



The Fibroblast Cell Numbers After Tooth Extraction by Topical Application of Egg White Gel Toward Iod Glycerin

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Abstract. Background: The results of the Indonesian Basic Health Research in 2018 stated that the index for tooth extraction reached 7.9%, higher than treatments with fillings (4.3%) and scaling (1.4%). Actions resulting from tooth extraction that are slow to heal can cause complaints including pain, swelling, bleeding, and even infection, so proper post-extraction management is needed to reduce the possibility of complications. The drug that is often used for wound healing is glycerin iodine, but iodine itself has irritating and toxic properties if it enters the blood vessels, so glycerin iodine needs to be given another alternative as an antiseptic or healing agent after tooth extraction. **Objectives:** This review aimed to determine the bioactive substances and the effect of Gallus domesticus egg white gel in increasing the number of fibroblast cells in the wound healing process after tooth extraction through a literature study from researchers which was used as a reference for making this literature review. **Method:** Data were obtained by data collection methods related to the study being studied and analyzed descriptively. **Results:** Several literatures conclude about bioactive substances and the effect of Gallus domesticus egg white gel in increasing fibroblast cells. These literatures discuss the effect of using egg white gel in the wound healing process that can stimulate fibroblast cells, antiviral, antibacterial, and growth factors. **Implications:** This review is expected to provide information in the health sector, especially in the oral cavity about the potential of Gallus domesticus egg white gel as a traditional medicine for wound healing which is relatively inexpensive, easy to obtain and practical.

Keywords: Fibroblasts · *Gallus domesticus* egg white · Glycerin iodine · Wound healing · Tooth extraction

1 Introduction

Tooth extraction is the removal of a tooth from its socket as a last resort treatment if it has been badly damaged and cannot be preserved [1]. The results of the 2018 Basic Health Research (RISKESDAS) stated that in Indonesia the index for tooth extraction reached 7.9%, higher than treatment with fillings (4.3%) and scaling (1.4%) [2].

Actions resulting from slow healing tooth extraction can cause complaints including pain, swelling, bleeding, impaired masticatory function, impaired speech function and even infection, so proper post-extraction management is needed to reduce the possibility of complications and accelerate post-extraction wound healing [3].

The wound healing process can be divided into three main phases including the inflammatory phase, the proliferative phase, and the maturation or remodeling phase [4]. Fibroblasts are key in the proliferative phase of wound healing, such as destroying fibrin clots, forming type III collagen, elastin fibers, glycosaminoglycans and proteoglycans and can be used as an indicator of accelerating the wound healing process [5].

The proliferation of fibroblasts at the wound healing stage may indicate a fast healing mechanism [6]. Wound healing is influenced by many factors including the type of medication used. The drug that is often used is glycerin iodine. Iodine itself has irritating and toxic properties if it enters the blood vessels, when used in high concentrations it can inhibit the wound granulation process, so glycerin iodine needs to be given another alternative as an antiseptic or healing agent after tooth extraction [7]. Researchers intended to use glycerin iodine as a positive control because this drug is often used daily in dental practice.

Natural ingredients as a source of active substances that can be used to accelerate wound healing, one of which is *Gallus domesticus* egg white. Treatment with *Gallus domesticus* egg white needs to be formulated in gel preparations to increase comfort in use and cover the distinctive odor of egg whites, besides that the drug applied topically in gel preparations is also more optimal because it does not experience first-pass metabolism in the liver, so researchers use a gel base this as a negative control [13].

This review aimed to determine the bioactive substances and the effect of *Gallus domesticus* egg white gel in increasing the number of fibroblast cells in the wound healing process after tooth extraction through a literature study from researchers which was used as a reference for making this literature review.

2 Method

The materials needed in the literature review research are literature related to *Gallus domesticus* egg white gel, tooth extraction, wound healing, and fibroblast cells. Tools used in searching for literature include laptops and search engines, including Google Scholar, Scencedirect, and Pubmed. Additional literature was taken from the bibliography of all relevant articles. A comprehensive literature search was carried out from 2013 to 2019. The literature used was in English and Indonesian.

3 Literature Review

3.1 Tooth Extraction

Tooth extraction is the removal of a tooth from its socket as a last resort treatment if it has been badly damaged and cannot be preserved [1]. Wounds are a form of tissue damage that can be caused by the results of medical actions, changes in physiological conditions and contact with heat sources. Wounds can be classified into two based on the time and healing process, namely acute wounds and chronic wounds. Acute wounds are tissue injuries caused by mechanical injury due to external factors, while chronic wounds are tissue injuries caused by prolonged infection [7].

3.2 Wound Healing

Wound healing is an important physiological process that involves cellular and biochemical responses to produce repair consisting of specialized structures that involve complex processes of serial coordination including bleeding, coagulation, initiation of acute inflammatory responses, regeneration, migration and proliferation of connective tissue, synthesis of extracellular matrix proteins, cell and tissue remodeling, and collagen deposition [8]. The wound healing process in general can be divided into 3 phases, namely the inflammatory phase, the proliferative phase, and the maturation (remodeling) phase [9].

3.3 Wound Healing Phase

The inflammatory phase initially occurs as a haemostatic reaction because the blood that comes out of the wound will come into contact with collagen and the extracellular matrix which can trigger the release of platelets that express glycoproteins on the cell membrane so that they can aggregate and form a mass that will fill the hollows in the wound forming a provisional matrix for inflammatory cells migration. The late inflammatory phase can be characterized by acute inflammatory cells and neutrophils that invade the inflammatory area and destroy bacteria and all foreign material. Pro-inflammatory cytokines such as $\text{TNF-}\alpha$, $\text{IL-1}\beta$, IL-6 are secreted by neutrophils which also secrete proteases to degrade the remaining extracellular matrix. Neutrophils will be phagocytosed by macrophages or die after neutrophils carry out their functions [7].

The proliferative phase aims to reduce the area of the lesioned tissue with contraction and fibroplasia, build a viable epithelial barrier to activate keratinocytes, besides this phase is responsible for the closure of the lesion itself, which includes angiogenesis, fibroplasia, and reepithelialization [9]. Fibroblasts have a very important role in this phase.

Fibroblasts are cells found in connective tissue that are responsible for bacterial phagocytosis. $\text{TGF-}\beta$ (transforming growth factor) and PDGF (platelet-derived growth factor) stimulate the structure of fibroblasts into myofibroblasts located at the edge of the ECM which promotes wound closure in the tissue. Fibroblasts are also key in the proliferative phase of wound healing, such as breaking down fibrin clots, producing collagen, elastin fibers, glycosaminoglycans and proteoglycans induced by $\text{TGF-}\beta$ to build a new

extracellular matrix to close the wound and help the wound re-epithelialization process [3]. The remodeling stage aims to achieve maximum tensile strength through reorganization, degradation, and resynthesis of the extracellular matrix. In the late stages of healing of these lesions, attempts to restore normal tissue structure occur, and the granulation tissue is gradually remodeled, forming a scar tissue that is less cellular and vascular and which shows a progressive increase in its collagen fiber concentration. This stage is characterized by maturation of the elements with profound changes in the extracellular matrix and early resolution of inflammation. During maturation and remodeling, most blood vessels, fibroblasts, and inflammatory cells disappear from the wound area due to emigration, apoptosis, or other unknown cell death mechanisms [9].

3.4 Fibroblast Cell

Fibroblast cells are used as an indicator of wound healing because these cells are the most dominant cells in the wound healing process [10]. The role of fibroblasts is important in the wound healing process at the stage of tissue repair and is responsible for the preparation of making protein structure products that will be used during the tissue repair process. Fibroblasts will actively move from the tissue around the wound into the wound area, then they will develop (proliferate) and secrete several substances (collagen, elastin, fibronectin, hyaluronic acid and proteoglycans) that function in building new tissue [11] (Fig. 1).

The healing process can be accelerated by the use of drugs to avoid infection in the socket after tooth extraction. The drug that is often used is glycerin iodine. The use of glycerin iodine after tooth extraction is useful in preventing infection in wounds that can cause severe complications [12].

3.5 Egg White Content

Egg white has the main content, namely protein consisting of ovotransferrin, lysozyme, ovomucin, ovomusid, ovalbumin and avidin. The content of ovotransferrin, lysosim and ovomucin have been reported to have antiviral and antibacterial effects. Another content of egg white is ovalbumin which also has the potential to be used as a drug carrier and as a source of amino acids for growth factors. The contribution of growth factors

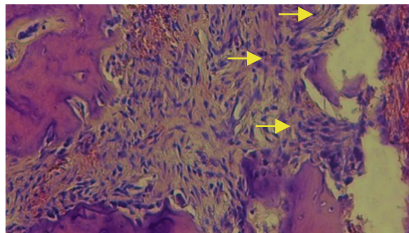


Fig. 1. Fibroblast cells in the apical portion of the rat tooth socket on the 3rd day after extraction with the application of *Gallus domesticus* egg white gel, viewed using a light microscope with a magnification of 200 times [12].

in wound healing is to stimulate fibroblast cells (connective tissue cells) to synthesize more collagen in the wound area. In addition, the protein content in egg whites is a lipid which also plays a role in growth factors [13].

3.6 Egg White Mechanism in Wound Healing

The mechanism of egg white in wound healing is to form new cell tissue and stimulate the restoration of damaged body tissue. The disadvantage of free-range chicken egg white is that it smells bad so it needs to be processed in gel preparations to increase comfort in use [14]. Egg white contains ovalbumin which has the potential to be used as a drug carrier and as a source of amino acids for growth factors. The contribution of growth factors in wound healing is to stimulate fibroblast cells (connective tissue cells) to synthesize more collagen in the wound area. In addition, the protein content in egg whites is a lipid which also plays a role in growth factors [13].

3.7 Gel

Gel preparations have a high water content so that they can increase hydration [14]. Moist conditions in the wound are necessary for the activity of growth factors such as TGF- β and EGF and better distribution of oxygen and nutrients. Moist conditions can also increase epithelial re-epithelialization and migration so that it can accelerate wound healing [15].

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