SYNTHESIS AND EVALUATION OF ^{105}RHODIUM(III) COMPLEXES DERIVED FROM DIAMINODITHIOETHER (DADTE) LIGANDS

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ABSTRACT

Seven analogoues of tetradentate acyclic diaminodithioether (DADTE) ligands were synthesized and characterized. $R_2SC(R_1)_2)CH_nN(CH_2)_mNCH_n((R_1)_2C)SR_2$ **222-gdm (L3)**: m = 1, n = 1, R_1 = –CH_3 and R_2 = -H; **222-gdm-pmBz (L4)**: m = 1, n = 1, R_1 = –CH_3, R_2 = –$CH_2C_6H_5OCH_3$; **232-gdm-pmBz (L7)**: m = 2, n = 1, R_1 = –CH_3, R_2 = –$CH_2C_6H_5OCH_3$, **232-gdm-Met (L8)**: m = 2, n = 1, R_1 = –CH_3, R_2 = –CH_3, **232-Met (L10)** m = 2, n = 1, R_1 = –H, R_2 = –CH_3, **323-Met** (**L12)**: m = 1, n = 2, R_1 = –H, R_2 = –CH_3 and **333-Met** (**L14)**: m = 2, n = 2, R_1 = –H, R_2 = –CH_3). Rh(III) complexes of these DADTE ligands were prepared and the effect of the ligand backbone size on the configuration (*cis* and/or *trans*) has been studied. ^{105}Rh radiolabeling studies were performed in order to investigate the optimum criteria for an ideal chelate such as high thermodynamic stability and kinetic inertness. Also, it is desirable that a single isomer with low lipophilicity properties is formed after complexation of the chelate. Complexation of **232-gdm-Met** with ^{105}Rh yielded a complex that fulfilled the minimum criteria. Coupling studies of **232-gdm-Met** to Bombesin(7-14)

analogues, Ahx-Met^{14}-BBN(7-14) and Ahx-NLeu^{14}-BBN(7-14), via an alternative approach have been accomplished. Finally, radiolabeling studies with **232-gdm-Met**-Ahx-BBN(7-14) analogues were investigated to achieve an efficient ^{105}Rh labeled BBN based target specific radiopharmaceutical.

Structural changes on the DADTE ligand system have been effected to provide a Rh(III)-DADTE complex with optimum properties for an ideal chelate for targeted therapy applications. The alternative approach developed to attach the ligands to peptides yields ^{105}Rh labeled Bombesin(7-14) without needing further functionalization on the ligand.