ORALLY-ADMINISTERED EMU OIL REDUCES DISEASE SEVERITY IN A MURINE MODEL OF COLITIS-ASSOCIATED COLORECTAL CANCER

THE UNIVERSITY
of ADELAIDE

Women's and Children's Hospital
ADELAIDE

LC Chartier^{1,2}, GS Howarth^{1,2,3}, IC Lawrance⁴, D Trinder⁴, SJ Barker^{1,2}, S Mashtoub^{1,2,4}

¹Discipline of Physiology, Adelaide Medical School, The University of Adelaide, South Australia ; ²Gastroenterology Department, Women's and Children's Hospital, South Australia; ³School of Animal & Veterinary Sciences, The University of Adelaide, South Australia; ⁴School of Medicine, The University of Western Australia

BACKGROUND

Ulcerative colitis & associated colorectal cancer

- Ulcerative colitis (UC) is an inflammatory bowel disease characterised by mucosal inflammation and ulceration of the colon and rectum¹
- UC symptoms include diarrhoea, weight loss, fever, abdominal pain and rectal bleeding
- Current treatments for UC are variably effective and patients are 60% more likely than the general population to develop colorectal cancer²

Emu Oil

- Oil derived from Emu adipose tissue has been used topically by Native Australian Aboriginal people to alleviate pain and reduce inflammation³
- Orally-administered Emu Oil has exhibited anti-inflammatory and reparative properties in animal models of gastrointestinal disease^{4,5,6,7}

HYPOTHESIS & AIM

It was hypothesised that orally-administered Emu Oil would decrease the severity of chronic colitis, thereby reducing the development of colorectal tumours in mice.

The aim was to determine if Emu Oil could reduce the severity of chronic colitis and number of tumours developed in an azoxymethane (AOM)/ dextran sulphate sodium (DSS) mouse model of colitis-associated colorectal cancer.

METHODS

- Mice were injected (i.p.) with saline or AOM (carcinogen; 7.4mg/kg) on day 0, followed by three DSS/water cycles (each consisting of 7 days water or DSS [2%w/v] and 14 days plain water)⁸
- Mice were orally-administered (via gavage) either water (160µL) or Emu Oil (80µL or 160µL) thrice weekly for 9 weeks
- Bodyweight (**Figure 1**) and disease activity index (DAI; bodyweight loss, general condition, stool consistency and rectal bleeding; **Figure 3**) were recorded daily⁴
- Mouse behaviour (burrowing; **Figure 2**) was analysed at the end of a DSS week and DSS/water cycle
- Colitis progression and tumour development (**Figure 4 & 5**) were assessed using a high resolution Karl Storz colonoscope (1.9mm outer diameter) at the end of each DSS/water cycle (**Figure 6**)⁸
- All mice were killed via CO₂ asphyxiation on day 63 of the trial
- Colon sections were collected and stained with H&E for quantitative crypt depth measurements (**Figure 7**)

Data were analysed using SPSS V17. p<0.05 was considered statistically significant.

RESULTS

Emu Oil attenuated bodyweight loss in AOM/DSS mice

Figure 1. Daily bodyweight change of mice (n=9/group). Data are expressed as mean (% change of starting bodyweight) ± SEM. ***p<0.001, **p<0.01, *p<0.05 compared to Saline + Water + Water, ^^p<0.001, ^p<0.01, ^p<0.05 compared to AOM + DSS + Water, ##p<0.01 compared to AOM + DSS + Emu Oil (80µL).

Emu Oil significantly increased burrowing activity of AOM/DSS mice on day 61 compared to AOM/DSS controls

Figure 2. Burrowing activity of mice (n=9/group). Data are expressed as mean amount burrowed (g) ± SEM. *p<0.05 compared to Saline + Water + Water, ^p<0.05 compared to AOM + DSS + Water

Emu Oil significantly reduced disease activity index compared to AOM/DSS controls

Figure 3. Daily disease activity index (DAI) score (n=9/group). Data are expressed as mean calculated DAI ± SEM. ***p<0.001, **p<0.01, *p<0.05 compared to Saline + Water + Water, ^^p<0.001, ^p<0.01, ^p<0.05 compared to AOM + DSS + Water, ##p<0.001, #p<0.01, #p<0.05 compared to AOM + DSS + Emu Oil (80µL).

Emu Oil reduced colitis severity and resulted in fewer small colonic tumours compared to AOM/DSS controls

Figure 4 & 5. Left (4); Colitis score calculated from scope videos (n=9/group). Data are expressed as mean colitis score ± SEM. ***p<0.001, ^p<0.01, ^p<0.05 compared to AOM + DSS + Water. **Right (5); Distal colonic tumours arranged into sizes (n=9/group).** Tumours were categorized depending on their diameters; small (<2mm), medium (2-3mm) and large (>3mm). ***p<0.001 compared to Saline + Water + Water, ^p<0.05 compared to AOM + DSS + Water.

Figure 6. Colonoscopy examples. Video representing an AOM/DSS control animal and colonoscopy still images

Colonic crypt depth increased in AOM/DSS mice compared to normal controls

Figure 7. Crypt depth of the proximal and distal colon (n=9/group). Data are expressed as mean crypt depth (µm) ± SEM. ***p<0.001, **p<0.01 compared to Saline + Water + Water.

SUMMARY & CONCLUSIONS

- Emu Oil attenuated bodyweight loss of AOM/DSS mice, while not significantly affecting bodyweight in normal animals
- Emu Oil reduced the severity of chronic colitis in a 9-week AOM/DSS model of colitis-associated colorectal cancer, evidenced by reduced DAI and scope colitis scores.
- AOM/DSS decreased burrowing activity, however, Emu Oil (low and high dose) significantly increased burrowing activity compared to AOM/DSS controls on day 61
- Emu Oil treatment resulted in significantly fewer small colorectal tumours compared to colorectal cancer controls, although total tumour number remained unaffected
- AOM/DSS increased colonic crypt depth compared to normal animals, with no effect exhibited by Emu Oil

Emu Oil reduced clinical indicators and resulted in fewer small colonic tumours compared to colorectal cancer controls. Additionally, this is the first study to investigate long-term administration of Emu Oil in normal animals. These results suggest the potential for Emu Oil to be used as a safe long-term treatment for UC and cancer management

Further investigation into cell kinetics, dosing and administration of Emu Oil would provide further insight into its mode of action and potential to be a novel therapeutic for gastrointestinal diseases

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