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INPLASY

Di(2-ethylhexyl) phthalate (DEHP) plasticizer: a systematic review of its migration in medical devices and toxicity

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - This protocol is being submitted retrospectively. The review team began the search and screening process on 13 November 2024. A PROSPERO registration was believed to have been completed prior to data extraction and was cited in the manuscript (CRD42024113926) and in an associated OSF data repository. It was subsequently confirmed that this PROSPERO record was never finalized or published. Data extraction for this review was completed on 13 November 2025. This INPLASY registration is submitted to provide a transparent, public record of the review's design and methods following identification of this administrative error.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202680067

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 August 2026 and was last updated on 17 August 2026.

INTRODUCTION

Review question / Objective To analyze recent evidence on di(2-ethylhexyl) phthalate (DEHP) migration from medical devices and its toxic effects through a systematic review, addressing the following question: What is the current evidence on DEHP migration from plasticized PVC medical devices, and what toxicological effects (reproductive, endocrine, hepatic, cardiovascular, cytotoxic, and genotoxic) are associated with DEHP/MEHP exposure in in vivo, ex vivo, and in vitro studies?

Rationale Growing evidence of the toxic effects of DEHP and other phthalates has generated considerable debate about their safety in invasive medical devices. Since DEHP binds non-covalently to PVC polymers, it can migrate into biological fluids during medical procedures such as blood transfusion, intravenous infusion, hemodialysis, and cardiopulmonary bypass. Although DEHP is classified in the CMR-1B category and several countries have restricted its use in medical devices, the direct relationship between DEHP exposure from medical devices and systemic toxic effects requires further elucidation. This review consolidates recent evidence on DEHP migration from plasticized PVC devices and its associated toxicological effects to inform regulatory and clinical decision-making.

Condition being studied Human exposure to di(2-ethylhexyl) phthalate (DEHP) released from

plasticized polyvinyl chloride (PVC) medical devices during clinical procedures, and the resulting toxicological effects documented in human, animal, and in vitro studies.

METHODS

Search strategy A systematic search was conducted in Scopus, ScienceDirect, and PubMed, with Google Scholar used for grey literature. MeSH terms and free-text terms related to "plasticizers", "phthalates", "DEHP metabolites", "medical devices", "migration", "toxicity", "cytotoxicity", "carcinogenic", and "endocrine disruptors" were combined using the Boolean operators AND, OR, and NOT to narrow or broaden results. Complete, reproducible search strings for each database are available as a supplementary file, following PRISMA-2020 recommendations.

Participant or population Studies reporting on: (a) patients exposed to DEHP-plasticized PVC medical devices during clinical procedures (e.g., ECMO, cardiopulmonary bypass, catheterization, hemodialysis, parenteral/enteral nutrition), and (b) animal models (rodent strains) and human/animal cell culture systems used to evaluate DEHP/MEHP toxicity. No restrictions were applied based on age, sex, or clinical setting.

Intervention Exposure to di(2-ethylhexyl) phthalate (DEHP) or its metabolite MEHP, either through contact with DEHP-plasticized PVC medical devices in clinical settings, or through experimental administration (oral, intragastric, intraperitoneal, or in vitro exposure) in animal models and cell cultures.

Comparator Not uniformly applicable across all included studies. Where present, comparators included pre- versus post-procedure exposure levels, DEHP-free/non-PVC alternative devices, and untreated/control groups in experimental studies.

Study designs to be included Original research articles, including observational/cross-sectional human exposure studies, ex vivo/direct migration assay studies, in vivo animal toxicity studies, in vitro cell culture studies, and relevant regulatory documents.

Eligibility criteria Inclusion: (a) publication year 2013–2025; (b) English language; (c) original articles and regulatory documents; (d) full text available; (e) subject areas: chemistry, biochemistry, and environmental sciences. Only studies scoring 26–28 ("excellent" quality) on the Downs and Black checklist were retained for synthesis.

Information sources Scopus, ScienceDirect, PubMed, and Google Scholar (grey literature).

Main outcome(s) DEHP and/or MEHP migration/leaching levels from medical devices (measured in biological fluids or clinical simulants), and toxic effects of DEHP/MEHP exposure (reproductive, endocrine, hepatic, cardiovascular, cytotoxic, and genotoxic).

Additional outcome(s) Identification of urinary and blood biomarkers of DEHP exposure (e.g., 5cx-MEPP, 5OH-MEHP, 5oxo-MEHP) and their relationship to procedure invasiveness and exposure duration.

Data management Search results were imported into Mendeley Desktop 1.19.8 for reference management and duplicate removal. Two independent reviewers screened titles/abstracts and full texts against the eligibility criteria and extracted data using a standardized form. Discrepancies were resolved by consensus between reviewers.
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Quality assessment / Risk of bias analysis Methodological quality was assessed independently by two reviewers using the Downs and Black checklist (27 items; scores range 0–28). Quality categories: excellent (26–28), good (20–25), fair (15–19), poor (≤14). Only studies rated "excellent" were included in the final synthesis.

Strategy of data synthesis A narrative/qualitative synthesis was performed, given the substantial heterogeneity in study designs, models, doses, and outcome measures. Studies were grouped into two thematic categories: (a) DEHP migration from plasticized PVC medical devices, and (b) DEHP/MEHP toxicity in vivo and in vitro. No meta-analysis was conducted.

Subgroup analysis Not applicable (qualitative/narrative synthesis; no meta-analysis was performed).

Sensitivity analysis Not applicable (no meta-analysis was performed).

Language restriction Only articles published in English were included.

Country(ies) involved Colombia.

Other relevant information Reference list available in the manuscript and in Supplementary File 1. Contributorship: Benavides-Henriquez HG (conceptualization, methodology, investigation, data curation, writing – original draft, writing – review & editing); Mendoza-Meza DL (conceptualization, methodology, formal analysis, investigation, writing – review & editing, supervision, project administration).

Keywords Diethylhexyl phthalate; plasticizers; medical devices; endocrine disruptors; toxicity tests.

Dissemination plans Submission of the completed systematic review to a peer-reviewed journal.

Contributions of each author

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