

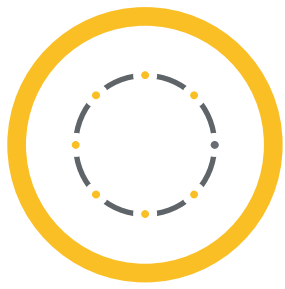


CARBOHYDE

SUGAR IS LIFE



Application of cyclodextrins in radiopharmaceuticals



Our Company

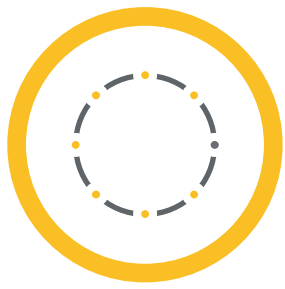
About CarboHyde

CarboHyde is a private preclinical pharma start-up, incorporated with the intention of developing carbohydrate-based APIs for different target indications and supporting other companies in this exciting journey.

We are a group of passionate carbohydrate-lovers who realized that there is a need for targeted industrial experience on advancing and broadening such innovative actives as the carbohydrate chemistry and analysis are probably the most challenging among all.

The company fosters several preclinical programs in various central nervous system (CNS) indications and other unmet medical needs while continuously working on exploring novel applications as well.

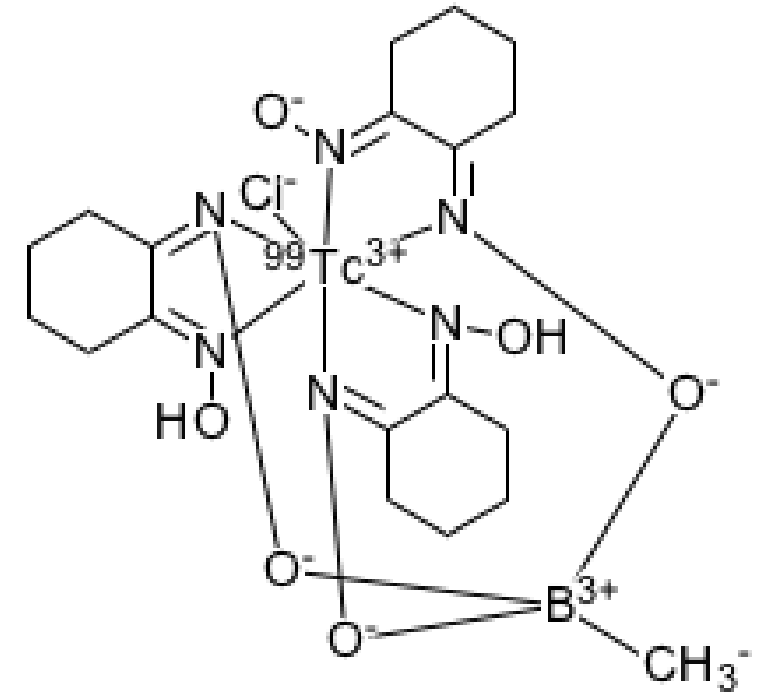




Applications in radiopharmaceutics

CardioTec i.v. solution

- Technetium Tc99m teboroxime solubilized by HPGCD
- Use - Myocardial Perfusion Imaging
- Developed by Bracco
- Approved in early 1990s by FDA
- Not widespread due to fast clearance



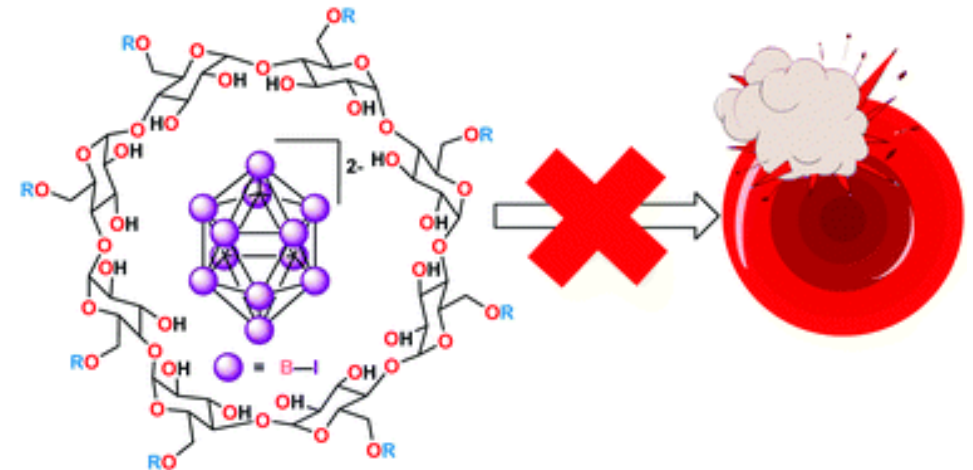
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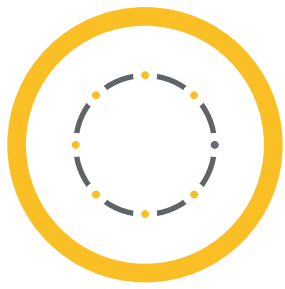


Applications in radiopharmaceutics

closo-dodecaiodododecaborate

- Use - $\text{Na}_2\text{B}_{12}\text{I}_{12}$ has many of the properties desired by an X-ray contrast agent but is lethal at the concentrations needed for medical imaging
- Results - presence of <1 equiv. of 2-hydroxypropyl- γ -cyclodextrin (as a solubilizer) prevents hemolysis (prevent membrane penetration and superchaotropic effect)
- Developed by University of California
(<https://doi.org/10.1039/D1CC06348K>)
- Status - academic research, cell studies





Applications in radiopharmaceuticals

18 F-labelled radiopharmaceuticals (primarily flurpiridaz)

- Use - the radio-labelled compound is stabilized by ascorbic acid + cyclodextrin (particularly HPBCD)
- Results - use of cyclodextrin as co-stabilizer improves the physical and radiochemical stability of a radiopharmaceutical compared to using a conventional stabilizer, compatible with plastic contact materials and can be a solubilizer as well.
- Developed by GE Healthcare (WO2021078814A1)
- Status - national phases
- Similar invention by others (Mallinckrodt - US07/836,644, 1992)

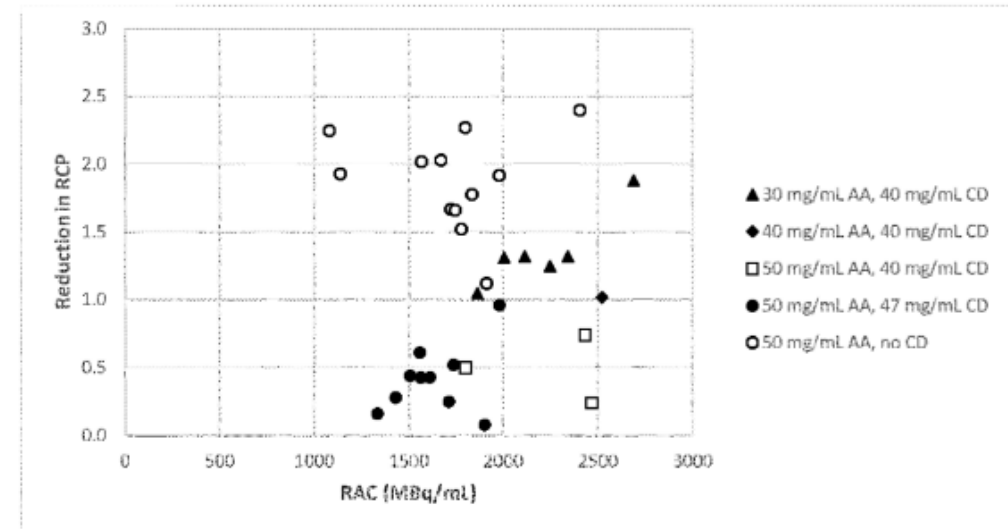
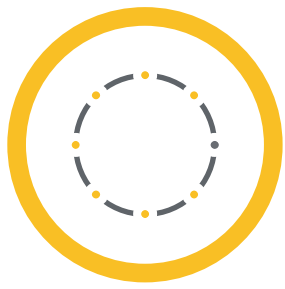
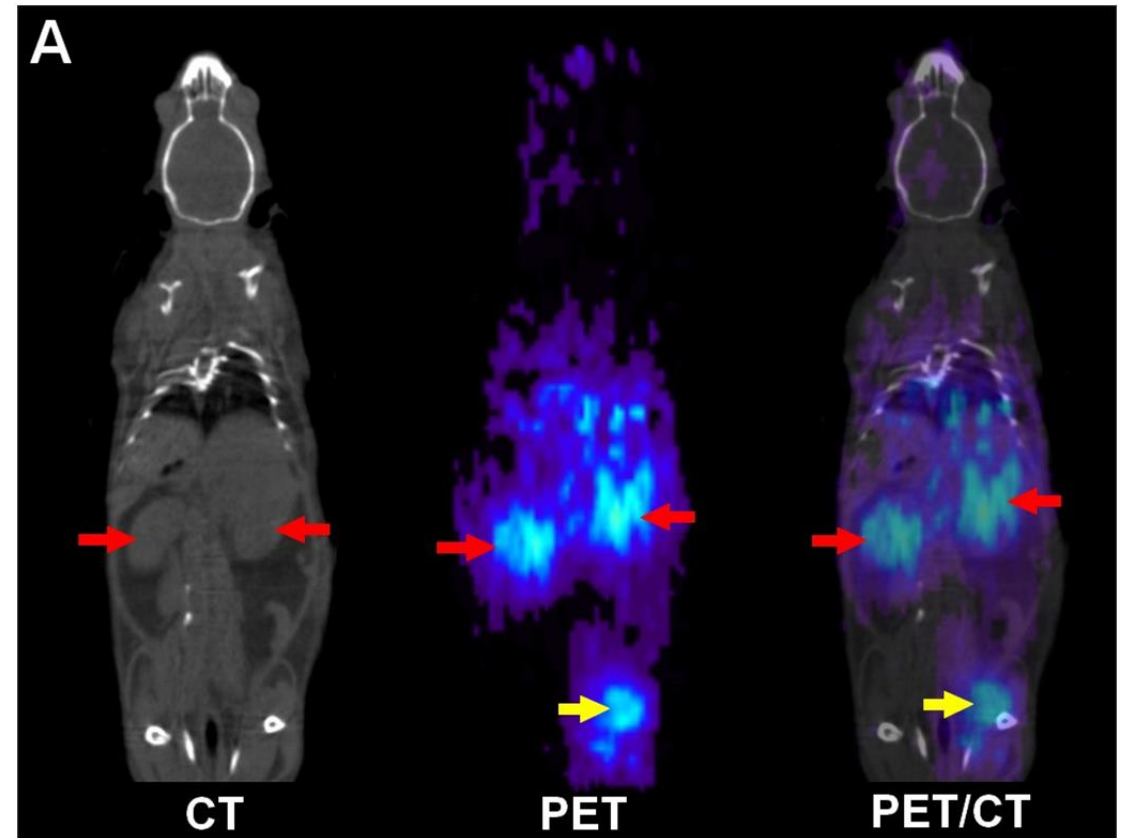
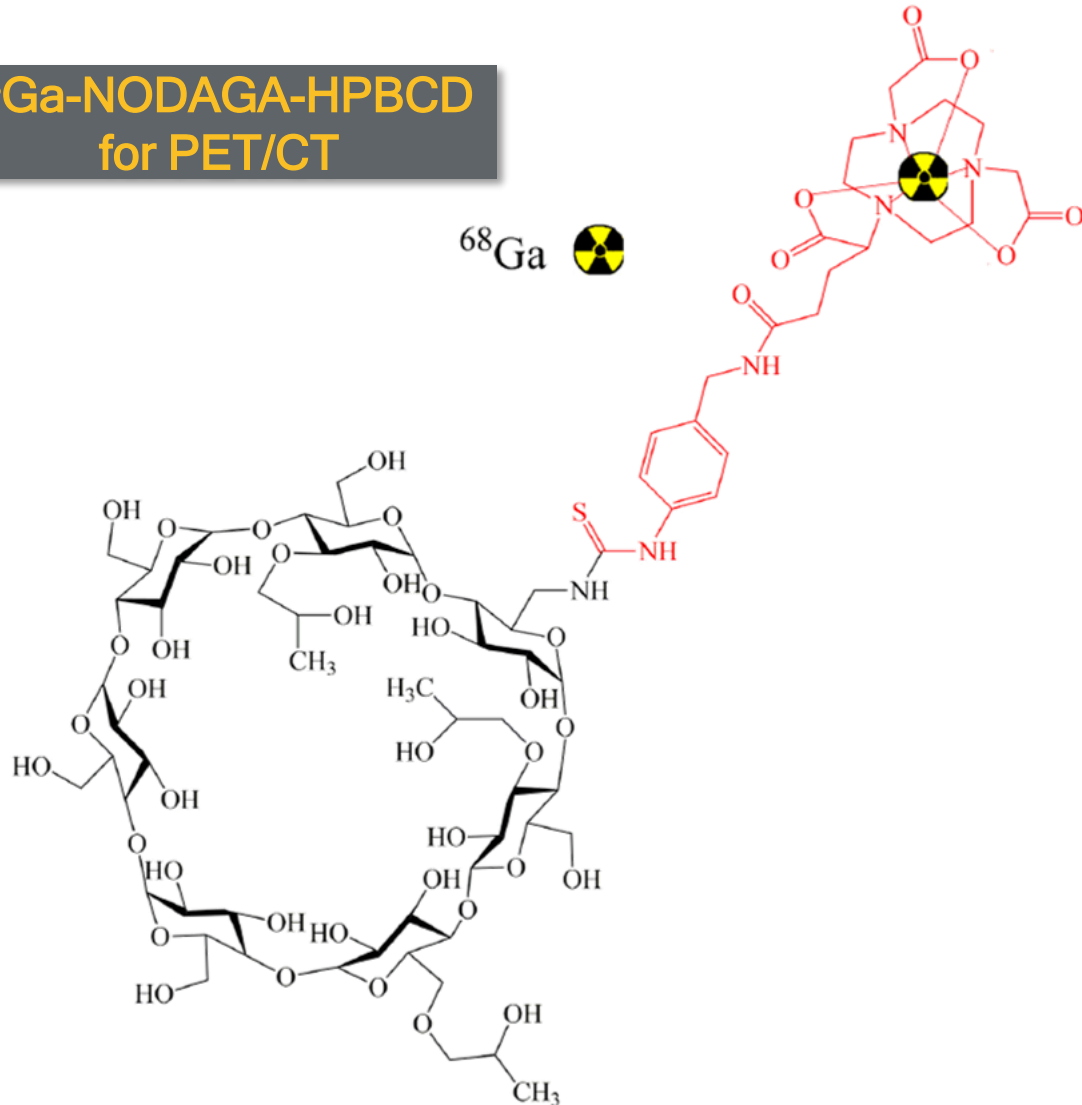


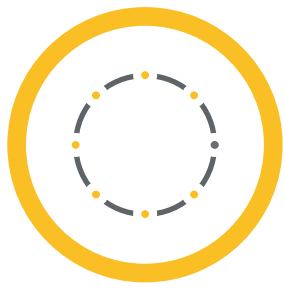
Figure 1



Applications in radiopharmaceuticals

**^{68}Ga -NODAGA-HPBCD
for PET/CT**

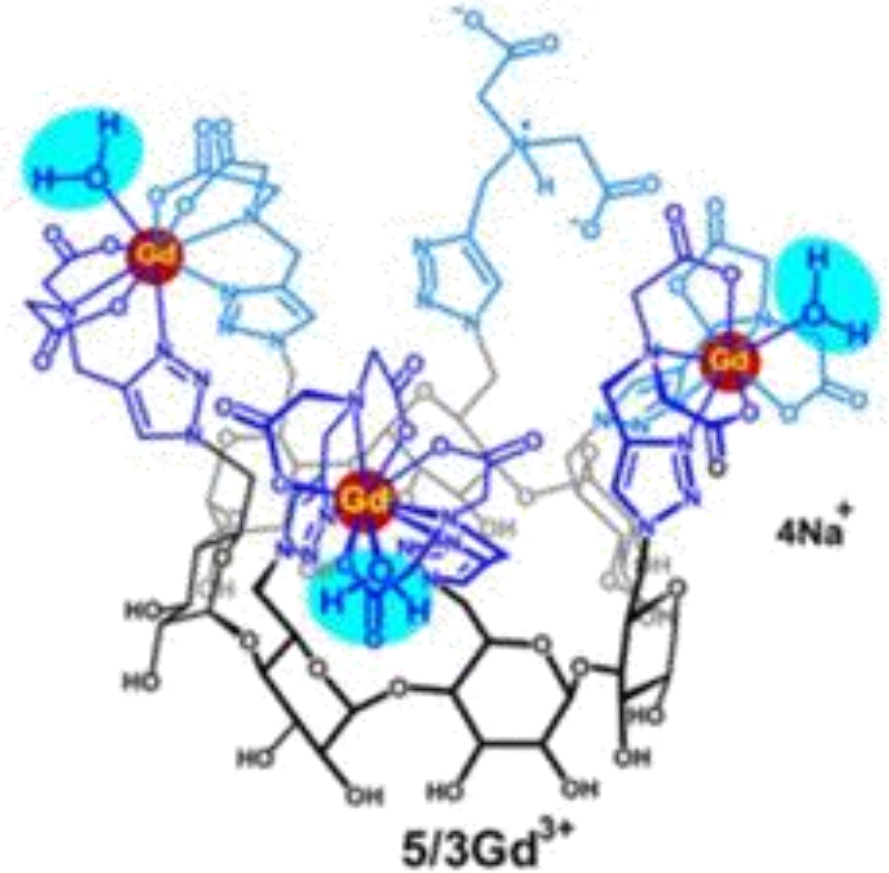




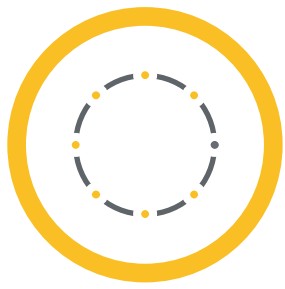
Applications in radiopharmaceutics

Improving contrast agents

- **Use:** complexation and delivery of Lanthanide Ions, mainly Gd and Y
- **Results:** stronger binding than DOTA, longer relaxation, high affinity; show significantly better abilities to alter T1 relaxivities of coordinated water than DOTA-Gd(III) and also some of the synthetic CD probes reported in the literature
- **Developed by:** Univ Calgary, CNRS France
- **Status:** patent granted, planning animal studies



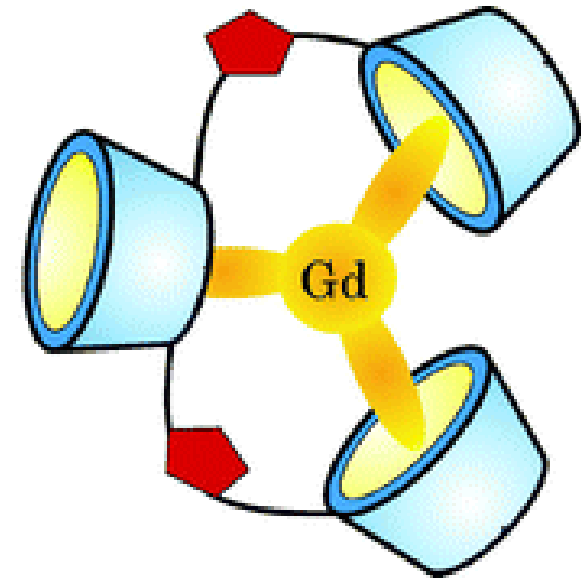
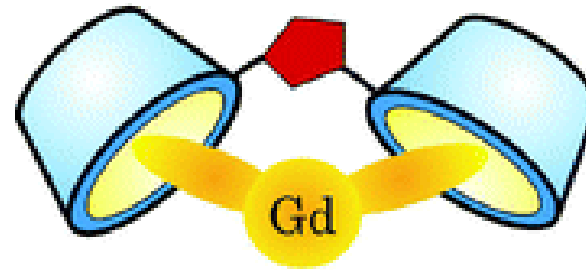
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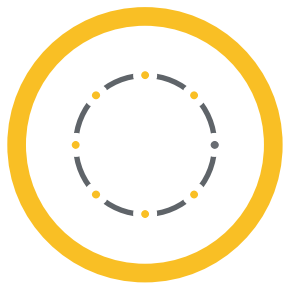
Applications in radiopharmaceutics

Improved CD chelators CD Dimers / Trimers

- **Use:** MRI agents
- **Results:** adducts with high selectivity, stability, relaxivity
- **Developed by:** University of Turin
- **Status:** Research



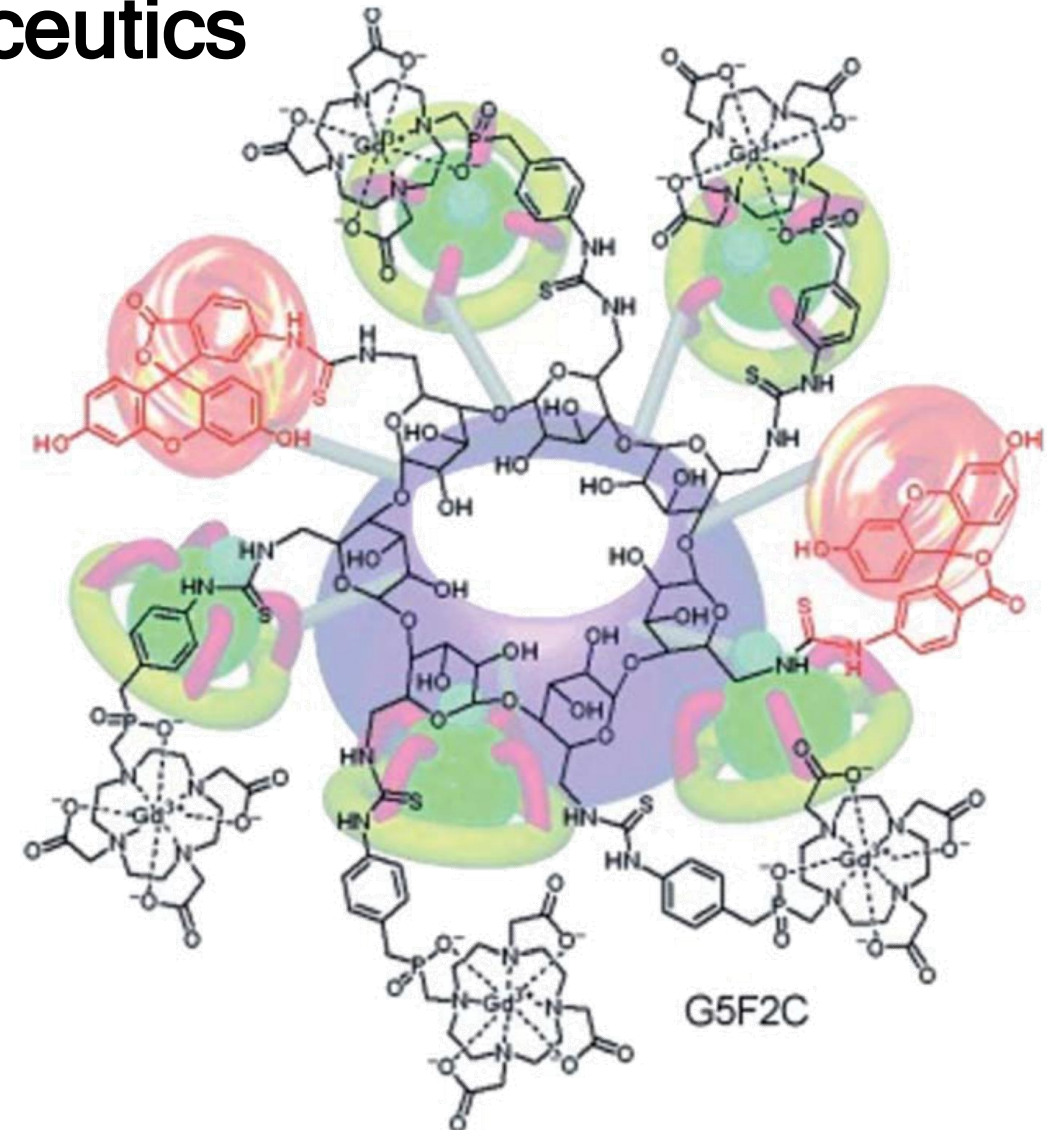
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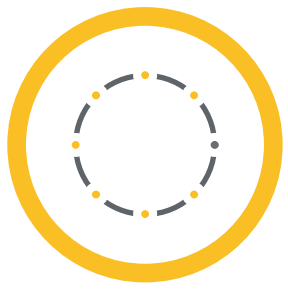
Applications in radiopharmaceuticals

Bimodal probes

- **Use:** simultaneous MRI and fluorescence properties.
- **Results:** DOTA and fluorescein immobilized on the same scaffold. Efficient probe to study in vitro pancreatic islets and rat mesenchymal stem cells. Low toxicity, good internalization observed by fluorescence and MRI phantom experiments. Quantitative fluorescent measurement proved that the contrast agent stayed in the intracellular space even after 24 hours allowing future in vivo imaging applications
- **Developed by:** Kotek
- **Status:** patent granted

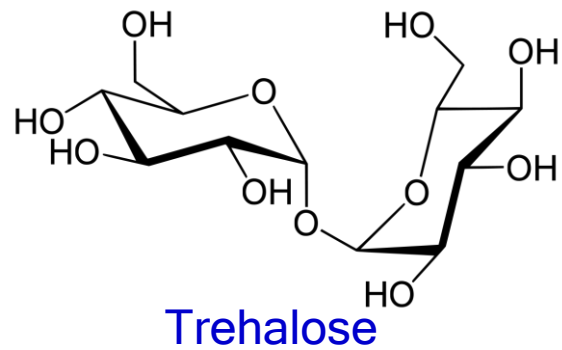
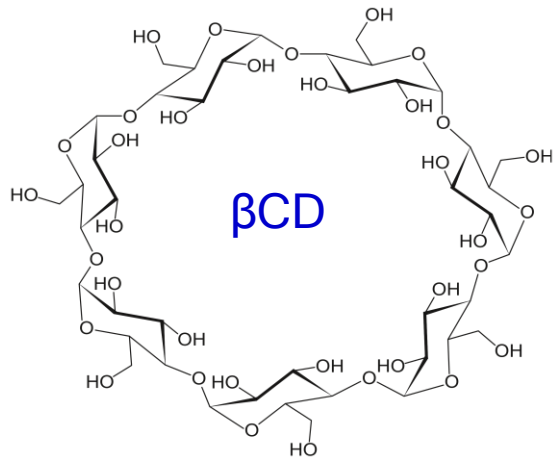


Structure



Carbohydrate Scaffolds for Multimodal Probes!

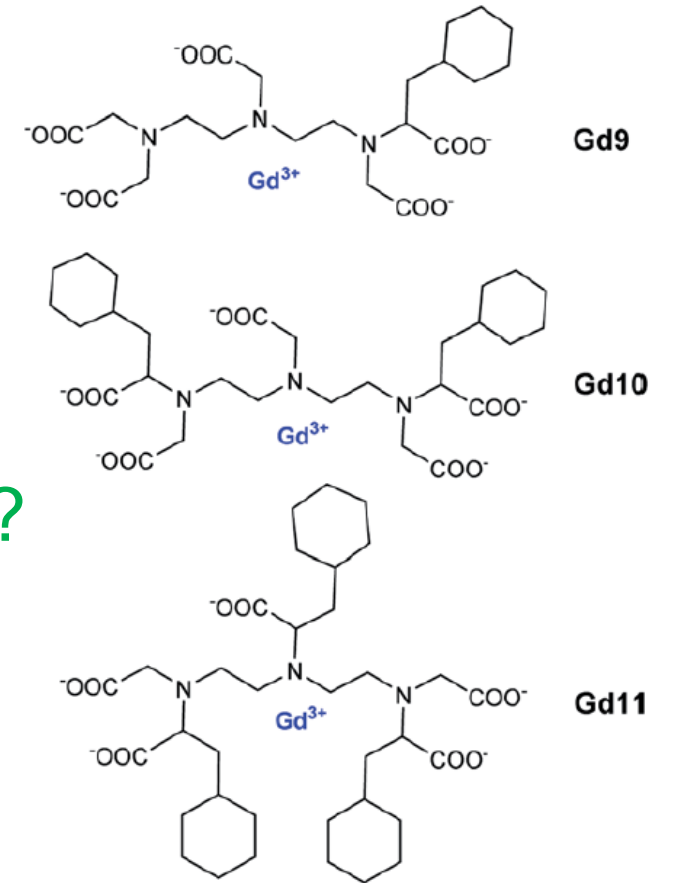
Carbohydrates



PET tracers

^{18}F
 ^{68}Ga
 ^{64}Cu
 ^{111}In
 $^{99\text{m}}\text{Tc}$

MRI contrast agents



Can we combine them all in one?