The effect of vitamins B2 and C on the development of mucositis

**Introduction**

Mucositis is considered one of the most debilitating side-effects of chemotherapy treatment, underpinned by inflammatory lesions through the alimentary tract. In the gut, mucositis is associated with symptoms such as diarrhoea, pain, neutropenia, bacteraemia and malnutrition. These complications require extensive supportive care measures resulting in the reduction in the dosage of chemotherapeutic drugs and consequently higher mortality in cancer patients [1]. It has recently been shown that chemotherapy drastically alters the diversity and composition of the intestinal microbiota. Although the specific bacteria affected vary depending on the type of chemotherapy agent used, a decrease in commensal bacteria is regularly reported in patients undergoing chemotherapy, coupled with an increase in a number of bacterial subtypes [2]. However, redox active compounds, such as vitamins B2 and C, were shown to reduce inflammation in the gut and to enhance the growth of anaerobic bacteria [3].

**Aim**

We aim at investigating the effects of vitamins B2 and C on the development of mucositis and on the composition of the gut microbiota in the methotrexate (MTX)-induced mucositis rat model.

**Materials and methods**

**Assessing bacterial growth**

To investigate the effect of vitamins B2 and C, alone or in conjugation, on the growth of six bacterial strains isolated from methotrexate-induced mucositis rats, their growth medium was enforced with different concentrations of these vitamins and the optimal density measured. Through microbial fuel cell (MFC) technique, the ability of bacteria to reduce the environment was measured by the current produced when vitamin B2 was added as electron transfer mediator (ETM).

**Methotrexate-induced mucositis rat model**

MTX-induced mucositis rats were intravenously injected with MTX (45 mg/kg) or saline solution (control). Vitamins B2 and C, alone or in conjugation, were daily administrated via oral gavage, starting one day before MTX treatment. Mucositis severity was determined by food intake, body weight and water intake. Blood was collected at days 0, 2, 4, 6 and 10 to measure plasma citrulline levels.

**Results**

1. **Vitamins B2 and C improve the growth of anaerobic bacteria under oxidative conditions**

2. **Blautia cocoides employs vitamin B2 for extracellular electron transport**

3. **Vitamin C ameliorates mucositis symptoms in rats**

**Conclusions**

- Anaerobic bacteria Blautia cocoides and Roseburia intestinals significantly grow better in the presence of oxygen, when a combination of 0.5 mM or 1 mM of both vitamins is added to the culture.
- Vitamin C supplementation (250mg/Kg/day) in rats attenuated the severity of mucositis reflected by changes in body weight, food intake and plasma citrulline.
- 60mg/Kg/day of vitamin B2 was found to have a negative impact on mucositis, suggesting that this dose has to be reduced.

**References**


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**Figure 1.** Schematic representation of the experimental design used for the in vivo study.

**Figure 2.** Growth curves of bacteria isolated from MTX-induced mucositis rats stimulated with Vitamins B2 and C. B. cocoides, B. intestinals, B. longum and E. coli were grown in YCFA medium, and vitamins were added to the medium. Experiment was performed under anaerobic conditions.

**Figure 3.** Microbial fuel cell (MFC). Like Fecalibacterium prausnitzii, Blautia cocoides are able to use riboflavin as an ETM, which suggests that riboflavin can be used by specific strict anaerobic bacteria to grow under oxidative condition.