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# *In vitro* study and characterization of cotton fabric PLA composite as a slow antibiotic delivery device for biomedical applications

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ABSTRACT

Wound treatment remains a challenge to many clinicians because of the complexities of the wound healing process. The choice of dressing depends on a number of factors such as wound type, location, and injury extension, as well as the patient's health status. All of these factors increase the complexity and difficulty of utilizing a single type of dressing. The focus of this study was centered on developing a woven cotton fabric polylactic acid (PLA) composite as a low drug delivery device for biomedical applications. A hand weaving method was employed in developing the fabric to control its porosity. Fabrics with three different pore sizes 0.5 mm, 1.0 mm, and 1.5 mm were developed with a natural cotton yarn of 36 Tex and the resulting fabrics were used for composite development. Three different PLA concentrations 0.01 g/mL, 0.03 g/mL, and 0.06 g/mL were used to study the effects of the PLA/fabric ratio on the mechanical properties. The antibiotic amoxicillin was used in the study. This drug release study was monitored by UV-Vis spectrophotometry, while mechanical testing was performed with the Instron 5566 universal materials testing system. The results suggested that drug-loading capacity increases with decreasing fabric porosity. The release profiles from these devices followed a two-stage pattern, and the release mechanism appears to be a mixed transport system. This includes diffusion and possibly super case II kinetics, as well as a release due to damage to the composite surface through dissolution. The amount of released concentration exceeded the minimum inhibitory concentration of amoxicillin against *Staphylococcus aureus*. Degradation of the fabric composites is suggested as influencing the drug release rate. The water absorption ability of composites decreases with increasing PLA concentrations. The mechanical properties of composites were consistent with the fabric's density and weight. To design the ideal wound dressing materials, consideration of all these aforementioned properties are required in order to incorporate the desired functions to support tissue regeneration and healing while limiting bacterial infections. The findings from this research suggest that the developed devices could be used for wound dressing applications on sites where a water-resistant dressing is required, thus aiding in the prevention of bacterial contamination of the primary dressing.

## 1. Introduction

Skin serves primarily as the essential barrier protecting organisms from their environment [1,2] and plays a role in thermoregulation. Skin is composed of three layers: epidermis, dermis, and hypodermis. The dermis layer provides support and nutrition to the epidermis. A wounded epidermis can stimulate self-regeneration and healing; however, this process is slow and can be affected by age and health status. Several strategies are available for the treatment of skin damage such as autografts, allografts, wound dressing, and tissue engineering substitutes [1]. In particular, a deeper dermal wound of more than 4 cm in diameter requires a graft for treatment. It is globally estimated that burns cause 265,000 deaths every year. In India, over 1,000,000 people are moderately or severely burnt every year. In 2016, over 486,000 burn injuries occurred and received medical treatment in the United States, with approximately 40,000 requiring hospitalization. Direct costs for the care of children with burns in the United States exceeded US$211 million. In Norway, costs for hospital burns management in 2007 reportedly exceeded €10.5 million [3]. Wound healing normally undergoes three phases: inflammatory, proliferation, and maturation. During these phases, damaged tissues are restored through coordinated signaling that constitutes the cutaneous healing response.

Despite the considerable progress in recent years, wound healing remains a challenge for many clinicians and researchers regardless of their professional discipline or experience in the development of novel and efficient wound dressings. Dressing choice should be based on the dressing's ability to provide or maintain a moist environment, enhance epidermal migration, promote angiogenesis and connective tissue

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synthesis, as well as allow gas exchanges between the wounded tissue and the environment. It must also maintain appropriate tissue temperature to improve the blood flow to the wound bed and enhance epidermal migration. Furthermore, it must provide protection against bacterial infection and debridement action to enhance leukocytes' migration. The dressing should be non-adherent to the wound for ease of removal after healing; it must also be sterile, non-toxic, and non-allergic [4]. However, it is difficult to find dressing materials that fulfill all these requirements, and the choice of the correct dressing depends on the wound type and stage, injury extension, patient condition, and involved tissues [5].

Traditional wound dressing products include gauze, honey pastes, plant fibers, animal fats, plasters, bandages (natural or synthetic), cotton, and wool used as primary or secondary dressings for protecting a wound from environmental and bacterial contamination [4,6,7]. However, some of these dressings do not meet the requirements for rapidly healing wounds, due to wound adherence causing ischemia/necrosis and frequent changes [7]. Gauze dressings made of woven and nonwoven fibers of cotton, rayon, and polyester afford some protection against bacterial infections. However, these dressings require frequent changing to protect against the maceration of healthy tissues.

Animal model studies have shown that when a wound is kept in a moist condition, as would have resulted from the application of an occlusive film dressing, epithelialization of the wound surface occurred at a much faster rate than in a dry condition, which was then regarded as the desirable condition. Studies on human wounds confirmed that the wound healing rate increased when the wound was kept in a moist condition [8].

Due to increasing environmental awareness, biocomposites are becoming the most important material. The development of eco-friendly products made from natural resources is increasing worldwide [9]. Natural fibers such as flax, cotton, hemp, silk etc. have been used to reinforce thermoplastics due to their advantages, such as low cost, low weight, acceptable specific strength, good thermal insulation properties, biodegradability, and, most important, renewability. As such, eco-friendly composites may be used for many applications including biomedical wound dressings [10,11]. It is suggested that natural fibers suitable for wound dressing include cotton, silk, and linen [12].

There is minimal literature [13] regarding the use of cotton woven fabrics, or PLA composites, as drug delivery devices for wound dressing applications. Our study aimed at providing a novel approach towards the preparation of cost-effective slow antibiotic delivery devices as wound dressing materials. In addition, these materials have some wide range applications for cellulose polymer composites materials for future wound care applications.

## 2. Materials and methods

### 2.1. Materials

Polylactic acid (PLA) 3052D (specific gravity = 1.24, Tg = 55–60 °C, MP = 200 °C) with Mw = 75,000 (g/mol) was obtained from Nature Works LLC Australia. Chloroform with a ≥99% assay, amoxicillin (potency: ≥90 μg per mg), and sodium hypochlorite (NaOCl) were obtained from Sigma Aldrich Kenya. Chemicals for PBS were purchased from a local supplier. Cotton yarns were kindly donated by Urafiki Textile Company, Tanzania.

### 2.2. Methods

#### 2.2.1. Preparation of cotton woven fabric

Fabrics with different pore size (0.5, 1.0, and 1.5 mm) were handmade using a cotton yarn of count 38 Tex on a 30 cm by 30 cm dimensional template with equally spaced warp and weft. The reason for hand-making was to control the pore size of the fabric, which affects the drug loading and dissolution. During the weaving process, yarns were inserted in the longitudinal direction that acted as the warp yarns were followed by the yarns in the horizontal direction and served as the weft yarns. After fabrication, the pore sizes of the fabrics were corrected by hand. Three samples from each pore size were made and stored in desiccators for further use.

#### 2.2.2. Antibiotic loading into the fabric

Hand-woven cotton fabrics were cut to 6 cm × 5 cm pieces and served as drug delivery devices. They were gently washed in 2% NaOCl in order to remove any residual oils and then thoroughly rinsed with distilled water. The cleaned specimens were dried in an oven at 50 °C for 48 h before use. Drug loading was done by making three different amoxicillin concentrations (0.10, 0.08, and 0.06 mg/mL) equivalent to 10%, 20%, and 30% w/w, respectively, in deionized water, and then the samples were totally immersed in the drug solutions for 10 min. After 10 min, the samples were put on Petri dish and allowed to dry under room temperature in a fume hood for 72 h. Weights of specimens were recorded before and after loading the drug.

#### 2.2.3. Preparation of woven fabric PLA composite

The woven cotton fabric PLA composites for this drug dissolution study were prepared using a solvent casting technique described previously [14,15]. Briefly, 0.01 g/mL, 0.03 g/mL and 0.06 g/mL of PLA solution in chloroform were prepared by dissolving an appropriate amount of PLA in chloroform under magnetic stirring on a hot plate and gently heating the mixture at 50° C until the PLA dissolved completely. Then drug-loaded samples were placed in a Petri dish, and then the solution of PLA was poured over until all samples were submerged completely. The process of composite development was carefully done to ensure a uniform distribution of PLA in the woven cotton fabric. Then solvent evaporation took place under small vacuum for 72 h after which the samples were stored in a desiccator for further studies.

Composites for mechanical testing, water absorption, and degradation studies were prepared by casting 150 mL of PLA solution of 0.01 g/mL, 0.03 g/mL, and 0.06 g/mL concentration on a 30 cm × 20 cm woven cotton fabric in a plate template covered by aluminum foil. The experiments were performed using cotton fabrics with different pore sizes, as mentioned above. The weights of the samples were recorded before and after composite development. Samples for mechanical testing were cut into 10 cm × 5 cm, a total of five samples were prepared for each pore size and PLA concentration. Degradation and water absorption studies were conducted on 4 cm × 4 cm composite specimens.

#### 2.2.4. Drug dissolution and quantification study

A drug dissolution study of woven cotton fabric and PLA composites was conducted under SINK conditions in phosphate buffered saline (PBS) (0.1 M, pH 7.4) at 37 ± 0.1 °C in a temperature-controlled oil bath shaker running at constant speed of 100 rpm. The experiment was designed so that each sampling time had its own independent samples running simultaneously under the same conditions and the experiments were each terminated after sampling. This was to avoid kinetic changes if some volume was to be taken and replaced with the fresh PBS solution. All drug concentrations were determined by a Milton Roy Spectronic 21D UV-Visible Spectrophotometer (Milton Roy Company, USA) at the maximum absorbance of amoxicillin, $\lambda_{max}$ = 496 nm using procedures described in Ref. [14]. The absorbance, which corresponds to the amoxicillin concentration, was measured from the dissolution samples and used to calculate the actual drug concentration using a calibration curve prepared for each set of measurements.

*2.2.4.1. Drug release kinetics.* Drug dissolution mechanisms from the composites were studied by fitting the dissolution results to various mathematical models selected from literature based on the known properties of the composites' constituents. The model characterized diffusion, dissolution or erosion, and mix or dissolution-diffusion