Platzer *et al.: Intrinsic Activity*, 2016; **4**(Suppl.3):A3.3
http://www.intrinsicactivity.org/2016/4/S3/A3.3
published online: 5 September 2016

INTRINSIC ACTIVITY

22nd Scientific Symposium of the Austrian Pharmacological Society: Joint Meeting with the Hungarian Society for Experimental and Clinical Pharmacology

Vienna, 8–10 September 2016

MEETING ABSTRACT

A3.3

Development of a multi-dimensional screening model to investigate the immune-modulatory effects of extractables and leachables from packaging materials

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Background: The plastic manufacturing process is accompanied by the addition of a variety of chemical compounds to achieve the designated properties of the synthetics. These additives are not bound to the polymer matrix and, therefore, become available due to migration out of the plastic. Risk assessment of migrating packaging components into final products entails significant challenges for regulators and manufacturers. Apart from the analytical requirements associated with the identification and quantification of extractables and leachables, adverse effects on human metabolism with regard to various impacts on human health are of particular concern. This work evaluates different extraction approaches requiring individual analytical techniques for the detection of very volatile, volatile and semi-volatile compounds.

Methods: Sampling included food contact materials, PVC medical devices and house dust. For determination of volatile and semi-volatile extractables, packaging materials and product containers were directly exposed to solvents with different polarities, ***e.g.*** hexane, methylene chloride, *tert*-methyl butyl ether, isopropanol and water over time (2 weeks to 6 months) at room temperature and/or thermal treatment with 60 °C. Solvent extracts were concentrated and injected into a 6890 gas chromatograph (GC, Agilent Technologies) coupled with a single quadrupole mass spectrometer (MS, Agilent Technologies) operated at 70 eV. Migration studies targeting volatile and semi-volatile leachables in aqueous products thermally stressed at 60 °C for two weeks were conducted. Additionally, direct static-headspace sampling of packaging materials and the aqueous sample material was performed using a 7697 headspace sampler (Agilent Technologies). For identification and quantification, a screening method with 210 reference substances including volatile and semi-volatile compounds ***e.g.*** phthalates, polycyclic aromatic hydrocarbons (PAH), linear hydrocarbons (C8–C40), solvents and individual reference standards was established.

Results: Depending on solvent polarity, different patterns of volatile and semi-volatile compounds were extracted from packaging materials, infusion sets, dialysis tubes, syringes, glas vials with stoppers and house dust. Comparable results including material-specific components were obtained for the hexane and the ether extracts, whereas substances derived from the production process or the material composition such as butylhydroxytoluol, styrene, methyl-acrylates, diethylphthalate, diethylhexylphthalate, 2-ethyl-1-hexanol, diisobutylphthalate and 9-octadecanamide were determined. By means of direct HS-GC-MS analysis of the aqueous extract ***e.g.*** 2-methyl-pentane, 3-pentene-2-one and 2-octane, unknown but structurally related hydrocarbons with m/z 43, m/z 45, m/z 57, m/z 71, m/z 85, m/z 98, m/z 112 and m/z 127 were detected. Using the internal data analyses method, these compounds were also identified in the final products.

Discussion: Although phthalates were replaced by alternative plasticizers in recent years, these compounds may also enter the human body by inhalation, enteral or parenteral uptake and may exert severe side effects on hormone metabolism promoting breast cancer, infertility or allergy. These experiments serve as part of a holistic approach to effectively evaluate and minimize the risk of leachables present in final products with regard to improvements in product quality, patient safety and consumer acceptance covering the production process and life-cycle management. Further studies regarding the biological activity will be conducted, including a validated quantification of identified migration compounds together with an investigation of the dose-dependent biological effects by means of an *in vitro* cell culture model.

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