Microchemical Journal 202 (2024) 110740

Contents lists available at ScienceDirect

Microchemical Journal

journal homepage: www.elsevier.com/locate/microc

Biocompatibility assessment of organic semiconductor pigments epindolidione and quinacridone

Sarka Hradilova [a], Tana Zavodna [a], Jan Belza [a], Mihai Irimia-Vladu [b], Niyazi Serdar Sariciftci [b], Cigdem Yumusak [b], Katerina Polakova [a,*]

[a] *Czech Advanced Technology and Research Institute (CATRIN), Regional Centre of Advanced Technologies and Materials (RCPTM), Palacký University Olomouc, Šlechtitelů 27, 779 00 Olomouc, Czech Republic*

[b] *Linz Institute for Organic Solar Cells (LIOS), Physical Chemistry, Johannes Kepler University Linz, Altenbergerstraße 69, 4040 Linz, Austria*

A R T I C L E I N F O

Keywords:
Semiconductor pigments
Epindolidione
Quinacridone
Biocompatible materials for bioelectronics
In vitro cytotoxicity
Biocompatibility

A B S T R A C T

Organic colorants epindolidione (EPI) and quinacridone (QUI) are commercially available hydrogen-bonded semiconductor pigments. Despite their suitable properties for bioelectronic applications, their biocompatibility has not been thoroughly examined yet. In this study, thin EPI and QUI layers were applied on well plates by vacuum deposition technique followed by short and long-term in vitro biocompatibility study. In vitro testing represents a relatively fast and cheap approach, especially suitable for screening testing and prioritization of materials for further research. LIVE/DEAD assay, cell cycle analysis, adhesion and morphology of NIH 3T3 mouse fibroblasts have been investigated up to 7 days using flow cytometry and fluorescent optical microscopy. In summary, no significant differences were observed in viability, cell morphology, or attachment capabilities between control cells and cells grown on the EPI or QUI surfaces or cells cultivated in medium harvested from EPI- or QUI-coated wells. Our results suggest that both pigments are highly biocompatible. The absence of adverse biological effects of EPI and QUI together with their low cost and availability indicate their high application potential in next-generation bioelectronic devices.

1. Introduction

Bioelectronics is currently a rapidly evolving field linking traditional electronic devices and sensing platforms with biology and medicine by stimulating and probing the biological cells and tissues [1–8], while offering new trends in the treatment of various non-efficiently treated diseases, such as neurodegenerative or chronic diseases [9,10]. Bioelectronics has already introduced a number of biomedical devices to monitor and manage certain health conditions [8,11–25]. The sensor and actuator electronic devices are designed to detect, stimulate and control bio-signals and even apply medical treatments, but the intrinsically different nature of these devices compared to the surrounding living tissue brings several challenges into play. Firstly, while the biological systems work in aqaueous environment utilizing electrochemical signals and ionic conduction, electronic devices work in crystalline form using electronic conduction only. Therefore, converging biology and electronics requires a fundamental condition to be met: mixed ionic/electronic conductivity [17] (see reference 17 and references therein). With this respect, the organic semiconductors and conductive polymers with the ability of interconverting ionic and electronic signals efficiently have significant advantages over their inorganic and oxide counterparts [12–14]. Secondly, the physical incompatibility caused by the mechanical mismatch between the rigid bioelectronic devices based on the inorganic materials and soft biological tissue creates undesirable cell reactions. Organic materials offer great interfacial stability providing better mechanical match between the flexible organic materials and soft tissue thanks to their stress release ability [15].

Third and arguably the most important aspect of the implant is its biocompatibility, which is essential for the fabrication of practical and sustainable bioelectronic devices that is not cytotoxic towards the surroundings cells and tissues and does not elicit undesirable cell response. There are several strategies to enhance the biocompatibility [8], however, they usually require additional fabrication techniques, as well as have limitations, such as poor mechanical and/or long-term stability in real clinical applications.

Taking into account all the above-mentioned aspects, we aimed to

* Corresponding author.
E-mail address: katerina.polakova@upol.cz (K. Polakova).

https://doi.org/10.1016/j.microc.2024.110740
Received 7 February 2024; Received in revised form 9 May 2024; Accepted 10 May 2024
Available online 11 May 2024
0026-265X/© 2024 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

evaluate the biocompatibility of hydrogen-bonded pigments epindolidione (5,11-Dihydroquinolino[3,2-b]quinoline-6,12-dione) (EPI) and quinacridone (5,12-Dihydroquinolino[2,3-b]acridine-7,14-dione) (QUI). Hydrogen-bonded pigments are a class of organic colorants that break the rules for obtaining semiconducting behaviour and they can be employed as semiconductors in various organic electronic applications [26–43]. Two critical features of hydrogen-bonded pigments are their low-cost availability and placement in the lowest toxicity group of commercial colorants. This combination of properties opens the intriguing possibility of cheap and sustainable electronic devices with inherent biocompatibility. The two additional critical aspects of these pigments that enable bioelectronics applications are namely the demonstration of stable semiconducting properties in aqueous environments (within a remarkably wide pH range of 2–10) [40] and their straightforward bioconjugation protocols that allow direct attachment of biomolecules to the amine groups present in hydrogen-bonded pigment-forming molecules [41]. However, implementation of pigments into bioelectronic devices requires biocompatibility evaluations. Organic semiconductor pigments are considered non-toxic, however, no or very few toxicological data are available for EPI. In the present study, we carried out for the first time a comprehensive in vitro biocompatibility study of EPI and QUI semiconductor pigments.

2. Materials and methods

2.1. Preparation of samples

Yellow color EPI is a heterocyclic compound and its molecular weight is 262.26 g/mol. Magenta color QUI is an organic heterotetracyclic compound and an organonitrogen heterocyclic compound with the molecular weight of 312.3 g/mol. Both pigments are poorly soluble in organic solvents. The pigments EPI and QUI were purchased from 1- Material and TCI EUROPE, respectively. To achieve electronic grade quality, the purification method was necessary [32]. It was shown that the purity level of the organic semiconductor pigments is directly correlated with the charge transport properties of these materials [32]. After that thin nanofilm layers (300 nm) of purified pigments have been prepared via physical vapor deposition (PVD) process by a custom-built organic evaporation system from Vaksis R&D and Engineering on the standard plastic cultivation well plates used for adherent cell lines (TPP tissue culture test plates). For the thin film deposition of the pigments EPI and QUI, a sufficient amount of pigment powder was sequentially placed into a crucible. The respective crucible was heated to 190 °C for EPI and 280 °C for QUI, where the sublimation started for the respective pigments. The sublimation and the thin film deposition were monitored by the quartz crystal inside the PVD system. For both pigments, when the sublimation rate became constant at 0.2 Å/s, the protective shutter under the well plates was opened, and the evaporation started and continued until the thickness reached 300 nm.

2.2. Cell culture

The murine cell line NIH3T3 purchased from American Type Culture Collection (ATCC, Manassas, VA, USA) was used for cytotoxicity testing. Cells were cultivated in DMEM (Life Technologies, Carlsbad, CA, USA). The culture medium contained (final concentrations in medium): 10 % fetal calf serum (FCS), L-Glutamine (2 mM), PenStrep (5 U penicillin, 50 μg streptomycin/mL). Cells were incubated at 37 °C and 5 % CO_2 atmosphere.

2.3. Cell viability – direct contact

Cell viability was assessed using a LIVE/DEAD™ Viability/Cytotoxicity Kit (Invitrogen) and a BD FACSVerse flow cytometer (BD Biosciences, San Jose, CA, USA). Wells of the 24-well plate coated with the testing materials (EPI and QUI) were sterilized by 70 % ethanol before the NIH3T3 cells were seeded at a density of 50,000 cells/well. Empty wells with the same treatment were included as blank controls to evaluate a potential interference of the dyes with the testing method. Heat-treated cells incubated at 60 °C for 30 min before measurements were used as a positive control. After incubation for 24 h, the supernatant containing detached cells was collected, cells were washed with phosphate-buffered saline (PBS; 0.1 M, pH 7.4) and detached using 0.25 % trypsin-EDTA solution (Gibco) for 5 min. Cells were collected in cell culture medium and added to the supernatant. PBS from the washing step was also collected and added to the supernatant. Collected cells were incubated with PI (10 μg/mL) and calcein-AM (in DMSO) for 30 min in the dark. Finally, the fluorescence signal was measured on a flow cytometer using the first two scatters (Forward scatter channel vs. Side scatter channel) and two fluorescence channels (red FL 2: ex. 488/em. 700 nm and green FL 3: ex. 488/em. 527 nm). The red PI signal marked dead cells that lost membrane integrity, whereas the green signal indicated live cells with active intracellular esterases that could catalyze the non-fluorescent calcein-AM to highly fluorescent green calcein. Three independent experiments were performed and mean and standard deviation ± (SD) were calculated.

2.4. Cell viability – extracts (ISO 10993-5 guideline)

A test method to assess the in vitro cytotoxicity of medical devices was performed according to the ISO 10993–5 guidelines. Briefly, the cell culture medium was incubated in the wells coated with EPI and QUI pigments. After 24 h, the extracts of the tested materials in the cell culture medium were collected. NIH3T3 cells were seeded at a density of 50,000 cells per well in a standard 24-well plate for 24 h, then medium was replaced with the material extracts. The cells were then cultured in the extracts for another 24–96 h, before the LIVE/DEAD assay was performed as described above. Medium applied to a 24-plate well without pigments was used as a negative control.

2.5. Cell adhesion

Visual determination of the cell morphology and adhesion was performed by using microscope Olympus IX 70 in a fluorescence mode. The effect of direct contact of cells with the pigment-covered chambers on cell adhesion ability was evaluated. Briefly, wells of 24-well plate coated with EPI and QUI were sterilized by 70 % ethanol before seeding NIH3T3 cells at a density of 50,000 cells/well. Wells coated with EPI/QUI without cells were included as blank controls to evaluate interference of the tested materials with the method. After 24 h, cells were detached with 0.25 % trypsin-EDTA solution (Sigma Aldrich), and mixed with fresh cell culture medium, transferred to new wells (non-coated with EPI/QUI) and observed under light microscopy after 24, 48, 72 and 168 h. The LIVE/DEAD assay was performed after 96 h cultivation. Before observation under the microscope, the medium was aspirated, replaced with fresh medium with fluorescent labels propidium iodide (PI) and calcein-AM at the final concentration of 10 μg/mL and 50 μM, respectively, diluted in DMSO. After 30 min incubation in the dark, the medium was replaced with PBS buffer.

2.6. Cell cycle

Changes in cell cycle phase were monitored using DNA kit (BD CycletestTM Plus DNA kit, Becton Dickinson, East Rutherford, NJ, USA) and BD FACSVerse flow cytometer (BD biosciences, East Rutherford, NJ, USA) after 24 h incubation on EPI/QUI layers. The fluorescent intensity of Propidium Iodide (PI) was measured using excitation 488 nm/emission 586 nm.

2.7. Endotoxin evaluation

The endotoxin lipopolysaccharide (LPS) quantification was

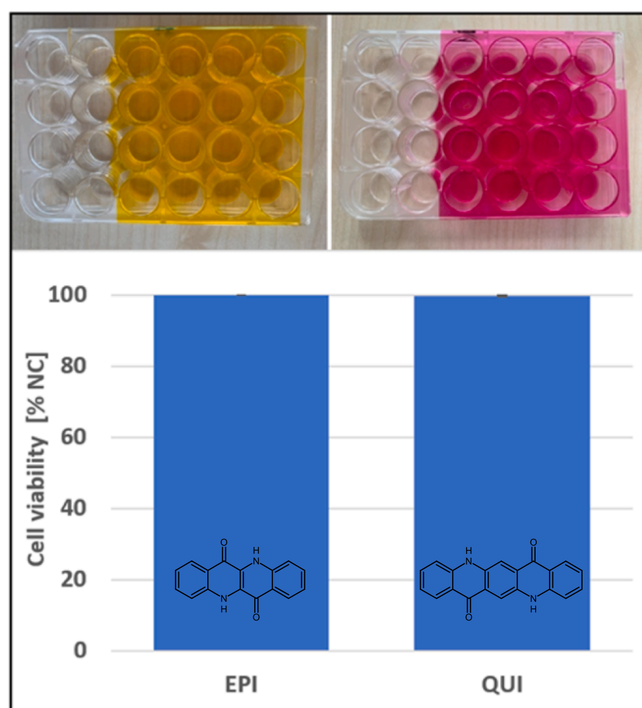

Fig. 1. (up) Pictures of well plates covered by thin layer of EPI (left) and QUI (right); (down) Viability of NIH3T3 cells after 24 h of incubation on EPI and QUI coatings. Results are expressed as a percentage of control (unexposed) cells. The values represent the mean ± standard deviation of three independent replicates.

performed according to the manufacturer's instructions using the Thermo Scientific, Pierce™ Chromogenic Endotoxin Quant Kit (Catalog number A39553, Waltham, MA). All reagents were equilibrated to room temperature prior to use, and great care was taken to use only endotoxin-free materials. A standard curve was generated using known endotoxin concentrations ranging from 0 to 1 EU/mL and run in parallel with the test samples. The test materials were incubated in phosphate-buffered saline (PBS) for 24 h at 37 °C before analysis. Standards and samples were maintained at 37 °C during the test. The colorimetric change in the wells of the 96-well microplate was measured at a wavelength of 405 nm using a Tecan Infinite M200 Pro Absorbance Spectrophotometer.

3. Results and discussion

Today's novel and exciting biomedical technologies are available in the market and influencing our daily lives by changing the way of our interaction with novel bioelectronic technologies. Organic semi-conducting materials are already recognized for integrated, cost-effective application due to their ease of use, especially with regard to production processes. They represent one of the most intense scientific developments in the field of bioelectronics over the past three decades. Organic technology relies on carbon-based semiconductor materials that deliver electronic devices with unique properties. The ability of electroactive materials to conduct ions, electrons, and holes opens up a new communication channel in life sciences and enables the fabrication of a large variety of biomedical devices.

Amon them, hydrogen-bonded organic pigments such as EPI and QUI are commercially available materials mostly used in the colorant industry, especially in robust outdoor paints, cosmetics, and printing inks. This class of materials are not normally produced for the electronic applications. Therefore, in this study, to achieve electronic grade quality, the purification method has been used, after that thin nanofilm

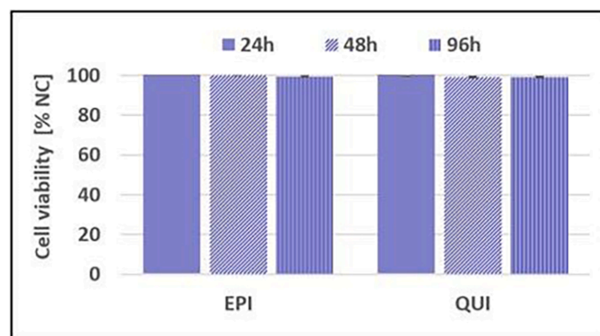

Fig. 2. Cytotoxicity of extracts of EPI and QUI tested according to the ISO standard for biocompatibility of medical devices after 24, 48 and 96 h. Results are expressed as a percentage of control (unexposed) cells. The values represent the mean ± standard deviation of three independent replicates.

layers (300 nm) of purified pigments have been prepared via PVD process and covered homogenously the whole surface of the commercial plastic 24 well plates chambers, see Fig. 1. This preparation method is advantageous not only from the perspective of following applications where it can be used for manufacturing of various types of bioelectronic devices (implants) but also from the point of view of easy handling during the in vitro experiments [44]. We could thus easily use commercial standard plastics coated with EPI and QUI as studied samples and the non-coated chambers as controls.

In vitro testing represents a relatively fast and cheap approach, especially suitable for screening testing and prioritization of materials for further research. First, we had to established the appropriate assays for studying biocompatibility of the pigments in general. The coloration of both EPI and QUI (see Fig. 1, upper line) caused interference with traditional absorbance-based assays using tetrazolium dyes, such as MTT or MTS (data not shown), leading to false positive or false negative results [45,46]. To minimize these interferences, we employed the LIVE/DEAD viability assay evaluated using flow cytometry. Flow cytometry is a fast, highthroughput and highly accurate technique providing information about each individual cell in the whole population with statistics. The fluorescence-based LIVE/DEAD assay reduced the risk of the interference of EPI/QUI in comparison to absorbance-based measurements.

Therefore, we tested biocompatibility of the EPI and QUI pigment coatings of cell culture plate wells by flow cytometry using LIVE/DEAD assay (LIVE/DEAD™ Viability/Cytotoxicity Kit (Invitrogen)) and a BD FACSVerse flow cytometer (BD Biosciences, San Jose, CA, USA) with two fluorescence probes (Propidium Iodide (PI) and Calcein-AM) to distinguish between the populations of dead and live cells. PI is able to intercalate into DNA of dead cells with a ruptured cell membrane, while live cells dispose active esterases that catalyse the non-fluorescent calcein-AM to highly fluorescent calcein.

Prior to cytotoxicity testing, cells were seeded onto the sterilized pigment-covered 24-well plates and incubated for 24 h. As shown in Fig. 1 (down), 24 h of direct contact with the studied materials did not cause decrease in cell viability compared to control cells grown in non-coated wells. To assess potential cytotoxic effects of extracts of the tested materials, we followed ISO standard protocol for testing biocompatibility of medical devices. The pigments-covered plates were incubated with cell culture medium only (without cells) for 24 h. Then, this medium was collected and further used for the cultivation of cells seeded in commercial plastic chambers without the pigment layer. After 24, 48 and 96 h of incubation, the LIVE/DEAD assay was performed using flow cytometry. Results presented in Fig. 2 show that extracts of any of the two tested pigments did not affect cell viability.

Other important parameters depicting normal physiological functions of the cells are changes in the cell morphology and cell adhesion. Cells grown on the pigments-covered plates for 24 h were detached by

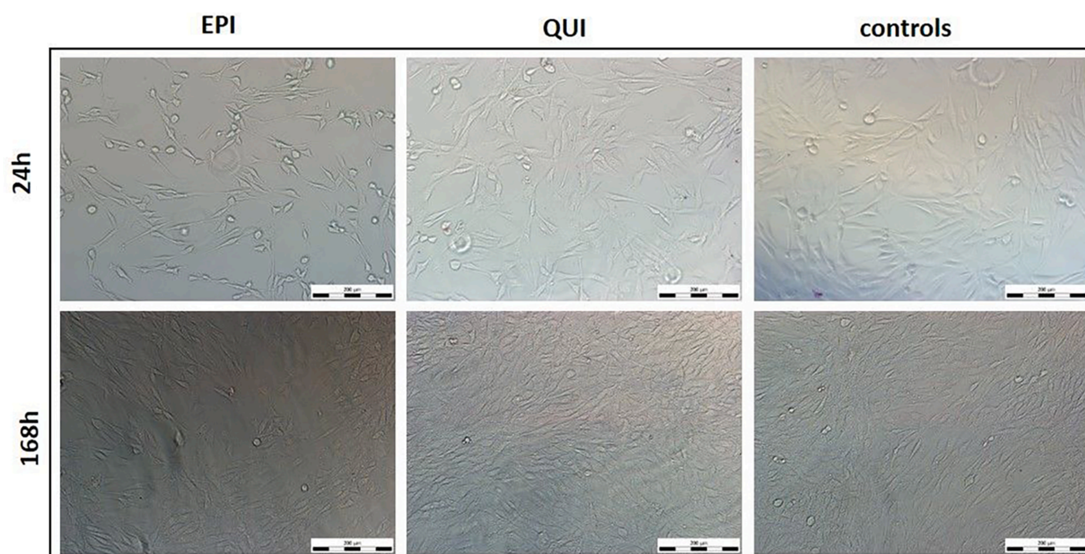

Fig. 3. Representative pictures of adhesion ability and morphology of NIH3T3 cells pre-incubated on EPI and QUI coating layers for 24hrs. Pictures show cells (up) 24 h, and (down) 168hrs after reseeding and incubation in standard non-coated wells.

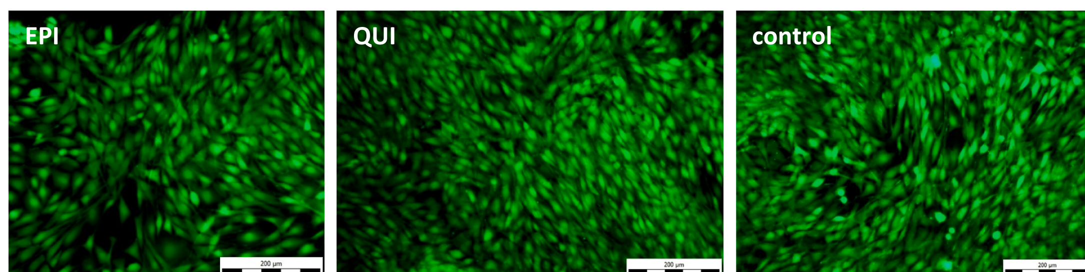

Fig. 4. Representative fluorescence optical microscopy pictures of NIH3T3 cells that were first grown on EPI and QUI coated plate wells for 24 h and then reseeded and cultivated in non-coated wells for 96 h. Green fluorescence from calcein in cytosol indicates live cells, no red signal from PI confirming no dead cells in the samples. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

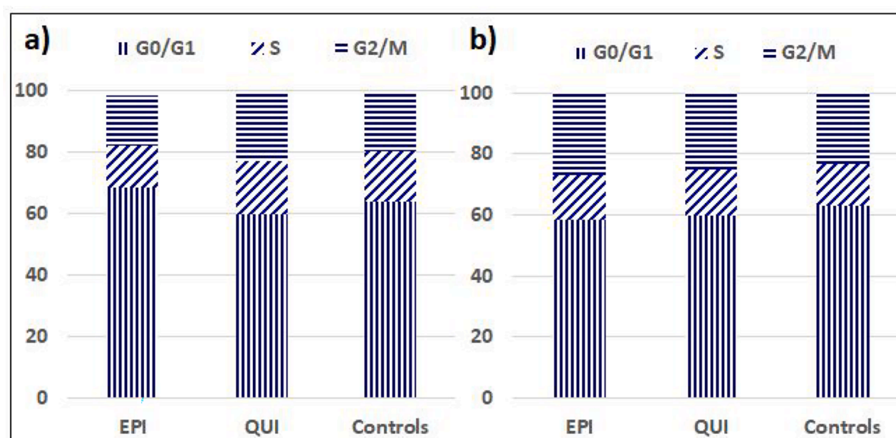

Fig. 5. Cell cycle phases in NIH3T3 cell after 24 h incubation with (a) EPI/QUI layers or (b) 24 h extracts of EPI/QUI in cell culture medium. Results are expressed as mean ± standard deviation of three independent replicates.

trypsinization and seeded on the commercial 24-well plate plastics. Then, adhesion ability and morphology of these cells were monitored after 24, 48, 72 and 168 h using optical microscopy. Representative images of cells keeping their adhesion capability after growing on the pigment layers 24 and 168 h are shown in Fig. 3. Moreover, proliferation rate/number of the cells was the same in the cells pre-incubated on the wells coated with the studied samples as in control cells that were originally seeded on the commercial (non-coated) plastics.

Viability of these cells was not affected for up to 96h days of incubation (Fig. 4). Moreover, no significant difference in the cell cycle profile in individual cell cycle phases between cells incubated on EPI or QUI layers and control cells has been observed which means that also

subcellular biocompatibility of the EPI and QUI pigments has been proven (Fig. 5).

At the end of this study we also tested if the materials contain endotoxin or are endotoxin-free. From the results (data not shown) the EPI and QUI showed the lower level of endotoxin than the absorbance achieved for the lowest tested endotoxin concentration (0.1 EU/ml), which means that both materials EPI and QUI prepared for this study are endotoxin-free and could be use as safe biocompatible materials in various bioelectronic and biomedical application in future.

4. Conclusion

In summary, a series of in vitro viability/cytotoxicity assays as well as cell morphological and adhesion assessment on EPI and QUI pigments were carried out on murine NIH3T3 cell line, a well-established cell line for biocompatibility screening. No differences were observed in viability, cell morphology or adhesion capability between control cells and cells grown on the EPI or QUI thin layers or cells cultivated with the medium harvested from EPI or QUI layers. The obtained results prove that these commercially available low cost pigments are highly biocompatible and are suitable for their further bioelectronic applications.

Extending our findings to the foundation for highly stable (without encapsulation) and biocompatible bioelectronic devices will be the next avenue of the research. This is yet an unsettled field with very high potential impact. It will explore avenues to grow novel bioelectronic devices. Furthermore, it will lead to bio-compatible electronic and optoelectronic biomedical implants and sensors. With the potential to monitor and improve the health of people, animals, plants, and ecosystems, there is room for vast academic and industrial growth in this sector.

Author contributions

Sample preparation: C.Y., M.I.V. Cytotoxicity measurement and dataanalysis: S.H., T.Z., J.B., K.P. Project idealization and guidance: N.S. S., C. Y., K.P. Paper writing: C.Y., K.P. All authors read and agreed on the final version of the manuscript.

CRediT authorship contribution statement

Sarka Hradilova: Writing – original draft, Methodology, Investigation, Data curation. **Tana Zavodna:** Writing – review & editing, Validation, Methodology, Data curation. **Jan Belza:** Data curation, Investigation, Methodology. **Mihai Irimia-Vladu:** Writing – original draft, Investigation, Conceptualization. **Niyazi Serdar Sariciftci:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition. **Cigdem Yumusak:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Katerina Polakova:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

We acknowledge the Research Infrastructure NanoEnviCz, supported by the Ministry of Education, Youth and Sports of the Czech Republic under Project No. LM2023066, by the Internal Grant Agency of the Palacký University Olomouc (grant No. IGA_PrF_2023_024). The work was supported from European Regional Development Fund – Project Excellence in Regenerative Medicine“ (No. CZ.02.01.01/00/22_008/0004562). Financial support of the Austrian Science Foundation (FWF) within the Wittgenstein Prize (Z222-N19) for Prof. Sariciftci is gratefully acknowledged.

References

[1] J. Rivnay, R.M. Owens, G.G. Malliaras, The Rise of Organic Bioelectronics, Chem. Mater. 26 (2014) 679–685.
[2] T. Someya, Z. Bao, G.G. Malliaras, The rise of plastic bioelectronics, Nature 540 (2016) 379–385.
[3] D.T. Simon, E.O. Gabrielsson, K. Tybrandt, M. Berggren, Organic Bioelectronics: Bridging the Signaling Gap between Biology and Technology, Chem. Rev. 116 (2016) 13009–13041.
[4] J. Rivnay, S. Inal, A. Salleo, R.M. Owens, M. Berggren, G.G. Malliaras, Organic electrochemical transistors, Nat. Rev. Mater. 3 (2018) 17086.
[5] G. Malliaras, I. McCulloch, Introduction: Organic Bioelectronics, Chem. Rev. 122 (2022) 4323–4324.
[6] J. Gurke, T.E. Naegele, S. Hilton, R. Pezone, V.F. Curto, D.G. Barone, E.J.W. List-Kratochvil, A. Carnicer-Lombarte, G.G. Malliaras, Hybrid fabrication of multimodal intracranial implants for electrophysiology and local drug delivery, Mater. Horizons 9 (2022) 1727–1734.
[7] J.T. Reeder, Z. Xie, Q. Yang, M.-H. Seo, Y. Yan, Y. Deng, K.R. Jinkins, S. R. Krishnan, C. Liu, S. McKay, E. Patnaude, A. Johnson, Z. Zhao, M.J. Kim, Y. Xu, I. Huang, R. Avila, C. Felicelli, E. Ray, X. Guo, W.Z. Ray, Y. Huang, M.R. MacEwan, J.A. Rogers, Soft, bioresorbable coolers for reversible conduction block of peripheral nerves, Science 377 (2022) 109–115.
[8] N. Zhou, L. Ma, Smart bioelectronics and biomedical devices, Bio-Design Manuf. 5 (2022) 1–5.
[9] Y. Jiang, A.A. Trotsyuk, S. Niu, D. Henn, K. Chen, C.-C. Shih, M.R. Larson, A. M. Mermin-Bunnell, S. Mittal, J.-C. Lai, A. Saberi, E. Beard, S. Jing, D. Zhong, S. R. Steele, K. Sun, T. Jain, E. Zhao, C.R. Neimeth, W.G. Viana, J. Tang, D. Sivaraj, J. Padmanabhan, M. Rodrigues, D.P. Perrault, A. Chattopadhyay, Z.N. Maan, M. C. Leeolou, C.A. Bonham, S.H. Kwon, H.C. Kussie, K.S. Fischer, G. Gurusankar, K. Liang, K. Zhang, R. Nag, M.P. Snyder, M. Januszyk, G.C. Gurtner, Z. Bao, Wireless, closed-loop, smart bandage with integrated sensors and stimulators for advanced wound care and accelerated healing, Nat. Biotechnol. 41 (2023) 652–662.
[10] C. Ni, C.V. Dinh, K.L.J. Prather, Dynamic Control of Metabolism, Annu. Rev. Chem. Biomol. Eng. 12 (2021) 519–541.
[11] C. Nicolini, Molecular bioelectronics, World Scientific Publishing Co., Singapore, 1996.
[12] J. Kim, R. Ghaffari, D.-H. Kim, The quest for miniaturized soft bioelectronic devices, Nat. Biomed. Eng. 1 (2017).
[13] S.R. Steinhubl, E.J. Topol, A skin patch for sensing blood pressures, Nat. Biomed. Eng. 2 (2018) 633–634.
[14] J.R. Sempionatto, M. Lin, L. Yin, E. De La Paz, K. Pei, T. Sonsa-ard, A.N. de Loyola Silva, A.A. Khorshed, F. Zhang, N. Tostado, S. Xu, J. Wang, An epidermal patch for the simultaneous monitoring of haemodynamic and metabolic biomarkers, Nat. Biomed. Eng. 5 (2021) 737–748.
[15] E. Song, Z. Xie, W. Bai, H. Luan, B. Ji, X. Ning, Y. Xia, J.M. Baek, Y. Lee, R. Avila, H. Y. Chen, J.H. Kim, S. Madhvapathy, K. Yao, D. Li, J. Zhou, M. Han, S.M. Won, X. Zhang, D.J. Myers, Y. Mei, X. Guo, S. Xu, J.K. Chang, X. Yu, Y. Huang, J. A. Rogers, Miniaturized electromechanical devices for the characterization of the biomechanics of deep tissue, Nat. Biomed. Eng. 5 (2021) 759–771.
[16] Y. Zhu, J. Li, J. Kim, S. Li, Y. Zhao, J. Bahari, P. Eliahoo, G. Li, S. Kawakita, R. Haghniaz, X. Gao, N. Falcone, M. Ermis, H. Kang, H. Liu, H.J. Kim, T. Tabish, H. Yu, B. Li, M. Akbari, S. Emaminejad, A. Khademhosseini, Skin-interfaced electronics: A promising and intelligent paradigm for personalized healthcare, Biomaterials 296 (2023) 122075.
[17] M. Irimia-Vladu, E.D. Glowacki, N.S. Sariciftci, S. Bauer, Green Materials for Electronics, Wiley-VCH, Weinheim, Germany, 2017.
[18] I. Willner, E. Katz, Bioelectronics: From Theory to Applications, (2005).
[19] A. Offenhäusser, R. Rinaldi, Nanobioelectronics – for Electronics, Biology, and Medicine (2009) 282.
[20] Y. Luo, M.R. Abidian, J.-H. Ahn, D. Akinwande, A.M. Andrews, M. Antonietti, Z. Bao, M. Berggren, C.A. Berkey, C.J. Bettinger, J. Chen, P. Chen, W. Cheng, X. Cheng, S.-J. Choi, A. Chortos, C. Dagdeviren, R.H. Dauskardt, C. Di, M. D. Dickey, X. Duan, A. Facchetti, Z. Fan, Y. Fang, J. Feng, X. Feng, H. Gao, W. Gao, X. Gong, C.F. Guo, X. Guo, M.C. Hartel, Z. He, J.S. Ho, Y. Hu, Q. Huang, Y. Huang, F. Huo, M.M. Hussain, A. Javey, U. Jeong, C. Jiang, X. Jiang, J. Kang, D. Karnaushenko, A. Khademhosseini, D.-H. Kim, I.-D. Kim, D. Kireev, L. Kong, C. Lee, N.-E. Lee, P.S. Lee, T.-W. Lee, F. Li, J. Li, C. Liang, C.T. Lim, Y. Lin, D. J. Lipomi, J. Liu, K. Liu, N. Liu, R. Liu, Y. Liu, Y. Liu, Z. Liu, Z. Liu, X.J. Loh, N. Lu, Z. Lv, S. Magdassi, G.G. Malliaras, N. Matsuhisa, A. Nathan, S. Niu, J. Pan, C. Pang, Q. Pei, H. Peng, D. Qi, H. Ren, J.A. Rogers, A. Rowe, O.G. Schmidt, T. Sekitani, D.-G. Seo, G. Shen, X. Sheng, Q. Shi, T. Someya, Y. Song, E. Stavrinidou, M. Su, X. Sun, K. Takei, X.-M. Tao, B.C.K. Tee, A.-V.-Y. Thean, T.Q. Trung, C. Wan, H. Wang, J. Wang, M. Wang, S. Wang, T. Wang, Z.L. Wang, P.S. Weiss, H. Wen, S. Xu, T. Xu,

H. Yan, X. Yan, H. Yang, L. Yang, S. Yang, L. Yin, C. Yu, G. Yu, J. Yu, S.-H. Yu, X. Yu, E. Zamburg, H. Zhang, X. Zhang, X. Zhang, X. Zhang, Y. Zhang, Y. Zhang, S. Zhao, X. Zhao, Y. Zheng, Y.-Q. Zheng, Z. Zheng, T. Zhou, B. Zhu, M. Zhu, R. Zhu, Y. Zhu, Y. Zhu, G. Zou, X. Chen, Technology Roadmap for Flexible Sensors, ACS Nano 17 (2023) 5211–5295.

[21] T.R. Ray, J. Choi, A.J. Bandodkar, S. Krishnan, P. Gutruf, L. Tian, R. Ghaffari, J. A. Rogers, Bio-integrated wearable systems: A comprehensive review, Chem. Rev. 119 (2019) 5461–5533.

[22] D.A. Bernards, R.M. Owens, G.G. Malliaras, Organic Semiconductors in Sensor Applications, Springer, Berlin Heidelberg, 2008.

[23] O. Parlak, A. Salleo, A. Turner, Wearable Bioelectronics, Elsevier, 2019.

[24] G. Srivastava, M. Khari, Bioelectronics and Medical Devices: Applications and Technology, (2021) 254.

[25] S.-H. Sunwoo, K.-H. Ha, S. Lee, N. Lu, D.-H. Kim, Wearable and Implantable Soft Bioelectronics: Device Designs and Material Strategies, Annu. Rev. Chem. Biomol. Eng. 12 (2021) 359–391.

[26] M. Irimia-Vladu, E.D. Gåowacki, P.A. Troshin, G. Schwabegger, L. Leonat, D. K. Susarova, O. Krystal, M. Ullah, Y. Kanbur, M.A. Bodea, V.F. Razumov, H. Sitter, S. Bauer, N.S. Sariciftci, Indigo - A natural pigment for high performance ambipolar organic field effect transistors and circuits, Adv. Mater. 24 (2012).

[27] E.D. Głowacki, G. Voss, L. Leonat, M. Irimia-Vladu, S. Bauer, N.S. Sariciftci, Indigo and Tyrian purple - From ancient natural dyes to modern organic semiconductors, Isr. J. Chem. 52 (2012) 540–551.

[28] D. Rand, M. Jakešová, G. Lubin, I. Vėbraitė, M. David-Pur, V. Đerek, T. Cramer, N. S. Sariciftci, Y. Hanein, E.D. Głowacki, Direct Electrical Neurostimulation with Organic Pigment Photocapacitors, Adv. Mater. 30 (2018) 1–11.

[29] Y. Kanbur, H. Coskun, E.D. Głowacki, M. Irimia-Vladu, N.S. Sariciftci, C. Yumusak, High temperature-stability of organic thin-film transistors based on quinacridone pigments, Org. Electron. 66 (2019) 53–57.

[30] C. Yumusak, A.J. Prochazkova, D.H. Apaydin, H. Seelajaroen, N.S. Sariciftci, M. Weiter, J. Krajcovic, Y. Qin, W. Zhang, J. Zhan, A. Kovalenko, Indigoidine – Biosynthesized organic semiconductor, Dye. Pigment. 171 (2019) 107768.

[31] M. Koehler, D. Farka, C. Yumusak, N. Serdar Sariciftci, P. Hinterdorfer, Localizing Binding Sites on Bioconjugated Hydrogen-Bonded Organic Semiconductors at the Nanoscale, ChemPhysChem 21 (2020) 659–666.

[32] C. Yumusak, N.S. Sariciftci, M. Irimia-Vladu, Purity of organic semiconductors as a key factor for the performance of organic electronic devices, Mater. Chem. Front. 4 (2020) 3678–3689.

[33] J. Richtar, M. Ciganek, A.J. Prochazkova, A. Kovalenko, H. Seelajaroen, M. Kratochvíl, M. Weiter, C. Yumusak, N.S. Sariciftci, V. Lukeš, J. Krajcovic, Adamantane Substitution Effects on Crystallization and Electrooptical Properties of Epindolidione and Quinacridone Dyes, ChemPhotoChem 5 (2021) 1059–1070.

[34] D. Saadi, C. Yumusak, I. Zrinski, A.I. Mardare, S. Romdhane, N.S. Sariciftci, M. Irimia-Vladu, M.C. Scharber, Magnetic Field Effect in Hydrogen-Bonded Semiconductor-Based Organic Field-Effect Transistors, Phys. Status Solidi Appl. Mater. Sci. 220 (2023).

[35] D. Saadi, F. Mayr, C. Yumusak, D. Wielend, M. Cobet, B. Kahraman, C.V. Irimia, Y. Kanbur, M. Bednorz, K. Kotwica, A. Ben Fredj, S. Romdhane, M.C. Scharber, N. S. Sariciftci, M. Irimia-Vladu, N,N′-Substituted quinacridones for organic electronic device applications, Mater. Adv. 4 (2023) 2214–2225.

[36] E. Daniel Głowacki, L. Leonat, M. Irimia-Vladu, R. Schwödiauer, M. Ullah, H. Sitter, S. Bauer, N. Serdar Sariciftci, Intermolecular hydrogen-bonded organic semiconductors-Quinacridone versus pentacene, Appl. Phys. Lett. 101 (2012) 20–24.

[37] E.D. Głowacki, M. Irimia-Vladu, M. Kaltenbrunner, J. Gsiorowski, M.S. White, U. Monkowius, G. Romanazzi, G.P. Suranna, P. Mastrorilli, T. Sekitani, S. Bauer, T. Someya, L. Torsi, N.S. Sariciftci, Hydrogen-bonded semiconducting pigments for air-stable field-effect transistors, Adv. Mater. 25 (2013) 1563–1569.

[38] E.D. Głowacki, M. Irimia-Vladu, S. Bauer, N.S. Sariciftci, Hydrogen-bonds in molecular solids-from biological systems to organic electronics, J. Mater. Chem. B 1 (2013) 3742–3753.

[39] E.D. Głowacki, G. Voss, N.S. Sariciftci, 25th anniversary article: Progress in chemistry and applications of functional indigos for organic electronics, Adv. Mater. 25 (2013) 6783–6800.

[40] E.D. Głowacki, G. Romanazzi, C. Yumusak, H. Coskun, U. Monkowius, G. Voss, M. Burian, R.T. Lechner, N. Demitri, G.J. Redhammer, N. Sünger, G.P. Suranna, S. Sariciftci, Epindolidiones-versatile and stable hydrogen-bonded pigments for organic field-effect transistors and light-emitting diodes, Adv. Funct. Mater. 25 (2015) 776–787.

[41] E.D. Głowacki, R.R. Tangorra, H. Coskun, D. Farka, A. Operamolla, Y. Kanbur, F. Milano, L. Giotta, G.M. Farinola, N.S. Sariciftci, Bioconjugation of hydrogen-bonded organic semiconductors with functional proteins, J. Mater. Chem. C 3 (2015) 6554–6564.

[42] M. Jakešová, D.H. Apaydin, M. Sytnyk, K. Oppelt, W. Heiss, N.S. Sariciftci, E. D. Głowacki, Hydrogen-Bonded Organic Semiconductors as Stable Photoelectrocatalysts for Efficient Hydrogen Peroxide Photosynthesis, Adv. Funct. Mater. 26 (2016) 5248–5254.

[43] A. Kovalenko, C. Yumusak, P. Heinrichova, S. Stritesky, L. Fekete, M. Vala, M. Weiter, N.S. Sariciftci, J. Krajcovic, Adamantane substitutions: A path to high-performing, soluble, versatile and sustainable organic semiconducting materials, J. Mater. Chem. C 5 (2017) 4716–4723.

[44] A. Cetkovic, A. Bellapianta, M. Irimia-Vladu, J. Hofinger, C. Yumusak, A. Corna, M. C. Scharber, G. Zeck, N.S. Sariciftci, M. Bolz, A. Salti, In Vitro Cytotoxicity of D18 and Y6 as Potential Organic Photovoltaic Materials for Retinal Prostheses, Int. J. Mol. Sci. 23 (2022) 8666.

[45] T. Malina, K. Poláková, C. Hirsch, L. Svoboda, R. Zbořil, Toxicity of Carbon Nanomaterials—Towards Reliable Viability Assessment via New Approach in Flow Cytometry, Int. J. Mol. Sci. 22 (2021) 7750.

[46] T. Malina, C. Hirsch, A. Rippl, D. Panacek, K. Polakova, V. Sedajova, M. Scheibe, R. Zboril, P. Wick, Safety assessment of graphene acid and cyanographene: Towards new carbon-based nanomedicine, Carbon N. Y. 211 (2023) 118093.