CHAPTER 1

Introduction

1.1 Historical background

Bleeding in the procedure is a clinical concern. Uncontrolled hemorrhage is an important problem in operation. During surgery, blood vessels are ruptured, and bleeding complication could lead to loss of blood volume and death [1,2,3,4]. Management of rapid clotting is a primary concern in the procedure [5,6]. Traditionally, gauze compression is commonly used to control hemorrhage in the site but it is not effective to activate coagulation and stabilize the clot while the prolonged pressure at the bleeding site may injure nerves or cell tissue [7,8]. Moreover, as gauze products has the risk of foreign-body reactions, inflammation because they do not have biocompatibility, and biodegradation properties, it is preferrable to remove it from the surgical site [9]. In the last few years, the hemostatic agent plays an important role as the most effective method to stop bleeding by providing a clot formation [5,9,10].

Several hemostatic agents with high effectiveness have been developed to control bleeding at a rapid rate [5,7]. The several commercial hemostatic agents was expensive [6]. Recently, health science researchers were interested in natural materials that are excellent in medical application. Biomaterials such as gelatin, rice starch, and chitosan are widely used in medical application. Several previous studies presented effective hemostatic abilities of these biomaterials [5,9,11]. According to research by the Science and Technology Research Institute, Chiang Mai University, the hemostatic materials should quickly stop bleeding, effectively absorb blood, can be degraded in the body within the specific period, and have no side effects [12]. For example, gelatin (Gel) is a widely used commercial hemostatic agent because it is a fast biodegradable material [5,13]. It easy to prepare from pork skin or bovine, and that is in the natural polyanion category [7,9,14]. In addition, Gel is composed of collagen and an amine group, in

which the protein chains have immobilized the water by gelatinization. Furthermore, Gel hemostatic agent exhibited early physical activation of hemostasis mechanism with hydrolysis properties, rapid swelling by protein chain increase absorbed a large amount of fluid or blood plasma serum, combined with thrombin, and released clot factors at the injury site, and this mechanism can lead to high rates of blood clotting and instantly stop bleeding [9,15]. Meanwhile, some previous study presented the good performance of rice starch (RS) in absorption. Accordingly, starch granule has a gelatinization property, the RS hemostatic agent provided high water absorption, and good biodegradability. The rice starch is a polysaccharide polymer with carbohydrate composition [16,17]. It is easy to find in Thailand, and low cost [18]. At the same time, chitosan has been widely studying in many applications. It comprises a linear polysaccharide with amine groups [1,19]. Chitosan (CS) is a natural polymer that can be used as a hemostatic agent [1,11,19]. The previous study presented that CS has hemostatic effect by electrostatic forces. Due to its positive charges an amino group of CS that can interact with the negative charges on red blood cells membranes [19,20,21]. This mechanism accelerates platelet adhesion and red blood cells (RBCs) aggregation leading to rapid clotting [20]. In the meantime, it forms a hydrophilic material due to the effect from hydrogen bonding, and covalent interaction absorbs blood serum protein. Furthermore, CS has excellent biological properties. For instance, biocompatibility, non-toxicity, biodegradability, oxygen barrier, antimicrobial activity, and blood coagulation [22]. Therefore, the mixing of CS, Gel, and RS may achieve effective blood absorption properties. Furthermore, the above-mentioned materials are local materials with low market value. Thus, the fabrication of these materials to be medical materials will be a method to value-add.

Currently, plasma jet technology has been introduced and implemented as a materials surface modification approach [23,24]. Atmospheric pressure plasma jet (APPJ) can enhance the wettability of materials surface, and without materials structure interruption [24,25]. Furthermore, the Ar/O_2 gas plasma leads to an etching process which decreases the surface tension and increase the surface roughness. This effect increases the hydrophilicity and absorption properties of materials [26,27,28]. Also, the combination of CS, Gel and, RS will be fabricated in various ratios to investigate the

most absorbable one. The most effective ratio will be treated by APPJ and differences will be investigated.

1.2 Research objectives

1.2.1 To analyze the physical properties and biological properties of naturally – derived hemostatic agent.

1.2.2 To investigate the atmospheric pressure plasma jet treatment condition on hemostatic agent properties.

1.2.3 To compare the properties between developing naturally – derived hemostatic agent between with and without atmospheric pressure plasma jet treatment.

1.3 Research scopes

1.3.1 Composition and mixing ratio of the naturally – derived hemostatic agent is based on the previous study (chitosan/gelatin/rice starch).

1.3.2 Variation of atmospheric pressure plasma jet condition is based on power, oxygen flow rate, and treatment time.

1.3.3 Physical properties of naturally – derived hemostatic agent will be studied based on the determination of porosity, the equilibrium swelling ratio testing, blood absorption testing, maximum volume of blood absorption, and clotting ability by hemoglobin leak testing.

1.3.4 Biological properties of naturally – derived hemostatic agent will be studied based on biodegradation by lysozyme, cell culture of fibroblast, biocompatibility testing and cytotoxicity by MTT assay.

1.4 Educational advantages

1.4.1 Achieve the physical properties and biological properties of naturally – derived hemostatic agent.

1.4.2 Obtain relationship between atmospheric pressure plasma jet conditions and properties of naturally – derived hemostatic agent.

1.4.3 Achieve the properties of naturally – derived hemostatic agent between with and without atmospheric pressure plasma jet treatment.