IICC 2021 International Industrial Chemistry Conference

Virtual

1st International Industrial Chemistry Conference

26-28th February 2021

Labeling and biodistribution of ^{99m}Tc- fludarabine for medical purposes

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Background and Objectives

Technetium-99m (^{99m}Tc) gamma emitters can be located using gamma cameras (planar imaging) or SPECT cameras (single photon emission computed tomography)(Yordanova et al., 2017) (Britton et al., 1990).Due to important physical and chemical properties of Techentium-99m i.e. 6 h half-life, gamma ray energy of 140 keV, easily available by ^{99}Mo/^{99m}Tc generator (1), minimal dose to patient, low cost, finest labeling yield even in harsh conditions and neutral pH etc makes it a best radioisotope for radiopharmaceutical applications (2-4)(It plays a vital role in diagnosis by labeling with various complexes like antibodies, peptides, steroids and some other small molecules). Some of the approaches are i.e. ^{99m}Tc labeled human serum albumin, ^{99m}Tc based human immunoglobulin, ^{99m}Tc-labeled red blood cells, ^{99m}Tc-methylene diphosphonate). Radiopharmaceuticals based on ^{99m}Tc have verified their significance with ideal physical characteristics ($t^{1/2}$ 6 h, 140 keV photon energy, no corpuscular radiation), high radiochemical purity, minimum labeling time (sometimes 10-30 min at room temperature), low cost, ^{99}Mo/^{99m}Tc generator commercial suitability and high biological efficacy .

Fludarabine phosphate has substantial activity againstlymphoid malignancies, particularly chronic lymphocytic leukemia (CLL) and low-grade non-Hodgkin'slymphoma (NHL).

The objective of this work was to demonstrate direct radiolabeling of fludarabine phosphate with ^{99m}Tc, quality control, biological evaluation and scintigraphic studies in mice.

Experimental and Results/Discussion

Labeling of fludarabine phosphate with technetium-99m was optimized by varying amount of precursor (fludarabine phosphate) 100-900 µg, stannous chloride 10-100 µg, incubation time 0-40 minutes and pH range of 3-11. These variations exhibit different radiolabeling efficiencies. The highest radiolabeling yield obtained by adding 500 µg of precursor, 30 µg of stannous and pH was adjusted to 8.5 by adding 0.1 N NaOH and 0.1 N HCl. At the end 3-4 mCi of technetium pertechnetate was added and allowed the compound to incubate for 30 minutes at room temperature 25±2° C.The reaction mixture volume was kept 1.25 ml each time. The radiochemical purity of ^{99m}Tc-Fludarabine was determined by instant thin layer chromatography and paper chromatography.

Biodistribution of ^{99m}Tc-Fludarabine

Biodistribution studies of Tc-Fludarabine were performed in normal (Balb-C) mice. Mice were injected intravenously in tail vain with an injection of 100 µl of ^{99m}Tc-Fludarabine having 0.4 mCi of technetium activity. The mice were sacrificed, weighed and biological distribution was evaluated in different organs of mice after anaesthesia with cotton swabs dipped in chloroform.

The in vivo study of ^{99m}Tc-Fludarabine in normal mice revealed that the large amount of drug was accumulated in kidneys (99.28±17.52) at 30 minutes post injection. ^{99m}Tc-Fludarabine illustrated a very rapid blood clearance and excreted through renal system. The accumulation of labeled compound was low in liver at both time points. The activity observed at 1 hour post injection showed uptake in kidney and intestine and then in liver i.e. 54.76±24.60, 22.52±16.00 and 13.28±5.29 respectively.

Conclusion

It showed sufficient binding affinity in vitro and the radiolabeling efficiency remained quite stable and consistent till 4 hours. In vivo biodistribution studies were carried out injecting 100 µl of ^{99m}Tc-Fludarabine (0.4 mCi) in tail vain of normal mice (n=2) which expresses highest uptake of the radioactivity in kidneys (54.76±24.60) and intestine (22.52±16.00) while the liver uptake (13.28±5.29) was low.

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