

USP Dietary Supplements Stakeholder Forum  
Tuesday, May 15, 2018

**Quantitative NMR use for Botanical RS Characterization  
Current Developments and Path Forward**

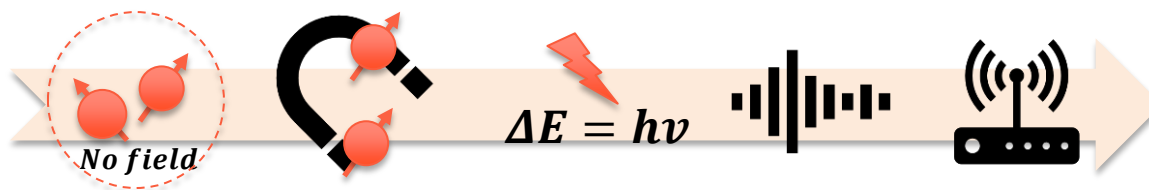
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# What is Nuclear Magnetic Resonance (NMR)?



- NMR traditionally used as a means of structure determination of organic molecules due to exceptional sensitivity to molecule structural fingerprint;
- NMR is also inherently quantitative (qNMR). It is a primary relative methodology suitable for measuring purity of reference materials, as well as determination of residual solvents and impurities;
- Besides small molecules, NMR is increasingly a method of choice for complex mixtures such as botanical extracts common in dietary supplements and herbal medicines, and biopolymers such as complex carbohydrates, polyphenols, peptides and small proteins.



# Research and Innovation (R&I) identified qNMR in 2018



## An area of interest for reference standard development

- Currently USP utilizes quantitative NMR (qNMR) as a standard analysis method in routine Reference Standard (RS) characterization. Additional applications are possible;
- Exploration of qNMR technology aligns with R&I's strategic goal of supporting USP in its development of new tools and methods for quality standards and applications;
- Focus on using **Dietary Supplements/Herbal Medicine** RS as a platform for establishing, troubleshooting and optimizing qNMR procedures and processes for specification assignment.
  - Potential application to small molecules, biologics, excipients and food ingredients.

# Adoption of qNMR as a routine method



## Potential tangible benefits to USP compendial testing

- Utilize qNMR as a standard analysis method in routine RS qualification (material characterization);
- Unbiased evaluation of sample composition and simultaneously quantify multiple compounds to complex natural products (Dietary Supplements/Herbal Medicine);
- Expand USP internal knowledge and characterization of the candidate RS materials;
- Solidify USP's scientific presence in the growing qNMR community.



## The digitalization of NMR spectrum

- Acquire high resolution of qNMR spectra, and implement structural elucidation for obtaining RS structural information;
- Utilize NMR data processing strategies, e.g., peak fitting, data fitting, etc., to match RS structural information and transform spectral information into digitally available data;
- Establish a digital NMR database for USP RS's
- Proof of concept: perform NMR simulation for test samples using the digital database and acquired RS structural information. The aim is to improve efficiency of qNMR analyses and to develop qNMR competitive with LC-based technologies.

## Current internal and external activities

**USP Scientific Fellow:** Dr. Yang Liu, started in January, 2018

- Graduated from Dr. Guido Pauli's lab at the University of Illinois, Chicago;
- Responsibilities include:
  - Conduct existing data/gap landscape analysis, and assist in the preparation of the strategic plan with input from all relevant groups;
  - Development and evaluation of applicable methods and procedures of qNMR for RS evaluation;
  - Feasibility evaluation of including qNMR as routine reference standard analysis for increased efficiency for new and continuous RS assessment;
  - Providing additional verification of material quality and fit for purpose prior to RS release;
  - Develop new methods, compile RS data, resolve inconsistencies.



## Current internal and external activities (continued)

### Project Status

- Review of current RS evaluation process. Discussions with appropriate groups;
- Develop prioritization criteria for method development testing;
- Evaluation of appropriate SW for quantum mechanic approach to data analysis;
- Laboratory work with simple molecules to establish method and process;
- Prioritization of botanicals in process.

# Thank You



**Empowering a healthy tomorrow**