

# Amelioration of the Pulmonary Toxic Effects of 4-ipomeanol in Mice by Fermentation of Mold-damaged Sweet Potatoes

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## Introduction

Stressed sweet potatoes infected with mold (*Fusarium sp.*) produce the furanoterpenoid 4-ipomeanol, which is pneumotoxic to cattle. Mechanical injury, chill injury, chemical injury, or infection with nematodes or fungi will stress sweet potatoes to produce toxic metabolites, which are further metabolized by *Fusarium sp.* The most abundant toxin produced is 4-ipomeanol. Pulmonary cytochrome P450 enzymes oxidize 4-ipomeanol to reactive species that cause pulmonary damage. Most of the pulmonary cytochrome P450 is contained in non-ciliated epithelial cells (Clara cells) that line bronchioles and bronchi. Within 1 day of ingestion, affected cattle develop interstitial pneumonia that causes an acute respiratory distress syndrome (ARDS). This can result in death from asphyxiation.

The risk of ARDS prevents the sweet potato from being used as cattle feed, which is unfortunate since there is an abundance of sweet potato waste in certain regions of the United States. The sweet potato is ranked 7th as a world crop. In 1995 approximately 1.3 billion pounds of sweet potatoes were produced in the United States. North Carolina alone produced 480 million pounds. Nearly 25% of the sweet potatoes harvested (approximately 1.8 million bushels) are culled, and are either dumped in a landfill or spread on crop land. Sweet potatoes have already been shown to have nutritional value equivalent to corn. Since pneumotoxicity excludes the sweet potato from use as a dietary source in cattle, we have begun investigating processing methods that may eliminate the furanoterpenoid toxins. To date our work suggests that simple processing methods may degrade the furanoterpenoids and eliminate pneumotoxicity.

## Materials and Methods

A mouse bioassay is to be utilized to confirm the reduction of toxicity. Intraperitoneal 4-ipomeanol induces pulmonary lesions in mice similar to that seen in cattle. The toxin also is nephrotoxic in male mice. We

have completed a preliminary mouse study in which CD-1 male mice received intraperitoneal synthetic 4-ipomeanol. There were 4 treatment groups (0, 35, 60 and 120 mg/kg body weight), and each group consisted of 5 mice. Within 5 hours of dosing, mice in the high-dose group became progressively dyspneic. By 5 hours post-dosing, 3 high-dose mice died, and the remaining 2 mice were euthanized. The other 3 dose groups were euthanized at approximately 30 hours post-dosing.

Treated mice had significant pulmonary and renal lesions similar to those previously described for 4-ipomeanol toxicity in mice. Lesion severity is dependent upon the dosage and duration of exposure. After 5 hours' exposure, the high dose group had hydrothorax, pulmonary edema, pulmonary vacuolar degeneration of the bronchial and bronchiolar epithelium, and renal tubule degeneration. After 30 hours' exposure, the middle and low-dose groups had severe bronchial and bronchiolar epithelial necrosis, and severe acute renal tubular necrosis. Negative control mice had no significant lesions.

We will utilize the 60-mg/kg level in a future mouse study, which will evaluate the efficacy of processing in the detoxification of moldy sweet potatoes. Planned is a study composed of 6 treatment groups, which are to be administered the following: corn oil (negative control), synthetic 4-ipomeanol (positive control), extract from clean non-processed sweet potatoes, extract from mold-damaged non-processed sweet potatoes, and extract from mold-damaged processed sweet potatoes. If processing is shown to detoxify mold-damaged sweet potatoes, we hope to develop a method to utilize these sweet potatoes as an economically viable and safe feed ingredient for cattle.

## Significant References

1. Doster A. R., *et al.* 1978. Effects of 4-ipomeanol, a product of Mold-Damaged Sweet Potatoes, on the Bovine Lung. *Veterinary Pathology*. 15:367-375.
2. Durham S. K., *et al.* 1985. Pulmonary Endothelial and Bronchiolar Lesions Induced by 4-Ipomeanol in Mice. *American Journal of Pathology*. 118:66-75.