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*Short communication*

# Extraction and Interaction study by HPLC-DAD method for screw cap PP 28 child-resistant used in packaging of drug product

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## Introduction

One of the essential before one pharmaceutical product is approved from regulatory agencies and to be released on the market, is to determine its purity, through determination of its impurity profile. Nowadays, migration and sorption of mobile chemical species from components used in the manufacture and storage of pharmaceutical products must be assessed.

The aim of the presented study is to evaluate the suitability and to justify the choice of the plastic material screw cap PP 28 child-resistant (CR) with tamper evident ring, embossed at the top and with PE-liner (pressure seal disc).

The compatibility of the screw cap PP 28 CR is tested by performing extraction and interaction studies for detection and identification of organic and inorganic compounds, possibly deriving from the screw cap, which potentially may interact with the final drug product during storage and use.

## Materials and methods

*Extraction and migration study*

The samples for Polypropylene (PP) outer cap, high-density polyethylene (HDPE) inner cap and polyethylene (PE) foam liner extractable testing were prepared from new, unused PP outer and HDPE inner caps and rings and PE foam liner, which were cut into small pieces (~ 0.5-1 $cm^2$ in size) before extraction. Molded screw caps were used instead of HDPE and PP granulate so that manufacturing influence can be taken into account (thermo-processing, molding, lubrication etc.). The extraction was performed by using ultra-sonic (US) bath and two specially selected solvent systems (placebo for oral solution adjusted to pH 3 and pH 5). The choice of solvents was made in accordance to the minimum and maximum specified pH values in the specification of the finished drug product, thus covering the extreme pH values at which the plastic components can be exposed during shelf life. The US (ultrasonic) extraction was performed by extracting ~ 27 g Polypropylene (PP) outer cap and ~ 35 g high-density polyethylene (HDPE) inner cap with tamper evident ring with 100 mL of placebo. Accordingly, same type of extraction was performed on ~ 2 g polyethylene (PE) foam liner with 50 mL of placebo. The extraction was conducted for about 2 hours, taking care that the ultrasonic (US) bath temperature did not exceed 35 °C as a result of the constant application of energy to the system.

After the extraction, the extracting solvents were filtered from the plastic pieces through 0.2 µm Regenerated Cellulose (RC) membrane filter before injecting. The samples for HPLC-DAD evaluation were analyzed directly without further processing. The HPLC-DAD screening was performed on Agilent 1260 HPLC system equipped with binary pump and diode-array detector. The following method parameters were used for the screening of samples and blanks: Column: Waters XTerra RP18 150 x 3.0 mm; 3.5 µm; Temp. 25 °C; Mobile phase A: 10 mM ammonium acetate B: acetonitrile; Flow 0.3 mL/min; Injection volume 20 µL;

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Wavelength: 210, 220, 230, 250 nm + UV spectra. The method is gradient (Petruševski et al., 2016).

*Sorption study*

Sorption studies were performed in order to investigate possible interactions between the selected screw cap and the formulation due to possible sorption of the active substance and preservative. For that purpose, initial analysis were preformed, afterwards bottles of finished product oral solution were stored for about three months at 25 °C/60% RH and 40°C/75% RH in inverted and non-inverted position.

Validated HPLC method was used for determining the content of API and Preservative in the drug product formulated as oral solution.

5 mL from oral solution were diluted to 50 mL with mobile phase, then filtered through 0.2 µm GHP filter into HPLC vial and analyzed. The nominal concentration of test and standard solution is 0.3 mg/mL of preservative and 0.1 mg/mL of API. The content is calculated from peaks area ratio in the chromatograms of the test and the standard solution respectively, at detection wavelength of 210 nm, on Thermo Ultimate Dionex system equipped with quaternary pump and diode-array detector. The following method parameters were used: Column Zorbax SB C8, 250 mm x 4.6 mm, 5 µm; Temp. 25 °C; Mobile phase A: Solution A (1.244 g pentane-1-sulfonic acid sodium salt in 1000.0 mL volumetric flask, dissolve with 600 mL water. Add 28 mL 85% ortho-phosphoric acid and dilute with water R) B: acetonitrile; Flow 1.8 mL/min; Injection volume 10 µL; Wavelength: 210 nm. The method is isocratic.

## Results and discussion

Representative UV chromatograms of analyzed placebo solutions, standards and tests solutions were obtained end evaluated after extraction and migration method. Values for Assay of API and preservative were collected after sorption method and compared to data values of untreated samples.

From the obtained data of sorption studies it can be concluded that the assay of API and preservative in finished product oral solution, as well as related and degradation products, are not significantly changed after storage of the original bottles for three months at 25 °C/60% RH and 40 °C/75% RH in inverted position.

The HPLC-DAD screening of the generated results for presence of extractable and leachable compounds revealed that all screw cap components do not contain any extractable compounds above the method detection limit, for any of the generated extracts, thus the selected packaging material does not affect the efficacy of the drug product.

The outcome from the analysis of inverted bottles with placebo and API oral solution is that there are no detected compounds deriving from the plastic screw cap PP 28 CR.

## Conclusion

The collected data demonstrate that the selected material is suitable in regards to the integrity and compatibility with the oral drug product (EMA, Guideline on Plastic Immediate Packaging Materials CPMP/QWP/4359/03). It can be concluded that there aren't any changes in the quality of the drug product.

## References

EMA, Guideline on Plastic Immediate Packaging Materials CPMP/QWP/4359/03. Microsoft Word - Guideline on Primary Plastic Packaging Materials.doc (europa.eu)

Petruševski, V., Jolevska, S.T., Ribarska, J.T., Chachorovska, M., Petkovska, A., Ugarković, S., 2016. Development of complementary HPLC-DAD/APCI MS methods for chemical characterization of pharmaceutical packaging materials, J. Pharm. Biomed. Anal. 124, 228–235. https://doi.org/10.1016/j.jpba.2016.03.005