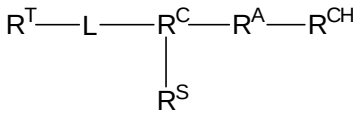
e.g. for radiodiagnosis or in the context of RGS or for radiotherapeutic applications. The optimized ligand structure was conceptually designed and comprises a common PSMA-inhibitor motif derived from highly potent radiohybrid PSMA diagnostics [23] and therapeutics [24], a tetraamine chelator for reliable complexation of a suitable radioisotope, such as technetium-99m, and a variable amino acid for the modulation of pharmacokinetic properties of the peptide. Such modifications have brought forth interesting PSMA radioligands for manifold applications [25-27].

Summary

In one aspect, the present disclosure refers to a compound of formula (1) or a salt thereof:



(1)

wherein

R^T is a PSMA binding group;

L is a linking group;

R^C is a trivalent coupling group;

R^S is a silicon-containing moiety of the formula -C(O)-R^{S3}-Si$R^{S1}R^{S2}$OH, wherein R^{S1} and R^{S2} are independently selected from C3-C10 alkyl, and R^{S3} is a group comprising a 6 membered aromatic ring;

R^A is an amino acid residue; and

R^{CH} is selected from

(i) a branched-chain, acyclic chelating moiety having 4 amino groups, and

(ii) a chelate moiety, wherein a radioisotope selected from ^{99m}Tc, ^{94m}Tc, ^{186}Re and ^{188}Re is chelated by the branched-chain, acyclic chelating moiety having 4 amino groups.

In one aspect, the present disclosure refers to the compound or salt as disclosed herein for use in diagnosing in *vivo* a disease which is associated with the overexpression of PSMA, wherein the disease is preferably cancer and more preferably prostate cancer and diagnosing preferably involves nuclear medicine tomography, more preferably single-photon emission computed tomography (SPECT).

In one aspect, the present disclosure refers to the compound or salt as disclosed herein for use in identifying *in vivo* diseased tissue which is associated with the overexpression of PSMA, wherein the diseased tissue is preferably cancer tissue and more preferably prostate cancer tissue.

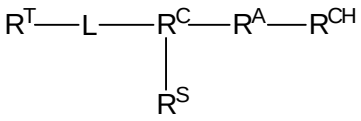
In one aspect, the present disclosure refers to *ex vivo* or *in vitro* use of the compound or salt as disclosed herein for identifying a tissue or cell which is associated with the overexpression of PSMA, wherein the tissue or cell is preferably a cancer tissue or cell and more preferably a prostate cancer tissue or cell.

In one aspect, the present disclosure refers to an *ex vivo* or *in vitro* method for identifying whether a tissue or cell overexpresses PSMA, comprising contacting the tissue or cell with the compound or salt as disclosed herein, wherein the tissue or cell is preferably a cancer tissue or cell and more preferably a prostate cancer tissue or cell.

In one aspect, the present disclosure refers to the compound or salt as disclosed herein for use in treating or preventing a disease which is associated with the overexpression of PSMA, wherein the disease is preferably cancer and more preferably prostate cancer.

Description

The PSMA-targeted ligand compounds in accordance with the invention are compounds of formula (1) or a salt thereof:



(1)

wherein

R^T is a PSMA binding group;

L is a linking group;

R^C is a trivalent coupling group;

R^S is a silicon-containing moiety of the formula -C(O)-R^{S3}-Si$R^{S1}R^{S2}$OH, wherein R^{S1} and R^{S2} are independently selected from C3-C10 alkyl, and are preferably *tert*-butyl, and R^{S3} is a group comprising a 6 membered aromatic ring, and is preferably benzenediyl;

R^A is an amino acid unit; and

R^{CH} is selected from

(i) a branched-chain, acyclic chelating moiety having 4 amino groups, and

(ii) a chelate moiety, wherein a radioisotope selected from ^{99m}Tc, ^{94m}Tc, ^{186}Re and ^{188}Re is chelated by the branched-chain, acyclic chelating moiety having 4 amino groups.

It has been found that the compounds in accordance with the invention combine a pronounced capability of binding as inhibitors to PSMA with general advantages compared to PSMA-I&S, such as reduced lipophilicity and reduced plasma protein binding (PPB). Thus, the compounds in accordance with the invention exhibit similar or even improved *in vitro* characteristics, while showing increased tumor-to-organ ratios in a variety of organs and in particular an increased tumor-to-kidney ratio, which is a critical parameter for radioligand applications in the diagnosis and the treatment of prostate cancer.