THE POTENTIAL OF A *SOLANUM TORVUM* EXTRACT AS A MUCOSAL IMMUNOMODULATOR IN ANTI-PARASITE VACCINE FORMULATIONS

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Introduction

Initial studies on vaccination against *Haemonchus contortus* in 1997 have shown that total worm protein extracts were able to elicit a partially protective immune response, however attempts to enhance this response with a powerful mucosal adjuvant namely *E. coli* heat-labile enterotoxin (HLT) failed. Based on our findings and current literature it was suggested that development of anti-parasitc vaccines should emphasise studies on immunostimulants that can enhance the response in the gut rather than selecting protein antigens from gel bands that were not likely to elicit protective immunity. Using rapid cell assay screening methods we have discovered an aqueous extract from *Solanum torvum* that is strongly mitogenic for splenic lymphocytes (Israf et al. unpublished data). We have tested this extract several times in a rodent-non-replicating antigen model and have shown that it is as effective as cholera toxin in enhancing mucosal immune responses. The results of these trials are presented.

Materials and Methods

Three trials were conducted with outbred female ICR mice. In trial 1, 10 groups of mice were given various doses of *Solanum* extract as an adjuvant to bovine serum albumin via the intraperitoneal route. Boosters were given and the immune response throughout a 4-month period was analysed. In trial 2 and 3, mice received similar doses as in trial 1 however the route of inoculation was via oral lavage. The main emphasis of these trials was to examine the ability of *Solanum* extracts to stimulate mucosal immune effector mechanisms towards ovalbumin. Assays used included enzyme immunoassay for detection of antibody isotypes in various tissues and serum. Enzyme immunospot was used to study cytokine responses of lymphoid tissue using monoclonal antibodies towards IFM-γ, IL-2, IL-4 and IL-5.

Results and Discussion

In trial 1: We demonstrated a significant enhancement in anti-BSA IgG titers when the lowest dose of *Solanum* was used (2 ug). We also demonstrated that following a final booster, the intestinal levels of both anti-BSA IgA and IgG were significantly elevated. Trial 2 demonstrated that an oral booster with ovalbumin/0.5 mg *Solanum* was able to significantly elevate intestinal and faecal IgA concentration and stimulate both Th1 and Th2 cells as determined by analysis of cytokine production. Trial 3 extended the findings of trial 2 in that it was shown that a very low dose of *Solanum* (2 ug) administered orally with ovalbumin was far more superior in generating both local and peripheral antibody and cytokine responses. This trial also demonstrated that 2ug of *Solanum* can enhance immune effector mechanisms in the lung, an example of enhanced mucosal homing. There is no doubt that this extract is truly stimulatory for lymphocytes and has great potential to replace the current mucosal adjuvants that are more toxic in nature. We plan to acquire further data on the mechanism of action and study the enhancing effects in a prototype *Haemonchus* vaccine.

Conclusions

Solanum extracts are very effective in enhancing local and peripheral effector mechanisms towards model protein antigens. They target lymphocytes by enhancing synthesis and secretion of antibodies and cytokines. However our data suggest that the crude extract contains both immunostimulatory and immunosuppressive factors. This theory is based on the fact that a reduction of the dose to as little as 2 ug leads to enhanced responses. It is therefore necessary to fractionate the components for future studies.

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