SCHOTT

The nature of glass with a focus on pharmaceutical glass

Technical white paper no. 1

The nature of glass

Technical white paper

Deep dive into the structure of glass used for pharmaceutical primary packaging

Background

“Glass is not just a pure coincidence” was the motto of Dr. Otto Schott (1851–1935), one of the founders of the SCHOTT company. Through his research, he was able to prove for the first time that the properties of glass can specifically be changed by certain chemical elements.These results are still valid today – over 100 years later.

But the history of glass starts even earlier. Over 5,000 years ago naturally occurring glass, obsidian, was used to produce hunting tools. Due to its shiny appearance and because it is easily stained it was used more and more for jewelry and decoration. The oldest known recipe for glass was found in the clay tablet library of the Assyrian king Assurbanipal (700 BC) which reads: “Take 60 parts sand, 180 parts ash from sea plants and 5 parts chalk – and you get glass”. This recipe represents a kind of glass which is still used nowadays, the so-called soda-lime glass.

But let us first have a look at the structure of glass in general. In the left picture of **figure 1** the structure of crystalline quartz is shown. It consists only of pure quartz sand (silica or SiO_2) which is arranged in a tetrahedron pattern. Its characteristic feature is its perfect symmetry. This perfect symmetry is described by the word “crystalline”. In the right picture the structure of amorphous quartz is shown. The atomic composition also only consists of pure SiO_2 but it shows a more chaotic arrangement. This structure is realized by melting the sand and letting it cool down rapidly.

The melting of quartz sand can be done by introducing heat into the system. This energy is used to break the bonds between the atoms whereupon they are able to move around freely in the system. The glass melt is liquid now. Upon cooling down, energy is leaving the glass melt to the environment **(see figure 2)**, the movement (frequency of movement) becomes slower and the atoms try to take positions like the organized crystal. Only their very high viscosity slows them down in such a manner that they freeze in the more chaotic spot they currently hold. Thus, the amorphous state is only created because the melted glass atoms do not have enough time to arrange into a crystal matrix. They simply freeze and get stuck in their liquid random position.

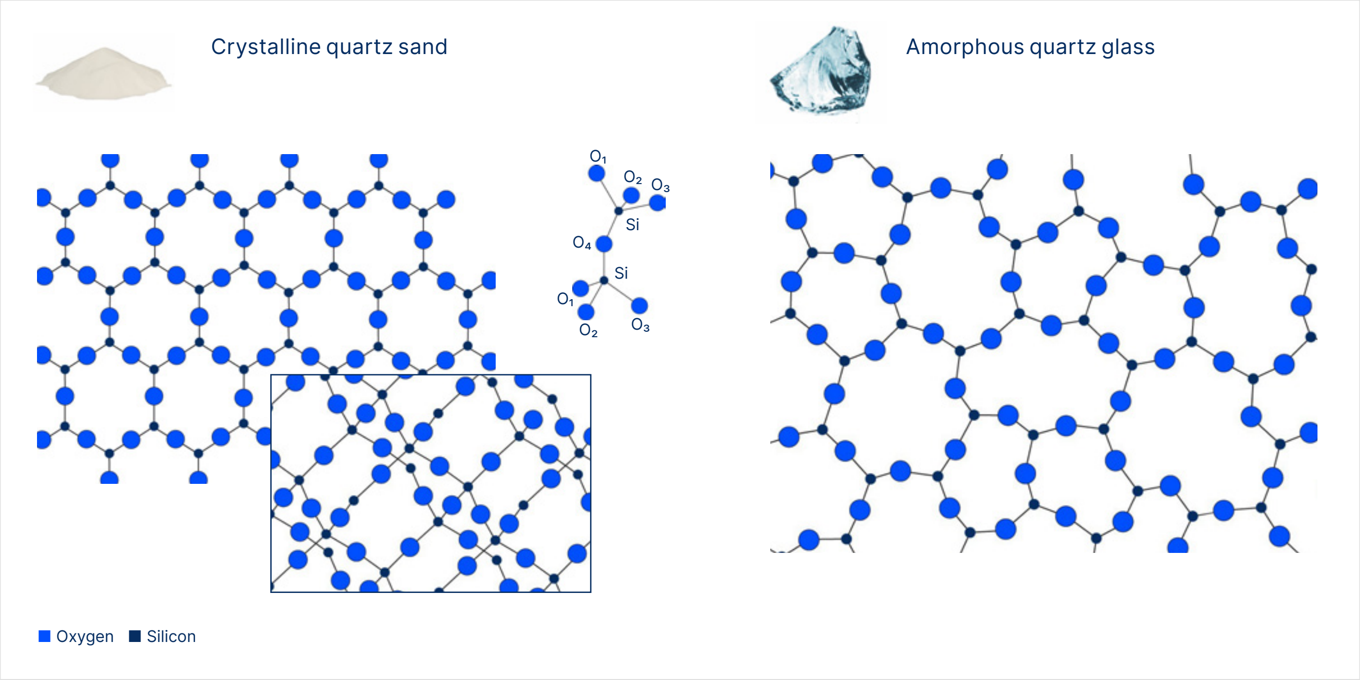

Figure 1 Structure of crystalline quartz sand (left) and structure of amorphous quartz glass (right)

This is different to most materials in nature. For example, if water is cooled down gradually, it reaches its melting point at precisely 0 °C where it promptly solidifies into a crystal structure (ice). Exactly this specific phase transition point is missing for the creation of an amorphous structure.

For glass the solidification process takes place in a temperature range, the so-called “annealing zone”. Below this range (for Type I glasses normally between 500 °C and 600 °C) the glass exists in its final solid structure whereas the glass is starting to get viscous above this zone. The annealing zone is mainly characterized by the transformation temperature T_g (glass temperature) which indicates the change between solid and liquid state.

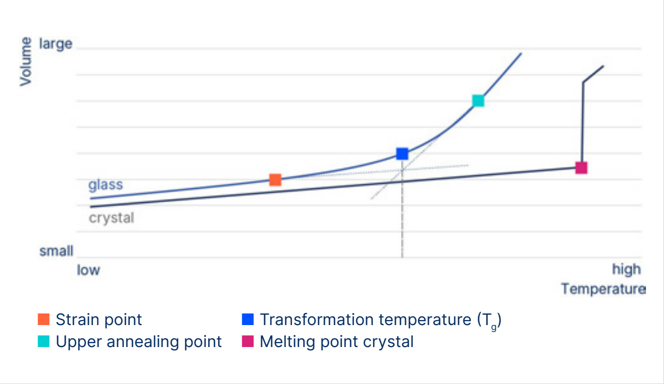

Figure 2 Solidification behavior of a crystal and the amorphous material glass shown in a temperature-volume diagram

Glass for pharmaceutical purposes

As silicon-oxygen-bonds belong to the strongest in nature, one main property of quartz is its very high melting temperature of over 2,000 °C. This makes it unfeasible to be used in pharmaceutical applications. To lower the melting temperature certain elements like alkali and alkaline earth metals (sodium, potassium, calcium, etc.) are added. These elements find their places inside the atomic glass network, thus increasing the space between the silicon and oxygen atoms. As they change the structure of the network they are also called “network modifiers”. Their addition significantly lowers the melting temperature of the glass and makes it much easier to be converted into pharmaceutical containers. In the old recipe ash of sea plants and chalk are added to the sand. Ash contains a lot of sodium and potassium whereas chalk mainly consists of calcium. As this lowered the melting temperature the glass manufacturing process was facilitated significantly. For the use as jewelry, decoration or food containers this was sufficient.

However, for the use in the pharmaceutical industry the containers are required to have a high chemical stability. And by the addition of the network modifiers the chemical resistance is lowered. To compensate for this, especially boron is added to the glass composition. It integrates into the network and thus stabilizes the same. The chemical stability is thereby increased again. In **figure 3** such typical structures for different glass types are shown. This basic composition of silicon, alkali (sodium, potassium) and alkaline earth metals (calcium), boron and aluminum is also called borosilicate glass. According to modern pharmacopoeias (e.g. USP and Ph.Eur.) borosilicate glass is a glass containing “significant amounts of boric acid, aluminum oxide, and alkali and / or alkaline earth oxides in the glass network. Borosilicate glass has a high hydrolytic resistance and a high thermal shock resistance due to the chemical composition of the glass itself; it is classified as Type I glass.”

The hydrolytic resistance is a more specific description of the chemical stability. Adding a greater amount of alkali and alkaline earth metals to the glass results in a soda lime glass, which has a lower chemical resistance or hydrolytic resistance resp. **(see figure 3).** Here USP (and Ph. Eur.) are stating that “soda-lime-silica glass is a silica glass containing alkali metal oxides, mainly sodium oxide, and alkaline earth oxides mainly calcium oxide, in the glass network. Soda-lime-silica glass has a moderate hydrolytic resistance due to the chemical composition itself; it is classified as Type III glass.” The increased amount of network modifiers in the Type III glass leads to a decrease in melting and working temperature. At the same time the hydrolytic resistance is lowered as well. As the hydrolytic resistance is an important quality criterion and certain drugs require a high quality the Type III glass is recommended (by USP and Ph. Eur.) to be used rather for non-parenterals, such as oral applications and powders.

With specific sulfate treatments (e. g. ammonium sulfate) a container of hydrolytic resistance class type III can be transformed into a container of type II. Type II glass is not a different chemical composition but rather a Type III glass, from which the sodium of the near-surface regions has been extracted and therefore increased its hydrolytic resistance. Thus, the surface of a Type II container would correspond to that of a Type I, but the glass grain test (representing the base glass) would correspond to that of a Type III glass.

Recently aluminosilicate glass for pharmaceutical applications has been discussed. The difference to borosilicate glass is the replacement of boron by a higher content of aluminum and alkali in the network. Without any further treatment – like chemical strengthening and subsequent washing / etching – this glass does not fulfill the current requirements for pharmaceutical packaging.

Apart from the melting and working temperature, other physical properties such as density, viscosity and thermal expansion are also significantly influenced by the glass composition. Accordingly, a higher content of network modifiers causes a lower density of the glass, a lower working point and a lower viscosity of the melt.

The working point is important for the converting process as it is the minimum temperature which has to be reached in order to properly convert the glass tubing. The coefficient of mean linear thermal expansion (CTE) is clearly increased and thus the resistance against thermal shock is lowered. The CTE determines how much a material changes in length and / or volume when it is heated or cooled down again. The lower the CTE is the more stable the glass is against temperature changes.

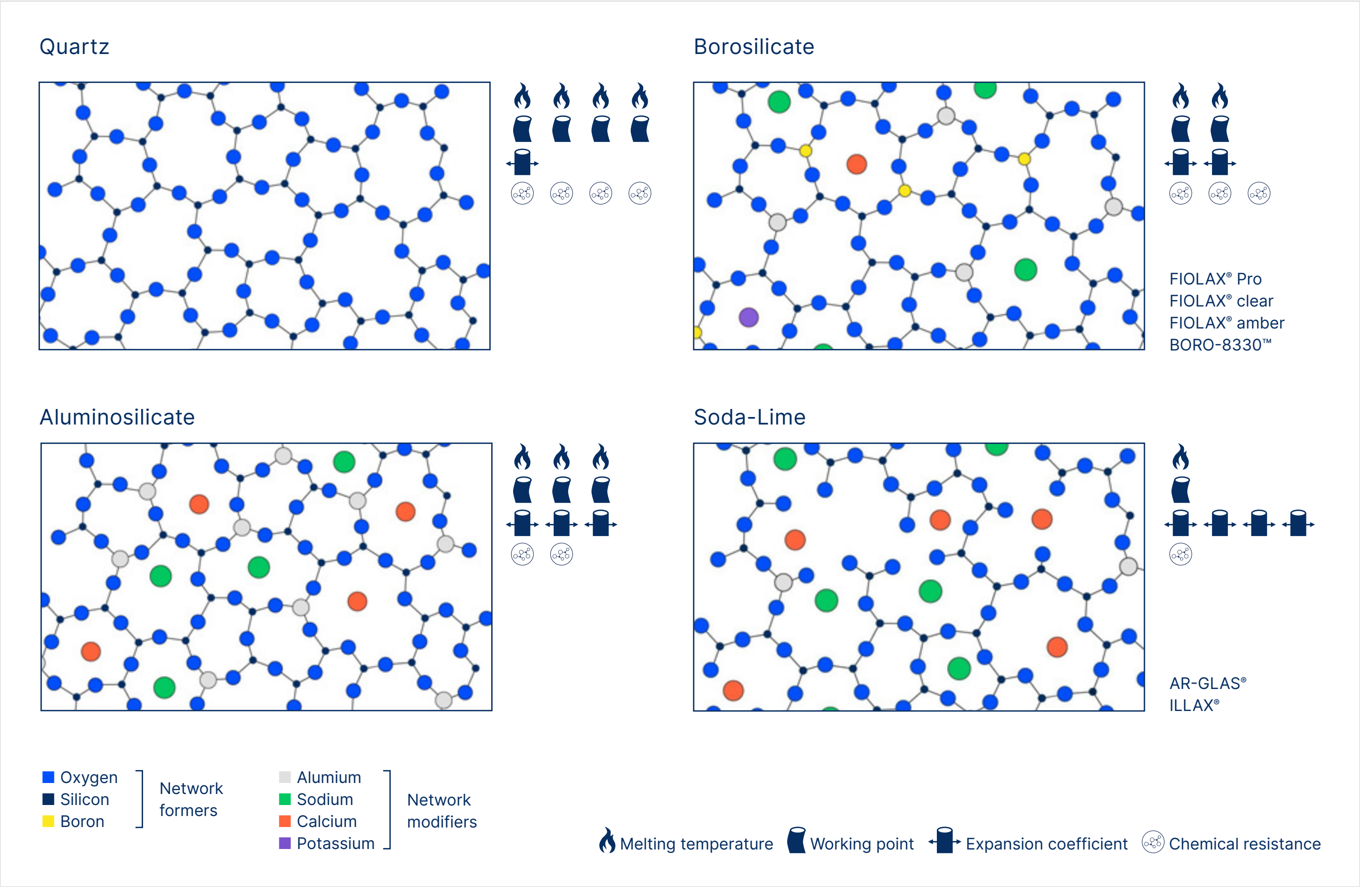

Figure 3 Schematic structure of different glass types

Classification of Type I glasses

Type I glasses can be further classified according to two different criteria:

Their CTE in borosilicate glass 3.3, 5.0 or 7.0

Their boron content in high, middle or low borosilicate glass

These classifications can also be seen in **table 1,** which provides an overview of the different types of glasses commonly used for pharmaceutical packaging. The borosilicate glasses all represent Type I glasses whereas soda lime represents Type III glass. It is apparent that with increasing network modifiers the working point decreases while the CTE increases.

	Type I Glasses			Type III Glass	Others
Glass type	Borosilicate 3.3	Borosilicate 5.0	Borosilicate 7.0	Soda-Lime	Aluminosilicate
Chinese classification	High borosilicate glass	Middle borosilicate glass	Low borosilicate glass	–	–
Composition [approx. % by weight]					
SiO_2	80 – 82	72 – 75	70 – 74	70 – 75	52 – 74
B_2O_3	12 – 13	9 – 11	5 – 8	0 – 1	–
Al_2O_3	2	5 – 7	4 – 6,5	2 – 4	10 – 25
Na_2O / K_2O	4	6 – 9	9 – 12	12 – 16	15 – 33
MgO / CaO / BaO	0	1 – 3	5 – 7	10 – 15	15 – 33
Physical properties					
Working point	1,260 °C	1,145 – 1,170 °C	1,030 – 1,100 °C	1,015 – 1,045 °C	1,240 – 1,330 °C
Transformation Temperature T_g	525 °C	565 – 575 °C	550 – 580 °C	525 – 540 °C	620 – 720 °C
Mean Coefficient of Thermal Expansion CTE $[10^{-6}\,K^{-1}]$	3.3	4.9 – 5.5	6.3 – 7.5	9.0 – 9.5	4.7 – 8.7

Example SCHOTT

	BORO-8330™	FIOLAX® Pro	FIOLAX® clear	FIOLAX® amber	AR-GLAS®
Glass type	Type I Glass Borosilicate 3.3	Type I Glass Borosilicate 5.0	Type I Glass Borosilicate 5.0	Type I Glass Borosilicate 5.0	Type III Glass Soda-Lime
Chinese classification	High borosilicate glass	Middle borosilicate glass	Middle borosilicate glass	Middle borosilicate glass	–
Composition [approx. % by weight]					
SiO_2	81	73	75	70	69
B_2O_3	13	11	10.5	7.5	1
Al_2O_3	2	7	5	6	4
Fe_2O_3	–	–	–	1	–
Na_2O	3.5	7	7	6.5	13
K_2O	0.5	< 1	–	1	3
BaO	–	–	–	2	2
CaO	–	< 1	1.5	< 1	5
TiO_2	–	–	–	5	–
MgO	–	–	–	–	3
Physical properties					
Working point	1,260 °C	1,170 °C	1,160 °C	1,165 °C	1,040 °C
Transformation Temperature T_g	525 °C	560 °C	565 °C	550 °C	525 °C
Mean Coefficient of Thermal Expansion CTE $[10^{-6}\,K^{-1}]$	3.3	5.2	4.9	5.4	9.1

Table 1 Overview of chemical and physical properties of different glass types available on the market

Light protection

Due to the amorphous structure of glass with "fixed" electrons there is almost no interaction of the glass with light. Therefore, visible light can pass through easily without significant absorption (see **figure 4,** left). This is described as highly transparent.

By the addition of metal ions – such as iron or titanium in FIOLAX® amber – this leads to an electronic interaction of the glass with light. UV and visible light cannot pass through the glass anymore, it is absorbed accordingly (see **figure 4,** right). In general, the darker the glass, the lower the transmission, which can give rise to UV protection of light-sensitive drug formulations.

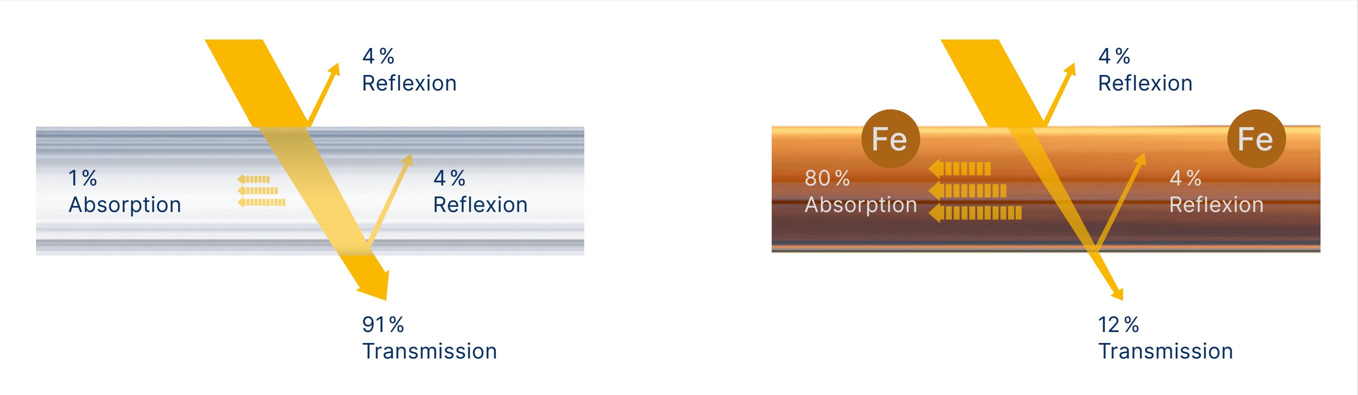

Figure 4 Exemplary comparison of the transmission behavior between clear (left) and amber glass (right)

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