

Comparison of VACUETTE® Serum Gel tubes with VACUTAINER® plain glass tubes for Therapeutic Drug Monitoring (TDM) in Serum

Background:

Greiner-Bio-One, Austria has sold plastic evacuated tubes (VACUETTE®) for venous blood collection since 1986.

VACUETTE® Gel Tubes incorporate an inert gel material into the blood collection tube. These gels have a controlled viscosity and a specific gravity intermediate to serum and clot. During centrifugation, the gel material forms an impermeable barrier between the serum and clot.

Gel Z has been in development since 2001 and has the same components as the last gel type (Gel P3), the difference being the production process, which has been optimised. The gel might be slightly more yellow in colour however provides the better performance than the last gel type as well as providing the advantage of a more stable barrier, which is particularly beneficial during transport.

Preanalytical handling remains the same and does not require any changes (i.e. centrifugation conditions, storage, transport, etc).

Study Objective:

The aim was to study the stability of a variety of commonly monitored drugs in serum after storage in VACUETTE® serum separator tubes on Gel Z or Gel P3N in comparison to a plain glass VACUTAINER® tube.

Study design:

Three tube types were evaluated in this study:

Sample Number	Description	Additive	Gel Type	Draw Volume
1	VACUETTE® 455071Z	Clot Activator	Gel Z	8 ml
2	VACUETTE® 455071	Clot Activator	Gel P3N	8 ml
3	VACUTAINER® 366441	-	-	10 ml

A serum pool was prepared by combining residual samples. This serum pool was split into two for each drug tested and each half was spiked with commercial quality control material (BioRad Muliquel Level III) to create a "low" and a "high" level to reflect the lower and the upper end of the therapeutic range. For each tube to be evaluated, two sets of duplicate tubes were labelled 0, 4, 24, and 48 h. 3.0 ml of "low" pool was aliquoted into one set of duplicate tubes and 3.0 ml "high" pool was aliquoted into the second set.

Immediately after aliquoting, the samples were analyzed in duplicate to obtain the "0 hours" values. The tubes were then stored at 4°C and the serum was analyzed in duplicate at 4, 24, and 48 h.

Sample Number	Level Tested	Time of measurement (h)
1	high low	0 – 4 – 24 – 48
2	high low	0 – 4 – 24 – 48
3	high low	0 – 4 – 24 – 48

The samples were analyzed for 15 TDM parameters on the following instruments according to manufacturer's instructions and protocols and using manufacturer's reagents:

Tested Drug	Analyzer
Acetaminophen	Beckman Coulter LX20 Analyzer
Carbamazepine	
Digoxin	Abbott AxSym Immunoassay Analyzer
Ethanol	Beckman Coulter LX20 Analyzer
Gentamycin	Abbott AxSym Immunoassay Analyzer
n-Acetyl Procainamide	
Phenytoin	
Phenobarbital	
Procainamide	
Salicylate	Beckman Coulter LX20 Analyzer
Theophylline	Abbott AxSym Immunoassay Analyzer
Tobramycin	
Valproic Acid	
Vancomycin	
Tricyclic Antidepressants	

Please find the results in the Annex.

Results – Evaluation:

There are two graphs shown for each drug tested, for one displaying low and the other displaying high drug quality control level (pink: VACUETTE® Gel Z, yellow: VACUETTE® Gel P3N, blue: Vacutainer® plain glass tube).

Please find the results in the Annex.

Results / Comments:

Percent recovery was calculated and was expected to fall within +/-10% of the initial time control tube values. Values falling below 90% or above 110% recovery were considered clinically significant.

Stability of the drug on the gel up to 48 hours was shown for all of the 15 drugs tested. These included the analgesics Acetaminophen, Carbamazepine, and Salicylate; the antibiotics Gentamycin, Tobramycin, and Vancomycin; the anti-epileptics Phenobarbital, Phenytoin, and Valproic Acid; the anti-arrhythmic drug Procainamide and its metabolite n-Acetylprocainamide; the cardiac glycoside Digoxin; the alcohol ethanol; tricyclic antidepressants and the anti-spasmodic Theophylline.

Conclusion:

The stability of therapeutic drugs in serum stored in gel tubes has been widely investigated. The absorption of drugs into the gel is dependent upon several factors including the chemical nature of the gel and of the drug itself, time on the gel, temperature of storage and volume of sample.

In this current study the stability of 15 drugs added to a serum pool under laboratory conditions was examined. Tubes containing Gel Z showed constant drug level over 48 hours for most of the analytes tested and no clinical significance was observed.

From these findings we conclude, that tubes containing Gel Z performed comparably to tubes containing Gel P3N and plain glass tubes, and that they are suitable for TDM studies.

References:

- (1) Dasgupta A., Yared M.A., Wells A., Time-dependent absorption of therapeutic drugs by the gel of the Greiner Vacuette® blood collection tube. TheDrugMonit. (2000)
- (2) Mutschler Ernst, Arzneimittelwirkungen. Wissenschaftliche Verlagsgesellschaft mbH Stuttgart, 7. Auflage (1996)

Annex / Results – Raw Data:

Concentration	Drug	Tube Type	Recovery after x hours [%]				
			0	4	24	48	
low	Acetaminophen	Gel Z	100	99,7	101,6	100	
		Gel P3N	100	103,0	102,3	98,3	
		plain glass tube	100	99,3	105,0	105,6	
high		Gel Z	100	102,3	100,9	101,4	
		Gel P3N	100	101,8	99,3	98,9	
		plain glass tube	100	99,8	95,8	96,5	
low		Carbamazepine	Gel Z	100	102,3	107,6	100
			Gel P3N	100	99,4	99,4	95,5
			plain glass tube	100	102,9	106,3	100,6
high	Gel Z		100	102,0	99,7	102,5	
	Gel P3N		100	99,7	96,7	94,4	
	plain glass tube		100	98,6	98,0	99,7	
low	Digoxin		Gel Z	100	109,1	100	109,1
			Gel P3N	100	100	100	109,1
			plain glass tube	100	100	100	109,1
high		Gel Z	100	100	100	95,2	
		Gel P3N	100	105,0	105,0	105,0	
		plain glass tube	100	95,2	100	100	
low		Ethanol	Gel Z	100	100	100	100
			Gel P3N	100	100	100	100
			plain glass tube	100	100	100	100
high	Gel Z		100	95,2	95,2	95,2	
	Gel P3N		100	95,2	95,2	100	
	plain glass tube		100	100	100	100	
low	Gentamycin		Gel Z	100	99,5	94,0	93,4
			Gel P3N	100	101,7	96,0	95,4
			plain glass tube	100	97,8	98,9	92,3
high		Gel Z	100	97,4	94,7	89,7	
		Gel P3N	100	102,7	100	100	
		plain glass tube	100	105,4	97,3	94,6	
low		n-Acetyl Procainamide	Gel Z	100	105,6	107,9	102,2
			Gel P3N	100	106,5	104,3	102,2
			plain glass tube	100	102,2	103	102,2
high	Gel Z		100	92,0	94,0	94,5	
	Gel P3N		100	97,9	100	102	
	plain glass tube		100	93,0	90,1	94,1	
low	Phenobarbital		Gel Z	100	100,5	97,3	94,0
			Gel P3N	100	100	100,6	103,9
			plain glass tube	100	104,3	100,4	104,3
high		Gel Z	100	102,2	97,5	98,8	
		Gel P3N	100	96,8	107,4	93,6	
		plain glass tube	100	98,0	93,6	98,4	
low		Phenytoin	Gel Z	100	101,9	102,7	97,7
			Gel P3N	100	103,6	102,0	104,8
			plain glass tube	100	101,2	108,3	101,6
high	Gel Z		100	97,7	101,6	97,7	
	Gel P3N		100	101,8	101,6	101,4	
	plain glass tube		100	96,7	99,4	97,3	
low	Procainamide		Gel Z	100	96,6	93,2	100

Concentration	Drug	Tube Type	Recovery after x hours [%]			
			0	4	24	48
high		Gel P3N	100	100,7	97,9	92,4
		plain glass tube	100	105,0	104,3	102,1
		Gel Z	100	93,8	96,6	91,8
		Gel P3N	100	106,3	106,6	102,6
low	Salicylate	plain glass tube	100	93,4	92,0	97,2
		Gel Z	100	92,3	88,5	103,8
		Gel P3N	100	88,9	92,6	111,1
		plain glass tube	100	92,0	92,0	100
high		Gel Z	100	100	100	100
		Gel P3N	100	100	100	105,6
		plain glass tube	100	105,9	105,9	111,8
		Gel Z	100	102,3	102,3	102,3
low	Theophylline	Gel P3N	100	100	102,3	100
		plain glass tube	100	100	102,3	100
		Gel Z	100	94,3	95,5	96,6
		Gel P3N	100	93,2	96,6	100
high		plain glass tube	100	94,4	93,3	97,8
		Gel Z	100	104,8	95,2	95,2
		Gel P3N	100	104,8	100	100
		plain glass tube	100	95,5	95,5	90,9
low	Tobramycin	Gel Z	100	100	92,7	102,4
		Gel P3N	100	100	100	105,0
		plain glass tube	100	95,0	102,5	105,0
		Gel Z	100	101,7	102,1	95,3
high	Valproic Acid	Gel P3N	100	97,6	96,7	99,2
		plain glass tube	100	106,7	111,2	105,4
		Gel Z	100	103,4	107,8	103,1
		Gel P3N	100	102,8	100,4	100
low	Vancomycin	plain glass tube	100	99,1	103,2	99,1
		Gel Z	100	93,9	85,4	93,9
		Gel P3N	100	101,3	113,2	106,6
		plain glass tube	100	102,4	100	92,7
high		Gel Z	100	95,1	99,4	98,1
		Gel P3N	100	105,2	109,1	104,5
		plain glass tube	100	97,6	94,0	95,8
		Gel Z	100	105,2	105,2	98,9
low	Tricyclic Antidepressants	Gel P3N	100	99,6	97,1	91,7
		plain glass tube	100	98,9	102,5	102,5
		Gel Z	100	104,5	102,9	98,8
		Gel P3N	100	98,8	102,7	99,8
high		plain glass tube	100	101,4	91,1	94,2



















