

ABSTRACT

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Title of Thesis: Study of interspecies differences in plasma protein binding of ^{18}F -labeled radiopharmaceuticals

In this thesis, the binding ability of three radiopharmaceuticals containing radionuclide ^{18}F to the plasma proteins was examined in bovine, pig, human and rat plasma, and the interspecies comparison was performed. Examined radiopharmaceuticals included ^{18}F -FDG, ^{18}F -fluorocholine and ^{18}F -thymidine. The two main methods used are equilibrium dialysis and ultrafiltration. These methods are based on separation of free ligand from the linked component. During the separation, semi-permeable membrane and special filters (AMICON and VIVASPIN) were used for equilibrium dialysis and ultrafiltration, respectively. Free fraction of drugs is considered to be an important parameter for the availability of the drug distribution into the tissues and cells, interaction with receptors, excretion and metabolism. All experiments were carried out at the physiological temperature of 37°C .

Obtained results indicate low plasma protein binding of the three radiopharmaceuticals in all studied species, which suggests that pharmacokinetics of ^{18}F -FDG, ^{18}F -fluorocholine and ^{18}F -thymidine would not significantly influence the plasma protein binding. The radiopharmaceutical with the highest ability of plasma protein binding was ^{18}F -thymidine, which reached $25.10 \pm 1.34\%$ in rat plasma sample (using ultrafiltration with filter VIVASPIN). However, this value is not generally considered as high. ^{18}F -FDG did not show the ability to bind to plasma proteins; free fraction was nearly 100 % in all species plasma samples, using either method.

In general, higher values of free fraction were measured with equilibrium dialysis approach when compared to ultrafiltration. However, no difference was found between filters AMICON and VIVASPIN. From the perspective of interspecies comparison, no difference in binding of studied radiopharmaceuticals to the plasma proteins in the four kinds of serum was found.

Key words

Radiopharmaceuticals, plasma proteins, equilibrium dialysis, ultrafiltration, ^{18}F -FDG, ^{18}F - fluorocholine, ^{18}F - thymidine, plasma binding ability