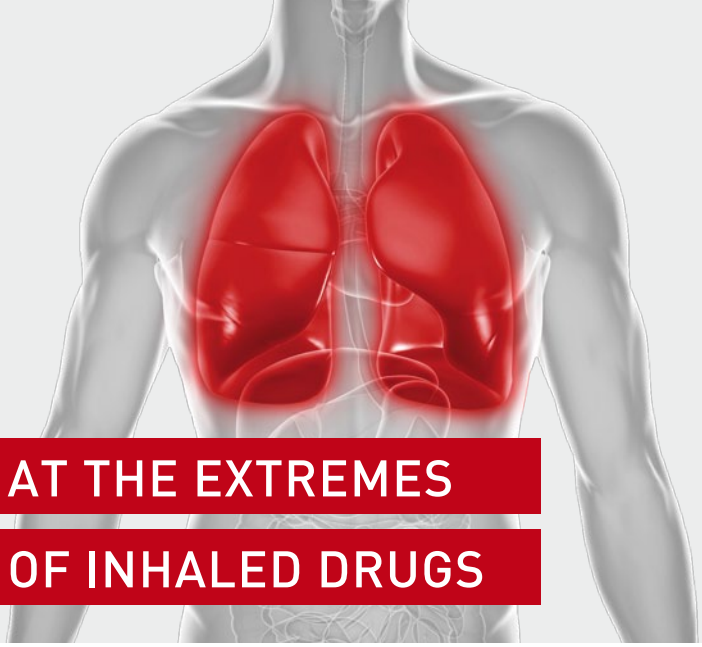

pharm analyt
BIOANALYSIS

BIOANALYSIS AT THE EXTREMES

BIOANALYSIS OF INHALED DRUGS

Inhaled drugs have extremely low systemic abundance, intended or not. Regardless of its purpose, quantification is necessary at the very least for regulatory requirement. Extremely low concentrations of the systemic active ingredients, in ever declining sample volumes (plasma) call for increasingly sensitive methods. At the same time regulatory and ethical demands are rising.

pharm-analyt has been catering to this demand for more than 2 decades, analyzing orally, inhaled and nasally administered Small Molecules and peptides in plasma. Our most sensitive assays are in the range of femtogram/mL plasma.

Bioavailability and disposition of azelastine and fluticasone propionate when delivered by MP29-02, a novel aqueous nasal spray

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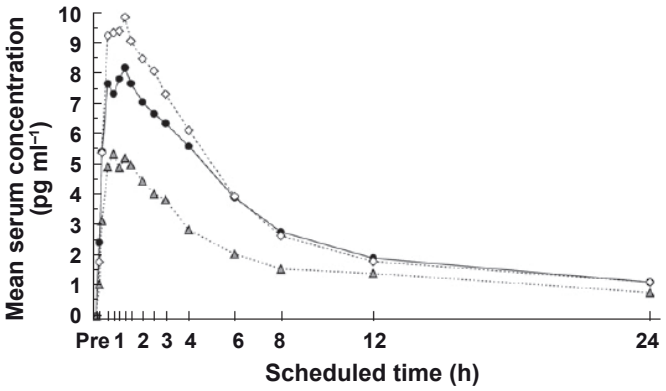


Figure 1

Study 1: Mean fluticasone propionate (FP) serum concetration-time cuvers after intranasal single dose administration of 200 µg FP delivered by trree different nasal spray products; ● MP29-02; ◇ MP29-02-FP-mono (i.e. MP29-02 formulation without azelastine); △ Marketed comparator product FP-BI (Fluticasone propionate Boehringer-Ingelheim/Roxane Laboratories Nasal Spray)

Examples of Inhalative Substances and Determination Limits:

Substance	Volume / Matrix	Calibration Range
Budesonide	0.5 mL plasma	5 - 1000 pg/mL
Ciclesonide + M1	1 mL serum	10 - 2000 pg/mL
Fluticasone Propionate	0.25 mL serum	3 - 1000 pg/mL
Fluticasone Propionate	1 mL serum	0.25 - 50 pg/mL
Formoterol	0.5 mL plasma	0.4 - 100 pg/mL
Salmeterol	0.25 mL serum	2 - 600 pg/mL

30 YEARS OF BRILLIANCE

DISTINGUISHING CORTISOL FROM CORTICOSTEROIDS IS CRITICAL AND WIDELY UNDERESTIMATED!

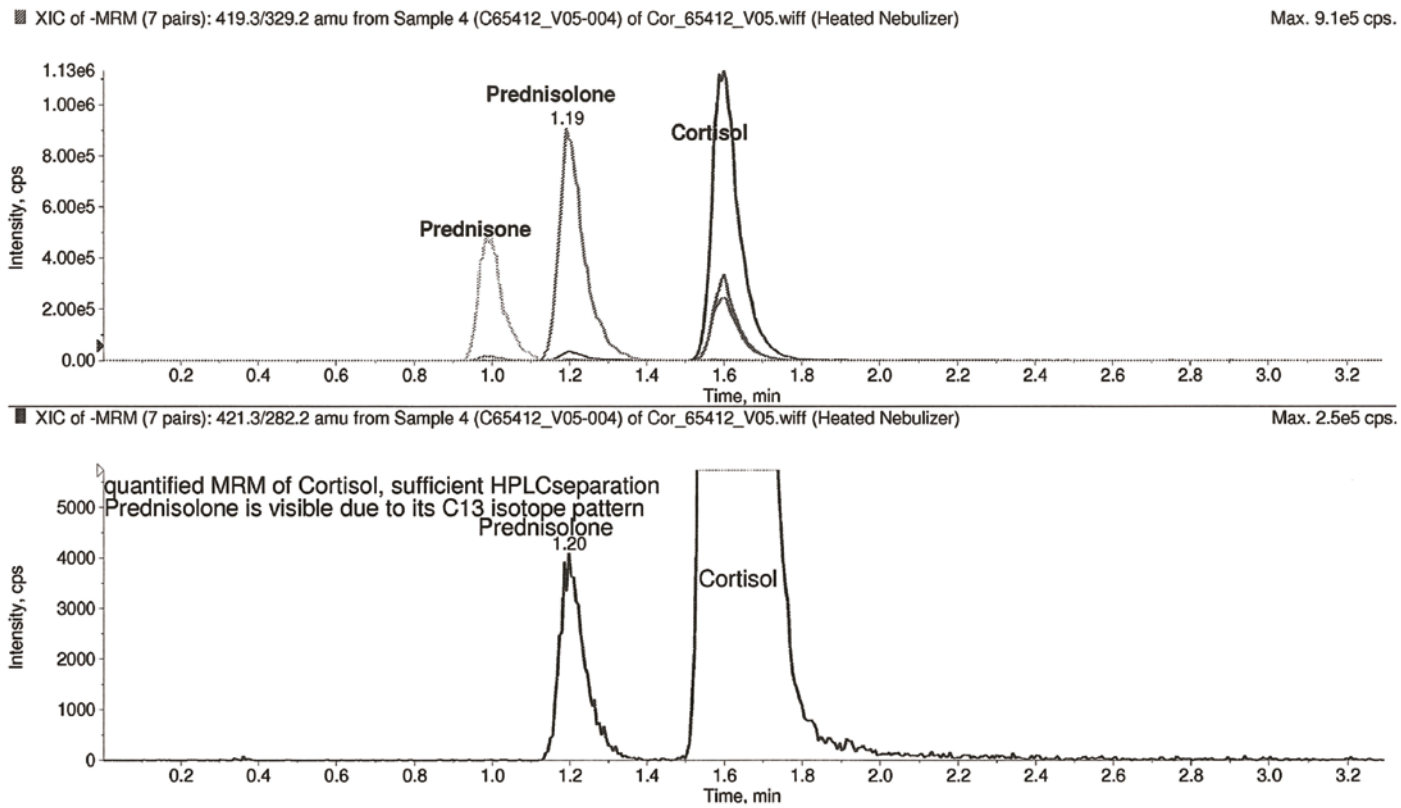
1000 ng prednisolone per mL plasma fakes ca. 10 ng cortisol per mL plasma!

Administering Corticosteroids (oral, topical, inhalative) and analyzing them by immunoassays, there´s the danger of so called “cross-reactions” resulting in wrong (higher) levels. When suppressing cortisol by corticosteroids the levels of native cortisol will decrease and escalate the problem further.

Even using the highly selective HPLC-MS/MS systems, “cross-reactions” can occur! For example, by application of prednisone (attention: metabolite is prednisolone) or initially prednisolone, the disturbing peak of prednisolone in the chromatogram is likely to bias the cortisol results.

In general, on reversed phase columns (C8, C18) prednisolone (MW 360) is not separable from cortisol (MW 362) and consequently adds to the sensitive iontrack of cortisol a signal of identical fragmentation!

Chromatogram of Interference Sample, Good Chromatographic Separation:



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