

Original article:**Evaluation of wound healing biomarkers of Interleukin 6 (IL-6), Vascular Endothelial Growth Factor (VEGF) and Matrix Metalloproteinases 9 (MMP-9) in post Lower Segment Caesarean Section (LSCS) patients consuming *Channa Striatus* extract**Julia Omar¹, Noorazliana Shafii², Ahmad Ezam Zainan³, KNS Sirajudeen⁴, Mohamed Rusli Abdullah⁵**Abstract:**

Background: Wound healing is a dynamic process which is divided into four phases; haemostasis, inflammatory, proliferation and tissue remodelling phases, that encompasses inflammatory cells, cytokines and growth factors. Interleukin-6 (IL-6), Vascular Endothelial Growth Factor (VEGF) and Matrix Metalloproteinase 9 (MMP-9) involve at the different phases of wound healing. *Channa striatus* (*C.striatus*) is a fresh water fish that is believed to have natural properties to promote wound healing. Currently, the effects of *C.striatus* on the cytokines and growth factors are not available. **Objective:** This study was conducted to evaluate the wound healing biomarkers; IL-6, VEGF and MMP-9 on post Lower Segment Caesarean Section (LSCS) women consuming oral *C.striatus* extract. **Methods:** This was a randomised, double-blinded study amongst LSCS women consuming *C.striatus* extract versus a placebo at Universiti Sains Malaysia Hospital and Raja Perempuan Zainab II Hospital from May 2011 to January 2013. After randomization, the treatment group received freeze dried *C.striatus* extract 500 mg daily while the placebo group received maltodextrin 500 mg daily for 6 weeks. Blood samples for IL-6, VEGF and MMP-9 were taken from both groups post-operatively at day 3, week 2, week 4 and week 6. The data were analysed using SPSS version 22. **Results:** A total of 39 patients from *C.striatus* and 34 patients from placebo group were included in this study. Within *C.striatus* group, the results of IL-6, MMP-9 and VEGF showed significant differences ($P<0.05$) for all the study period. Between group comparison showed significant difference ($P<0.05$) on week 4 and week 6 for IL-6 and MMP-9 whereas VEGF showed significant difference ($P<0.05$) on day 1, day 3, week 4 and week 6. The trend of IL-6 and MMP-9 exhibit decreasing trend in both groups however, VEGF in *C.striatus* group exhibit increasing trend till week 6 compared to placebo group. **Conclusion:** This study showed *C.striatus* extract had effects on IL-6, VEGF and MMP-9 in post LSCS women.

Keywords: *Channa striatus*; lower segment caesarean section; wound healing; Interleukin-6; MMP 9; VEGF

Bangladesh Journal of Medical Science Vol. 19 No. 03 July'20. Page : 520-526
DOI: <https://doi.org/10.3329/bjms.v19i3.45870>

Introduction

Wound healing is divided into four distinct and overlapping phases of haemostasis, inflammatory, proliferation and tissue remodelling¹. It encompasses

a variety of cells and inflammatory markers. Interleukin-6 (IL-6) involves in the systemic changes during inflammation and infection². It plays a crucial role in inflammation, particularly

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have attributed to the above findings⁷. *C.striatus* is also known to produce polyunsaturated fatty acids which regulate prostaglandin synthesis inducing wound healing¹⁸. In this study the level of wound healing markers (IL-6, MMP-9) between group were statistically significant different from week 4 until week 6. IL-6 and MMP-9 levels were higher in *C.striatus* group compared to the placebo group. However, VEGF levels were increasing till week 6. This findings correlated well with the parallel study done by Ab Wahab *et al.* (2014) which showed an improvement in term of wound cosmetic appearance using visual analogue scale among *C.striatus* group at the end of week 6^{19,20}. This findings indicate that the effectiveness of *C.striatus* extract starts at week 4 onwards enhancing the production of VEGF during proliferation and remodelling phase. At this particular week, keratinocytes migration and collagen production via fibroblast are in progress to establish healing response. Perhaps, the high content of amino acid and fatty acids in *C.striatus* had triggered more productions of VEGF through the influence of IL-6 which play a role in the regulation of VEGF and in turn stimulate angiogenesis and vascularity. Increase vascularity stimulates the endothelial sensitivity to produce growth factors which further induce VEGF expression in a positive feedback loop⁴.

Similar pattern was observed in both IL-6 and MMP-9 over time (Figure 1 and Figure 2). Both groups exhibit similar pattern with a peak at the beginning of inflammation phase (1- 3 days) and decreasing gradually till week 6. This confirms that IL-6 and MMP-9 levels are high during haemostasis and inflammation phase that last several days and act as a defence mechanism triggered by pro-inflammatory cells. Both cytokines started decreasing from week 2 onwards until the final phase as the number of pro-inflammatory cells will subsequently be replaced by tissue building cells such as fibroblast, myofibroblast, keratinocytes and epithelial cells.

The trend of VEGF between both groups showed different magnitude where VEGF trend in *C.striatus* showed an increasing trend compared to VEGF in

placebo that showed a decreasing trend from day 1 until week 6 (Figure 3). *C.striatus* had triggered more productions of VEGF. A study done by Holmes and Zachary (2005) reported that the biological and signalling roles of the VEGF receptors have not yet been fully defined although there was a significant progress made towards elucidating the mechanisms mediating the angiogenic effects of VEGF²¹. This study was not followed on and the level and trend of VEGF after 6 weeks could not be elicited.

As a conclusion, this study showed that the oral administration of *C.striatus* extract had effects on wound healing process. High concentration of amino acid, EPA and DHA in *C.striatus* extract is believed to exert the effectiveness as wound healing properties. Both cytokines IL-6 and MMP-9 exerted effects at week 4 and above. However, VEGF trend could not be elicited as increasing trend was seen till week 6. Further study is needed to understand the detailed effects of *C.striatus*.

Conflict of interest

We declare that we have no conflict of interest.

Author's contribution

Data gathering and idea owner of this study: Julia Omar, Ahmad Ezam Zainan

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Acknowledgements

We acknowledge the financial assistance received from Universiti Sains Malaysia, Kubang Kerian, Kelantan through RUI grant (Grant No. 1001/PPSP/812081).