Synthesis and evaluation of ^{64}Cu labeled chromene derivative for the diagnosis of SK-BR-3

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Breast cancer is the most common female cancer and the second most common cause of female cancer-related deaths with more than one million new cases diagnosed per year throughout the world. Chromene derivatives have demonstrated numerous biological activities, and 6-alkyl- amino-2,2'-di-functionalized-2*H*-chromene derivatives was reported to have anticancer activity by inhibition of receptor tyrosine kinase (RTK). In this study, we synthesized chromene derivative (CRM) that inhibits HER2 (human epidermal growth factor receptor 2, 180 kDa) and ^{64}Cu labeled, that to study the potential of PET tracer for the diagnosis of HER2 overexpression breast cancer.

The 6-amino-2-methyl-2-phenethyl-2*H*- chromene (CRM) compound was synthesized starting from 2-hydroxy-5-nitroacetophenone via 4 steps which produce an overall yield of 26%. SK-BR-3 cell line, HER2 overexpressed breast cancer cells, was treated with the CRM at different concentrations to confirm the cytotoxicity (IC_{50} = 19 μM). The result confirmed that the CRM inhibits colony formation of SK-BR-3 by anchorage independent colony assay, and also confirmed that CRM inhibited the expression of HER2 protein by western blotting analysis.

The precursor (NOTA-Bn-SCN-CRM) was synthesized with 89% yield by introducing *p*-SCN-Bn-NOTA into CRM. For the diagnosis of SK-BR-3, ^{64}Cu-NOTA-Bn-SCN-CRM was synthesized by radioisotope ^{64}Cu labeled to precursor, with a radiochemical yield of 90%. The radiochemical purity of the labeled compound was analyzed to be 98% and the specific activity was 3.7 GBq/μmol. Moreover, the stability was found to be more than 94% for 24 hours and the lipophilicity was 0.15. In addition, ^{64}Cu-NOTA-Bn-SCN-CRM was cultured in SK-BR-3 cell line and cell uptake was measured by gamma counter. As a result, the cell uptake rate increased with respect to time, and the maximum uptake was examined to 1.9 ± 0.4% at 24 h.

Through this study, ^{64}Cu-NOTA-Bn-SCN-CRM was synthesized and evaluated as a potential radiotracer for PET. Furthermore, experimentally evaluated the anti-cancer effect of CRM to SK-BR-3 cell line and proved the possibility of simultaneous diagnosis of HER2 overexpression breast cancer as a pharmaceutical.

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