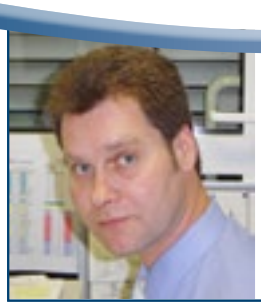
APPLICATIONS



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In addition to chromatography, Dr. Behr has an absolute love for heavy metal music and skiing in the Alps.

Related Substances Assay of the Drug Product Dienogest on a Kinetex® 3.5 µm XB-C18 Column According to Ph. Eur. Monograph 2732

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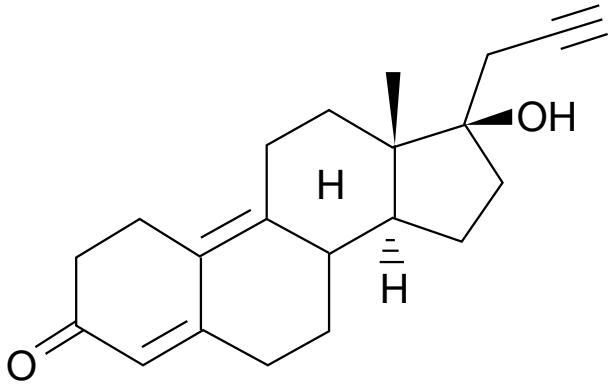
In this technical note, we report the separation between Dienogest and Impurity F {(17-hydroxy-3,3-dimethoxyestra-5(10),9(11)-dien-17α-yl)acetonitrile} using a Kinetex 3.5 µm XB-C18 HPLC column according to the Ph. Eur. Monograph 2732 related substances assay.

Introduction

The European Pharmacopoeia (Pharmacopoea Europaea, Ph. Eur.) is a single reference work for the quality control of medicines in the signatory states of the Convention on its elaboration. The official standards published within provide a legal and scientific basis for quality control during the development, production, and marketing processes. They concern the qualitative and quantitative composition and the tests to be carried out on medicines, on the raw materials used in production of medicines and on the intermediates of synthesis. All producers of medicines and/or substances for pharmaceutical use must therefore apply these quality standards in order to market their products. Dienogest is primarily an oral contraceptive used in combination with ethinylestradiol. However, the compound is also given in isolation for the treatment of endometriosis under the trade name Visanne.

Figure 1.
Dienogest



Materials and Methods

The analysis was performed using an Agilent® 1100 equipped with a multiple wavelength UV detector. The Kinetex 3.5 µm XB-C18 column used for analysis was obtained from Phenomenex (Torrance, CA, USA). All solvents were purchased from Honeywell (Morristown, NJ, USA) and Sigma-Aldrich (St. Louis, MO, USA). Ph. Eur. Standard Dienogest for system suitability CRS (containing impurity F) Y0001782 was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allée Kastner CS 30026 F - 67081 STRASBOURG (France).

Ph. Eur. Monograph 2732

Ph. Eur. Monograph 2732 system suitability reference solution A. Dissolve 2.5 mg of Dienogest for system suitability CRS (containing impurity F) in 2 mL of acetonitrile and dilute to 5.0 mL with water.

Column:
- *size: l = 0.25 m, Ø = 4.6 mm*
- *stationary phase: end-capped extra-dense bonded octadecylsilyl silica gel for chromatography (3.5 µm)*
- *temperature: 35 °C*

Mobile Phase:
- *A: Acetonitrile/Water for chromatography (10:90 V/V)*
- *B: Water for chromatography/acetonitrile (10:90 V/V)*

Gradient: 10 % mobile phase B for 3 min to 90 % mobile phase B in 50 min

Flow Rate: 1.0 mL/min

Detection: spectrophotometer at 210 nm

Injection: 15 µL

Relative retention with reference to Dienogest (retention time = about 19 min): impurity F = about 1.1

System suitability: reference solution (A):
- *resolution: minimum 4.0 between the peaks due to Dienogest and impurity*

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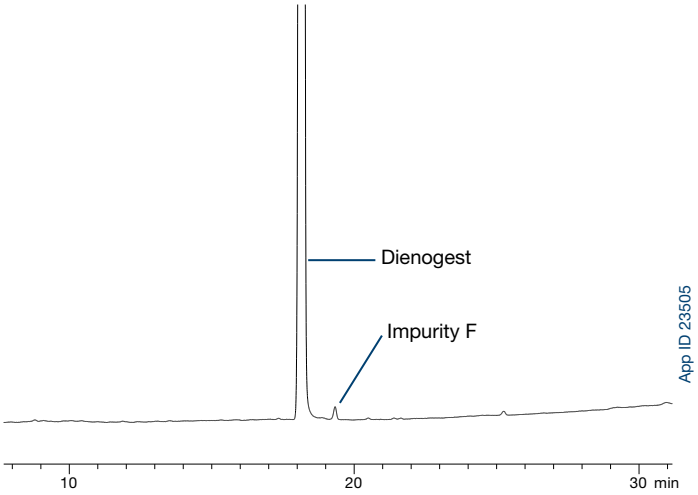
Result and Discussion

In this technote we report the separation between Dienogest (the Active pharmaceutical ingredient) and related impurity F ((17-hydroxy-3,3-dimethoxyestra-5(10),9(11)-dien-17α-yl)acetonitrile) per the related substances section of Ph. Eur. Monograph 2732, as shown in **Figure 2**. The resolution between Dienogest and the related substance F is 6.22 which passes the system suitability minimum resolution requirement of 4.0.

Figure 2.
Dienogest reference solution (A) on a Kinetex® 3.5 µm XB-C18, 150 x 4.6 mm, R_s= 6.22



Conclusion

The results shown above demonstrate that Kinetex 3.5 µm XB-C18, 150 x 4.6 mm column can be successfully used to analyze Dienogest according to Ph. Eur. Monograph 2732. Resolution between the API and impurity F for system suitability was 6.22 which is well above the minimum of 4.0 required by the Ph. Eur. monograph method.

Kinetex 3.5 µm Analytical Columns		SecurityGuard™ ULTRA Cartridges*
Phases	150 x 4.6 mm	3pk
XB-C18	00F-4744-E0	AJ0-8768 for 4.6 mm ID

* SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

guarantee

If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to other products of the same phase and dimensions, return the product with comparative data within 45 days for a FULL REFUND.

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