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# Examination of the effects of dimethyl sulfoxide on PEDOT: PSS-based materials used in thermoelectric power systems developed for intracorporeal active implanted devices

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## Abstract

With the increasing use of active implantable medical devices (IMDs), studies to meet their energy needs have focused on wireless energy transfer and thermoelectric generators. Materials, which are one of the most critical research topics in thermoelectric power systems, are expected to have low thermal conductivity and high electrical conductivity. Recently, organic polymers, especially poly (3,4-ethylenedioxythiophene) poly styrene sulfonate, have been preferred due to concerns over the toxicity of inorganic materials. However, using solvents such as dimethyl sulfoxide to prepare high-concentration solutions of poly (3,4-ethylenedioxythiophene) poly styrene sulfonate (PEDOT: PSS) may raise biocompatibility issues. This study investigates the effects on electrical conductivity, Seebeck coefficient, and biocompatibility after mixing different dimethyl sulfoxide solutions with PEDOT: PSS. As a result of these analyses, the highest electrical conductivity, 156.15 S/cm, was achieved with a 15/85 (v/v) dimethyl sulfoxide-water solution. The highest Seebeck coefficient was obtained at 26.27 µV/K for the film prepared with a 10/90 (v/v) dimethyl sulfoxide-water solution. Biocompatibility tests were performed according to ISO 10993-5 and ISO 10993-12 standards with the L929 cell line. It revealed that higher dimethyl sulfoxide (DMSO) ratios lead to increased toxicity in PEDOT: PSS samples. Furthermore, the group with the highest biocompatibility, which shows over 70% cell viability even at a 1:1 (v/v) extract ratio, was found as the group with a 1:1 extract ratio that contains 1% PEDOT: PSS. These findings provide insights into optimizing PEDOT: PSS formulations for enhanced electrical performance while maintaining biocompatibility, contributing to the development of safer and more efficient thermoelectric power sources for implantable medical devices.



## Introduction

The quality of human life decreases due to various diseases, many of which require regular monitoring or treatment. The most common active implantable devices, such as cochlear implants and pacemakers, are the primary method for managing these conditions. Over the past 20 years, FDA approvals have expanded the use of neurostimulation devices, which are now increasingly employed in the treatment of sleep apnea, depression, seizures, epilepsy, pain, urgency urinary incontinence, and movement disorders (Austelle et al.,

2022; Keser & Feng, 2023; Lucente et al., 2024; Stauss & Honma, 2018). According to a study conducted in 2022, the global market value of wearable devices reached 27 billion USD, indicating a growing demand for these technologies. Similarly, the market value of active implantable devices reached 22 billion USD. The combined market value of these two sectors is projected to reach 100 billion USD by 2030 (Gao et al., 2024). Pacemakers, one of the most widely used IMDs, are used by approximately three million people worldwide, with 600,000 new devices implanted each year (Amar et al., 2015; The PLOS ONE Staff, 2019). Although these widely used IMDs are quite costly procedures in terms of both device and surgical expenses, they positively affect people's lives, thereby improving patient outcomes and quality of life. Active implantable devices remain within the body, continuously monitoring changes and responding in real time, which positively affects human health. The most critical factor in managing this process is meeting the energy requirements. The most common method of powering these devices is through internal batteries. The lifespan of batteries used in implanted devices varies with treatment times and power requirements, which vary depending, for example, on the frequency of epileptic seizures and the stimulation amplitude set by the doctor (Karthikeyan et al., 2020; Zhang et al., 2013). However, due to the limited working life of these batteries, patients often require repeated surgeries. This process not only carries the risks inherent in each operation but also negatively affects the psychological state of the patient (Mohammed Ibrahim et al., 2024). To minimize these issues, systems requiring external charging units are employed. These systems are based on charging methods that use electromagnetic fields. In such a system, the charger is placed on the receiver coil of the active implant device at certain times. During this time, energy transfer can only occur momentarily (Akinaga, 2020). Alternatively, when a thermoelectric-based energy production system is used, continuous operation can be achieved. A thermoelectric module placed inside the body allows for continuous energy production by utilizing the temperature gradient between the body's internal temperature and the external environment (Chen & Wright, 2012). This generated energy can be further enhanced by increasing the temperature difference, and it can also be supplemented by an electromagnetic charging system when needed. To achieve this, the temperature gradient can be enhanced by further lowering the body's external temperature with an ice cassette, thereby increasing the amount of energy generated. Thermoelectric modules have a characteristic feature known as the Seebeck coefficient, which represents the ratio between the temperature difference and the voltage generated (Beltrán-Pitarch et al., 2018; Jaziri et al., 2020; Misra et al., 2015; Shen et al., 2025; Suarez et al., 2016; Zoui et al., 2020). Traditionally, these materials are inorganic materials derived from $Bi_2Te_3$ in commonly used modules. However, these materials lack flexibility and biocompatibility and do not have the desired properties for implantation inside the body. To address these limitations, there is growing interest in organic-based conductive polymers (such as poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT: PSS), polyaniline (PANI), etc.) (Liu et al., 2024). PEDOT: PSS is the most commonly used in thermoelectric studies (Bharti et al., 2018; Nath et al., 2014). In recent years, PEDOT: PSS has been preferred in thermoelectric materials due to its water solubility, ease of processing, and stability. While the PEDOT polymer exhibits high conductivity, it faces issues with water solubility. When used with polystyrene sulfonate (PSS), known as a counterion, the problem of water solubility is resolved. However, the PSS anion suppresses the conductive properties of the PEDOT polymer, preventing the achievement of the desired high electrical conductivity (Akdemir et al., 2025; Panigrahy & Kandasubramanian, 2020; Xu et al., 2019). High electrical conductivity is crucial for materials intended for use in thermoelectric devices.

Studies have shown that adding polar solvents and performing post-treatment processes can increase the electrical conductivity of PEDOT: PSS. These processes can shorten π-π stacking, remove accumulated PSS anions, and result in various phase separations (Nan et al., 2025; Toolan et al., 2016; Zhu et al., 2017). Polar solvents with a high boiling point, such as ethylene glycol (EG), dimethyl sulfoxide (DMSO), dimethylformamide (DMF), glycerol, and sorbitol, not only help disperse the material within the film but are also used in post-treatment materials (Alam et al., 2024; Asri et al., 2022; Cruz-Cruz et al., 2010; Khasim et al., 2017; Li et al., 2019; Yamaguchi et al., 2018). For example, in a study conducted by Dong and Portale in 2020, they examined the effects of DMF and DMSO on PEDOT: PSS. As a result, they noted that DMSO was more effective on PEDOT: PSS, as it facilitated better phase separation (Dong & Portale, 2020). Similarly, in their 2020 improvement studies, Vedovatte et al. (2020) opted to use DMSO to enhance PEDOT conductivity. However, high concentrations of DMSO raise biocompatibility concerns, making it essential to investigate and optimize this concentration (Munesada et al., 2023). Another critical factor in these studies is the concentration of PEDOT: PSS in solution. While most studies in the literature have used 1.1-1.3 wt % PEDOT: PSS, the impact of different PEDOT concentrations has not yet been thoroughly examined. Considering the biocompatibility criteria, we hypothesize that high thermoelectric properties can be achieved with high PEDOT: PSS ratios and DMSO concentrations. In line with our hypothesis, primarily a commercially available PEDOT: PSS solution was lyophilized and purified. Solutions with 1, 3, and 5% PEDOT: PSS were then prepared by adding DMSO-water mixtures in the required ratios. Thin films were produced from these obtained solutions using the doctor blade method and

allowed to dry. The thermoelectric properties, specifically electrical conductivity and Seebeck coefficient, were evaluated on the resulting films, and biocompatibility tests were conducted to ensure suitability for implantation in the body.

The aim of this study is to evaluate the impact of varying DMSO-water solution ratios on the electrical conductivity, Seebeck coefficient, and biocompatibility of PEDOT: PSS films used in thermoelectric power systems for active implantable medical devices. By investigating these properties, the study aims to identify the most effective DMSO concentration that maximizes electrical performance while minimizing biocompatibility risks, thereby addressing the energy needs of medical implants with safer and more effective organic polymers.

## Materials and Methods

### Materials

In the study, a solution containing 1-1.3 wt % poly (3,4-ethylenedioxythiophene) poly styrene sulfonate (PEDOT: PSS), with a product code 483095 from Sigma Aldrich, was used. Additionally, DMSO from Carlo Erba was used to facilitate the dispersion of PEDOT: PSS.

For the cytotoxicity tests, the following materials were used: high-glucose DMEM (Gibco, Lot: 2687500), fetal bovine serum (FBS, Gibco, Lot: 10270-106), L-glutamine (Gibco, Lot: 2437202), gentamicin (Capricorn, Lot: CP214333), 0.25% trypsin-EDTA (Multicell, Lot: 325542084), DMSO (AppliChem, Lot: 2006643), and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Cell Biolabs, CBA-252, Lot: 4022080).

### Methods

In this study, a commercially available PEDOT: PSS solution with a concentration of 1-1.3% was lyophilized to obtain PEDOT: PSS in sponge form. It was lyophilized at -50$^{o}$C and 0.04 mbar for 3 days. Subsequently, DMSO/water (v/v) solutions were added to the polymer in ratios of 5/95, 10/90, 15/85, and 30/70 to achieve PEDOT: PSS concentrations of 1, 3, and 5%. These mixtures were stirred using a magnetic stirrer for 72 h. Afterward, the mixtures were formed into films using the doctor blade technique, resulting in a thickness of 100 microns. The films were left to dry at room temperature at 25 $^{o}$C for 24 h, and their electrical conductivity was measured using the 4-point probe method with a 2450 Keithley Source Meter device. Additionally, measurements were taken with a lab-made Seebeck coefficient device (Özkan et al., 2024). Furthermore, the cytotoxicity test of the produced polymeric material was performed following the ISO-10993-5 standard.

### Preparation of Polymeric Material and Extraction

The sample, with a thickness of less than 0.5 mm and a surface area of 6 cm², required 1 mL of culture medium for the cytotoxicity test, as calculated according to ISO 10993-12 (2021) standards. The material was sterilized using ethylene oxide gas and ventilated for 3 days prior to use. Samples that were sterilized by ethylene oxide were incubated at (37 ± 1) °C for (24 ± 2) h statically in a $CO_2$-free incubator in serum-free cell culture medium containing 0.1% gentamicin. The extraction medium volume relationship was determined as 6 cm²/mL for surface area/volume due to the material thickness being <0.5 mm according to ISO 10993-12 (2021). Since the surface area of the material was 6 cm², the material was extracted with 1 mL of extraction medium. After 24 h of incubation, 10% FBS and 1% L-glutamine were added to extracts. This extract was named as a 100% (1:1) extract. The prepared extracts were then prepared by serial dilution with cell culture medium. The dilution process starts with the undiluted extract 1:1, then continues with serial dilutions of 1:2, 1:4, 1:8, and 1:16 (v/v) with cell culture medium.

### Cell Culture and MTT Cytotoxicity Test

The mouse fibroblast cell line (L929) (ATCC CCL-1) was cultured in high-glucose DMEM medium containing 10% fetal bovine serum (FBS) and 0.1% gentamicin at 37°C with 5% $CO_2$ and 95% humidity. Simultaneously with the extraction, the L929 cells were detached using 0.25% trypsin-EDTA, and the L929 cells were seeded at a concentration of 1 x $10^5$ cells/mL into a 96-well plate, followed by incubation for 24 h at 37ºC with 5% $CO_2$. The culture medium was then replaced for the set cytotoxicity test. The media were replaced by the positive control group, the group incubated with the media containing 10% DMSO, which had a negative effect on the cells; the negative control group, the group incubated with the media that had no effect on the cells, and the extraction groups at ratios of 1:1, 1:2, 1:4, 1:8, and 1:16. After 24 h, all culture media were replaced with serum-free high-glucose DMEM medium containing MTT (0.5 mg/mL). The cells were then incubated for 3 h in the dark at 37°C with 5% $CO_2$ and 95% humidity. Following incubation, the medium was removed, and then, 100 µL of DMSO was added to each well. The formazan crystals were allowed to dissolve on a shaker for 10 min. Absorbance values were measured using a spectrophotometer (BioTek Synergy HTX) at wavelengths of 570 and 690 nm and were analyzed using 'GraphPad Prism version 8.4.2'. The percentage of cell viability was calculated using the following formula:

% Cell viability =

[100 × (sample abs)/ (negative control abs)] (1)

In the MTT test, three samples from each experimental group were tested (n=3). In the evaluation of the results obtained from the MTT tests, mean values and standard deviations were determined. Statistical differences were evaluated using one-way ANOVA with a significance level of $P<0.05$.

## Results and Discussion

### Electrical Conductivity

The hydrophilic nature of DMSO enables it to bind to the excess PSS present in PEDOT: PSS, which causes insulation. Therefore, improvement studies on PEDOT: PSS films showed that the addition of DMSO increased electrical conductivity (Cruz-Cruz et al., 2010). Additionally, the ratio of conductive polymer within the film directly affects electrical conductivity. The electrical conductivity results, presented in Figure 1, illustrate the effect of varying DMSO concentrations (5%, 10%, 15%, and 30%) on films containing different PEDOT: PSS ratios (1%, 3%, and 5%). Electrical conductivity measurements were taken from 10 different areas of a film, and the average values were given. As shown in the graphs, both an increase in the DMSO ratio and an increase in the PEDOT: PSS ratio led to higher electrical conductivity. Although the highest DMSO ratio yields improved electrical conductivity with different PEDOT ratios, this improvement is limited compared to other ratios, likely due to saturation of the film with DMSO.

In light of these findings, a detailed comparison of the different DMSO ratios in the 5% PEDOT: PSS with the highest electrical conductivity is shown in Figure 2. A comparative analysis in Figure 2, focusing on the 5% PEDOT: PSS group, reinforces the trend where conductivity increases steadily from 5% to 15% DMSO. However, further increasing the DMSO concentration to 30% does not yield substantial improvements, indicating a limit to the enhancement effect of DMSO. As discussed earlier, a higher DMSO concentration enhances the electrical conductivity of PEDOT: PSS films. This improvement may occur because DMSO facilitates phase separation by selectively reducing the insulating effect of excess PSS, thereby increasing the mobility of charge carriers within the polymer network.

The electrical conductivities were analyzed using a two-way ANOVA to determine the effects of PEDOT: PSS and DMSO concentrations. The analysis revealed a significant influence of both PEDOT: PSS concentration (*****P<0.0001*) and DMSO concentration (*****P<0.0001*). Additionally, there is a strong interaction between PEDOT: PSS and DMSO concentrations (*****P<0.0001*).

### Seebeck Coefficient

Seebeck effect measurements were performed by recording temperature data at five different points on the film. The final value was obtained by calculating the average of these measurements. In Figure 3, the effects of various DMSO and PEDOT: PSS ratios on these parameters are examined in detail. The Seebeck coefficient results, depicted in Figure 3, reveal a different trend compared to conductivity. While increasing PEDOT: PSS concentration enhances the Seebeck coefficient, an increase in DMSO concentration does not contribute significantly. When analyzed in detail, the Seebeck coefficient generally increases with higher PEDOT: PSS concentrations. This trend occurs because a higher PEDOT: PSS content enhances charge carrier density, which contributes to improved thermoelectric performance. However, increasing the proportion of DMSO does not seem to affect the Seebeck coefficient, indicating that it primarily acts to increase electrical conductivity. These results indicate that DMSO increases electrical conductivity by affecting polymer morphology and phase separation; however, it does not significantly alter the thermoelectric properties because the Seebeck coefficient is largely determined by the intrinsic properties of the PEDOT: PSS system.

The Seebeck coefficients were analyzed using two-way ANOVA to determine the effects of PEDOT: PSS and DMSO concentrations. The analysis revealed a significant influence of PEDOT: PSS concentration (****P<0.001*), while DMSO concentration showed no statistically significant effect on Seebeck coefficients (*P=0.3121*). Moreover, the effect of PEDOT: PSS concentration on Seebeck coefficients is affected by the DMSO concentrations (****P<0.0001*).

### MTT Cytotoxicity Test

To determine the applicability of parametric tests, the results were checked for normal distribution. Given that more than two dependent groups were compared, a one-way ANOVA was conducted, as it is an appropriate method for analyzing normally distributed datasets. The MTT test was performed three times (n=3); however, the number of independent experiments can be increased to support the statistical robustness of the results. The critical values are expressed as *P≤0.05, **P≤0.01, ***P≤0.001, and ****P≤0.0001. The cytotoxicity analyses after 24 h of incubation with extracts are shown below. According to ISO-10993-5 standards, a decrease in cell viability below 70% indicates that the material is cytotoxic.

a) 5% PEDOT: PSS

In the 10% DMSO/90% water group, cell viability exceeded 70% only at the 1:4, 1:8, and 1:16 concentration ratios (Figure 4b). In Figure 4b, the adjusted P value in the 1:4 extract is 0.0722 and is not significant. In all other compositions and concentrations, the material exhibited a cytotoxic effect. (Figure 4a, c, and d).

b) 3% PEDOT: PSS

In the group containing 5% DMSO/95% water, no cytotoxic effect was observed at the 1:4, 1:8, and 1:16 concentration ratios (Figure 5a). In Figure 5a, the adjusted P value for the 1:4 concentration ratio is 0.071, while it is 0.069 for the 1:8 concentration ratio and 0.999 for the 1:16 concentration ratio. The 1:8 and 1:16 concentration ratios are not statistically significant. However, cytotoxic effects were observed at various concentrations in the other groups (Figure 5b, c, and d).

c) 1% PEDOT: PSS

In the film containing 5% DMSO/95% water, high cell viability (>70%) was observed at all concentrations,

indicating no cytotoxic effects (Figure 6a). In Figure 6a, the adjusted P values are >0.999, 0.9980, 0.3481, and 0.7930 for extract ratios of 1:2, 1:4, 1:8, and 1:16, respectively. Furthermore, the adjusted P value is not significant for extract ratios of 1.2, 1:4, 1:8, and 1:16. However, in the film containing 10% DMSO/90% water and 15% DMSO/85% water, cytotoxic effects were observed in all concentrations except for the 1:16 ratio (Figure 6b and c), suggesting that higher DMSO concentrations significantly reduce cell viability. In the other films with different amounts of DMSO and water, cytotoxic effects were observed at all concentrations (Figure 6d).

Treatment of cells with DMSO increases cell apoptosis (Costa et al., 2017). In general, an inverse relationship was observed between cell viability and extraction rates in MTT results. There are multiple reasons why DMSO causes toxic effects on cells and triggers apoptosis. One of these is that it disrupts the structural integrity of the cell membrane by creating pores in the plasma membrane (Chan et al., 2014). DMSO compromises cellular integrity, elevates oxidative stress, and leads to the overproduction of reactive oxygen species, which may induce necrosis or apoptosis (Tamagawa et al., 2022). However, the damage that DMSO causes to the cell depends on factors such as exposure time and DMSO concentration (Costa et al., 2017). Therefore, toxic effects are observed in PEDOT: PSS with high DMSO concentrations. However, no toxic effects were observed according to ISO-10993-5 standards, only at a 1:1 ratio in 1% PEDOT: PSS. Although there are cells that show toxic effects even at 0.5% DMSO concentrations, the existence of a non-toxic extract group at 1:1 concentration is promising (Gallardo-Villagrán et al., 2022). However, this result may be due to the absence of direct exposure of DMSO to the cells in the same environment. For this reason and to increase the application areas of the produced material in daily life, more research should be done on the amount of DMSO released from PEDOT: PSS. Additionally, the lower toxicity of DMSO in this group may be attributed to its lower concentration compared to the other groups.

On the other hand, PEDOT: PSS has recently been frequently used in biomaterial applications due to its biocompatibility and lack of carcinogenic and cytotoxic effects (Chung et al., 2023). There is even evidence that scaffolds produced by combining different biopolymers with PEDOT: PSS support cell adhesion and proliferation (Ruzaidi et al., 2021). The findings show that DMSO improves electrical conductivity by changing the polymer's structure, breaking up the PSS matrix, and helping PEDOT chains align more effectively. However, when the DMSO concentration becomes too high, it can reduce biocompatibility, likely because of greater solvent retention and its impact on cell membrane permeability (Cruz-Cruz et al., 2010; Gallardo-Villagrán et al., 2022).

## Conclusion

Commercially available PEDOT: PSS was lyophilized to concentrate the polymer. This study bridges the gap in existing research, as most prior studies have primarily focused on enhancing conductivity through solvent engineering without adequately addressing biocompatibility concerns associated with high-DMSO formulations. By systematically analyzing the impact of DMSO concentration on both conductivity and cytotoxicity, this study offers important lessons for biomedical applications.

The findings demonstrate a distinct balance between electrical performance and biocompatibility. While increasing DMSO concentration enhances conductivity by promoting phase separation and charge carrier mobility, higher DMSO levels negatively impact cell viability, as confirmed by MTT cytotoxicity tests. At 15% DMSO, the highest conductivity (156.15 S/cm) was achieved; however, consistent with previous reports that PEDOT:PSS films with ~10–15% DMSO provide optimal performance and higher concentrations tend to degrade film morphology (Gasiorowski et al. 2013) our findings indicate that films containing ≥10% DMSO also pose cytotoxicity risks, limiting their direct applicability in biomedical contexts.

Although the material exhibits toxic effects, it can be effectively isolated under appropriate conditions to prevent any leakage into the environment or harm to human health. For instance, protective coatings or composite structures can be employed to ensure that the material does not leach out. In this context, it is possible to develop thermoelectric materials through designs that minimize toxic effects. This enables the safe use of the resulting materials and offers suitable alternatives for thermoelectric applications.

Moreover, Seebeck coefficient data indicate that while higher PEDOT: PSS content improves thermoelectric efficiency, excessive DMSO does not proportionally enhance thermoelectric performance. These findings suggest that adjusting the PEDOT: PSS ratio rather than relying solely on DMSO is a more effective strategy for maintaining high performance while ensuring biocompatibility.

The limitation of this study is that PEDOT: PSS, which has low thermal conductivity but high electrical conductivity, causes biocompatibility problems at high electrical conductivity concentrations. In future studies, studies can be conducted on the formation of the material with different materials in order to prepare high concentration PEDOT: PSS solutions.

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## Author Contributions

First Author: Investigation, Formal Analysis, Writing – Original Draft. Second Author: Conceptualization, Data Curation, Methodology, Visualization and Writing -original draft. Third Author: Project Administration, Supervision, Methodology, Writing -review and editing. Fourth Author: Supervision, Writing - review and editing. Fifth Author: Formal Analysis. Sixth Author: Conceptualization, Visualization. Seventh Author: Methodology, Writing – Review & Editing.

## Conflict of Interest

The authors declare that they have no known competing financial or non-financial, professional, or personal conflicts that could have appeared to influence the work reported in this paper.

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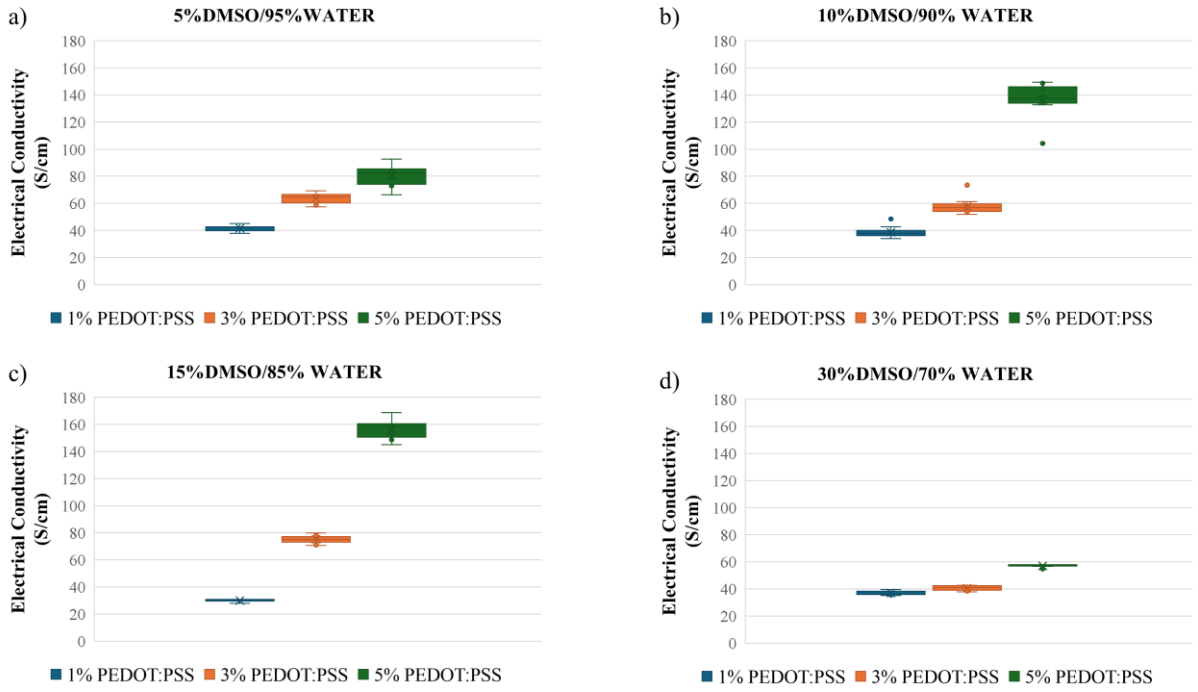


**Figure 1.** The electrical conductivities of films prepared with different ratios of PEDOT: PSS was added to DMSO-water solutions of varying concentrations a) 5% DMSO/95% water b) 10% DMSO/90% water c) 15% DMSO/85% water d) 30% DMSO/70% water.

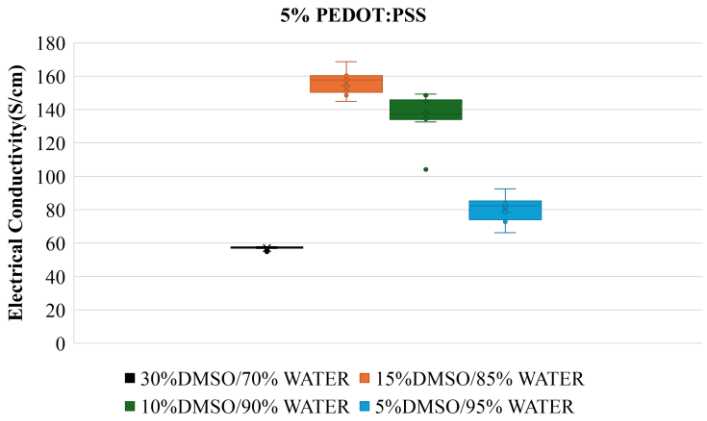


**Figure 2.** The electrical conductivities of films prepared with 5% PEDOT: PSS added to DMSO-water mixtures at different concentrations.

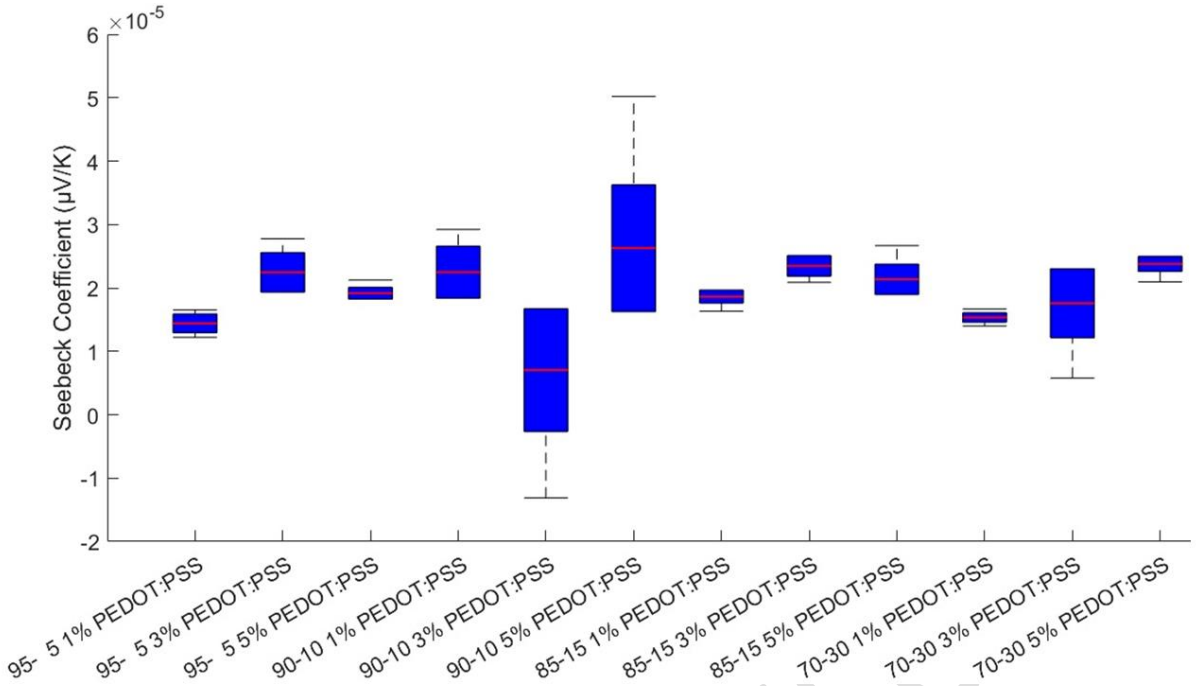


**Figure 3.** The Seebeck Coefficient measurements of films prepared with different ratios of PEDOT: PSS was added to DMSO-water solutions of varying concentrations.

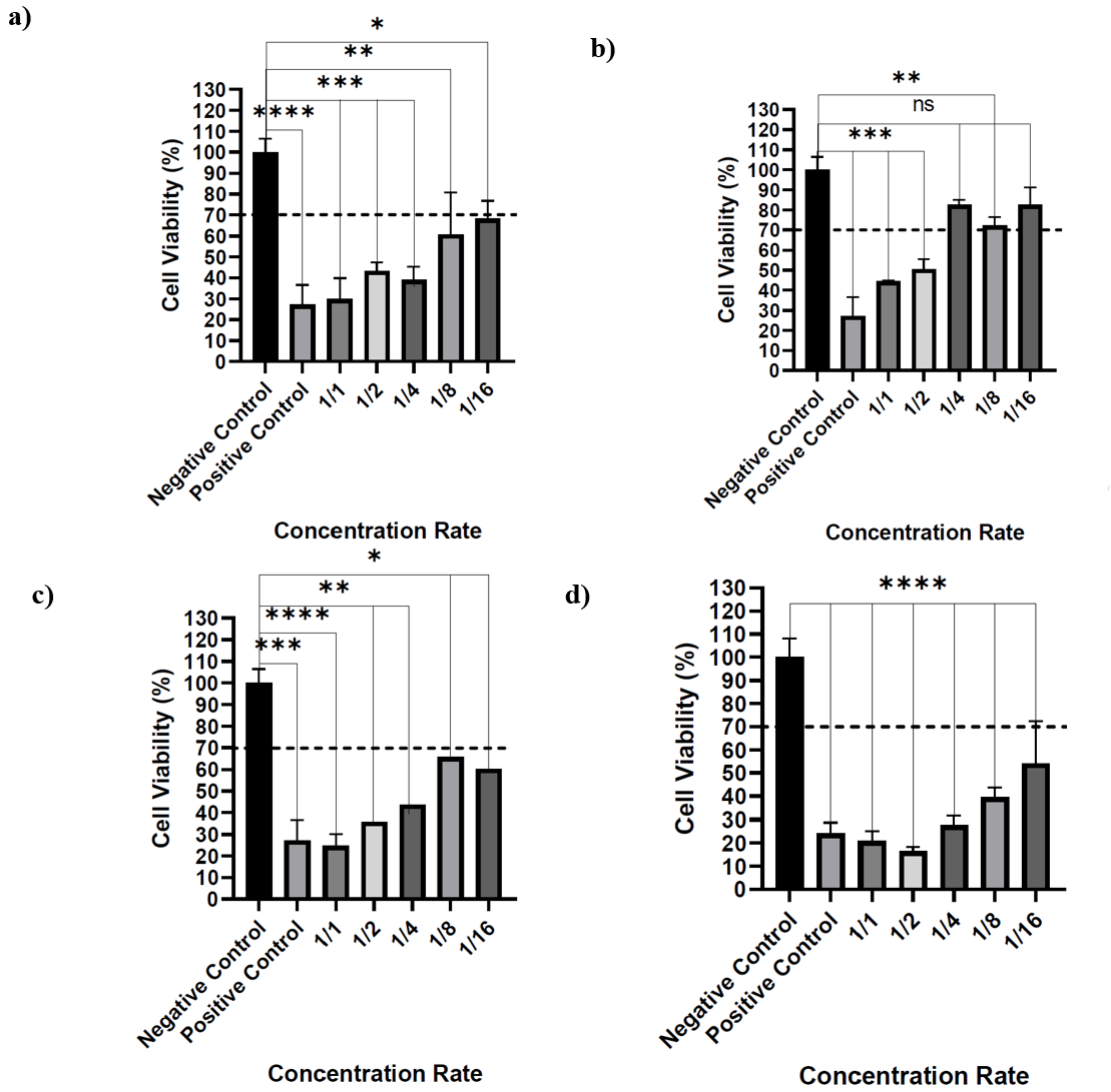


**Figure 4.** Cell viability % graph of films containing 5% PEDOT: PSS and different DMSO-water ratios: a) 5% DMSO/95% water b) 10% DMSO/90% water, c) 15% DMSO/85% water, d) 30% DMSO/70% water.

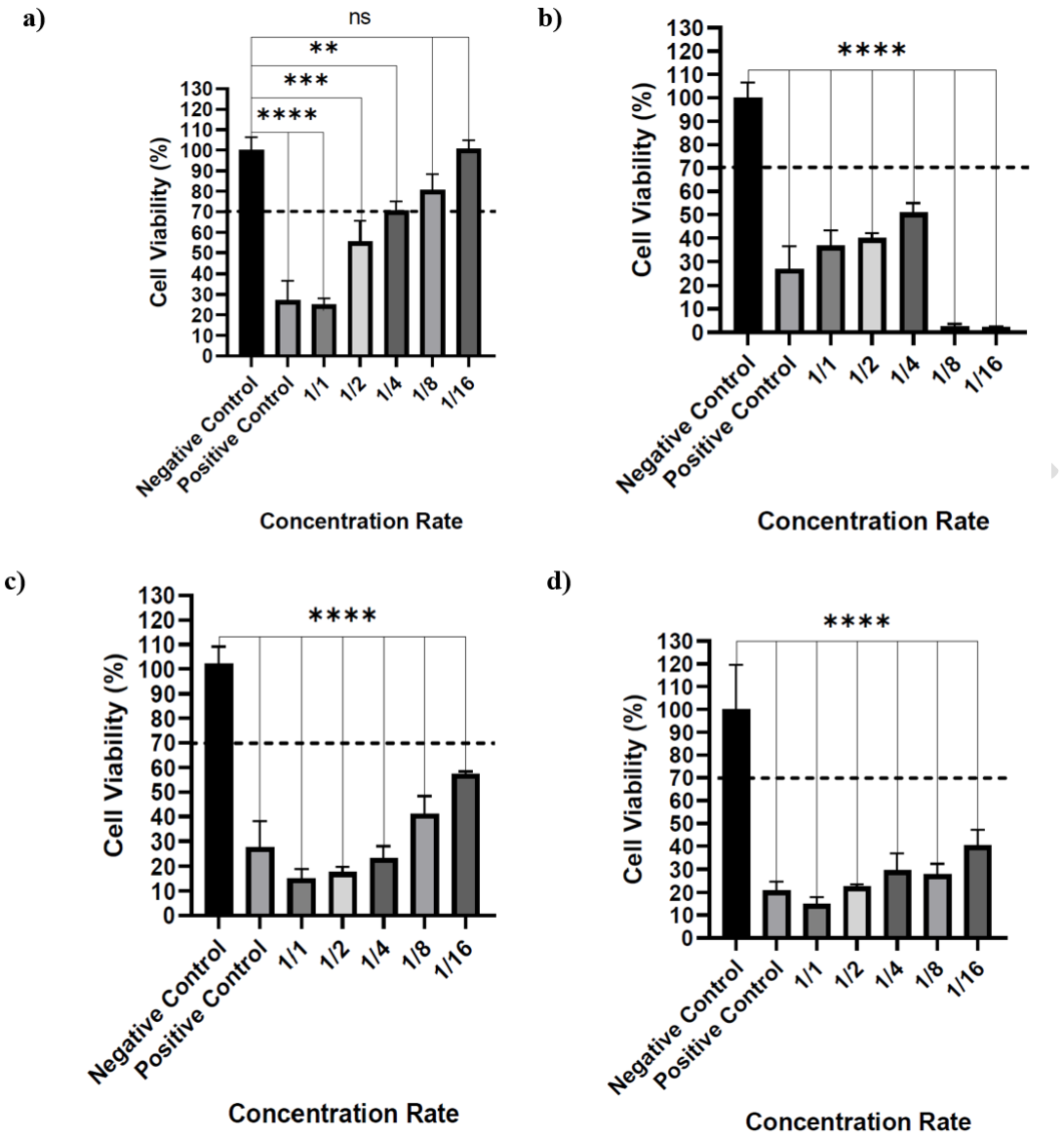


**Figure 5.** Cell viability % graph of films containing 3% PEDOT: PSS and different DMSO-water ratios: a) 5% DMSO/95% water b) 10% DMSO/90% water, c) 15% DMSO/85% water, d) 30% DMSO/70% water.

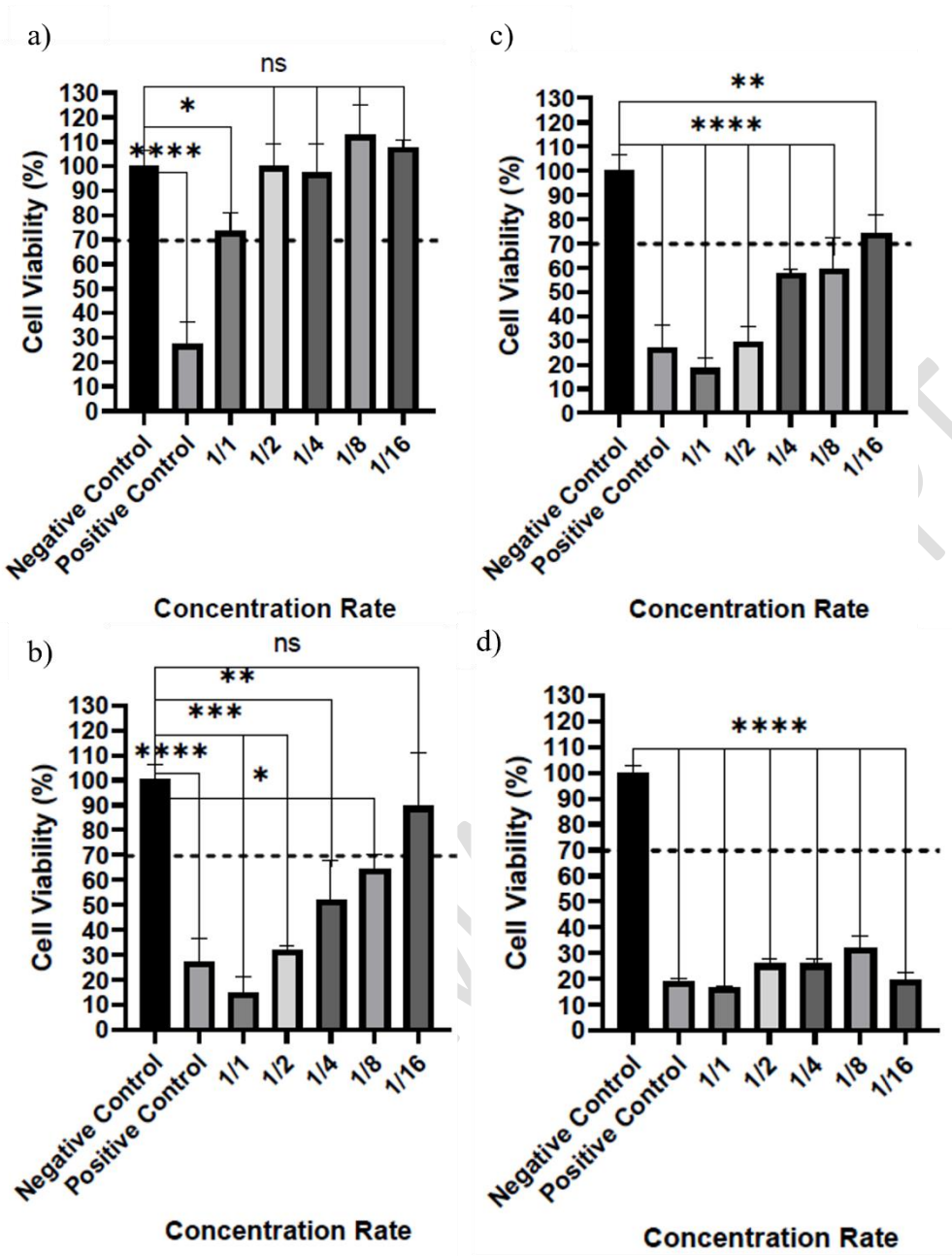


**Figure 6.** Cell viability % graph of films containing 1% PEDOT: PSS and different DMSO-water ratios: a) 5% DMSO/95% water b) 10% DMSO/90% water, c) 15% DMSO/85% water, d) 30% DMSO/70% water.