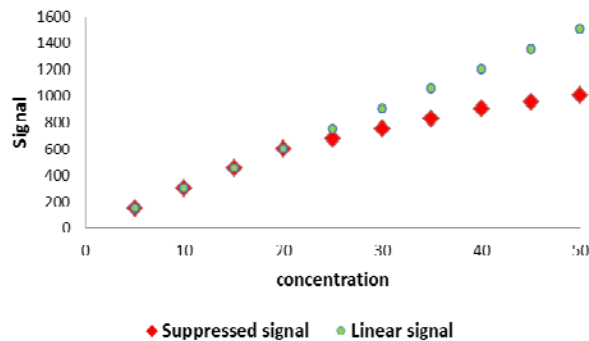


CURRENT SITUATION

Mass spectrometry is an established technology in almost all research fields of the life-sciences. Additionally, it is now becoming a cutting edge technology in the fields of **clinical diagnostics** and **personalized medicine**. A key application is the quantification and/or assessment of fold changes of molecules derived from primary and secondary metabolism.



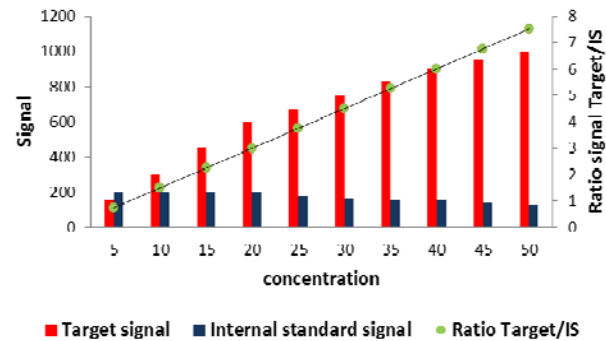
Samples derived from human origin contain a wide variety of metabolites at a wide range of concentrations, additionally the matrix (e.g. blood) is often very complex. Therefore quantification and quality control via mass spectrometric determination of metabolite concentrations for biomedical research is often laborious and inefficient. Through unintentional variations in sample preparation and measurement, the repeatability of analytical results is often compromised. This is also true for samples from cell culture.



As shown above, matrix effects and saturation of the detector disturb quantitative investigations of relevant metabolites. A method to overcome those problems is the addition of stable isotope-labelled internal standards.

SOLUTION

ISOTOPIC solutions offers internal standards produced by *in-vivo* labelling. Using this method, cells are grown on an isotopically enriched ^{13}C growth media. These cells can be harvested and extracted to obtain an isotopically enriched extract of the metabolome that can be exploited as internal standard for a plethora of metabolites.



The principle is very simple: An external calibration as well as the samples are spiked with the same amount of internal standard mixture from **ISOTOPIC solutions**. As the signal of the target molecule and the signal of the internal standard are evenly influenced by matrix effects and saturation of the detector, the ratio of both signals will yield a linear calibration function.

The principles of isotope dilution guarantee a compensation of the error sources. This leads to an improvement in the linearity of the measurement signal and thus a significant improvement of the results.

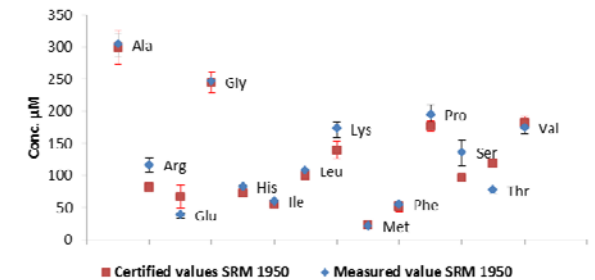
WE OFFER NEARLY THE WHOLE METABOLOME OF YEAST WITH ^{13}C -ISOTOPE LABELLING IN ONE SOLUTION

APPLICATION EXAMPLE

^{13}C -labelled yeast extracts as internal standard for LC-MS/MS based Amino acid quantification in human plasma NIST SRM 1950:

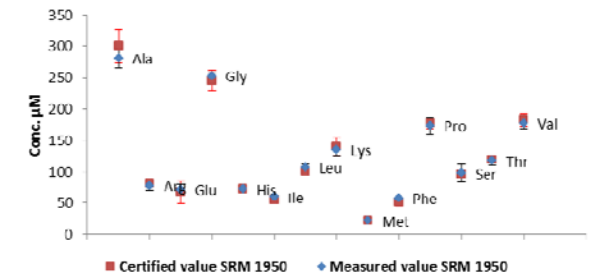
To prove the applicability of *in-vivo* synthesized internal standard extracts for real life clinical samples we used SRM 1950 (Standard Reference Material, metabolites in frozen human plasma). SRM 1950 provides certified concentration values for a variety of metabolites. In this example we covered 14 certified amino acids. We defined the values in the certificate as our target values and evaluated calibrations with and without the internal standard on their applicability and figures of merit.

AA concentration in SRM 1950 (1:1000) without internal standardisation



As depicted above it can be seen that not all amino acids were quantified correctly. In fact for 6 amino acids, the measured and the certified value were not in agreement.

AA concentration in SRM 1950 (1:1000) with internal standardisation



The application of *in-vivo* labelled standards from **ISOTOPIC solutions** resulted in a significant improvement of trueness and precision. All 14 Amino acids have been quantified according to the certificate. [Method: RPLC-MS/MS Agilent: 1290/6490]

FOR MORE INFORMATION VISIT
www.isotopic-solutions.com