

Emu Oil Promotes Intestinal Repair in Rat Models  
of Enteric Inflammation

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## ABSTRACT

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Several disorders of the gastrointestinal (GI) tract including ulcerative colitis, chemotherapy-induced mucositis and non-steroidal anti-inflammatory drug (NSAID)-induced enteropathy, are characterised by inflammation, ulceration, mucosal damage and malabsorption. Treatment options are variably effective, highlighting the need to broaden therapeutic approaches, including adjunctive strategies. Emu Oil, derived from subcutaneous and retroperitoneal Emu adipose tissue, is a rich source of fatty acids (FA). Despite limited rigorous scientific studies, topically applied Emu Oil has demonstrated potent anti-inflammatory properties *in vivo*. Previously, orally administered Emu Oil improved intestinal architecture in a rat model of mucositis, with early indications of enhanced intestinal repair. Accordingly, this thesis investigated the effects of orally administered Emu Oil in rat models of colitis (colonic damage), NSAID-enteropathy (small intestinal [SI] damage) and on the time course of SI repair in chemotherapy-induced mucositis.

In the current study, Emu Oil improved colonic tissue damage associated with dextran sulphate sodium-induced colitis in Sprague Dawley rats and facilitated the repair process (**Chapter 2**). Improvements were indicated histologically by reduced intestinal damage severity scores and enhanced crypt compensatory elongation in the colon. These findings suggested the potential for Emu Oil to augment conventional treatment approaches for colitis. The effectiveness of Emu Oil in the colon provided impetus to further investigate Emu Oil action proximally, in the SI. In a rat model of chemotherapy (5-Fluorouracil; 5-FU)-induced mucositis, Emu Oil maintained SI villus height and crypt depth during the phase of maximal damage (**Chapter 3**). This was followed by an enhanced compensatory mucosal thickening, suggesting an acceleration of the repair process. Furthermore, Emu



Oil significantly decreased myeloperoxidase (MPO) activity, indicative of acute inflammation, in the jejunum and ileum of 5-FU-injected rats. Potent anti-inflammatory properties of Emu Oil were reaffirmed in NSAID (Indomethacin)-induced enteropathy, whereby MPO activity in the jejunum and ileum of Indomethacin-treated rats was markedly decreased following Emu Oil administration (**Chapter 4**).

Treatments for diseases such as coronary artery disease and GI disorders seek to minimise oxidative damage by free radicals through the use of antioxidants. Oils derived from ratites (flightless birds) predominantly comprise FA varying in composition between ratite species. The influence of farm location, rendering method, duration and storage mode was investigated for free radical scavenging activity (RSA) against 2,2-diphenyl-1-picrylhydrazyl and primary oxidation status of Ratite Oils (**Chapter 5**). Emu Oil conferred the greatest RSA compared to Ostrich and Rhea Oil, potentially attributed to its high unsaturated FA: saturated FA ratio and non-triglyceride fraction minor constituents. Rendering and storage variables impacted on Emu Oil RSA and primary oxidation.

This thesis identified Emu Oil as a safe, renewable and economical means to augment pharmaceutical options for GI disorders. A new mechanism of action for Emu Oil could represent a promotion of repair from injury together with decreased SI inflammation. This suggests potential for Emu Oil as an adjunct to conventional treatment approaches for colitis, cancer management and long-term NSAID usage.

## DECLARATION

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This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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**(1) SM Abimosleh, CD Tran, GS Howarth.** Emu Oil: a novel therapeutic for disorders of the gastrointestinal tract? *Journal of Gastroenterology and Hepatology* 2012 May;27(5):857-61

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**(2) SM Abimosleh, RJ Lindsay, RN Butler, AG Cummins, GS Howarth.** Emu oil increases colonic crypt depth in a rat model of ulcerative colitis. *Digestive Diseases and Sciences* 2012 Apr;57(4):887-96

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## Appendices

(3) KY Cheah, SEP Bastian, TMV Acott, **SM Abimosleh**, KA Lymn, GS Howarth. Grape Seed Extract Reduces Selected Disease Markers in the Proximal Colon of Dextran Sulphate Sodium-Induced Colitis in Rats. *Digestive Diseases and Sciences* 2012 Nov (epub ahead of print) DOI 10.1007/s10620-012-2464-1

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(4) AK Samanta, VA Torok, NJ Percy, **SM Abimosleh**, GS Howarth. Microbial fingerprinting detects unique bacterial communities in the faecal microbiota of rats with experimentally-induced colitis. *Journal of Microbiology* 2012 Apr;50(2):218-2

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(5) CD Tran, R Katsikeros, **SM Abimosleh**. Current and Novel Treatments for Ulcerative Colitis. *Ulcerative Colitis from Genetics to Complications*. InTech 2012: 189-211

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(6) R Raghu Nadhanan, **SM Abimosleh**, YW Su, MA Scherer, GS Howarth, CJ Xian. Dietary emu oil supplementation suppresses 5-fluorouracil chemotherapy-induced inflammation, osteoclast formation, and bone loss. *American Journal of Physiology Endocrinology and Metabolism* 2012 Jun;302(11):E1440-9

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**Date**

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*~ In loving memory of my dear friend Pat ~*

*“If we never had a cloudy day with wind and rain and thunder,  
we would never see a rainbow and rejoice in all its wonder...” Pat Westin*

## PUBLICATIONS ARISING FROM THIS THESIS

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**SM Abimosleh**, CD Tran, GS Howarth. Emu Oil: a novel therapeutic for disorders of the gastrointestinal tract? *Journal of Gastroenterology and Hepatology* 2012 May;27(5):857-61

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**SM Abimosleh**, CD Tran, GS Howarth. Emu Oil Expedites Small Intestinal Repair Following 5-Fluorouracil-Induced Mucositis in Rats. *Experimental Biology and Medicine* 2012; Under review

**SM Abimosleh**, CD Tran, GS Howarth. Emu Oil Reduces Small Intestinal Inflammation in the Absence of Clinical Improvement in a Rat Model of Indomethacin-Induced Enteropathy. *Evidence-Based Complementary and Alternative Medicine* 2012; Under review

*Publications arising from conferences*

**SM Abimosleh**, Z Lotfollahi, J Papini, L Hoyle, D Stomaci, E Penascoza, CD Tran, KA Lymn, RN Butler and GS Howarth. Orally-administered Emu Oil maintains intestinal goblet cell numbers and improves barrier function in a rat model of chemotherapy-induced mucositis.

1. Multinational Association of Supportive Care in Cancer (MASCC), New York, USA. *Supportive Care in Cancer* 2012; 20(1):627
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*2<sup>nd</sup> Prize for Best Oral Presentation*

**SM Abimosleh**, CD Tran, GS Howarth. Emu Oil Promotes Repair From Chemotherapy-Induced Intestinal Mucositis In Rats

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*Poster of Merit Prize*

**S Mashtoub**, RJ Lindsay, KA Lymn, TWV Acott, R Yazbeck, AG Cummins, RN Butler, GS Howarth. Emu oil increases crypt depth but only minimally affects other indicators of colonic integrity in a rat model of colitis. AGW, Sydney, NSW. *J Gastro Hepatol* 27: A239-A247 (2009)

## **THESIS STRUCTURE**

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This thesis is presented as a ‘Thesis by Publication’ and includes a combination of published manuscripts and papers under review. Each manuscript is formatted according to the journal specifications.

Furthermore, additional publications arising from the research described in this thesis are included as Appendices.