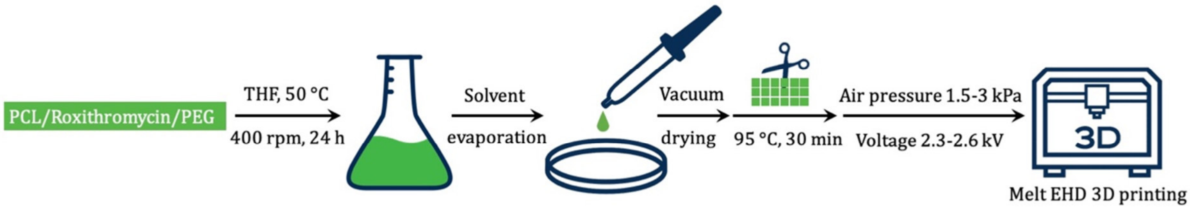
How Contact Angle Measurement Can Help Develop Materials for Anti-Infective Bone Implants

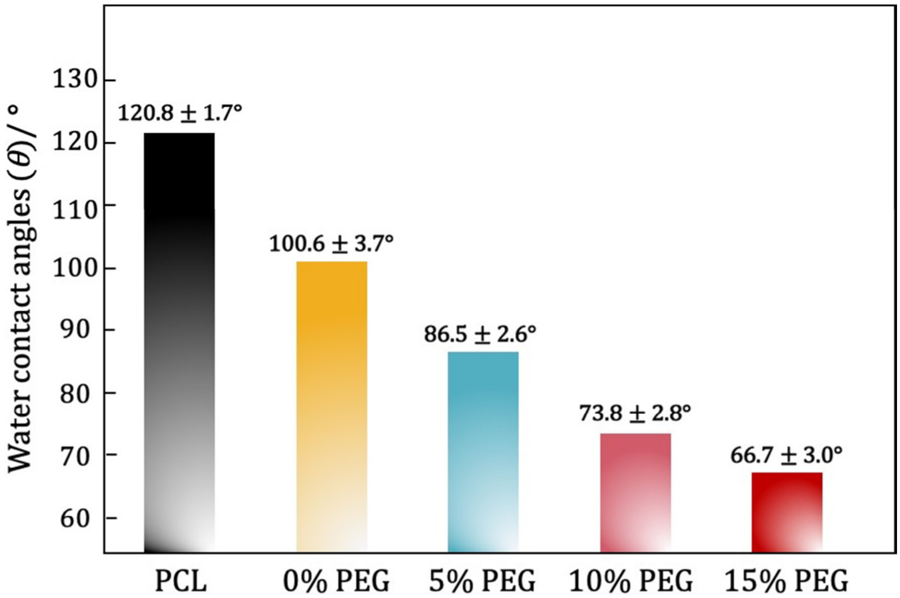
Bone defects usually result from trauma, neoplasm, congenital defects, infection or failed arthroplasty. Nowadays, modern orthopedic surgical techniques have proved to be reliable for the reconstruction of these defects. The current strategies consist of autologous bone graft, allogeneic bone graft, and biomaterial scaffold graft. Autologous bone graft, which involves the transport of bone from one site to another location in the same patient, remains the gold standard for bone defects. However, it faces the challenges of donor morbidity and insufficient bone supply. Meanwhile, allogeneic bone graft, which means the transfer of bone from a donor to the defect site of the patient, has the limitation of immune rejection. Biomaterial scaffold graft, which uses a supporting biomaterial like in tissue engineering applications to repair or restore damaged tissues, is the most promising treatment and has been extensively studied for bone repair. Until now, various methods have been reported to fabricate potential biomaterial scaffold grafts. Poly(ε-caprolactone) (PCL) is one of the most widely used tissue engineering materials with good biocompatibility, biodegradability and ideal mechanical properties. However, the application of PCL in tissue engineering is still limited by its hydrophobicity. To improve PCL systems, Bai et al. recently developed a composite scaffold with better hydrophilicity as an anti-infective bone implant.

In this work, a composite scaffold consisting of poly (ε-caprolactone) (PCL)/polyethylene glycol (PEG)/roxithromycin (ROX) was constructed *via* melt electrohydrodynamic (EHD) 3D printing as shown in **Picture 1**.



Picture 1: *The preparation process of the PCL/PEG/ROX composite materials (PCL: PEG: ROX* = 95:0:5, 90:5:5, 85:10:5, 80:15:5*)*

In brief, PCL, PEG and ROX with different weight ratios were added to tetrahydrofuran (THF) and mixed for 24 h (50 °C, 400 rpm). Then the solution was transferred to a glass dish for solvent evaporation, following by vacuum for 2-3 h. Afterwards, the PCL/PEG/ROX composites were cut, molten and then placed into the melt EHD 3D printing device to generate the desired structure. Scanning electron microscope (SEM) showed that the composite scaffolds with different PEG content all displayed homogeneous morphology and uniform three-dimensional stacked structure with a fiber diameter of around 8 µm. Specifically, the scaffold with 15% PEG exhibited the worst stacking morphology and wider distribution of fiber diameter, attributed to the addition of PEG which would largely decrease the viscosity of melt and reduce the spinnability. Next, Fourier Transform Infrared Spectroscopy (FTIR) was applied to successfully verify the introduction of ROX and PEG into PCL fibers. Previous studies have demonstrated that a moderate hydrophilicity of the scaffold is quite significant for cell adhesion and proliferation. Hence, hydrophilic PEG was introduced into the fibers to improve its wettability and the further cell behavior on the scaffolds. The thus formed composite scaffolds were analyzed by contact angle measurements to study the surface wettability. As shown in **Picture 2**, the water contact angle of pure PCL scaffold which is a typical hydrophobic material was 120.8 ± 1.7°. PCL/ROX scaffold with 0% PEG had a water contact angle around 100.6 ± 3.7° due to the presence of the hydroxyl groups in ROX. The addition of PEG showed a significant effect on the surface hydrophilicity, while the water contact angle decreased from 86.5 ± 2.6° to 66.7 ± 3.0° with the increase of PEG content from 5% to 15%.

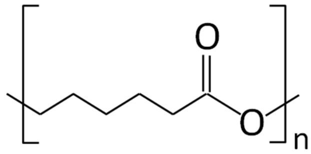


Picture 2: *Characterization of Surface Wettability of Pure PCL and PCL/ROX scaffolds with various PEG contents*

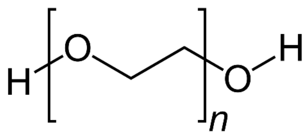
The effect of polymer mixtures on the wettability

Different functional groups strongly influence the wettability of a surface. Following the basic chemical principle of **"same likes same"** it can be understood, that water with its two O-H bonds is more affine towards **more polar PEG** that also possesses O-H groups at the terminus and a high oxygen to carbon ratio compared to **less polar PCL** resulting in a better wettability (smaller contact angle).

Furthermore the **content of terminal groups** which depends on the molecular weight of the polymer is **highly important for its polarity**. While the PCL used in this paper had a very high molecular weight of 50000 resulting in only little terminal groups, the PEG had a molecular weight of 6000 resulting in much more terminal O-H groups and a higher polarity. The lower the molecular weight of the PEG the stronger it will increase the wettability.
In order to improve the wettability of a biopolymer it will help to add polar components such as PEG.



PCL (MW 50000)



PEG (MW 6000)

Moreover, further drug release, antibacterial activity and cell work were conducted to study the potential anti-infective effect of PCL/PEG/ ROX scaffold. Herein, ROX was used as a local antibiotic to prevent and treat the infection during bone repair. It was illustrated that the scaffolds with 0%, 5%, 10%, and 15% PEG displayed an initial short-term burst release and subsequent long-term sustained ROX release behavior, accordingly releasing 76.3%, 87.6%, 88.9% and 91.4% of ROX until 24 h respectively. The disc diffusion assay and dynamic contact assay against E. coli and S. aureus showed that the ROX-loaded scaffolds exhibit excellent antibacterial activity, especially for Gram-positive bacteria like S. aureus which is also the main bacteria in bone infection. Also, MTT assay and immunostaining analysis demonstrated that PCL/ROX scaffold with 5% PEG led to the highest cell viability. This data indicated the moderate hydrophilicity of materials was beneficial to cell adhesion and growth, while too high hydrophilicity was not beneficial to protein adsorption.

Overall, the authors described that PCL/PEG/ROX composite scaffolds fabricated by melt EHD 3D printing possess good biocompatibility and anti-bacterial activity. Key properties of the scaffolds, such as drug release and cell adhesion, could be easily controlled by tuning the hydrophilicity of the materials. The increase of PEG content from 5% to 15% could decrease the water contact angle from 86.5 ± 2.6° to 66.7 ± 3.0°. This research thus offers considerable prospects in the fabrication of anti-infective implant materials with controlled hydrophilicity properties during bone repair.

An optical contact angle analyzer OCA 100 (DataPhysics Instruments GmbH, Germany) was used in this research.

For more information, please refer to the following article:

Melt electrohydrodynamic 3D printed poly (ε-caprolactone)/polyethylene glycol/roxithromycin scaffold as a potential anti-infective implant in bone repair; Jianfu Bai, Han Wang, Wei Gao, Feng Liang, Zixu Wang, Ying Zhou, Xingzi Lan, Xun Chen, Nian Cai, Weimin Huang, Yadong Tang; *International Journal of Pharmaceutics* **2020**, 576, 118941; DOI: 10.1016/j.ijpharm.2019.118941