Frontiers in Engineering
ISSN Print: 3104-4298
ISSN Online: 3104-4301
CD ISSN: 3104-431X
https://doi.org/10.63313/FE.9025

Quantitative 2D HSQC with Non-Uniform Sampling for the Determination of Paracetamol in Compound Preparations

Chang Zhang. Shoufeng Wang*
Sichuan University of Science & Engineering, Zigong 643000, China
*Corresponding author. E-mail address: shoufeng.wang@163.com (S. Wang).

How to cite this paper: Zhang, C., & Wang, S. (2026). Quantitative 2D HSQC with non-uniform sampling for the determination of paracetamol in compound preparations. Frontiers in Engineering, 2(2), 1–11. ISSN Print: 3104-4298, ISSN Online: 3104-4301.
https://doi.org/10.63313/FE.9025
Published: 2026-10-16

Copyright © 2026 by author(s) and Erytis Publishing Limited.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/
CC BY 4.0

Abstract

Paracetamol (APAP) is a common active ingredient of compound cold preparations, and its routine one-dimensional 1H-NMR quantification is compromised by overlap with the aromatic signals of co-formulated caffeine and chlorpheniramine. A rapid method based on two-dimensional 1H−13C HSQC combined with non-uniform sampling (NUS) was established: with DMSO-d6 as the extraction solvent and 1,4-dinitrobenzene (δH = 8.45 ppm) as internal standard, the cross-peaks at δH/δC = 7.33/121.26 and 6.67/115.44 ppm serve as two independent quantitative channels, requiring neither chromatographic separation nor an analyte-matched reference standard. Under the optimised conditions the acquisition time per sample was 26′35″, one quarter of that of uniformly sampled HSQC (108′25″). The method was linear over 0.625–40.0 g·L−1 (R2 = 0.9999) with LOD 0.397 g·L−1 and LOQ 1.20 g·L−1; precision was 0.5 %–0.74 % RSD, 48 h stability 0.83 % RSD, and recovery 98.15 %–99.89 %. The results for ten commercial preparations (capsules, tablets and a granule) deviated from the pharmacopoeial HPLC method by less than 4 % — Bland–Altman bias +0.93 % with 95 % limits of agreement of −2.1 % to +3.9 % and no significant systematic bias (paired t-test, p = 0.09) — and from the label claims by less than ±2 %; the lowest content verified experimentally was 1.2 % w/w, and lower contents were not examined and should not be extrapolated. The method is simple to operate, determines APAP in compound preparations rapidly and accurately, and provides a reference for the quality control of manufacturers and regulatory authorities.

Keywords

Quantitative NMR; 2D HSQC; Non-uniform sampling; Paracetamol; Compound preparations; Method validation

1. Introduction

Paracetamol (APAP) is one of the most widely used antipyretic-analgesics and the core active of compound cold preparations, present in the majority of marketed

capsules, tablets and granules. APAP is safe at therapeutic doses, but overdose causes severe liver injury, and it has become the leading drug-induced cause of acute liver failure [1]. Its content is strictly controlled in China: Part I of the Chinese Pharmacopoeia (2020 edition) specifies explicit content limits for APAP-containing compound cold preparations — for example, Compound Ganmaoling Granules must contain 90.0 %–110.0 % of the labelled amount of APAP per sachet [2]. In these preparations APAP coexists with caffeine, chlorpheniramine maleate and vitamin C in a complex matrix, so a simple, rapid and accurate determination of APAP is of practical significance for manufacturers and regulatory authorities.

High-performance liquid chromatography (HPLC) is the most common technique for the determination of APAP [2-3]. In addition, ultraviolet spectrophotometry is simple to operate and widely available, and titration, as a classical volumetric method, is suited to the assay of high-content raw materials. Chromatographic methods are specific and sensitive, but they consume analyte-matched reference standards of established purity, involve time-consuming sample preparation and separation, and identify the analyte by retention time alone, providing no structural information on the substance measured. In recent years quantitative NMR (qNMR) has become an important analytical tool [4-6], widely applied in food, natural-product and pharmaceutical analysis. Because the area of a resonance is proportional to the number of nuclei contributing to it, quantification can be performed against a single certified internal standard rather than a matched standard of the analyte itself; the measurement is non-destructive and confirms the assignment of the integrated signal as it quantifies [5,7]. Instrumental reproducibility and quantitative reliability are the principal advantages of qNMR over chromatographic techniques.

These advantages of one-dimensional qNMR, however, do not transfer automatically to compound preparations: several actives are present in the same formulation, their aromatic proton signals are close together and cannot be baseline-resolved in a one-dimensional 1H spectrum, and direct integration necessarily introduces a systematic error. Adding a second frequency dimension addresses the problem at its origin: a 1H–13C HSQC experiment spreads the crowded proton spectrum over the much wider 13C chemical-shift range, and the quantification of individual compounds in mixtures through HSQC cross-peaks has precedents [8-9]. What prevents routine use is the acquisition time. Non-uniform sampling (NUS), which records only a subset of the indirect-domain points and reconstructs the spectrum with algorithms that exploit the sparsity of the frequency-domain signal [10-12], offers a route towards routine two-dimensional quantification; yet the trade-off between sampling density, indirect-domain points and quantitative accuracy has not been systematically mapped. Here, using ten commercial compound cold preparations, we establish an APAP quantification method based on 2D HSQC with NUS, validate it according to ICH Q2(R2) [13], and compare it with the

pharmacopoeial HPLC method, providing a reference for the rapid determination of APAP in compound preparations.

2. Experimental

2.1. Instrumentation and Reagents

NMR spectra were acquired on a Bruker Avance III HD 600 MHz spectrometer equipped with a 5 mm BBO probe (Bruker, Germany). HPLC analysis was performed on an Agilent 1100 system with an Agilent ZORBAX Eclipse XDB-C18 column (250 × 4.6 mm, 5 μm). Auxiliary equipment included Eppendorf pipettes, a Vortex 3000 mixer (WIGGENS, Germany), a JOYN-30AL ultrasonic bath and a TG-18 centrifuge (Shuke, Sichuan).

NMR solvents DMSO-d6 (99.9 % D), CDCl3 (99.8 % D), C3D6O (99.8 % D) and D2O (99.9 % D) were obtained from Shanghai Titan. Paracetamol (C8H9NO2, 99.0 %) and 1,4-dinitrobenzene (C6H4N2O4, 99.0 %) reference standards were purchased from Shanghai Aladdin or Shanghai Titan. Methanol was of HPLC grade, and water was prepared on a Milli-Q Academic system.

2.2. Samples

Ten commercial compound preparations (A–J) were purchased from pharmacies and comprised capsules (A–E: Gan-te-ling, Jin-gan, Gan-yu, Vitamin C Yinqiao and Compound Ganmao-ling Capsules), tablets (F–I: Refined Yinqiao Jiedu, Compound Ganmao-ling, Vitamin C Yinqiao and Gan-tong Tablets) and a granule (J: 999 Compound Ganmao-ling Granule), all produced by pharmaceutical manufacturers. Label claims and dosage forms are listed in Table 3.

2.3. Sample Preparation

Powdered tablets or capsule contents (30.0 mg, or 50.5 mg for granule J) were dissolved in 900 μL DMSO-d6 under ultrasonication (250 W, 40 kHz) and centrifuged (5000 r/min, 20 min). A 540 μL aliquot of the supernatant was transferred to a 5 mm NMR tube and mixed with 60 μL of the 1,4-dinitrobenzene internal standard solution (50.0 g·L−1) on a vortex mixer. Three technical replicates were averaged for each sample.

2.4. HSQC(NUS) Acquisition

Spectra were acquired with the hsqcetgp pulse sequence with FnTYPE set to non-uniform sampling, O1P = 5.269 ppm, SW(F2) = 9.8 ppm, SW(F1) = 165 ppm, TD(F2) = 1024 and RG = 203, at 298 K. TD(F1) and NS were set to 256 and 16 respectively following the optimisation described in Section 3.2, and the NUS ratio was 25 %. Reconstruction of the non-uniformly sampled data followed the compressed-sensing procedure implemented in the spectrometer software. All acquisition and processing parameters that influence cross-peak intensity —

polarisation-transfer delays, spectral windows, receiver gain and reconstruction settings — were held constant for calibration standards, recovery samples and commercial preparations alike, so that any systematic response factor is absorbed into the calibration.

2.5. Reference HPLC Method

Paracetamol was determined by HPLC following the method for paracetamol effervescent tablets in Part II of the Chinese Pharmacopoeia (2020 edition) [2] and the method of Liu et al. [3]. Chromatographic conditions: Agilent ZORBAX Eclipse XDB-C18 column (250 mm × 4.6 mm, 5 μm); methanol-water (40:60) as the mobile phase; detection at 254 nm; column temperature 25 °C; flow rate 1.0 mL·min−1; injection volume 20 μL. A reference stock was prepared by dissolving 18.0 mg of APAP reference standard in methanol to 10 mL and was serially diluted to 0.00350, 0.0300, 0.0500, 0.110, 0.220, 0.450 and 0.900 g·L−1; regression of peak area against concentration gave the calibration curve Y = 43155X + 216.63 (R2 = 0.9995). For sample preparation, 5.6 mg of powdered tablets or capsule contents (50.5 mg for granule J) was dissolved in 1 mL of methanol in a 2 mL tube; a 10 μL aliquot was diluted to 1 mL with methanol (100-fold) and filtered through a 0.2 μm membrane before injection. For the recovery test, aliquots of a Gan-yu Capsule sample of known content were spiked with 10, 30 and 50 μL of the 0.900 g·L−1 working solution (0.009, 0.027 and 0.045 mg of APAP) at low, medium and high levels, each in triplicate; the measured recoveries ranged from 98.03 % to 101.52 % with RSDs of 0.55 %–1.56 %.

3. Results and Discussion

3.1. Choice of Quantitative Cross-Peaks and Extraction Solvent

Paracetamol gives five 1H signals, at δH = 1.98, 6.67, 7.33, 9.44 and 9.86 ppm. The signals at 9.44 and 9.86 ppm arise from the amide and phenolic protons; both broaden with solvent composition and concentration and are unsuitable for integration. The methyl signal at 1.98 ppm is overlapped by baseline structure from excipients. The two aromatic signals at 6.67 and 7.33 ppm each show a single, well-resolved HSQC correlation, to carbons at δC = 115.44 and 121.26 ppm respectively, and were therefore used as quantitative peaks. 1,4-Dinitrobenzene gives a single aromatic resonance at δH = 8.45 ppm (δC = 125.59 ppm) that is clear of all analyte and co-formulant signals, and was used as internal standard (Figure 1). The value of the second dimension is evident from the proton shifts alone. The quantitative peak at δH = 7.33 ppm lies 0.23 ppm from the chlorpheniramine signal near δH = 7.10 ppm and 0.19 ppm from the caffeine signal near δH = 7.52 ppm — 138 Hz and 114 Hz respectively at 600 MHz — so that the three would not be baseline-resolved in a one-dimensional spectrum at the concentrations present in these preparations. Distributing the same signals over the 13C dimension separates

them, and both APAP cross-peaks are free of interference in the two-dimensional plane (Figure 1). Detection remains on the proton channel, so sensitivity is governed by the proton rather than by the carbon nucleus, and the second dimension serves to separate rather than to detect.

DMSO-d6 was selected as the extraction and NMR solvent: CDCl3 did not extract paracetamol from the formulation matrix, while C3D6O and D2O gave lower extraction efficiencies.

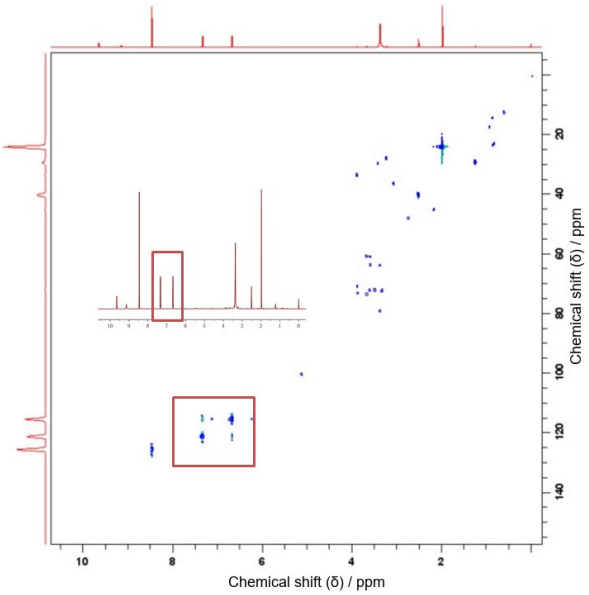


Figure 1. HSQC(NUS) spectrum of a representative compound preparation, showing the cross-peaks of paracetamol at (δH/δC) 7.33/121.26 and 6.67/115.44 ppm and the 1,4-dinitrobenzene internal standard at (δH/δC) 8.45/125.59 ppm.

3.2. Optimisation of NUS Acquisition Parameters

Three parameters govern both acquisition time and the fidelity of the reconstructed spectrum: the NUS ratio, the number of time-domain points in the indirect dimension TD(F1), and the number of scans NS. Each was varied while the others were held constant.

- NUS ratio. At TD(F1) = 128 and NS = 16, raising the NUS ratio from 25 % to 100 % changed the cross-peak integrals at δH = 6.67 and 7.33 ppm by less than the run-to-run scatter, while the acquisition time increased from 13′56″ to 54′23″ (Table 1, Figure 2). A ratio of 25 % was adopted.

- TD(F1). At NS = 16 and NUS = 25 %, increasing TD(F1) from 128 to 2048 raised the integrals up to TD(F1) = 256, after which they remained constant, whereas the acquisition time continued to increase steeply (Table 2). TD(F1) = 256 was adopted.

- NS. Beyond NS = 16 the integrals were stable while the acquisition time continued to grow. NS = 16 was adopted.

Under these conditions the acquisition time per sample was 26′35″, against 108′25″

for the uniformly sampled experiment at the same TD(F1), a four-fold saving. The reconstructed cross-peak volumes agreed with those of the fully sampled reference to within 1.5 %, comfortably inside the 2 % RSD budget expected for content-uniformity work [13] (Figure 2).

The insensitivity of the integrals to sampling density deserves comment, because it is what makes the four-fold saving quantitative rather than merely cosmetic. Sparse sampling degrades an indirect dimension in two ways: it distorts the lineshape, and it distributes reconstruction artefacts across the spectrum. Both effects are governed by the ratio of sampled points to the number of genuine peaks, not by the sampling percentage alone. The aromatic region of these preparations contains a small number of well-separated cross-peaks, so that 25 % of the Nyquist grid still supplies many more points than the signal has degrees of freedom, and the reconstruction converges on volumes matching the fully sampled data. The corollary is that 25 % is a property of this spectrum and not a universal constant: a matrix with substantially higher cross-peak density, a crude plant extract or a biofluid for instance, would require a higher minimum density, and the optimum should be re-established rather than transferred.

Table 1. Effect of the NUS ratio on acquisition time at TD(F1) = 128, NS = 16.

NUS / %	Acquisition time
25	13′56″
50	27′25″
75	40′54″
100	54′23″

Table 2. Effect of TD(F1) on acquisition time at NS = 16, NUS = 25 %.

TD(F1)	Acquisition time
128	13′56″
256	27′26″
512	54′30″
1024	108′54″
2048	218′45″

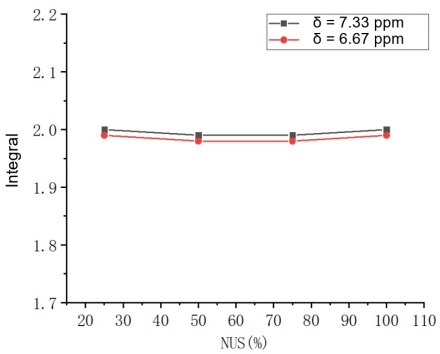


Figure 2. Effect of the NUS ratio on the integrals at δH = 7.33 and 6.67 ppm (TD(F1) = 128, NS = 16): the integrals remain stable between 25 % and 100 %, while the acquisition time rises from 13′56″ to 54′23″.

3.3. Calibration, Validation and the Basis of Quantification

Two parallel calibration curves were constructed over 0.625–40.0 g·L−1, one for each quantitative cross-peak:

- δH = 7.33 ppm: Y = 0.2033 X − 0.0114, R2 = 0.9999
- δH = 6.67 ppm: Y = 0.2041 X − 0.0162, R2 = 0.9999

Limits of detection and quantification, calculated as 3.3σ/S and 10σ/S (σ being the residual standard deviation of the fitted curve and S its slope), were 0.397 and 1.20 g·L−1 at δH = 7.33 ppm, and 0.541 and 1.64 g·L−1 at δH = 6.67 ppm. Precision was assessed in two ways that answer different questions: seven replicate measurements of a single sample solution gave RSD = 0.5 %, describing instrument and reconstruction repeatability, while five independent preparations of a homogeneous batch gave RSD = 0.74 %, describing the sample-preparation step. Stability was confirmed by re-analysing the same solution at 0, 2, 4, 8, 12, 24 and 48 h (RSD = 0.83 %), so that overnight queues do not compromise results. Recovery, determined by adding 100 µL of a 100 g·L−1 working solution (10 mg of APAP) to three aliquots of a preparation of known content, was 98.15–99.89 % (mean 98.74 %, RSD = 1.00 %), within the 98–102 % range expected of a pharmacopoeial assay.

It should be stated plainly that this is a relative quantification. An HSQC cross-peak volume is not proportional to the number of contributing nuclei in the way that a directly detected 1H integral is: it depends additionally on the efficiency of polarisation transfer, on the one-bond coupling constant of the particular C-H pair, and on relaxation during the transfer and acquisition periods. Different chemical environments therefore give different response factors, and two peaks of the same molecule need not yield equal volumes. The procedure accommodates this without requiring the individual factors to be known. The analyte volume is measured relative to a certified internal standard, and the ratio is converted to concentration through an external calibration prepared from the same analyte under identical acquisition conditions. Because every parameter that affects transfer efficiency was held constant across standards and samples (Section 2.4), the response factor is reproducible and is absorbed into the calibration slope. What the method requires is therefore not absolute proportionality but a stable, reproducible response, which is what the calibration, recovery and stability data above establish.

The two quantitative channels provide an internal check on that stability. Their calibration slopes differ by only 0.4 % (0.2033 against 0.2041), and across the ten commercial preparations the contents derived from the two cross-peaks agreed to within 0.9 % (paired differences averaging +0.09 % with 95 % limits of agreement of ±0.65 %). A response factor established for one aromatic C-H pair thus applies to the other, and the measurement is not being distorted by a peak-specific artefact.

3.4. Analysis of Commercial Compound Preparations

Ten preparations spanning all three dosage forms were analysed (Table 3, Figure 3). Relative deviations from the pharmacopoeial HPLC method were all below 4 % (range 0.05–3.5 %), and the HSQC(NUS) results agreed with the label claims to within ±2 %. The largest deviation from HPLC occurred for the granule (J, 3.5 %), which also had by far the lowest analyte content (label claim 1.2 %) and consequently the smallest cross-peak volumes; a larger sample mass was taken for this formulation (50.5 mg against 30.0 mg) to compensate, and the agreement nonetheless remained within the acceptance level.

To place the agreement on a formal footing, the paired results were analysed by the Bland–Altman method (Figure 4). The mean relative difference (bias) of the 7.33 ppm channel against HPLC was +0.93 %, with a 95 % confidence interval of −0.16 % to +2.02 % that includes zero; a paired t-test against zero gives t = 1.92 (df = 9, p = 0.087), so no significant systematic bias between the two methods could be detected. The 95 % limits of agreement, −2.07 % to +3.92 %, lie inside the ±4 % acceptance band, and the differences showed no dependence on analyte content (r = −0.26, p = 0.47): the agreement is uniform from the granule at 1.2 % w/w to the capsules above 60 % w/w. The second cross-peak gives an equivalent picture (bias +0.84 %, limits of agreement −2.39 % to +4.06 %, p = 0.14), and against each other the two channels differ by only +0.09 % with limits of agreement of ±0.65 %.

Table 3. Paracetamol contents of ten compound preparations determined by HSQC(NUS) and HPLC.

No.	Medicine	Dosage form	Label / %	HSQC(NUS) at 7.33 ppm / %	HSQC(NUS) at 6.67 ppm / %	HPLC / %	Relative deviation / %
A	Gan-te-ling Capsule	Capsule	25.0	24.81	24.78	24.54	1.2
B	Jin-gan Capsule	Capsule	55.5	55.06	54.89	55.03	0.05
C	Gan-yu Capsule	Capsule	62.5	62.29	62.12	62.26	0.05
D	Vitamin C Yinqiao Capsule	Capsule	31.8	31.75	31.55	30.70	3.4
E	Compound Ganmao-ling Capsule	Capsule	16.8	16.75	16.75	16.70	0.3
F	Refined Yinqiao Jiedu Tablet	Tablet	17.6	17.28	17.28	17.51	1.3
G	Compound Ganmao-ling Tablet	Tablet	18.26	18.17	18.17	18.16	0.05
H	Vitamin C Yinqiao Tablet	Tablet	21.0	21.00	20.96	20.88	0.7
I	Gan-tong Tablet	Tablet	39.06	38.83	38.74	38.23	1.6
J	999 Compound Ganmao-ling Granule	Granule	1.2	1.19	1.20	1.15	3.5

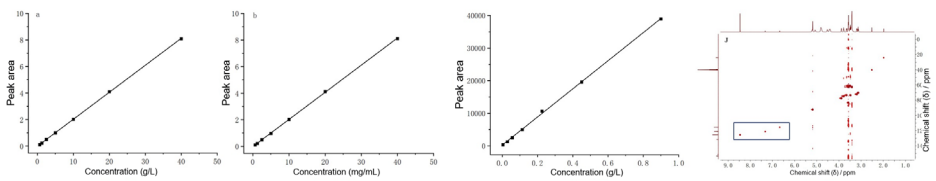


Figure 3. Cross-validation against HPLC: (left) HSQC(NUS) calibration curves of the paracetamol reference standard at δH = 7.33 and 6.67 ppm; (middle) HPLC calibration curve of the reference standard; (right) representative HSQC(NUS) spectrum of a commercial

preparation (sample J, 999 Compound Ganmao-ling Granule). Relative deviations between the two methods for all ten preparations are given in Table 3.

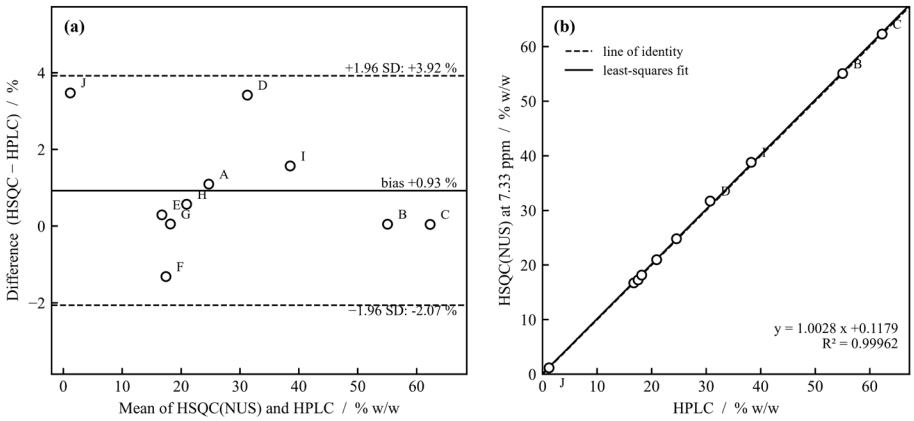


Figure 4. Method comparison between HSQC(NUS) (7.33 ppm channel) and HPLC for the ten preparations of Table 3. (a) Bland–Altman plot of the relative difference against the mean of the two methods; the solid line marks the bias (+0.93 %) and the dashed lines the 95 % limits of agreement (−2.07 % to +3.92 %). (b) HSQC(NUS) results against the HPLC reference, with the line of identity (dashed) and the least-squares fit y = 1.0028x + 0.1179 (R^2 = 0.99962).

3.5. Scope and Limitations

Three limitations should be noted. First, all measurements were made on one 600 MHz spectrometer in a single laboratory, and inter-laboratory reproducibility was not assessed; transfer of the protocol requires the calibration to be re-established on the receiving instrument. Second, the optimum NUS ratio is tied to the cross-peak density of the spectrum, as argued in Section 3.2, and should be re-determined for matrices whose two-dimensional spectra are substantially more crowded. Third, only paracetamol was quantified; extension to other actives in the same preparations, caffeine for instance, would require identifying interference-free cross-peaks and re-establishing the calibration, but not a change of principle.

4. Conclusions

A 1H–13C HSQC experiment with non-uniform sampling determines paracetamol in commercial compound preparations without chromatographic separation and without an analyte-matched reference standard. The second frequency dimension removes the overlap with caffeine and chlorpheniramine that prevents direct one-dimensional 1H integration, and non-uniform sampling reduces the acquisition to 26′35″, a quarter of the uniformly sampled experiment, without measurably altering cross-peak volumes. Calibrated against a certified internal standard, the method is linear over 0.625–40.0 g·L−1 (R2 = 0.9999), precise to better than 1 % RSD, accurate to within 4 % of the pharmacopoeial HPLC method across ten preparations with no statistically significant bias (Bland–Altman limits of agreement −2.1 % to +3.9 %) and within ±2 % of their label claims, and the two independent

quantitative cross-peaks agree with each other to within 0.9 %. The lowest content verified experimentally was 1.2 % w/w; below this level the method was not tested and should not be presumed valid. Because the response of a cross-peak depends on the transfer efficiency of the individual C-H pair, the procedure is explicitly a relative one, calibrated under fixed acquisition conditions; within that constraint it is rapid, simple and specific, and provides a valuable reference for the quality control of high-dose actives in compound preparations.

Declarations

Author contributions: C.Z. performed the NMR and HPLC experiments, analysed the data and drafted the manuscript; S.W. designed and supervised the study and revised the manuscript; both authors discussed the results and approved the final manuscript.

Funding: This research received no external funding

Data availability: The NMR and HPLC data supporting the findings of this study are available from the corresponding author on reasonable request.

Conflicts of interest: The authors declare no competing financial interests.

References

[1] Larson, A.M., Polson, J., Fontana, R.J., et al. (2005) Acetaminophen-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study. Hepatology, 42, 1364-1372. https://doi.org/10.1002/hep.20948

[2] Chinese Pharmacopoeia Commission (2020) Pharmacopoeia of the People's Republic of China, 2020 Edition, Parts I and II. China Medical Science Press, Beijing.

[3] Liu, M.H., Zhang, Y., Li, C.H., et al. (2019) Determination of Paracetamol in Compound Ganmao-ling by HPLC. Chinese Journal of Pharmaceutical Analysis, 39, 912-918.

[4] Pauli, G.F., Jaki, B.U. and Lankin, D.C. (2005) Quantitative 1H-NMR: Development and Potential of a Method for Natural Products Analysis. Journal of Natural Products, 68, 133-149. https://doi.org/10.1021/np0497301

[5] Holzgrabe, U., Deubner, R., Schollmayer, C. and Waibel, B. (2005) Quantitative NMR Spectroscopy—Applications in Pharmaceutical Analysis. Journal of Pharmaceutical and Biomedical Analysis, 38, 806-812. https://doi.org/10.1016/j.jpba.2005.01.050

[6] Bharti, S.K. and Roy, R. (2012) Quantitative 1H NMR Spectroscopy. TrAC Trends in Analytical Chemistry, 35, 5-26. https://doi.org/10.1016/j.trac.2012.02.007

[7] Pauli, G.F., Chen, S.N., Simmler, C., et al. (2014) Importance of Purity Evaluation and the Potential of Quantitative 1H-NMR as a Purity Assay. Journal of Medicinal Chemistry, 57, 9220-9231. https://doi.org/10.1021/jm500734a

[8] Palmer, A.G., Cavanagh, J., Wright, P.E. and Rance, M. (1991) Sensitivity Improvement in Proton-Detected Two-Dimensional Heteronuclear Correlation NMR Spectroscopy. Journal of Magnetic Resonance, 93, 151-170. https://doi.org/10.1016/0022-2364(91)90036-S

[9] Hu, K., Westler, W.M. and Markley, J.L. (2011) Simultaneous Quantification and Identification of Individual Chemicals in Metabolite Mixtures by Two-Dimensional Extrapolated Time-Zero 1H−13C HSQC (HSQC0). Journal of the American Chemical Society, 133, 1662-1665. https://doi.org/10.1021/ja1095304

[10] Hyberts, S.G., Milbradt, A.G., Wagner, A.B., Arthanari, H. and Wagner, G. (2012) Application of Iterative Soft Thresholding for Fast Reconstruction of NMR Data

Non-Uniformly Sampled with Multidimensional Poisson Gap Scheduling. Journal of Biomolecular NMR, 52, 315-327. https://doi.org/10.1007/s10858-012-9611-z

[11] Mobli, M. and Hoch, J.C. (2014) Nonuniform Sampling and Non-Fourier Signal Processing Methods in Multidimensional NMR. Progress in Nuclear Magnetic Resonance Spectroscopy, 83, 21-41. https://doi.org/10.1016/j.pnmrs.2014.09.002

[12] Kazimierczuk, K. and Orekhov, V.Y. (2011) Accelerated NMR Spectroscopy by Using Compressed Sensing. Angewandte Chemie International Edition, 50, 5556-5559. https://doi.org/10.1002/anie.201100370

[13] International Council for Harmonisation (2023) ICH Harmonised Guideline Q2(R2): Validation of Analytical Procedures. ICH, Geneva.