Wound Healing and Antioxidant Evaluations of Alginate from *Sargassum ilicifolium* and Mangosteen Rind Combination Extracts on Diabetic Mice Model

Pugar Arga Cristina Wulandari 1, Zulfa Nailul Ilmi 1*, Saikhu Akhmad Husen 2, Dwi Winarni 2, Mohammad Amin Alamsjah 3, Khalijah Awang 4, Marco Vastano 5, Alessandro Pellis 5,6*, Duncan MacQuarrie 5 and Pratiwi Pudjiastuti 1,*

1 Department of Chemistry, Faculty of Science and Technology, Airlangga University, Surabaya 60115, Indonesia; cristinapugar@gmail.com (P.A.C.W.); zulfanailuilmi@gmail.com (Z.N.I.)
2 Department of Biology, Faculty of Science and Technology, Airlangga University, Surabaya 60115, Indonesia; saikhu-a-h@fst.unair.ac.id (S.A.H.); dwi-w@fst.unair.ac.id (D.W.)
3 Department of Marine, Faculty of Fisheries and Marine, Airlangga University, Surabaya 60115, Indonesia; alamsjah@fpm.unair.ac.id
4 Department of Chemistry, Faculty of Science, University of Malaya, Kuala Lumpur 50603, Malaysia; khalijah@um.edu.my
5 Department of Chemistry, University of York, Heslington, York YO10 5DD, UK; marco.vastano@york.ac.uk (M.V.); alessandro.pellis@boku.ac.at (A.P.); duncan.macquarrie@york.ac.uk (D.M.)
6 Department for Agrobioechnology, IFA-Tulln, Institute for Environmental Biotechnology, University of Natural Resources and Life Sciences, Konrad Lorenz Strasse 20, Tulln an der Donau, 3430 Vienna, Austria

* Correspondence: pratiwi-p@fst.unair.ac.id; Tel.: +62-856-3390-952

** Abstract:** A diabetic foot ulcer is an open wound that can become sore and frequently occurs in diabetic patients. Alginate has the ability to form a hydrophilic gel when in contact with a wound surface in diabetic patients. Xanthones are the main compounds of mangosteen rind and have antibacterial and anti-inflammatory properties. The purpose of this research was to evaluate the wound healing and antioxidants assay with a combination of alginate from *S. ilicifolium* and mangosteen rind combination extracts on a diabetic mice model. The characterization of alginate was carried out by size exclusion chromatography with multiple angle laser light scattering (SEC-MALLS) and thermogravimetric analysis (TGA). The M/G ratio of alginate was calculated by using proton nuclear magnetic resonance (1H NMR). The antioxidant activity of mangosteen rind and the combination extracts was determined using the DPPH method. The observed parameters were wound width, number of neutrophils, macrophages, fibrocytes, fibroblasts, and collagen densities. The 36 male mice were divided into 12 groups including non-diabetic control (NC), diabetes alginate (DA), alginate–mangosteen (DAM), and diabetes control (DC) groups in three different groups by a histopathology test on skin tissue. The treatment was carried out for 14 days and mice were evaluated on Days 3, 7, and 14. The SEC-MALLS results showed that the molecular weight and dispersity index (D) of alginate were 2.77 × 10^4 Dalton and 1.73, respectively. The M/G ratio of alginate was 0.77 and described as single-stage decomposition based on TGA. Alginate, mangosteen rind extract, and their combination were divided into weak, medium, and strong antioxidant, respectively. The treatment of the DA and DAM groups showed a decrease in wound width and an increase in the number of fibrocytes, fibroblasts, and macrophages. The number of neutrophils decreased while the percentage of collagen densities increased for all the considered groups.

**Keywords:** alginate; *Sargassum ilicifolium*; mangosteen rind; wound healing; diabetic mice

1. Introduction

Diabetes mellitus (DM) is a metabolic disease caused by the disruption of the glucose metabolism in the body [1]. DM can cause changes in skin homeostasis resulting in...