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Rapid Screening of Skin Lightening Products for the Corticosteroid Clobetasol Propionate Using Direct Analysis in Real Time (DART) with Mass Detection

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Abstract

In this application note we describe a powerful detection method for the rapid qualitative determination of active ingredients (AIs) and other ingredients in cosmetics samples using a direct ionization technique with mass detection. The direct analysis of cosmetic samples using DART coupled with the ACQUITY QDa Mass Detector provides molecular ion information while allowing samples to be analyzed very rapidly and without the need for time-consuming sample preparation or chromatographic method development.

Benefits

- Rapid screening of cosmetics samples for clobetasol propionate
- Reduced need for sample prep
- No LC method development
- Ease of use

Introduction

Skin whitening/lightening agents in cosmetics are often used to produce a more even skin tone, usually to the face and neck, but sometimes they can be used more extensively over larger areas of skin.[1-3] The use of pharmaceutical active ingredients (AIs) such as corticosteroids is prohibited for use in cosmetics due to the potential undesirable side effects that can occur.[1-5] Corticosteroids are highly effective drugs which are used to treat inflammatory skin conditions such as eczema and psoriasis. Topical preparations are usually in the form of creams, ointments, or gels. Long term use of corticosteroids can cause side effects including pustular psoriasis, permanent skin atrophy, and systemic effects such as hypertension, contact dermatitis, and diabetes.[4,5] EU (1223/2009) and US regulations, require that all cosmetic products be safe for human use.[6,7] Regardless of the regulations against using corticosteroids in cosmetics without a prescription, they can still be found in cosmetics marketed as skin lightening products, due to their effectiveness.[1-3]

In this study, cosmetic products were obtained from online vendors. The samples were analyzed using a DART[8-11] source (IonSense, Saugus, MA, USA) coupled with Waters ACQUITY QDa Mass Detector. DART is a desorption atmospheric pressure chemical ionization (APCI) method where a heated ionized gas (helium or nitrogen) is directed towards a target positioned between the DART source exit and the inlet tube leading to

the ACQUITY QDa Detector's ion block. Ions are generated in open air for analysis by mass detection. This mode of analysis typically allows samples be analyzed with little or no time-consuming sample preparation.

The analysis of cosmetics samples was accelerated and simplified in this study using the direct ionization method. When direct ionization techniques are used in combination with mass detection it has the potential to provide a powerful detection method for the rapid qualitative determination of AI's and other ingredients in cosmetics samples.

Experimental

Instrumentation and software

Ambient ionization was performed using the DART source with subsequent mass detection using the ACQUITY QDa. MassLynx Software was used for data acquisition and interpretation. The DART interface software was used to control the ionization settings and sampling speed.

DART conditions

Ionization mode:	negative
Temp.:	350 °C
Sampling speed:	1.0 mm/sec
Grid voltage:	350 V

MS conditions

MS system:	ACQUITY QDa (Performance option)
Ionization mode:	negative
Cone voltage:	10 V

Mass range:	100 to 600 Da
Sampling rate:	5 Hz

Sample analysis

The standard compounds including clobetasol propionate, arbutin (a glycosylated hydroquinone), and four parabens (Figure 1) were dissolved in methanol and sequentially diluted to prepare the working solutions. Cosmetic samples including gel and cream formulations were obtained from internet vendors in the US. The cosmetic samples were transferred directly to the QuickStrip cards (Figure 2A) using a pipette tip for analysis with the DART-MS in negative ion mode, and helium gas heated to 350 °C. The sampling speed was set to 1 mm/s. Each sample on the card is analyzed consecutively as it traverses the DART-MS interface (Figure 2B).

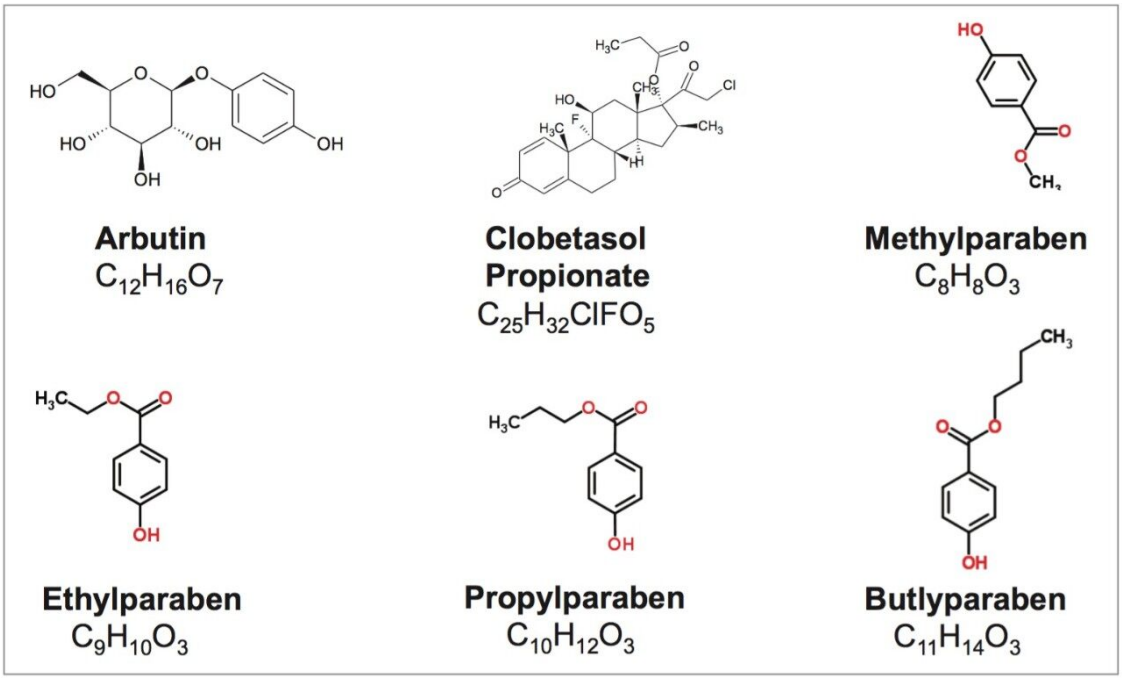

Figure 1. Empirical formulas and structures for arbutin, clobetasol propionate and parabens etc. that were analyzed in the study.

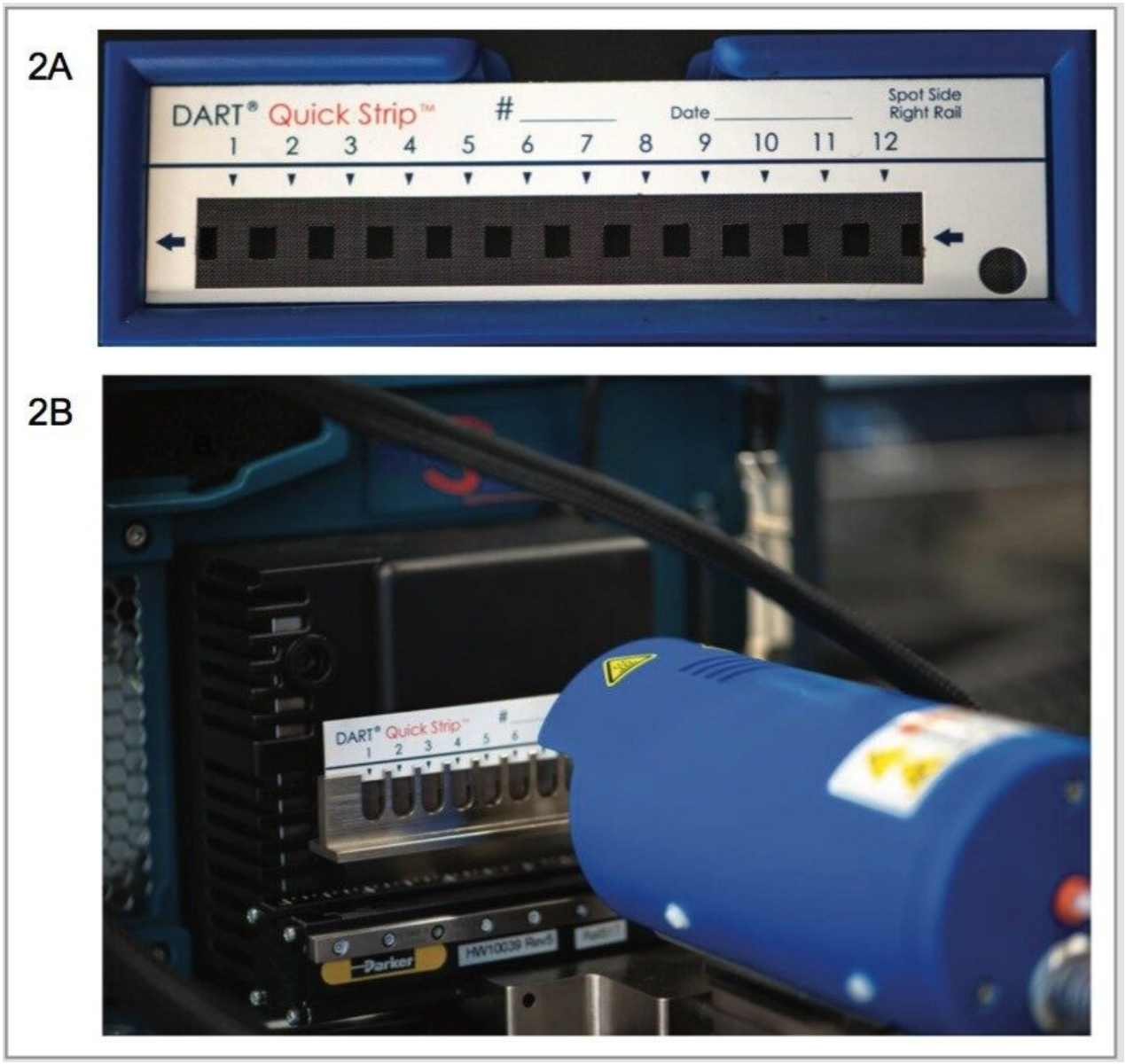

Figure 2. A. QuickStrip card used for sampling, B. automated multi-sample analysis.

Results and Discussion

Figure 3 shows the combined and subtracted spectra resulting from the analysis of a solvent standard of clobetasol propionate, a skin lightening cream, and finally a skin lightening gel sample which did not declare the presence of clobetasol propionate on the label. The packaging for the skin lightening cream sample listed

the presence of clobetasol propionate at a level of 0.05% w/w.

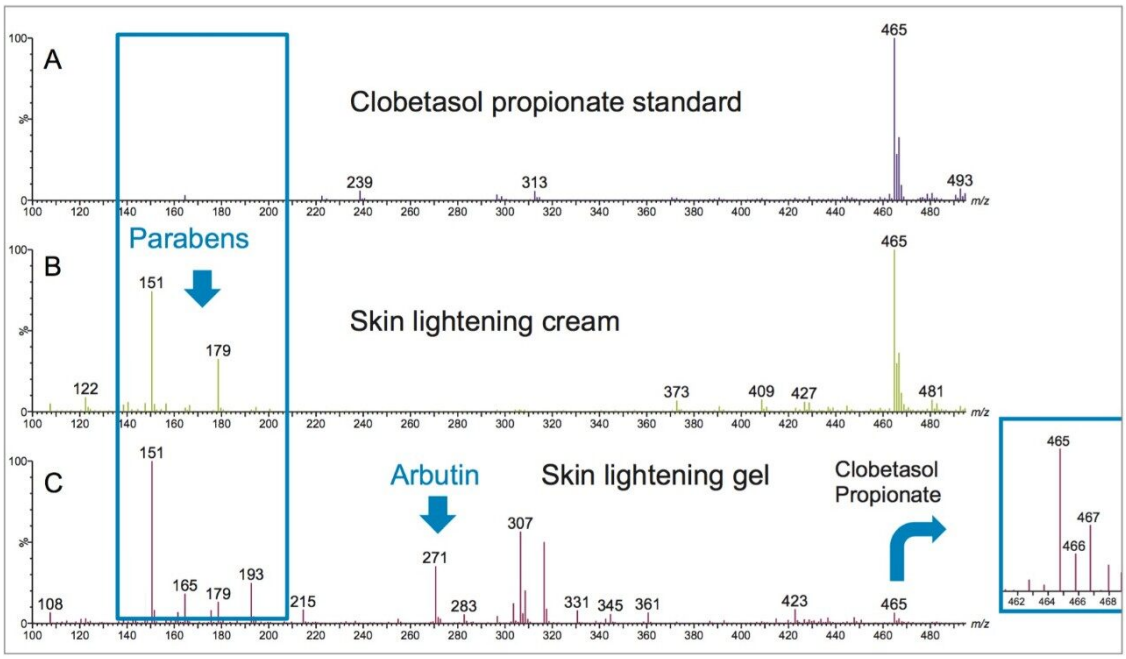

Figure 3. A. Spectra from the direct analysis of clobetasol propionate standard; B. a skin lightening cream sample containing clobetasol propionate at 0.05% w/w; C. a skin lightening gel sample. In this example the y axis is normalized to the most intense peak in the spectrum.

Clobetasol propionate, with an [M-H]- ion corresponding to a mass-to-charge ratio (*m/z*) of 465 was observed in the spectrum resulting from the analysis of a solvent standard (100 µg/mL). The isotopic pattern observed reflects the chlorine present in the chemical structure of clobetasol propionate (Figure 1) providing extra confirmation and increased confidence in the identification of the corticosteroid in both of the cosmetics samples. The same m/z and isotopic patterns were observed in both the gel and cream samples.

The *m/z* 271 observed in the skin whitening gel sample indicated by the arrow in Figure 3C corresponds to the [M-H]- ion of arbutin which was listed as an ingredient on the product label. Arbutin is frequently used as a skin lightening agent in cosmetics, and currently, its use is not restricted.[2] In addition, *m/z*'s representative of four parabens were observed in both samples. Parabens (Figure 1) are used as microbial inhibitors and are commonly found in cosmetic products.[11-13] Based on the observed *m/z*'s detected, the presence of methylparaben (*m/z* 151) and ethylparaben (*m/z* 165) was suspected in both samples, along with propylparaben (*m/z* 179) and butylparaben (*m/z* 193) in the lightening gel sample. These results were confirmed in a previous Waters application note using UHPLC with PDA and mass detection.[14]

Conclusion

- The direct analysis of cosmetic samples using DART coupled with the ACQUITY QDa Mass Detector provides molecular ion information while allowing samples to be analyzed very rapidly and without the need for time-consuming sample preparation or chromatographic method development.
- Clobetasol propionate is a highly effective drug that is widely used in dermatology; however its use requires a prescription from a licensed physician. The cosmetic skin lightening cream sample listed the presence of clobetasol propionate on the product information, however the product was sold without a prescription. In the skin lightening gel sample analyzed, the presence of clobetasol propionate was detected, but not declared on the label or the enclosed product information. Inaccurate or insufficient labeling of the cosmetics products increases the likelihood of adverse side effects, as cosmetics are usually used over long time periods with no medical supervision.
- In the current study the DART-MS has shown potential for the rapid screening of cosmetics samples suspected to contain clobetasol propionate. For precise and accurate quantitation, LC-MS can be used on the screened samples that test positive for the presence of clobetasol propionate and other cosmetics additives.

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