Identification and Quantitation of Mixture Components of Formulated Products by NMR

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Introduction

It has become increasingly important for chemists and analysts to be able to test and determine the various components that may be present in mixtures, both qualitatively and quantitatively, to solve a wide variety of scientific problems. NMR spectroscopy has emerged as a powerful, non-destructive analytical technique that provides unique information that may not be readily accessible by other means to support the needs of various industries, including polymers, pharmaceuticals, consumer products, and nutrition, to name a few. Here we present a set of analyses that help in the understanding and characterization of a sample from the beverage industry. We present improved capabilities in DOSY analysis, as well as newly integrated tools for processing, database searching, interpretation, and reporting. These tools are developed in order to make these analyses more accessible to the user by being both quicker and simpler to interpret.

Test Product: Energy Drink

Medicinal Ingredients

Ingredient	Quantity in 250 mL
taurine	1000 mg
glucuronolactone	600 mg
caffeine	80 mg
niacin (niacinamide)	18 mg
pantothenic acid (calcium d-pantothenate)	6 mg
vitamin B6 (pyridoxine HCl)	2 mg
riboflavin	1.65 mg
vitamin B12 (cyanocobalamin)	1 mcg

Non-medicinal Ingredients

carbonated water
sucrose
glucose
Citric acid (sodium citrate)
inositol
flavours
caramel

Medicinal Ingredients in sugar-free

Ingredient	Quantity in 250 mL
taurine	1000 mg
glucuronolactone	600 mg
caffeine	80 mg
niacin (niacinamide)	18 mg
pantothenic acid (calcium d-pantothenate)	6 mg
vitamin B6 (pyridoxine HCl)	2 mg
riboflavin	1.65 mg
vitamin B12 (cyanocobalamin)	1 mcg

Non-medicinal Ingredients in sugar-free

carbonated water
citric acid
inositol
acesulfame k
aspartame
flavors
xanthan gum
caramel
contains a source of phenylalanine

Table 1. Ingredient list of a popular Energy Drink and a Sugar-Free Energy Drink [1].

1D and 2D NMR Analysis of Energy Drinks

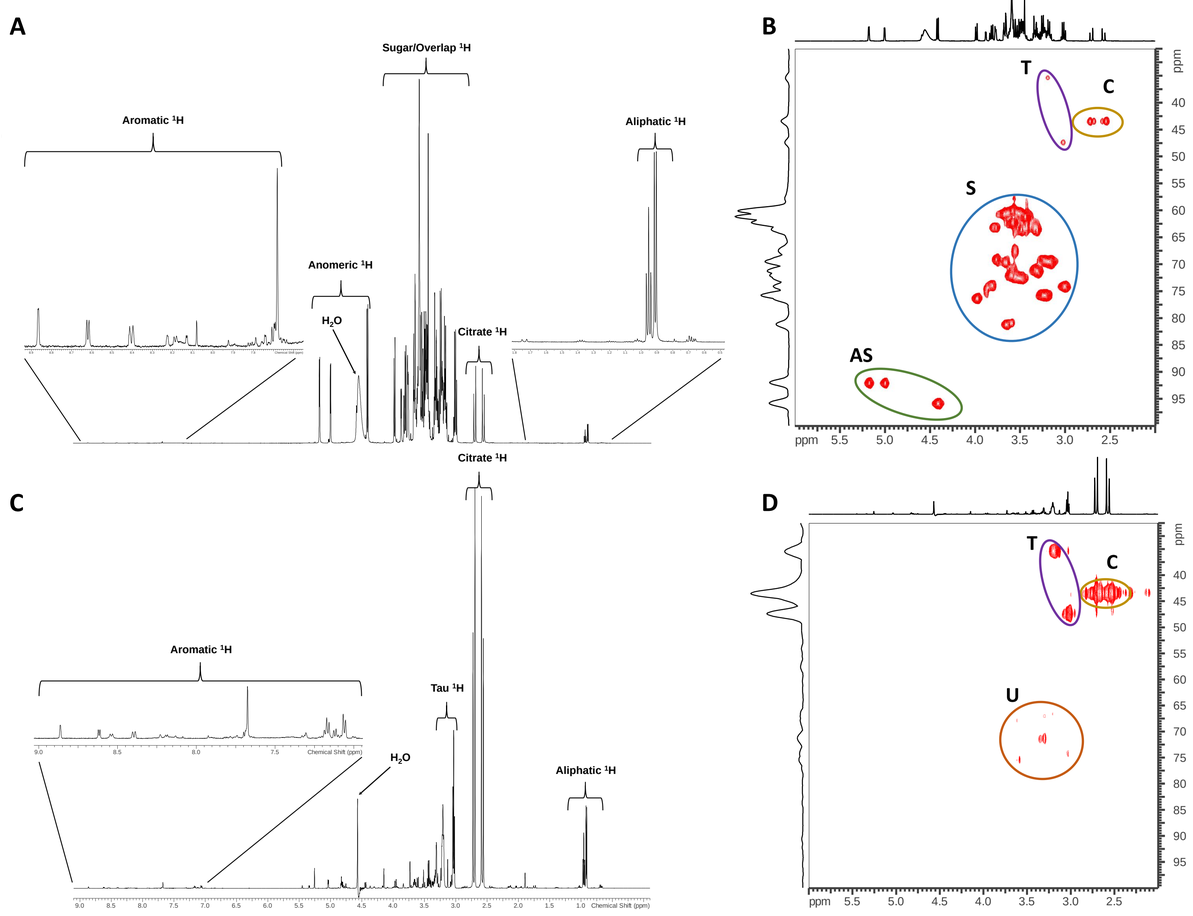

Figure 1. NMR analysis of a commercially available Energy Drink (A & B) and a Sugar-Free Energy Drink (C & D); (A) ^{1}H NMR spectrum with major overlapping functional group ^{1}H signals labelled; (B) the corresponding ^{1}H-^{13}C HMQC spectrum, highlighting the main types of components present; (C) ^{1}H NMR spectrum of the Sugar-Free Energy Drink with the major functional groups labelled (less overlap with the elimination of ^{1}H signals from sugars); (D) corresponding ^{1}H-^{13}C HMQC spectrum highlighting the main types of components present [1].

The increase in ^{13}C chemical shift dispersion allows for the direct assignment of taurine (Tau) based on chemical shift knowledge which can be related to the ^{1}H NMR of the sugar-free drink, however it still substantially overlaps with the sugar ^{1}H signals in (A). Symbols: citrate (C), taurine (T), overlapping sugars (S), Anomeric sugar signals (AS), trace unknowns (U). Note that complete identification of all mixture constituents by these techniques alone may not be possible, due to proprietary information and ambiguous ingredients, such as "flavors" which likely give rise to the aliphatic ^{1}H signals [1] and may require additional resources such as comprehensive database searching/matching.

Diffusion Ordered Spectroscopy (DOSY)

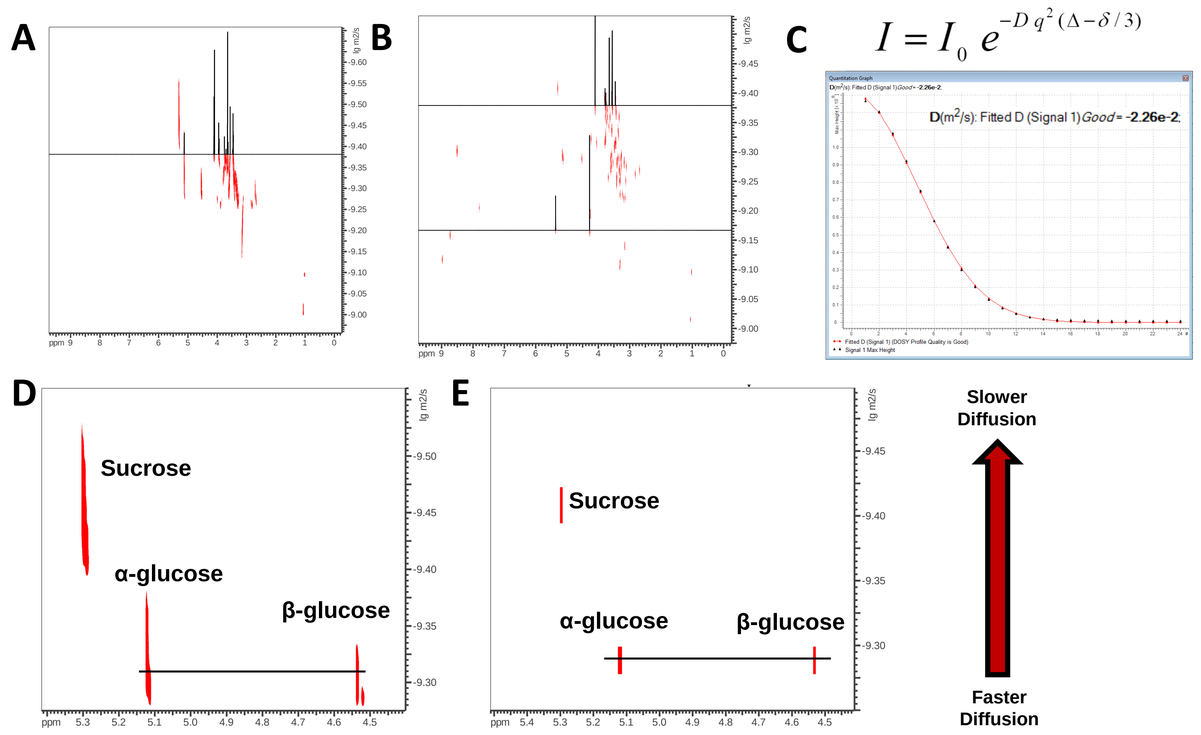

Figure 2. DOSY Analysis of Energy Drink acquired using parameters described elsewhere [2]; (A) a standard DOSY contour plot that contains substantial overlap in the diffusion dimension with a 1D cross section slice displayed at a specific D coefficient; (B) a DOSY transformation performed after peak fitting and deconvolution to decrease overlap and increase dispersion; (C) a "D" coefficient quality plot of the anomeric ^{1}H signals highlighting the resulting D coefficient and that the Δ (diffusion time) & δ (length of gradient) were accurately applied; (D,E) DOSY plots of the anomeric ^{1}H region highlight that sucrose diffuses more slowly than glucose and corresponding "slice extraction" can reveal single component spectra. Note that the Peak Fitted contour plot results in less overlap and more accurate "D" coefficient determination.

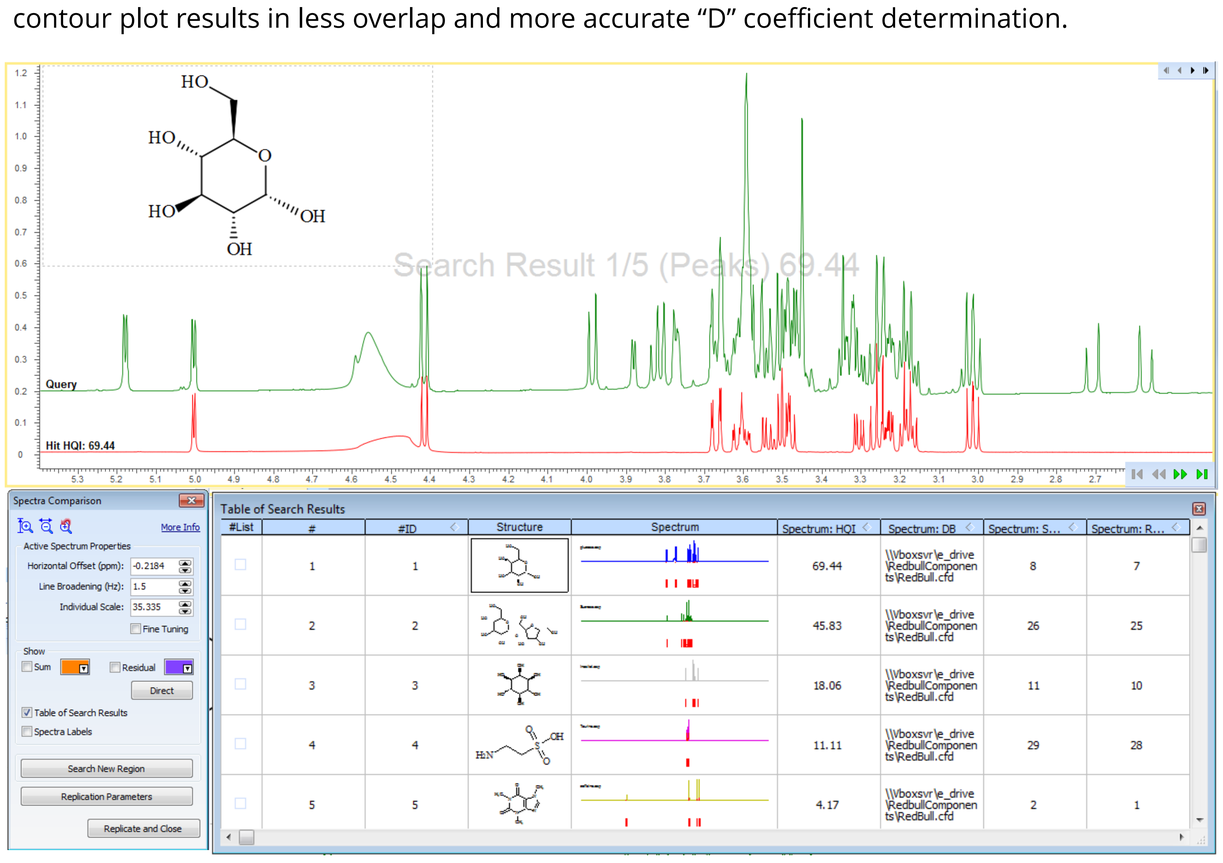

Figure 3. Highlights of the newly developed mixture search functionality that allows for a seamless workflow to quickly identify, quantify, and verify components likely present in the mixture. Upon completion of a search, the results are automatically tabulated and residual curves are extracted for additional analysis if required. This tool aids in the analysts' workflow, allowing for fast and efficient component determination and reporting of results.

Conclusions

Multiple NMR spectroscopic techniques have been applied to effectively determine the number, type, and quantity of components of a test product without requiring data from additional analytical techniques. In particular, the updated mixture searching and database integration allows for rapid identification of mixture constituents through semi-automated tools and manual analysis. Modernized software improves workflows and provides the capability to rapidly determine constituents in a complex mixture, moving from data collection to reporting in a rapid fashion.

Acknowledgements

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PHARMASEA

References

[1] Simpson *et al.*, *J. Chem. Edu.* **2009**, 86, 360. [2] Wu *et al.*, *J. Magn. Reson. A* **1995**, 115, 123.

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