Summary of Anthraquinone Literature

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Natural Occurrence and Residues:

Anthraquinone substances are naturally found in a number of plants. Senna (Cassia angustifolia) is used for its laxative properties and its extract contains sennoside B. Daily oral administration of Senna extract at 10 mg/kg to male winstar rats for up to 28 weeks did not produce aberrant crypt foci or malignant tumors in rat colons(Mascolo 1999)

Hydroxyanthraquinones are a naturally occurring component of rhubarb(Xiaoyu 2001) . Analysis of rhubarb indicated that the concentration of physcion, emodin, aloe-emodin and rhein ranged from 0.89 to 1.16; 1.04 to 1.32; 1.10 to 1.13; and 0.93 to 1.02, respectively. The EPA registered biopesticide chitosan (poly-D-glucosamine) induces the plants resistance to defend against pathogenic fungi(Chitosan Fact Sheet 2003). One of the effects of chitosan is the stimulation of anthraquinones(Vasconsuelo 2005). The anthraquinone emodin is present in 17 different plant families comprising 94 plant species. These even include commonly consumed vegetables such as peas , beans and lettuce(Izhaki 2002).
In studying anthracene and phenanthrene in corn and wheat in England(Wild 2005) grown in treated soil, these compounds as well as anthraquinone and hydroxanthraquinone were found in roots, but no detectable levels of either compound were found in the shoots or above ground foliage of plants. In recent studies conducted on 9, 10 anthraquinone with the formulated product Avipel , corn seed was treated at one or five times the anticipated labeled rate. Corn was grown under lights and sampled over time. At 42 days after planting in both the 1X and 5X rates there were no detectable residues of 9,10-anthraquinone in corn shoots (Owen 2005). The IR-4 Project will be conducting GLP field trials in corn to determine residues in 2006 http://www.ir4.rutgers.edu/Food_Use3.cfm?prnum=09613 .

Mutagenicity/Carcinogenicity

Innes et al. (1969 NCI) conducted a subchronic oral study with a daily dosage of 9,10-Anthraquinone at 464mg/kg (1206 ppm) to 18 male and female mice daily from 7 days until 18 months of age and there were an additional 36 control mice . Upon necropsy at 18 months it was determined that there was no significant increase in tumors.

The mutagenic activity of 9, 10- Anthraquinone was evaluated in a GLP Salmonella-Escherichia coli/Mammalian –Microsome Reverse mutation assay in the presence or absence of exogenous enzymes derived from Aroclor induced rat live(Lawlor 1997). Doses ranged from 500 to 15.7 micrograms per plate.There was no positive increase in the number of revertants per plate of any of the tester strains either in the presence or absence of induced rat liver microsomal enzymes(Lawlor 1997).

An additional Reverse mutation Assay was conducted with 1-OH-Anthraquinone (Mecchi 2001). In this study there was a positive increase in the mean number of revertants per plate with tester strain TA1537 in the presence of induced rat liver(S9). No positive increases were observed in the mean number of revertants per plate with any other strain/activation condition combination.

In a study involving measurement of chromosomal abberations in Chinese Hamster Ovary cells(Murli 1997), 9, 10- Anthraquinone was utilized at 0.0166 to 498 microgram/ml. There was a 57% and 9% reduction in the mitotic index of the culture dosed with 166 microgram/ml with and without metabolic activation, respectively.

Functional groups can play an important role in activity. Anthraquinone esters (Jin 2001) and anthracene derivatives have been shown to be anticancer and antitumor agents. Therefore it is critical to consider the form and purity of anthraquinone when interpreting toxicology studies

The National Toxicology Program has conducted a carcinogenicity study on Anthraquinone(http://ntp.niehs.nih.gov/files/494_Web.pdf). The 9, 10 anthraquinone that they used also contained 9-nitroanthracene (C2) and was a form developed by the oxidation of anthracene(AQ-OX). This is a different from the anthraquinone used in Flight Control or Avitect .
The conclusions of the NTP study (page 10) are that there is some evidence of carcinogenicity in male rats and clear evidence of carcinogenicity in female rats. There was clear evidence of carcinogenicity in mice , but decreases in leukemia in male and female rats. On pages 17 to 22 of the NTP report, it outlines the supporting and dissenting opinions about the proper title of the study (to qualify that the study was based on testing anthracene based anthraquinone) . On page 18, Dr Irwin (the lead author from NTP) confirmed that purified anthraquinone was not a mutagen nor was 1 hydroxy anthraquinone, but characterized 1-hydroxyanthraquinone as a carcinogen. The initial decision of the technical review committee was 7 for and 6 against having the title be anthracene based anthraquinones (page 20). There was additional debate about the contaminant at a later meeting and 2 of 7 scientists on the technical review panel voted to retain the title of Anthracene based anthraquinones(page 22). There were additional motions and suggestions for qualifying the type of anthraquinone which were objected too by Dr Irwin so in the end , the fact that the anthraquinone tested was anthracene based was purged from the title, abstract and body of the report.