CHAPTER 1

INTRODUCTION

1.1. Historical Background

There is an increasing rate of requirements for obtaining safer and more effective therapeutic methods for wound coverage and skin tissue repairing in a variety of clinical situations, such as the acute skin wounds, the burned wound, and the chronic skin ulcers. The split thickness skin autograft is the dominant desirable therapeutic method for coverage of excised burn wounds while the available donor sites for autografting are so limited, especially when facing patients with a very large area of the burned wound. Those wound coverages require repeated harvesting from those available donor sites, which will lead to pain and scar at those donor sites that will extend the time for skin recovery and then those patients will have to stay longer in the hospital (Huang and Fu 2011). Since the limited applications of autografts and allografts, and the tremendous need of clinical applications for wound regeneration in those patients with various wound situations, the bioengineered skin substitutes have been developed quickly and that provided new alternative methods for the clinicians to restore skin and solve a variety of skin defects (Rendon, Berson et al. 2010, Shishatskaya, Nikolaeva et al. 2016, Yang, Cho et al. 2016). The substitutes should have some fundamental properties to guarantee that they can create a proper environment for promoting the wound healing, such as having appropriate physical and mechanical properties and having a controlled degradation rate. The desirable materials of skin substitutes should fulfill the following requirements: 1) be able to maintain the local moist environment of skin, 2) be able to protect the wound from side-infection, 3) should have the ability to absorb the wound fluids and exudates, 4) be able to minimize the wound surface necrosis, 5) be able to prevent the wound d

ryness, 6) be able to stimulate the cell growth and differentiation, and 7) be elastic, non-toxic, non-antigenic, biocompatible and biodegradable (MacNeil 2007).

In terms of those characteristics, a variety of biomaterials both from the natural origin and the artificial origin have been applied to the medical applications such as the chitosan, alginate, collagen, gelatin, polyglycolic acid, polycaprolactone and polylactic acid. All those substances are currently the most used materials for tissue engineering applications since those materials have great capacity to reproduce the properties match to the native organic skin tissues.

Gelatin is derived from the hydrolysis of collagen. Gelatin acts as a very frequently-used material for producing the tissue engineering scaffolds because gelatin owns a very good dissoluble ability within the water. Good biodegradability and it is cheap for large scale production that make gelatin a good choice of biomaterials to produce of tissue engineering scaffolds. Because gelatin is produced from collagen, so it has the main peptide sequences or structures of collagen, which means that gelatin has some common features of collagen such as RGDs that could promote cell adhesion and migration. Furthermore, gelatin possesses the very excellent foaming ability, therefore it always works as a suitable colloid stabilizer and foaming agent (Santoro, Tatara et al. 2014, Shevchenko, Eeman et al. 2014). Previous study showed that photocurable hydrogel made from pure gelatin possessed ultrasoft property which induced neural differentiation in adipose derived stem cells (Kantawong, Kuboki et al. 2015). When hydroxyapatite was added to pure gelatin, the material could induce neural differentiation in hMSCs (Kantawong, Tanum et al. 2016). If gelatin is applied alone as the material of scaffold, it would not be able to obtain the scaffolds that can provide enough mechanical and physical properties for skin regeneration. Thus, combination of gelatin and chitosan with a proper ratio was developed and successfully applied in biomedical fields (Parvez, Rahman et al. 2012).

Polyvinyl alcohol (PVA) is one of the most frequently used material and also the oldest artificial polymer hydrogels (Vashisth, Nikhil et al. 2016). The PVA has a good biocompatibility and it has been proven in many advanced biomedical applications,

such as the wound dressing (Ahmed, Mandal et al. 2017, Saeed, Mirzadeh et al. 2017), the drug delivery systems (Tavakoli and Tang 2017), and the contact lens production (Kita, Ogura et al. 1990). However, the elasticity of PVA hydrogel is not sufficient to match native skin elasticity since the PVA always acts as a stiff membrane and has limited hydrophilicity characteristics that limits its functions when applying it alone as a wound dressing polymeric material (Kamoun, Chen et al. 2015, Kamoun, Kenawy et al. 2017).

The chemical name of the chitosan is (1-4)-linked-2-amino-2-deoxy-b-glucan (Suh and Matthew 2000, Croisier and Jerome 2013). Chitosan is a by-product of N-deacetylation of chitin. The chitosan plays as an essential constituent of crab and shrimp shells, and cuticles of insects (Bano, Ghauri et al. 2014, Figueiredo, Moura et al. 2015) which has an excellent biocompatibility and a very good wound healing capability and antimicrobial activity (Goy, Morais et al. 2016). The chitosan can form membranes after mixing with a proper amount of cross-linker agent. These membranes present the three-dimensional networks, which have the good ability to absorb and retain a huge amount of water while being able to maintain their structures. In addition, the chitosan membranes have been widely used in the field of medicine (such as the tissue engineering, burns dressing materials and controller of drug release systems) and packaging material for food (Baldino, Cardea et al. 2014).

Since a single material or polymer is not able to create a proper environment for applications of skin regeneration, to obtain the better potential materials for using in clinical skin substitutes, this study had fabricated a composited scaffold by blending the gelatin, polyvinyl alcohol and chitosan together with a proper ratio. The blended scaffolds were tested to see if they can overcome the weakness of a single material, and if they own the super-duper properties for wound healing which could provide the significant information for further studies.

1.2. Purpose of study

1.2.1. To study and fabricate Gelatin-PVA- Chitosan scaffold as a promising material for wound skin regeneration.

1.2.2. To study the physical and mechanical properties of Gelatin-PVA-Chitosan scaffold in a variety of fabrication methods.

1.2.3. To study the degradation rate, porosity and water capacity of the scaffolds.

1.2.4. To study cell viability and mRNA relative gene expression by using the blended scaffolds.

1.3. Research Scope

1.3.1. Fabricated blended scaffolds by blending Gelatin, PVA and Chitosan together with variety and different ratios.

1.3.2. Detect the physical properties of the specimens that included pore size, surface morphology and microstructure.

1.3.3. Measure the porosity of the scaffolds.

1.3.4. Measure the swelling capacity.

1.3.5. Test the biodegradation rate.

1.3.6. Analyze the bioactivity of the scaffolds in vitro experiment.

1.4. Education Advantages

The highlighted advantage or significance of this research is to reveal the developing potential of Gelatin-PVA- Chitosan scaffold for skin wound regeneration. This research focuses on improving the scaffolds' characterization method and the fabrication processes of scaffolds by using the more complicated method and more suitable materials which should give them both more accurate and valued results. According to this point, the improvement which may promote the application of biomaterial.

In terms of academic benefit, the advantage of this research is the providing of the significant information for the further studies. If this knowledge can be utilized in the future, then more opportunities will be given to patients because of its valuable information.