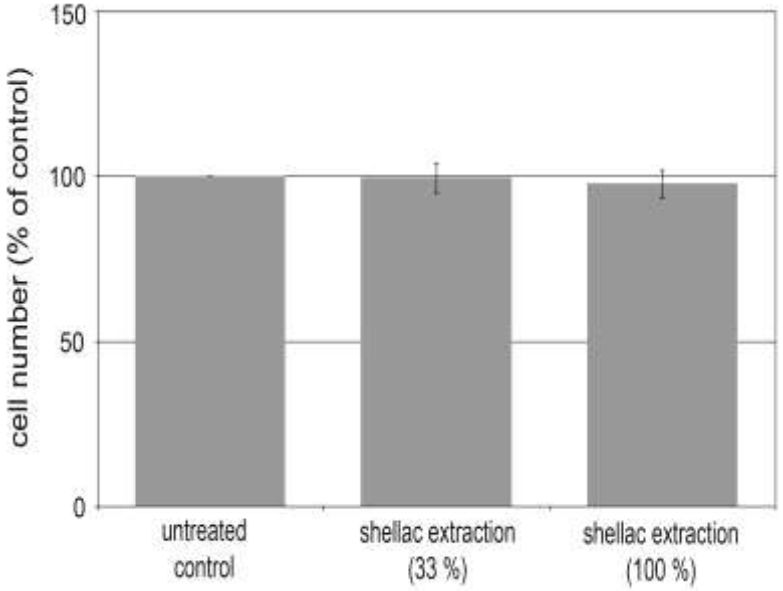
- Investigation of metabolic activity

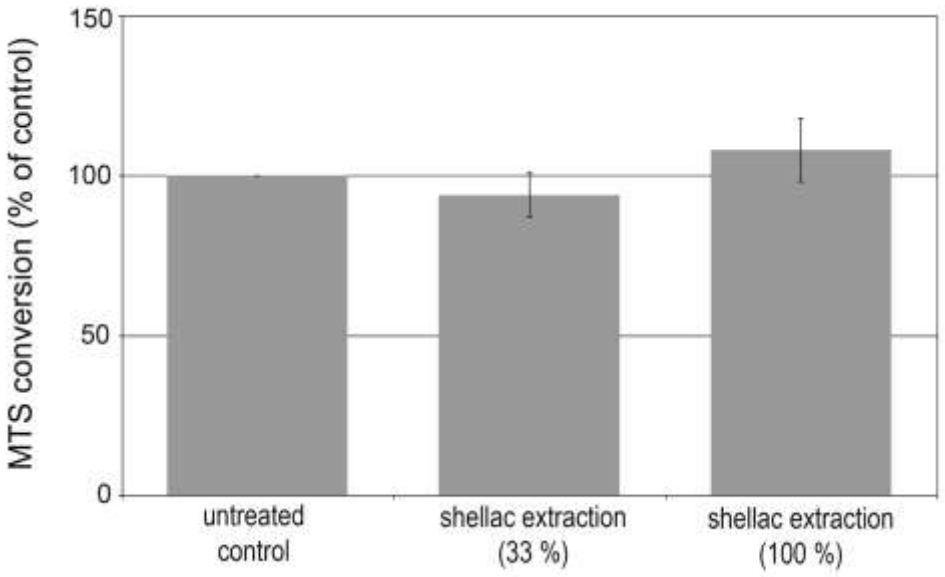
- Investigation of pro-inflammatory response

Evaluation of metabolic activity

• Shellac extraction products did not show any impairment of EC and SMC viability, proliferation as well as metabolic activity.

Metabolic cell activity



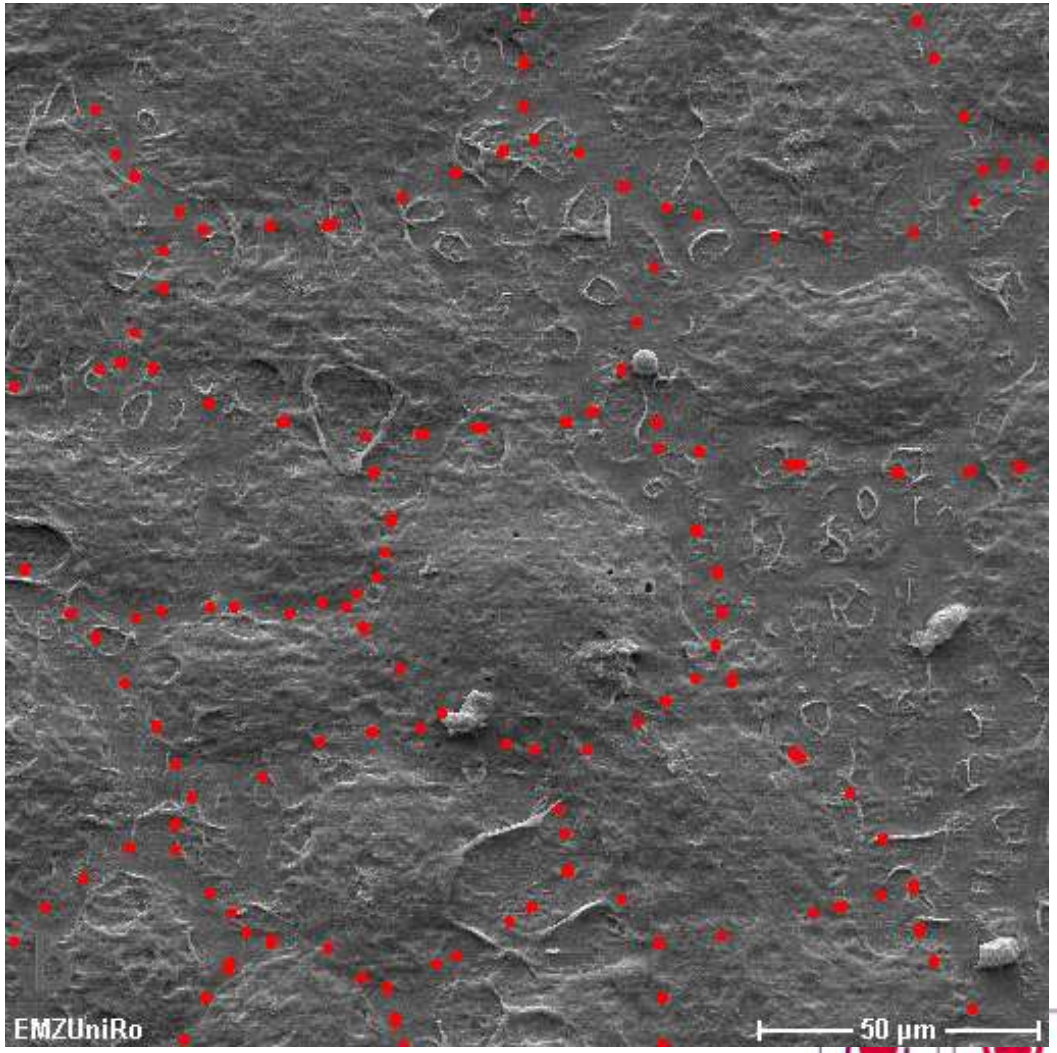


Courtesy of Kirsten Peters[1*]

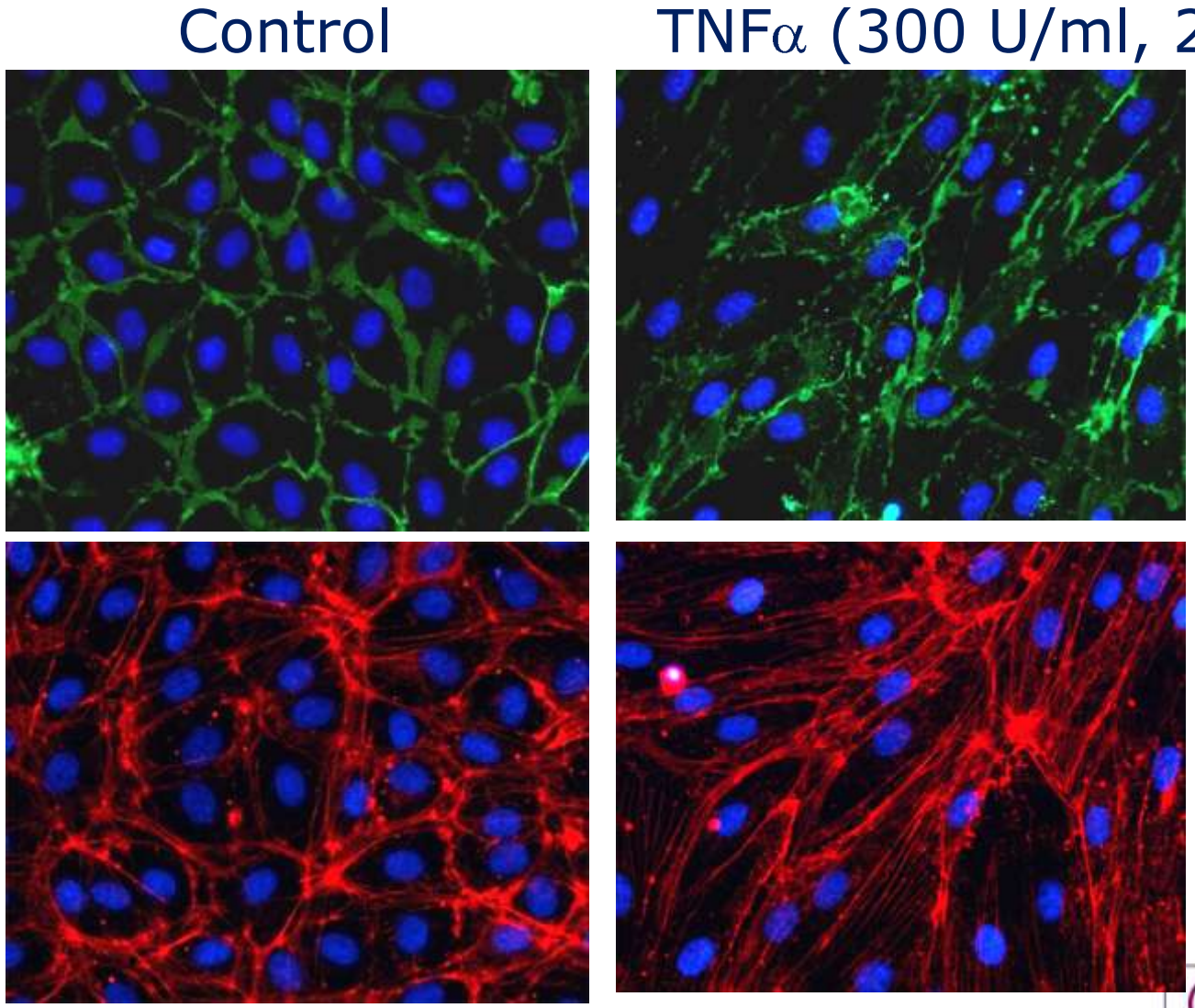
[1]Arbeitsbereich Zellbiologie (*Nachwuchsgruppe), Universität Rostock

Endothelial cell phaenotype in contact to shellac

- Human dermal EC (HDMEC) in vitro in direct contact to shellc coating (SEM)



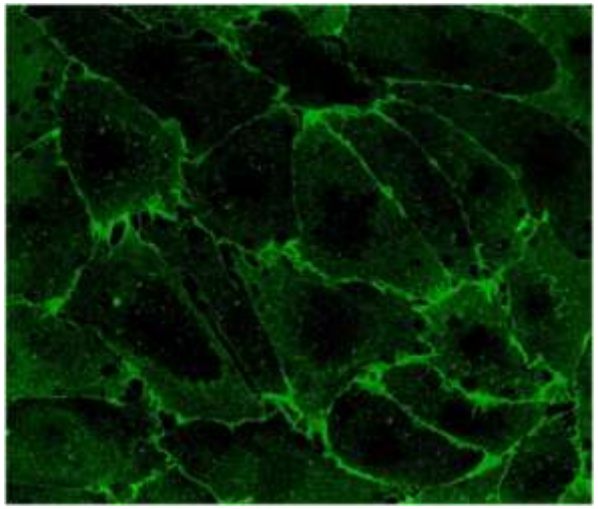
Interendothelial contacts *in vitro*



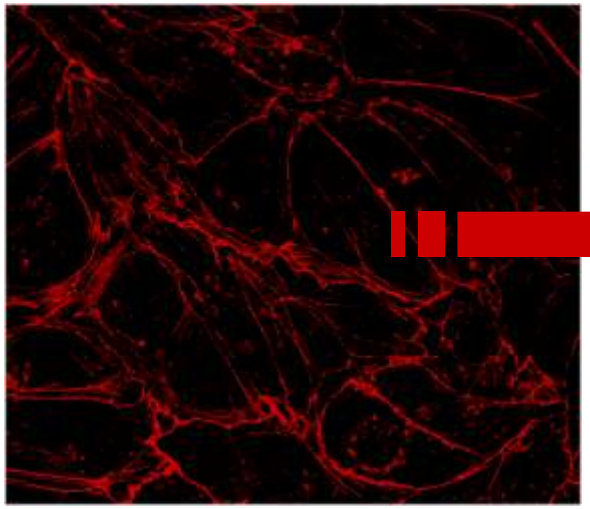
Interendothelial contacts *in vitro*

Human dermal EC (HDMEC) *in vitro* after 24 h cell culture supernatants with Shellac extraction products

CD31



F-Aktin

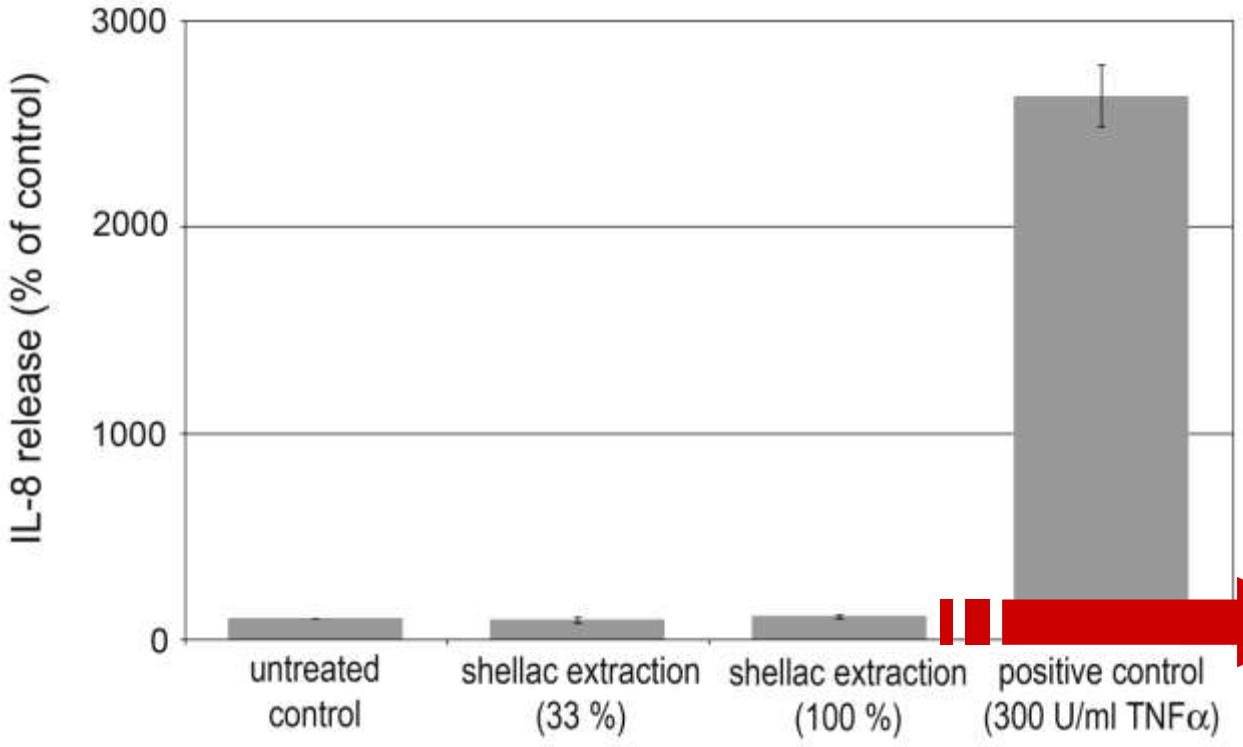


No sign of activation

Pro-inflammatory activation?

IL-8-release

- Shellac extraction product (24 h extraction)
- Exposition of confluent Human dermal EC (HDMEC) with extraction product (24 h extraction)
- TNFα as positive control group



No increase in pro-inflammatory activation (shown by IL-8 release) observed

Summary and Conclusions

- Neither direct contact to shellac-coated materials nor exposure to shellac extraction products did impair EC and SMC viability and function in vitro.

- Thus, shellac is a promising candidate for coating of drug-eluting intra-vascular devices.