

Effect of Garcinia Mangostana Linn Fruit Peel Ethanolic Extract on Fibroblast Cell Migration

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ABSTRACT

Wound healing is the survival process against disruptor of living cells or tissues. Many attempts have tried to develop the products for promoting wound healing process. Garcidine®, a hospital formula containing 10% w/v ethanolic extract of Garcinia mangostana Linn fruit peel in propylene glycol base, is the topical anti-septic product for treating open wound. This current study aimed to determine wound healing efficiency of Garcidine® by using fibroblast cell migration model. Cell migration of Garcidine® treated fibroblast cells was compared to that of 10%w/v povidone iodine. The results revealed that Garcidine® was superior to 10% w/v povidone iodine in increasing fibroblast cell migration within 12 hours of treatment. Cytotoxic effect on fibroblast cells was not evidenced in both formulations. Therefore, this finding suggests that Garcinia Mangostana Linn fruit peel ethanolic extract is the promising natural product for treating open wound due to the efficacy in increasing fibroblast cell migration.

Keywords: Garcinia Mangostana Linn; Cell Migration; Wound Healing

Introduction

Wound is the disruption of cellular and anatomical living tissue. It can be produced by chemical, physical and microorganism attacking the tissue and is a major cause of organ abnormal function and disability [1]. Wound healing is a survival process for protecting and regenerating damage tissue. The healing process is triggered since tissue injury; platelets are activated and attracted into the injury area. Platelet aggregation induces the release of clotting factor that results in the deposition of a fibrin clot at the site of injury. Immune cells also interact with fibrin clot and release the cytokines and growth factors such as interleukin-1 beta (IL-1 β), tumor necrosis factor alpha (TNF- α) and transforming growth factor beta (TGF- β). Fibroblasts cells obviously response to TGF- β and then perform collagen deposition for repairing the injury tissue [1,2]. Due to fibroblasts responsibility to collagen production, they are usually studied for estimating wound healing process by

using cell migration and proliferation models [3]. Many studies used fibroblast cells for predicting wound healing promotion activity [1,3]. Garcinia mangostana Linn. has many chemical compounds that present various bio-activities? There was a study reported on wound healing promotion activity of G. mangostana in Sprague-Dawley rats by inducing skin epithelialization and wound contraction [4]. Moreover, xanthenes isolated from G. mangostana presented potent anti-microbial [5,6] and anti-inflammatory activities [7,8]. Both activities play crucial role in wound healing promotion. Garcidine® is a topical anti-septic product containing G. mangostana peel extract in propylene glycol. The formula is formulated according to Thailand National List Essential Medicines recommendation [9]. Current study aimed to investigate wound healing promotion activity of Garcidine® by using fibroblast cell migration model.

Materials and Methods

Garcidine® (10% w/v *Garcinia mangostana* Linn fruit peel ethanolic extract in propylene glycol) was obtained from Chaopraya Abhaiphubejhr Hospital, Prachinburi Province, Thailand. The extraction was described in brief; dry *G. mangostana* fruit peel powder 600g was macerated with 95% ethanol 800 g for 24 hours. An extract solution was collected. The maceration process was repeated 3 times with fresh ethanol. The extract solutions were filtered and pooled before evaporation at 60°C using rotary evaporator. Garcidine® was prepared as 10% w/v *G. mangostana* fruit peel extract in propylene glycol. Scar-plate was purchased from Gibco (Gibthai, Thailand). Dulbecco's Modified Eagle Medium (DMEM), Penicillin/Streptomycin, Trypsin and dimethyl sulfoxide (DMSO) and 3-2, 5-diphenyltetrazolium bromide were cell culture grade and purchased from Gibco (Invitrogen, USA). Fibroblast cells were isolated from neonatal circumcision foreskin. The process of skin collection was approved by Naresuan University Institutional Review Board with approval number 0140/62.

Fibroblast Cells Isolation

Dermis layer was dissected from foreskin and settled on cell culture plate. Culture tissue was maintained with DMEM containing 10% fetal bovine serum and 1% penicillin/streptomycin for 5 days. The cells were incubated in 95% RH, 5% CO₂ environment at 37°C. They were then sub-cultured at 80% confluence.

Cytotoxic Testing

Fibroblast cells were added into 96 wells-plates with 1x10⁴ cells/well and incubated for 24 hours. Then the cells were treated by Garcidine® or 10% w/v povidone iodine (a commercial topical anti-septic product) at various concentrations and re-incubated for 24 hours. Fifty microliters of 1 mg/ml MTT solution were added into each well. The incubation was done for formazan crystal formation for 3 hours. Cell viability was determined by measuring absorbance at 595 nm comparing with the untreated cells [10].

Cell Migration Testing

Fibroblast cells were added into Scar-plate with 3.5x10⁴ cell/channel. The cells were allowed to adhere for 24 hours in DMEM containing 10% fetal bovine serum and 1% penicillin/streptomycin. The septum was removed to create a channel between cells and then they were treated with Garcidine® or 10% w/v povidone iodine for 24 hours. Cell migration was observed and photographed using invert light microscope at 12 and 24 hours after treatment. Decrease of channel distance was calculated by using Image J computer software.

Results

Both Garcidine® and 10% w/v povidone iodine did not show any cytotoxic effect on fibroblast cells. The cell viability was greater than 90% in all treated concentration for both formulations. The results of cytotoxic test are showed in Figure 1. According to Figure 1, both Garcidine® and 10% w/v povidone iodine did not show any cytotoxic within the range 0.20 – 100.00µg/mL. Therefore, designed concentration of both samples for cell migration testing was 100µg/mL. Results of cell migration after treated with Garcidine® and povidone iodine were also compared with the control (untreated cells). After treated with test formulations, the cell morphology and migration were photographed at 12 and 24 hours. The images of cell migration are presented in Figure 2. Garcidine® obviously induced fibroblast cells migration across the channel space. On contrary, fibroblast cells treated with 10% w/v povidone iodine showed a limited migration when comparing to untreated cells and cells treated with Garcidine®. The decrease of channel distance presented in percent migration was calculated using ImageJ. The data indicated that fibroblast cells treated with Garcidine® was significantly decrease the channel distance more than that of the cells treated with 10%w/v povidone iodine and the control (Figure 3).

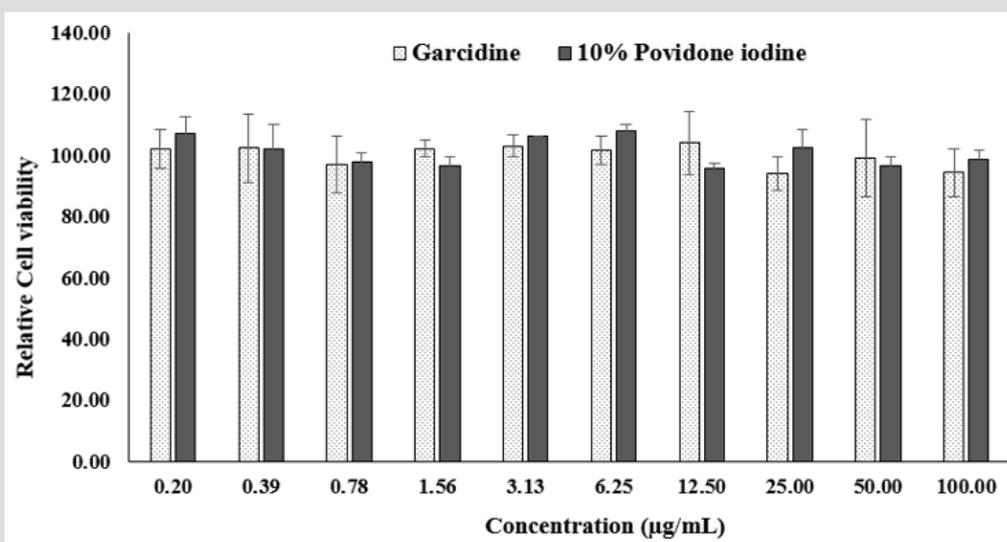


Figure 1: Relative cell viability after being treated with various concentration of Garcidine® or 10% w/v povidone iodine for 24 hours.

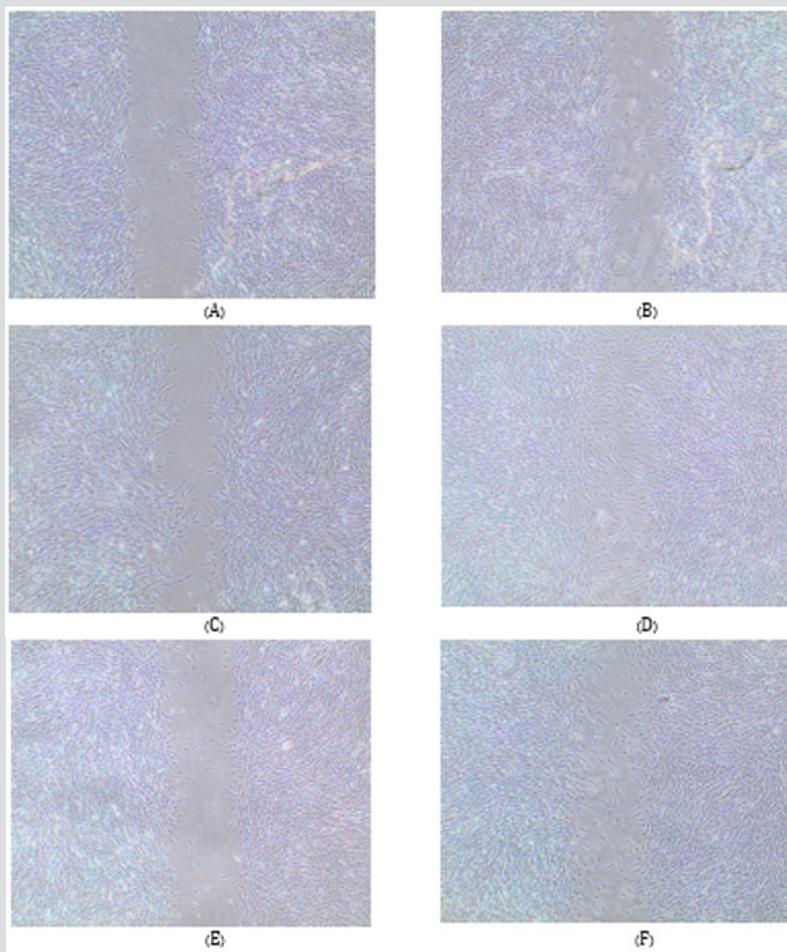


Figure 2: Cell migration after being treated with 100 µg/mL of 10% w/v povidone iodine for 12 hours (A) 24 hours (B) 100 µg/mL of Garcidine® for 12 hours (C) 24 (D) and Control cells at 12 hours (E) and 24 (F).

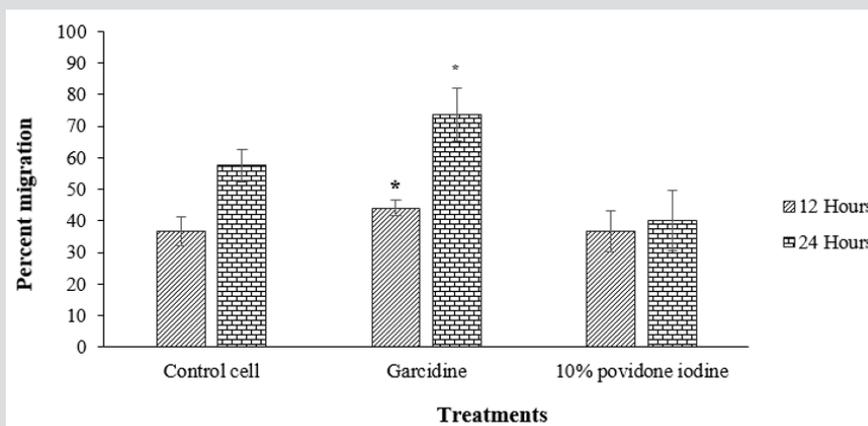


Figure 3: Percent migration of fibroblast cells at 12 and 24 hours after being treated with Garcidine® or 10% povidone iodine; *significantly different from control cell p<0.05.

Discussion

The effectiveness of Garcidine® (10% w/v Garcinia mangostana Linn fruit peel ethanolic extract in propylene glycol) in promoting cell migration was evidenced. Garcidine®, the anti-septic product, has been used for treating fresh and chronic wounds in local Thai hospital according to Thailand National List Essential Medicines recommendation. The result revealed that Garcidine® was non-

toxic on fibroblast cells. In addition, Garcidine® also induced fibroblast cells migration better than the commercially available topical anti-septic product, 10% w/v povidone iodine. Migration of fibroblast cells is a significant phenomenon for wound closure. They are the indicator of wound healing process [2]. Migration of Garcidine® treated cells was the effect of G. mangostana peel extract. The extract could promote wound healing by inducing the wound

to be at epithelization stage [4]. In case of povidone iodine, the result indicated that fibroblast cells were limited in cell migration when comparing to Garcidine® and the control. There were reports indicated that povidone iodine inhibited human fibroblast proliferation [11], although it was diluted till below cytotoxic concentration [12]. According to the current study, G.mangostana fruit peel ethanolic extract is a promising topical anti-septic ingredient of natural origin for treating open wound dues to it affect not only for preventing bacterial infection but also for promoting wound healing without cytotoxic effect on fibroblast cells.

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