Extraction and Isolation of Cyclopamine from Veratrum californicum
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Abstract
The Veratrum californicum is a plant native to the western United States that initially received negative publicity as the origin of birth defects in sheep throughout mountainous grazing lands in Idaho. Upon rigorous investigation by researchers at the University of Idaho, it was discovered that the V. californicum produces a potent anti-cancer agent; cyclopamine. Cyclopamine is a steroidal alkaloid that inhibits the hedgehog mechanism, which is integral to cell growth and maturation. Cyclopamina, a craniofacial defect, is commonly observed in newborn infants when the hedgehog mechanism is inhibited by cyclopamine during gestation. In-vivo and in-vitro studies of certain cancer cell lines have shown decreased tumor growth through inhibition of the hedgehog mechanism. Pancreatic, breast, prostate and colorectal cancer cell lines have shown diminished cell proliferation when treated with cyclopamine. The purpose of this study was to extract, isolate, purify, and characterize cyclopamine from V. californicum throughout a seasonal period.

Cancer Applications
Modern medicine has found a positive use for cyclopamine in cancer research. In cancer research, the hedgehog pathway is perceived to be abnormally active, therefore resulting in an overproduction of cells and the creation of a tumor. Studies have shown that cyclopamine, the constituent responsible for cyclopia from the V. californicum, is able to diminish the growth of certain cancers.2 Successful in vitro studies have shown that cyclopamine can diminish the proliferation of breast, prostate, colorectal, pancreatic cell lines and also of melanoma, glioblastoma brain tumors and small cell lung cancers (Fig. 3).2

Future Directions
-Modifying extraction procedures
-Streamlining isolation methods
-Maximizing purified cyclopamine yields
-Establishing ideal characterization processes

Results and Conclusion
-Prior work reports a ~18% yield of cyclopamine from powdered dried V. californicum. The initial extractions yielded 0.14% and 0.26% of combined alkaloid extract. A subsequent duplicate extraction yielded 0.19% crude product.

Analytical Methods
In parallel to the processing of plant material, characterization of a commercial cyclopamine standard was performed. An Infrared spectrum (IR) of the standard was also collected using a Perkin Elmer Spectrum One instrument (Fig. 8). Carbon (Fig. 10) and Proton (Fig. 11) Nuclear Magnetic Resonance (NMR) spectroscopy data were acquired using a Bruker Avance III 600 MHz NMR equipped with a T1X indirect detection probe. Standard was spotted on a silica TLC plate, eluted with 90:10:0.5 Chloroform: MeOH: NH4OH and visualized with 2:1:97 Vanillin: H2SO4: MeOH and heated to 110°C

Acknowledgements
Thanks to Dr. Don Warner, Dr. Eric Brown, Emily Drussel, Petr Malek, Emma Baker, Bryan Martin, Jessica Brookhouse, Erik Sheldon, Wally Baker, and Gerry Chingas. NSF CRIF/MU; NMR Spectrometer (CHE-0639251) Funded by the National Science Foundation REU Program (CHE-1005159).