

EXTRACTABLES AND LEACHABLES: A COMPLEX ANALYSIS



Technology Advantage: Agilent Intuvo 9000 GC with MS-HES



Introduction

Extractables analysis involves exposing packaging materials to strong conditions (elevated temperatures to simulate a worst-case scenario or appropriate solvents to mimic pharmaceutical properties) to determine potential compound migration. In leachables analysis, a pharmaceutical product is analyzed at normal conditions to observe actual compound migration. Compound migration involves correlating extractables to leachables¹.

Sources of extractables and leachables are often plastic and elastomeric components, ink and adhesives from labels, and degradation products from processing, storage, and sterilization. A phthalate, such as DEHP (*bis*(2-ethylhexyl) phthalate), is an example of a plasticizer that is added to packaging material for flexibility, with the potential to leach into the product.

The impact of various extractable or leachable compounds on final product properties is not well known. Therefore, the ability to detect and identify extractables and leachables present in various products is desirable. The Agilent Intuvo 9000 Gas Chromatograph, coupled to a mass spectrometer equipped with a high efficiency source (HES) provides a simple means of detection with additional advantages over conventional gas chromatographs:

- Simplified column installation
- Innovative inert flow path²
- Smaller footprint

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A redesigned modular flow path simplifies column installation while the innovative inert flow path maintains chromatographic integrity. Lastly, the 9000 Intuvo GC is only 27 cm wide affording additional flexibility, especially in laboratories with limited bench space.

Experimental

A 9000 Intuvo GC was coupled to an MS-HES. A standard 30 m Intuvo HP-5ms Ultra Inert column was installed and run at 1 mL/min. A phthalate standard obtained from Sigma-Aldrich was diluted to 500 ppb, 50 ppb, and 5 ppb, and analyzed in Selected Ion Monitoring mode (SIM). Extracts from a 5 % lidocaine transdermal patch and plastic film-backing were analyzed in Scan mode¹.

Results and Discussion

A phthalate standard was first analyzed to determine method conditions. By using SIM, phthalates were identified down to 5 ppb. Excellent peak shape was obtained (Figure 1).

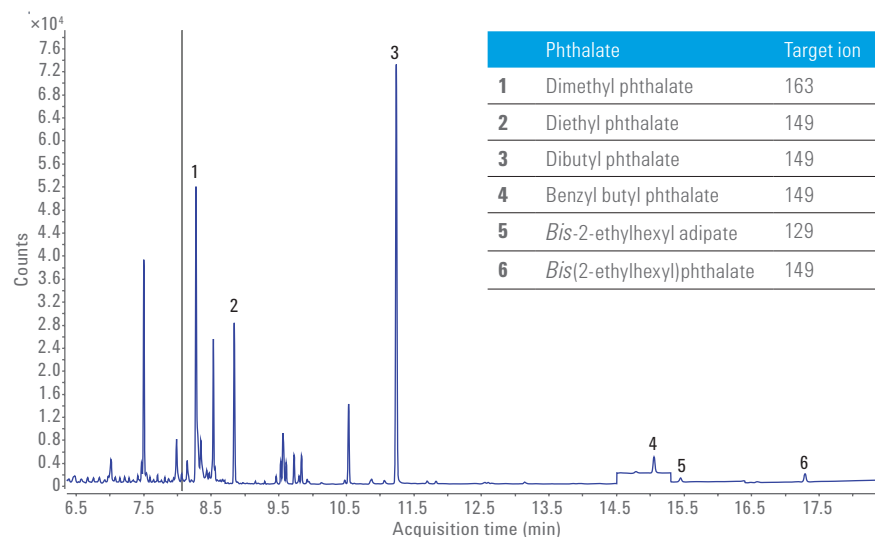


Figure 1. Phthalate standard at 5 ppb was analyzed with the Agilent 9000 Intuvo GC and an MS-HES using a 30 m Intuvo HP-5ms UI column.

Solvent extracts of lidocaine patches and films were evaluated using the same method parameters, but without SIM. As expected, the largest response from the patch was the active pharmaceutical ingredient, lidocaine, with parabens also present at high levels. Interestingly, a small amount of terephthalate was also present in the patch extract (Figure 2). The film shows small amounts of the patch ingredients (parabens and lidocaine) due to close interaction, while also containing terephthalate (Figure 3).

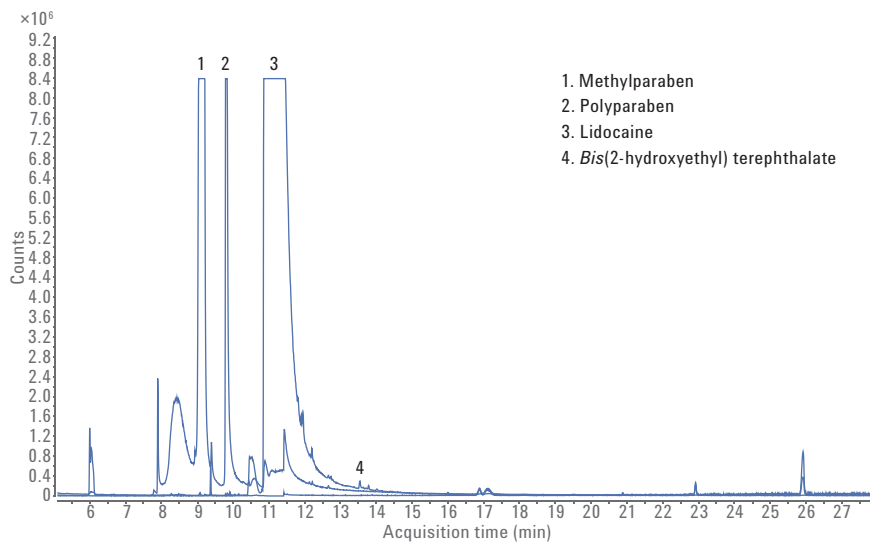


Figure 2. The extracted ion chromatogram for the dichloromethane extraction of a 5% lidocaine transdermal patch shows paraben A, paraben B, lidocaine (active ingredient), and terephthalate.

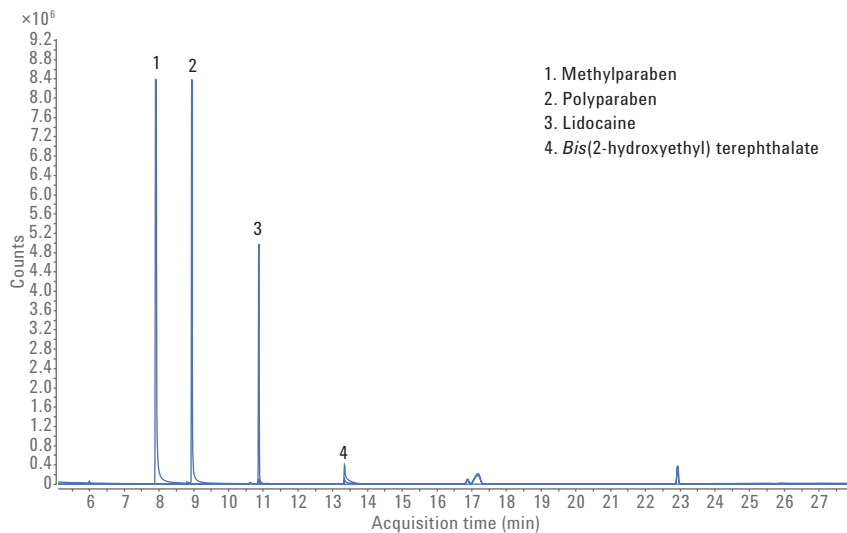


Figure 3. The extracted ion chromatogram for the dichloromethane extraction of a 5% lidocaine transdermal patch shows paraben A, paraben B, lidocaine, and terephthalate.

Conclusion

The Agilent 9000 Intuvo GC, coupled to an MS-HES and an 30 m Intuvo HP-5ms UI column, delivers symmetric peak shapes and high sensitivity for phthalate analysis in the context of extractables and leachables. Active and inactive ingredients were identified from extracts of both the transdermal patch and the plastic film backing. This demonstrates the ability of the 9000 Intuvo GC to analyze complex samples while enhancing the user's experience through innovative flow path and connection technology.

References

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2. Multiresidue Pesticide Analysis Improving Peak Shape Consistency, *Agilent Technologies*, publication number 5991-7175EN, **2016**.

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