



Formulation of Biotech products


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Stabilizers:

- Includes antioxidants, preservatives,
- Proteins rich in oxidizable amino acids like methionine, cysteine, tryptophan, tyrosine and histidine are liable to oxidative degradation.
- So, we can avoid or prevent that by:
 - 1) Replacement of oxygen by inert gases in the vials.


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2) Addition of antioxidant like ascorbic acid, acetyl cysteine, GSH, sodium disulfide and alpha tocopherol, are frequently used at a concentration of about 0.05-0.1%.

3) Chelating agents can be incorporated to bind copper, iron, calcium and manganese. Ethylenediamine tetraacetic acid **EDTA** is commonly used at a concentration of about 0.01%-0.05%.

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■ Certain proteins are formulated in multiple injection systems, then contamination with M.O. may be occurred after administration of first dose, therefore preservatives are needed.

■ Preservatives used in concentrations that are bacteriostatic rather than bactericidal in nature.

■ Examples: thimerosal, p-hydroxy benzoic acids, phenol, benzyl alcohol and chlorobutanol


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Osmotic agents:

- Are added for adjusting the tonicity like saline and monosaccharide (dextrose) or disaccharide solutions.
- These excipients may not be inert?? They may influence protein structural stability.
- For example, sugars and polyhydric alcohols can stabilize the protein structure through the principle of **preferential exclusion**.

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- These additives (water structure promoters) enhance the interaction of the solvent with the protein and are themselves excluded from the protein surface layer, the protein is preferentially hydrated.
 - A strong preferential exclusion effect enhances the tendency of protein to self associate.


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Lyo-protectant/cake formers:

- Are typical excipients used in a freeze-dried protein formulation for protection of the physical structure of the protein, like sugars and albumin
- Their mechanisms are not fully understood. Factors that might play a role are:
 - 1) They replace water as stabilizing agent (water replacement theory).
 - 2) They increase the T_g of the cake/frozen system.
 - 3) They will absorb moisture from the stoppers.

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- 4) They slow down the secondary drying process and minimize the chances for over-drying of the protein. Over-drying might occur when residual water levels after secondary drying become too low.

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Carrier systems (bulking agents):

- Are typical excipients used in a freeze-dried protein formulation for elegance shape and blowout prevention like mannitol and glycine.
- Blowout is the loss of material taken away by the water vapor that leaves the vial. It occurs when little solid material is present in the vial.