



COMPATIBILITY AND STABILITY ASSESSMENT OF A SODIUM GLYCEROPHOSPHATE FORMULATION MIXED IN BAGS FOR NEONATAL TOTAL PARENTERAL NUTRITION

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BACKGROUND AND IMPORTANCE

At the end of 2018 there was a shortage and withdrawal from the market of D-fructose-1,6-diphosphate (Esafosfina), a phosphate source for the extemporaneous preparation of bags for neonatal total parenteral nutrition (TPN). Therefore, a solution of sodium glycerophosphate (Natriumglycerophosphat-Ampulle Fresenius) was imported from abroad. This solution is different because it contains L-malic acid as an excipient. No stability data on Natriumglycerophosphat-Ampulle Fresenius in TPN bags were found in the literature.

AIM AND OBJECTIVES

To test the compatibility and stability of Natriumglycerophosphat-Ampulle Fresenius in TPN bags we prepared.

MATERIAL AND METHODS

Neonatal TPN formulations are customised: therefore, we identified three test formulations, with varying concentrations of phosphate, calcium and magnesium (critical components), with and without lipids.

Turbidity and pH controls were planned at appropriate time intervals (0, 24, 48, 72 and 96 hours after preparation) and under different storage conditions (room temperature, refrigerated and at 37°C).

These controls were performed either with lipid free or with all in one formulations (all components, including lipids, are mixed in the same bag).

bag No1		bag No2		bag No3	
glucose 50%	41,96 ml	glucose 50%	31,82 ml	glucose 50%	17 ml
TPH 6% (amino acids solution)	115,44 ml	TPH 6% (amino acids solution)	78,94 ml	TPH 6% (amino acids solution)	115,7 ml
water for injection	20,6 ml	water for injection	58,53 ml	water for injection	2,07 ml
NaCl 2 mEq/ml	2,02 ml	NaCl 2 mEq/ml	1,34 ml	NaCl 2 mEq/ml	1,49 ml
KCl 2 mEq/ml	2,36 ml	KCl 2 mEq/ml	1,07 ml	KCl 2 mEq/ml	1,19 ml
sodium glycerophosphate	4,04 ml	sodium glycerophosphate	1,51 ml	sodium glycerophosphate	2,8 ml
calcium gluconate 10%	15,17 ml	calcium gluconate 10%	5,77 ml	calcium gluconate 10%	11,63 ml
magnesium sulfate 10%	0,84 ml	magnesium sulfate 10%	0,67 ml		
		zinc sulfate 10 mg/10 ml	0,53 ml		

RESULTS

In lipid free formulations there was no formation of a precipitate at room temperature or under refrigerated conditions.

The absorbance of the solutions at 600 nm (turbidity reading) remained below 0.010, which means no evidence of precipitation.

There was precipitate formation under storage condition at 37°C (after 72 hours in test bags No1 and No2 and after 96 hours in bag No3).

The determining factors of the formation of this precipitate are alteration and degradation of the amino acids and the resulting pH reduction.

In all in one formulations, we assessed stability with a microscope.

Coalescence started in a bag 48 hours after preparation.

Solution pH ranged from 5.5 to 6.5.

Bags without lipids

room temperature				refrigerated				37°C			
		ABS 600 nm	pH			ABS 600 nm	pH			ABS 600 nm	pH
T0	Bag No1	0,000	6,13	T0	Bag No1	0,000	6,13	T0	Bag No1	0,000	6,13
	Bag No2	0,001	5,98		Bag No2	0,001	5,98		Bag No2	0,001	5,98
	Bag No3	0,001	6,03		Bag No3	0,001	6,03		Bag No3	0,001	6,03
24 hours	Bag No1	0,001	6,13	24 hours	Bag No1	0,001	6,12	24 hours	Bag No1	0,001	6,08
	Bag No2	0,000	5,96		Bag No2	0,001	5,96		Bag No2	0,001	5,94
	Bag No3	0,000	6,02		Bag No3	0,002	6,02		Bag No3	0,002	5,98
48 hours	Bag No1	0,001	6,1	48 hours	Bag No1	0,001	6,1	48 hours	Bag No1	0,001	6,08
	Bag No2	0,001	5,97		Bag No2	0,001	5,98		Bag No2	0,001	5,94
	Bag No3	0,001	6,02		Bag No3	0,001	6,03		Bag No3	0,002	5,98
72 hours	Bag No1	0,002	6,06	72 hours	Bag No1	0,002	6,1	72 hours	Bag No1	0,257 *	5,84
	Bag No2	0,003	5,94		Bag No2	0,003	6		Bag No2	0,104 *	5,8
	Bag No3	0,002	5,99		Bag No3	0,002	6,02		Bag No3	0,005	5,93
96 hours	Bag No1	0,001	6,05	96 hours	Bag No1	0,001	6,08	96 hours	Bag No1	-	-
	Bag No2	0,001	5,94		Bag No2	0,001	5,99		Bag No2	-	-
	Bag No3	0,002	6,01		Bag No3	0,002	6,02		Bag No3	0,189 *	5,88

* evidence of precipitation

after one week at room temperature...

		ABS 600 nm	pH
one week	Bag No1	0,001	6,14
	Bag No2	0,001	5,95
	Bag No3	0,001	6,02

Bags with lipids at room temperature

		pH	particle size (nm)	dispersity	zeta potential
T0	Bag No1	6,4	335 ± 2	0,046	-28
	Bag No3	6,02	334 ± 4	0,051	-26
24 hours	Bag No1	6,41	343 ± 5	0,101	-24
	Bag No3	6,01	342 ± 6	0,031	-24
48 hours	Bag No1	6,4	385 ± 6	0,24 *	-24
	Bag No3	6,01	314 ± 3	0,103	-24

* particles 4000 nm

CONCLUSION AND RELEVANCE

Sodium glycerophosphate (Natriumglycerophosphat-Ampulle Fresenius) can be mixed with the usual components for neonatal TPN.

In the test formulations there was no physical or chemical incompatibility.

Lipid free formulations were stable for at least 96 hours. All in one formulations should be infused within 24 hours, especially if the amount of lipids is high.



<https://www.eahf.eu/25-3PC-001>