A Sustainable and Technically Smart Spectrophotometric Manipulation of PAXLOVID; A Comprehensive Ecological and Analytical Performance Rating

PC-02

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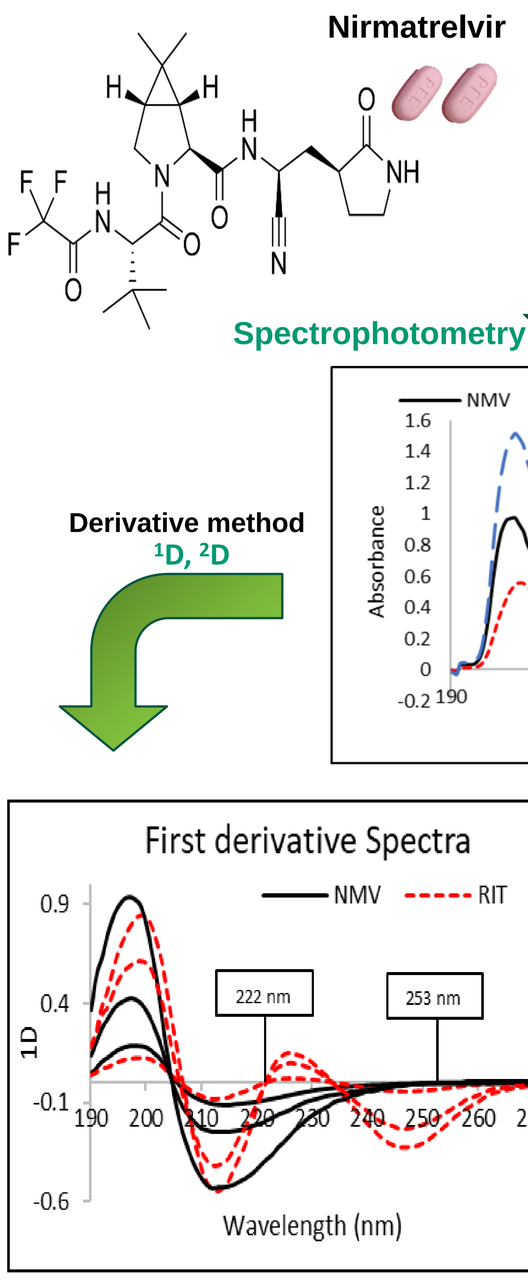
Introduction

COVID-19 still is a serious global health issue causing digestive, respiratory illnesses, neurological and mental issues.

Paxlovid (Nirmatrelvir **NMV** co-packaged with Ritonavir **RIT**) has been identified as a promising solution as an oral antiviral drug with 89% reduction in hospitalization or death within five days. [1]

However, no spectrophotometric assay has been identified for Paxlovid component determination. So, simple, green, and reproducible **spectrophotometric methods** have been developed for the quantitation of NMV and RIT in bulk and pharmaceutical dosage form. **Analytical and ecological reviews** have been performed to compare the results achieved by suggested methods and reported ones. Green analytical chemistry (GAC) and white analytical chemistry (WAC) principles also influence the selection of environmentally friendly solvents, waste reduction, and general sustainability of analytical procedures.

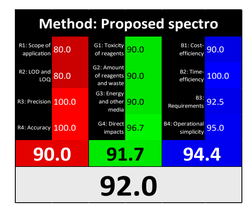
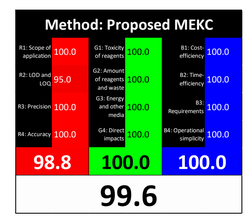
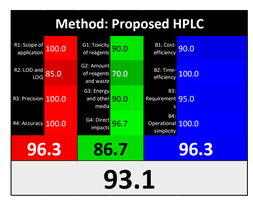
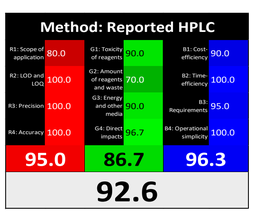
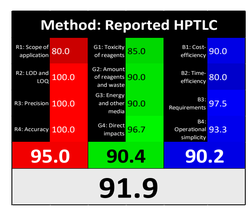
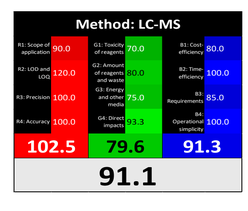
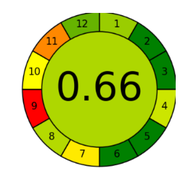
Materials and Methods



Results

Analyte	NMV			RIT		
Method	**¹D**	**²D**	**DWZ**	**¹D**	**²D**	**DWZ**
Wavelength (nm)	222	222	Δλ (231-248)	253	253	Δλ (251-272)
Linearity range (µg/mL)		10-250			10-250	
LOD (µg/mL) [a]	1.37	2.65	2.69	3.22	2.43	2.75
LOQ (µg/mL) [b]	4.14	8.04	8.14	9.75	7.35	8.35
Regression coefficient	0.9999	0.9998	0.9998	0.9996	0.9998	0.9997
Slope	0.0009	0.0004	0.0010	0.0010	0.0008	0.0028
S_b of slope [c]	1.03E-05	9.74E-06	2.32E-05	2.74E-05	1.58E-05	6.39E-05
Intercept	-4.44E-04	3.47E-18	-2.93E-03	2.70E-03	2.11E-03	4.56E-03
S_a of intercept [d]	3.73E-04	3.53E-04	8.41E-04	9.75E-04	5.75E-04	2.32E-03

Analytical and Ecological performance rating of Analytical methods analyzing PAXLOVID

Method name	RGB12 MODEL	AGREE	LOQ (µg/mL)
Proposed Spectrophotometric Ethanol Number of analytes:2			**NMV RIT (mentioned above)**
Reported MEKC-DAD[2] BGE: 50mM borate buffer containing 25 mM SDS Number of analytes:2 Run time: 7 min.			**NMV 0.21 RIT 0.13**
Reported HPLC-DAD[2] Mobile phase: ACN: ammonium acetate buffer (50:50 v/v). Number of analytes:2 Flow rate: 1 mL/ min. Run time: 7 min.			**NMV 0.6 RIT 0.96**
Reported HPLC-DAD [3] Mobile phase: ethanol: water (80:20 v/v). Number of analytes:2 Flow rate: 1 mL/ min. Run time: 7 min.			**NMV 2.78 RIT 1.95**
Reported HPTLC [4] Mobile phase: methanol-water -2% urea solution of β-cyclodextrin (40:10:5) Number of analytes: 2. Run time: around 20 min.			**NMV 2.22 RIT 1.23**
Reported LC-MS [5] Mobile phase: 0.1% v/v formic acid in water and methanol (36:64, v/v). Number of analytes: 2. Flow rate: 0.8 mL/ min Run time: 7 min.			**NMV 50 RIT 10 ng/mL**

Spider greenness index table

	Water score	EtOH Score	MeOH Score	ACN Score
Health impact	4.38	3.56	3.25	3.13
General properties	1.44	1.31	1.31	1.13
Odor	5	-3	-3	-3
Fire Safety	5.00	-0.17	0.17	-0.17
Stability	5.00	2.86	2.71	1.14
Mean average	4.16	0.91	0.89	0.45

Conclusions

This study investigates and validates simple, sustainable, and earth-friendly spectrophotometric manipulations for RIT and NMV quantification in bulk powder, synthetic admixtures, and co-packed tablets. It is the first spectrophotometric analysis for the mixture under study, offering ease of use, time, and cost efficiency. The greenness assessment protocol uses solvent evaluation, penalization strategies, and color-coded strategies, making these methods highly recommended for quality control purposes.

References

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2. Elbordiny, H.S., et al., *Tailoring two white chromatographic platforms for simultaneous estimation of ritonavir-boosted nirmatrelvir in their novel pills: degradation, validation, and environmental impact studies.* RSC Adv, 2023. **13**(38): p. 26719-26731.
3. Imam, M.S., et al., *Adjusted green HPLC determination of nirmatrelvir and ritonavir in the new FDA approved co-packaged pharmaceutical dosage using supported computational calculations.* Sci Rep, 2023. **13**(1): p. 137.
4. Imam, M.S., et al., *Simultaneous green TLC determination of nirmatrelvir and ritonavir in the pharmaceutical dosage form and spiked human plasma.* Sci Rep, 2023. **13**(1): p. 6165.
5. Liu, C., et al., *Simultaneous determination of nirmatrelvir and ritonavir in human plasma using LC-MS/MS and its pharmacokinetic application in healthy Chinese volunteers.* Biomed Chromatogr, 2022. **36**(11): p. e5456.