

LABILE BLOOD COMPONENTS PLASMA COLLECTED, PROCESSED AND STORED IN DEHP-FREE CONTAINERS

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INTRODUCTION

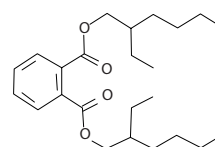
Use of diethylhexyl phthalate (DEHP) as a polyvinyl chloride (PVC) plasticiser for medical devices is now discouraged since this plasticiser has been found to be toxic in animal experiments. During blood storage, DEHP leaches slowly from PVC bags into blood components intended to be transfused to patients. Toxicological studies suggest that DEHP is a reproductive toxicant potentially leading to a lower potential of sexual reproduction. The European Directive 2007/47/EC advises to use alternatives to DEHP-PVC as far as possible.

The plasticizer DINCH is an alternative to DEHP in the manufacture of blood bags. DINCH has a very low migration rate and an excellent toxicological profile:

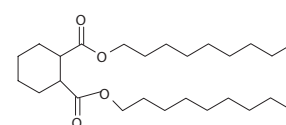
- no testicular toxicity, nor impairment of fertility, nor teratogenicity;
- no carcinogenic potential.

Although alternative PVC plasticizers are known for decades, demonstration has to be made

whether blood component storage is not adversely influenced. The present study focuses on the in vitro effects on leukodepleted plasma for fractionation and provides comparison between DINCH-PVC and DEHP-PVC containers during 1 year.



DEHP
(di(2-ethylhexyl)
phthalate)



DINCH (1,2-Cyclohexanedicarboxylic
acid, diisononylester).

MATERIALS AND METHODS

CONTAINERS:

30 quadruple bag systems with in-line whole blood filter (MACOPHARMA - France) made of DINCH-PVC and 30 identical units made of DEHP-PVC have been used in order to compare characteristics of blood components stored in both plastic materials.

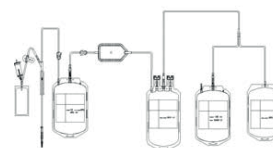
BLOOD COMPONENTS:

450 – 480 ml of blood was collected in 63 ml of citrate phosphate dextrose (CPD) solution from 60 healthy donors for the preparation of RBC and plasma. 100 ml of SAG-M solution was used as an additive solution for RBC. 30 whole blood units were stored at 2 - 6°C for 8 hours and 30 units during 18-24 hours. Once separated by centrifugation, the plasma was collected in a transfer bag and frozen.

STUDY OF PLASMA CHARACTERISTICS:

Tests (see list of tests in the Table of Results below) were performed at D1, D14, M6 and M12 on 30 samples per container type. Plasma proteins, QT, ACT, fibrinogen, Factor V, Factor VIII, activated ATIII; plasminogen, α2-antiplasmin, Factor XIIa, TAT complex, C3a, C5a, D-dimers, F1+2, FPA and C1 inhibitors were also controlled after a 24 month storage period on 5 samples. Controls at D1 were performed before plasma freezing. The same validated test methods were used for both types of containers.

The statistical comparison of biological characteristics between the two types of PVC was done using SPSS PSAW.



Schematic representation of the blood bag system

Blood group	O	A	AB	B
Number of donations	12+12	12+12	2+2	4+4
%	40%	40%	7%	13%

Distribution of blood groups

MIGRATION OF PLASTICISERS:

In parallel samples were kept to measure comparatively the migration of DINCH versus DEHP from containers into the plasma during 1 year. The plasticizer's concentration is measured by HPLC with UV detection.

RESULTS AFTER 12 MONTH STORAGE

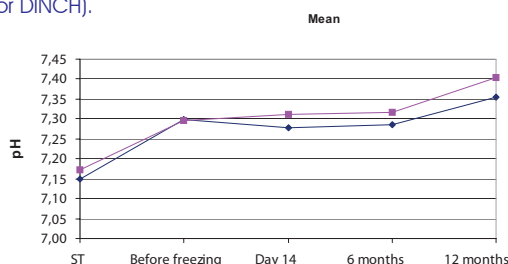
		pH	K ⁺ (mEq/L)	Proteins (g/L)	Albumin (g/L)	IgG (g/L)	IgA (g/L)	IgM (g/L)	Cholesterol (g/L)	Triglycerides (g/L)	QT (%)	ACT (s)	Fibrinogen activity (g/L)
DEHP	Mean	7,36	3,87	60,30	37,91	8,18	1,75	1,11	1,53	0,97	85,47	38,16	2,44
	SD	0,07	0,38	2,65	1,39	1,36	0,72	0,35	0,28	0,52	8,11	4,63	0,61
DINCH	Mean	7,40	3,79	59,67	37,58	8,30	1,84	1,10	1,48	0,97	84,20	37,83	2,39
	SD	0,07	0,27	4,05	2,03	2,53	0,69	0,29	0,27	0,52	6,55	3,19	0,70
Significance		S	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

		Factor VIII activity (IU/ml)	Factor IX activity (IU/ml)	Factor XI activity (IU/ml)	Factor XII activity (IU/ml)	Factor II activity (IU/ml)	Factor V activity (IU/ml)	Factor VII activity (IU/ml)	Factor X activity (IU/ml)	vWF:Ag activity (IU/ml)	vWF:RCO activity (IU/ml)	C protein (%)	S protein (%)
DEHP	Mean	0,65	0,88	0,55	0,99	0,86	0,81	0,88	0,88	1,01	0,82	105,23	74,10
	SD	0,27	0,18	0,13	0,31	0,10	0,16	0,23	0,16	0,42	0,24	17,65	20,77
DINCH	Mean	0,73	0,87	0,59	1,07	0,84	0,78	0,87	0,90	1,05	0,87	101,93	79,38
	SD	0,24	0,15	0,13	0,30	0,07	0,12	0,21	0,12	0,31	0,27	14,99	23,69
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

		Activated ATIII (%)	Plasminogen (%)	2- antiplasmin (IU/ml)	Facteur VIIa (ng/ml)	Factor XIIa (ng/ml)	D-dimers (ng/ml)	C1 inhibitor	C3a (ng/ml)	C5a (ng/ml)	Cleaving prot. activity (IU/ml)	TAT complex (µg/l)	F 1+2	FPA
DEHP	Mean	98,63	98,30	1,02	74,33	32, 10	0,30	97,10	159,09	0,31	25,07	8,86	243,30	22,40
	SD	9,33	18,14	0,10	39,09	16, 90	0,12	16,14	81,52	0,15	37,87	19,92	230,37	15,10
DINCH	Mean	99,80	94,73	1,00	69,43	34, 33	0,29	101,37	137,31	3,66	36,75	6,02	210,83	19,57
	SD	7,64	14,07	0,10	30,06	16, 14	0,10	16,24	23,00	18,39	43,08	14,35	127,10	11,71
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

DISCUSSION

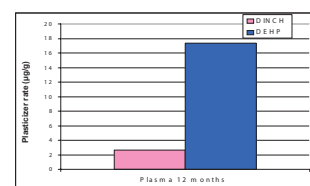
Statistical tests show that only pH differs lightly but significantly (higher pH value for DINCH).



There is a lower migration of plasticiser into the plasma stored in PVC-DINCH containers.

Plasticiser rate (µg/g)	Mean	Mini	Maxi
DEHP	17,4	14,6	19,9
DINCH	2,6	1,9	3,4

DINCH leaching in plasma is decreased by 85% compared to DEHP



CONCLUSION

Leukodepleted fractionation plasma prepared and stored in PVC DINCH bags is conform to the regulatory characteristics of blood labile products. A 12 month storage period doesn't alter the quality of fractionation plasma. DINCH leaching in plasma is lower than DEHP leaching. PVC-DINCH is a DEHP-free material suitable for plasma storage, as it is for RBC storage (previous communication). Platelet storage for 7 days is currently under investigation.