Omega 3 formulated in a juice/whey drink and in a juice/curcumin drink decrease tumour growth and improve muscle wasting in tumour-bearing mice

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Background and aims: The aim of the present investigation is to evaluate the effects of a juice containing essential nutrients (marine omega-3 fatty acids (EPA and DHA), a polyphenol rich juice, vitamin D3, essential amino acids and dietary fibre) (CAX) and one juice enriched also with curcumin (CUR) alone or in combination with a chemotherapeutic agent (SORAFENIB) in a mouse cancer cachexia model.

Juice treatment –both CAX and CUR– significantly reduced primary tumour growth (Figure 1). Sorafenib treatment also reduced primary tumour growth although no additive effect was observed on this parameter when juice treatment was applied to sorafenib-treated mice. No effects on metastasis measurements were observed.

In spite of the tumour reduction, the chemotherapy treatment did not result in changes in body weight. In combination with sorafenib, CAX had an important effect on reducing body weight loss. CUR treatment also had an effect without chemotherapy (Figure 2).

Tumour inoculation and treatment

Tumour-bearing animals were divided into two major groups, untreated (no chemotherapy) and treated (chemotherapy) daily with Sorafenib (90mg/kg body weight, intraperitoneally (i.p.) from day 4 after tumour injection). The animal groups were divided into subgroups of 8 animals:

control group: Milk-based isocaloric placebo-treated animals (PLAC).

treated groups:
- Nutrifriend 2000 (CAX)
- Nutrifriend 3000/curcumin (CUR)

The juices were given in the form of jellified blocks according the following doses:

- PLAC: 1 g of jellified juice (for a mouse weighing 25 g)
- CAX: 826 mg/kg in 2 g of jellified juice (for a mouse weighing 25 g)
- CUR: Mouse dosing: 616 mg/kg in 1 g of jellified juice (for a mouse weighing 25 g)

A clear statistically significant increase was observed in tibialis muscle when the animals were treated with either CAX or CUR (Figure 3). In combination with sorafenib, CAX treatment also resulted in larger tibialis muscle. In sorafenib-treated mice, juice treatment –either CAX or CUR– resulted in a marked tendency to increase in grip force.

Concerning adipose weights, juice treatment resulted in a clear significant increase in both eWAT and dWAT (CAX) and BAT mass (CUR). This effect was observed in combination with chemotherapy in WATd (Table 1).

It is concluded that administration of omega-3 and omega-3/curcumin-enriched fruit juices may have beneficial effects on muscle wasting and could be part of a multi-modal therapy for cancer cachexia.

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**Figure 1. Tumour weight (mg)**

Results are mean ± S.E.M. for the number of animals indicated in parentheses. PLAC: placebo. CAX: Nutrifriend 2000. CUR: Nutrifriend 3000/curcumin. PLAC+C: placebo+sorafenib. CUR+Sorafenib: Nutrifriend 3000+sorafenib. Statistical significance of the results by full factorial two-way ANOVA (fixed factors: juice treatment and sorafenib treatment). Statistical significant differences by post hoc Duncan test. Different letters indicate significant differences between groups.

**Figure 2. Body weight (% growth decrease).**

Results are mean ± S.E.M. for the number of animals indicated in parentheses. PLAC: placebo. CAX: Nutrifriend 2000. CUR: Nutrifriend 3000/curcumin. PLAC+C: placebo+sorafenib. CUR+Sorafenib: Nutrifriend 3000+sorafenib. Statistical significance of the results by full factorial two-way ANOVA (fixed factors: juice treatment and sorafenib treatment). Statistical significant differences by post hoc Duncan test. Different letters indicate significant differences between groups.

**Figure 3. Tibialis weight (mg/100g IBW)**

Results are mean ± S.E.M. for the number of animals indicated in parentheses. Tissue weights are expressed as mg/100g of initial body weight. WATd: white adipose dorsal; WATe: white adipose epigastrial. WATd+WATe: sum of the two adipose tissue pads, BAT: brown adipose tissue. Statistical significance of the results by full factorial two-way ANOVA (fixed factors: juice treatment and sorafenib treatment). Statistical significant differences by post hoc Duncan test. Different letters indicate significant differences between groups.

**Table 1. Adipose tissue weights.**

Results are mean ± S.E.M. for the number of animals indicated in parentheses. Tissue weights are expressed as mg/100g of initial body weight. WATd: white adipose dorsal; WATe: white adipose epigastrial. WATd+WATe: sum of the two adipose tissue pads, BAT: brown adipose tissue. Statistical significance of the results by full factorial two-way ANOVA (fixed factors: juice treatment and sorafenib treatment). Statistical significant differences by post hoc Duncan test. Different letters indicate significant differences between groups.