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Research Article

Letter to do Editör: Residual Solvent Detection in Avermectin Sodium: A Comparison of Current Analytical Approaches

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Introduction

Residual solvent analysis remains an essential component of pharmaceutical and veterinary drug quality control, particularly for fermentation-derived compounds such as avermectin sodium. Organic solvents are widely employed during extraction, purification, and formulation processes, and their incomplete removal may compromise product safety, efficacy, and regulatory compliance. Consequently, the selection of an appropriate analytical method for residual solvent determination is of considerable importance [1,2].

Gas chromatography with flame ionization detection (GC-FID) continues to be the most widely adopted technique for routine quantification of residual solvents. The method offers excellent sensitivity, robustness, and relatively low operating costs. When combined with headspace sampling (HS-GC-FID), matrix interference from non-volatile components of avermectin sodium is substantially minimized, enabling reliable quantification of volatile organic compounds. The simplicity of instrumentation and widespread availability make HS-GC-FID the preferred choice in quality control laboratories [2].

Gas chromatography coupled with mass spectrometry (GC-MS) provides significant advantages over GC-FID in terms of analyte identification and selectivity. While GC-FID relies solely on chromatographic retention times for identification, GC-MS generates characteristic mass spectra that facilitate confirmation of unknown or co-eluting compounds. This capability is particularly valuable during method development, impurity profiling, and investigations involving manufacturing deviations. However, the higher acquisition and maintenance costs, together with increased technical complexity, often limit GC-MS to reference laboratories or research applications rather than routine batch release [2,3].

Direct injection GC methods have also been reported for solvent analysis, but they are generally less suitable for avermectin sodium because the sample matrix may contaminate the injection system and reduce column lifetime. Headspace sampling offers clear advantages by introducing only volatile analytes into the chromatographic system, thereby improving reproducibility and reducing maintenance requirements. Consequently, headspace techniques are increasingly regarded as the analytical standard for pharmaceutical residual solvent testing [2].

Emerging technologies have further expanded analytical possibilities. Comprehensive two-dimensional gas chromatography (GC×GC) significantly enhances chromatographic resolution, allowing improved separation of complex solvent mixtures. Likewise, hyphenated techniques incorporating high-resolution mass spectrometry provide exceptional analytical confidence for trace-level impurity identification. Despite these advantages, their high operational costs and sophisticated data processing requirements currently limit their widespread implementation in routine industrial settings [1,4].

From a regulatory perspective, analytical methods should comply with the recommendations outlined in the International Council for Harmonisation (ICH) Guideline Q3C concerning residual solvents. Method validation should include assessments of specificity, linearity, precision, accuracy, detection and quantification limits, robustness, and system suitability. Because avermectin sodium is a complex fermentation-derived active pharmaceutical ingredient, matrix effects should also be carefully evaluated during method validation to ensure analytical reliability [4].

Considering current analytical capabilities, HS-GC-FID appears to provide the optimal balance between sensitivity, robustness, throughput, and cost-effectiveness for routine monitoring of residual solvents in avermectin sodium. GC-MS serves as an excellent complementary technique whenever confirmation of analyte identity or investigation of unexpected impurities is required. Future developments in automated headspace systems, multidimensional chromatography, and artificial intelligence-assisted spectral interpretation may further improve analytical efficiency while reducing operator-dependent variability [5].

Conclusion

The choice of analytical methodology should be guided by the intended application, regulatory expectations, laboratory resources, and required analytical confidence. Continued refinement of chromatographic techniques will contribute substantially to ensuring the quality, safety, and regulatory compliance of avermectin sodium products used in veterinary medicine and agriculture [6].

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