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TITLE: Real Time in-situ Monitoring of Drug Product Degradation Using Water Proton NMR

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Field
Pharmaceutical

Technology
Technology Key Words

Advantages
NMR
Quality Control
Vaccine
Drug Manufacturing
Freeze-Thaw

Status
Available for licensing

Patent Status
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External Reference

Taraban, M.B., Briggs, K.T., Merkel, P., Yu, Y.B. (2019) Flow Water Proton NMR: In-Line Process Analytical Technology for Continuous Biomanufacturing. Anal. Chem. 91, 13538-13546.

Briggs, K.T., Taraban, M.B., Yu, Y.B., (2018) Water proton NMR detection of amide hydrolysis and diglycine dimerization. Chem. Commun. 54, 7003-7006.

Summary
This technology uses NMR spectroscopy to measure changes in the NMR signal of water, which is sensitive to changes in the chemical environment of the drug molecules it interacts with. This patented method allows for continuous monitoring of drug product degradation.

Market
The monitoring of drug products is essential to ensure their quality and efficacy during their manufacturing, transportation, and storage. Traditional methods for monitoring drug product degradation are time-consuming, labor-intensive, and destructive, often requiring expensive equipment and trained personnel.

However, the non-destructive monitoring of drug products using real-time in situ monitoring of drug product degradation using water proton NMR technology is quick and easy to perform.

Pharmaceutical products that are discarded due to degradation pose a significant financial impact, with up to 50% of pharmaceutical products not used as intended, leading to significant waste and financial loss. It is estimated that the value of pharmaceutical products that are discarded annually due to degradation is up to $15 billion.

Technology
Nuclear Magnetic Resonance (NMR) spectroscopy is a technique that allows us to determine the structure and chemical environment of molecules. The NMR spectrum provides information about the chemical environment and molecular structure of the sample.

In the case of the present invention, the NMR signal of water is used as a reporter for the solutes (APIs and/or excipients) dissolved in it. Water is chosen as a reporter because it has a high concentration in most drug products and its NMR signal is sensitive to changes in the chemical environment of the solutes it interacts with.

The NMR signal of water can be characterized by two relaxation rates, R1 and R2, which are related to different aspects of the water molecule's interactions with its environment. R1, also known as the longitudinal relaxation rate, measures the rate at which the water molecule returns to its equilibrium state after being excited by a radiofrequency pulse. R2, also known as the transverse relaxation rate, measures the rate at which the excited water molecule loses its coherence due to interactions with its environment.

Changes in the chemical environment of the solutes dissolved in water can affect the NMR signal of water, resulting in changes in R1 and/or R2. For example, if an API undergoes chemical degradation, it may release reactive species that can interact with water molecules and affect the NMR signal of water. By measuring the changes in R1 and/or R2 of water over time, it is possible to monitor the chemical stability of the drug product.

The method described in the present invention involves measuring the R1 and/or R2 of water in suspect drug samples. The R1 and/or R2 values of a control sample that has not undergone chemical degradation can be determined by the manufacturer and provided as a reference range. If the measured R1 and/or R2 values of a drug product sample fall outside of the reference range, it is an indication that the sample has undergone chemical degradation and should be rejected.

One advantage of this method is that it is non-destructive and non-invasive, meaning that the drug product sample does not need to be opened or tampered with in any way. This

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makes it a useful tool for monitoring the chemical stability of drug products throughout the manufacturing, transportation, and storage process.

Another advantage is that the method is quantitative, meaning that it provides a numerical value that can be used to assess the degree of chemical degradation that has occurred. This allows for a more accurate determination of whether a drug product sample is acceptable for use or not.

Technology Status

Ready for licensing.

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