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Studying the Biological Efficacy of Radiation-Treated Radiolabeled DOTA-Bombesin-Decorated Nanoconstructs as Potential Nanosized Drug Delivery Systems

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Aim: The over-expression of neuropeptide receptors in human breast or prostate cancer leads to potential application of these peptides as new generation of agents for cancer diagnosis and therapy. In this study, we have developed 177Lu-labeled bombesin (BBN) based albumin nanoparticles (Alb-NPs) and papain nanoparticles (Pap-NPs), thus resulting highly specific radiolabeled nanoconstructs decorated with DOTA-BBN, and used as emerging novel 'nanotheranostics'for pre-clinical imaging. The synthesis of gold nanoparticles was developed by the use of green technology, through the stabilization with natural gums (Arabinoxylan - AX isolated from ispaghula seed husk).

Methods: As a part of IAEA CRP, the albumin nanoparticles (Alb-NPs) were prepared in Argentina while papain nanoparticles (Pap-NPs) were prepared in Brazil by ionizing radiation cross linking. Particle size of Alb-NPs was tailored by changing the water/ethanol ratio in the protein solution, reaching particles in the range of 20 nm to 40 nm. The biological efficacy of DOTA-Bombesin-(Alb-NPs) was tested in Pakistan after labeling with 177Lu. The quality control was performed by using ITLC-SG strips as stationery phase. There was a good separation with radiochemical purity (RCP) of 97.3 %. The biological efficacy of 177Lu-DOTA-Bombesin-(Alb-NPs) was tested by determining *in vivo* uptake through imaging scintigraphy in normal rabbit models and biodistribution in normal mice. A solution of 177Lu-AlbNPs-DOTA-Bombesin (2 mCi ml-1) was injected intravenously into the ear vein of rabbits (n = 3). Dynamic study acquisition comprised of 10 frames of 60 sec each. It was followed by anterior and posterior whole body Static images acquired at 15 min, 24h, 48h, 72h, and 96h, post injection. All of these protocols have been established and are further applied to novel bombesin-derivatized (radiation-treated) nanoconstructs from other partner labs.

Results: Radiolabeling and quality control was established for 177Lu-Alb-NPs-DOTA-Bombesin. The effect of activity on labeling efficacy was studied by varying the amount of activity from 5 mCi to 30 mCi by keeping all parameters constant. Similarly, the effect of volume over labeling efficacy was studied by varying the amount of volume from 10 to 200 µl. The maximum labeling efficacy was found at 10 µl and beyond 50 µl, the solution became turbid. Regarding imaging scintigraphy in normal rabbit models, immediately after the injection of radiolabeled nanoconstruct, activity was observed to form the blood pool that was visible in dynamic study of 15 min. In static images, it was further observed that the compound showed a slower uptake with a significantly higher retention time in liver and spleen, thus leading to sufficient renal excretion to allow absorption of the labeled compound into tumor, with rapid body clearance.

Conclusion: In summary, this approach might be further extended to tumor-specific targeting by using BBN derivatives as carrier of chemotherapeutic agents. Imaging studies performed with 177Lu-Alb-NPs-DOTA-Bombesin demonstrate its ideal therapeutic potential to be further developed as a feasible theranostic agent, during this CRP.

Country/Organization invited to participate

Pakistan

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