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Preparation and characterization of thermosensitive artificial skin with a Sandwich structure

Ying Tu [a], Mingbing Zhou [a], Zhijun Guo [a], Yubao Li [a], Yi Hou [a], Danqing Wang [b,*], Li Zhang [a,**]

[a] Analytical & Testing Center, Research Center for Nanobiomaterials, Sichuan University, Chengdu 610064, China
[b] West China Second University Hospital, Sichuan University, Chengdu 510100, China

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ABSTRACT

A thermosensitive artificial skin composed of gelatin–chitosan (Gel–CS) scaffold as dermis and poly(N-isopropyl acrylamide) (PNIPAAm) grafted microporous polyurethane (PU) membrane as epidermis bound together by gelatin was prepared, and its morphological structure, water vapor permeability rate (WVPR) and *in vivo* biological properties were investigated. The results showed that the as-prepared artificial skin showed a "Sandwich" structure and its WVPR was 804 g/m^2 day, close to those from commercial skin dressings (426–2047 g/m^2 day). The *in vivo* tests indicated that the "Sandwich" artificial skin could effectively accelerate wound closure in a rat model with full-thickness skin loss and the epidermis could easily peel off after wound healing.

1. Introduction

As the biggest organ of body, skin loss caused by accident, trauma, war, burn and disease has become one of the most serious problems in clinic [1–3]. As we know, full-thickness skin defects in large scale cannot repair spontaneously [4,5]. By far, a variety of commercially available artificial skins have been successfully used clinically to protect the wound from bacterial infection and provide a moist and healing environment, among which, Integra™ has been used more widely [6–9]. However, the dense silicone rubber membrane in Integra™ often results in subdural effusion after implantation, inducing wound infection [10]. So the porous membranes have been tried to substitute dense silicone rubber membrane. Nevertheless, the improved artificial skin still had an obvious deficiency, that is, during the wound healing, porous membrane was difficult to separate from the surface of the newly formed tissues and caused secondary damage [11,12]. Considering this, some researchers selected a thermosensitive polymer material to compound with the temporary artificial skin epidermis, and the epidermis is easy to peel off after wound healing [13–15]. PNIPAAm is the most widely used thermosensitive polymer with a lower critical solution temperature (LCST), when the temperature is over or below the LCST, an obvious phase transformation for PNIPAAm hydrogel will occur, making the epidermis easily peel off.

Polyurethane (PU) is an excellent medical elastomer material with good mechanical strength and biocompatibility. Gel–CS scaffold resembles extracellular matrix, enhances tissue regeneration, provides nanotopographical clues for cell migration and proliferation and displays excellent biodegradability. So an artificial skin using PU-g-PNIPAAm membrane as epidermis and Gel–CS scaffold as dermis bound together by the interlayer of gelatin was prepared and characterized.

2. Experimental

Preparation of the artificial skin with "Sandwich" structure: Microporous PU membrane was fabricated according to our previous work reported in reference [16]. PU film was grafted with N-isopropyl acrylamide (NIPAAm) monomer using ultraviolet irradiation, and the product was referred as PU-g-PNIPAAm. Gel–CS scaffold was also prepared following a previously described methodology [17]. And the detailed fabrication process of the artificial skin with "Sandwich" structure is shown clearly in Fig. 1.

Characterization of the "Sandwich" artificial skin: PU-g-PNIPAAm membrane and Gel–CS scaffold as well as the as-prepared "Sandwich" artificial skin were digitally photographed, and then, gold coated samples were analyzed by means of scanning electron microscopy (SEM, Jeol JSM-6500LV, Japan).

* Corresponding author. Tel.: +86 28 85411552.
** Corresponding author. Tel.: +86 28 85411552.
E-mail addresses: danqingwang@163.com (D. Wang), zhangli9111@126.com (L. Zhang).

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PU-g-PNIPAAm membrane and the "Sandwich" artificial skin were fixed on a centrifuge tube full of distilled water and the edge was sealed well. The initial weight of the tube full of distilled water was determined and recorded as W_0, and the tube was placed in a desiccator with constant temperature (about 25 °C) and humidity. The weight of the permeable tube at time t was denoted as W_t. The slope of the curve of mass change versus time was denoted as L, which was calculated by $L = W_0 - W_t/t$. Thus the water vapor permeability rate (WVPR) was calculated according to the following formula:

$$WVTR = L/S$$

where S was the testing area (m^2).

Healthy adult SD rats (250–300 g) were obtained from the animal laboratory of Sichuan University. Prior to the test, rats were anesthetized with 3% pentobarbital sodium solution and the dorsal surface were shaved and sterilized with iodine. Then full-thickness skin defects with a surface area of $1.5 \times 1.5\ cm^2$ each were made

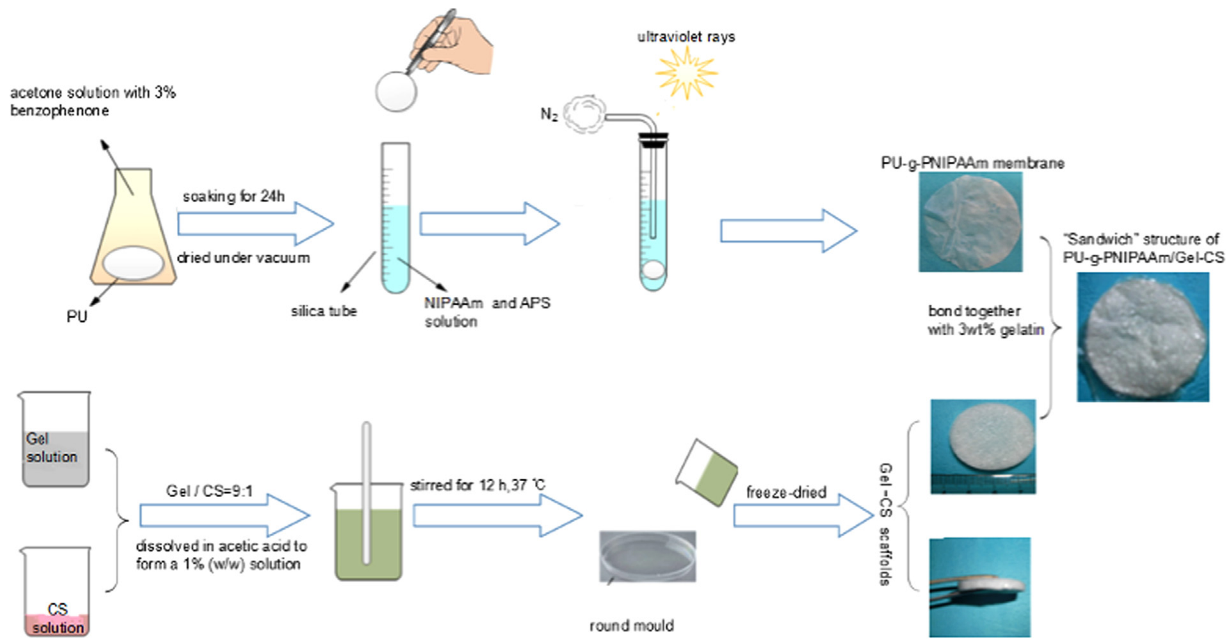

Fig. 1. The fabricating process of the "sandwich" artificial skin.

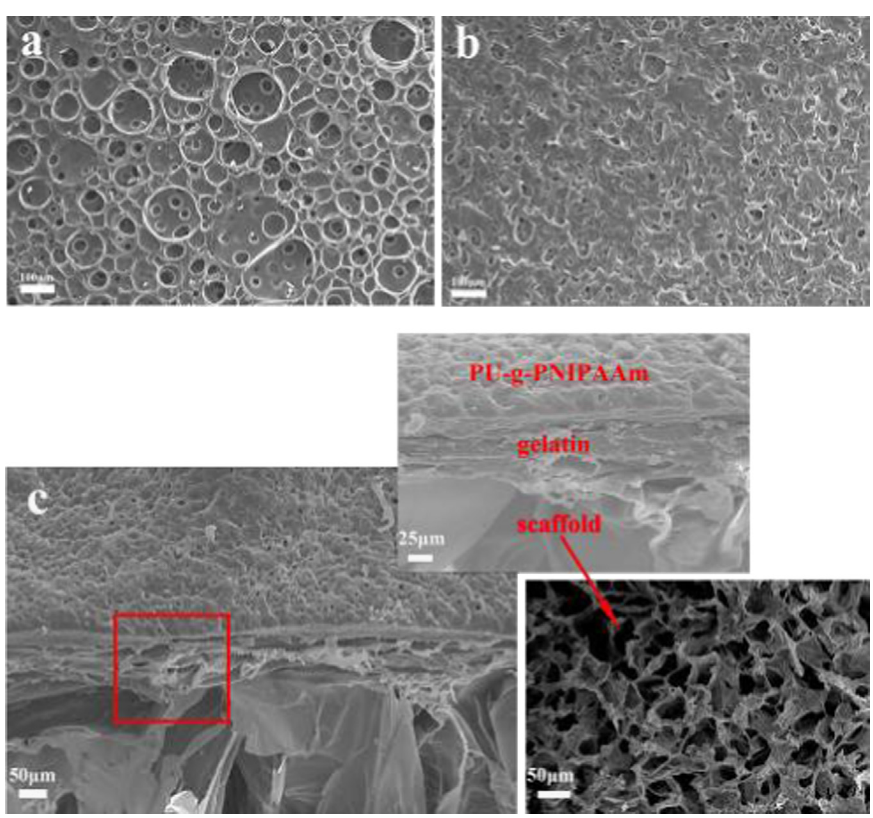

Fig. 2. SEM images of PU (a) and PU-g-PNIPAAm (b) membranes and PU-g-PNIPAAm/Gel–CS artificial skin (c).