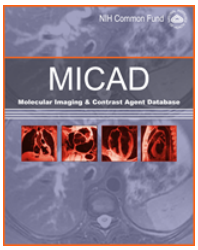
U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Chopra A. 2-Deoxy-2-[18F]fluorosorbitol . 2008 Jan 14 [Updated 2008 Feb 6]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/



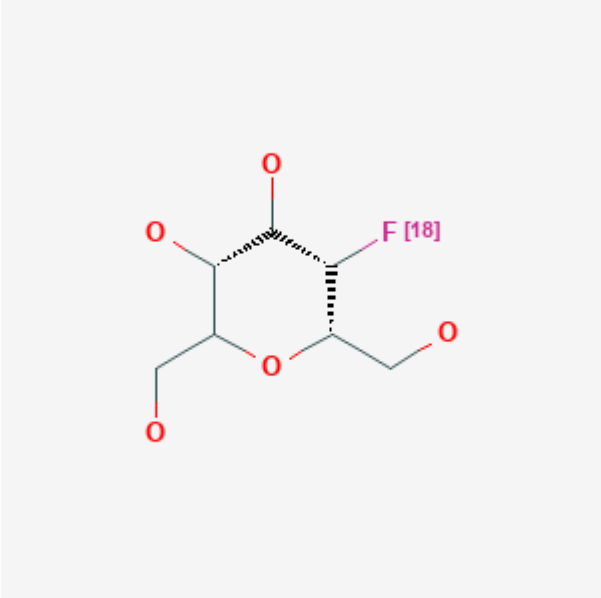
2-Deoxy-2-[18F]fluorosorbitol

[18F]FDS

Arvind Chopra, PhD[1]

Created: January 14, 2008; Updated: February 6, 2008.

Chemical name:	2-Deoxy-2-[18F]fluorosorbitol
Abbreviated name:	[18F]FDS
Synonym:	
Agent Category:	Compound
Target:	Brain tumors and inflammation
Target Category:	Cellular accumulation after phosphorylation
Method of detection:	Positron emission tomography (PET)
Source of signal:	18F
Activation:	Yes
Studies:	• *In vitro* • Rodents



Click on the above structure for additional information in PubChem.

Background

[PubMed]

The glucose analog 2-deoxy-2-[18F]fluoro-D-glucose ([18F]FDG) is a recommended radiochemical that is often used for the detection and posttherapy monitoring of commonly occurring cancers such as Hodgkin's disease and non-Hodgkin's lymphoma (1). The 18F-labeled FDG is transported into the cell by the glucose transporters, is phosphorylated, and remains trapped in the cell without further metabolism. So, this glucose analog can be used to monitor the uptake of glucose by the cells, but it can not be used to track glucose metabolism within the cell (2). Neoplastic cells are highly proliferative and have a high rate of glucose metabolism compared to normal tissue, and they tend to accumulate [18F]FDG, which can be used to detect and monitor various cancerous lesions by positron emission tomography (PET) (3, 4). In addition, glucose is the main source of energy for the

Author Affiliation: 1 National Center for Biotechnology Information, NLM, NIH, Bethesda, MD 20878; Email: micad@ncbi.nlm.nih.gov.

brain because this tissue has a very high concentration of neurons that can not metabolize free fatty acids (5). However, because [^{18}F]FDG produces high background interference in the brain, it is difficult to detect cancerous lesions in the brain tissue with this radiochemical (6).

Li et al. have evaluated the use of 2-deoxy-2-[^{18}F]fluorosorbitol ([^{18}F]FDS) for the detection of lesions that are not easily detected with [^{18}F]FDG, particularly in the brain (6). This was based on the fact that FDS is structurally similar to glucose, does not use the glucose transport system for entry into cells, probably is not metabolized in the brain, and can be synthesized easily by the reduction of FDG (7). This chapter describes the *in vitro* and *in vivo* imaging studies carried out with [^{18}F]FDS.

Synthesis

[PubMed]

The synthesis of [^{18}F]FDS was described by Li et al. (6). Briefly, sodium borohydride was added to a solution of [^{18}F]FDG in saline. The mixture was stirred at 35°C for 15 min. The reaction was quenched (the investigators did not describe how the reaction was quenched), and the pH was adjusted to 7.4. The mixture was subsequently filtered through an Alumina-N Sep-Pak cartridge, and the filtrate was analyzed by radio thin-layer chromatography. Using acetonitrile and water as the eluent for thin-layer chromatography, the Rf values for [^{18}F]FDS and [^{18}F]FDG were 0.33 and 0.54, respectively. The total time required for the synthesis was ~30 min with a yield (decay-corrected) of 81 ± 4%. Based on [^{18}F]FDG, the specific activity of [^{18}F]FDS was reported to be 100–200 TBq/mmol (270–540 Ci/mmol). The investigators did not report the stability of the labeled product (6).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The uptake and efflux of [^{18}F]FDS and [^{18}F]FDG were compared with U87MG cells, a glioblastoma-astrocytoma cell line (6). To determine the uptake of [^{18}F]FDS and [^{18}F]FDG, the cells were respectively exposed to the radiochemicals for 10–180 min in glucose-free medium, and the cells were lysed after washing to determine the accumulation of radioactivity. For the efflux study, the cells were respectively exposed to the radiochemicals for 180 min as described above and then washed to remove the labeled compounds from the growth medium. The cells were then recultured in glucose-free medium for 15–180 min, washed with the same medium, and lysed to determine the accumulated radioactivity. Approximately 40% of the total [^{18}F]FDG was taken up by the cells, whereas only ~0.1% of the total [^{18}F]FDS accumulated in the cells. A rapid efflux of [^{18}F]FDS from the cells, which reached equilibrium in ~10 min, was observed. However, with [^{18}F]FDG the efflux was gradual and did not reach equilibrium even after 180 min. Although [^{18}F]FDG uptake by the U87MG cells was influenced significantly by the presence of glucose (it decreased the uptake) or insulin (it increased the uptake), no such effect was observed with either agent on the [^{18}F]FDS uptake by these cells (6).

Animal Studies

Rodents

[PubMed]

PET studies were performed with [^{18}F]FDS and [^{18}F]FDG in a murine model of mice either bearing xenograft tumors or after the induction of inflammation (6). To generate the xenograft tumors, U87MG cells were injected either subcutaneously in the front legs or intracranially in athymic mice (n = 3 mice per time point), and the tumors were allowed to engraft for 3–4 or 6–7 weeks, respectively. In another study, glioma tumors were

generated with intracranial injections of highly tumorogenic GL-26 cells (originally from the National Cancer Institute, Bethesda, Maryland) in syngenic C57BL/6 mice (n = 3 mice per time point) as described above; the mice were subjected to PET imaging 25–30 days after tumor inoculation. The mice were injected with radioactive FDG or FDS, and the PET images were obtained at different time points for the tumor and the major organs (liver, heart muscle, intestines, and kidneys). The U87MG tumor uptake was calculated to be 2.43% of the injected dose/gram tissue (% ID/g) at 15 min after injection, and the tumor/major organ ratios were also determined. From these ratios it was evident that [^{18}F]FDS was a suitable tracer to detect brain lesions because it had a tumor/brain ratio of up to 13.6 compared to ratio of 0.5–4.5 for the other organs. Compared to [^{18}F]FDS, the uptake of [^{18}F]FDG was high in both the U87MG tumors and the normal brain tissue (6). In the GL-26 model, a high uptake of [^{18}F]FDS (6.38% ID/g) was also observed in the tumors, which were clearly visible with this radiochemical. In comparison, [^{18}F]FDG was unable to distinguish between the neoplastic and normal tissue in the brain.

To induce inflammation, a solution of 12-O-tetradecanoyl-phorbol-13-acetate (TPA) in acetone was applied to the inner and outer surfaces of the right ears of three BALB/c mice (6). The untreated left ear served as the control for each animal. An edematous swelling was noted within 6 h of TPA application on the right ear, at which point the mice were subject to PET imaging after the administration of either [^{18}F]FDG or [^{18}F]FDS. Both labeled compounds showed a higher accumulation in the inflamed ear compared to the control ear. Although the accumulation of radioactivity was higher for [^{18}F]FDG compared to [^{18}F]FDS, with a right ear/left ear uptake ratio of 3.44 ± 0.25, the uptake ratio was higher (4.21 ± 1.33) for the labeled sorbitol derivative. The investigators reported that it was more difficult to detect the inflamed ear with [^{18}F]FDG *versus* [^{18}F]FDS using PET because of the interference of high brain activity (6).

Other Non-Primate Mammals

[PubMed]

No references are currently available.

Non-Human Primates

[PubMed]

No references are currently available.

Human Studies

[PubMed]

No references are currently available.

Supplemental Information

[Disclaimers]

NIH Support

Some studies reported in this chapter were funded by NCI grants R01 CA119053, R21 CA121842, R21 CA102123, ICMIC P50 CA114747, CCNE U54 CA119367, and R24 CA93862.

References

1. Juweid M.E. 18F-FDG PET as a Routine Test for Posttherapy Assessment of Hodgkin's Disease and Aggressive Non-Hodgkin's Lymphoma: Where Is the Evidence? J Nucl Med. 2008; **49** (1):9–12. PubMed PMID: 18077522.
2. Smith T.A. The rate-limiting step for tumor [18F]fluoro-2-deoxy-D-glucose (FDG) incorporation. Nucl Med Biol. 2001; **28** (1):1–4. PubMed PMID: 11182558.
3. Brahimi-Horn M.C., Pouyssegur J. Hypoxia in cancer cell metabolism and pH regulation. Essays Biochem. 2007; **43** :165–78. PubMed PMID: 17705800.
4. Chung, H.H., W.J. Kang, J.W. Kim, N.H. Park, Y.S. Song, J.K. Chung, and S.B. Kang, The clinical impact of [(18)F]FDG PET/CT for the management of recurrent endometrial cancer: correlation with clinical and histological findings. Eur J Nucl Med Mol Imaging, 2008.
5. Tomlinson D.R., Gardiner N.J. Glucose neurotoxicity. Nat Rev Neurosci. 2008; **9** (1):36–45. PubMed PMID: 18094705.
6. Li, Z.B., Z. Wu, Q. Cao, D.W. Dick, J.R. Tseng, S.S. Gambhir, and X. Chen, The Synthesis of (18)F-FDS and Its Potential Application in Molecular Imaging. Mol Imaging Biol, 2007.
7. Scott M.E., Viola R.E. The use of fluoro- and deoxy-substrate analogs to examine binding specificity and catalysis in the enzymes of the sorbitol pathway. Carbohydr Res. 1998; **313** (3-4):247–53. PubMed PMID: 10209867.