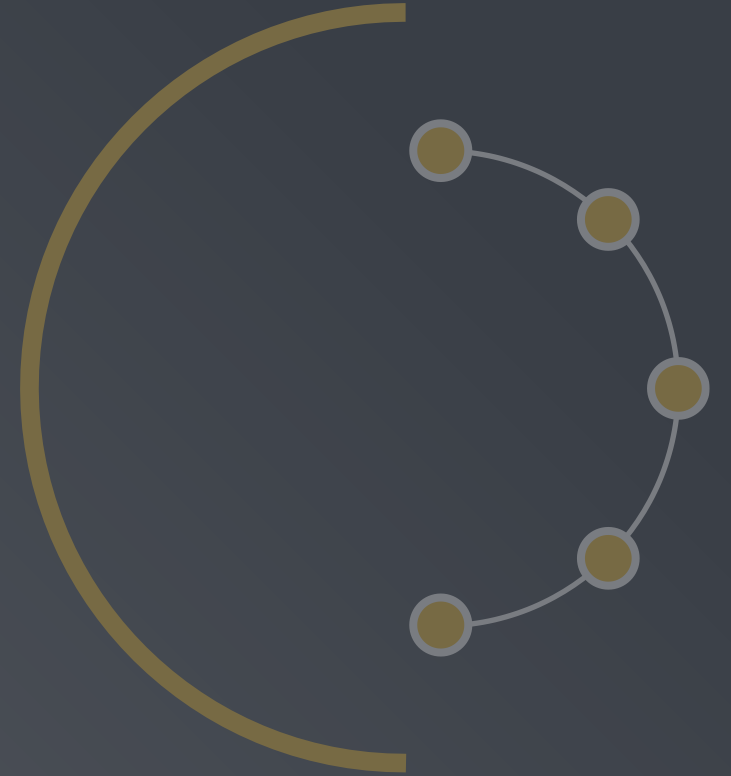


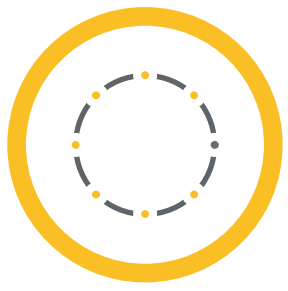


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Cyclodextrins

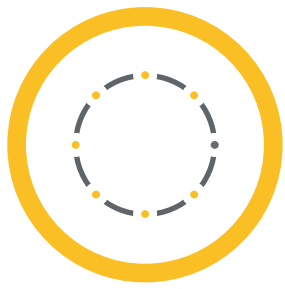
Uses in Covid-19



Outline

Cyclodextrins in the 1st, 2nd and 3rd lines of antiviral combat

- How to avoid COVID infection with the help of CDs?
 - Protective gears
 - Topical liquids
 - Vaccines
- What are the options if we need to cope with the infection?
 - Cyclodextrin-based formulations
 - Cyclodextrins as active ingredients



Prevention - Protective gears

HeiQ Viroblock® NPJ03 facemask containing silver nanoparticles and methyl-beta-cyclodextrin

Cidaltex® - cyclodextrin polymers fixed on fibers



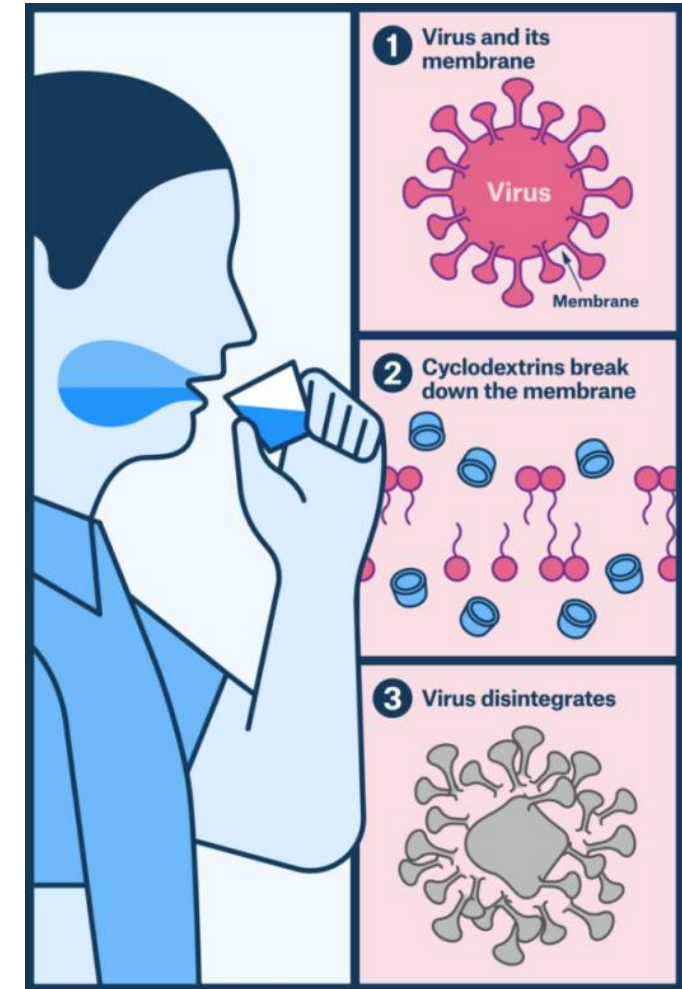
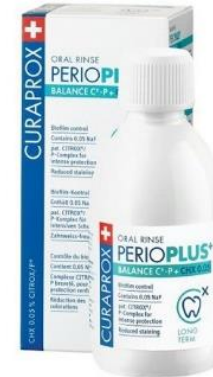
-  FILTRATION CAPABILITIES OF FFP2 GRADE MASKS
-  MICROBIAL CLEANLINESS: MEDICAL-GRADE
-  NO SIDE EFFECTS TO THE BODY
-  DECONTAMINANT REMAINS FIXATED TO INTERNAL MASK FIBERS
-  SOFT FABRIC: NON-ABRASIVE AND SAFE TO THE SKIN
-  EXCELLENT BREATHABILITY PERFORMANCE

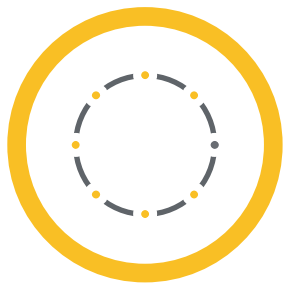


Prevention - Sprays and rinses

Curaprox Perio Plus Regenerate® mouth-rinse from Switzerland containing BCD

- Therapy: mouthrinse with beta-cyclodextrin (0.1%) and citrox
- MOA: cholesterol sequestering (lipid rafts) → inhibition of viral entry, replication and virucidal activity
- Results: reduces the viral load in the mouth after a single rinse
- Development status: trial completed (176 participants), results not posted (NCT04352959)
- Clinical results: significant beneficial effect on reducing SARS-CoV-2 salivary viral load 4 h after the initial dose.
- For long-term (7 day) effect, the benefit appears limited compared with placebo
- 14.80 CHF



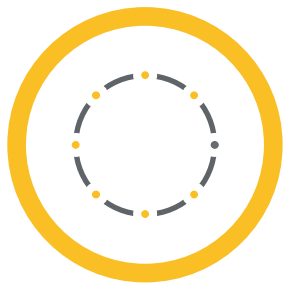


Prevention - Sprays and rinses

Endovir stop oral/nasal spray with ACD (Magi Euregio - WO2022079498A1)

- Therapy: alpha-cyclodextrin (0.2%) and hydroxytyrosol, oral spray
- MOA: sphingolipid and phospholipid sequestering (lipid rafts)
- Result: 50 volunteers did not become positive
- 149 healthy volunteers considered at higher risk of SARS-CoV-2 infection using nasal spray for 4 weeks
- None of the volunteers became positive to SARS-CoV-2
- Marketed in Italy (<https://www.endovir.it/>)





Prevention - Vaccines

J&J ad26.cov2.s: cyclodextrin as cryoprotectants

- The era of vaccines (from 2021) - changes in research focus
- EUA (FDA and EMA) in March 2021
- Janssen incorporated HPBCD into their Covid-19 vaccine
- HPBCD is used as a cryoprotectant
- MoA is unclear
- Uses as adjuvants in COVID vaccines - not yet
- Uses as DDS in mRNA vaccines - not yet



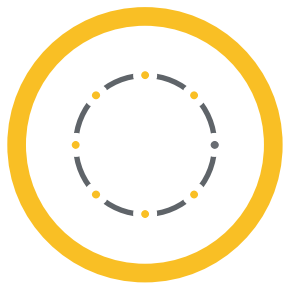


Treatment - CD-based formulations

Cyclodextrins used to formulate actives - a selection

- Paxlovid (without CD)
- NCE (Pfizer)
- HPBCD is a potent solubilizer of PF-07321332
- Intravenous (iv) doses for PF-07321332 were administered as a solution in 10% DMSO/30% PEG400/60% deionized water to rats
- 5% (v/v) PEG400:95% (v/v) of 23% HPBCD in aqueous sodium phosphate buffer pH = 6.0 was administered to the monkeys
- Still without CD

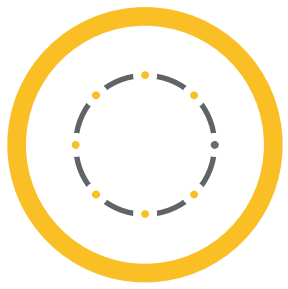




Treatment - CD-based formulations

Cyclodextrins used to formulate actives - a selection

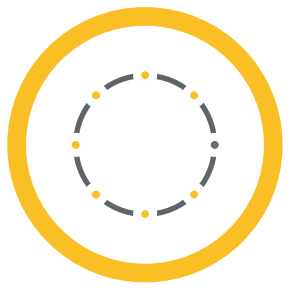
- Inhalable cyclodextrin-based formulation of a repurposed drug niclosamide (antihelminthic/vet)
- Bronchodilating effects also inhibits the release cytokines
- Antibacterial activity for pulmonary superinfections
- Positive commentary published in The Lancet
- Clinical phases II-III are still ahead



Treatment - CD-based formulations

Remdesivir

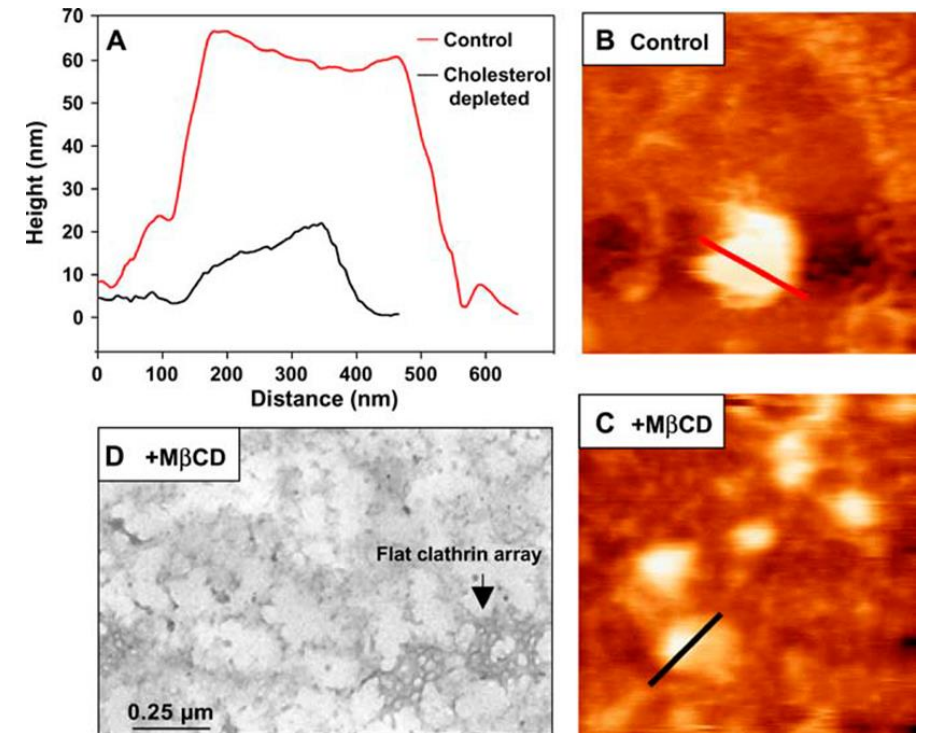
- 97% SBECD, 3% remdesivir
- FDA approval to treat Covid-19 (May/Oct, 2020)
- Only approved treatment in 2020
- WHO suggested against use (Nov, 2020)
- July, 2021 - summary concludes no mortality benefit
- Still in protocol in the developed markets
- Combination therapy with baricitinib (Eli Lilly)
- 24th best selling drug in 2021 globally (5.5+ B USD)
- January, 2022 - Veklury approved for non-hospitalized patients too + kids (12-) at high risk of disease progression
- April, 2022 - critical review on the role of remdesivir - depends on which one you read
- April, 2022 - approved in young patients (28 days of age and older)



Treatment - CDs as antivirals

Cyclodextrins - MoA and historical uses

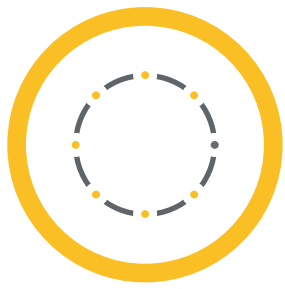
- CDs possess broad-spectrum antiviral activity
- Studies on HIV, herpes simplex, influenza, RSV and Zika viruses
- MoA
 - Inhibition of viral entry
 - Inhibition of viral replication
 - Cholesterol sequestering and virucidal activity
 - Autophagy induction
- Typically used CDs
 - Methyl-BCD
 - Sulfated CDs



Martin-Acebes et al 2016 Progress in Lipid Research | <https://doi.org/10.1016/j.plipres.2016.09.005>

Frankel et al 2006 Biophysical Journal | <https://doi.org/10.1529%2Fbiophysj.105.073692>

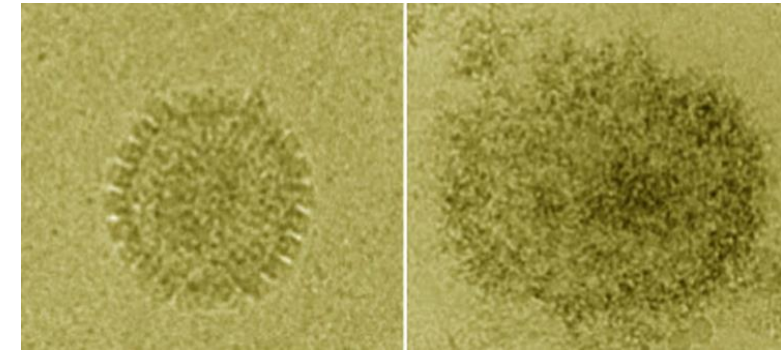
Fatmi, et al 2021 Current Drug Delivery | <http://dx.doi.org/10.2174/1567201817666200917124241>



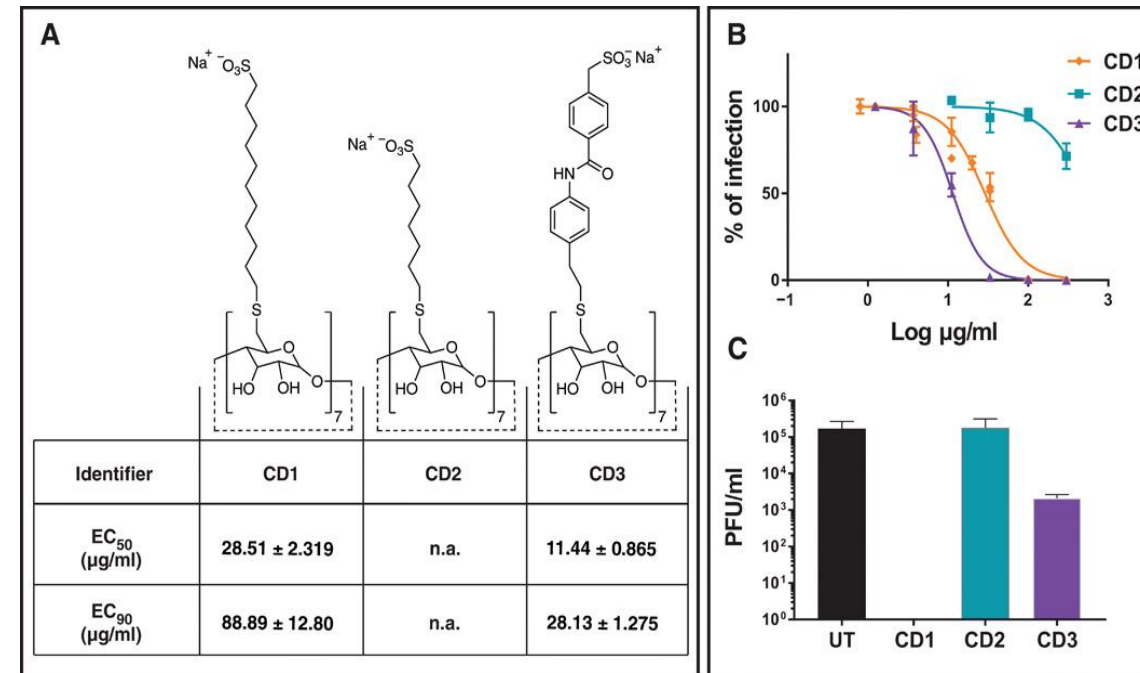
Treatment - CDs as antivirals

The best-timed paper in the topic

- Published 29th Jan 2020
- Evaluating modified, tailor-made CD against HSV-2
- Candidate proved to be active against several HS-dependent [heparan sulphate-dependent] viruses
- „exhibits a broad-spectrum virucidal, irreversible mechanism of action, presents a high barrier to viral resistance, and is biocompatible”
- High hopes for Covid, establishing Asterivir
- No news (public) about the company
- No news about activity against SARS-CoV2



Before / after CD
(HSV)





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