

**Poisonous Plant Research Laboratory**  
**REGISTRATION NUMBER: 87-G-0001**  
**EXPLANATION FOR THE USE OF ANIMALS LISTED IN COLUMN E**

The 2016 Annual Report of Research Facility for the Poisonous Plant Research Laboratory indicates laboratory mice have been used in studies involving pain and distress for which the use of appropriate anesthetic, analgesic or tranquilizing drugs would have adversely affected the procedures, results or interpretation of the research. Research conducted at this institution involves experiments to determine the toxicity of plant compounds using a median lethal dose (LD<sub>50</sub>) protocol in a laboratory mouse model. In the case of all LD<sub>50</sub> experiments, animals are intensively monitored during the experiment. Previous experience with LD<sub>50</sub> experiments in laboratory mice at this laboratory have provided specific criteria for each plant compound indicating likely death. Laboratory mice meeting these criteria are euthanized to minimize pain and distress. All compounds used with the animals in this report are extremely acute toxins, with death occurring within minutes after IV injection. All animals that survive are quickly euthanized after it is apparent they survived the treatment. Therefore, any pain and distress experienced by the animals is minimized by euthanizing the animals.

Some of the LD<sub>50</sub> experiments performed at the Poisonous Plant Research Laboratory involve the investigation of plant compounds for which the toxicity and mechanism of action is not known. The experimental status of the plant compounds being tested means that little or no information is available regarding possible drug-drug interactions. Co-administration of pain relieving compounds alters their toxicity, and therefore would skew the true toxicity values of the compounds. Therefore, the use of pain relieving substances is avoided in these experiments.

Results from a literature search with PubMed suggests that commonly used pain medications such as opioids [1-3] and non-steroidal anti-inflammatory agents [4-6] may alter the response to bioactive molecules like plant compounds and other drugs. Furthermore, it is well documented that bioactive plant products in Human medicine and Veterinary medicine have the potential for adverse effects [7-9]. Due to the confounding effects of drug-plant compound interactions, pain relieving substances are not routinely administered to laboratory mice in LD<sub>50</sub> experiments.

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8. Singh, D., et al., *Herbs-are they safe enough? an overview*. Crit Rev Food Sci Nutr. 2012. 52:876-98.
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