resultados indicam que a resistência à CDDP na linhagem SCC-25 pode estar associada ao aumento da expressão dos genes AKR1C1, CCND1, CCND3 e ERCC1, bem como à redução da expressão do gene SLC31A1, o que sugere que esses genes desempenham um papel na quimiorresistência. Esses achados reforçam o potencial desses genes como biomarcadores para um futuro painel de predição de resistência à cisplatina no CCECO. No entanto, novos estudos devem ser realizados em outras linhagens de tumores, assim como em modelos animais, para validar esses resultados.

Palavras-chave: Biomarcadores, Câncer de cabeça e pescoço, Cisplatin, Quimiorresistência.

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A BORON COMPLEX DESIGNED FOR FLUORINE-18 LABELING AIMING FOR PET IMAGING APPLICATION

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A B S T R A C T

Introduction/Justification: Positron emission tomography (PET) is a rapidly expanding clinical modality worldwide due to the availability of compact medical cyclotrons and automated chemistry for the production of radiopharmaceuticals. Despite the availability of various positron-emitting radionuclides such as carbon-11 [11C], fluorine-18 [18F], and gallium-68 [68Ga], 18F has gained more importance and preeminence in research and diagnostic nuclear medicine due to its appropriate half-life of 110 min. Currently, 18F-fluorodeoxyglucose [18F]FDG is the most used radiopharmaceutical for the detection of various neurological disorders and cancer diseases. Since standard 18F-fluorination methods to form carbon-fluorine bonds have some limitations, such as low yield and the requirement for harsh reaction conditions, inorganic approaches, including the formation of boron-fluorine-18 bonds, have the potential to give high specific activities at room temperature, forming a bond that is stable in vivo. The boron complex is planned to be used in fluorine-18 labeling, aiming to develop a potential radiopharmaceutical for PET. **Objectives:** This work aims to produce a new boron compound with a trivalent and tetradentate chelating agent, relatively stable in air and in solution, but reactive in the presence of fluoride ions, to form an inert fluorinated species, aiming for its use in fluor-18 labeling and application in PET imaging. **Materials and Methods:** A tetradentate trivalent chelator, named 3-((bis-(2-hydroxyethyl)amino)methyl)-2-hydroxy-5-methylbenzaldehyde (abbreviated as H3L), was synthesized as previously described and used to prepare a neutral tetracoordinated boron complex, named [BL], by its equimolar quantitative reaction with boric acid in acetonitrile under reflux conditions overnight, as a white solid, which was filtered, dried, and characterized. By spectroscopic monitoring, the formation of a new species was observed in methanol solution from [BL] and NaF, supposedly forming Na[BFL]. The structures of the [BL] molecule and of the [BFL]1- anion were theoretically calculated by DFT methods. **Results:** The H3L free ligand and the boron complex were satisfactorily characterized by diverse techniques, including mass spectrometry, FT-IR, UV-Vis, and NMR spectroscopies (1H, 13C, and 11B) and single crystal X-ray diffraction. The complex [BL] was formed upon deprotonation of three hydroxyl groups in the free ligand, whose oxygens formed the coordination sphere together with the nitrogen atom. The coordination compound has a distorted tetrahedral coordination geometry, which might favor the formation of the bond between the boron atom and the fluoride ion, which is a strong nucleophile, by weakening the boron-nitrogen bond but keeping the oxygen donor atoms strongly coordinated to the boron center. **Conclusion:** Both, the free ligand and the boron complex have been successfully synthesized and characterized. The complex forms a new species in the presence of fluoride. X-ray diffraction on a single crystal of [BL] confirms its structure. The boron center is tetracoordinate with the ligand L3-, which coordinates trianionically and tetradentate through one nitrogen and three oxygen donor atoms. The obtained boron complex exhibited reactivity upon fluoride in solution, resulting in the formation of a novel species, confirming its potential application in [18F]fluoride labeling.

Keywords: Boron, Fluorine-18, Polyvalent chelator, Radiopharmaceutical.

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PREPARATION OF PHOSPHATIDYLSERINE LIPOSOMES FOR 99MTC RADIOPHARMACEUTICALS ENCAPSULATION

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A B S T R A C T

Introduction/Justification: Liposomes are microscopic vesicles containing an aqueous core surrounded by a lipid bilayer, enabling lipophilic and hydrophilic drugs to be encapsulated. Due to this characteristic, they have been used as transporters of substances to treat or diagnose diseases, including radiopharmaceuticals. **Objectives:** This work aims to prepare liposome from phosphatidylserine, encapsulate 99mTc- MDP inside it, and compare murine 4T1 breast cell tumor uptake for 99mTc-MDP and 99mTc-MDP-liposome. **Materials and Methods:** Liposome was prepared by adding 90 mg of phosphatidylserine in a chloroform/methanol solution at a concentration of (9:1). The solvents were evaporated in a desiccator until the lipids formed a film at the bottom of the vial. The radiopharmaceutical 99mTc-MDP was obtained from the reconstitution of a lyophilized kit with a 99mTcO4- solution, according to radiolabeling instructions. The liposome was reconstituted with saline and 99mTc-MDP was added; the solution was sonicated for 10 min. The purification and encapsulation of percentage were done by size exclusion filtration in an Amicon® 10 kD filter, including two water washes. Murine 4T1 breast cancer cells were grown in RPMI-1640 culture medium supplemented with 10% fetal bovine serum, under 37°C in a humidified atmosphere with 5% CO2 and seed at 5 × 104 cell/well and stood overnight in culture conditions. 99mTc-MDP and 99mTc-MDP-liposome were added to wells, in triplicate, and stood in culture conditions for 15, 30, 60 and 120 min. Culture medium was removed, cells were washed twice with PBS, the cells were detached from the wells, and radioactivity was measured in a gamma counter. The cell internalization percentage was determined by dividing cells counts by a standard sample. **Results:** The 99mTc-MDP encapsulation in the liposome reached an average of 68 ± 26% (n = 3), determined by size exclusion filtration. In vitro tumor cells uptake for 99mTc-MDP fluctuated between 0.2% during interval time. On the other hand, 99mTc-MDP-liposome tumor cells uptake had 0.7% ± 0.1% (15 min), 0.8 ± 0.2% (30 min) 0.9 ± 0.2% (60 min) and 1.2 ± 0,4 (120 min). **Conclusion:** The experiments demonstrated the feasibility of liposome production and their use for encapsulate 99mTc-MDP radiopharmaceutical. Loaded 99mTc-MDP-liposome had significantly high tumor uptake compared to 99mTc-MDP alone, demonstrating the effectivity of the phosphatidylserine liposome in delivering radiopharmaceuticals in tumor cells.

Keywords: 99mTc, Liposome, Phosphatidylserine, Radiopharmaceuticals.

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AUTOIMMUNE ENCEPHALITIS AND PARANEOPLASTIC SYNDROMES: A CLINICAL AND FDG-PET/CT STUDY

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A B S T R A C T

Introduction/Justification: Autoimmune encephalitis (AE) is a debilitating neurological disorder characterized by inflammation of brain tissue. Frequently, it is associated with the detection of highly specific antibodies, as such as NMDA, Yo, GAD, Hu, among others. Oftentimes, this condition is expressed as a paraneoplastic syndrome (PNS), for which the neurological manifestation precedes the tumor diagnosis up to 4 years in about two-thirds of the patients. **Objectives:** This work applied the review of clinical findings and FDG-PET/CT images analysis to characterize and explore the outcomes of patients diagnosed with AE, both clinically and by antibodies test. **Materials and Methods:** The study includes 37 patients, aged from 13 to 75 (47.08 ± 20,00 years), 65% female, who had been presented neurological manifestations of encephalitis and PNS. The group of patients was divided according to the antibodies detected (NMDA, Yo, Hu, LGI1, GAD, Amphiphysin, Aquaporin-4), being also studied a group of patients with negative antibodies and untested. Retrospectively, the clinical records were analyzed by the neurology staff, being the clinical manifestations and the results of antibodies tests correlated with FDG-PET/CT brain images, analyzed by an expert in nuclear medicine. **Results:** Among the groups studied, 24.3% had suspicion or confirmed neoplasia (most of them breast or thyroid lesions), being 49% of the patients positive for antibodies related autoimmune encephalitis (AE). In the pretreatment phase, patients with Yo antibodies, manifested epilepsy and cerebellar ataxia, with FDG-PET/CT revealing hypermetabolism in the basal ganglia, cingulate gyri, thalamus, and midbrain, with hypometabolism in the cerebellar hemispheres. Hu antibodies has been associated with epilepsy, sensitive and behavior alterations, being the hypermetabolism in the cingulate gyrus and hypometabolism in the cerebellar hemispheres identified in the PET/CT images; on the other side, GAD antibodies resulted in higher FDG uptake in the thalamus and midbrain, with hypometabolism in the