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Immunomodulatory and anti-inflammatory potential of a malleable protein matrix composed of concentrated fermented whey proteins

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A novel nutraceutical ingredient, the malleable protein matrix (MPM), is obtained from the fermentation of pasteurized whey with a unique probiotic strain isolated from kefir grains. It is also composed of capsular exopolysaccharides, vitamins, minerals (such as Ca) and peptides generated during the fermentation process. MPM is a complex biological mixture in which synergistic effects between the components are expected. Immunocompetent-animal studies have shown that MPM increases the polymorphonuclear cell counts(1), but also modulates the overall level of glutathione in circulating cells(1)and cytokine production (Fig. 1). These results suggest that MPM exerts a definitive stimulation of the innate immunity and that consumption of MPM could be either beneficial or detrimental on the immune system.

In order to assess the resulting effect of MPM, an oxazolone-induced atopic contact dermatitis model (ACD) was used to induce systemic inflammation. The results showed that MPM did not promote any detrimental side effects. On the contrary, MPM exhibited a positive and significant anti-inflammatory effect comparable with that of hydrocortisone but without the side effects(2). Using this model a marked reduction in ear inflammation was demonstrated in MPM-treated mice, and this effect was correlated with inhibition of neutrophil extravasation in the tissue(2). The *in vivo* 'air pouch' model, which represents the pathological characteristics of arthritis, also demonstrated a 50% inhibition of neutrophil infiltration in MPM-treated mice, which was correlated with an important reduction in cytokine and chemokine production following stimulation (J Beaulieu, D Girard, C Dupont and P Lemieux, unpublished results).

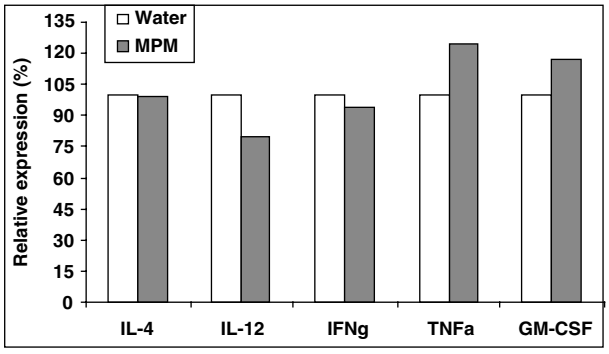

Fig. 1. Systemic cytokine production in healthy mice treated with water or MPM for 2 weeks. IFNg, interferon-γ; TNFa, TNFα; GM-CSF, granulocyte-macrophage colony-stimulating factor.

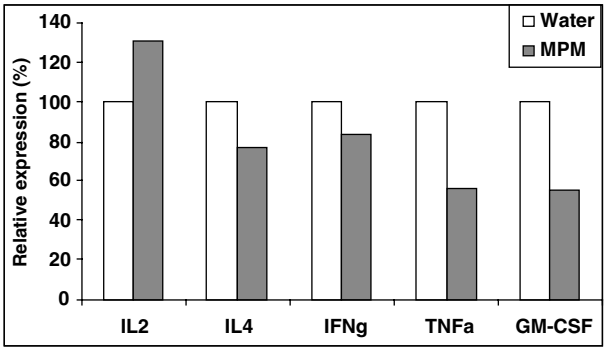

Fig. 2. Systemic cytokine production in the ACD model in water- or MPM-treated mice. IFNg, interferon-γ; TNFa, TNFα; GM-CSF, granulocyte-macrophage colony-stimulating factor.

The evaluation of cytokine production in healthy animals indicates that the stimulation of immunity is not related to activation of classical T-helper 1 or T-helper 2 pathways (Fig. 1). Furthermore, in the ACD model the cytokine production also indicates that these pathways are not implicated in the anti-inflammatory effect of the MPM, and IL-2 appears to have a role in the mechanism of action (Fig. 2). The modulation of cytokine production in animal models suggests that MPM regulates a newly-discovered subpopulation of lymphocytes that acts specifically on neutrophils, which could explain the dual effects obtained with MPM, i.e. the capacity to stimulate immunity as well as exhibiting important anti-inflammatory effects. This mechanism of action has not previously been associated with a nutraceutical product, suggesting that MPM may become an alternative and a functional food of choice for those individuals suffering from autoimmune diseases, as well as being able to stimulate infectious defence.

1. Beaulieu J, Dubuc R, Beaudet N, Dupont C & Lemieux P. (2007) *J Med Food* **10**, 67–72.
2. Beaulieu J, Dupont C & Lemieux P. (2007) *J Inflamm (Lond)* **4**, 6.