3PC-013

RADIOPHARMACEUTICAL SINGLE-VIAL COLD KIT FORMULATION OF FAPI-04, AN EXPERIMENTAL VECTOR FOR GALLIUM-68 PET IMAGING IN ONCOLOGY

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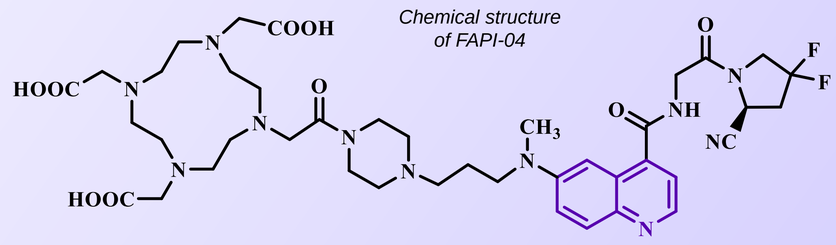
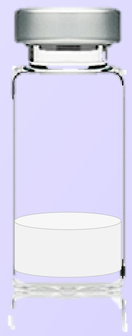
WHAT WAS DONE

- **FAPI-04** radiolabeled with **gallium-68** is a promising quinoline-based, DOTA-conjugated molecule for **tumor microenvironment** PET imaging.[1]
- To date, **[^{68}Ga]Ga-FAPI-04** is considered an **experimental radiopharmaceutical**, with a tedious and intricate radiolabeling process.[2]
- The formulation of FAPI-04 in a **single-vial cold kit (SVCK)**[3] was therefore studied.

Chemical structure of FAPI-04





Single vial cold kit = lyophilisate containing:

- *Filler agent*
- *FAPI-04*
- *Buffer*
- *Anti-radiolysis compound*

Ready for direct ^{68}Ga radiolabeling

WHY IT WAS DONE

- The development of a SVCK formulation of FAPI-04 would **simplify the preparation** of [^{68}Ga]Ga-FAPI-04.

HOW IT WAS DONE

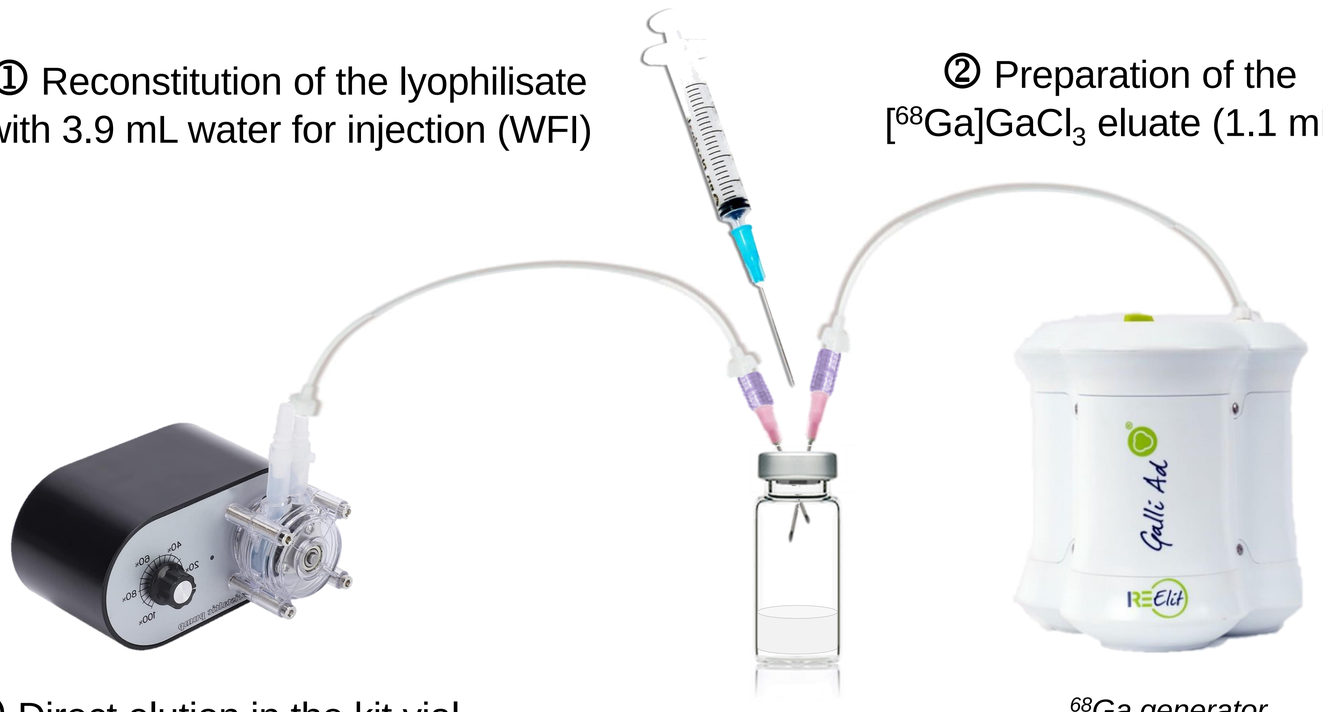
- **Various parameters** (type and amount) involved in the formulation of FAPI-04 as a SVCK were investigated: **filler** (bulk agent), **buffer**, **anti-radiolysis compound**, **FAPI-04 quantity**.
- Optimal conditions for successful radiolabeling of [^{68}Ga]Ga-FAPI-04 were identified.

WHAT WAS ACHIEVED

1) Design of the radiolabeling protocol

① Reconstitution of the lyophilisate with 3.9 mL water for injection (WFI)

② Preparation of the [^{68}Ga]$GaCl_3$ eluate (1.1 mL)



③ Direct elution in the kit vial using a peristaltic pump

Kit vial containing the filler agent, buffer and FAPI-04 lyophilisate

^{68}Ga generator (GALLIAD®, IRE Elit)

④ Heating step, 97°C, 10 min

⑤ Quality controls: TLC, HPLC

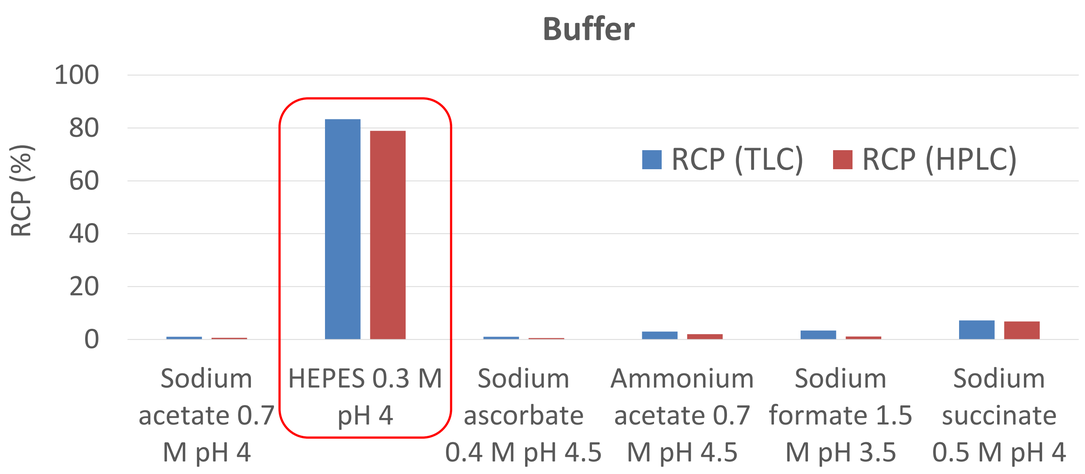
2) Filler selection

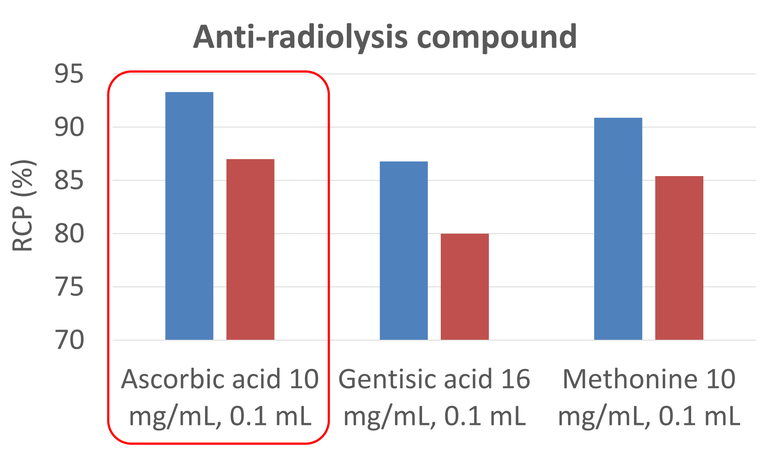
- 5 fillers commonly used were tested
- Each vial also contained 280 mg HEPES buffer and 30 µg FAPI-04 for test ^{68}Ga radiolabeling

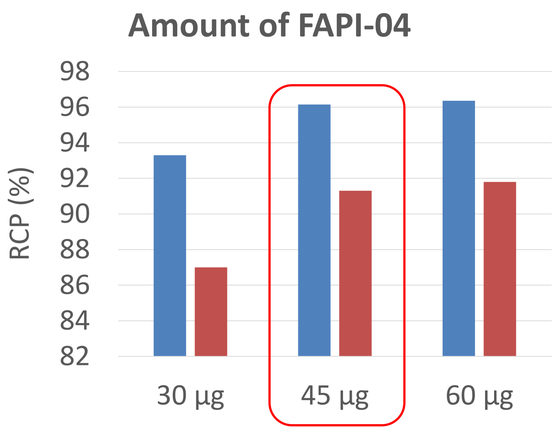
Filler	Amount of filler (mg)	Appearance after freeze-drying	Reconstitution (3.9 mL WFI)	Test radiolabeling (RCP measured by TLC)
Trehalose	98	Oily, amorphous	5 min shaking	-
	195		5 min shaking	-
	390		5 min shaking	pH = 3.9 ; RCP = 93.2%
	780		Not soluble	-
	1560	Amorphous	Not soluble	-
Sorbitol	98	Amorphous	5 min shaking	-
	195		5 min shaking	-
	390		5 min shaking	pH = 3.9 ; RCP = 88.7%
	780		Not soluble	-
	1560		Not soluble	-
Glycine	98	Crystalline	15 sec shaking	pH = 3.9 ; RCP = 4.75%
	195		15 sec shaking	-
	390		15 sec shaking	-
	780		Not soluble	-
	1560		Not soluble	-
Mannitol	**50**	**Neat**	**15 sec shaking**	**pH = 3.8 ; RCP = 89.5%**
	98		15 sec shaking	-
	195		5 min shaking	-
	390		5 min shaking	-
	780		Not soluble	-
	1560		Not soluble	-
Sucrose	98	Bubbly, amorphous	15 sec shaking	pH = 3.8 ; RCP = 71.4%
	195		15 sec shaking	-
	390		15 sec shaking	-
	780		Not soluble	-
	1560		Not soluble	-

➢ **50 mg mannitol** was retained for further assays

3) Buffer, anti-radiolysis compound and amount of vector selection







WHAT IS NEXT

- After careful selection of the ingredients involved in the SVCK formulation of FAPI-04, optimal conditions involved **50 mg mannitol**, **280 mg HEPES buffer**, **2.6 mg ascorbic acid** and **45 µg vector** ⇨ PRC >96% in TLC, >91% in HPLC.
- HEPES considered as an impurity by Ph. Eur.[4] ⇨ A **terminal purification** with a **SPE cartridge** would allow HEPES residues < 50 µg/mL.

[1] T. Lindner *et al*., Development of quinoline-based theranostic ligands for the targeting of fibroblast activation protein. *J Nucl Med* **2018**, *59*, 1415–1422. **[2]** C. Da Pieve *et al*., New fully automated preparation of high apparent molar activity ^{68}Ga-FAPI-46 on a Trasis AiO platform. *Molecules* **2022**, *27*, 675. **[3]** N. Lepareur. Cold Kit Labeling: The Future of ^{68}Ga Radiopharmaceuticals? *Front Med* **2022**, *9*, 812050. [4] European Directorate for the Quality of Medicines & Healthcare (EDQM), **2022**. Gallium (^{68}Ga) edotreotide injection. *European Pharmacopoeia 11.0*, 2482, 1274–1276.