August 30, 2022

**Ms. Alvina Wu**

**Managing Editor**

**Molecules**

I would like to submit to Biomed Research International, the article entitled: **“Characterization of Polyphenolic compounds from *Bacopa procumbens* and their effects on wound healing process”** co-authored by Adriana Martínez-Cuazitl, María del Consuelo Gómez-Garcia, Oriana Hidalgo-Alegria, Olivia Medel Flores, José Alberto Núñez-Gastélum, Eduardo San Martín Martínez, Ada Ríos-Cortés, Marío Garcia-Solis, and myself, for your editorial consideration. The manuscript deals with the characterization of wound healing effects of *B. procumbens* compounds by *in vitro* assays including proliferation, cell adhesion and migration, modulating cell differentiation and the reduction of artificial scratch area. Then, Bioactive compounds from aquoethanolic extract were characterized by HPLC-QTOF-MS, polyphenolic compounds from *Bacopa procumbens* were included in a hydrogel for *in vivo* assays using a rat excision wound model. Histological, histochemical and mechanical analyses showed that polyphenolic compounds from *Bacopa procumbens* treatment accelerates wound closure in at least 48 h; reduce inflammation, increasing cell proliferation and deposition and organization of collagen in earlier times. These changes resulted in the formation of a scar with better tensile properties. Immunohistochemistry and RT-PCR molecular analyses demonstrated that treatment induces: *i)* overexpression of transforming growth factor beta (TGF-β); and *ii)* the phosphorylation of Smad 2/3 and ERK1/2, suggesting the central role of some polyphenolic compounds from *Bacopa procumbens* to enhance wound healing, modulating TGF- β activation. The article has not been published and is not being submitted simultaneously or published elsewhere. All the authors have contributed and read the paper and have given permission to be included as co- authors.

Thanks for yo d attention

ur kin

Dr. David Guillermo Pérez Ishiwara (Ph.D). National Polytechnic Institute

Tel: 5255 57296000 ext 55534

e-mail: ishiwaramx@yahoo.com.mx, dperez@ipn.mx