



# Preparation of Innovative PEG/Tannic Acid/TiO<sub>2</sub> Hydrogels and Effect of Tannic Acid Concentration on Their Hydrophilicity

Serbülent Türk<sup>1,2\*</sup>, Burak Ünlü<sup>1,2</sup>, Mohammad Sukri Mustapa<sup>3</sup>

<sup>1</sup>Sakarya University, Biomedical, Magnetic and Semiconductor Materials Application and Research Center (BIMAS-RC), 54187 Sakarya, TURKEY

<sup>2</sup>Sakarya University, Biomaterials, Energy, Photocatalysis, Enzyme Technology, Nano & Advanced Materials, Additive Manufacturing, Environmental Applications and Sustainability Research & Development Group (BIOENAMS R&D Group), 54187 Sakarya, TURKEY

<sup>3</sup>Faculty of Mechanical and Manufacturing Engineering, Universiti Tun Hussein Onn Malaysia, MALAYSIA

\*Corresponding Author

DOI: <https://doi.org/10.30880/ijie.2021.13.07.030>

Received 1 September 2021; Accepted 15 September 2021; Available online 30 September 2021

**Abstract:** Hydrogels are materials that can be used in biomedical and medical applications and have gained increasing interest in recent years. In order to obtain a wide variety of properties, hydrogels containing more innovative components still need to be produced and investigated. In this study, for this purpose, an innovative injectable polyethylene glycol (PEG)/tannic acid (TA)/TiO<sub>2</sub> hydrogels were prepared and their properties were investigated. TA, used as a crosslinker for PEG, was used in different concentrations (400 mg, 800 mg, and 1.2 g) in hydrogel preparation to analyse the effect of tannic acid on the properties of the obtained hydrogels. PEG/0.4TA/TiO<sub>2</sub>, PEG/0.8TA/TiO<sub>2</sub> and PEG/1.2TA/TiO<sub>2</sub> hydrogels prepared by using FeCl<sub>3</sub> to increase the crosslink density in its content and by adding TiO<sub>2</sub> due to its antimicrobial properties, were characterized by UV-VIS spectroscopy, FTIR and contact angle measurements. . With the UV-VIS and FTIR spectra, it is seen that TA/Fe<sup>3+</sup> metal complexes are formed and the three-dimensional hydrogel network is successfully completed with the help of these metal complexes formed by the addition of FeCl<sub>3</sub>. In addition, the contact angle measurements of the PEG/0.4TA/TiO<sub>2</sub>, PEG/0.8TA/TiO<sub>2</sub> and PEG/1.2TA/TiO<sub>2</sub> hydrogels were found to be 18°, 27° and 27° degrees, respectively, and the hydrophilicity of the hydrogels was reached at constant value in the samples added 0.8 g TA. The obtained new injectable PEG/TA/TiO<sub>2</sub> hydrogel is promising for use in biomedical and medical fields, thanks to its contact angle values of less than 90° for biocompatibility and its biocompatible components.

**Keywords:** Tannic acid, PEG, TiO<sub>2</sub>, hydrogel

## 1. Introduction

Hydrogels are three-dimensional polymeric networks that show hydrophilic properties. These networks can be built by physical or chemical bonding that can change the properties of hydrogels. Properties such as flexibility or

\*Corresponding author: [serbulentturk@sakarya.edu.tr](mailto:serbulentturk@sakarya.edu.tr)

2021 UTHM Publisher. All rights reserved.

[penerbit.uthm.edu.my/ojs/index.php/ijie](http://penerbit.uthm.edu.my/ojs/index.php/ijie)

mechanical strength also depend on the crosslinkers that are used for the formation of hydrogels. Hydrogels can absorb the water in the medium and swell due to their hydrophilicity. Hydrogels are also insoluble in both organic and inorganic solvents. With all these properties, hydrogels are used as biomaterials such as wound dressing [1], contact lens [2] and membrane [3] or used in biomedical applications such as sensors [4,5].

Polyethylene glycol (PEG) is widely used in biomedical applications. It is a hydrophilic polymer and soluble in water which makes it a good hydrogel candidate. PEG is also a biocompatible and flexible material and has low toxicity. In addition, PEG has low interaction with the blood components and has been already approved by Food and Drug Administration (FDA) [6]. PEG is a particularly good material for biomedical applications due to all these properties. Tannic acid (TA) is a plant polyphenol that is a mixture of gallic acid and glucose molecules. One of the important properties of tannic acid is its adhering ability on various substrates such as inorganic or organic substrates, hydrophilic or hydrophobic substrates [7]. In addition, TA has phenolic hydroxyl groups that can easily form hydrogen bonds. This hydrogen bonding ability of TA helps it to connect hydrophilic polymer chains. Therefore, phenolic hydroxyl groups of TA make it a good ligand to some metals such as  $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Co}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Mn}^{2+}$  and  $\text{Cu}^{2+}$  [8–10] While tannins also are capable of inhibiting the growth of some life forms such as fungi, bacteria and viruses, TA has antimicrobial and antioxidant activities [11].

Titanium dioxide is a semiconductor metal oxide that has properties like biocompatibility, ability to absorb UV light [12]. Therefore,  $\text{TiO}_2$  is an excellent antimicrobial agent [13,14] and has a wide area of use such as solar cells [15], cosmetics [16], wound healing [17] and food preservation [18]. Hydrogel formation with non-covalent interaction such as hydrogen bonding gives the ability of self-healing [19] and shape-memory [20] properties. Hydrogels using TA as crosslinker have structure, which have both ionic binding and complexation. While ionic binding is forming between polymer and TA via hydrogen bonding, the complexation forms between metal ions and TA that was bonded polymer. This metal ion acts as a center and binds TA more than one depending on the metal coordination number. With all these bindings a three-dimensional network emerges, and hydrogel formation occurs. While TA is an ideal binder for hydrogel formation, controlling parameters of the hydrogel formation such as concentration or pH must be adjusted carefully when using TA as a crosslinker. The change at the pH or concentration will affect the protons on the hydroxyl groups of TA, so complexation of TA with metal ions will change.

In this work, innovative PEG/TA/ $\text{TiO}_2$  hydrogels were designed for biomedical applications. Although PEG/TA hydrogels have been studied before, there is no paper that uses  $\text{TiO}_2$  as an additive to increase the internal cross-linking, strengthen their mechanical strength and enhance their antibacterial properties of PEG/TA hydrogels. Therefore, it was investigated that how different concentration of TA affects the property of prepared hydrogels in this paper. While TA was used as a crosslinker in hydrogels, its concentration affects the formation of the 3D network and property of hydrogel because of the high amount of hydroxyl groups over TA.

## 2. Materials and Methods

### 2.1 Materials

Polyethylene Glycol (PEG8000) and sodium hydroxide (NaOH) were purchased from Sigma Aldrich, iron (iii) chloride hexahydrate ( $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ ) and tannic acid were purchased from Merck. All chemicals were analytical grade and used without further purification.

### 2.2 Preparation of PEG/TA/ $\text{TiO}_2$ Hydrogels

To synthesize hydrogels, the first 4 g PEG was dissolved in 7.5 mL deionized water. While stirring, TA solution (400 mg, 800 mg, and 1.2 g in 2 mL water) was added to PEG solution. The mixture was stirred until a transparent solution was obtained. Then 0.5 mL  $\text{FeCl}_3$  solution (64 mg  $\text{FeCl}_3$  contained) in water was added to the mixture slowly. As a third component,  $\text{TiO}_2$  nanoparticles synthesized as in our previous study [21] were added to the hydrogel composite as 0.2 g for each sample in the hydrogel solution. Finally, gelation was done by adjusting the pH to 6 by adding 3M NaOH solution. Samples were named with PEG/0.4TA/ $\text{TiO}_2$ , PEG/0.8TA/ $\text{TiO}_2$  and PEG/1.2TA/ $\text{TiO}_2$  according to the amount of added TA respectively.

### 2.3 Measurement and Characterization

Hydrogels were coated on microscope glasses with the help of syringes and solid UV measurements were performed after drying at room temperature for 2 days. The solid-state absorption spectra were recorded at room temperature using SHIMADZU UV-2600 UV-vis spectrophotometer, with  $\text{BaSO}_4$  as reference. The Fourier transform

infrared spectroscopy of hydrogel samples was performed with Perkin Elmer Spectrum Two FTIR spectrophotometer. Hydrophilicity and wettability and of the samples were measured by measuring the contact angle using a video-based contact angle device (Attention optical tensiometer). The drop was recorded with a camera, and the recorded image was handled with the drop snake analysis plugin of the software to get the contact angle. Images of the contact angles for each sample were obtained 5 seconds after dropping of 4  $\mu\text{L}$  drops.

### 3. Results and Discussion

The formation mechanism of this three component (PEG, TA and  $\text{TiO}_2$ ) hydrogels is shown in Scheme 1. TA works as linkers to functionalize PEG polymer chains via H-bonds. TA binds polymers to the ternary complex with the aid of both  $\text{TiO}_2$  and  $\text{Fe}^{3+}$ , and multiplex coordination results in cross-linking of TA-linked PEG polymer chains.

Both the crosslink density and the combination of the self-forming fragments in the polymers directly contribute to the properties of the obtained materials and form the basis of gelation. At low crosslink density, the interaction of polymers is not strong enough to form gels, while high crosslink density induces strong interactions between polymers, thus resulting in precipitation. In the PEG/TA/ $\text{TiO}_2$  system, the fragment density can be easily adjusted by varying the concentration of polymer and TA.

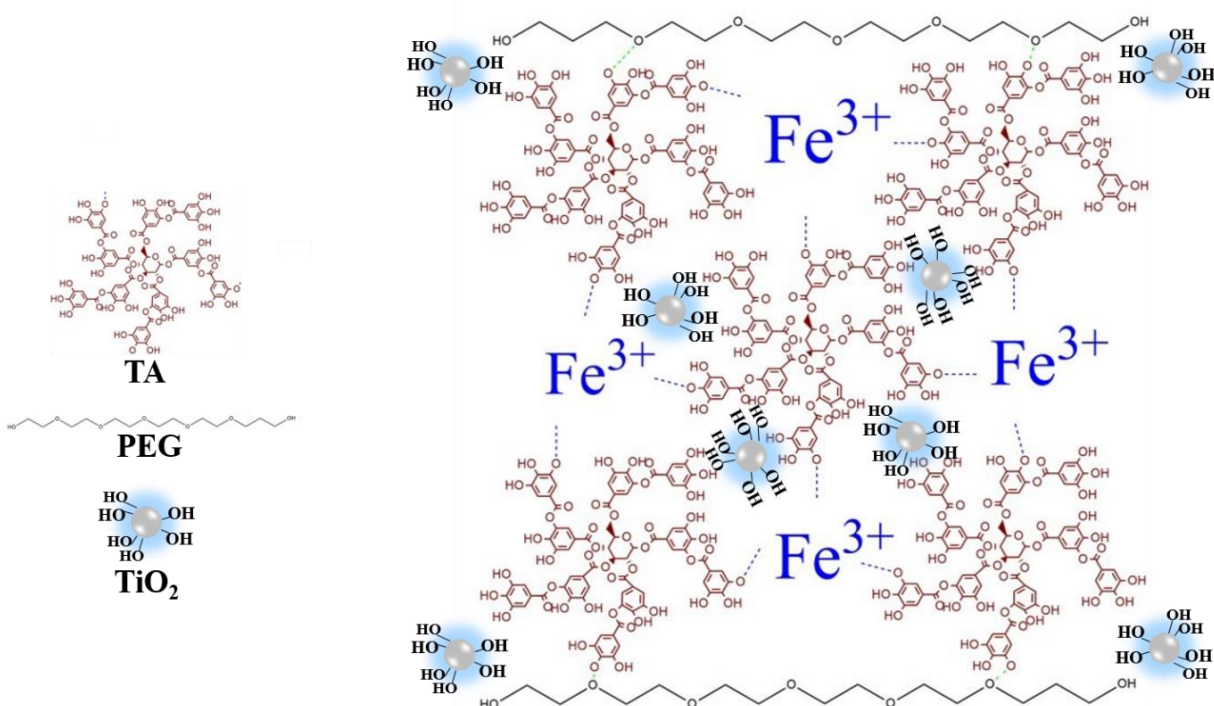
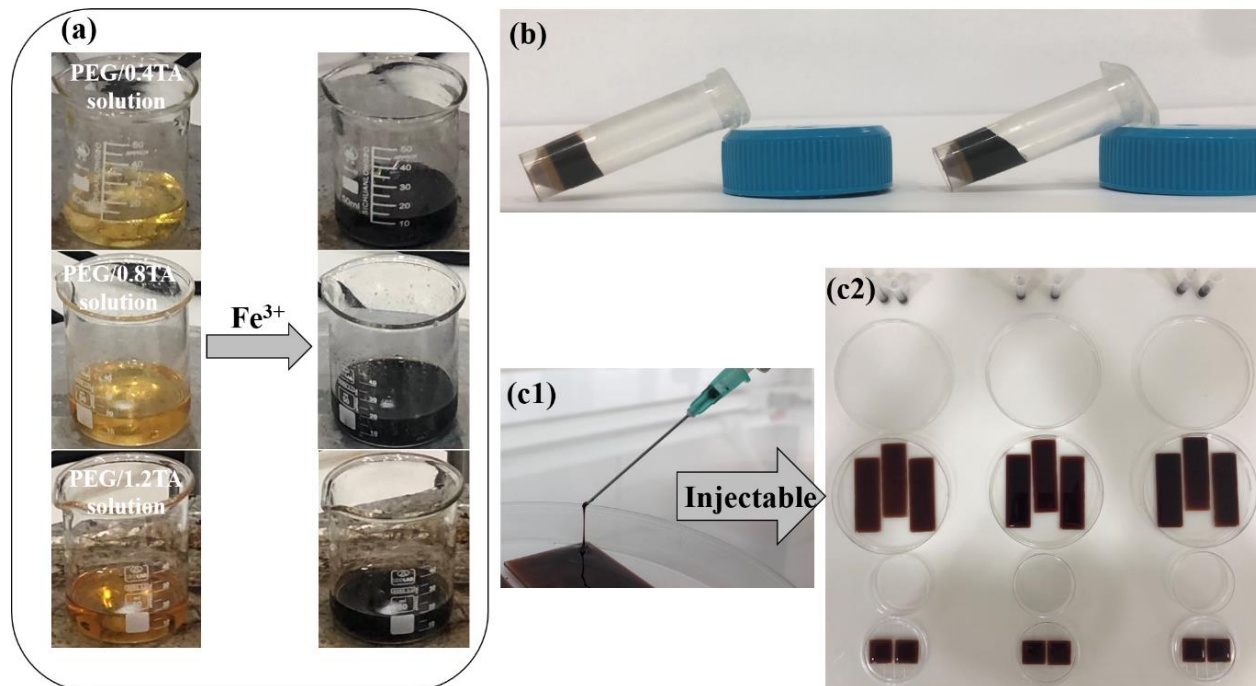


Fig. 1 - Three-Dimensional structure of prepared PEG/TA/ $\text{TiO}_2$  hydrogels

As can be seen in Fig. 1a, a color change occurred after the addition of three different  $\text{FeCl}_3$  solutions prepared. This color change indicates that the  $\text{Fe}^{3+}$  complex is formed. It was observed that the viscosity of the three separate hydrogel samples we obtained was high and the viscosity of the hydrogels increased after 24 hours in open containers at room temperature. As can be seen in Fig. 1b, while the left-hand sample gelled after being kept with its mouth open, it was observed that the right-hand sample with its mouth closed was more fluid. As shown in Fig. 1 c1-2, the hydrogels obtained for performing the characterizations were transferred to the microscope glasses with the help of a syringe and it was observed that they were injectable.



**Fig. 1 - Preparation and obtaining stages of hydrogel samples. (a) The color change observed after the addition of  $FeCl_3$  to the prepared PEG/TA solutions, (b) The decrease in the fluidity of the produced hydrogels after 1 day at room temperature, (c1,c2) Transfer of the obtained injectable hydrogels to microscope glasses for characterizations with the help of a commercial syringe.**

After coating the prepared hydrogel samples, solid-state UV-VIS spectra were measured as shown in Fig. 2. Three absorption peaks (212 and 265/365 nm) were observed in the absorption spectrum of the PEG/1.2TA/TiO<sub>2</sub> hydrogel. They correspond to three absorption peaks (212 and 265/365 nm) due to the B-band (absorption band characteristic of aromatic compounds) and K-band (characteristic absorption band in conjugated double bond) corresponding to  $\pi-\pi^*$  transitions [22]. In the absorption spectrum of PEG/1.2TA/TiO<sub>2</sub>, the red-shifted phenomenon may be attributed to the strong conjugation and inter/intra-molecular interaction between the molecule segments of PEG and TA in hydrogels. A broad band ranging from 415–700 nm in the visible light region has been attributed to ligand-to-metal charge transfer (LMCT) transitions, d–d transitions, or ligand domain transitions. Also, the double excitations here are due to simultaneous excitations of two adjacent magnetically bound  $Fe^{3+}$  cations [23]. Therefore, between 200–365 nm PEG/1.2TA/TiO<sub>2</sub> hydrogel absorbance is highest among all hydrogel samples. Also, PEG/0.4TA/TiO<sub>2</sub> and PEG/0.8TA/TiO<sub>2</sub> hydrogel samples have similar absorbance intensity at the same region. This can be attributed to exceeding TA amount over 800 mg, surplus amount of TA does not contribute for formation of hydrogel network.

As can be seen from Fig. 3, there is a broad peak between 3500-3000  $cm^{-1}$  in the FTIR spectra of all hydrogel samples. These broad peaks can be attributed to physical water, which is swallowed by hydrogels due to the hydrophilic nature of samples. All characteristic peaks of tannic acid (C=O bond at 1716  $cm^{-1}$ , aromatic C-C bonds at 1613  $cm^{-1}$  and 1448  $cm^{-1}$ ) and polyethylene glycol (C-O bond at 1280 and 1242  $cm^{-1}$ ) can be seen in FTIR spectra. In addition, there are peaks at 527  $cm^{-1}$  for all hydrogel samples that expressed Fe-O bindings. These peaks correspond to the main hydrogel network connection of tannic acid between PEG molecules. Therefore, same difference intensity phenomenon can be seen in FTIR spectra as can be seen in UV-VIS spectra. While PEG/0.8TA/TiO<sub>2</sub> have lower intensity than PEG/0.4TA/TiO<sub>2</sub>, peak intensities of PEG/1.2TA/TiO<sub>2</sub> is higher than PEG/0.8TA/TiO<sub>2</sub>. This can be due to excess amount of TA could not play role when formation of hydrogel network occurs.

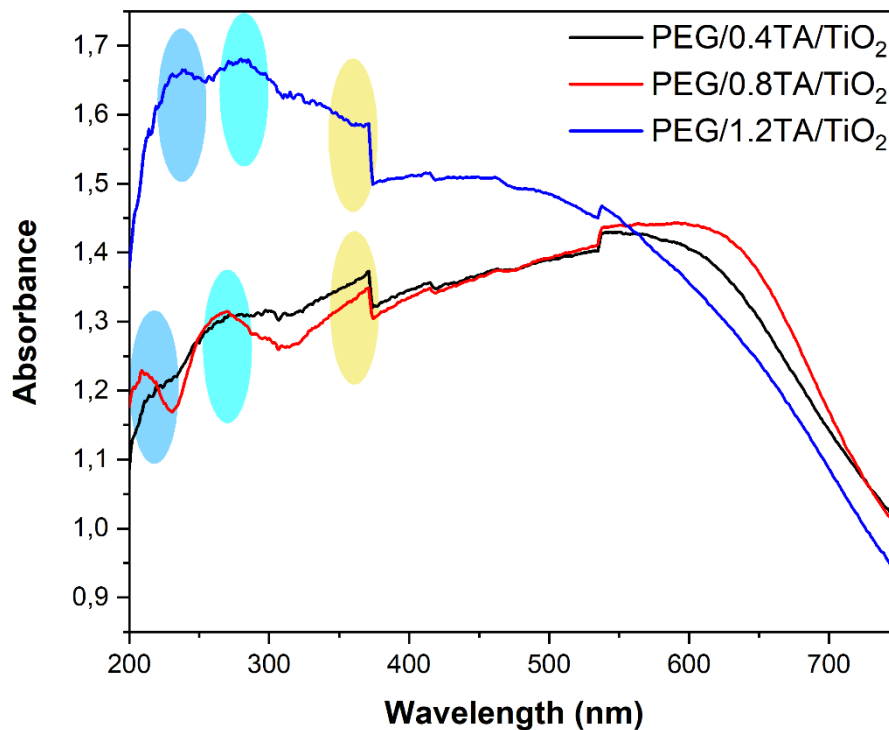


Fig. 2 - Solid-state UV-Vis spectra of PEG/TA/TiO<sub>2</sub> hydrogels

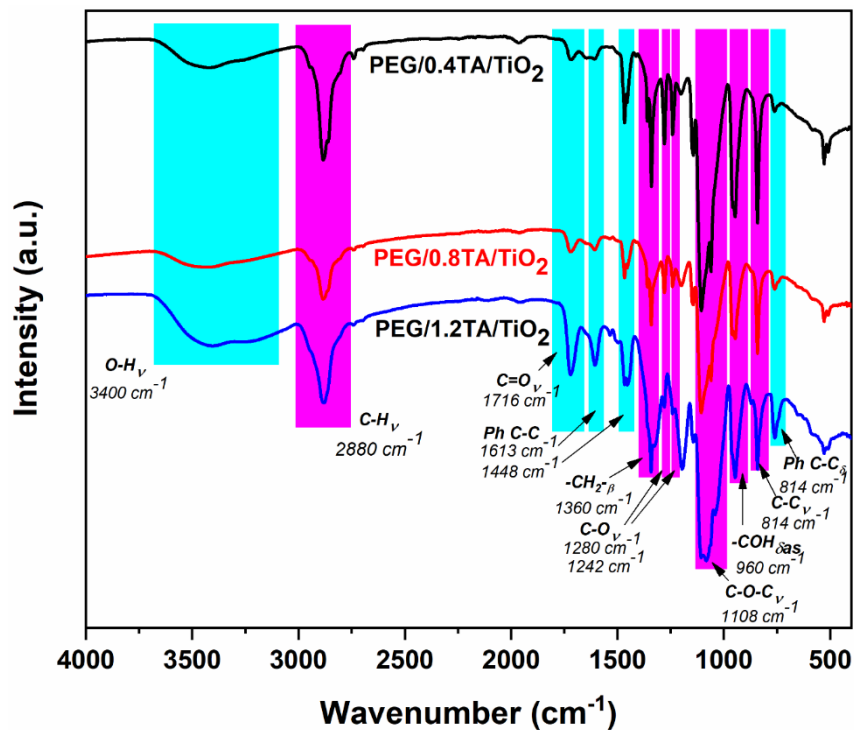


Fig. 3 - FTIR spectra of PEG/TA/TiO<sub>2</sub> hydrogels.

Contact angle measurements were performed using the sessile drop method for the motion of the three-phase contact line between DI water (4 ml) and hydrogel coated surfaces, which were shown in Fig. 4. The contact angles

of the hydrogel coated microscope glass surfaces containing tannic acid at 0.4, 0.8 and 1.2 ratios were obtained as 18°, 27° and 27°, respectively.

Since the contact angle measurements were below 90°, it was observed that the obtained hydrogel surfaces were hydrophilic. Since it is known that hydrophilic surfaces are preferred in biomedical fields, prepared hydrogels are suitable for biomedical use in this respect. In addition, it was observed that the contact angle increased with the increase of the tannic acid ratio from 0.4 to 0.8, and no significant change was observed after the tannic acid ratio increased to 1.2, and the contact angle remained constant. The increase in the contact angle from 18° to 27° is thought to be due to the formation of hydrogen bonding of TA with the -OH functional groups of PEG molecules on the hydrogel surface. Thus, it was interpreted that the functional groups containing oxygen that would interact with the water on the surface decreased.

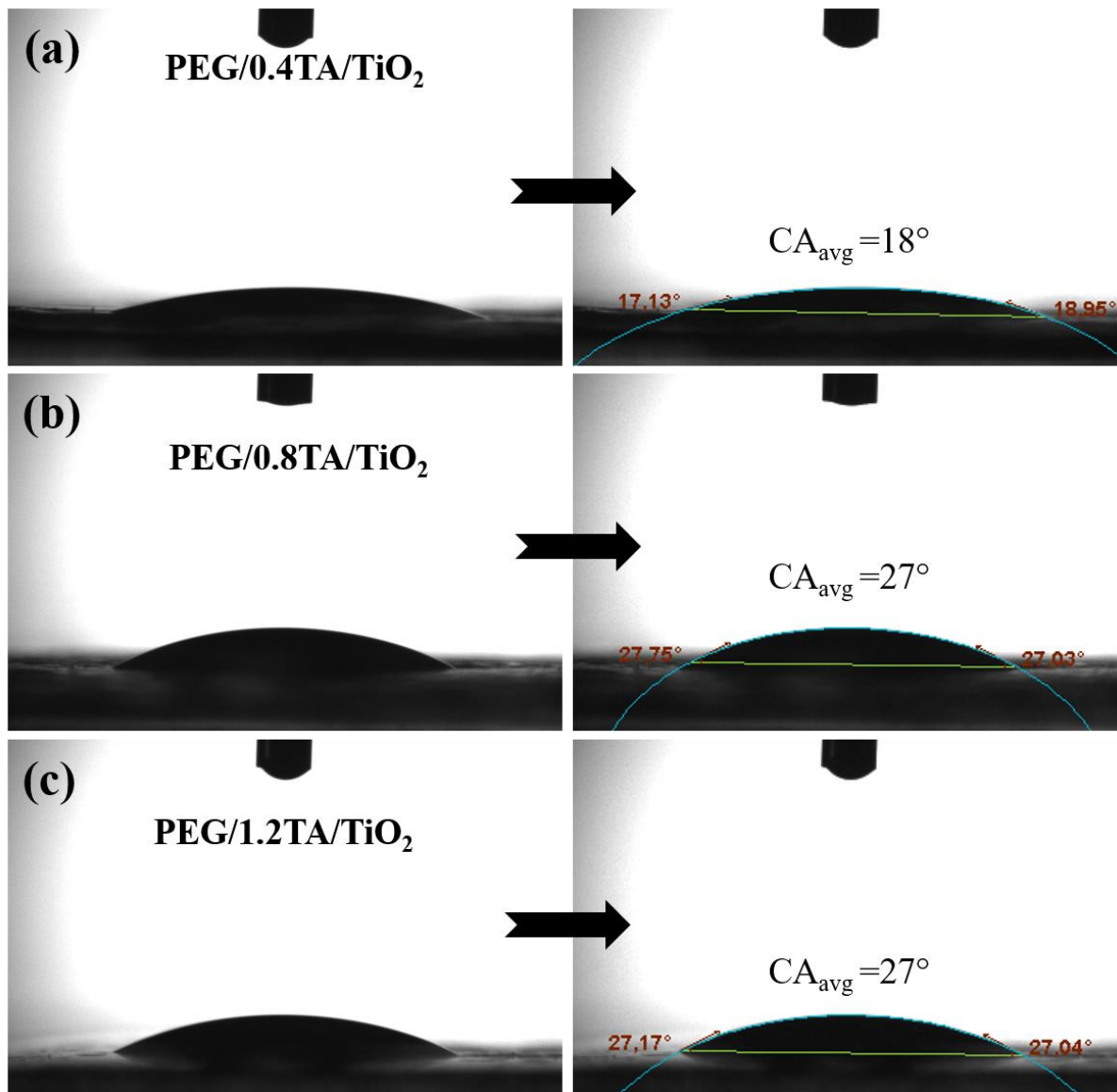


Fig. 4 - Contact angle measurements of PEG/TA/TiO<sub>2</sub> hydrogels obtained using software.

It is thought that there are two factors in the contact angle remaining constant at 27° in the second concentration increase. As the first factor, it is thought that after the addition of TA, it causes an increase in the wetting angle on the surface as a result of the interaction of the functional groups containing oxygen in the PEG molecule with TA, while

as the second factor, it also causes an increase in the contact angle as a result of the placement of the oxygen-containing functional groups on the TA on the surface, It is thought that the contact angle remains constant due to these two factors.

#### 4. Conclusion

PEG/TA/TiO<sub>2</sub> hydrogels with different TA amounts were synthesized successfully. It has been seen from UV-VIS and FTIR spectra that PEG/TA/TiO<sub>2</sub> hydrogels were successfully synthesized. With the increased amount of TA, the hydrophilicity of hydrogels was decreased until the 0.8 g TA added hydrogel. For PEG/0.8TA hydrogel, hydrophilicity is reached a fixed value and even adding more TA, the hydrophilicity of hydrogel remains the same for the PEG/1.2TA/TiO<sub>2</sub> hydrogel sample. According to the characterization results, it is believed that obtained hydrogels can be used for biomedical applications. The prepared PEG/TA/TiO<sub>2</sub> hydrogels with an in-vitro gelling feature will provide a great convenience in terms of injecting them into the skin surface for wound healing since TiO<sub>2</sub> is also known to have antibacterial properties.

#### Acknowledgement

The author would like to acknowledge the Biomedical, Magnetic and Semiconductor Materials Application and Research Center (BIMAS- RC) and Biomaterials, Energy, Photocatalysis, Enzyme Technology, Nano & Advanced Materials, Additive Manufacturing, Environmental Applications and Sustainability Research & Development Group (BIOENAMS R&D Group), Sakarya, Turkey also Faculty of Mechanical and Manufacturing Engineering, Universiti Tunn Hussein Onn Malaysia, Malaysia.

#### References

- [1] A. Dabbaghi, A. Ramazani, N. Farshchi, A. Rezaei, A. Bodaghi, S. Rezayati, Synthesis, physical and mechanical properties of amphiphilic hydrogels based on polycaprolactone and polyethylene glycol for bioapplications: A review, *J. Ind. Eng. Chem.* (2021). doi:<https://doi.org/10.1016/j.jiec.2021.05.051>
- [2] L. Xinming, C. Yingde, A.W. Lloyd, S. V. Mikhailovsky, S.R. Sandeman, C.A. Howel, L. Liewen, Polymeric hydrogels for novel contact lens-based ophthalmic drug delivery systems: A review, *Contact Lens Anterior Eye.* 31 (2008) 57–64. doi:<https://doi.org/10.1016/j.clae.2007.09.002>
- [3] U. Klueh, I. Ludzinska, C. Czajkowski, Y. Qiao, D.L. Kreuzer, Crosslinked basement membrane-based coatings enhance glucose sensor function and continuous glucose monitoring in vivo, *J. Biomed. Mater. Res. Part A.* 106 (2018) 7–16. doi:<https://doi.org/10.1002/jbm.a.36206>
- [4] R. Jin, J. Xu, L. Duan, G. Gao, Chitosan-driven skin-attachable hydrogel sensors toward human motion and physiological signal monitoring, *Carbohydr. Polym.* 268 (2021) 118240. doi:<https://doi.org/10.1016/j.carbpol.2021.118240>
- [5] M. Yang, X. Ren, T. Yang, C. Xu, Y. Ye, Z. Sun, L. Kong, B. Wang, Z. Luo, Polypyrrole/sulfonated multi-walled carbon nanotubes conductive hydrogel for electrochemical sensing of living cells, *Chem. Eng. J.* 418 (2021) 129483. doi:<https://doi.org/10.1016/j.cej.2021.129483>
- [6] L. Meabe, H. Sardon, D. Mecerreyes, Hydrolytically degradable poly(ethylene glycol) based polycarbonates by organocatalyzed condensation, *Eur. Polym. J.* 95 (2017) 737–745. doi:<https://doi.org/10.1016/j.eurpolymj.2017.06.046>
- [7] W. Yan, M. Shi, C. Dong, L. Liu, C. Gao, Applications of tannic acid in membrane technologies: A review, *Adv. Colloid Interface Sci.* 284 (2020) 102267. doi:<https://doi.org/10.1016/j.cis.2020.102267>
- [8] H. Ejima, J.J. Richardson, K. Liang, J.P. Best, M.P. van Koeveden, G.K. Such, J. Cui, F. Caruso, One-Step Assembly of Coordination Complexes for Versatile Film and Particle Engineering, *Science* (80-. ). 341 (2013) 154 LP – 157. doi:10.1126/science.1237265
- [9] T. Liu, M. Zhang, W. Liu, X. Zeng, X. Song, X. Yang, X. Zhang, J. Feng, Metal Ion/Tannic Acid Assembly as a Versatile Photothermal Platform in Engineering Multimodal Nanotheranostics for Advanced Applications, *ACS Nano.* 12 (2018) 3917–3927. doi:10.1021/acsnano.8b01456
- [10] S. Çakar, M. Özacar, Fe–tannic acid complex dye as photo sensitizer for different morphological ZnO based DSSCs, *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.* 163 (2016) 79–88. doi:<http://dx.doi.org/10.1016/j.saa.2016.03.031>
- [11] F. Heidari, I. Akbarzadeh, D. Nourouzian, A. Mirzaie, H. Bakhshandeh, Optimization and characterization of tannic acid loaded niosomes for enhanced antibacterial and anti-biofilm activities, *Adv. Powder Technol.* 31

- (2020) 4768–4781. doi:<https://doi.org/10.1016/j.appt.2020.11.008>
- [12] M. Mesgari, A.H. Aalami, A. Sahebkar, Antimicrobial activities of chitosan/titanium dioxide composites as a biological nanolayer for food preservation: A review, *Int. J. Biol. Macromol.* 176 (2021) 530–539. doi:<https://doi.org/10.1016/j.ijbiomac.2021.02.099>
- [13] A. Ali, S. Ahmed, A review on chitosan and its nanocomposites in drug delivery, *Int. J. Biol. Macromol.* 109 (2018) 273–286. doi:<https://doi.org/10.1016/j.ijbiomac.2017.12.078>
- [14] S.G. Ullattil, S.B. Narendranath, S.C. Pillai, P. Periyat, Black TiO<sub>2</sub> Nanomaterials: A Review of Recent Advances, *Chem. Eng. J.* 343 (2018) 708–736. doi:<https://doi.org/10.1016/j.cej.2018.01.069>
- [15] M.M.I. Megat Hasnan, N. Nayan, N.K.A. Hamed, Z. Azman, M.K. Ahmad, M.S. Mohamed Ali, M.Z. Mohd Yusop, I.M. Noor, Improvement of facile hydrothermal TiO<sub>2</sub> rutile nanorod-flower using second HiPIMS deposition for DSSC performance enhancement, *Opt. Mater. (Amst.)* 117 (2021) 111149. doi:<https://doi.org/10.1016/j.optmat.2021.111149>
- [16] K. Fournier, N. Marina, N. Joshi, V.R. Berthiaume, S. Currie, A.E. Lanterna, J.C. Scaiano, Scale-up of a photochemical flow reactor for the production of lignin-coated titanium dioxide as a sunscreen ingredient, *J. Photochem. Photobiol.* 7 (2021) 100040. doi:<https://doi.org/10.1016/j.jpap.2021.100040>
- [17] M.H. Razali, N.A. Ismail, K.A. Mat Amin, Titanium dioxide nanotubes incorporated gellan gum bio-nanocomposite film for wound healing: Effect of TiO<sub>2</sub> nanotubes concentration, *Int. J. Biol. Macromol.* 153 (2020) 1117–1135. doi:<https://doi.org/10.1016/j.ijbiomac.2019.10.242>
- [18] M. Gumiero, D. Peressini, A. Pizzariello, A. Sensidoni, L. Iacumin, G. Comi, R. Toniolo, Effect of TiO<sub>2</sub> photocatalytic activity in a HDPE-based food packaging on the structural and microbiological stability of a short-ripened cheese, *Food Chem.* 138 (2013) 1633–1640. doi:<https://doi.org/10.1016/j.foodchem.2012.10.139>
- [19] X. Dai, Y. Zhang, L. Gao, T. Bai, W. Wang, Y. Cui, W. Liu, A Mechanically Strong, Highly Stable, Thermoplastic, and Self-Healable Supramolecular Polymer Hydrogel., *Adv. Mater.* 27 (2015) 3566–3571. doi:10.1002/adma.201500534
- [20] W. Guo, C.-H. Lu, R. Orbach, F. Wang, X.-J. Qi, A. Ceconello, D. Seliktar, I. Willner, pH-stimulated DNA hydrogels exhibiting shape-memory properties., *Adv. Mater.* 27 (2015) 73–78. doi:10.1002/adma.201403702.
- [21] B. Ünlü, S. Çakar, M. Özacar, The effects of metal doped TiO<sub>2</sub> and dithizone-metal complexes on DSSCs performance, *Sol. Energy.* 166 (2018) 441–449. doi:10.1016/j.solener.2018.03.064
- [22] J.-J. Wang, R.-C. Zhang, D.-J. Zhang, Y.-F. Shi, Y.-H. Zhang, X.-L. Lu, E.-N. Wang, F. Jin, Modulated preparation and structural diversification of metal–organic frameworks based on 4,4',4''-(1H-imidazole-2,4,5-triyl)tripyridine ligand, *Inorganica Chim. Acta.* 427 (2015) 240–247. doi:<https://doi.org/10.1016/j.ica.2015.01.010>
- [23] L.H. Wee, M. Meledina, S. Turner, K. Custers, S. Kerkhofs, G. van Tendeloo, J.A. Martens, Hematite iron oxide nanorod patterning inside COK-12 mesochannels as an efficient visible light photocatalyst, *J. Mater. Chem. A* 3 (2015) 19884–19891. doi:10.1039/C5TA05075H