Glass Surface Technology

Influence of aggressive screening conditions and glass composition on the Extractables and Leachables from glass containers

Glass vials from different manufacturing process (moulded and tubing) and suppliers are compared :
Part I Glass composition and Extractables Moulded Tubing
Part II Extractables with 1660 Solutions
Part III Leachables with 1660 Solutions

Part I Glass compositions and Extractables

- 2 main Glass Types for containers : borosilicate and sodalime silicate glass
- Borosilicate glass has better chemical resistance but is more difficult to melt and shape
- In Pharma, 3 Glass Types are regulated based on max Hydrolytic Resistance

Type I : borosilicate

Type III: soda-lime silicate

Type II : soda-lime silicate glass with Internal Sulfur Treatment

%		Borosilicate	Sodalime Silicate
Network Formers	SiO2+Al2O3	73	75
	B2O3	12	
Network modifiers	Na2O K2O	10	14
	CaO BaO ZnO MgO	5	11

Part I Composition by X-Ray Fluorescence Spectrometry – Moulded and Tubing Type I

(%)	Molded	Tubing 1	Tubing 2
Network Formers	85.7	90.2	91.1
Network Modifiers	14.2	9.6	8.7

- Stronger network for bulk tubing glass, less modifiers
- Network modifiers needed to soften the glass to shape the vials for molded glass

Main elements (%)	Moulded Flint	5ml Tubing 1	10ml Tubing 2
SiO_2	69,1	70,8	74,3
Na_2O	6,1	7,1	7,2
K_2O	3,1	1,2	0,0
CaO	1,1	1,2	1,5
MgO	0,0	0,2	0,0
Al_2O_3	4,0	7,3	5,6
Fe_2O_3	0,02	0,03	0,02
B_2O_3	12,6	12,1	11,2
BaO	2,8	0,1	0,0
TiO_2	0,02	0,01	0,03
ZnO	1,1	0,0	0,0

Part I Hydrolytic Resistance Comparison in (ml) HCl N/100

Standard test for Pharma Glass - Hydrolytic stability, expressed by the resistance to the release of soluble mineral substances into water under the prescribed conditions of contact between :

- the inner surface of the container (Test A, surface test according to European Pharmacopeia, 3.2.1)
- glass grains (Test B, glass grain test according to European Pharmacopeia, 3.2.1)

The hydrolytic resistance is evaluated by titrating released alkali.
The glass grain test is performed on crushed glass pieces, so represents the chemical resistance of the bulk glass

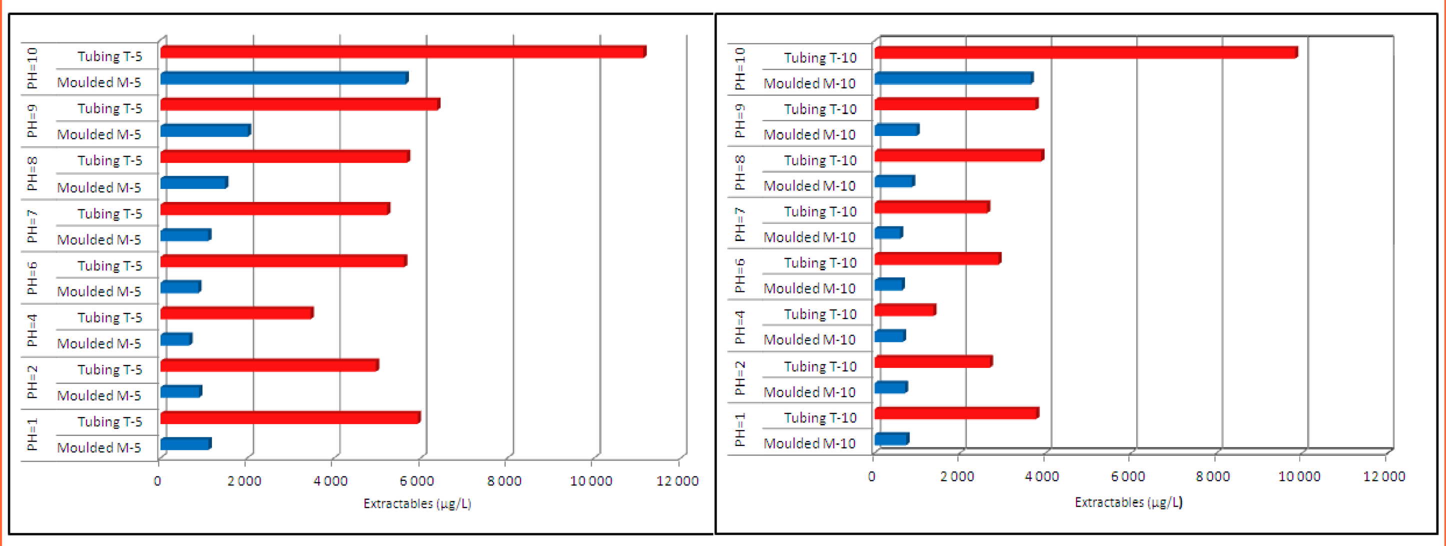
	Type I Molded	Tubing T-5
Grain Hydrolytic Resistance (ml)	0.53	0.43

Better grain resistance for Tubing than molded because more network formers and less modifiers, Type I Limit 1 ml

	Molded M-5	Tubing T-5	Molded M-10	TubingT-10
Vol 90% (ml)	8.1	8.3	12.25	12.4
Type I Limit	1	1	0.8	0.8
Surface Hydrolytic Resistance (ml)	0.15	0.50	0.17	0.41

More critical for product interaction
All vials are lower than type I surface limit, as required
Better surface Hydrolytic resistance for molded vials

Part I Total Extractables by ICP after 1h at 121°C – 5 &10ml Moulded Tubing

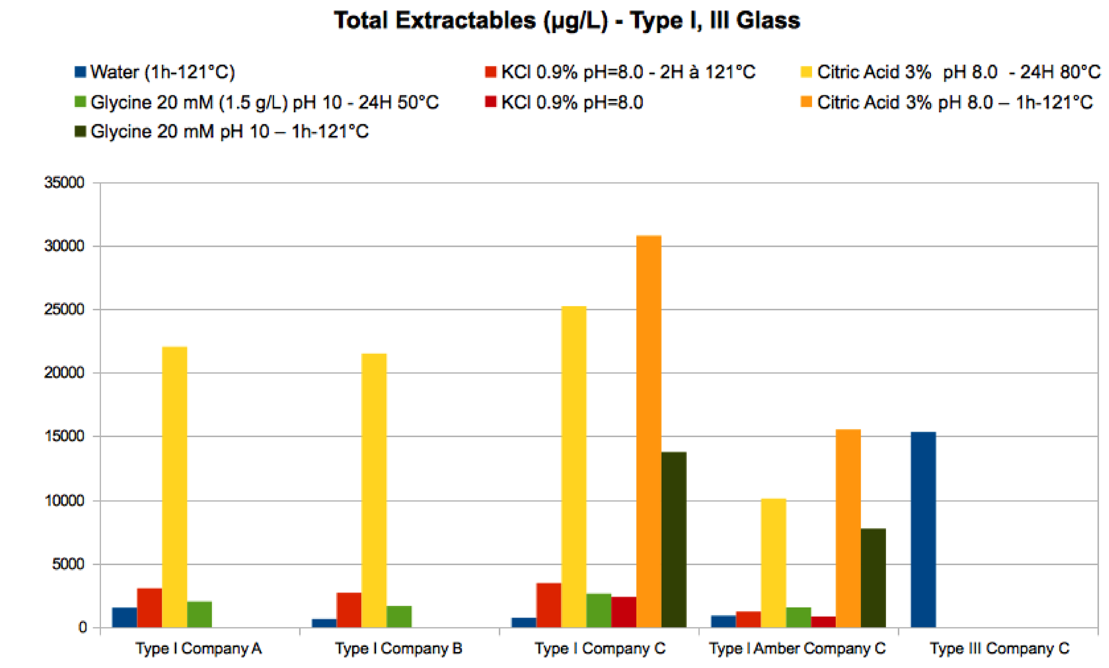


Less elements extracted with Molded vials, for all pH
Higher pH (10 or more) causes higher extractions
Less extraction in volume for bigger vials, lower surface/volume ratio

Part II Extractables Evaluation with <1660> Solutions

3 Solutions for New USP 1660 Chapter to evaluate glass containers
- KCl 0.9% pH 8.0 Autoclave for 2H at 121°C (2 1h autoclave cycles)
- 3% Citric Acid at pH 8.0 for 24h at 80°C
- 20 mM (1.5g/L) Glycine at pH 10.0 for 24h at 50°C

NaOH (contains K) added to bring pH to the right level, so Na and K not measured in extracted solutions
Autoclave samples closed with borosilicate lab glass, Other vials closed with aluminum foil
Glass Samples : 100ml Type I moulded vials from different glass makers
ICP Preparation
Acidification HNO3 Suprapur 2% before ICP-OES measurement
Equipment Calibration with certified PE multielements solution and acidification HNO3 Suprapur 2%
Results
Equipment : Emission Spectrometry ICP (Perkin Elmer Optima 7300 DV)
The blank solution is analyzed and subtracted from the autoclaved solutions



Citric Acid at pH 8 is more aggressive than the other solutions
Same Glass types are similar with same chemical solution and testing procedure
Extractions depend on : solution, glass composition and extraction conditions

Glass Composition					
(%)	Type I Company C	Type I Amber Company C	Type III Company C	Type I Company B	Type I Company A
SiO_2	69.1	65.4	72.9	66.3	67.4
Na_2O	6.1	7.3	11.9	9.6	8.3
K_2O	3.1	2.2	0.8	1.1	1.9
CaO	1.1	0.5	12.1	0.8	1.3
MgO	0.0	0.0	0.1	0.5	0.3
Al_2O_3	4.0	6.6	2.2	5.5	5.6
Fe_2O_3	0.02	0.86	0.03	0.06	0.03
B_2O_3	12.6	11.6	0.0	12.8	12.0
BaO	2.8	2.0	0.0	2.7	2.7
TiO_2	0.02	2.70	0.03	0.02	0.05
ZnO	1.1	0.7	0.0	0.6	0.4

All glass are type I or Type III glass (Hydrolytic Resistance better than limit)

Composition differences (Flint vs. Amber) impact chemical resistance

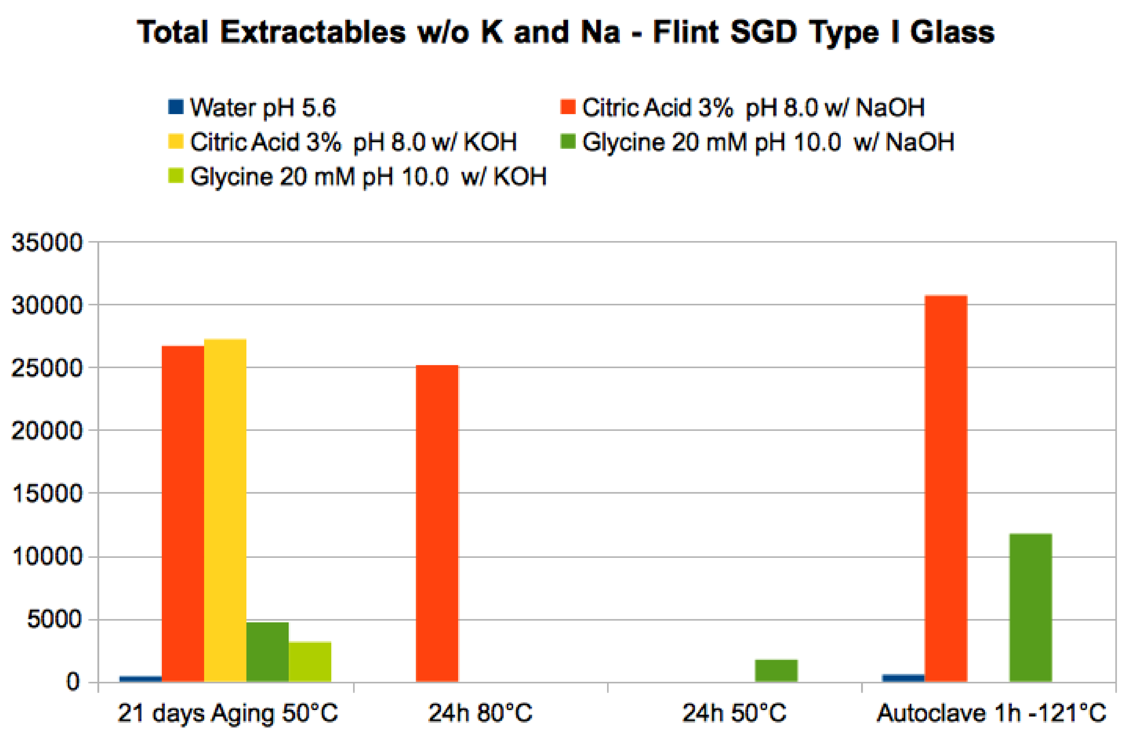
Part III Leachables Testing using <1660> Solutions

Same 1660 Solutions as previous part, with pH adjusted 2 ways
- Demineralized water at pH 5.6
- 3% Citric Acid at pH 8.0, pH adjusted with NaOH
- 3% Citric Acid at pH 8.0, pH adjusted with KOH
- 20 mM (1.5g/L) Glycine at pH 10.0, pH adjusted with NaOH
- 20 mM (1.5g/L) Glycine at pH 10.0, pH adjusted with KOH

Glass Samples : 100ml Type I moulded Flint SGD vials

All containers closed with Omniflex Helvoet stoppers

21 days aging at 50°C



All results with Citric Acid are similar, higher than Glycine and water

Adjusting the pH with KOH or NaOH gives similar results

Conclusions

Evaluating Extractables and Leachables is an important step in designing a product, comparing all aspects (visual/shape, functions, product protection, ...cost...)

Not all (glass) vials are equal for chemical resistance : it depends on process, glass composition and product composition, as well as storage conditions

Glass Surface Technology is working on innovative solutions to evaluate and improve chemical interactions, including functional treatments for packaging.

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