GLASS FORMULATIONS FOR ANTIBACTERIAL APPLICATIONS

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HyMedPoly

Drug-Free Antibacterial Hybrid Biopolymers for Medical Applications

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Objectives of Hymedpoly re - Antibacterial glass materials

- Develop bioactive glasses with different charge potential and ion release rates, including:
  - Complex phosphate glasses adjusted to engineer both charge potential and biodegradation rate.
  - Silica glasses: bioactive glasses with a mesoporous structure to act as a reservoir for natural antibacterial inhibitors.
- Characterise surface and chemical properties
- Evaluate their antimicrobial properties through *in vitro* tests characterising aspects such as microbial adhesion, proliferation assays and biofilm formation

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Glass

- The nature of glass
- Composition
- Preparation and formats
- Examples
- Possible applications

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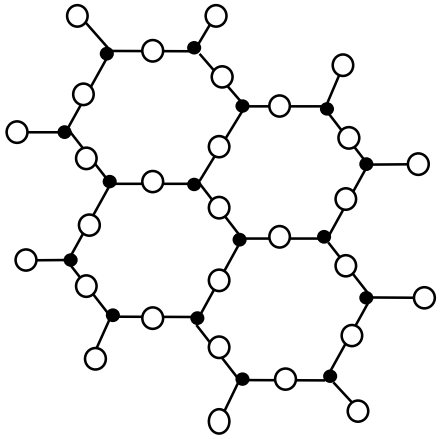
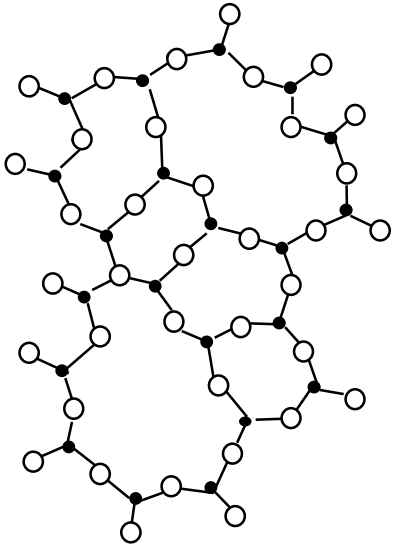
Glass structure



Crystalline Silica



Vitreous Silica

Vitrification – Transformation to a Glass

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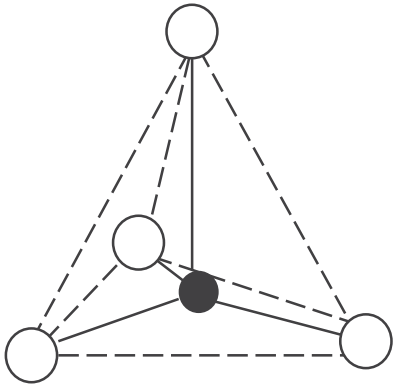
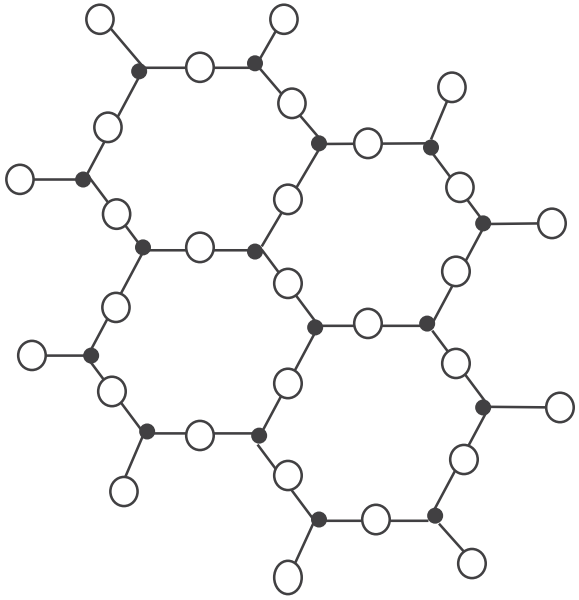
Glass structure (network diagram)100% SiO_2

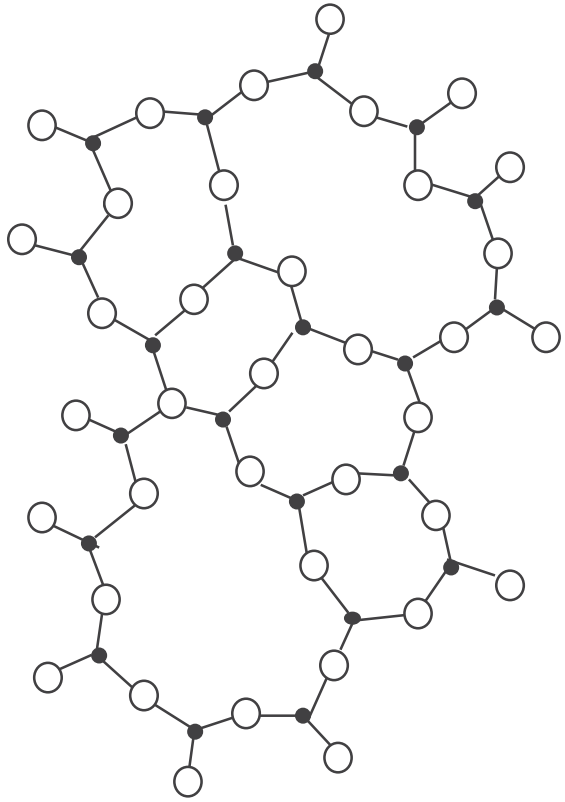
Two dimensions



Silicon - oxygen tetrahedron



Crystalline silica



Glassy silica

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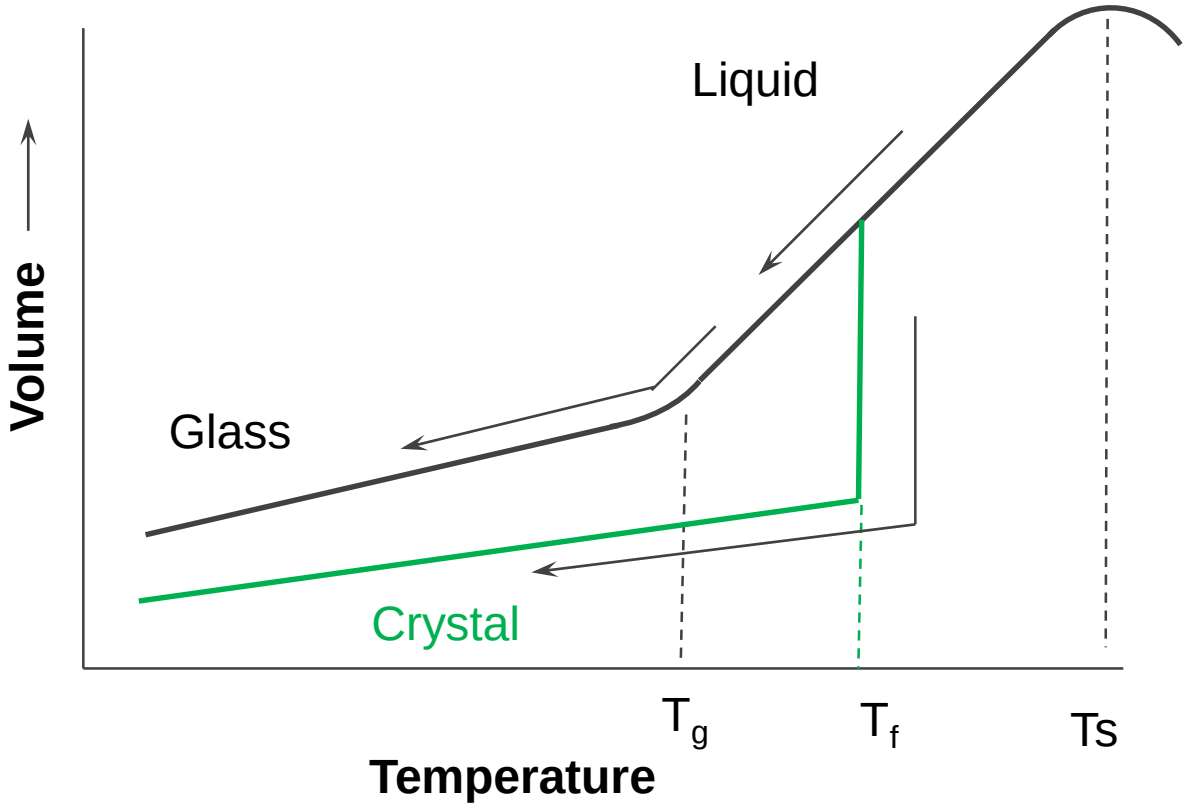
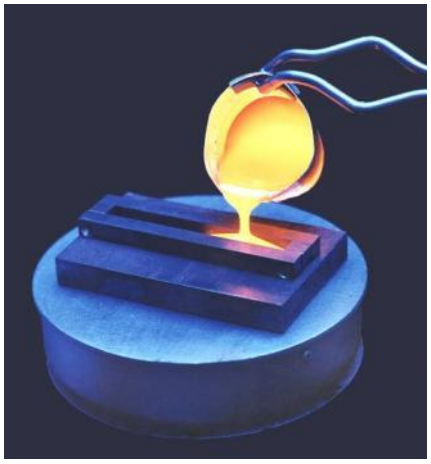
The glassy state



Volume-temperature curves for crystallisation and glass formation showing liquid melting temperature T, and glass transformation range T_g

Glass – basic constituents

Structural Role	Oxide
Network Former	SiO_2
	B_2O_3
	P_2O_5
Intermediate	Al_2O_3
	TiO_2
	ZrO_2
Network Modifier	MgO
	CaO
	SrO
	BaO
	PbO
	ZnO
	Na_2O
	Li_2O
	K_2O



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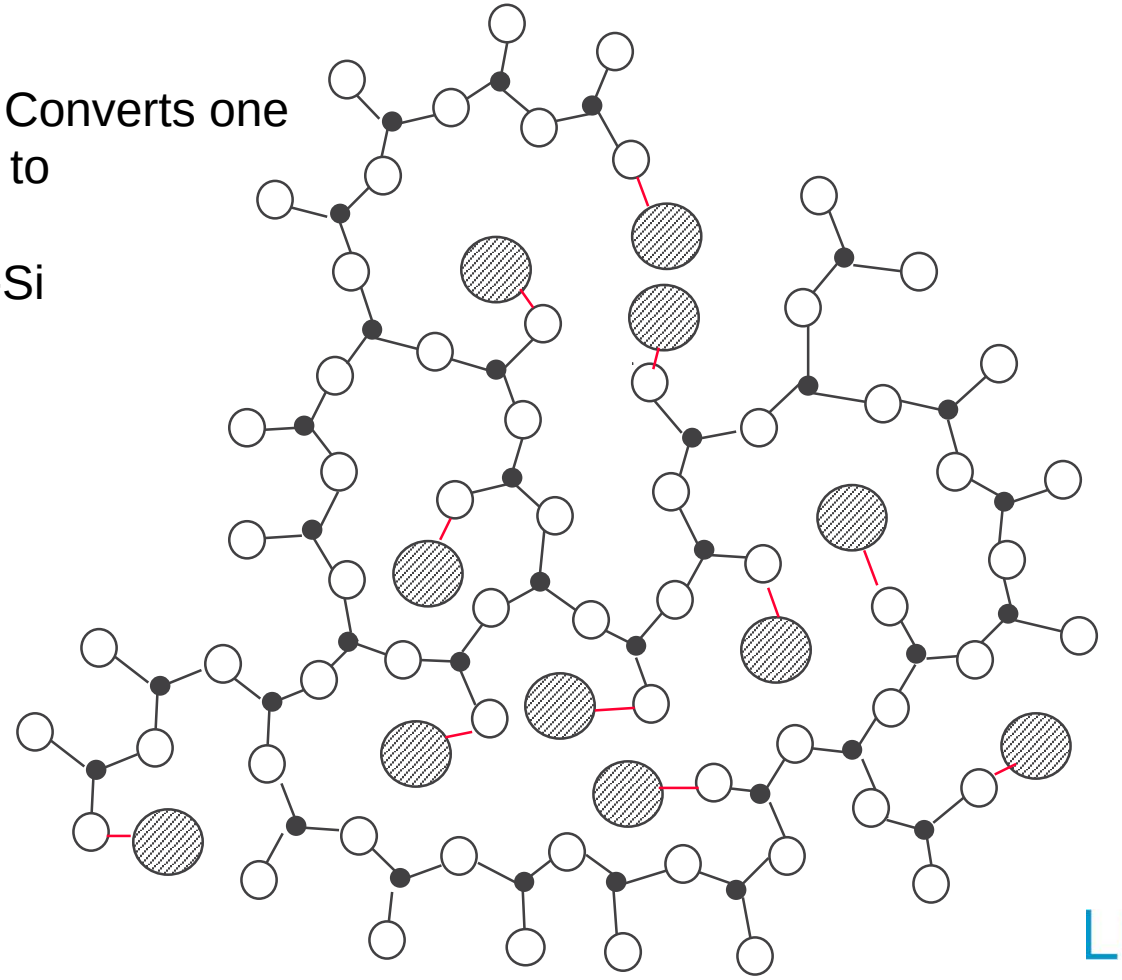
Glass structure
silicate network disrupted by Na_2O

Each Na_2O Converts one Si-O-Si unit to

Na^+

$Si\text{-}O^-$ $^-O\text{-}Si$

Na^+



Si

O

Na

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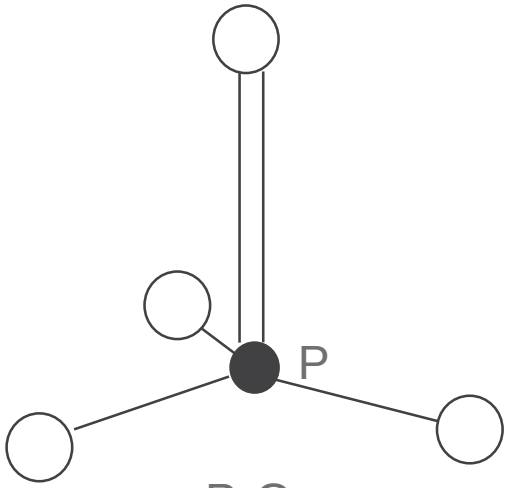
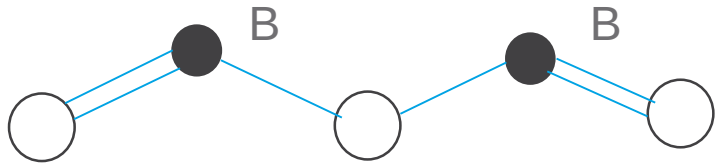
Phosphate and borate glasses



P_2O_5



B_2O_3

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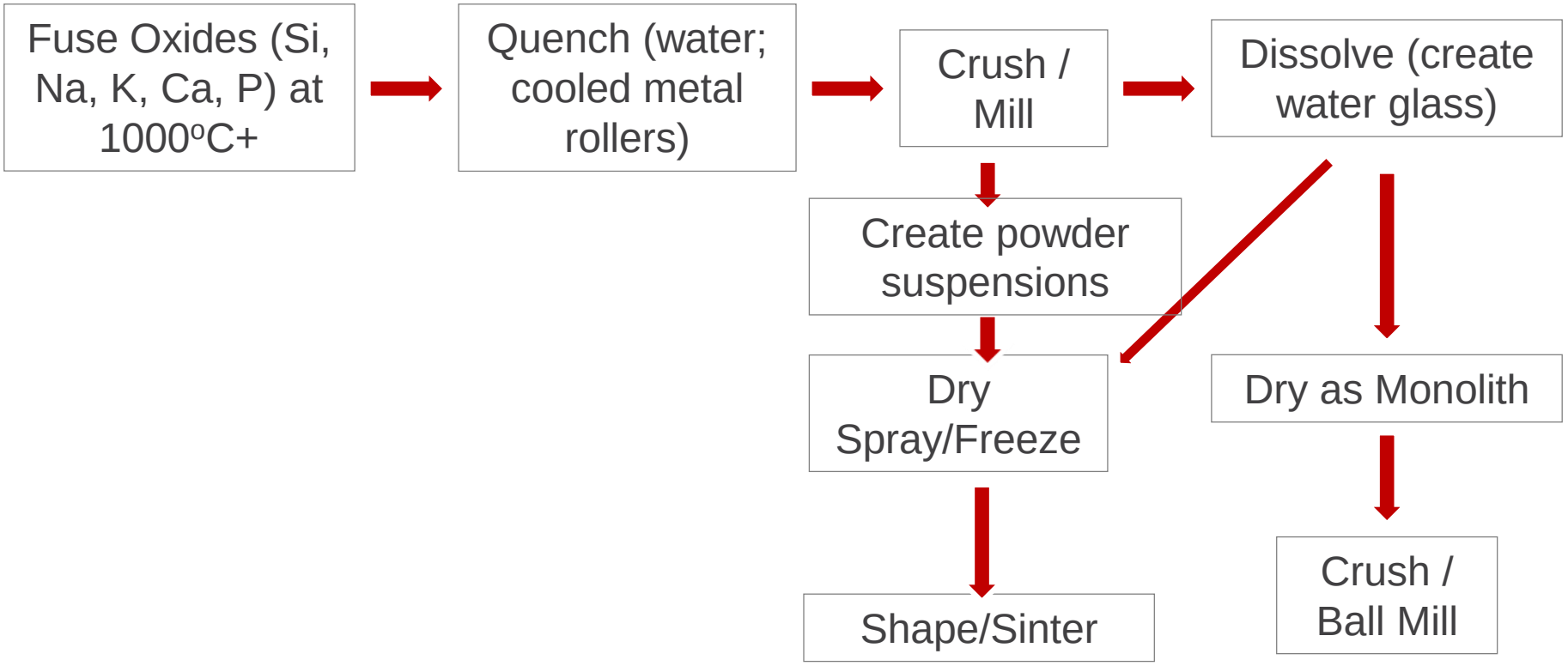
Glass preparation by fusion



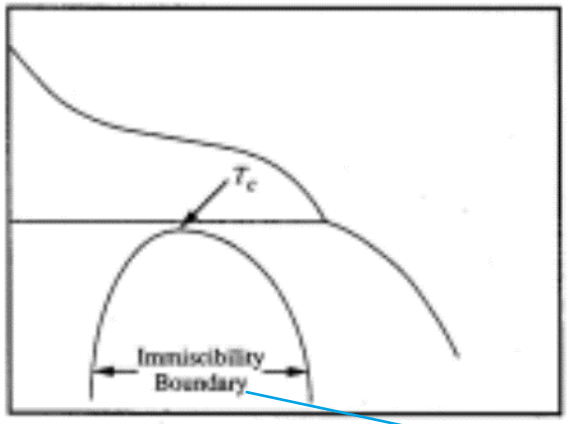
Glass preparation by fusion

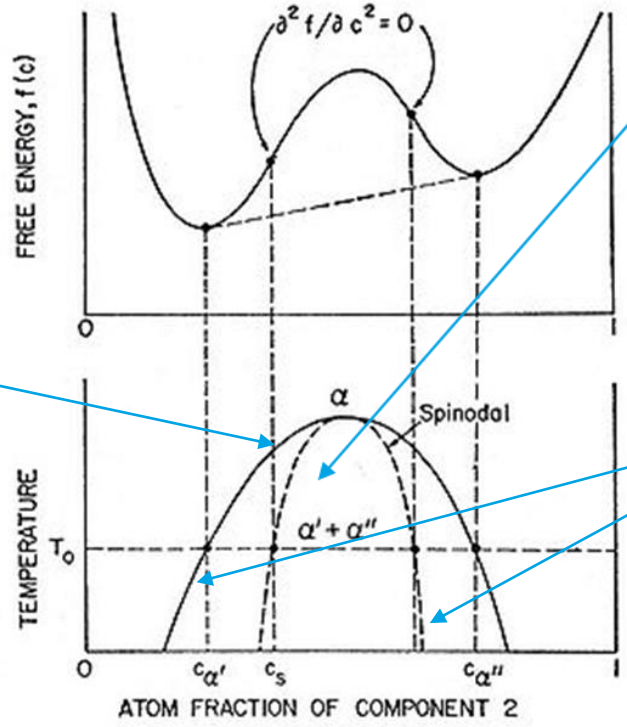
Melt Quenched
on a steel plate

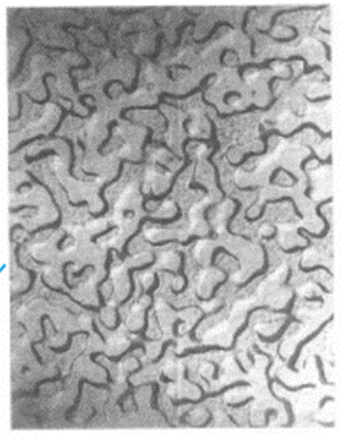
Cooled glass

Product as powder
frit or shapes

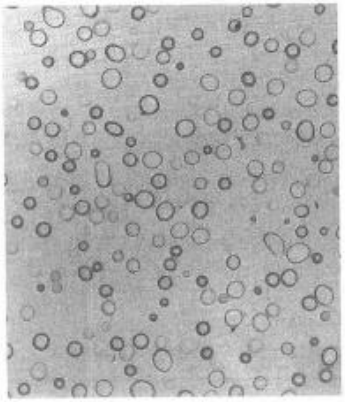
Phase separation in glasses







Spinodal



Nucleated

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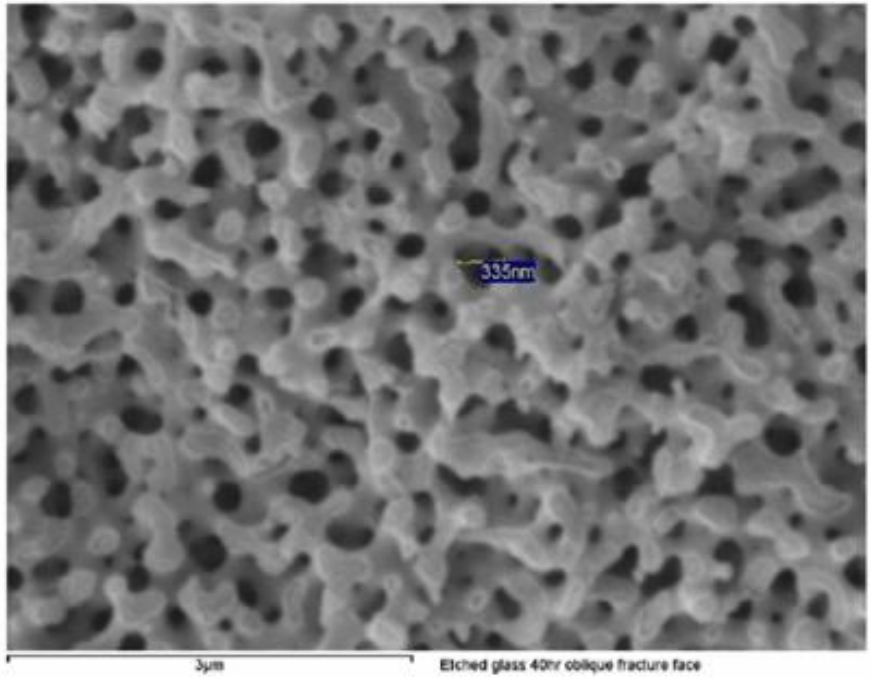
Phase separation



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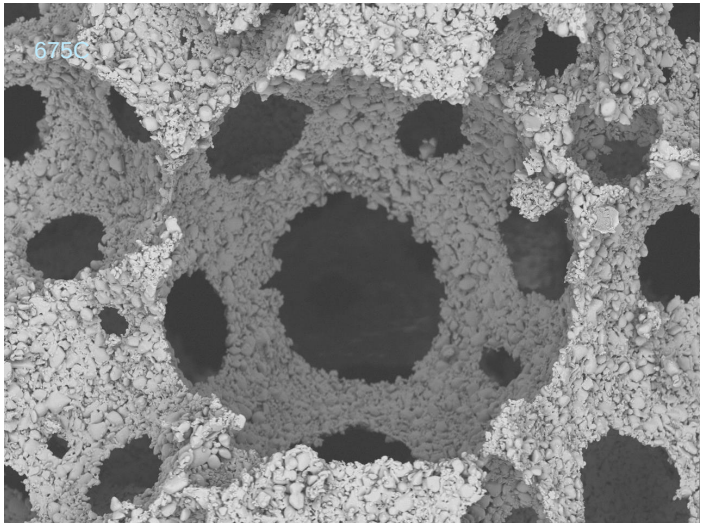
Glasses prepared via fusion

- Wide compositional and dissolution ranges
- Shaped or crushed for use or processing
- Used as a functional material, active ingredient or as a carrier
- May be shaped post formation to enhance performance: foams, spheres, fibres
- Volatile active loading by impregnation



Foamed Particulate Glass*

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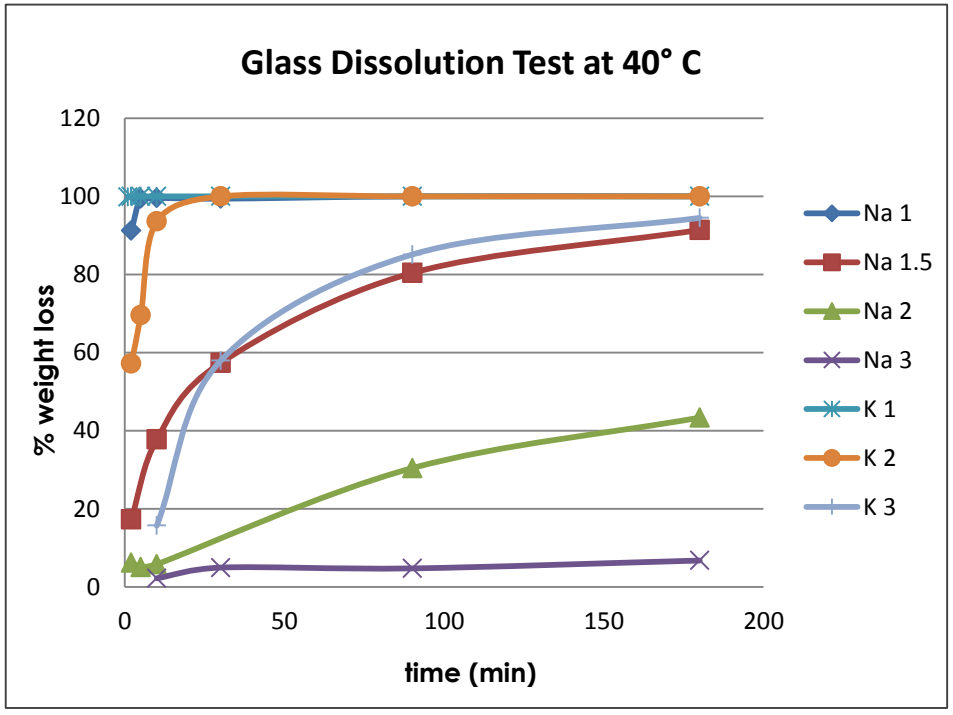
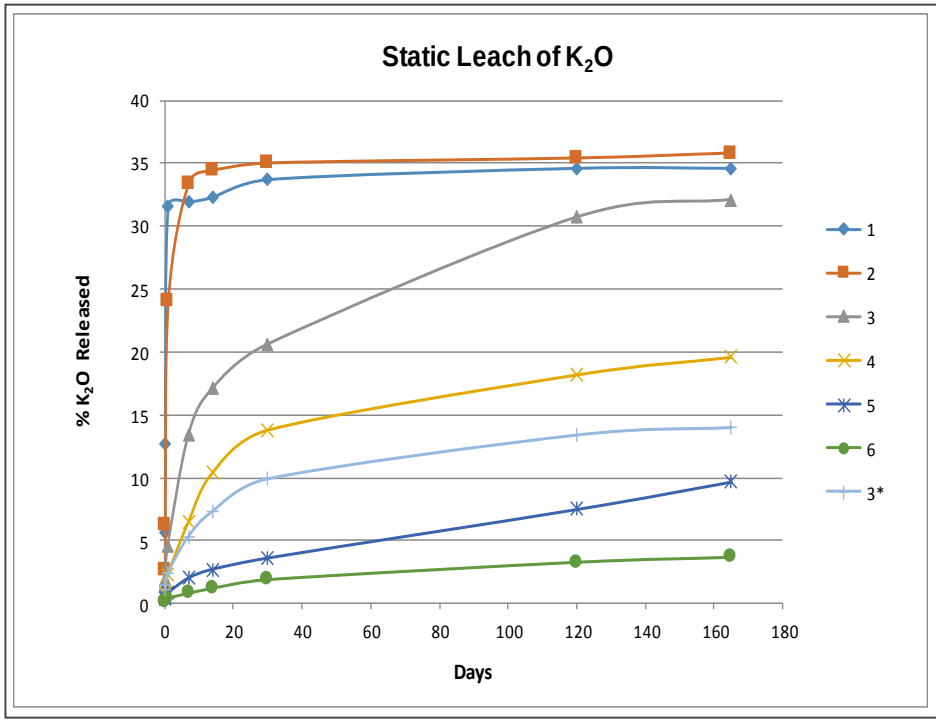
Control of dissolution - silicates





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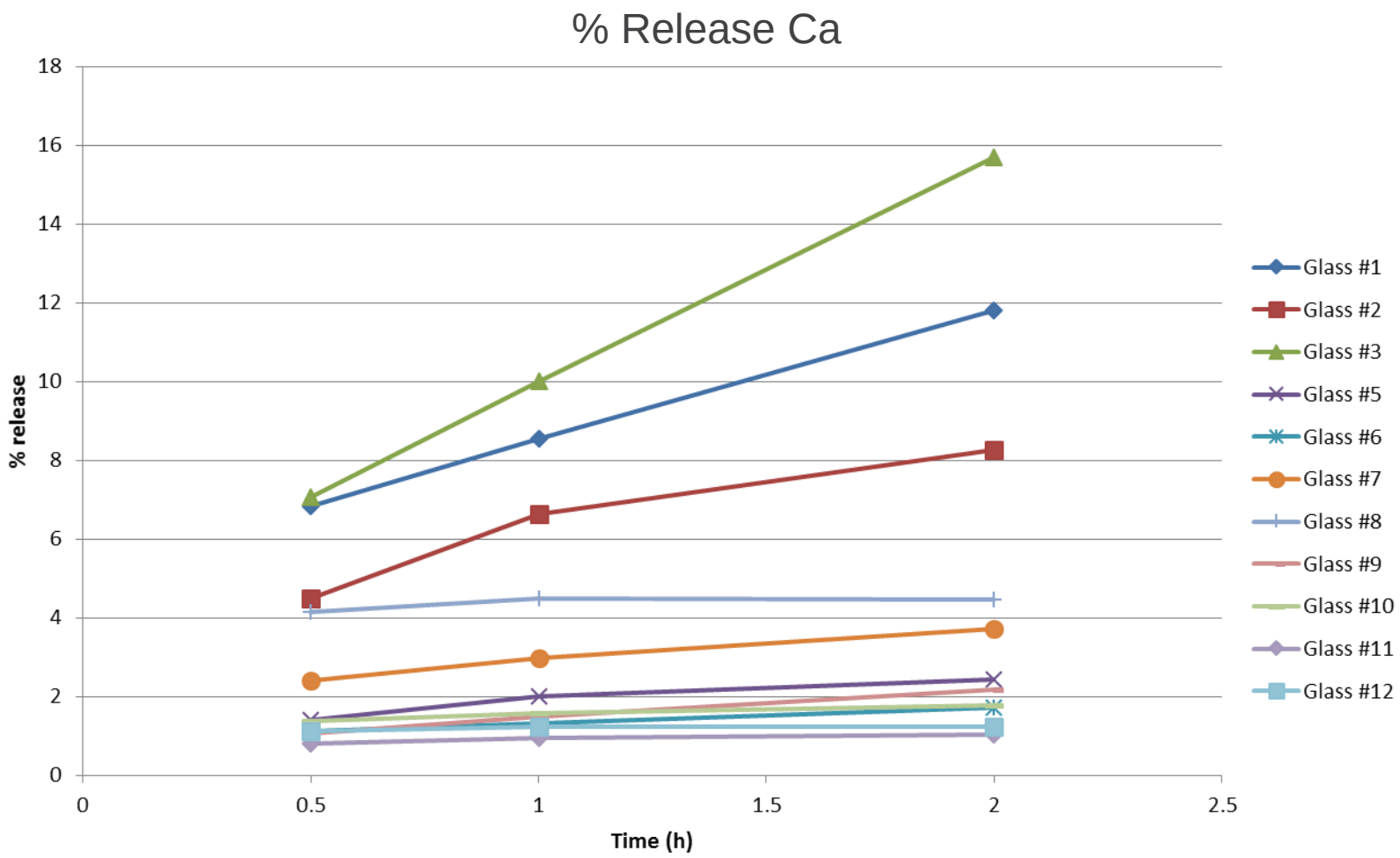
Control of dissolution – phosphate glass



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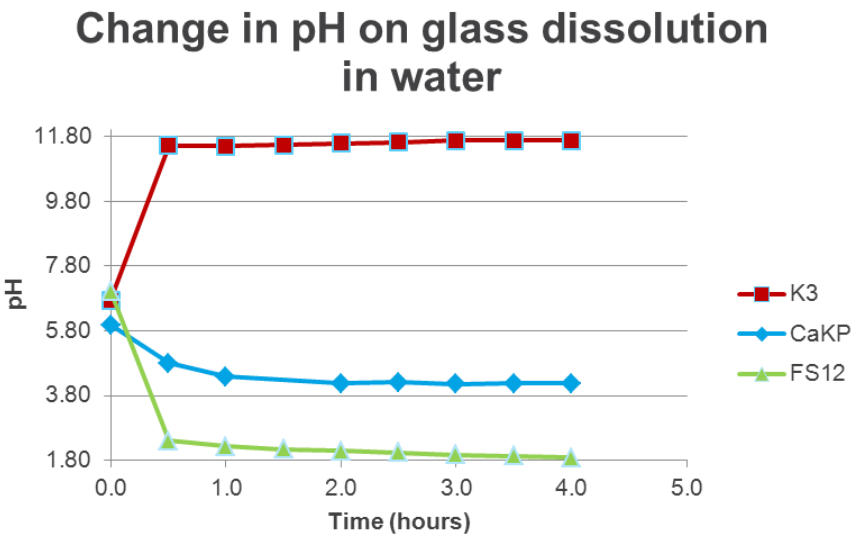
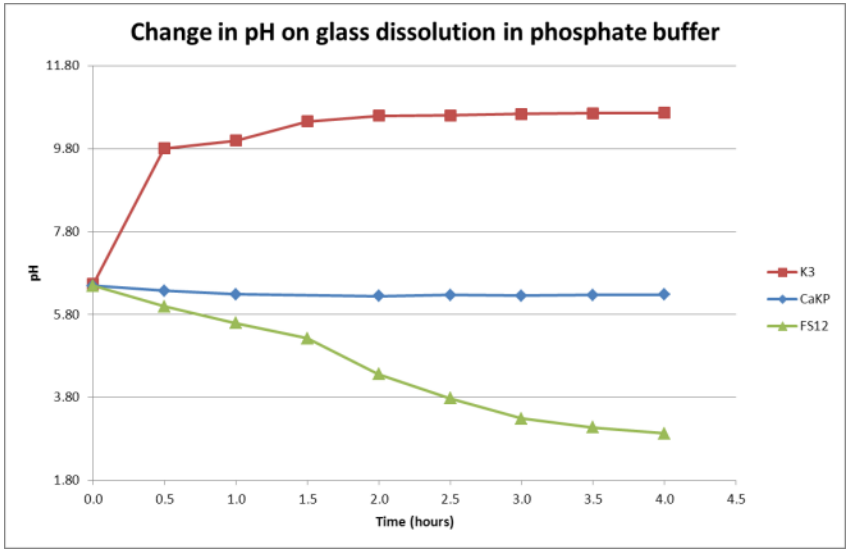
Effect of composition on pH





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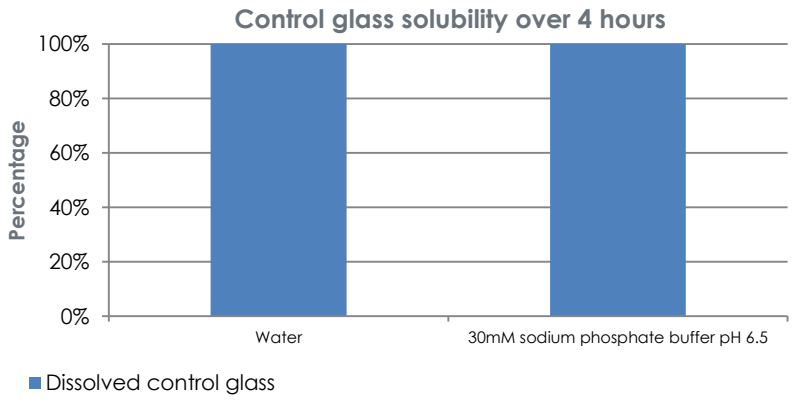
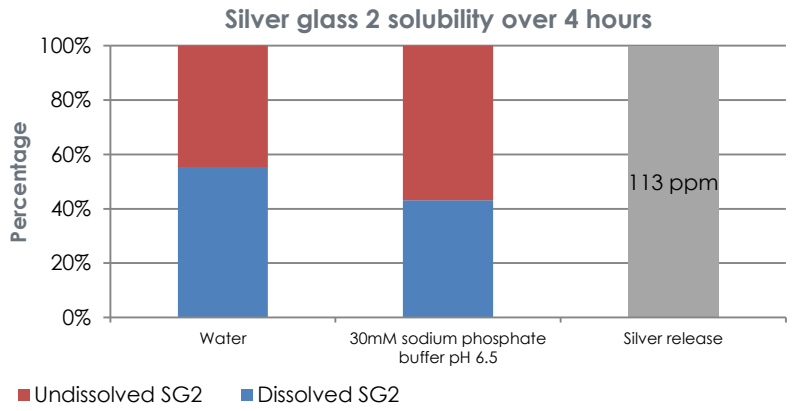
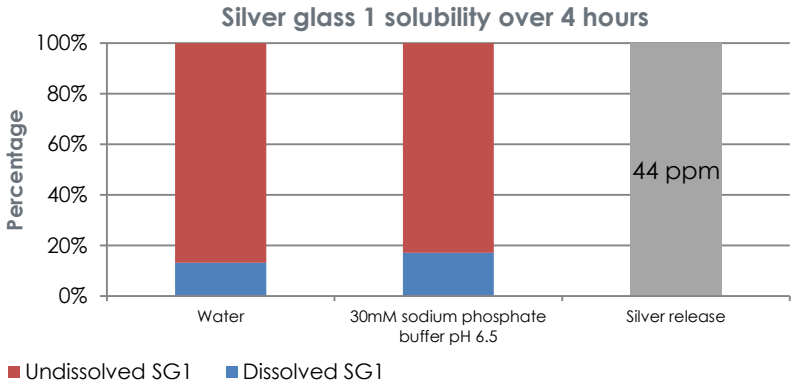
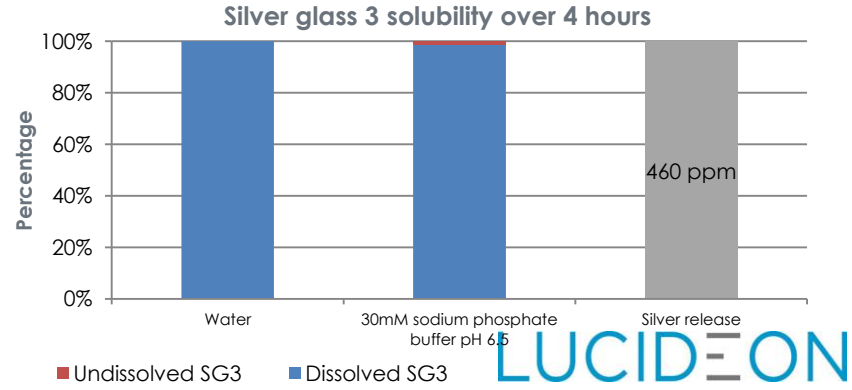
Control of dissolution - Ag

- 3 glasses from same compositional family
  - All contain same level of silver (4.3 Wt % Ag_2O)
  - All have different gross dissolution and silver (Ag) release rates









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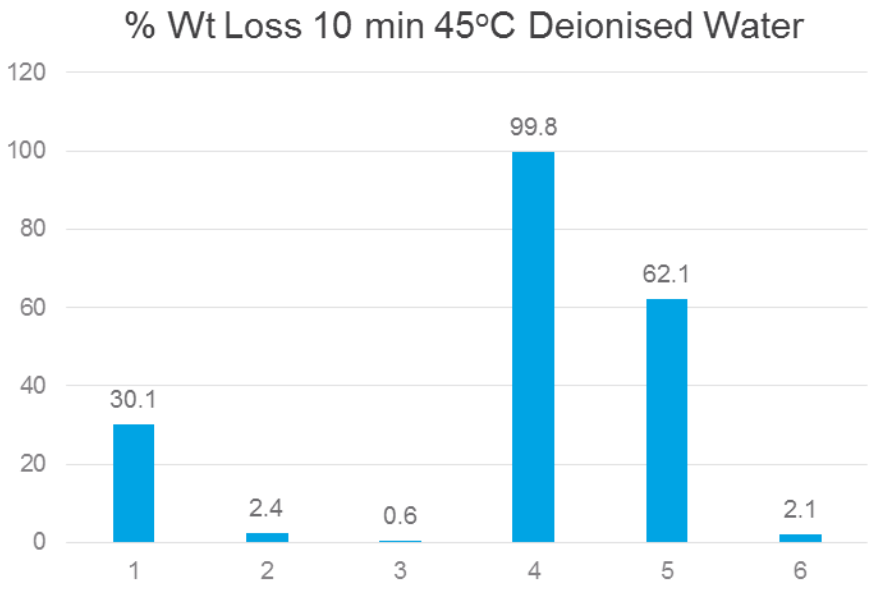
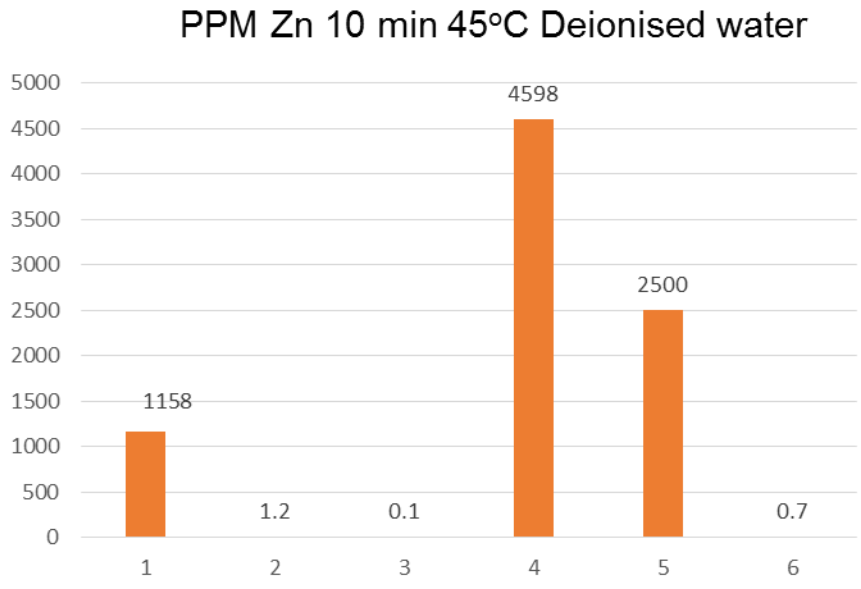
Control of dissolution – Zn





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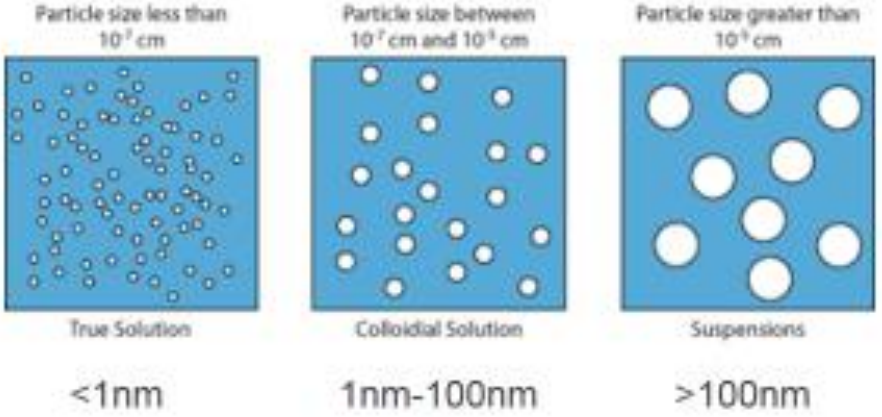
Glass preparation via chemical routes

Sol-gel processing

Sol: A colloidal suspension of solid particles in a liquid

Gel: A substance which contains a continuous solid phase enclosing a continuous liquid phase



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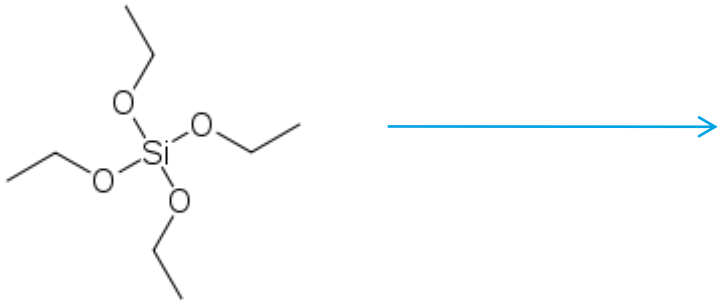
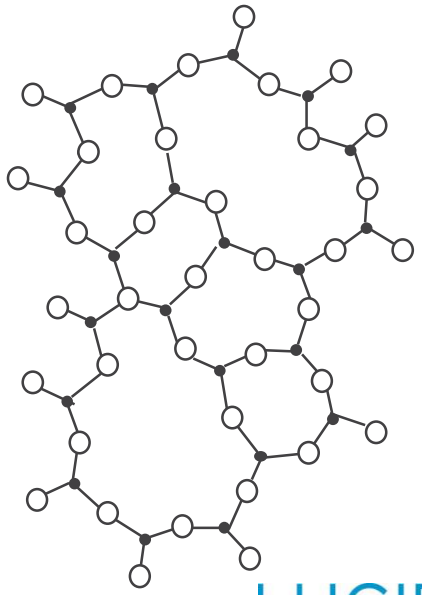
Sol-gel processing

- Most commonly used to produce porous silicates

TEOS → Silica

$Si(OEt)_4$ → $SiO_2 . n(H_2O)$





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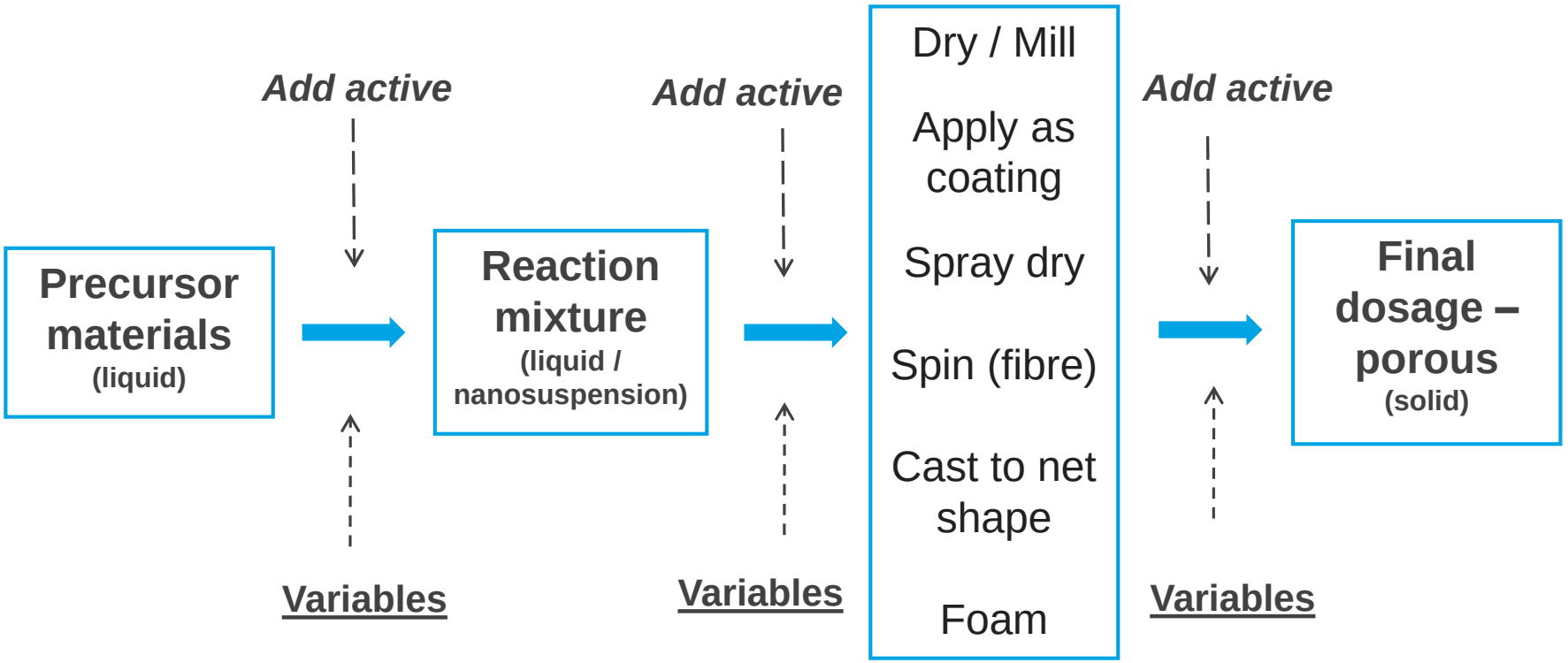
Sol-gel processing



Modification of the process i.e. Active addition and reaction parameters influences product microstructure and release rate not the chemistry of the carrier

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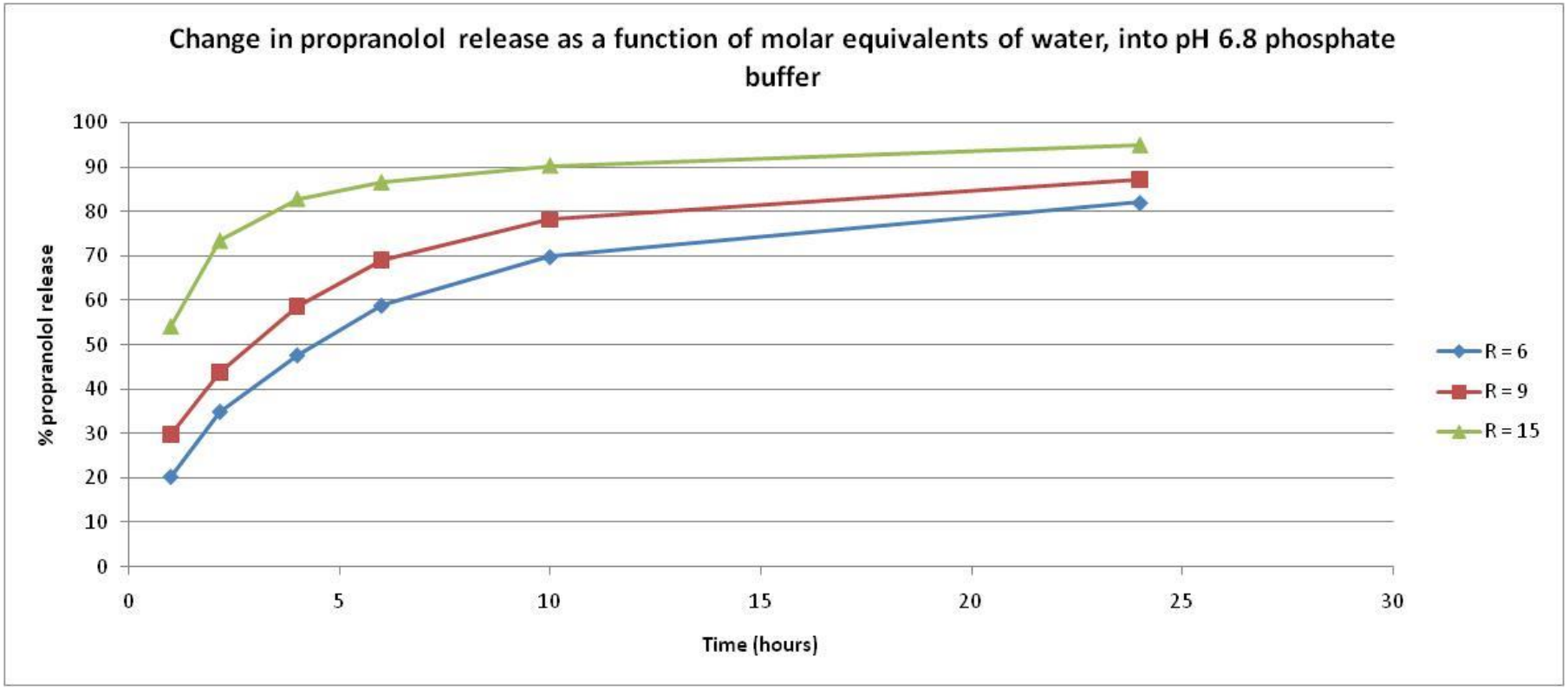
Sol-gel processing



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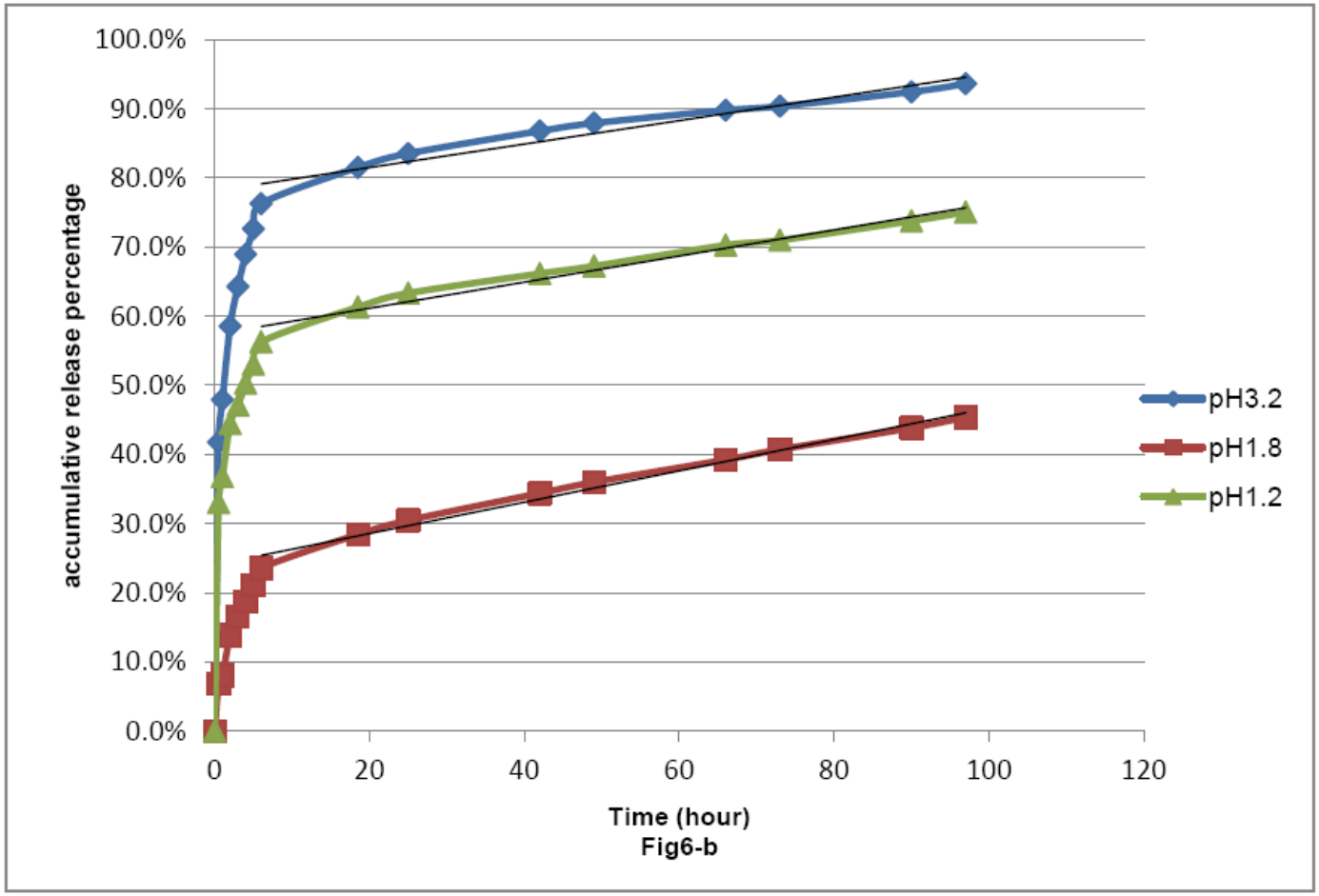
Sol-gel processing



Methadone release into pH 7.3 phosphate buffer - KCL

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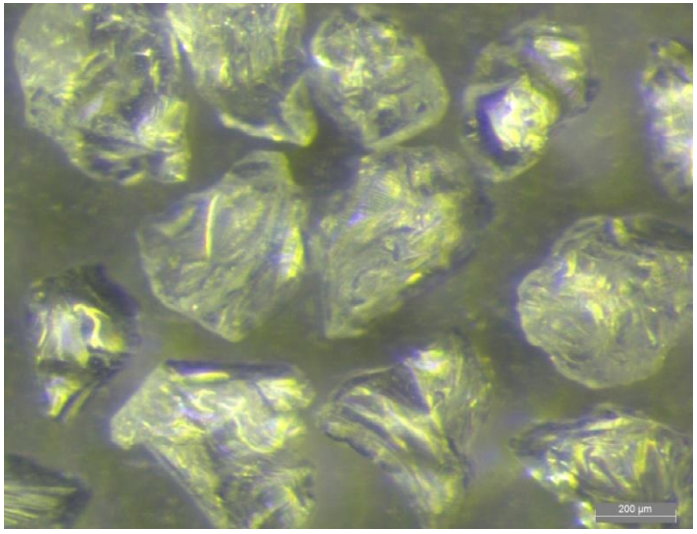
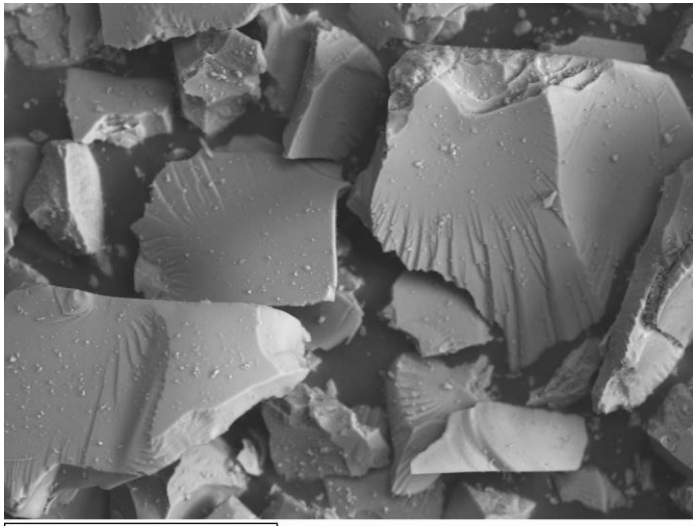
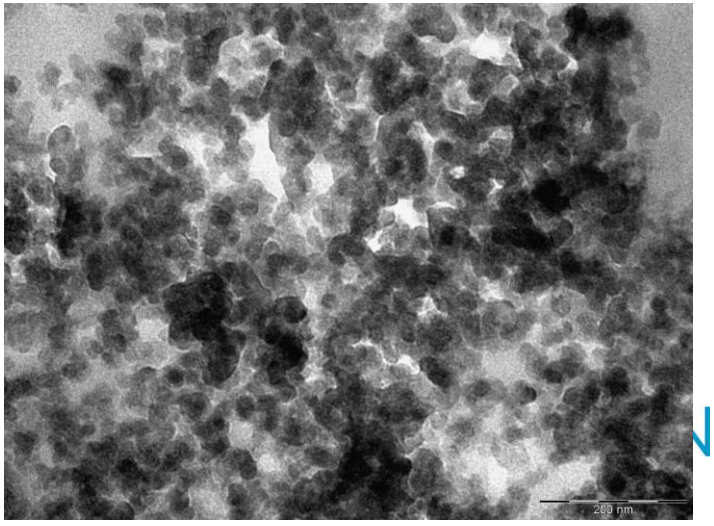
Sol-gel processing

Standard process – allow gel to form, dry, mill, desired PSD (from <1um – 1000um)

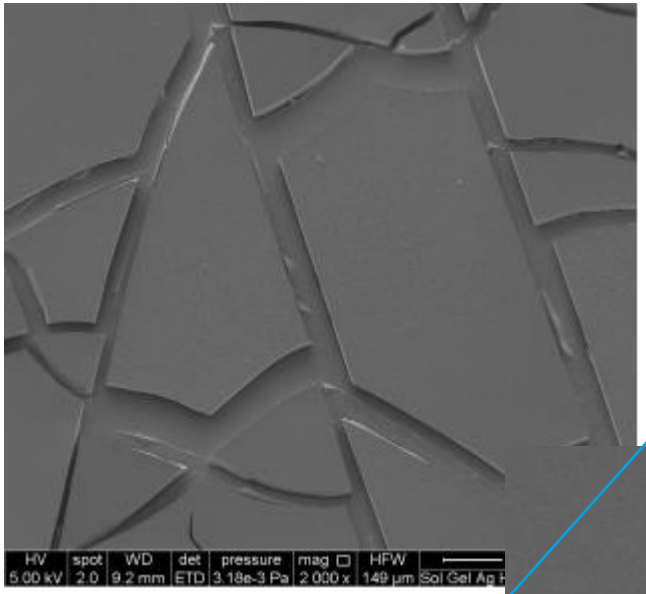
- Dry / Mill
- Apply as coating
- Spray dry
- Spin (fibre)
- Cast to net shape
- Foam



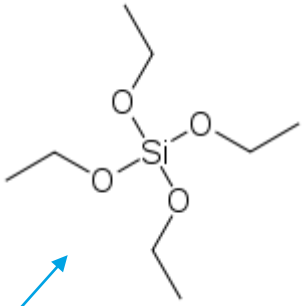


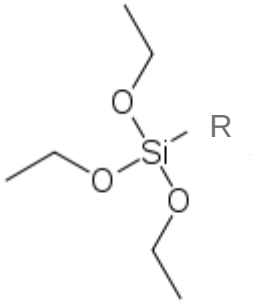


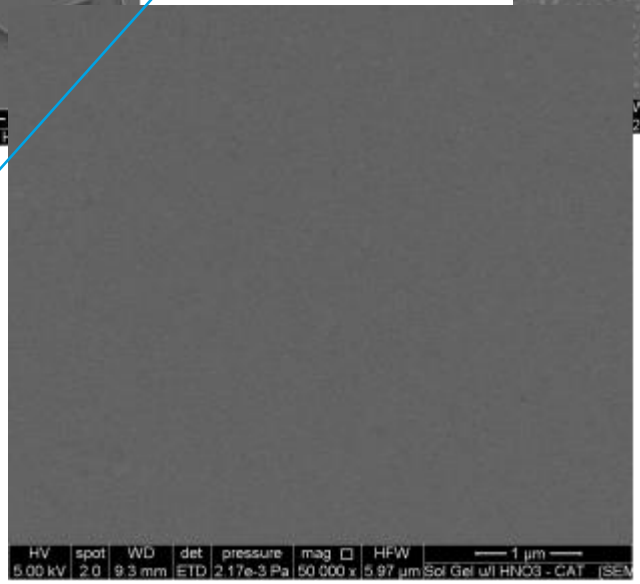
Sol gel coatings with silver



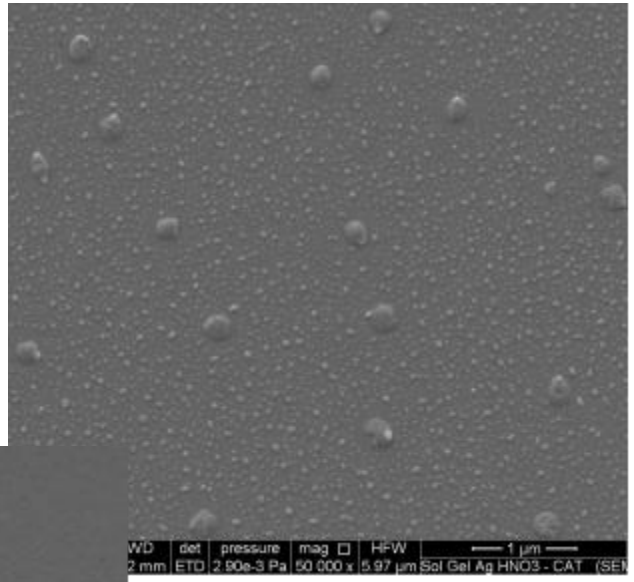
Cracked coating







Intact coating dispersed active



Intact coating with agglomerated active

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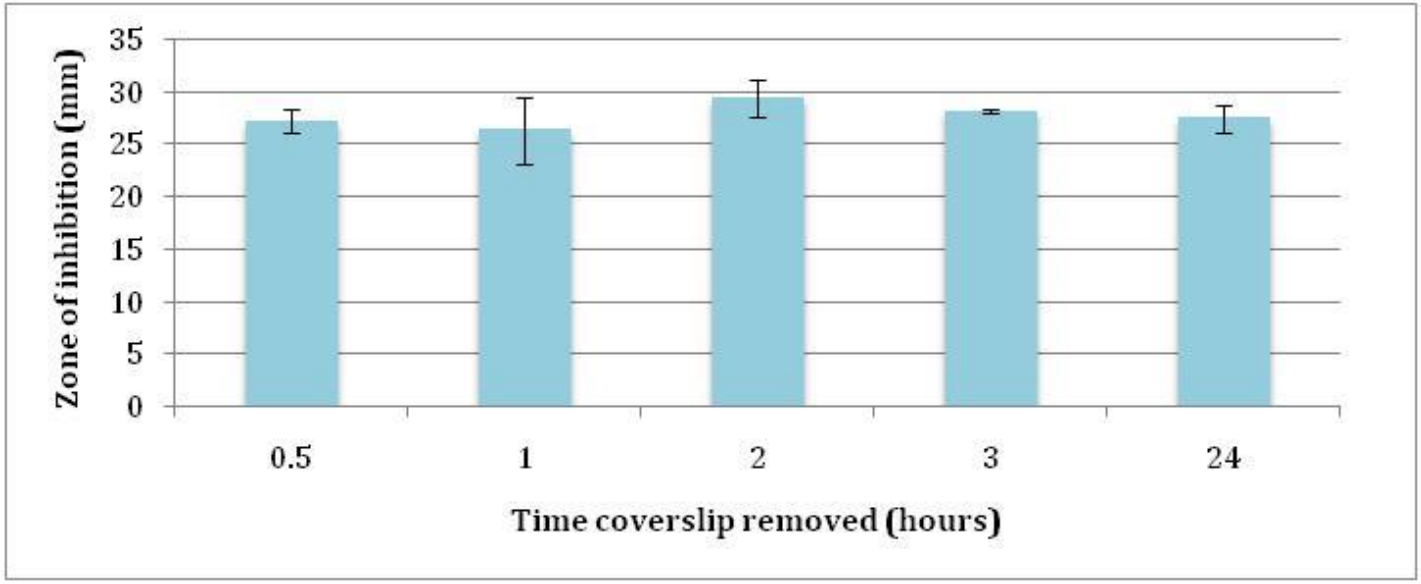
Case study: Silver release – porous carrier



- Antibacterial efficacy of silver-films tested against *E. Coli*
- Material has fast onset of action which is maintained for 24 hours

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Actives worked with

APIs

Propranolol hydrochloride
Naloxone hydrochloride
Oxycodone hydrochloride
Rapamycin
Guaifenesin
Ibuprofen sodium salt
Nifedipine
Methadone hydrochloride
AZD7295
Bicalutamide
Olaparib

Fragrances

Limonene
Linalool
β-ionone
α-hexylcinnamaldehyde
Methyl dihydrojasmonate

Others

Urea
Metaldehyde
Food dye
Ag^{+}

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Sol-gel vs melt-quench

Sol-gel	Melt-quench
Low temperature (RT-100°C)	High temperature (1000-1500°C)
Structured formed by solubilising ions in a solvent	Structure formed by making ions molten
Products are porous & high surface area	Products are dense & low surface area
Limited compositional range (for glasses)	Wide compositional range
Delivery of organic actives and ions	Delivery of active ions
Reagents relatively expensive, but cheap process	Reagents cheap, but process high energy (cost)

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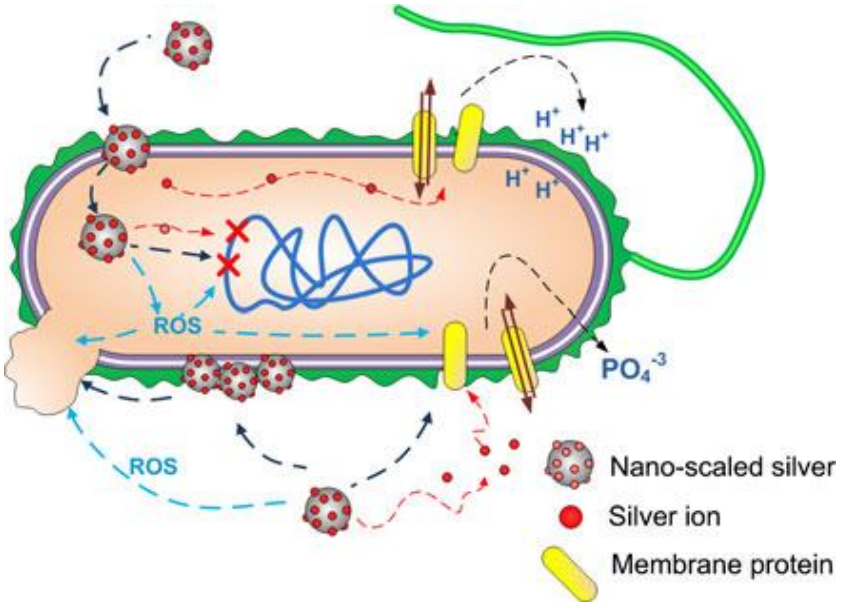
Antibacterial effect - Oligodynamic metals

Bismuth

Copper

Zinc



Gallium

Tin

Boron

Silver

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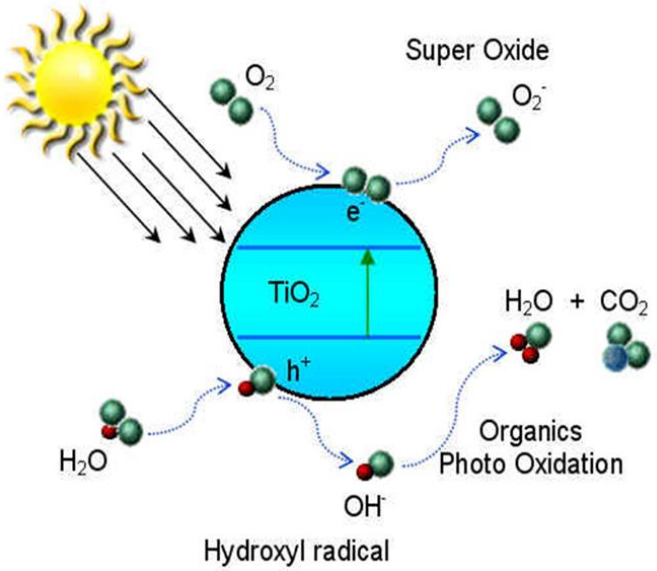
Photocatalytic effect



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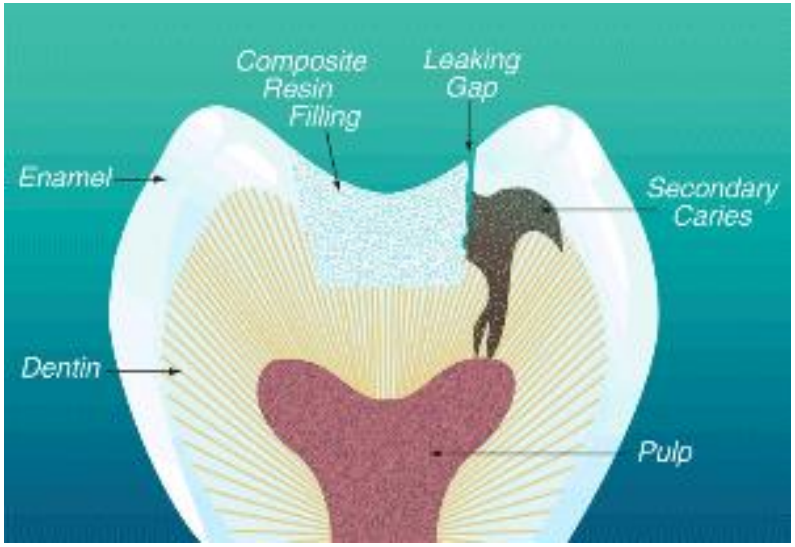
Antibacterial glass applications



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Objectives of Hymedpoly re Antibacterial glass materials

- Development of drug free antimicrobial technologies for medical applications such as implants and wound care.

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Thank you

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