

Publication

4-Hydroxynonenal - A Toxic Leachable from Clinically Used Administration Materials

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The migration of chemicals from processing materials into biopharmaceuticals can lead to various problems. Leachables from administration materials, with no possibility of further clearance, are of particular concern. Released chemicals can be toxic or react with formulation components, thereby impacting product safety. Therapeutic proteins, which are susceptible to chemical modifications, have highest risk to be affected.; The aim of this study was to identify a previously unknown leachable compound from clinical administration sets, which was present above the applied generic safety threshold.; Extracts of commonly used clinical administration sets were analyzed using a recently established specific assay allowing the identification and quantification of the α,β -unsaturated aldehyde 4-hydroxynonenal (HNE) in a drug product surrogate solution. HNE was quantified after derivatization with 2,4-dinitrophenylhydrazine (DNPH) and liquid extraction of the formed hydrazone by LC-MRM analysis.; Potentially genotoxic HNE was a leachable compound from all tested administration sets, in parts exceeding safety thresholds for genotoxins. The HNE-releasing polymer was identified as PVC.; Clinical administration sets should be, like manufacturing materials and container closure systems, in the focus of routine leachables studies. Manufacturers of clinical administration sets should show responsibility to avoid the presence of safety concerning chemicals, like HNE.

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