Monitoring of Manufacturing Changes and Formulation Excipients on Solid Oral Dosage Forms of Furosemide Using Chemometrics and Laser-Induced Breakdown Spectroscopy (LIBS)

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Background: LIBS, an atomic spectroscopy technique, analyses the elemental content of gaseous plasma discharged from the sample as a result of laser ablation. The study purpose is to evaluate the potential of LIBS to monitor the influence of manufacturing changes and formulation excipients on solid dosage forms of furosemide and assess the utility of chemometrics to determine API and excipient concentrations.

Methods: A LIBS spectrometer equipped with a pulsed Nd:YAG laser was utilized to produce the gaseous plasma at the tablet surface, without sample preparation. Calibration sets prepared under cGMP conditions differing in their avicel/lactose (0-100%) and magnesium stearate excipient compositions were used to monitor the LIBS furosemide signal intensity (e.g. Cl or S). Test sets (50/50 avicel/lactose) were prepared to monitor excipient changes during manufacturing. A chemometrics training set from broadband spectrum (e.g. CN, CH, C2) was developed. Chemometrics was used to evaluate multivariate spectra of the formulation excipients.

Results: The avicel/lactose excipient ratio significantly affected the furosemide LIBS signal. The calibration set containing lactose, had 70% of the furosemide signal intensity of a calibration set containing only avicel. Test formulation sets of 50/50 avicel/lactose were accurately predicted. In addition, chemometrics accurately determined furosemide or magnesium stearate content.

Conclusions: The impact of excipient changes on the LIBS signal can provide a novel approach to monitoring major or minor compositional or manufacturing changes. Chemometrics may assist with the accurate prediction of API and excipient content in drug product formulations demonstrating the potential of LIBS for PAT monitoring of drug products.