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Fragmentation of Pharmaceuticals with DART-MS-MS

Introduction

Over-the-counter pharmaceuticals contain active ingredients, which, if incorrectly measured or selected, could significantly impact the effect they take on consumers' health. We studied the fragmentation patterns of some of the active ingredients in these medicines in attempt to determine a new way of ascertaining the contents of the pharmaceuticals we trust.

The active ingredients in over-the-counter Walgreen's Mucus Relief and CVS Cold & Flu Plus tablets will be analyzed. DART-MS-MS with a Thermo Triple Quad will be used to determine the optimal collision energy for standards of these ingredients, as well as reveal their fragmentation patterns. The pharmaceuticals will then be analyzed under these optimal conditions to determine whether DART-MS-MS is capable of detecting the fragments when all ingredients are combined.

Active ingredients tested from Mucus Relief:

- Guaifenesin
- Phenylephrine

Active ingredients tested from Cold & Flu:

- Dextromethorphan
- Phenylephrine

Results

Standards were made into 10 ng/µl solutions in 1:1 water:methanol. The standards were each detected by DART-MS full scan, and were then analyzed using DART-MS-MS with the application of various voltages. The optimal collision energy was considered that which produced the most fragment ions at relative abundances higher than that of the parent ion.

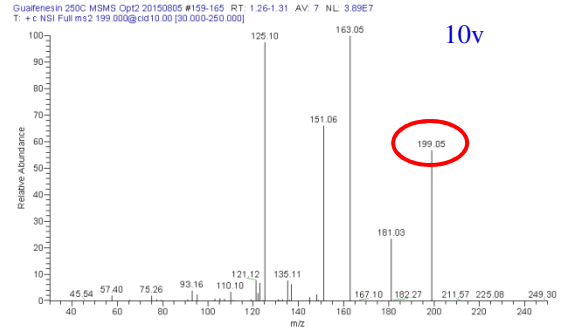

Fig.1: DART-MS-MS spectra of Guaifenesin standard (199.0 m/z)at 10v

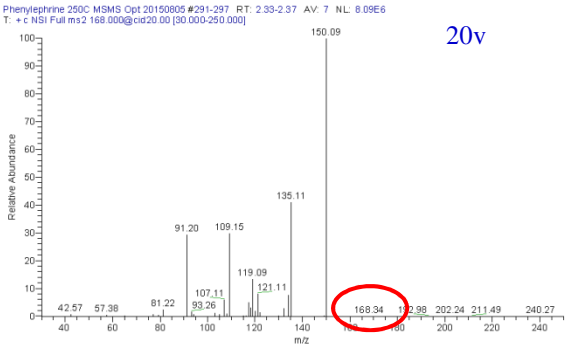

Fig.2: DART-MS-MS spectra of Phenylephrine standard (168.0 m/z) at 20v

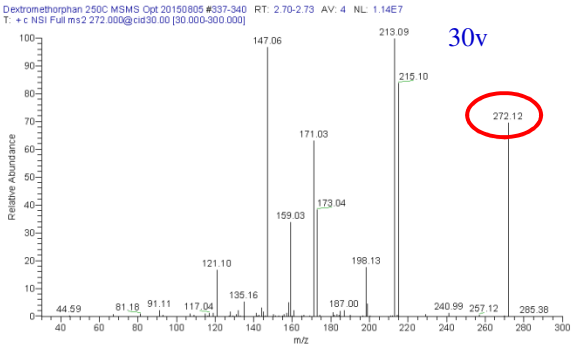

Fig.3: DART-MS-MS spectra of Dextromethorphan standard (272.0 m/z) at 30v

Analysis of Pharmaceuticals

Next, Mucus Relief and Cold & Flu tablets were disolved in 1:1 water:methanol at similar concentrations to the standard solutions, and analyzed under the optimal DART-MS-MS conditions.

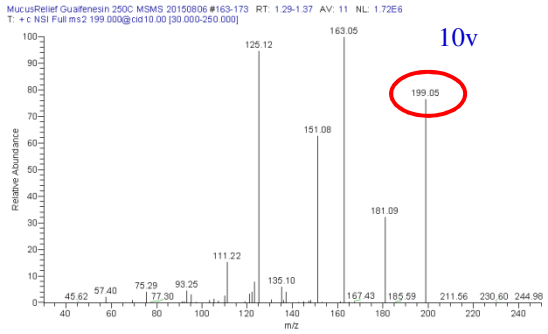

Fig.4: DART-MS-MS spectrum of Guaifenesin in Mucus Relief at 10v

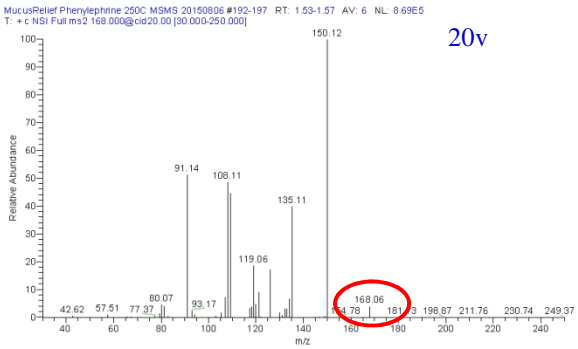

Fig.5: DART-MS-MS spectrum of Phenylephrine in Mucus Relief at 20v

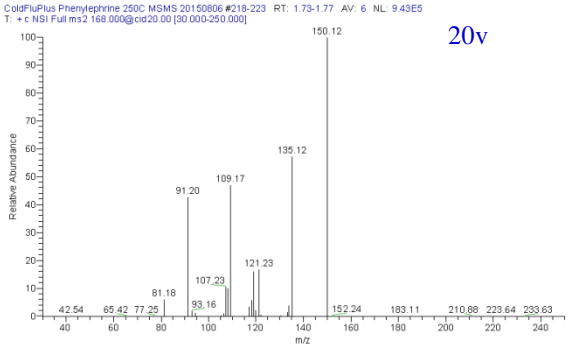

Fig.6: DART-MS-MS spectrum of Phenylephrine in Cold & Flu at 20v

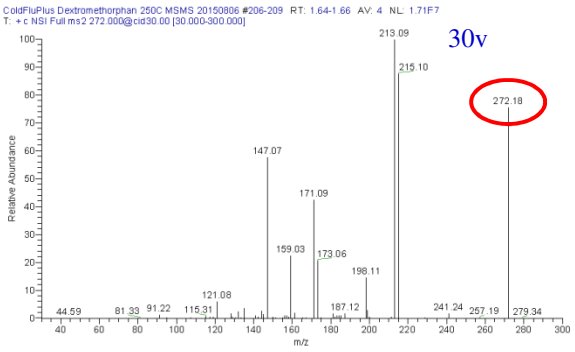

Fig.7: DART-MS-MS spectrum of Dextromethorphan in Cold & Flu at 30v

DART-MS-MS analysis of the dissolved tablets proved to be capable of providing spectra nearly identical to the those of pure standard samples.

Experimental

Procedure:

- 10 ng/µl solutions of Guaifenesin, Phenylephrine Hydrochloride, and Dextromethorphan Hydrobromide standards were created in 1:1 water:methanol
- 3 µl spots of the solutions were spotted on Quickstrip cards and analyzed first with DART-MS full scan in positive-ion mode, using helium gas heated to 250˚C
- Standard solutions then analyzed with DART-MS-MS in positive-ion mode, using helium gas heated to 250˚C, applying collision energies ranging from 10-30v
- CVS Cold & Flu Daytime softgel dissolved in 1:1 water:methanol at 2 mg/mL (about 20 ng/µl dextromethorphan, 10 ng/µl phenylephrine)
- Mucus Relief Daytime tablet dissolved in 1:1 water:methanol at 50 ng/µl (about 12.5 ng/µl guaifenesin) and at 1.67 µg/µl (about 10 ng/µl phenylephrine)
- Solutions analyzed on Quickstrip cards with DART-MS-MS in positive-ion mode, using helium gas heated to 250°C, applying collision energies determined optimal for each standard (Guaifenesin 10v, Phenylephrine 20v, Dextromethorphan 30v)

Conclusion

DART-MS-MS was able to fragment chemical standards of the active ingredients in Mucus Relief and Cold & Flu tablets. Using the collision energies determined to be optimal for each standard through this first experiement, nearly the same spectra were obtained by analyzing the dissolved tablets themselves with DART-MS-MS.

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