Water NMR: A Noninvasive QA/QC Tool for Biopharmaceuticals

Key Investigator
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Field
Analytical Chemistry, Quality control, Quality Assurance

Technology
Water NMR

Advantages
Enables analysis without opening the vial; no sample prep needed

Adaptable to high-throughput screening

Status
Available for licensing

Patent Status
PCT/US2014/033833
US 10,267,754
US Application 16/369,534

UMB Docket Reference
BY-2013-101, BY-2017-009 & BY-2017-055

External References
Taraban MB, et al (2017) ACS, Epub Apr 25, 2017

Feng Y, et al. (2015) *Chem Comm.* 51, 6804-6807

Taraban MB, et al. (2015) *J Pharm Sci*. 104, 4132-4141.

Summary
Aggregation is a significant problem in biopharmaceutical manufacturing and long-term storage, as aggregated proteins may lose their biological activities, alter concentration, distribution, and kinetics, and aggravate immunogenicity. As the number of biomacromolecule-based, nanoparticle-conjugated, and non-biological complex drugs increases, aggregation in aqueous solutions has become increasingly problematic for the quality control of products. UMB researchers have developed a magnetic resonance relaxometry method, Water NMR, to reliably and non-invasively identify and calculate protein and peptide aggregation in nanoparticle and micron-sized particle-containing products, without opening the vial or storage container. As water is present in most particle pharmaceutical formulations, this technique provides a universally applicable method to assess the degree of aggregation in a sample.

Market
Aggregation can occur at any stage of product development and is one of the biggest hurdles in most processes, including production, administration, shipping, and storage. Technologies for analyzing complex drugs solutions are invasive, requiring the solution to be drawn out of the container or a probe inserted into the solution to obtain quality control measurements. These approaches compromise drug product quality assurance for that specific vial and result in drug waste. The cost of quality assurance/quality control can be significant, especially for complex drugs, where the manufacturing cost also is very high. This noninvasive quality control tool has the potential to greatly reduce manufacturing costs and limit costs and pitfalls of product recalls. WaterNMR is a simple, fast, inexpensive, noninvasive, broadly applicable analytical tool that may be used to screen protein, nanoparticle, and micron-sized particle-containing formulation conditions. Its applications include 1) aiding and testing the stability of biopharmaceutical formulations 2) monitoring biopharmaceuticals during process development, 3) analyzing every vial for product release during manufacturing, 4) monitoring quality during transportation and storage, and 5) ensuring lack of aggregation just before administration. It does not require sample preparation, can be optimized to take less than 1 minute per sample, has a strong and sensitive signal detection, and is adaptable for high-throughput screening. Compared to current methods of detection, it is also cost-effective and reduces drug waste.

Technology
UMB researchers have discovered that the transverse relaxation rate (R_2) of water increases depending on the extent of protein aggregation and the size distribution of the aggregates. Using magnetic resonance relaxometry, this can be measured and used to calculate protein and peptide aggregation in aqueous solutions without opening the vial or storage container. Water NMR allows for noninvasive measurement of NMR signals with a simple benchtop NMR instrument. It has the potential to be used during formulation research, for quality control during production, just before administration, and following long-term storage.

Technology Status
Water NMR has been tested in biological, nanoparticle-containing, and non-biological complex drug solutions, where it was found to quantify a change in concentration of a biopharmaceutical, detect surfactant micellization and monitor protein aggregation. The inventors have also recently shown that Water NMR outperforms conventional techniques such as SEC, DLS, and MFI. Water NMR was most consistently sensitive to increases in soluble and insoluble aggregates, including subvisible particles (Taraban et al. 2017).

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