Troubleshooting and FAQs for KLEPTOSE® cyclodextrins

ROQUETTE

created by

PE PHARMA EXCIPIENTS

What are ß-Cyclodextrins (ß-CDs)?

β-Cyclodextrins (β-CDs) are cyclic oligosaccharides with a bucket-like structure having a hydrophobic internal cavity and a hydrophilic exterior.

This unique structure allows for the formation of inclusion complexes, where lipophilic compounds are non-covalently bound within the cavity.

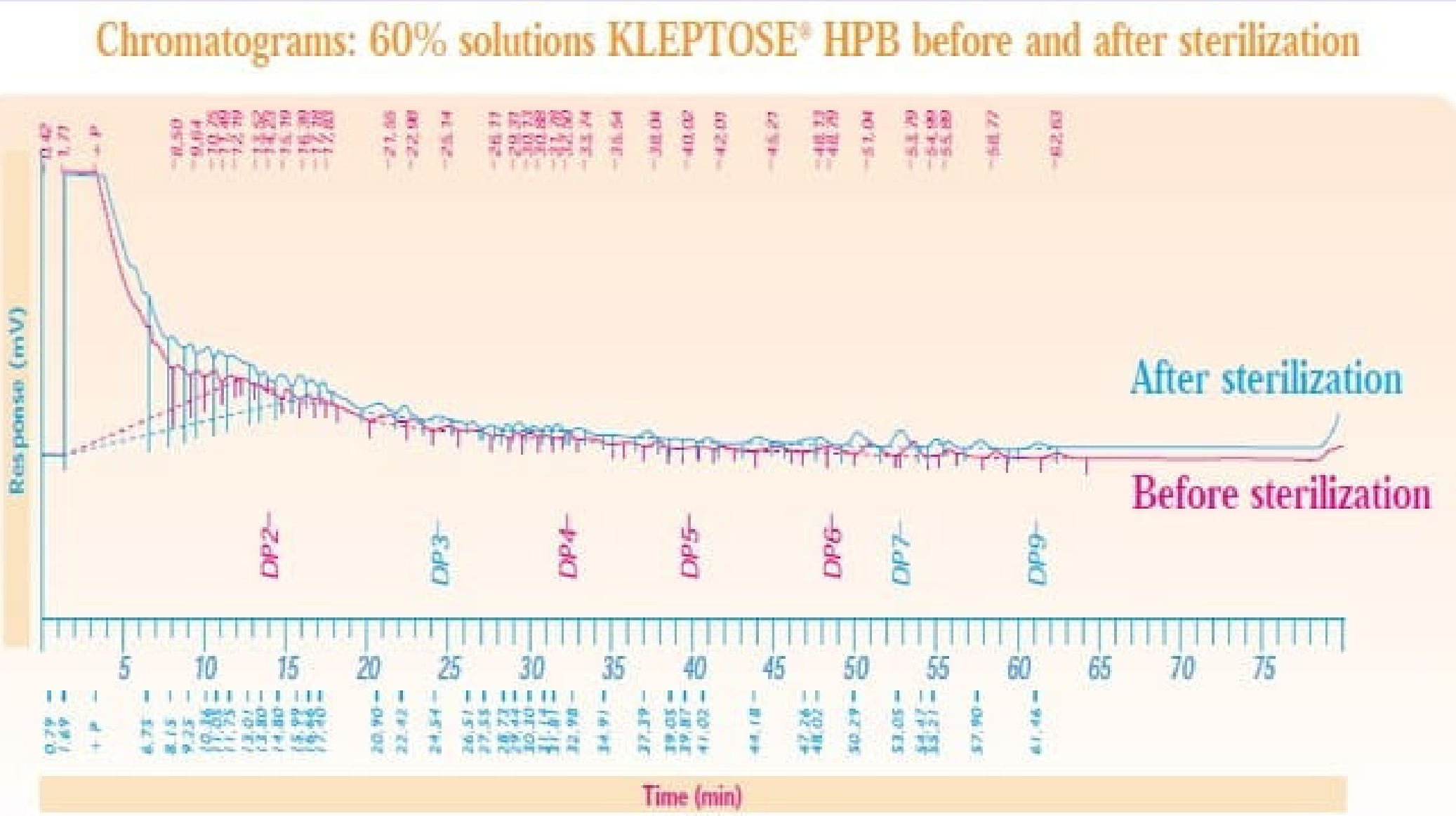
Are cyclodextrins stable during sterilization?

Cyclodextrins are not sensitive to filtration or autoclaving processing conditions.

Aqueous HPBCD solutions of various concentration (from 10 % to 60 % of KLEPTOSE® HP and KLEPTOSE® HPB) were sterilized for 15 minutes at 121 °C.

No degradation of hydroxypropyl-β-cyclodextrin solutions occurred during sterilization.

An example of the chromatogram for 60 % solution KLEPTOSE® HPB before and after sterilization is shown below:



Source: Roquette

What is/are the difference(s) between the oral and parenteral grades of KLEPTOSE® HP?

The molar substitution of both the oral and parenteral grades of KLEPTOSE® HP are the same, and are both generally used in small molecule applications.

The key difference of the parenteral and oral grades of KLEPTOSE® HP are listed in the table below.

	KLEPTOSE® HP Oral grade	KLEPTOSE® HP Parenteral grade
Route of administration	Oral, topical	Parenteral, ophthalmic and topic
Endotoxin controlled	*Not applicable*	Yes
CEP	No	Yes
DMF	US DMF Type IV	US DMF Type II and IV

Does hydroxypropyl-ß-cyclodextrin function as a surfacant?

Hydroxypropyl-ß-cyclodextrins are not surfactants.

Unlike a surfactant, they do not have a critical micellar concentration (CMC) value.

However, it has been reported that hydroxypropyl-ß-cyclodextrins exhibit some surface active properties:

It was observed that the surface tension generally decreases as the concentration of hydroxypropyl-ß-cyclodextrin increases.

What is/are the key difference(s) between the parenteral and biopharma grades of KLEPTOSE® HP and KLEPTOSE® HPB?

The molar substitution of both the parenteral and biopharma grades of KLEPTOSE® HP and KLEPTOSE® HPB are the same.

Both are low endotoxins grades that are suitable for parenteral dosage forms.

However, the key difference is that KLEPTOSE® HP Biopharma and KLEPTOSE® HPB Biopharma undergoes additional testing beyond the monograph, such as Beta Glucans, DNAse, protease, residual DNA, ICH Q3D elemental impurities, and pesticides levels.

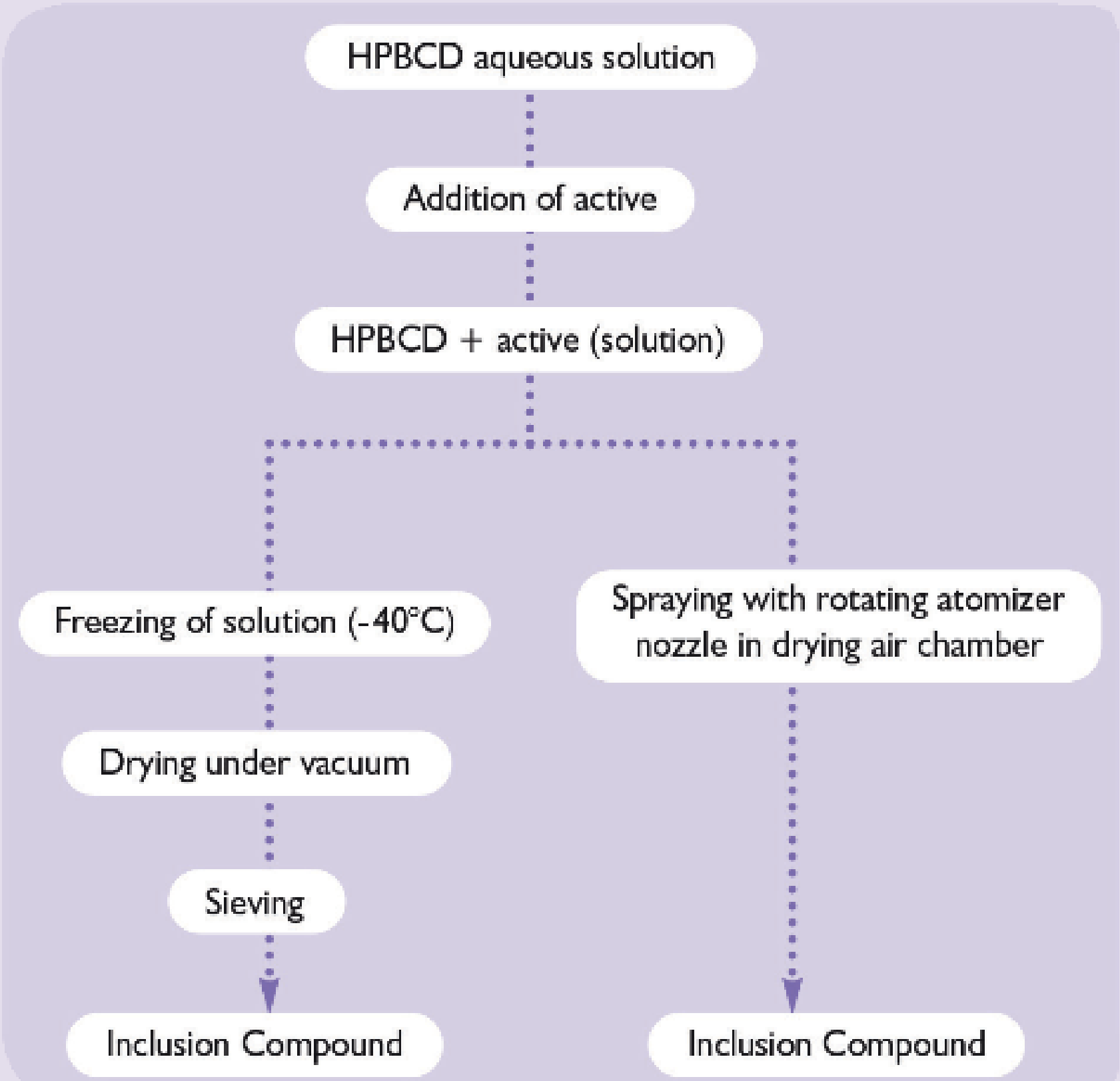
How do I prepare an inclusion complex between my API/drug/NME/NCE and a cyclodextrin ?

Inclusion compounds with cyclodextrins can be prepared in various ways, such as spray-drying, freeze-drying, kneading, physical mixing, etc.

The preparation method may be selected from some preliminary trials to determine the complexation efficiency for the given method.

To prepare complexes in the solid form, the solvent needs to be removed in the final step of the process.

With the hydroxypropyl-β-cyclodextrins (HPBCD), the preparation of inclusion compounds or complexes in aqueous media is very simple.



How do I analyze inclusion complexes between cyclodextrin and my API/NBE/protein/large molecule?

Usually a combination of analytical techniques are used to understand the complexation between the guest molecule and cyclodextrin due to the inherent limitations and sensitivity of the respective techniques.

Nuclear magnetic resonance (NMR) spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, differential scanning calorimetry (DSC), power X-ray diffraction are some of the common methods employed.

How are inclusion complexes between my API/drug/NME/NCE and cyclodextrin formed?

In the presence of water, cyclodextrins (host molecule) can form inclusion complexes with many drugs (guest molecule) by taking up (some lipophilic part of) the molecule.

Drug molecules in the complex are in rapid equilibrium with free molecules in the solution.

No covalent bonds are formed or broken during the complex formation.

What is the safety profile of cyclodextrins?

Native cyclodextrins and cyclodextrin derivatives such as hydroxypropyl-β-cyclodextrin are used in marketed pharmaceutical products.

The safety profiles of native cyclodextrins are well established, and they are accepted as food additives and “generally regarded as safe” (GRAS).

What is the difference between the hydroxypropyl-ß-cyclodextrin, KLEPTOSE® HP and HPB?

Roquette has developed a range of substituted hydroxypropyl-β-cyclodextrins with different degrees of substitution that are described by the molar substitution level.

KLEPTOSE® HP has a higher degree of molar substitution (0.81-0.99) compared to KLEPTOSE® HPB (molar substitution range of 0.58-0.68).

Both KLEPTOSE® HP and HPB are available in oral, parenteral and biopharma grades that are suitable for taste masking, solubility improvement and stability improvement of active molecules and therapeutic proteins.

What are the types of cyclodextrins offered by Roquette for pharmaceutical or nutraceutical applications?

Roquette has a range of native and modified hydroxypropyl-β-cyclodextrins (HPBCD) for use in many dosage forms:

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	Products:	Key attributes:
Native β-cyclodextrins	KLEPTOSE®	Standard β-cyclodextrin grade
	KLEPTOSE® 10	For aerosol use and improved mouthfeel (very fine particle size)
	KLEPTOSE® 200 F	For improved mouthfeel (fine particle size)
	KLEPTOSE® 4%	Less than 4% loss on drying
	KLEPTOSE® 7%	Less than 7% loss on drying
	KLEPTOSE® DC	Directly compressible grade
Modified hydroxypropyl-β-cyclodextrins	KLEPTOSE® HPB Oral	Medium molar substitution; oral grade
	KLEPTOSE® HPB Parenteral	Medium molar substitution; parenteral grade
	KLEPTOSE® HPB Biopharma	Medium molar substitution; biopharma (low endotoxin)
	KLEPTOSE® HPB-LB Parenteral	Medium molar substitution; parenteral grade
	KLEPTOSE® HP Oral	High molar substitution; oral grade
	KLEPTOSE® HP Parenteral	High molar substitution; parenteral grade
	KLEPTOSE® HP Biopharma	High molar substitution; biopharma (low endotoxin)

When should I consider the use of cyclodextrins in my formulations?

The use of cyclodextrins in small molecule drug formulations can be considered, for example when...

1. **... the active ingredient is poorly water soluble, which may then affect the bioavailability.**
2. **... the time required to reach the effective blood level of the orally administered drug is too long because of slow dissolution rate and/or incomplete absorption.**
3. **... there is a need to formulate an aqueous eye drop or injectable solution containing a poorly water soluble active ingredient.**

... and many more ...

Visit the Roquette supplier page at https://www.pharmaexcipients.com/excipient-suppliers-list/roquette/ for more information.

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