

CHAPTER I
INTRODUCTION

I. INTRODUCTION

Today's development of novel vaccines stresses the need for edible vaccines that are inexpensive, easily administered and capable of being stored and transported without refrigeration. Without these characteristics developing countries find it difficult to adopt vaccination as the central strategy for preventing their most devastating diseases. A promising approach to inexpensive and effective vaccines is production in plants that are commonly consumed. It has been demonstrated that transgenic plants have the capacity to synthesize and accumulate antigenic proteins that retain the immunological properties of their native counterparts in infectious viruses or bacteria (Arntzen, 1997; Wong *et al.*, 1998). Transgenic plants have some remarkable features that make them particularly well suited for bioproduction of vaccines. These include 1) low production cost, 2) improved reliability, 3) elimination of injections, 4) capacity for the production of multicomponent vaccines, 5) ease of storage, and 6) scalability or the potential for large scale production to world wide markets and populations (Cramer *et al.*, 1999; Richter and Kipp, 1999). Research has been conducted on plants such as maize and soybean for livestock and tomato and potato for human use as a food source for the production and delivery of edible vaccines. However, tobacco provides a better system for initial feasibility studies. Tobacco is the easiest crop to genetically engineer and is widely used to test suitability of plant-based systems for bioproduction of recombinant proteins. In addition, tobacco is an excellent biomass and prolific seed producer, which shortens the time for scaling up (Cramer *et al.*, 1999).

Two major obstacles have been encountered in developing vaccines in plants. First the expression level of foreign antigens tends to be low, and second, co-expression of an adjuvant may be required to facilitate appropriate immune responses. An adjuvant is a substance that enhances the immune response to an antigen with which it is combined. The mechanism by which adjuvants augment the immune response is poorly understood. Their primary effect appears to be the retention of antigen at the inoculation site so that the immunogenic stimulus persists for a longer period of time. Adjuvants also activate macrophages and sometimes have direct effects on lymphocytes. Ricin, a plant

toxin that survives the human digestive process, has been proven to stimulate an immune response to antigens and could therefore serve as a suitable adjuvant.

The research described here forms part of a large multi-institutional project, the overall objective of which is the production in plants of a vaccine that protects against the tropical disease, amebiasis. The goal is to elicit a protective antibody response against the carbohydrate recognition domain of the cell surface lectin of the causative parasite, *Entamoeba histolytica*, via a plant-produced antigen. The success of this project will depend on development of an effective animal model for vaccine studies, demonstration that the CRD antigen can trigger protective immunity, development of plant-based expression systems for high-level antigen/adjuvant production, and identification of effective protein-based adjuvants for co-expression with or fusion to the *E. histolytica* antigen. In the research described here, expression of ricin in tobacco as tested under control of different promoters and the expressed ricin was tested for activity. The future aim is to co-express ricin as adjuvant for a suitable vaccine against amebiasis.