Original Article

Comparison of hydrogel polymerisation and conditioning for wearable sweat chloride sensing application

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ABSTRACT

This paper details the development of a wearable Cl^- ion-selective electrode for use in cystic fibrosis patient monitoring. Ag/AgCl electrodes were adapted with a Cl^--saturated poly 2-hydroxyethyl methacrylate (pHEMA) hydrogel mixture to act as a reference electrode. The length of time which the pHEMA was conditioned in the solution, as well as the concentration of the conditioning solutions were variables examined during the development of the device and compared to the conditioning process of similar devices from literature. In contrast to other studies, it was found that a 3M KCl condition did not produce a stable Cl^- concentration within the gel. Instead, conditioning the pHEMA in a 1 M KCl solution for 25 hours produced electrodes which exhibited strong sensitivity toward the Cl^- concentration of test solutions, over a range of $1\ mM^{-1}$ M. The electrodes demonstrate sufficient stability that plans are in place to conduct a healthy volunteer study to examine their efficacy whilst placed on the skin of participants.

KEYWORDS: wearable, chloride, pHEMA, hydrogel, potentiometric, cystic fibrosis.

1. INTRODUCTION

Cystic fibrosis (CF) is a genetic disease which affects the body's ability to regulate chloride transport across various epithelial cells throughout the body. One consequence of the disease is an inability in the sweat glands to resorb chloride (Cl^-), leading to CF sufferers displaying elevated Cl^- levels in their sweat. A new generation of CF treatments are emerging which target the proteins affected by the genetic mutations, aiming to re-instil their ordinary function, thus improve Cl^- transport throughout the body [1]. The efficacy of these treatments can be gauged by monitoring the concentration of sweat Cl^- in a patient over the course of treatment. The gold standard technique of sweat Cl^- measurement, the CF sweat test, is time-consuming and unsuitable for monitoring the temporal changes in patients' sweat Cl^-. Therefore, the development of a wearable device capable of serially monitoring sweat Cl^- levels of individual patients quickly and non-invasively could be used to investigate not only the treatment's efficacy in treating a wide range of CF patients but also aspects such as the drug's durability in maintaining these changes. Such a device would be of great significance within this field as well as areas such as health and wellbeing monitoring.

This paper introduces a wearable sweat Cl^- monitor developed by our research group and compares it to examples of similar devices found in literature.

1.1. Precedents

There are a number of previous examples of research teams using hydrogel-adapted Ag/AgCl electrodes as a Cl^- sensor. The device described by

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Dam, Zevenbergen, and van Schaijk [2] utilises a UV-cured HEMA gel mixture (cured for 25 mins under UVB lamp), conditioned in 3M KCl for a prolonged period of time, to create the reference electrode. Alongside an array of Ag/AgCl working electrodes, these were incorporated into a wearable platform and tested on subjects, in which a sterile gauze was used to direct the sweat onto the collection area. The paper stated that the electrodes were stable for over a week in fluid and possessed a sensitivity toward chloride of 58 mV/dec [2]. However, to date there does not seem to be any further development of a commercial device. Subsequent papers from the same authors have focussed on ion-selective electrodes (ISEs) pertaining to potassium and sodium [3, 4]. Choi *et al.* have also utilised chloride-saturated gel as a reference for a chloride ISE device [5-7]. The first paper published by this group investigated the effect a salt bridge has on the potentiometric performance of a chloride sensor, namely how its geometry affected the equilibration between the reference and test solutions. On-body tests were carried out by integrating the setup into a wristband. A reference chamber filled with 1 M KCl saturated hydrogel (with internal Ag/AgCl electrode) and salt bridge was used in conjunction with a Ag/AgCl working electrode. A sensitivity of 50 mV/dec was reported by the team [5]. The group's follow-up paper detailed the development of a wearable potentiometric sweat Cl⁻ sensor with an integrated salt bridge. This device utilised a 1 M KCl-saturated agarose gel on top of Ag/AgCl as a reference electrode. This was covered with a UV-curable resin. The salt bridge consisted of a small hole between the reference electrode setup and the test liquid (sweat) [6]. The group claimed that the device displayed a sensitivity of 58.5 mV/dec. They have since used their device in direct comparison to the Sweat Test for the measurement of sweat Cl⁻ concentration, returning a correlation coefficient of 0.97 [7].

Although the design of such ISEs is relatively simple, there are a number of drawbacks. Due to being in direct contact with any solution under investigation, the hydrogel's high capacity for absorbance means that over time it often takes on an excess of water causing the layer to expand. The added liquid means that Cl⁻ ions are able to slowly leach out, causing a drift in the measured

potential and, hence, the device's sensitivity over time [4, 8].

2. MATERIALS AND METHODS

2.1. HEMA gel mixture

Similar to the study by Dam *et al.* [2], the hydrogel mixture consisted of four constituents: UV-sensitive 2-hydroxyethyl methacrylate (HEMA, Sigma Aldrich, Product No. 128635); polyvinylpyrolidone K-90 (PVP K-90, Sigma Aldrich, Product No. 81440) used as an emulsifier; 2,2-dimethoxy-2-phenylacetophenone (DMPAP, Sigma Aldrich, Product No. 196118) as a photoinitiator; and ethylene glycol dimethacrylate (EGDMA, Sigma Aldrich, Product No. 335681) as a crosslinking agent. To make the hydrogel mixture, a sealable glass container was affixed to an IKA KS 130 Basic orbital shaker (IKA, Staufen, Germany) and the speed set to 320 rpm. 18.6 ml of HEMA was then pipetted into the container, prior to incremental addition of 2 g of PVP (to avoid clumping and aid emulsion), followed by 0.8 g of DMPAP and 95 μl of EGDMA. The beaker was sealed and kept on the orbital shaker for a further 2-4 hours to aid the emulsion of the gel. The mixture was stored in the fridge at 5 °C.

2.2. Electrode

Woundsense® Ag/AgCl electrodes (Ohmedics, Glasgow) were adapted for this work. Consisting of two parallel Ag/AgCl electrodes screen printed on a polyethylene substrate, they are primarily designed as a disposable sensor to monitor the moisture of a wound without disturbing the wound dressing [9]. The first adaption was to remove the porous film layer to expose the electrode contacts. A disposable, plastic inoculation loop of inner diameter of 4 mm was secured to the electrode substrate using a segment of toupee tape. Two 4 mm holes were punched through the tape before application such that the electrode contacts would remain uncovered. An inoculation loop (inner diameter: 4 mm; depth: 1 mm) was then removed from its stem and secured over the right hand electrode contact. Figure 1 depicts this stage of the electrode's development.

2.3. HEMA polymerization

A Multipette Plus positive displacement pipette (Eppendorf, Hamburg, Germany) was used to deposit
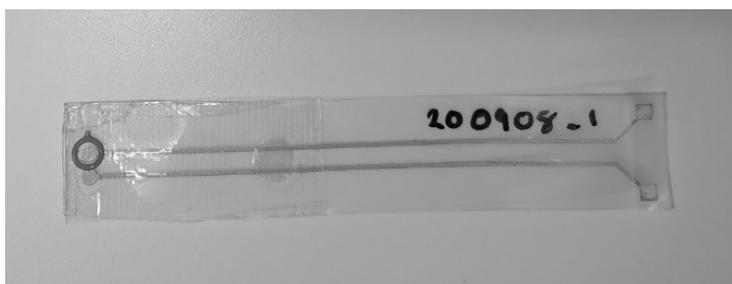
Figure 1. Woundsense electrode adapted with well for HEMA hydrogel mixture.

15 µl of the HEMA hydrogel mixture into the well created by the inoculation loop. Following the deposition of the HEMA hydrogel mixture onto the electrode surface, it must immediately be polymerised to prevent leakage from the well. The hydrogel's mechanism of polymerisation is *via* the absorption of UV radiation by the DMPAP photoinitiator component of the mixture, which absorbs UV radiation in the range of 310-390 nm [10-12]. A purpose-built UV LED array, shown in Figure 2, was manufactured to provide the source of UV light. Six 365 nm LEDs (Osram, MA, USA) were fixed to the lid of a light-tight, aluminium box (Hammond Manufacturing, Ontario, Canada) using CW2400 epoxy resin (Chemtronics, USA). The LEDs were serially linked to form an array which allowed 6 HEMA electrodes to be polymerised simultaneously. The electrodes, with freshly deposited HEMA mixture, were placed directly under the LEDs within the main segment of the box. The lid was then immediately secured on, and the power cables connected to the power source set to 30 V and 570 mA. These conditions were maintained for 15 minutes, an exposure time which was found to be optimum by experimentation, at which point the power source is turned off, the cables removed and the electrodes transferred out of the box before they go on to be conditioned.

2.4. pHEMA gel conditioning

Following polymerisation, the pHEMA samples were conditioned by submerging them in a 20 ml, 1 M KCl DI water solution. An amount of KCl was weighed directly into a sealable, plastic bijou container and 20 ml of DI water added to create a solution of known Cl$^-$ concentration. Up to three electrodes can fit into the containers to be conditioned. Once the pHEMA samples on the electrodes are submerged within the solution, the containers are sealed, and the electrodes left to condition for a set period of time. Through experimentation, a conditioning period of 25 hours within the 1 M KCl solution was found to produce electrodes with consistent and sensitive potentiometric responses to incident Cl$^-$ concentrations.

When the conditioning time had elapsed, the electrodes were removed and rinsed with DI water to remove any residue from the conditioning solution. They were gently dabbed dry on a paper towel and placed in an oven set at 40 °C for 2 hours. It was found that electrodes which are stored dry after being conditioned had a better potentiometric performance than those stored in KCl solutions – as you would find with many commercial reference electrodes. For this reason, an oven drying step at 40 °C for 2 hours was incorporated to aid the drying process so that electrodes could be tested soon after being removed from the conditioning solution.

2.5. Open circuit potentiometry

Unless otherwise stated, a Palmsens Electrochemical Interface (Houten, Netherlands) was used to perform open circuit potentiometry to record the open circuit potential (OCP) of the pHEMA - modified Woundsense electrode. It was configured in a two-lead mode by connecting the potentiostat's RE and CE clips together. Excel 2016 (Microsoft, Redmond, WA) was used to plot and analyse the data obtained.

3. RESULTS

3.1. pHEMA Cl$^-$ conditioning

Following the HEMA hydrogel's UV polymerisation, it is in a dry and glassy state. When a crosslinked
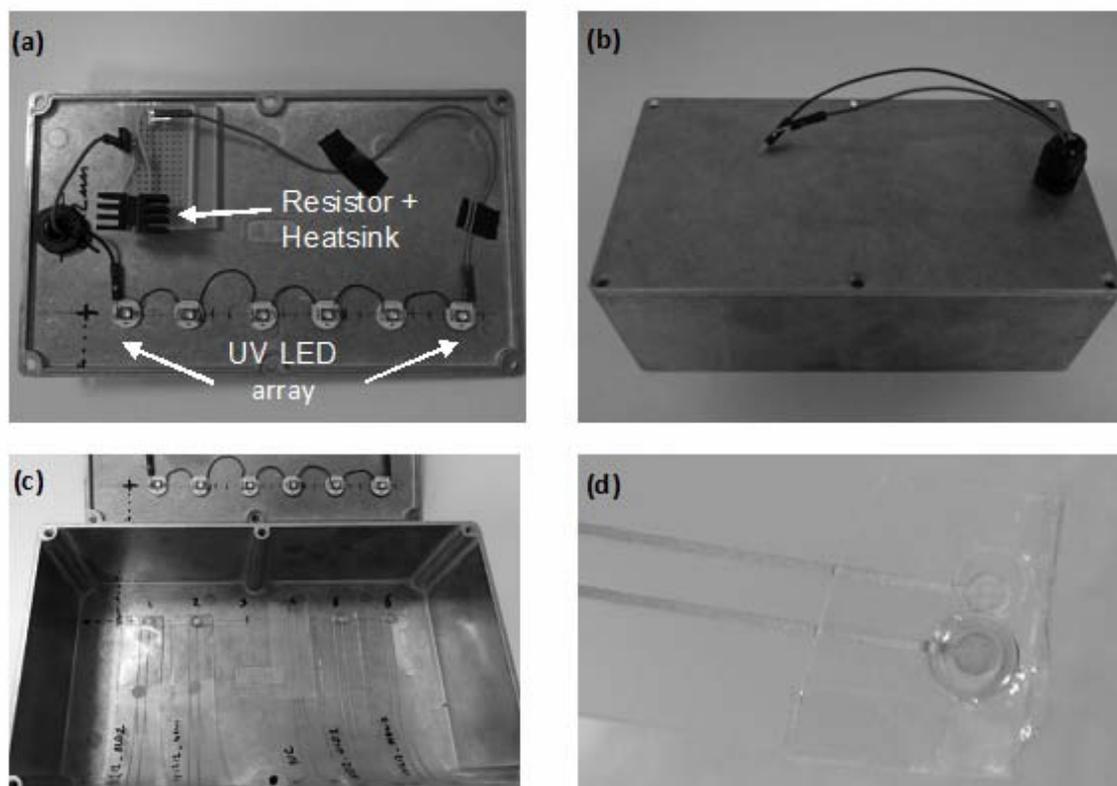
Figure 2. (a) UV LED circuit configuration, on base of aluminium box lid, used to polymerise HEMA mixture on electrodes. **(b)** View of setup with lid in place, and power leads unconnected. **(c)** View of setup with lid removed, showing how the electrodes are positioned within the box. **(d)** Example of electrode with HEMA sample, contained within well, polymerised by the LEDs.

hydrogel like pHEMA is exposed to a solution, the molecular chains of the polymer undergo relaxation, allowing the solution to penetrate further into the hydrogel volume [13-15]. This process is illustrated in Figure 3, adapted from a study by Brazel & Peppas [13]. Through this mechanism we attempt to establish a stable Cl⁻ concentration within the gel barriers above the electrode contact, enabling it to be utilised as a reference electrode (RE). Figure 4 shows a pHEMA hydrogel sample before and after the conditioning process, where it has gone from a dry, glassy state to a swollen, opaque one due to the absorption of the solution.

As Figure 3 suggests, the point at which the hydrogel has become fully saturated is dependent upon the length of time it is in contact with the solution. To analyse this, the OCP of the pHEMA hydrogel electrode was monitored, with respect to a commercial 3M KCl Ag/AgCl reference electrode, whilst conditioning in the KCl DI water solution.

A plot of the pHEMA electrode's potential throughout the conditioning period was subsequently obtained. Equation 1 presents a rearranged form of the Nernst equation, where C_{WE} and C_{RE} represent the Cl⁻ concentrations at the surfaces of the electrodes connected to the WE and RE leads of the potentiostat, respectively.

$$C_{WE} = C_{RE} \times 10^{\left(-\frac{V_{meas}}{0.059}\right)} \quad (1)$$

By substituting the measured potential values, V_{meas}, into equation 1, an estimate of the effective Cl⁻ concentration forming within the gel barrier layers can be made. The Cl⁻ concentration can then be plotted with time, allowing its progress to be tracked over the conditioning period. It has been stipulated in the literature [2, 5] that the pHEMA electrode must possess a steady and consistent potential in order to perform the role of a RE. Within the plots obtained from the conditioning
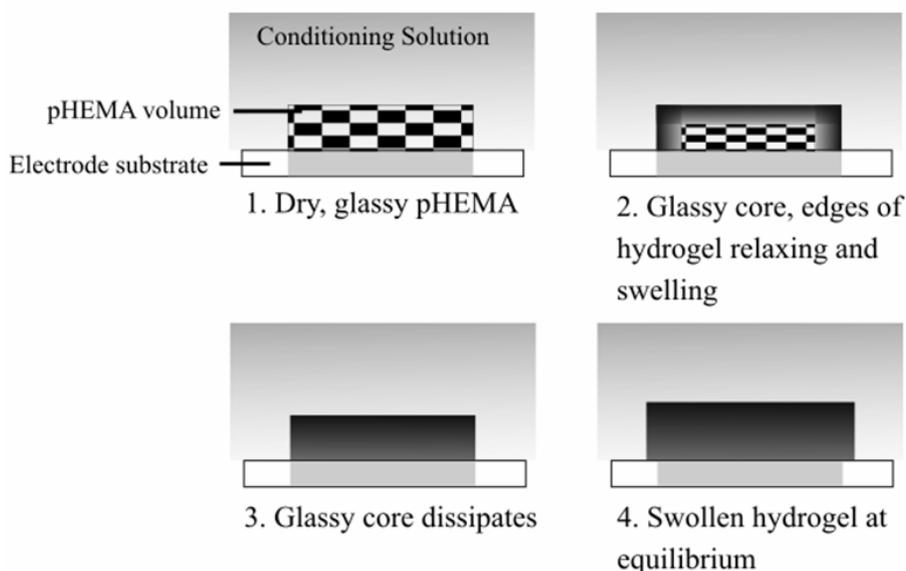
Figure 3. Schematic of water sorption progression in an initially dry, glassy pHEMA hydrogel [13].

(a)

(b)
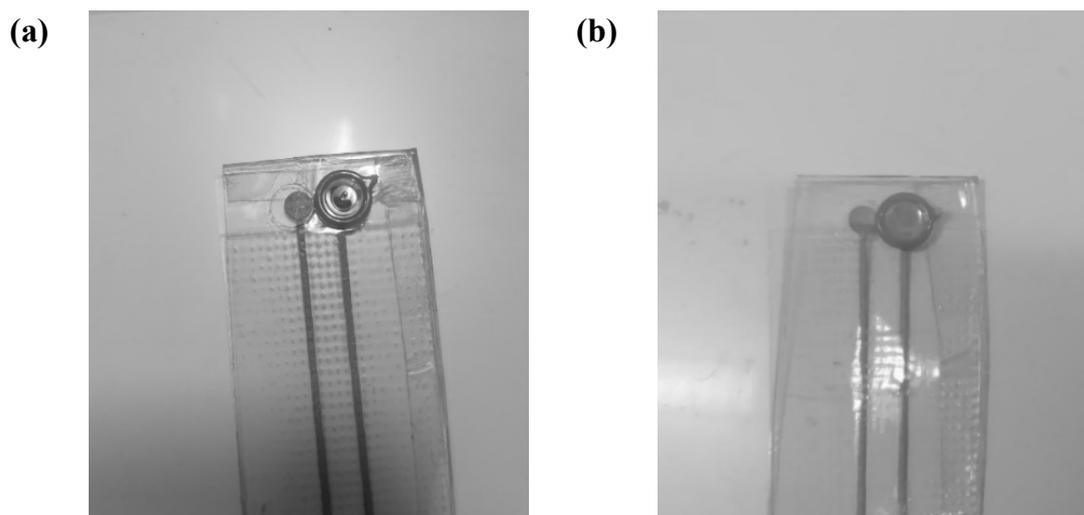
Figure 4. Woundsense electrode with: **(a)** dry, glassy pHEMA hydrogel before KCl DI water solution conditioning; **(b)** swollen, opaque pHEMA after conditioning.

process this should be characterised by a sustained plateau in both measured potential and estimated Cl⁻ concentration within the effective barrier of the pHEMA hydrogel. The plots can therefore be used to gauge the appropriate length of the conditioning time.

3.1.1. KCl conditioning

The potentials of three pHEMA electrodes were measured against a commercial 3 M KCl RE whilst they were conditioned in 1 M, 2 M, and 3M KCl DI water conditioning solutions, respectively. Figure 5 shows the conditioning profiles obtained from these observations. The corresponding calculations of the pHEMA gel barrier Cl⁻ concentration are shown in Figure 6. The sensitivity of the electrodes towards the presence of Cl was evaluated by measuring their potentiometric responses to a range of concentrations of KCl test solutions and performing

(a)   **(b)**
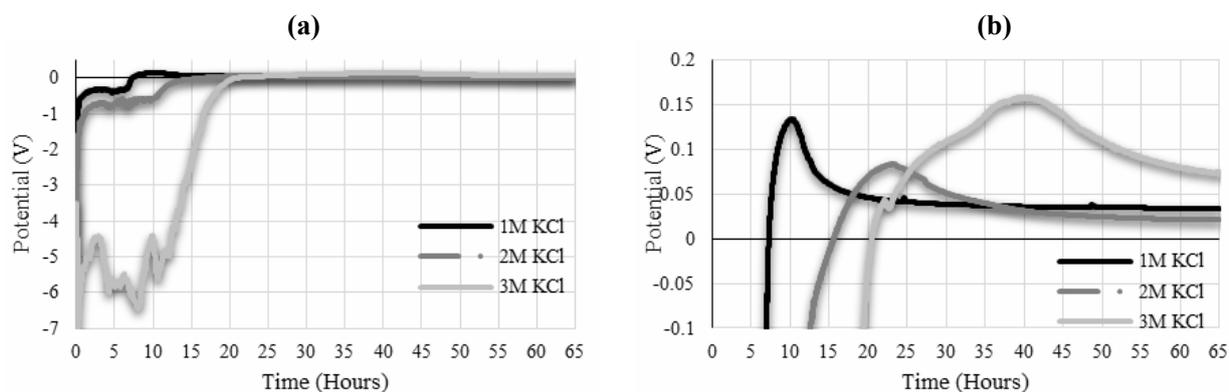
Figure 5. Potentials of three pHEMA electrodes, each measured against a commercial RE, whilst conditioning in KCl solutions of concentration 1 M, 2 M, and 3 M, respectively. (a) Potentials recorded over full measurement period. (b) Focus on the measured potentials recorded time periods in which there are peaks in the measured potentials.
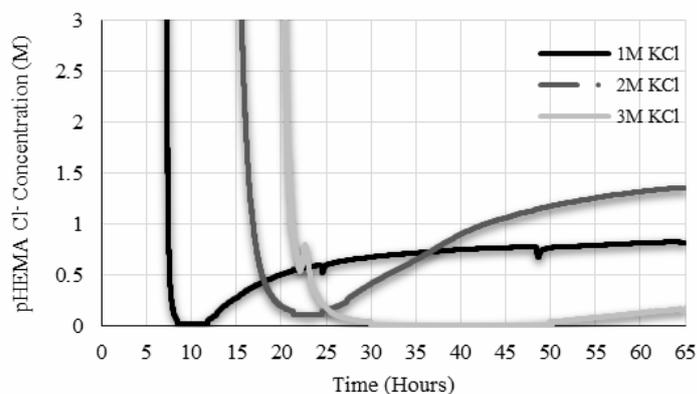
Figure 6. Effective barrier Cl⁻ concentrations estimated within pHEMA gel electrodes throughout their respective conditioning processes.

linear regression analysis. The potentiometric responses of electrodes conditioned in 3 M KCl for 25 hours and 65 hours are shown in Figures 7 and 8, and the response of electrode conditioned in 1 M KCl for 25 hours is shown in Figure 9. A summary of the experimental finding is provided in Table 1.

4. DISCUSSION

4.1. Conditioning

As noted earlier, the research by Dam *et al*. and Choi *et al*. utilised Cl⁻ -saturated hydrogels as reference electrodes in Cl⁻ ISE setups. In particular, Dam *et al*. [2] used an identical gel pHEMA composition. They reported that a stable potential was measured after the gel had been left conditioning in a 3 M KCl solution for 17 hours. Conditioning lasted at least 24 hours. This duration differs from that exhibited in Figure 5(b). Whilst they found that conditioning the gel in a 3 M KCl solution produced electrodes with a high degree of sensitivity to Cl⁻ and were reproducible, our own testing with a 3 M KCl conditioning solution could not replicate these results, with no clear sign of a steady potential being reached after >65 hours of conditioning. Studying the form of the 3M KCl conditioning profile provides an insight into why this did not yield favourable electrodes.

From Figure 5(b) it is apparent that each of the profiles follows roughly the same pattern: an equilibration from an initially large potential, before reaching a peak, and gradually plateauing in potential. The 3 M KCl profile, however, exhibits
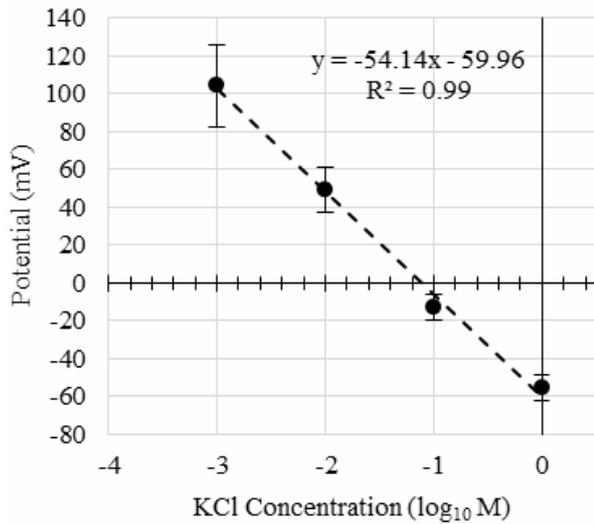
Figure 7. Potentiometric responses of four pHEMA electrodes, conditioned in 3M KCl for 25 hours, toward KCl test solutions of concentrations 1 mM, 10 mM, 100 mM, and 1 M. Data points represent the mean potentiometric responses ± SD (n = 4) to test solutions (104.30 ± 21.99mV; 49.14 ± 11.97mV; -12.93 ± 6.89mV; and -55.48 ± 7.1mV respectively). Results of linear regression analysis are also shown.

Figure 9. Potentiometric responses of four pHEMA electrodes, conditioned in 1 M KCl for 25 hours, toward KCl test solutions of concentrations 1 mM, 10 mM, 100 mM, and 1 M. Data points represent the mean potentiometric responses ± SD (n = 4) to test solutions (147.83 ± 3.85mV; 107.33 ± 2.92mV; 51.17 ± 4.37mV; and 6.33 ± 3.36mV respectively). Results of linear regression analysis are also shown.

Figure 8. Potentiometric responses (n=1) of electrodes conditioned in 3 M KCl for 90 hours toward KCl test solutions of concentrations 1 mM, 10 mM, 100 mM, and 200 mM.

a more prolonged plateauing in comparison to the other profiles, with a steady potential only being approached at the end of the 65-hour observation period. This is also highlighted in the estimated

barrier concentration where after 65 hours of conditioning the concentration remains in flux and reaches a magnitude of around 0.2 M, a fraction of the 3 M conditioning solution concentration. These observations suggest that a steady effective barrier Cl concentration has not yet been reached within the hydrogel, a theory which is supported by the potentiometric tests carried out on electrodes conditioned in 3 M KCl solutions for 90 hours. Figure 8 shows an electrode exhibiting little-to-no sensitivity toward Cl⁻ test solutions after conditioning as such. This suggests that conditioning the pHEMA hydrogel for a prolonged period may have an adverse effect on the potentiometric performance of the electrode. The possible reasons for this are discussed in Section 4.2.

Electrodes conditioned in 3M KCl for 25 hours, the length of time used by Dam *et al.* [2], exhibited a high degree of sensitivity (54.16 mV/dec) toward the Cl⁻ concentration of test solutions. However, they also demonstrated poor reproducibility with the magnitudes of the measured responses to the test solutions varying from electrode to electrode, as demonstrated by the large values of deviation shown in Figure 7. This perhaps owes to the 25-hour

Table 1. Summary of electrode conditioning and performance characteristics.

Conditioning Solution Concentration (M)	Conditioning Time	Notes
3	25 hours	• Effective barrier Cl⁻ concentration still in flux (Figure 6). • Electrodes display strong sensitivity toward test solutions (Figure 7). • Higher variability in potentiometric responses of electrodes i.e. poorer reproducibility compared to 25 hours 1M KCl condition (Figure 7).
	>65 hours	• No indication of steady Cl⁻ concentration within gel barrier (Figure 6). • Effective barrier Cl⁻ concentration at very low level (Figure 6). • Electrodes display poor sensitivity toward test solutions (Figure 8).
1	25 hours	• Stable measured potential / effective Cl⁻ concentration observed (Figures 5 (b), 6). • Magnitude of effective barrier Cl⁻ concentration approaching that of the conditioning solution (Figure 6) • Consistent potentiometric responses with good sensitivity toward test solutions (Figure 9).

conditioning time falling within the initial, high-flux phase of equilibration exhibited in the conditioning profile, Figure 5(b). The lack of sensitivity exhibited by the electrode in Figure 8 coupled with the large flux in effective barrier Cl⁻ concentration after 25 hours of conditioning meant that a 3 M KCl conditioning process was unsuitable and an alternative was required.

In contrast to the 3 M KCl conditioning profile, the 1 M KCl profile reaches a steady concentration of magnitude similar to that of the conditioning solution after around 25-30 hours of conditioning. This suggests that the pHEMA hydrogel has become saturated with Cl⁻ ions such that the electrode would provide a stable potential. This is supported by the strong average potentiometric response of 48.07 mV/dec shown by the electrodes conditioned in 1M KCl for 25 hours, Figure 9. Although this sensitivity is less than that of the 3 M KCl condition, and those reported in literature [2, 6], the small levels of deviation shown across the entire test concentration range in Figure 9 demonstrate that the 1 M KCl condition is a highly reproducible method of conditioning, and one which was chosen for the continued development of the Cl⁻ sensors.

4.2. Effect of solution concentration on conditioning profile

A notable feature observed in Figures 5(b) and 6 is that the concentration of the conditioning solution seems to affect the dynamics of the solution's uptake within the hydrogel. It is worth considering first the relationship between the concentration of the conditioning solution and the time taken to record a steady effective barrier concentration. Assuming that the penetrant transport through the hydrogel is purely dictated through Fick's 1st law, equation 2, then one would expect a steady state to occur, and a steady concentration to be measured, more rapidly with increasing concentration of conditioning solution.

$$J = -D \frac{\partial C}{\partial x}. \tag{2}$$

Here, J is the flux of penetrant ($m^{-2}s^{-1}$), D is the diffusion coefficient (m^2s^{-1}), and C is the concentration of the penetrant (M). Conversely, in Figure 6, there is an apparent delay in the time taken to reach a steady effective barrier concentration with increasing conditioning solution concentration. Studies have found that the transport of solutes through swellable hydrogels such as pHEMA may be non-Fickian in nature and dictated by the relaxation of the polymer as it transitions from a glassy to a swelled state, termed Case II transport [16, 17]. Often, however, it is the case that the penetrant transport through a hydrogel is a combination of Fickian and Case II [15,18], mathematically described by the relationship [13, 19]:

$$\frac{\partial C}{\partial t} = \frac{\partial}{\partial x}\left(D_{1,2}\frac{\partial C}{\partial x} - vC_1\right), \qquad (3)$$

where C_1 is the concentration of penetrant, $D_{1,2}$ is the diffusion coefficient, and v is the velocity (ms^{-1}) of the penetrant front. The '-vC_1' term characterises the constant velocity Case II transport of the system. Hopfenberg and Frisch [19] studied the transport of hydrocarbons through glassy polystyrene. They found that Case II transport occurred when penetrant activity was relatively high (activity: 0.5-1), and was accompanied by time-dependent anomalies in diffusion [19]. Studies have demonstrated that Case II transport can occur in pHEMA hydrogels including those containing PVP [13, 15], similar to the composition used in our investigations. This may explain the apparent increase in the time taken to reach a steady concentration with the increase in conditioning solution concentration observed in Figure 6. Further study would be needed to investigate this.

A point touched upon earlier was that of the poor potentiometric performance of electrodes conditioned in a 3 M KCl solution for 90 hours. A study conducted by Lee and Bucknall [20] examined the swelling behaviour and network structure of UV-polymerised hydrogels. It was found that immersion in high concentration saline solutions for prolonged periods led to the partial disintegration of the polymer networks of n-vinyl-2-pyrrolidone (VP) and HEMA hydrogels (similar composition to the hydrogel used in our studies). In addition, they noted that cracking may occur when the hydrogel is exposed to the saline solution. This is known as crazing, and was noted by Hopfenberg and Frisch [19], among others [13, 15], to occur when penetrants of high activity (defined by the authors as 0.85-1) [19] apply stress to the dry polymer network as they are absorbed. In these scenarios, therefore, the hydrogel's ability to act as a matrix to retain a steady Cl concentration and perform as a RE, could be compromised. This may explain the poor potentiometric performances of electrodes conditioned in 3 M KCl solutions for prolonged periods of time.

These points suggest that there is a balance to be struck when conditioning the pHEMA hydrogel, between ensuring that the barrier gel layers possess a steady Cl concentration and limiting the time in which it is exposed to the potentially destructive saline solution. Consequently, a 3 M KCl conditioning solution was deemed unsuitable for this application.

4.3. Double layer

Another feature of the conditioning profiles is that of the large potentials recorded in the initial hours of observation. It is possible that these are the result of a double layer effect. Notably, there is interest in the use of certain polymers to form electric double layer capacitors (EDLC), or supercapacitors. Conventional capacitors store energy within a dielectric material *via* an electric field, where the capacitance is given by:

$$C = \frac{\varepsilon A}{d}, \qquad (4)$$

where ε is the absolute permittivity of the dielectric (F m^{-1}), A is the surface area of the capacitor (m^2) plates, and d is the separation between them (m). EDLCs utilise electrode materials with large surface areas, like porous hydrogels, to store energy through the enhanced double layer effect which occur when they come in contact with an electrolyte solution [21-24]. This is illustrated in Figure 10.

It should be noted that normal metallic electrode contacts will not be perfectly smooth, as is illustrated in Figure 10(a) above and will contain imperfections which increase their surface area. The extent of this in comparison to the materials used to create EDLCs, however, is insignificant. Such a device was developed using UV-polymerised pHEMA hydrogel in the study conducted by Kim, Kannan, and Chung [25]. Whilst conventional dielectric capacitors typically have capacitances in the nF to µF range, capacitors exploiting materials with large surface areas and electrolytes can have capacitances ranging from 10 µF-100 mF [26, 27]. Typically these have operating potentials of around 1-100 V [26]. Capacitance is defined as the ratio of charge, Q, to the voltage, V, across the capacitor, meaning capacitors utilising materials of large surface area can store ~10 C of charge [26].

Using the Palmsens potentiostat to perform an impedance spectroscopy reading on the pHEMA electrode when it is first placed into the conditioning solution, it was estimated that the capacitance of the configuration during this period could be as
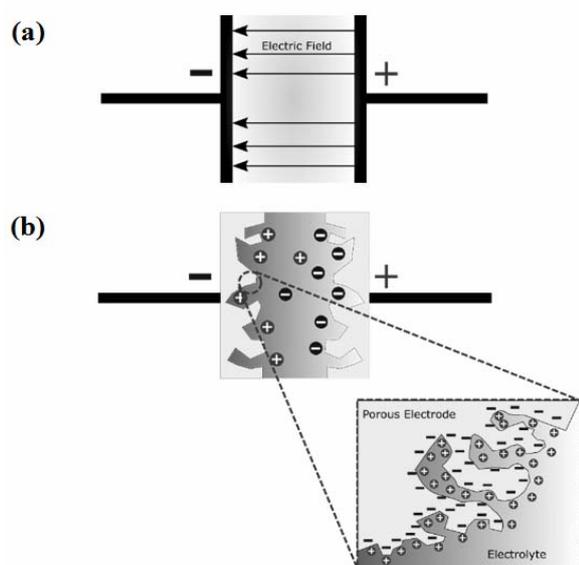
Figure 10. Schematic representations of electric charge storage in: **(a)** a conventional capacitor, through the generation of an electric field within a dielectric material; and **(b)** an electric double layer capacitor (EDLC) utilising the large surface area of a porous material to enhance the electric double layer effect [22].

high as 0.7 mF, comparable to the magnitudes of the capacitors utilising materials of large surface areas quoted above. Although this was not investigated in depth in the current work programme, such tests suggested that the capacitive properties of the sensor are high and initial currents could subsequently have large spikes from $C \times dV/dt$ capacitive current effects. It is plausible, therefore, that the large potentials recorded in the initial stages of the pHEMA hydrogel's conditioning could be the result of the formation of electric double layers enhanced by the large surface area of the pHEMA.

5. CONCLUSION AND FURTHER STUDIES

This paper detailed the work undertaken to develop a CF patient monitor in the form of a wearable Cl⁻ ion-selective electrode. Woundsense Ag/AgCl electrodes were adapted through the deposition of a HEMA hydrogel mixture onto one of the substrate's two electrode contacts. The HEMA mixture was polymerised using a purpose-built UV LED array and the resultant pHEMA electrodes were then immersed in a KCl DI water solution to facilitate the hydrogel's saturation with Cl⁻ ions. This allowed the pHEMA-covered electrode to be utilised as a reference electrode. Alongside the unaltered Ag/AgCl working electrode, the electrode pair formed a compact Cl⁻ concentration cell configuration where the measured potential is proportional to the Cl⁻ concentration of the solution with which the electrodes are in contact.

The length of time which the pHEMA is conditioned in the KCl solution, as well as the concentration of the conditioning solutions were variables examined during the development of the device. It was found that conditioning the pHEMA in a 1 M KCl solution for 25 hours produced electrodes which exhibited strong sensitivity of 48.07 mV/dec toward the Cl⁻ concentration of test solutions, over a range of 1 mM^{-1} M. This compares well to the sensitivities of 58 mV/dec and 58.5 mV/dec of Cl⁻ sensitive hydrogel electrodes reported in the literature [2, 6].

The electrodes exhibited excellent levels of reproducibility, and sufficient levels of stability, that a healthy volunteer study is viewed as the next stage of testing. These tests would involve placing the electrodes on the participant's forearms and gauging their ability to monitor the Cl⁻ content of their sweat or an artificial sweat solution. If successful, the study would demonstrate the ability of the device to operate in a real-world environment.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

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