

Attenuation of proteolysis and muscle wasting by Curcumin C3 Complex® in MAC16 colon tumour-bearing mice

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Cachexia is defined as the progressive wasting of body tissues that primarily affects muscle and adipose tissue. Patients suffering from sepsis, trauma, AIDS and many types of cancer exhibit cachexia. In case of cancer, it is one of the most important factors leading to early morbidity and mortality, accounting for up to 30% of all deaths; particularly more pronounced in pancreatic and head–neck cancers.

Various inflammatory mediators like cytokines, including TNF- α , interferon-gamma, IL-6, leukaemia inhibitory factor and mediators, including proteolysis-inducing factor and lipid mobilising factor, are known to play a role in the development of cachexia. However, attempts at neutralising these cytokines or mediators have had only limited success so far. Recent attempts have been made to supplement diets with nutrients, such as Curcumin that specifically inhibits muscle proteolysis.

Objective:

To understand the effect of Curcumin C3 Complex® (Curcumin) on attenuation of muscle proteolysis using *in vitro* and *in vivo* models.

Study Design:

- Cytotoxic effects of Curcumin were evaluated in proliferating human skeletal myoblast cells
- Protein degradation in response to serum starvation was assayed in skeletal muscle cells
- Murine MAC16 tumour cells were injected in nude–nu male mice (aged: 6–7 weeks) to induce cachexia
- The body weight of the animals and progression of tumour growth were recorded every day post–tumour implantation, once the tumour was palpable
- Proteasome assay was carried out in both muscle extracts of MAC16 tumour-bearing mice as well as in serum-starved human skeletal muscle cells to assess the effect of Curcumin

Results and Discussion:

- At 0.5 µg/ml Curcumin concentration was very effective in significantly inhibiting ($p < 0.05$) tyrosine release by 30% and maximum inhibition (i.e. 60%) was seen at 2.5 µg/ml concentration
- At the end of the study (day 21 post-treatment) indicated that both low and high doses of Curcumin showed a net increase in body weight by 24% ($p < 0.05$) and 35% ($p < 0.05$), respectively
- Curcumin also improved weights of gastrocnemius muscle by 30% ($p < 0.05$) and 58% ($p < 0.05$) at both low and high doses, respectively
- Curcumin also inhibited muscle proteolysis by inhibiting chymotrypsin-like proteasome 20S activity by 22–25% ($p < 0.05$) compared to placebo

Conclusion:

Curcumin treatment resulted in the prevention and reversal of cachexia in cachectic animals bearing MAC16 tumours, thus possess an effective adjuvant therapy potential against cachexia.

