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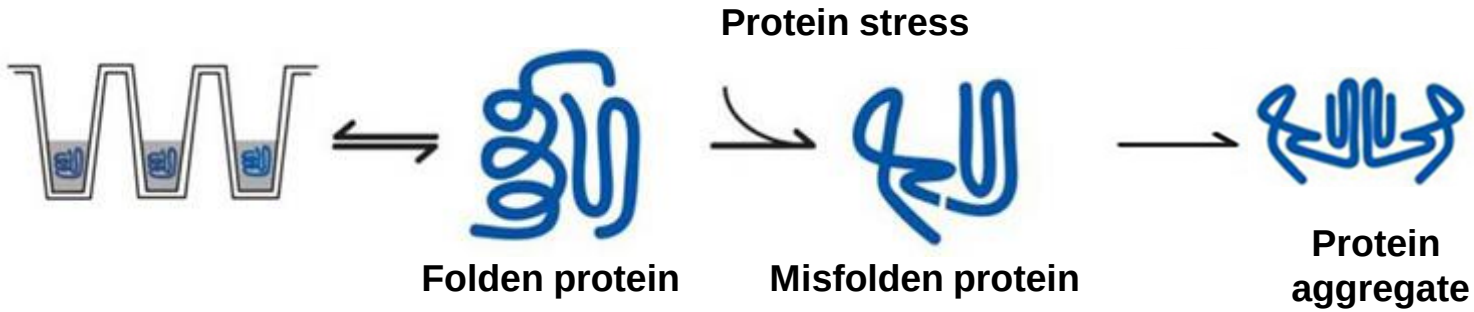
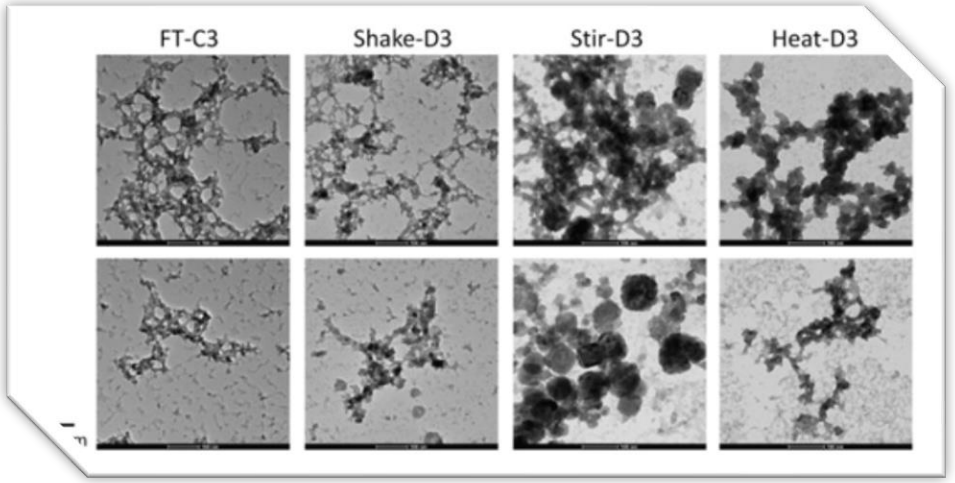
Cyclodextrins

Uses in protein formulations

Outcomes of Protein Aggregation



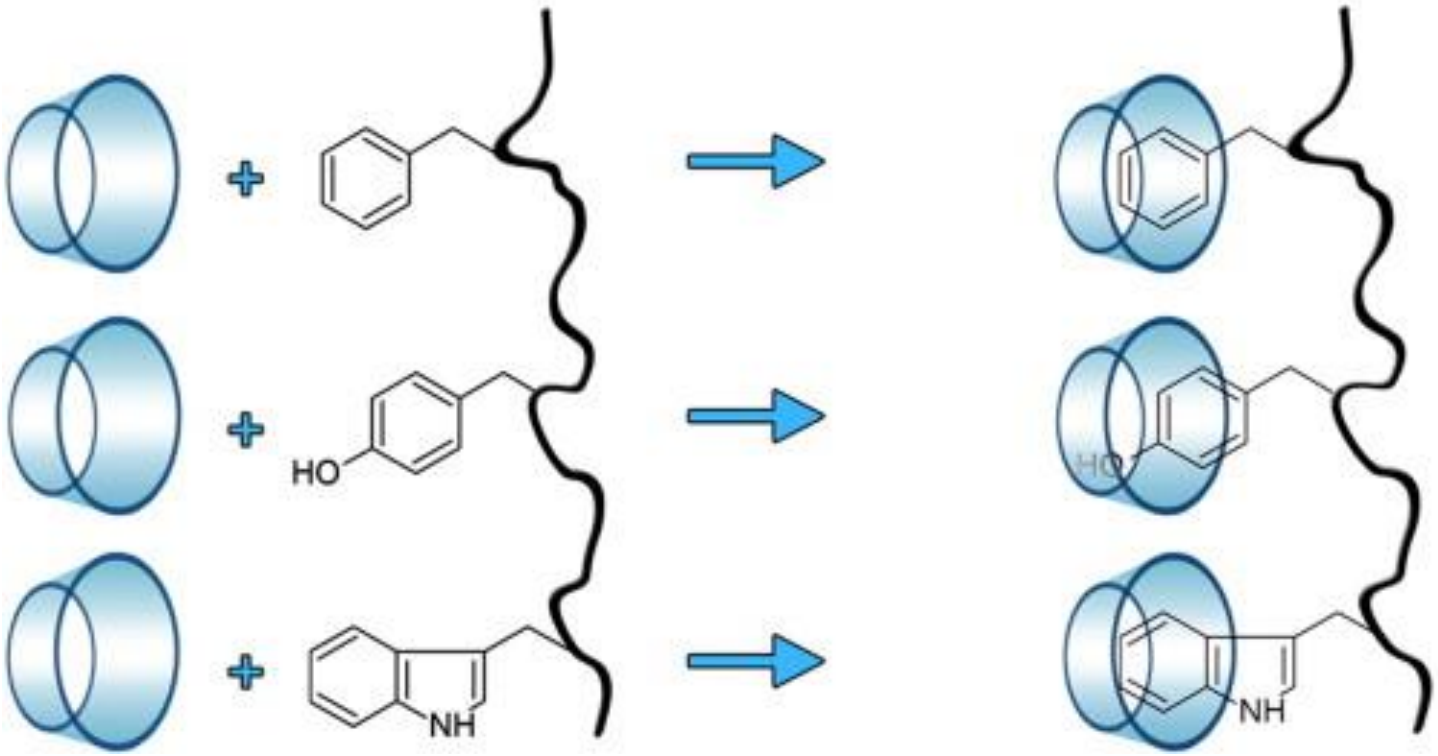
- Decreased efficiency
- Altered pharmacokinetics
- Immunogenicity, irritation, anaphylaxis
- Short shelf-life, poor stability



Monoclonal antibodies are particularly prone to aggregation

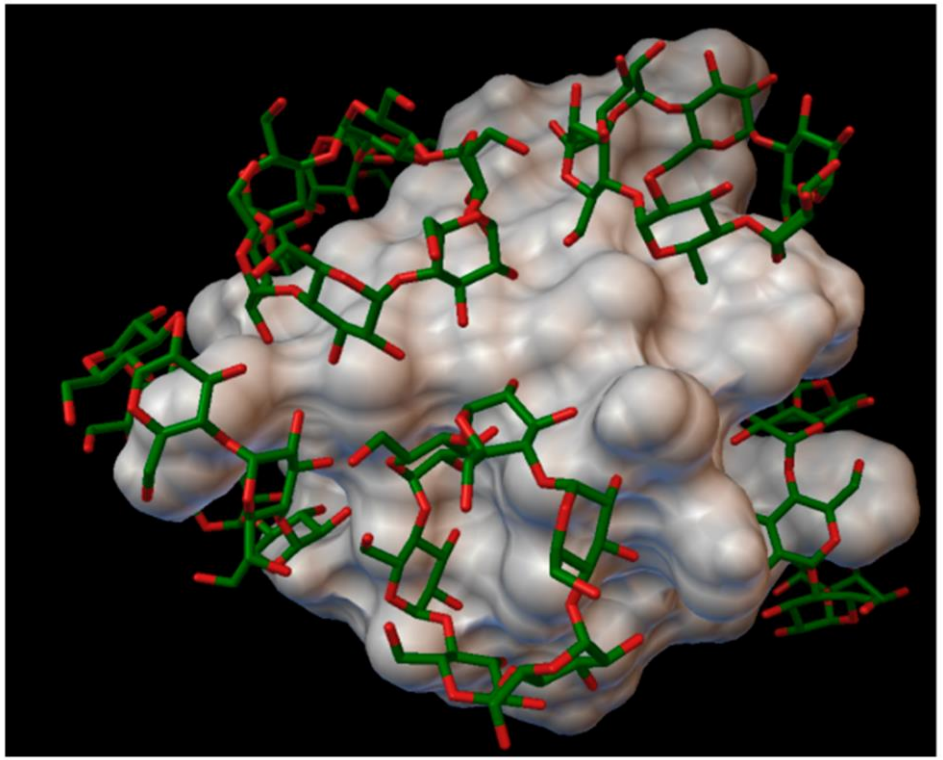
CD-Proteins Interactions

CDs are able to interact with proteins and polypeptides on several levels. The classical inclusion involves aromatic amino acids.



Tim Serno et al., https://doi.org/10.1016/j.addr.2011.08.003

Cyclodextrin's effect on insulin aggregation

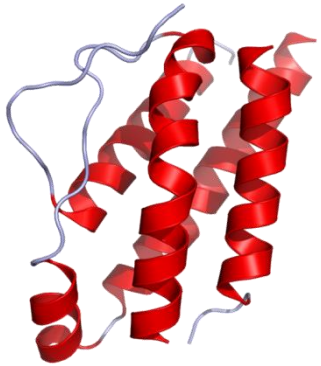


Several CD molecules cover a single proteins simultaneously.

CDs were found to be useful for improving the pharmacological performance of various insulin
formulations aimed for different routes of administration – oral, nasal, pulmonary, etc.

Emese Sipos et al., Molecules 2022, 27(2), 465

Interaction of CDs with Interleukin-2



Interleukin-2

Freee drying

Redissolution in buffer

Interleukin-2 aggregation

Citrate buffer, sucrose

0.5% HPBCD

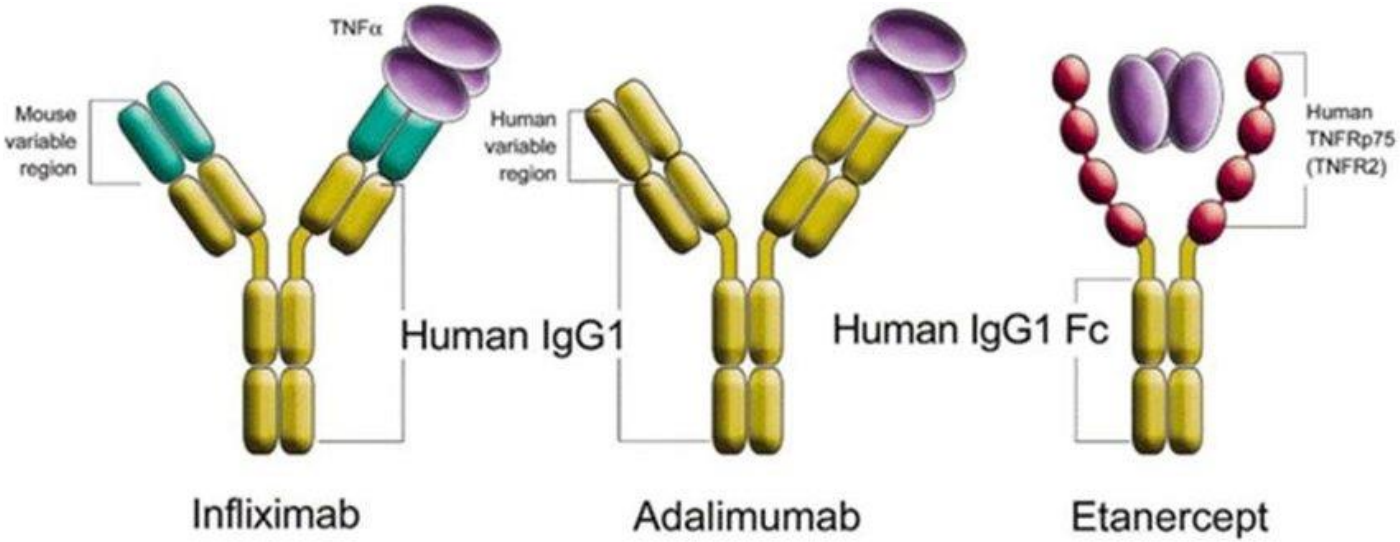
Safer than current excipients (e.g. Tween), no peroxide formation, corresponding immunogenicity, degradation.
Prevention of aggregation, delayed folding.
Less protein adsorption onto container surface.
Reduced/maintained viscosity, improved injectability.
Life-cycle management.

Stabilizer for Monoclonal Antibodies

Open Access Article

Polysorbates versus Hydroxypropyl Beta-Cyclodextrin (HPβCD): Comparative Study on Excipient Stability and Stabilization Benefits on Monoclonal Antibodies

by Hailong Zhang [1,*], Shiqi Hong [1], Sarah Si Kai Tan [1], Tao Peng [1], Lucas Yuan Hao Goh [1], Kwan Hang Lam [1], Keat Theng Chow [1] and Rajeev Gokhale [2,*]



Physicochemical stability excipient

HPβCDs: stable under heat, autoclavation, light and oxidative stress. Chemical structure unchanged.

Polysorbates (PS): degrade under heat-stress and autoclavation severely decompose upon light irradiation and significantly hydrolyse and oxidize.

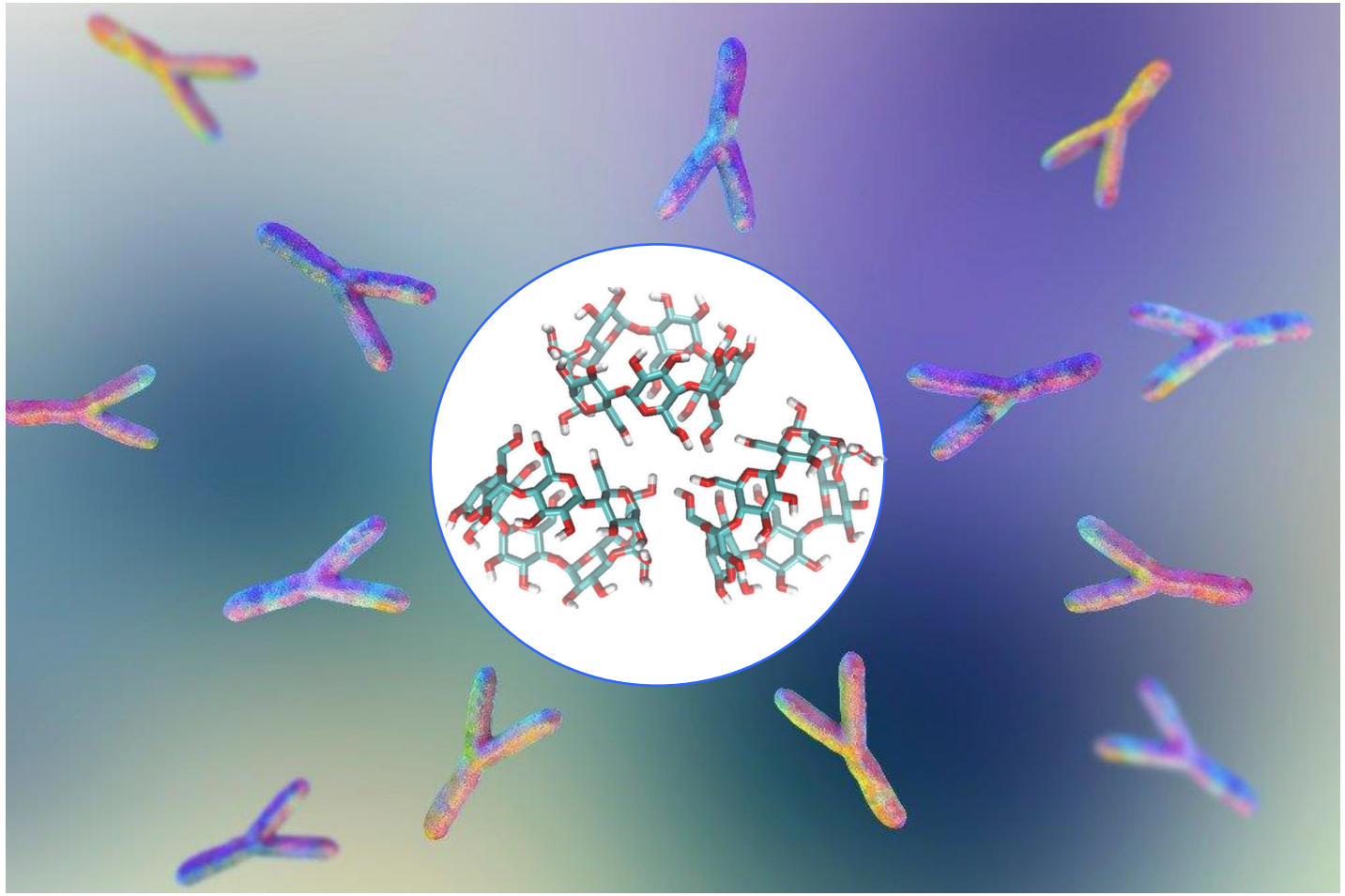
Physicochemical stability of monoclonal antibodies

HPβCD formulations: decrease in protein aggregation, superior monomer and total protein recovery compared to PS-containing formulations.

HPβCD formulations: reduce both agitation and thermal stress-induced protein aggregation and prevents subvisible particle formation compared to PS.

Molecules 2022, 27(19), 6497

Monoclonal Antibody for Detection of CDs



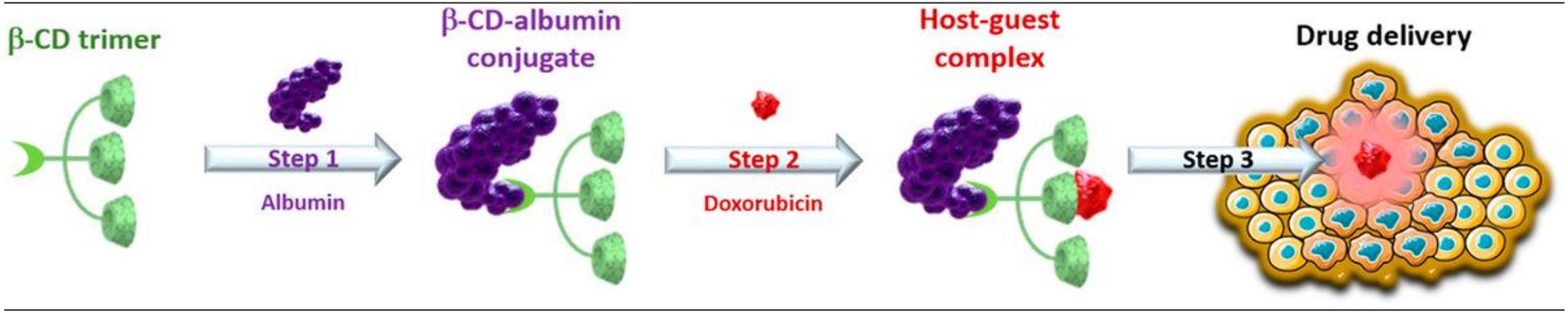
The monoclonal antibody to BCD was generated by using a conjugate of glucosaminylmaltosyl-BCD and bovine serum albumin as an antigen.

The monoclonal antibody was IgM/κ and reacted with β-CD with high specificity. The epitope recognized seemed to be located on the secondary side of the β-CD

The immunoassay was useful to determine BCD in biological fluids such as human plasma and urine.

Koji Ikura et. Al., Cytotechnology 40: 23–29, 2002

Monoclonal Antibody-CD conjugates



β-cyclodextrin trimer binds to circulating albumin to form the corresponding bioconjugate in the bloodstream. This latter can then entrap doxorubicin following its i.v. administration via the formation of a host–guest inclusion complex and deliver the drug in tumors.

This way the β-cyclodextrin trimer improved the therapeutic efficacy of doxorubicin in C57BL/6 mice associated with an increased deposition of doxorubicin in malignant tissues when used in combination with the β-cyclodextrin trimer compared to the administration of the drug alone.

Sébastien Papot et al., Bioconjugate Chem. 2022, 33, 6, 1138–1144

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For any questions:

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