Investigation of Preventative Treatment Options for Pressure Ulcers

Kirsten Black , Sean Minderlein, Alex Hudson ,Kartik Warikoo
College of Engineering and Computing
Miami University

Abstract

The health care system currently lacks a product that both treats and prevents the progression of sub-dermal pressure ulcers. Not much is known about the formation of sub-dermal pressure ulcers however it is widely accepted that lack of blood supply, and thus lack of oxygen, is the cause. The purpose of this investigation is to develop a device that supplies oxygen from an external reservoir, at a controlled rate, to the location of a subdermal pressure ulcer. Since skin is a large diffusional barrier to oxygen the incorporation of microneedles into the devices allows for increased and possibly uninhibited gas diffusion. We plan on using this data to creating a device that would effectively treat the progression of pressure ulcers, or more generically a device that would be able to diffuse gas to a sub-dermal tissue.

Introduction, Problem Statement, Objectives

Pressure ulcers, commonly known as bedsores, are defined as a localized injury to the skin and/or underlying tissue usually over a bony prominence as a result of pressure or pressure in combination with shear (NPUAP). The Agency of Healthcare Research and Quality reports that pressure ulcers present an annual burden of 9.1 to 11.6 billion dollars on the US health care system, a drastic increase from 1.2 billion reported in 2006 (Linder-Ganz *et.al*). Pressure ulcers cause 60 thousand deaths annually and are most prevalent in patients that are bedridden, wheelchair bound, or immobile (AHRQ). The NPUAP has created four classes to describe the extents and depths of pressure ulcers: non-blanchable erythema, partial thickness, full thickness skin loss, and full thickness tissue loss. An additional category was added for “suspected deep tissue injury”, defined as purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear (NPUAP). This last category is of particular interest because very little is known about its development and progression.

Pressure ulcers develop in two different ways, superficially and sub-dermally. Superficial pressure ulcers are initiated by moisture, heat, frictional, and shear forces in the skin near the

epidermal tissue. Due to the location of generation they tend to be less severe, easy to identify, and easier to treat because they are contained in the regenerative tissue and therefore reversible. The second form of generation is sub-dermal, also called deep tissue injury (DTI) pressure ulcers. Sub-dermal pressure ulcers are more clinically relevant than superficial pressure ulcers due to the fact that DTIs alone affect 10% of all hospital patients and lead to osteomyelitis, sepsis, and death (Linder-Ganz *et.al*). These are thought to initiate adjacent to bony prominences and erode the local soft tissue surrounding the bony prominences, typically muscle first. The specific details about the development of sub-dermal pressure ulcers are still unknown, including a single damage threshold (OOmens *et.al*). However, it is known that the prolonged pressure to a localized area blocks the flow of blood through vascularized soft tissue, preventing the transport of oxygen, nutrients, and disposal of metabolic byproducts, which are all essential to tissue viability and development (Linder-Ganz *et.al*).

Literature review has shown that there is uncertainty in the field about the best way to treat pressure ulcers. Treatments and preventative measures currently employed only target superficial pressure ulcers which are less severe and easier to treat. The health care system is currently lacking a product that both treats and prevents the progression of sub-dermal pressure ulcers. The goal of this project is to create a device that delivers oxygen at a controlled rate from a chemical reaction to the location of a sub-dermal pressure ulcer, supplying the affected cells with one of the necessary compounds they needs to survive.

In order to create this device, three specific objectives will be completed to develop the final product. The first objective is to demonstrate oxygen delivery that can be worn as an adhesive patch without attached tanks or bulky equipment. The second objective is to measure oxygen diffusion, propagated by a chemical reaction, through skin with and without the use of microneedles. The last objective is to produce controlled oxygen delivery rates through microneedles over extended periods of time. By completing these objectives, the final device will be an oxygen-generating patch that delivers oxygen through the skin to the site of the pressure ulcer by microneedles.

Background

There is a demand for a device that can both treat an existing ulcer as well as prevent subdermal pressure ulcers from progressing to the point of necrosis of the outer layers of skin. Of the current treatment methods, some apply to both superficial and sub-dermal sores. Repositioning is the most common method of treatment and prevention for patients that are immobile and thus at high risk for bedsores. The purpose of repositioning is to alleviate the affected tissue from pressure and shear stress (Mayo Clinic). A problem with this treatment method is that it has to be done very frequently, about every 15 minutes for wheelchair bound patients, which can be extremely difficult for patients with mobility issues. Another method of treatment includes support surfaces such as air mattresses and bed cushions which have the same goal as repositioning - to reduce pressure. Other common treatments are continual cleaning and wound dressing to prevent infection as well as proper hygiene and nutrition to promote the body's natural ability to heal. A more invasive treatment is the surgical removal of damaged tissue or debridement, which includes the body's natural or chemical enzymes to break down the dead tissue (Mayo Clinic). Two treatments that are used for more severe cases of pressure ulcers are

negative pressure therapy and hyperbaric oxygen therapy. Negative pressure therapy uses a device that attaches a bandage to the wound and a pump to create a negative pressure environment surrounding the damaged cells to encourage blood flow through vascularized tissue where it was previously blocked (Gupta *et.al*). Hyperbaric oxygen therapy vastly increases the supply of oxygen, which in turn improves the healing. This technique is used for other types of chronic wound care as well as pressure ulcers (Kranke *et.al*). All of the current treatments are painful yet very effective. According to the Agency for Healthcare Research and Quality, the cost of treating a pressure ulcer for the patient is between $20,900 and $151,700 per ulcer. Therefore, there exists a demand for a sub-dermal pressure ulcer treatment which is less painful, less expensive, and more effective.

Through literature and patent review, a device was discovered that had a similar goal of delivering oxygen to pressure ulcers. Oxyband is marketed to treat superficial pressure ulcers instead of sub-dermal pressure ulcers (Rosati), which are the focus of this project. While the concept of delivering oxygen to pressure ulcers in order to prevent tissue necrosis was the same, the mechanisms by which the oxygen is delivered differ. Oxyband patches contain an oxygen reservoir behind a semi-permeable layer through which the oxygen diffuses into the ulcer, as opposed to an oxygen-generating chemical reaction diffusing through microneedles (Rosati). Since our goal was to create a patch with a sustained effective life, further searches were required to determine a viable mechanism of oxygen-generation.

Online research into oxygen generating compounds led to the discovery of multiple research projects on the topic from the Wake Forest Institute for Regenerative Medicine at Wake Forest University, of which two held potential to be viable components in our design. The first project examined if oxygen generating biomaterials were able maintain cell viability while simultaneously maintaining the structural integrity of a three-dimensional scaffolding from which the oxygen is produced (Harrison, 2009). Poly(d,l-lactide–co–glycolide) (PLGA), with an 85:15 molar ratio of lactic to glycolic acid, was formed into the porous scaffolds using paraffin molding techniques (Harrison, 2009). Calcium peroxide (CPO) particles, which were incorporated into the pores of the scaffolds during the molding process, caused the formation of small oxygen bubbles on the surface of the scaffolds when they were placed in water (Harrison, 2009). Although a product was created which was able to bolster cell survival under hypoxic conditions via oxygen production, it ultimately was not right for inclusion in this project due to conflicts with the methods of delivery.

The second study dealt with a film laced with a polymeric oxygen-generating compound which was inserted subcutaneously to help prevent cell necrosis. This film more closely resembled the design that we want to employ, although it would remain on the surface of the skin rather than being placed beneath it. As with the first study, the biomaterial PLGA was used as the base through which the oxygen-generating compound would be delivered, albeit this time as a film with a molar ratio of 50:50 lactic to glycolic acid (Harrison, 2007). The oxygen generating Sodium percarbonate (SPO) was incorporated into the films using a solvent casting process (Harrison, 2007). Figure 2 shows the amount of oxygen, in mL, per gram of SPO that was released over a roughly three day period (Harrison, 2007). The amount of oxygen released was measured as the volume of the water displaced by the generation of the oxygen gas.

In vivo research was conducted on sixteen nude mice (*Mus musculus*) which were randomly split into two groups; one group received films treated with the sodium bicarbonate,

and the second, a control group, received just the PLGA films without the sodium bicarbonate. Skin flaps measuring 30 x 10 mm were made on the backs of the mice, and the 20 x 10 mm films were inserted subcutaneously in between layers of muscle and skin, before the flaps were sewn shut using absorbable sutures (Harrison, 2007). The amount of necrotized tissue was then measured after two, three, and seven days and skin samples were analyzed using histology. Results, as depicted in Figure 3, showed a significant difference in the extent of necrosis over the first three days but became increasingly more comparable as the seventh day neared (Harrison, 2007). The amount of oxygen produced and necrosis prevented made the film viable for application into our project.

Design Approach

Stage 1: Demonstrate oxygen delivery from a lightweight and compact enclosable substance.
Hypothesis: Chemical reaction of CaO_2 or NaH_2O_2 and water will produce oxygen at a rate similar to that of systemic oxygen delivery patches.
Rational: The chemical reaction of CaO_2 or NaH_2O_2 and water produces pure oxygen, with by products that can be consumed by the human body. Our research into the subject of hyperbaric oxygen therapy suggested treatments of 100% oxygen at pressures of 2-2.5 ATA for 60-90 minutes once, or twice daily. During this time, the elevated tissue oxygen levels enhances the healing process. The benefits of hyperbaric oxygen therapy are well established for the healing of pressure ulcers and new developments in topically applied oxygen delivery have shown similar outcomes. The results from both treatments are directly correlated to systemic oxygen delivery to the damaged and oxygen deprived skin tissue. When there is healthy blood circulation, the body provides a tissue with pO_2 of approximately 39 mmHg. In the case of pressure ulcers, the oxygen level in the tissue can drop down to almost zero due to injury, infections, and/or reduced blood flow. This drop in pO_2 to a dangerously low level results in necrosis and slowed healing. Optimal tissue healing apparently occurs when pO_2 rises to between 50 and 80 mmHg for a sustained period of time.

Measurements of the gas production from the reaction using an inverted test tube method. This is the simplest method that can be used to measure gas production, and it involves the placing of an inverted, graduated cylinder, containing a reaction vessel inside of it, into a large beaker of water. The house vacuum system was then used to remove the majority of the air from the formed air pocket, drawing water up into the graduated cylinder. This creates a chamber that allows for the gas produced in the reaction vessel to be contained and measured.
Driving scientific question: Can relatively simple lab experiments involving chemical reactions replicate oxygen production levels that match the levels produced by topically applied systemic oxygen delivery patches and by hyperbaric oxygen therapy? In hyperbaric oxygen therapy, hemoglobin in the circulating blood becomes fully oxygenated. The partial pressure of oxygen is directly proportional to the oxygen that is physically dissolved in plasma and can meet the tissues oxygen requirements. The increments in oxygen supply may factor in the ability for the compromised tissues to survive and be maintained until healed.
Stage 2: Measure the diffusion of oxygen from a chemical reaction through skin both with and without micro-needles. We wish to see how much oxygen from the reaction permeates through

skin via the microneedles, as well as without, in order to see how much oxygen will be able to diffuse across this barrier. More specifically, we want to take our data and apply it to the real world application of pressure ulcers. We can use known constants for the diffusion rate of oxygen through sub-dermal tissue and the constants for the material that will eventually house the chemical reaction to calculate the amount of oxygen that will reach the tissue from the site of reaction. This model will show us the rate at which the oxygen being generated in the reaction is getting to the lower tissue layers, which can be utilized to model the oxygen diffusion from the patch to the site of necrosis.

Hypothesis: The addition of micro-needles will increase the rate at which oxygen will diffuse through a skin substitute.

Rational: Since the dermal layers are a large barrier to gas diffusion, the addition of microneedles will allow the oxygen to more easily diffuse to the areas where it is most needed by bypassing the dermal layer. We already possess the microneedles, now we have to implement them in a device that houses our oxygen generating reaction. We are testing to see how oxygen diffuses through the skin substitute over time so that a model of it can be created later on. We feel it is imperative at this stage to create a model based off of our experimental data to see how the reaction is carrying on and how we can proceed with making a pressure ulcer treatment. With the model we can then move on to our next objective and fine tune the product.

Henry's law can be utilized for the rate at which the gas diffuses into the material and then diffuses out of it into the surrounding fluid. Using this mass balance law, we can calculate the flow rate of oxygen out of the needles. After we find the flow rate of oxygen out of the needles, we can use known diffusion constants for skin and other biological tissue to calculate the amount of oxygen that diffuses through the needles. We know the amount of oxygen that diffuses out of capillaries into passive muscle tissue or muscle tissue that is not contracted (Wilson et al). This method will be able to tell us the amount of oxygen that is diffusing through to the pressure ulcer site as well as tell us the amount of oxygen at the site of needle entry. This model for diffusion will be important later on as we try to implement the patch to fit a real physiological system.

The plan for measuring this stage is as what was performed before, using inverted test tube methods however there needs to be skin fastened on top of both reaction vessels. For the microneedle array just pressing the skin onto it as the needles hold it in place allows for the reaction to work. For the control test the skin will be held in place by a plastic ring, this will ensure that the skin will not blow off due to high pressure.

Driving scientific question: How does oxygen diffuse out of the micro-needle apparatus and though a skin substitute? Also, how would that translate to actual physiological states?

Stage 3: Measure the diffusion of oxygen from a chemical reaction that is housed in a multi layered super-dermal patch. Finalizing a design for a superficial patch that will house a chemical reaction that would be able to diffuse oxygen to sub-dermal layers of pressure ulcer. Creating a patch for clinical would have to incorporate 4-layer system. The initial or outside layer is a waterproof plastic that would block any unwanted moisture from the surrounding environment that would disrupt and skew any levels of oxygen being produced. It was also important to add a strong skin adhesive to the outer edge of the patch that would help keep the patch from moving from the site of infection. The second layer of the prototype patch was that of a 2.0 mm thick multi-layered gauze. This layer would be the first layer that would act as a boundary as well as a

primer layer to the reaction vessel. The third segment of the patch contained simple supermarket gelatin. The pre-packaged powered gelatin was mixed with a fourth cup of water and microwaved for a minute to liquefy. Approximately 1.5ml -2.0ml of liquid gelatin was pipetted across the surface of the gauze layer of the patch and was set at room temperature overnight. This allowed the gelatin to solidify and give rigidity to the prototype. It was important to add a gelatinous layer as its role was to act as the main vessel that houses the SPO/water reaction. Finally, the last layer of the patch was the actually SPO/water reaction that would face directly to the site of the ulcer.

Hypothesis: A multi-layered patch that will be able to house a SPO/water reaction can be created to produce and diffuse oxygen levels necessary to treat sub-dermal pressures ulcers.

Rational: Designing a system from which to deliver oxygen to sub-dermal levels of pressure ulcers was an important aspect of this project. It was determined that approximately .500g of SPO with 2ml of water would produce enough oxygen needed to help treat patient with pressure ulcers, but there needed to be a method or system to deliver such high oxygen levels to the site of infection. Creating a super-dermal patch that could easily house half a gram of SPO and 2ml of water without losing any reagents and thus minimizing any loss oxygen that is need to diffuse sub-dermally. The apparatus in which oxygen levels where tested was the inverted test tube method we have been using for oxygen production rates of SPO and CPO. The only alteration that needed to be made was do create a boat/vessel a sample of the patch had to be held in. Having a holding vessel for the patch as it is in the inverted test tube as extremely important because excess water could not enter the area of the patch where SPO and water was reacting over time as this would alter the levels of oxygen being produced. The vessel was simply lined completely with gauze and the liquefied gelatin (1.5ml) was pipetted inside. As the gelatin was left to set it was able to take the shape of the vessel covering every piece of surface area for the SPO and water to react. This did not limit to the amount of SPO that could be tested in addition to any excess moisture in the apparatus would absorbed by the excess gauze covering the testing vessel.

Driving scientific question: Can a super-dermal, multi-layered patch act as housing vessel for a chemical reaction that will diffuse oxygen to sub-dermal layers of a pressure ulcer?

Results and Data Interpretation

Previous work from the prior team determined that the microneedle patch will have a surface area of 5 cm^2 and contain a field of microneedles that the oxygen will diffuse through. Each individual needle will be between 10 and 1000 µm in length. The base width will be 50 µm, the tip width will be 20 µm, and the diameter of the center will be 10 µm. In order to provide the microneedles with a substantial feed of oxygen, the needle patch will be affixed to a systemic oxygen delivery patch that can be applied topically to the afflicted area. The patch is a development on the previous team's work, providing a tankless source of pure oxygen.

After researching chemical reactions that produce oxygen, which would increase the shelf life of the product and not produce any harmful byproducts, we settled on the two Wake Forest papers that utilized sodium percarbonate and calcium peroxide. Both chemicals react with water to eventually form oxygen and create non-toxic and non-harmful byproducts in the meantime.

The two chemicals were bought from Sigma Aldrich for the purpose of this experiment. Utilizing stoichiometry and ideal gas laws, we calculated that one gram of sodium percarbonate will produce approximately 120 milliliters of oxygen; one gram of calcium peroxide will produce 167 milliliters of oxygen at 20 degrees Celsius and one atmosphere of pressure.

The reaction of just sodium percarbonate in water at room temperature was investigated to determine the amount of oxygen generated using the inverted test tube method. This reaction took around three days to react completely, generating approximately 70 ml of gas per one half gram of sodium percarbonate (SPO). Three trial runs were conducted and generated similar results of a sigmoidal curve (Table 3). It was assumed that any volume generated in the graduated cylinder was the desired product, oxygen, because gaseous oxygen product of the reaction and carbon dioxide remains in solution. When comparing the experimentally generated moles of oxygen to the calculated moles of oxygen generation there was around a 70% conversion. This percent conversion was set to be the standard and what was desired when the reaction was run with microneedles and then with mirconeedles and skin. The calcium per oxide (CPO) reaction was not nearly as efficient, it would produce only a few milliliters of gas per one half gram in a weeks' time. Due to these less then promising results, experimentation with CPO was ceased.

After obtaining repeatable results from the sodium percarbonate and water reaction, the next measurements obtained were of SPO and water in a reaction vessel attached to the microneedle array. The purpose of this reaction was to measure any diffusional barriers that the needles presented. For this experiment a luer lock syringe attached to the microneedles to house the reaction. The reaction measured one half gram of SPO with water that was not measured, this caused the data to have large amounts of error. This error lead to more stringent control on how much water was added to the reaction environment. The inverted test tube method of measurement was employed again. From data collection it appeared that the needles do not present any barrier of gas production, as the amount of gas measured over time is the same as what would be expected given the reaction kinetics.

The next step in experimentation was to determine if the microneedle length was sufficient to bypass the epidermis, which poses a problematic diffusional barrier to oxygen. To explore this idea, the ability of the needles to increase the gas diffusion through dermal layers was measured. The testing model was skin, obtained from poultry, more specifically *Gallus Gallus domesticus* (Kroger, Oxford OH). Although this species does not have dermal layers that are exactly like that of humans, it would be close enough to allow the modeling of the diffusional barrier that human skin presents to the microneedles and to the atmospheric oxygen in general. The inverted test tube method of measurement was employed again as it is the simplest method we had to measuring gas production. The results clearly show that the needles allow for a steady diffusion of gas through the dermal barrier, opposed to the extremely limited diffusion that is exhibited in the non-needle trials.

From the experimentation, it was observed that the reaction rates of the sodium percarbonate reaction were similar when no microneedles were used and when microneedles and skin were used (Figure 4). Therefore, the microneedles do not present any diffusional barrier to oxygen and the length of the microneedles is sufficient to bypass the epidermal layer of tissue on a human patient. This conclusion is particularly important because sub-dermal pressure ulcers develop adjacent to boney prominences and do not deteriorate the outer layer of skin, as do

superficial pressure ulcers. Therefore the outer layer of skin is intact and prevents the diffusion of oxygen. These results show that the microneedles will penetrate the epidermis and deliver necessary oxygen to the site of the sub-dermal pressure ulcer.

Due to the nature of the formation of most subdermal pressure ulcers, target areas for patch placement are not usually exposed to the air in the room, but instead are pressed against the bed or chair that the patient is situated in. Because of this fact, the reaction would not be taking place at room temperature, but instead at a higher temperature which was approximated to be human body temperature (37˚C). This necessitated the completion of another set of experiments to determine the rate of the reaction at this elevated temperature level. In order to do this, the large beaker of water in the inverted test tube set up was replaced by a hot water bath maintained at 37˚C to simulate an in vivo environment. Three control trials were run with no chemical to ensure that no oxygen was generated, as well as that the mixing motion used to keep the bath at a homogenous temperature would not introduce external oxygen into the test chamber. During these tests it became evident that, with the higher temperature, evaporation of water from the reservoir would become problematic if not monitored and dealt with accordingly. To counteract the loss due to evaporation and keep water levels where they need to be, small amounts of water were poured into the bath. To reduce the air bubbles created by pouring the water and keep them from entering into the test chamber, the added water was poured down the inside wall of the bath, causing minimal surface disturbance.

Three experimental trials were run, each using approximately 0.5 g of SPO and 2 ml of deionized water. It was hypothesized that the rate of reaction would be increased at a higher temperature; but the rate was even faster than expected, with the reaction completing in around six to seven hours. This lead to measurements taken at too large of time intervals for the first trial. The data collected did not give an accurate representation of the reaction over time and thusly was dismissed from consideration. To allow for a higher degree of accuracy in the data, measurements for the second and third trials were taken every thirty minutes until three identical readings were recorded to ensure the reaction had reached completion. The data points between the two trials were almost identical, with only a few, slight variations. Both trials yielded approximately 60 ml of oxygen produced and, just as with the room temperature trials, generated sigmoidal curves (Figure 5).

Because of the drastic increase in reaction rate observed between running SPO trials at room temperature and body temperature, CPO was again considered as a possible chemical choice. If CPO's rate of reaction increased similarly, it could be used to create a patch that would generate oxygen over a longer period of time. Hypothetically, if the CPO generated little to no oxygen over the first six to seven hours, and then started producing viable amounts of oxygen for an extended period of time, the SPO and CPO could then possibly be used in conjunction to create a reaction that starts quickly (from the SPO) and continues for longer (from the CPO), requiring less bandage changes and maintenance. Since CPO does not react at room temperature, a patch incorporating it would theoretically have a longer shelf life and would only start to react once applied to the patient. Two trials using the CPO in the water bath at 37˚C were performed, but when barely 8 ml of oxygen was produced after 36 hours (far longer than a patch should be applied), the third trial was scratched and CPO was again dismissed as a viable option.

After the patch was assembled with all the layers necessary. It was time to test how much oxygen could be produced by the prototype. A bottle cap was used as a holding vessel

throughout the testing of the patch. The initial controls were run with a patch that did not include a layer of SPO/water reaction. After the testing vessel was placed in the vacuumed inverted test tube, no oxygen was produced over a period of three days. Three trials were then run following the control experiments. Due to the limited surface area of the patch that could be tested within the inverted test tube, only 0.2534 g and 0.2567 g of SPO (with 1 ml of H_2O) were tested and only 1.50 ml of oxygen was produced. Theoretically, there should have been approximately 5 ml of oxygen being produced. Due to the small, flat surface area being tested, undissolved SPO as well was the water falling into the testing vessel. In addition some oxygen bubbles were getting trapped in the gelatinous layer as the layer failed to solidify entirely. In order to attain the theoretical amount of oxygen the surfaces of the patch had to be modified for testing purposes only. The vessel was simply lined completely with gauze and the liquefied gelatin was pipetted inside. As the gelatin was left to set, it was able to take the shape of the vessel covering every piece of surface area for the SPO and water to react. This did not limit to the amount of SPO that could be tested so 0.5734 g of SPO was tested with 2ml of water (Figure 6). Over four days, minimal water and almost no SPO was lost and approximately 62 ml of oxygen was produced, resulting in a 73.3% yield of oxygen. More trials need to be conducted, but this trial clearly shows a multi layered patch can house a chemical reaction that can produce oxygen levels high enough to diffuse and treat sub dermal pressure ulcers.

Impact

Developing a skin patch that is able to house an oxygen producing chemical reaction and diffuse sufficient levels oxygen to sub dermal layers of the skin via an attachment of microneedles can revolutionize the treatment of sub-dermal pressure ulcers. We were able to develop an efficient alternative to other sub dermal pressure ulcer treatments in today's industry.

Future plans

One main objective for the future is to fully develop this patch beyond a prototype. There are several points that need to be addressed to get to this point. One of the main ones is to fine tune the rate of oxygen production so that it reflects the rate due to body temperature. Testing the patch at physiological temperature of 37^{o}C may cause problems due to the fact that gelatin has a melting point of 35^{o}C. This could alter oxygen production levels as well as the rate of oxygen production since oxygen may get caught in the gelatinous matrix. A possible solution to the issue is to use a layer of keratin that has a melting point of 110^{o}C.

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Appendix

Table 1: Data collected from experimental trials using CPO and water in the inverted test tube apparatus.

Chemical	SPO	Trial 1	moles	
mass	0.174	grams	0.002230769	
Date	9/15/14	Estiated O2	0.001115385	
Time (hrs)	Volume (ml)	net volume(ml)	moles o2	exp/est
0	70	0	0	0
1	70	0	0	0
2	70	0	0	0
3	70	0	0	0
4	70	0	0	0
5	70	0	0	0
23	72	2	8.2984E-05	0.07439948
27.5	72	2	8.2984E-05	0.07439948
45.5	73	3	0.000124476	0.11159922
48.5	74	4	0.000165968	0.14879896
168	74	4	0.000165968	0.14879896

Chemical	SPO	Trial 2	moles	
mass	0.539	grams	0.00691026	
Date	9/15/14	Estiated O2	0.00345513	
Time (hrs)	Volume (ml)	net volume(r	moles o2	exp/est
0	34	0	0	0.0
1	35	1	4.1492E-05	0.0
2	35	1	4.1492E-05	0.0
4	35	1	4.1492E-05	0.0
5	36	2	8.2984E-05	0.0
6	36	2	8.2984E-05	0.0
25	66	32	0.00132774	0.4
27.5	66	32	0.00132774	0.4
46	77	43	0.00178416	0.5
48	78	44	0.00182565	0.5
50	79	45	0.00186714	0.5
52.5	80	46	0.00190863	0.6
53.5	81	47	0.00195012	0.6
54.5	81	47	0.00195012	0.6
56	82	48	0.00199162	0.6
58	83	49	0.00203311	0.6
60	84	50	0.0020746	0.6
70.5	88	54	0.00224057	0.6
74	89	55	0.00228206	0.7
77	90	56	0.00232355	0.7
94	94	60	0.00248952	0.7
168	102	68	0.00282146	0.8

Chemical	SPO	Trial 3	moles	
mass	0.537	grams	0.00688462	
Date	9/22/14	Estiated O2	0.00344231	
Time (hrs)	Volume (ml)	net volume(r	moles o2	exp/est
0	68	0	0	0.0
1.5	69	1	4.1492E-05	0.0
4	70	2	8.2984E-05	0.0
5	70	2	8.2984E-05	0.0
6	72	4	0.00016597	0.0
24.5	96	28	0.00116178	0.3
25.5	98	30	0.00124476	0.4
27	100	32	0.00132774	0.4
30	104	36	0.00149371	0.4
42.5	118	50	0.0020746	0.6
49.5	120	52	0.00215758	0.6
50	120	52	0.00215758	0.6
52	120	52	0.00215758	0.6
63	122	54	0.00224057	0.7
67	124	56	0.00232355	0.7
85	124	56	0.00232355	0.7
87	124	56	0.00232355	0.7
113	124	56	0.00232355	0.7
168	124	56	0.00232355	0.7

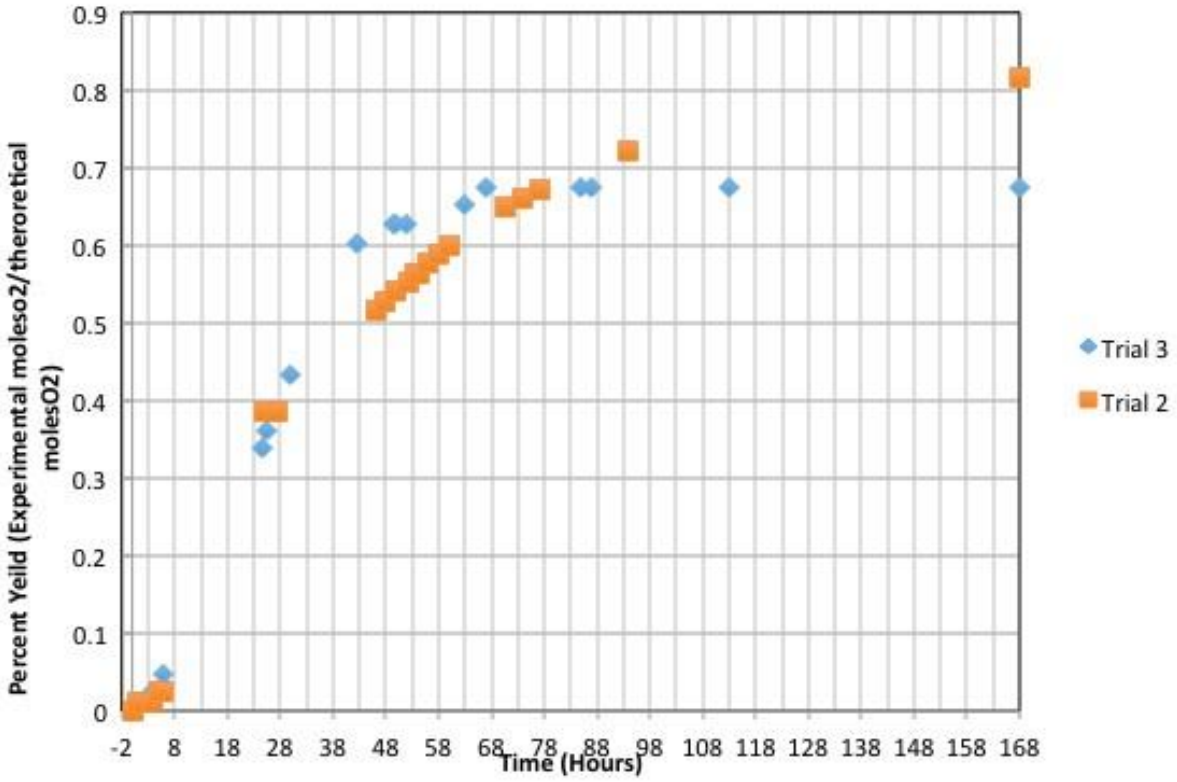

Figure 3: Graphical representation of experimentally obtained moles of oxygen divided by the estimated moles by time employing the SPO and water reaction in the inverted test tube apparatus.

Table 2. Data collected from SPO trials taking place in $2cm^2$ surface area of patch

	control (0.000g SPO)	**0.5743g SPO**
Hours	Oxygen Produced (ml)	
0	0	0
4	0	3
14	0	8
19	0	12
21	0	19
35	0	24
47	0	38
57	0	52
69	0	62
75	0	62
85	0	62
96	0	62

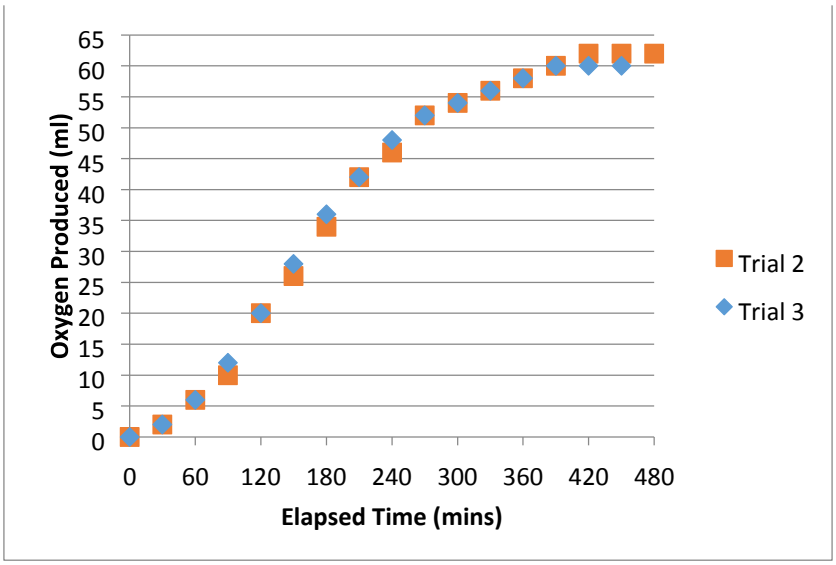

Figure 5. Graphical representation of oxygen produced over time by the SPO and water reaction in the test tube apparatus at 37°C

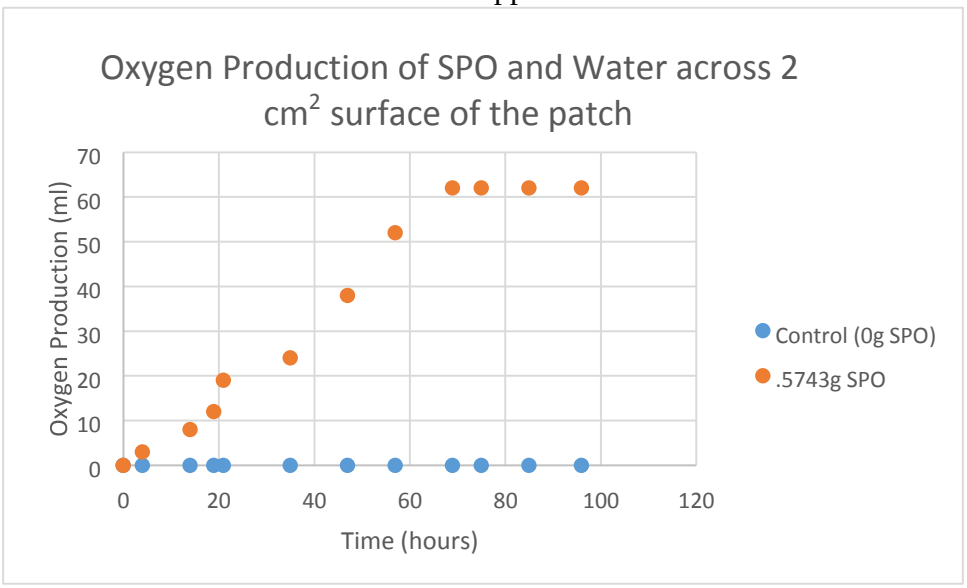

Figure 6: Graphical representation of oxygen produced with 2ml of water and .5743g of SPO on $2cm^2$ surface area of patch prototype