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Review article

ANALYTICAL METHODS FOR SIMULTANEOUS DETERMINATION OF DOLUTEGRAVIR AND LAMIVUDINE IN FIXED-DOSE COMBINATION FORMULATIONS: A CRITICAL REVIEW

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Abstract

The fixed-dose combination of dolutegravir (DTG) and lamivudine (3TC) requires robust and reproducible analytical methods for analysis and stability testing. This review aims recent literature on simultaneous assay methods, with emphasis on stability-indicating reversed-phase liquid chromatography (HPLC/UHPLC/UPLC) and also summarizing spectrophotometric and HPTLC alternatives. A comparative table summarizes chromatographic conditions, validation parameters and practical considerations. We discuss method strengths, limitations, and recommend priorities for impurity profiling and greener workflows.

Key words: Dolutegravir, Lamivudine, RP-HPLC, UPLC, Stability-indicating, Validation, Fixed-dose combination

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1. Introduction

Dolutegravir (DTG) and lamivudine (3TC) are widely adopted antiretrovirals co-formulated in fixed-dose regimens. Accurate simultaneous quantification in tablets is essential for assay, content uniformity and stability testing. Because DTG and 3TC differ in polarity, UV absorbance and chemical stability, analytical methods must balance selectivity, sensitivity and operational simplicity.

2. Overview of Analytical Techniques

Reversed-phase chromatography (RP-HPLC, UHPLC, and UPLC) is mostly preferred in the recent literature for simultaneous DTG/3TC studies because of its specificity and flexibility to stability-indicating procedures. UV/derivative spectrophotometry and HPTLC are complementary methods that have been reported; they are less selective than chromatography but can be helpful for quick screening in situations when equipment is scarce. Although they are more frequent for regular tablet assays, bioanalytical LC-MS/MS technologies are well-established for plasma analysis (Table 1)

3. Validation and Stability Considerations

The ICH Q2(R1) parameters are frequently followed by published methods, which report linearity (often $r^2 > 0.999$), accuracy (recoveries usually 98–102%), and precision. Importantly, forced degradation (acid/base hydrolysis, oxidation, thermal and photolytic stress) is used in many publications to show that the assay is selective and that the degradation products do not co-elute with DTG or 3TC peaks[1–3,5]. PDA detectors are widely used for peak purity confirmation.

4. Discussion

A practical balance between throughput and specificity is shown by trends in the literature. RP-HPLC techniques offer strong separation windows that are helpful for impurity profiling, whereas UHPLC/UPLC techniques reduce analysis time and solvent consumption, which advantages high-volume QC labs. The formulation matrix should be taken into account when choosing a method because coated tablets, high excipient loadings, and poorly soluble APIs (particularly DTG) can make extraction and chromatographic behavior more difficult. Although their weak selectivity renders them inappropriate for stability or impurity research, spectrophotometric and HPTLC approaches are nonetheless useful in situations where chromatographic access is limited. The creation of LC-MS/MS techniques for low-level degradants and the use of AQbD concepts to establish method-operable design spaces and enhance transferability between labs are emerging priority

Table 1: Comparative Summary of Representative Methods

Study (author, year)	Technique	Column / Conditions	Detection / λ (nm)	Key validation / notes
Godela R. et al. 2020[1]	Stability-indicating RP-HPLC	XBridge Phenyl C18 250×4.6 mm, 5 µm; Methanol:0.1% TFA (85:15); 0.8 mL/min	PDA / 258	RTs: 3.4 (3TC), 5.0 (DTG); linearity and forced-degradation studies reported
Patel K. et al. 2021[2]	RP-HPLC (stability indicating)	Hypersil BDS C18 250×4.6 mm, 3.5 µm; Phosphate buffer pH 3.0:ACN (60:40); 1.5 mL/min	PDA / 232	Validated per ICH Q2(R1); good accuracy and precision
Sowjanya A. 2024[3]	Stability-indicating RP-HPLC	Discovery C18 250×4.6 mm, 5 µm; 0.1% perchloric acid:ACN (55:45); 1.0 mL/min	UV / 230	Low LOD/LOQ reported; %RSD < 1
Reddy M.S. et al. 2023[4]	RP-UPLC	HSS C18 50×2.1 mm, 1.6 µm; KH2PO4:MeOH (70:30); 0.3 mL/min	PDA / 260	Short run times (≈1–2 min); validated for tablets
BEH Shield UPLC method (JPRI) 2022[5]	UPLC stability-indicating	BEH Shield RP18 2.1×100 mm, 1.7 µm; KH2PO4 pH3:MeOH (30:70); 0.5 mL/min	PDA / 258	Designed for degradant separation in DTG/3TC tablets

5. Future Perspectives

Suggested areas for analytical development consist of: (i) Study of degradation pathways by LC–MS/MS impurity analysis (ii) environmentally friendly chromatography—including shorter columns, more efficient stationary phases, and lower ratios of organic solvents; (iii) inter-laboratory studies for method transfer to verify robustness; and (iv) dissolution testing method development with stability-indicating assays for in-process monitoring.

6. Conclusion

Reversed-phase chromatographic methods, particularly when configured as stability-indicating, are the most reliable approaches for simultaneous DTG/3TC assay in fixed-dose formulations. UPLC/UHPLC methods offer throughput and solvent savings, while rigorous validation—including forced degradation and peak purity assessment—remains essential for regulatory acceptance.

7. References

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