

PLASTICIZER DEHT

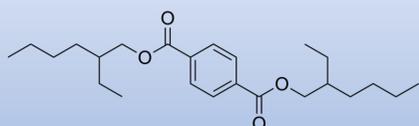
PROVIDES ADEQUATE BLOOD COMPONENT QUALITY: A POTENTIAL SUBSTITUTE TO DEHP IN BLOOD BAGS

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DEHT

di(2-ethylhexyl) terephthalate



A structural isomer of DEHP, with no reported resemblance of the DEHP toxicity pattern

• BACKGROUND

Updated European Union regulations (EU) 2017/745 restricts usage of the phthalate plasticizer di(2-ethylhexyl) phthalate (DEHP) in future blood bags. This increases the urgency to find a non-phthalate, substitute plasticizer that does not compromise blood component quality.

• AIMS

To investigate whether di(2-ethylhexyl) terephthalate (DEHT), can be an acceptable substitute to DEHP in PVC blood bags through:

- Assessment of the quality of RBCs (irradiated and non-irradiated, paired with two different additive solutions; SAGM and PAGGSM), plasma and platelets collected and stored in PVC-DEHT blood bag systems
- Comparison of the results to corresponding DEHP storage

• MATERIALS & METHODS

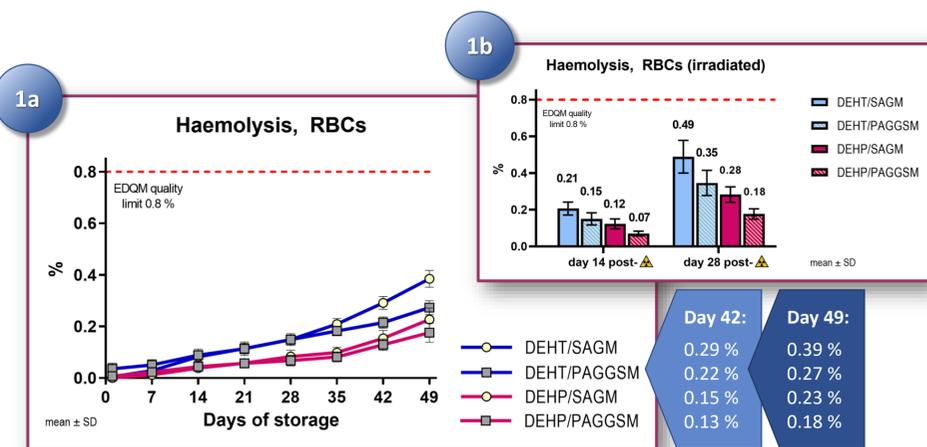
RBC study arms (4): DEHT/SAGM, DEHT/PAGGSM, DEHP/SAGM and DEHP/PAGGSM. Plasma and platelet study arms (2): DEHT and DEHP.

Blood component	N, total (N, each study arm)	Plasticizer	Additive solution	Sampling days	Analysis parameters
Red blood cell (RBC) concentrates	64 (16)	DEHT DEHP	SAGM PAGGSM	1, 7, 14, 21, 28, 35, 42, 49	Haematocrit, haemoglobin, haemolysis, mean corpuscular volume (MCV), RBC microvesicle (RMV) count, RMV phosphatidylserine translocation, pH, extracellular potassium ions (K ⁺), glucose, lactate, ATP, 2,3-DPG
Red blood cell (RBC) concentrates • X-ray irradiated on day 2	60 (15)	DEHT DEHP	SAGM PAGGSM	2 pre-irradiation 14, 28 post-irradiation	Haematocrit, haemoglobin, haemolysis, MCV, RMV count, RMV phosphatidylserine translocation, pH, extracellular K ⁺ , glucose, lactate
Fresh frozen plasma (FFP)	32 (16)	DEHT DEHP	N/A	0 pre-freezing 0, 7, 14 (FVIII only) post-thawing	Factor (F) V, FVII, FVIII, FX, FXI, FXIII, von Willebrand Factor, protein C, protein S-free, α-1-antitrypsin, fibrinogen, triglycerides
Buffy coat platelet concentrates (PC)	16 (8)	DEHT DEHP	PAS-E	2, 5, 7	Count, mean platelet volume (MPV), extracellular lactate dehydrogenase (LDH), pH, glucose, lactate, bicarbonate, ATP, JC-1, CD62P, CD42b, PECAM-1, response capacity to agonist stimulation (PAC-1; collagen, ADP, thrombin), swirling

➤ All bags, including collection, were made of either PVC-DEHT or PVC-DEHP, ensuring no cross-contamination, except for the PC storage bag which was plasticized with BTHC and tubes of either DEHT or DEHP (PCs passed briefly through the I-Platelet Pooling set (Kansuk, Turkey) with tubes of DEHP during processing). All components were leucofiltered. Whole blood was separated within 8 hours of donation.

• RESULTS

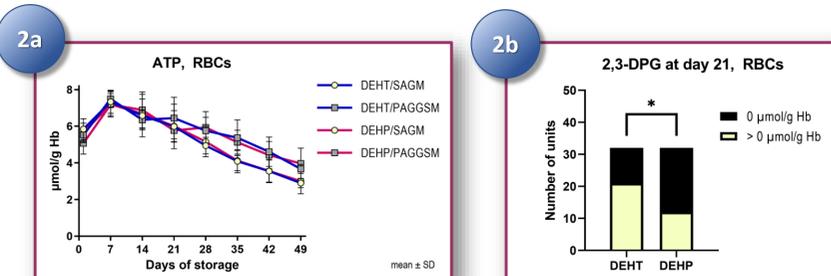
➤ RBCs had acceptable membrane stability and no difference in metabolism



➤ **Haemolysis:** For non-irradiated RBCs (fig. 1a), all four study arms remained below half of the EDQM quality limit (0.8 %) at day 49, though the level was significantly higher in DEHT from d14 ($P < 0.001$). The irradiated units (fig. 1b) were an amplified reflection of the non-irradiated. PAGGSM appeared to be favourable to SAGM independent of plasticizer.

➤ **RBC microvesicle (RMV) count** showed a similar pattern to haemolysis in highest-to-lowest order at end of storage, both in non-irradiated and irradiated units. Noteworthy, for non-irradiated units, DEHT/PAGGSM remained similar to DEHP up to/including day 42.

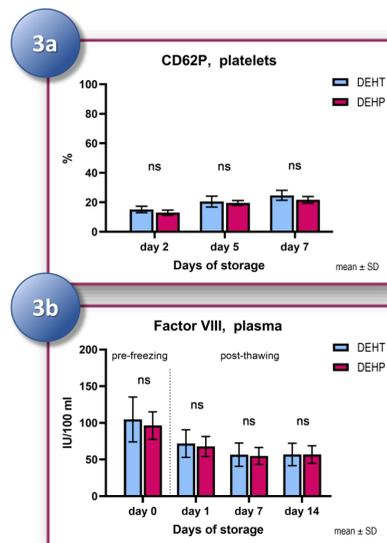
➤ **Extracellular K⁺:** There was no indication of disadvantageous K⁺ levels in DEHT; in fact, for non-irradiated RBCs, the concentration was 5-10 % lower ($P < 0.001$) in DEHT at storage end, whereas differences were smaller in irradiated RBCs.



➤ **The metabolic parameters and MCV** were not influenced by plasticizer, but a generally faster metabolism rate was observed with SAGM, which gave better ATP preservation (fig. 2a) and less RMV phosphatidylserine translocation in the PAGGSM arms.

➤ **2,3-DPG** preservation (fig. 2b) was slightly favourable in DEHT storage, as a higher percentage of DEHT-stored RBCs had some 2,3-DPG left at d21 (DEHT: 66%, DEHP: 38%, $P < 0.05$).

➤ Platelets and plasma were similarly preserved



➤ **Platelets:** Similar reactivity, activation and metabolism at all measuring points (ns) demonstrated an overall high quality independent of plasticizer, here illustrated through similar levels of activation marker CD62P (fig. 3a).

➤ **Plasma:** There were no differences (ns) in FFP coagulation factors/inhibitor preservation throughout storage, here illustrated by similar decrease in factor VIII regardless of choice of plasticizer (fig. 3b).

SUMMARY

DEHT-plasticized PVC blood bags provide adequate storage quality for both irradiated and non-irradiated RBCs. PAGGSM may be slightly preferential to SAGM as additive solution, though SAGM remains an acceptable choice.

FFP coagulation factors and platelet lesion profile are equally affected in both plasticizers throughout storage.

CONCLUSION

We consider PVC-DEHT blood bags a recommendable non-phthalate candidate for future blood component collection and storage.

Read the full publication:

<https://onlinelibrary.wiley.com/doi/10.1111/vox.12982>

