# Development of Stability Indicating Method and Characterization of Degradation Impurity of Nirmaltrelvir in Its Self-Emulsifying Drug Delivery System

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**Abstract :** A stability-indicating reverse phase high performance liquid chromatography (RP-HPLC) method was developed and validated for estimating Nirmatrelvir in its self-emulsifying drug delivery system (SEDDS). The separation of Nirmatrelvir and its degradation products was accomplished by employing an Agilent Zorbax Eclipse plus C18 (250 mm x 4.6 mm, 5 μm) column, through which the mobile phase 5 mM phosphate buffer (pH 4.0) as mobile phase A and Acetonitrile as mobile phase B in a ratio of (40:60 % v/v) was pumped at a flow rate of 1.0 mL/min, through the HPLC system. Chromatographic separation and elution were monitored by a photo-diode array detector at 210 nm. Stress studies have been employed to evaluate this method's ability to indicate stability. Nirmatrelvir was exposed to several stress conditions, such as acid, alkali, oxidative, photolytic, and thermal degradations. Significant degradation was observed during acid and alkali hydrolysis, and the resulting degradation product was successfully separated from the Nirmatrelvir peak, preventing any interference. Furthermore, the primary degradant produced under alkali degradation conditions was identified using UPLC-ESI-TQ-MS/MS. The method was validated in accordance with the International Council on Harmonization (ICH) and found to be selective, precise, accurate, linear, and robust. The apparent permeability of Nirmatrelvir SEDDS was $4.20 \pm 0.21 \times 10^{-6}$ cm/sec, and the average proportion of free drug recovered was 0.5%. The method developed in this study was feasible and accurate for routine quality control evaluation of Nirmatrelvir SEDDS.

**Keywords :** Nirmatrelvir, SEDDS, degradation study, HPLC, LC-MS/MS

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