## Supplementary information

# Development, cross-validation and greenness assessment of capillary electrophoresis method for determination of alpelisib in pharmaceutical dosage forms – an alternative to liquid chromatography

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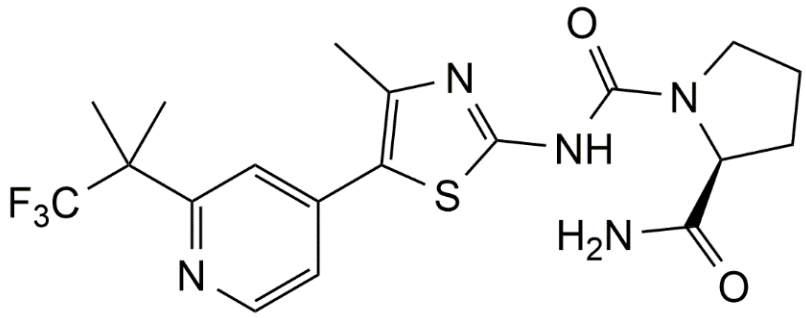


**Figure S1**. Chemical structure of alpelisib. Drawn by ChemDraw Professional 15.0 (PerkinElmer, Shelton, CT, USA)

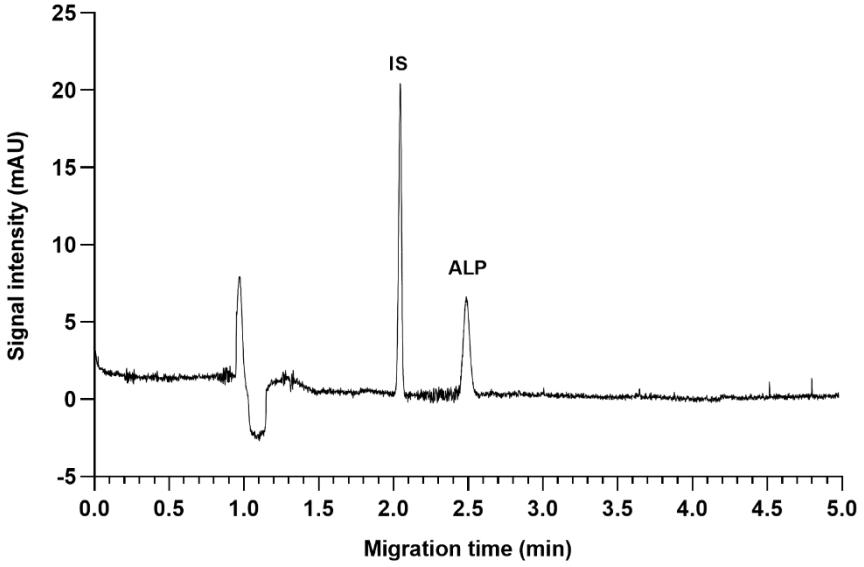


**Figure S2**. MEKC electropherogram of ALP and IS, 25 mM borate at pH 9.3, 20 mM SDS, 30 kV, 30 °C

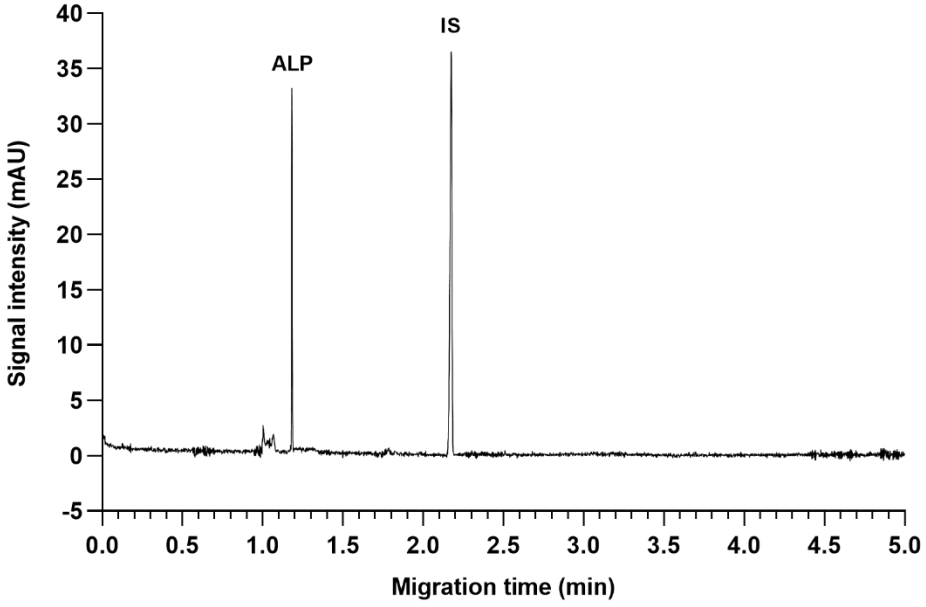


**Figure S3**. Electropherogram of ALP and IS, 25 mM borate at pH 9.3, 10% MeOH, 30 mM borate, 30 °C, 30 kV

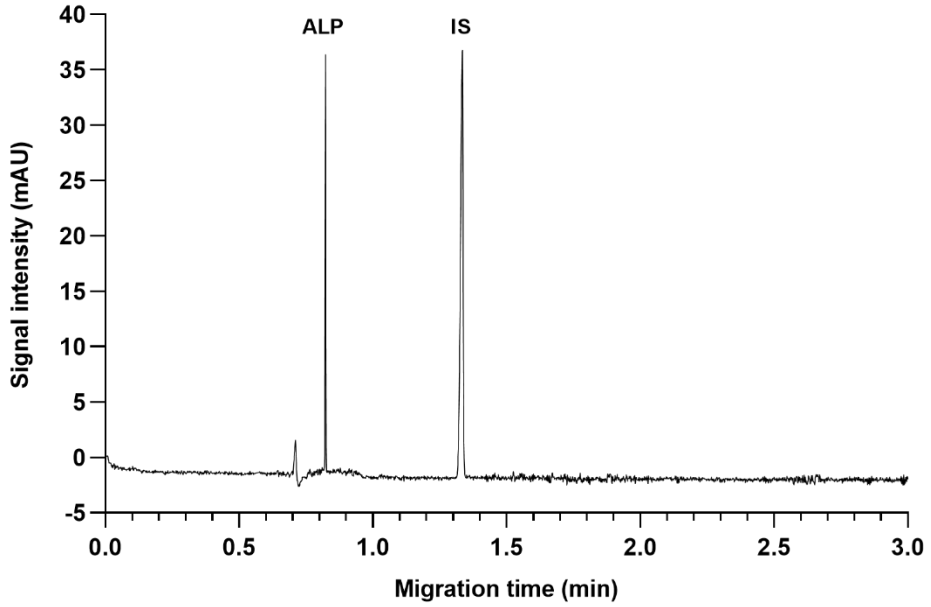


**Figure S4**. Electropherogram of ALP pharmaceutical dosage form with added IS at 50 µg/mL, 25 mM borate at pH 9.3, 30 kV, 30 °C

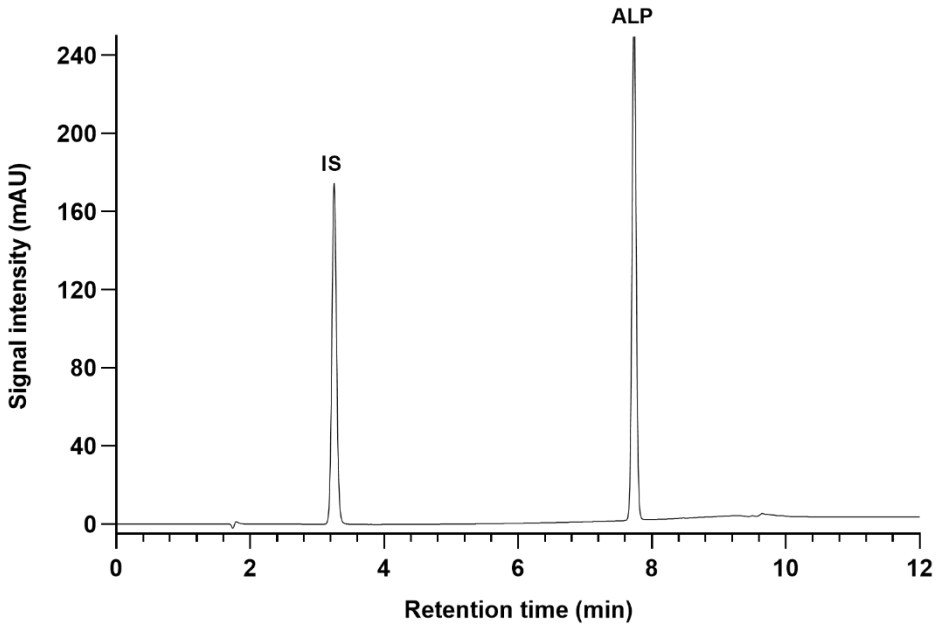


**Figure S5**. Chromatogram of ALP pharmaceutical dosage form with added IS at 50 µg/mL, detection at 315 nm

**Table S1**. Inputs for calculation of AGREE scores for CE and LC methods

| Principle | Weight | CE | LC |
|---|---|---|---|
| Sampling | 1 | External sample preparation (reduced steps) | External sample preparation (reduced steps) |
| Amount of sample (g or mL) | 2 | 0.02 | 0.02 |
| Positioning of analytical device | 1 | at-line | at-line |
| Major steps | 1 | 3 or fewer | 3 or fewer |
| Automation; sample preparation | 1 | semi-automatic, not miniaturized | semi-automatic, not miniaturized |
| Derivatization | 1 | no | no |
| Amount of waste (g or mL) | 2 | 0.15 mL | 16 mL |
| Number of analytes, samples per hour | 2 | 1 analyte, 7 samples per hour | 1 analyte, 3 samples per hour |
| Energy | 2 | 0,015 kWh | LC |
| Bio-based reagents | 1 | Some are bio-based | Some are bio-based |
| Use of toxic reagents | 2 | Yes, 0.01 mL | Yes, 9.5 mL |
| Threats | 1 | Highly flammable | Highly flammable |

**Table S2**. AGREE scores for individual greenness criteria for CE and HPLC methods

| Principle | Weight ($w_i$) | CE score ($s_i$) | LC score ($s_i$) |
|---|---|---|---|
| Sampling | 1 | 0.30 | 0.30 |
| Amount of sample (g or mL) | 2 | 1.00 | 1.00 |
| Positioning of analytical device | 1 | 0.33 | 0.33 |
| Major steps | 1 | 1.00 | 1.00 |
| Automation; sample preparation | 1 | 0.25 | 0.25 |
| Derivatization | 1 | 1.00 | 1.00 |
| Amount of waste (g or mL) | 2 | 0.9488 | 0.3231 |
| Number of analytes, samples per hour | 2 | 0.4210 | 0.2152 |
| Energy | 2 | 1.00 | 0.50 |
| Bio-based reagents | 1 | 0.50 | 0.50 |
| Use of toxic reagents | 2 | 0.80 | 0.2108 |
| Threats | 1 | 0.80 | 0.80 |

AGREE score can be calculated according to the following equation where $w_i$ is the weight factor for the greenness principle $i$ with a corresponding individual score $s_i$.

$$AGREE\ score = \frac{\sum_{i=1}^{12} w_i s_i}{\sum_{i=1}^{12} w_i}$$

AGREE scores for CE and HPLC methods are then calculated as follows:

$$AGREE\ score\ (CE) = \frac{\sum_{i=1}^{12} w_i s_i}{\sum_{i=1}^{12} w_i} = \frac{12.5196}{17} = 0.7364$$

$$AGREE\ score\ (HPLC) = \frac{\sum_{i=1}^{12} w_i s_i}{\sum_{i=1}^{12} w_i} = \frac{8.6782}{17} = 0.5105$$