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INPLASY

A Scoping Review Protocol: Handheld Raman Spectroscopy for Screening Quality of Pharmaceuticals

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ADMINISTRATIVE INFORMATION

Support - No external support.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 September 2026 and was last updated on 20 September 2026.

INTRODUCTION

Review question / Objective Primary review question: What evidence exists regarding the capability of handheld or portable Raman spectroscopy to assess the identity and quality of finished pharmaceutical products, including quality changes associated with substandard composition, degradation or storage-related stress, and how might this evidence inform future pharmacy-based assessment of unused medicines returned by patients as part of efforts to reduce avoidable medicines waste?

The review question and eligibility criteria are structured using the Population, Concept and Context (PCC) framework recommended in Joanna Briggs Institute (JBI) methodological guidance for scoping reviews.

Population/source of evidence: finished pharmaceutical products intended for human use, including authentic commercial products, field-collected or suspect medicines, deliberately altered or substandard models, storage-stressed products, vaccines and finished herbal medicines where a medicine-quality application is explicit.

Concept: handheld, hand-held, portable, miniaturised or genuinely field-deployable Raman spectroscopy for pharmaceutical identity or quality assessment. Conventional Raman is the core technology; handheld spatially offset Raman spectroscopy (SORS) and portable surface-enhanced Raman spectroscopy (SERS) will also be included but analysed separately because their sampling characteristics and likely pharmacy applicability differ.

Context: laboratory, community or hospital pharmacy, medicine-market, supply-chain, post-market surveillance, customs/border, regulatory and other field settings worldwide.

Objectives are to:

(1) map current applications of handheld Raman for finished-pharmaceutical quality assessment;
(2) distinguish authentication/gross falsification from detection of quantitatively substandard products, degradation and storage-related change;
(3) evaluate non-destructive and through-packaging approaches relevant to intact returned medicines; (4) compare conventional Raman, SORS and SERS in terms of analytical performance and practical requirements;
(5) summarise reference methods, chemometrics, limitations and field readiness;
(6) identify evidence gaps relevant to future community- or hospital-pharmacy assessment of unused patient-returned medicines; and
(7) consider the potential implications of analytically robust pharmacy-level quality assessment for medicines-waste reduction and sustainable pharmacy, without making sustainability an eligibility criterion.

Background Medicines prescribed and dispensed to patients are not always fully used and may subsequently be returned to community or hospital pharmacies. In the United Kingdom, such medicines are generally accepted for disposal because post-dispensing storage and handling cannot be assured and visual inspection alone cannot confirm continued pharmaceutical quality. This creates both a patient-safety concern and a sustainability challenge, as potentially usable medicines and the resources associated with their manufacture, packaging and distribution are lost. Studies of returned medicines suggest that some products may remain unopened, within shelf life and potentially suitable for reuse under controlled conditions. The Dutch ROAD study demonstrated that redispensing can reduce medicine waste when safeguards such as sealed packaging, remaining shelf life and time-temperature monitoring are applied. However, these approaches rely mainly on indirect indicators and do not provide direct chemical assessment of medicine quality.
Handheld Raman spectroscopy offers rapid, potentially non-destructive molecular analysis with little or no sample preparation and has been applied to pharmaceutical authentication, falsified/substandard medicine detection and quantitative quality assessment. Spatially offset Raman spectroscopy (SORS) may additionally allow analysis through intact packaging, while surface-enhanced Raman spectroscopy (SERS) can improve sensitivity but may require sampling or substrates. The existing evidence has largely focused on pharmaceutical surveillance rather than patient-returned medicines. This review will therefore map the capabilities, limitations and practical relevance of handheld and portable Raman technologies for assessing the quality of finished pharmaceutical products, with particular emphasis on non-destructive testing and potential pharmacy-based application.

Rationale This scoping review addresses whether handheld Raman spectroscopy could support objective quality assessment of unused prescribed medicines returned by patients, rather than such medicines being treated automatically as waste. The review does not assume that returned medicines should currently be redispensed. In the UK, post-dispensing storage and handling are usually unknown, and visual inspection alone cannot confirm continued pharmaceutical quality. Patient safety and product quality therefore remain primary, while sustainability provides an important rationale for reducing avoidable medicines waste where quality can be demonstrated. Handheld Raman spectroscopy is attractive because it is rapid, potentially non-destructive, requires minimal consumables and can be used outside conventional laboratories. Although most existing evidence relates to authentication, counterfeit/substandard medicines and field screening, these studies can clarify its ability to assess identity, quantitative or chemical changes, analyse medicines through intact packaging, and identify limitations relevant to community or hospital pharmacy. Existing reviews have considered portable vibrational spectroscopy more broadly, while medicines-waste literature highlights the sustainability implications of unused medicines. This review therefore focuses specifically on handheld/portable Raman spectroscopy for finished pharmaceuticals, including its analytical performance, ability to detect quality-related changes, non-destructive and through-packaging applications, and potential relevance to future pharmacy-level assessment of returned medicines.

METHODS

Strategy of data synthesis PubMed/MEDLINE and Scopus were searched from database inception to 13 September 2026. The search strategy was developed using the Population, Concept and Context (PCC) framework [1,2] and adapted to the syntax of each database. Four core concepts were combined: Raman spectroscopy; handheld/portable or field-deployable technology; medicines/pharmaceutical products; and pharmaceutical quality assessment.
The core search structure was:
(Raman OR "Raman spectroscopy") AND (handheld OR "hand-held" OR portable OR mobile OR miniatur* OR "field deployable" OR "field-

deployable") AND (medicine* OR drug* OR pharmaceutical* OR tablet* OR capsule* OR "finished pharmaceutical product*") AND (quality OR authentication OR identity OR identification OR counterfeit* OR falsif* OR substandard OR screening OR potency OR assay OR degradation)
The quality concept includes degradation to capture studies evaluating quality-related chemical changes as well as product authentication. The Scopus search was restricted to English-language articles. Publication-type filters were not applied in PubMed because relevant experimental studies may be indexed under broad publication categories such as Journal Article; non-primary publications will instead be excluded during screening. Reference lists of included studies and relevant reviews will also be screened to identify additional eligible studies. Before final synthesis, the database searches will be updated using the same core strategy to identify any newly published studies. Search results will be combined and deduplicated using bibliographic identifiers and title matching.

Eligibility criteria Population/source of evidence: Original experimental studies evaluating finished pharmaceutical products intended for human use. Eligible samples include authentic commercial medicines; unused or returned medicines where studied; field-collected, suspect or falsified products; deliberately altered/model products representing low/high API or other defects; medicines subjected to controlled temperature, humidity, light or other storage/stability stress; vaccines; liquid medicines; and finished herbal medicinal products where a pharmaceutical-quality application is explicit.
Concept: Handheld, hand-held, portable, miniaturised or genuinely field-deployable Raman spectroscopy used to assess medicine identity, authentication, falsification, substandard quality, API content/potency, degradation/stability, storage-related change, formulation/product discrimination, adulteration/contamination or another finished-product quality attribute. Conventional handheld Raman is eligible. Handheld/portable SORS is eligible, including non-destructive measurement through packaging. Portable SERS is eligible where Raman detection remains handheld/portable, but it will be analysed separately because SERS may require sampling, extraction and/or an enhancing substrate.
Context: Laboratory and real-world settings, including community or hospital pharmacy, medicine markets, supply chains, regulatory laboratories, post-market surveillance programmes, customs/border or international-mail facilities and other field settings in any country. Studies do not need to involve patient-returned medicines directly; broader finished-product evidence is eligible where it informs the analytical capability or limitations relevant to the future pharmacy use case.
Comparators/reference standards: No comparator is mandatory. Where present, reference methods may include HPLC/UPLC, LC-MS, mass spectrometry, TLC, UV-visible spectroscopy, dissolution or other pharmacopoeial testing, stability-indicating assays, benchtop spectroscopy or authenticated reference products.
Publication type: Original peer-reviewed experimental research, including analytical validation, comparative studies, laboratory evaluations, stability/degradation investigations, field surveys and field implementation/evaluation studies.
Exclusions: Conventional benchtop Raman as the sole Raman technology; Raman microscopy without a portable application; raw API, excipient or pharmaceutical raw-material identification alone; manufacturing-process/PAT or formulation-development studies without an explicit finished-product quality, assay or stability application; non-pharmaceutical chemical, food, agricultural, environmental or clinical-diagnostic applications; illicit-drug/forensic studies unless samples are explicitly finished pharmaceutical products relevant to medicine quality; reviews, systematic/scoping reviews, meta-analyses, editorials, commentaries, letters without primary experimental data, conference-only reports and non-peer-reviewed preprints. No date restriction will be applied. Only English-language publications will be included.

Source of evidence screening and selection Source selection will follow JBI scoping-review guidance. Screening will be conducted in two stages: title/abstract screening followed by full-text eligibility assessment. Duplicate records will first be removed using DOI, PMID, title and bibliographic matching. Each unique record will then be assessed against the predefined technology, product, quality-purpose, sample, Raman-modality and publication criteria. A primary reviewer will perform screening and a second reviewer will independently verify decisions before the final evidence set is established. Full-text eligibility decisions will be independently checked; disagreements will be resolved through discussion and, where required, adjudication by a third reviewer. Reasons for full-text exclusion will be recorded using standardised categories.
Records will be retained for full-text review where eligibility is clear or cannot be determined reliably from the abstract, particularly when instrument portability, finished-product status, through-

packaging measurement, storage/degradation relevance or the distinction between pharmaceutical versus illicit-drug samples is uncertain. Studies of SERS and SORS will not be excluded solely because they differ from conventional Raman; instead, practical compatibility with non-destructive pharmacy screening will be charted and interpreted separately. The selection process will be reported using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) flow diagram, showing database-specific yields, duplicates removed, records screened, full texts assessed and final included sources of evidence.

Data management Search records and screening decisions will be managed in a structured Microsoft Excel database. Each record will retain a unique review identifier and source database. Deduplication will be undertaken using DOI and PMID, followed by normalised title and bibliographic matching. A standardised data-charting form, informed by JBI recommendations [4], will capture study characteristics; medicine/API and dosage form; sample characteristics; relevant storage or stress conditions; Raman instrument and modality; measurement through or outside packaging; spectral processing and chemometrics; reference method; quality attribute assessed; analytical performance; limitations; and indicators of field or pharmacy applicability.
Additional fields will assess relevance to returned medicines, including non-destructive testing, through-packaging analysis and whether testing requires opening or consuming the product. Sustainability-related information, such as medicine waste, material or reagent use, product destruction, cost/resource use and environmental outcomes, will be extracted where reported but will not be required for study eligibility. Data will be verified against the full text before synthesis, with disagreements resolved by reviewer consensus.

Reporting results / Analysis of the evidence Evidence will be analysed descriptively and narratively in accordance with JBI guidance. Study characteristics will be summarised using counts, percentages and ranges where appropriate, and mapped by publication year, country, medicine/product class, dosage form, setting, Raman modality, quality-assessment purpose and reference method. The synthesis will distinguish between identity/authentication and falsification detection; quantitative or substandard-quality assessment; degradation or stability assessment; non-destructive or through-packaging analysis; and field or pharmacy-based applications. Conventional Raman, spatially offset Raman spectroscopy (SORS) and surface-enhanced Raman spectroscopy (SERS) will be considered separately where appropriate. Sustainability-related findings will be summarised descriptively as reported in the eligible studies.

Presentation of the results Results will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) and JBI guidance. Study characteristics will be presented in structured evidence tables including author/year, country and setting, medicine/API, dosage form, sample characteristics, Raman instrument and modality, sampling configuration, quality-assessment application, reference method, analytical performance and study conclusions. Graphical or tabulated summaries will be used where appropriate to present publication trends, geographical distribution, Raman modalities, dosage forms and quality-assessment applications. Sustainability-related outcomes will be reported where available.

Language restriction Yes. Only studies published in English will be included.

Country(ies) involved United Kingdom.

Keywords Handheld Raman spectroscopy; Pharmaceutical quality; Returned medicines; Medicines reuse; Pharmaceutical waste; Sustainable pharmacy; Storage stability; SORS; SERS; Non-destructive analysis.

Dissemination plans The completed scoping review will be submitted to a peer-reviewed journal in pharmaceutics, pharmaceutical analysis or pharmacy practice. Findings may also be presented at relevant conferences and shared with stakeholders interested in medicines quality, pharmacy practice, medicines waste and reuse, sustainability, and regulatory science.

Contributions of each author

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