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Research Article

APPLICATION OF 3D PRINTING IN ELECTRO INDUCED DRUG DELIVERY BASED ON WOUND TEMPERATURE

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ABSTRACT

An attempt is made through this work to device and develop a new type of wound dressing with drug delivery system. The developed drug delivery system for wound care and management is designed and fabricated, where the management of the drug delivery system is by the wound temperature of the human body. There are three main parts to the device namely; temperature transistor sensor, Arduino Nano processor, and battery. The device is placed on the skin of the patients which holds the drug in the medical chamber. The temperature of the wound is raised above the normal the device delivers a responsive drug delivered to the chronic wound and aid in appropriate healing of the wound based on the patients metabolic rate, which is a function of body temperature.

Keyword: Drug Delivery, Wound Temperature, Additive Manufacturing, 3d Printing, Electro induced drug delivery

INTRODUCTION

Smart drug delivery carriers which are placed over the body release the right amount of drug at right place and right time to enable the delivery of the drug. There is a great need for newer method of drug delivery, this is particularly for wound dressing for prolong or chronic wounds. In the health care practices, the furthermost predominant activity is wound care[1]. The wound is classified into acute and chronic wound which is shown in figure 1.Briefing about wounds pointed it out the difference based on wound healing. Acute wounds are moved through the stages of healing within the expected timeframe[2]. Discussing about chronic wounds, stated that these does not follow the healing phases subsequent in a prolonged recovery[3]. Meanwhile, a chronic wound is categorized as the one that fails to heal within four weeks, and which shows no sign of improvement within eight weeks though the cause may vary. Wound care and healing has common behaviors that carryout for all care and treatments [4].

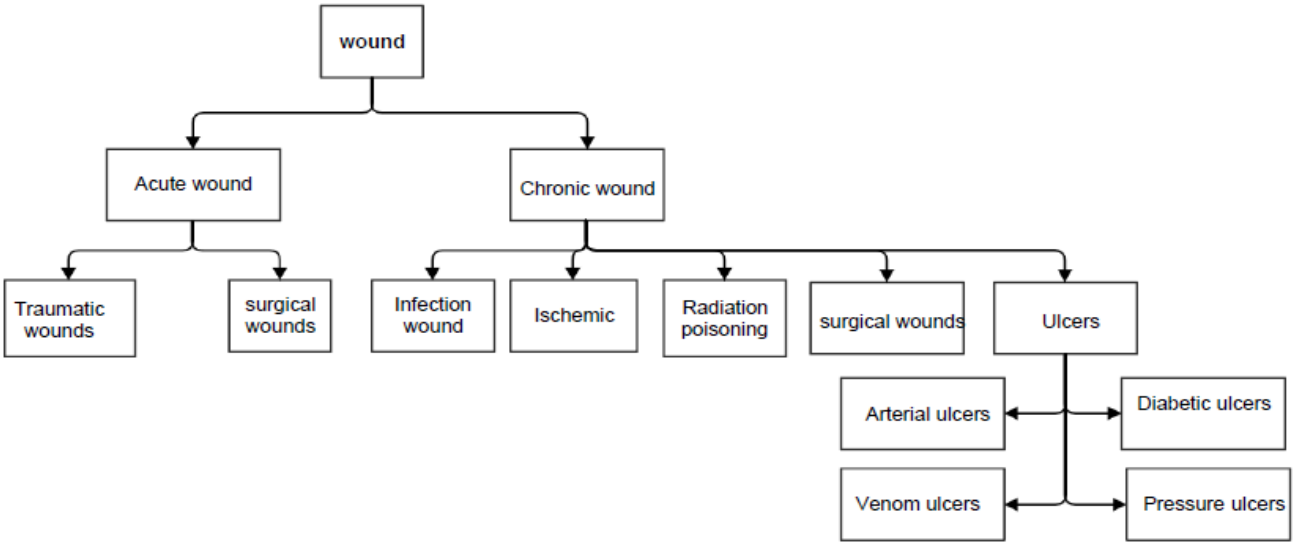

Figure: 1 Types of wound

Additive Manufacturing (AM) is a layer by layer manufacturing and also known as 3D printing, is currently being stimulated as the trigger of a new industrial revolution. These technologies are used to make customized products without any tool or mold[5]. Moreover, AM enables the production of complex and integrated functional designs in one-step process, thereby also potentially reducing the need for assembly work. By using this technology of direct digital manufacturing processes, the transfer of direct 3D data in to a physical product is possible. Furthermore, the AM can also manufacture functionally integrated parts in a single fabrication step. The core benefit from this technology is applied in aerospace, automobile and medical sectors[6].

The traditional wound dressing is used for treating chronic wound by therapies that consist of several dressing changes with repeated application of wound healing medicines. The result of this new method wound dressing is designed and fabricated in such that it would deliver a responsive drug to the wound. Here in this paper, it is proposed to use the wound properties namely; temperature as a driving parameter to allow the responsive drug delivery towards treating the chronic wound. This dressing is manufactured with help of AM based upon the wound properties and patient criteria.

Literature Review

Currently, wound dressing which are used for the drug delivery are cotton gauze, cotton, adhesive bandage, these dressings are manufactured in bulk and stored in the hospital as a stock[7]. These readily available wound dressings are directly used for the patients at the hospitals with specific wound care. This traditional wound dressings are directly persuaded in wound with the bulk of medicines, which tends to affect the healing time and produces side effect[8]. For this reason a modern health care wound management system with advanced drug delivery are found to be a requirement.

The advanced drug delivery type involves three types namely; thermo responsive, electro responsive and magnetic responsive. Thermo responsive drug delivery system utilizes temperature sensitive hydrogels that changes the temperature triggers the drug in response to temperature[9]. Electro responsive drug delivery delivers drug by external stimulate poly electrolyte which contains relatively high concentrated ionization. This drug delivery system is applied by means of biomimetic actuators[10]. The magnetic responsive drug delivery system is based on magnet targeted to wound site that pulls the drug towards the magnet field and it can applied to the cancer treatment[11].

The electro responsive drug delivery is that the medicine is placed between the electrodes; the drug is deswelled by applying current[10] . The research on smart drug delivery system for the chronic wounds showed it by using stimulated responsive polymers[11]. The method can be stimulated by various environments alike; temperature, electric, magnetic fields.

These advanced drug delivery methods effectively deliver drug through pores, these pores become the responsive drug delivery system. Research showed that additive manufacturing or 3D printing used for the drug delivery in the micron scale applied and is expected to make possible for the fabrication of controllable drug-delivery[6]. conducted study on 3D printing methods that are used to scan the patient's broken bone and build the physical model with parameters like density, pore interconnectivity; pore size and shape, it results with high mechanical strength and reduced inflammation[12].

Investigation shows that 3D porous chitosal scaffolds was fabricated with various pores design and mechanical properties of various anisotropic with 50µm diameter[1]. A study conducted by[14]expressed a wound dressing is used for healing by using series of micro porous silicon rubber membrane with different pore sizes. Study shows the wound healing is done by using pores to control the absorbency of the wound dressing with chemical composition CNF[15].

Another parameter for the wound is temperature for wound healing. The study by revealed that for a normal cell growth wound needs a normal temperature 37°[7]. Meanwhile the study conducted by shows that the patients with diabetic foot ulcer shows temperature of the wound is greater than 2°Celsius compared with their normal skin temperature[16]. Concluded that, chronic venom diseases are measured through infrared temperature device and it shown that for patients above 70 age group had temperature which is nearly 1.2°C above the normal wound temperature[17].

From the literature review, it was observed that pores, temperature and type of drug delivery are more important for healing chronic wound, which needs continuous drug delivery to increase the healing of the wound. In order to achieve an effective drug delivery system a suitably manufacturing technology have to identified Additive manufacturing technology is succeeded in various fields by verification of design, and functional test. Recently, investigators studied to fabricate functional parts that can be customized incorporate in this drug delivery system.

DESIGN AND DEVELOPMENT

Understanding the need for a suitable drug delivery system, this section details about a novel design involved in drug delivery system for treatment of chronic wounds. The drug delivery wound dressing method reported here utilizes the temperature of the wound from the human body to sense through the sensor and supplies drug through the pores to the wound. The wound dressing model is designed in a 3D modelling software "SOLIDWORKS" in which dimensions to the model and some of the critical parts are designed for 300 microns. When it comes to product development the main material used for the model is Vero clear. Figure 2 shows the design of the model considering the design specification, and dimension of the product.

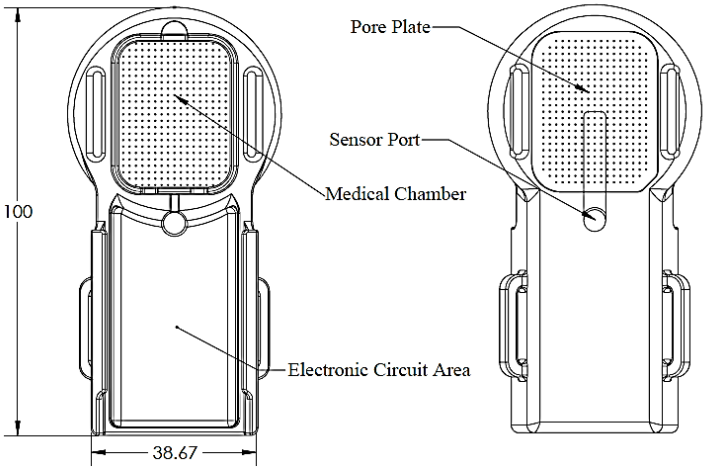

Figure 2: Design of 3D printed wound dressing model

In this wound dressing method, thermistor are used, where, resistance varies with temperature. The temperature response will be varying and the thermistor typically supports higher precision within a limited temperature range [usually −90 °C to 130 °C]. Assuming, that the relationship between resistance and temperature is linear, then:

$$\Delta R = k\Delta T$$

Where,
ΔR = change in resistance
ΔT = change in temperature
k = first-order temperature coefficient of resistance

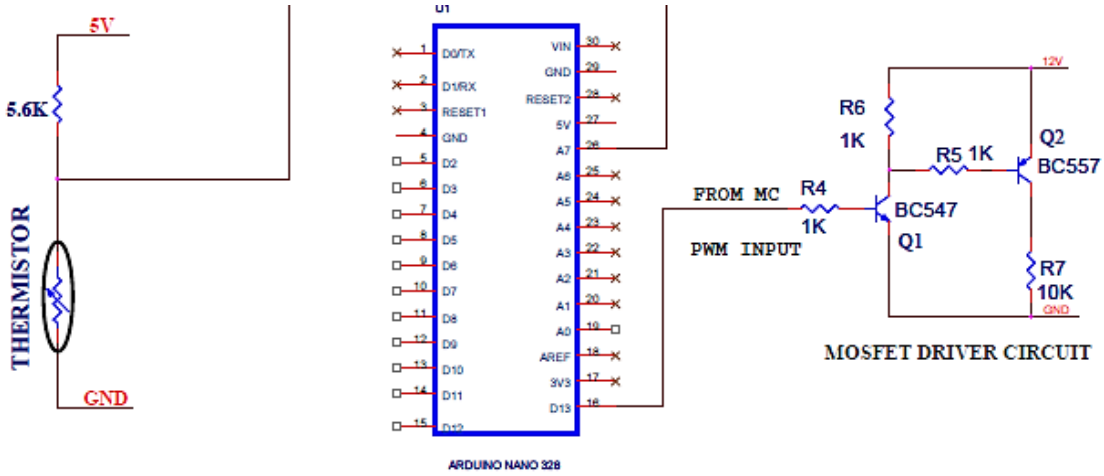

Figure: 3 Schematic diagram of temperature control circuit for model wound dressing

Arduino nano is a processor board based on ATmega168 (Arduino Nano 2.x). Figure 3 shows schematic diagram of a circuit for the model. This logic is used to control the temperature in the wound which indicate the inflammatory due to microbes. In this case, temperature change will occur in the wound. In the circuit, the temperature change will be measured by the thermistor and the value is given to the microcontroller. The microcontroller will compare the thermistor temperature value with the normal temperature value of the wound. If the thermistor temperature is higher, then the microcontroller will actuate model drug to inject. The model will deliver the drug containing anti-inflammatory medicine for the chronic wound through pores. If the usage of model drug has any reduction in the temperature through the inducing agents, then the drug delivery will immediately be cut-off.

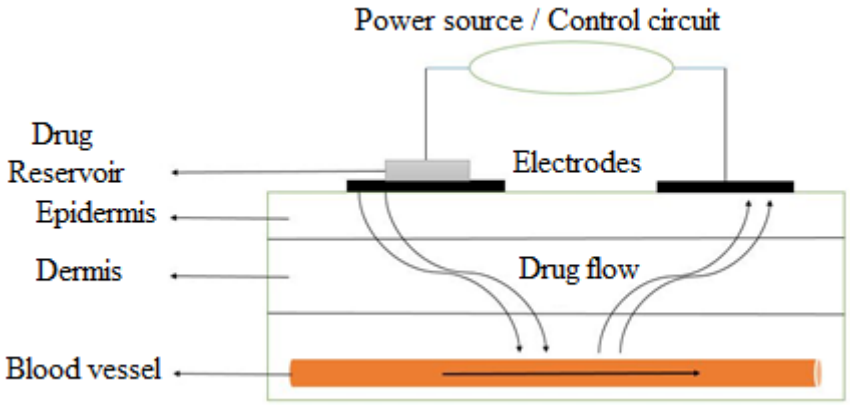

Figure 4 Model electro induced drug delivery

The model shown in figure 4 above is the electro induced drug delivery system, which is implemented by use of a drug reservoir in the main component with a perforated base facing towards the wound through which the drug diffuses. Here a flow inducing electrode is placed in the 3D printed wound dressing and on the bottom of the part which is in contact with skin. The electrode which contacts skin acts as the neutral electrode which draws the drug from the reservoir through electro induced diffusion. The control circuit with the battery pack is placed inside the compartment in the dressing, and the pathway for the circuit conduits is also provided.

FABRICATION AND TESTING

The wound dressing model is fabricated and analyzed for various pore size and for varied voltage ranges, as described in the table 1. Drug delivery system for wound care and management is fabricated with temperature sensor and control board. This device is designed with different pores to prove the model can be operated in a wider temperature range, this is with the aid of a temperature sensor and control units. The temperature is the main parameter which is used to examine the device. Then model experiment is conducted with different pores of the wound dressing and tested with the model drug.

Table: 1 Model drug delivery with different pores

Pores in mm	0.3	0.35	0.45	0.5	1
Drug delivered point	125 mv	136 mv	158 mv	22 mv	13 mv

Figure 2, describes the basic test that is carried out to check for functionality of the developed device. Device consists of a thermistor which measures the temperature which is heated at the bottom of drug delivery system for wound care and management device. As temperature increases above the body temperature, a certain quantity of voltage is released by the control unit. Voltage released with respect to the temperature raise is measured in a digital multimeter which corresponds to the voltage value. An approximated value of 200mV is released for every seconds of a temperature raise.

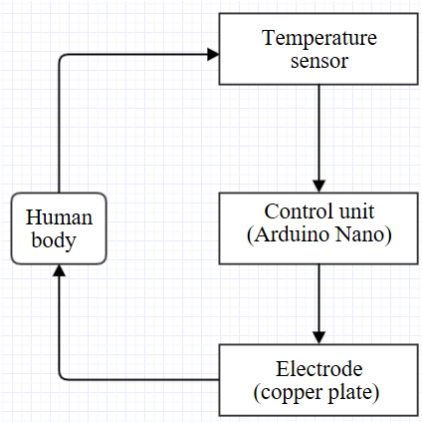

Figure 4 Model of the temperature based drug delivery

EXPERIMENTAL RESULT

Illustrates the design model of wound dressing device that is carried out using SolidWorks modeling. The model is designed based on wound properties and pore size. Proceeding further is to develop the model by using an Additive Manufacturing (AM) technology. Selected AM will be based on complex design and the availability of the machine. Polyjet printing based AM technology is selected to develop the designed wound dressing model. The component of the wound dressing model is printed individually and assembled and was found out to be a functional working prototype.

In order to check for the functional working, control circuits as shown in figure 3 is assembled together with the requirements for producing electric induced current. The control circuits are set along with the pore size and with diffusion voltage setup, which controls the rate of diffusion and the amount of drugs to be delivered. The pore size can be configured depending on the age, medical condition, drug composition and drug concentration. The whole set is tested for working condition by passing electric current. Continuous monitoring of the test is carried out and it was identified that below the temperature of 37°C there is no voltage release and when the temperature rises above 37°C, 200 mV of voltage is released and as a result it leads to effective drug delivery to the wounds.

The test carried out gave satisfactory results and thereby prototype is electro induced with functionally working model for effective drug delivery that can be used for wound care management.

CONCLUSION

In conclusion, a drug delivery model was made powered by temperature of the wound in the human body. The device can be used for delivery of drug to chronic wound. These models were created with a material Vero clear, transistor sensor, Arduino Nano processor, and battery for temperature transducer .The experimental verification and result data analysis have been carried out on a model drug to act as the input data to the control circuit for induced drug delivery. Furthermore, designing of the actual product is carried out after considering the customized body fit product complexity and the future variation and development that can be done in the product. The designed component is used to create a functional prototype of the product.

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