**Evaluation of Digestive Transformation and Passive Permeability of Plant and Marine Natural Products**

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**Overview**

Pharmaceutical products are subjected to rigorous testing throughout the FDA drug approval process. While many of these drugs originate from natural products, most natural compounds are routinely under-researched and unregulated outside of this pathway. In vitro testing allows compounds to be tested in physiological environments that mimic how drug absorption, distribution, metabolism, and excretion may occur within the body, prior to these products being used in animal or human studies. Leaf and root extracts from *Withania somnifera*, Ashwagandha, were subjected to simulated gastrointestinal environments to see how their metabolomic profiles and passive permeability capabilities may have been affected. Analytical techniques employed include the parallel artificial membrane permeability assay (PAMPA) and metabolomic profiling. Future projects will apply these same techniques to marine natural products.

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**Plant Extraction**

- Certified plant samples purchased from American Herbal Pharmacopeia®
- Leaf and root material pulverized to increase surface area for extraction
- Samples extracted in an analogous method to commercial tincture preparation

**Experimental Design**

- Withaferin A retention time and m/z validated
- Pectinase incubation of root extract
- Assays performed on the natural product and related synthetic compounds using the procedures described above.

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**Assessing Oral Absorption**

- The primary mechanism of oral bioavailability is passive diffusion through the lining of the small intestine.
- PAMPA mimics small intestine absorption. During a 5-hour incubation period, permeable compounds in donor wells pass through an artificial lipid membrane to acceptor wells where they are detected via LC-MS.

**Results: Ashwagandha Root**

Transformation of Root Extract from Enzymatic Incubation:

- Distinctive differences in metabolite profiles are observed after metabolic transformations of extracts.

**Application to Antiviral Marine Natural Products**

- In collaboration with virologists at Virginia Tech and medicinal chemists at George Mason University, UNCW’s Drug DISCOvery group has identified a compound produced by a marine bacteria that inhibits mosquito-borne encephalitis alphaviruses (Venezuelan, eastern and western equine encephalitis viruses – VEEV, EEEV, and WEEV).
- These deadly viruses currently have no FDA-approved antiviral therapeutics.

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**Bioactive Natural Products in Ashwagandha**

- Withaferin A
- Withanolide A
- Anti-inflammatory
- Hepatoprotective
- Anti-drug resistance

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**References**


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**Application to Antiviral Marine Natural Products**

- Homoseongomycin is currently the lead compound identified for treatment of VEEV.
- Homoseongomycin has shown both lack of cytotoxicity and inhibition of viral replication.

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