S20-1 Synthesis and SAR of a New Class of Tetrahydroquinoline Derivatives as Potent and Selective SSTR2 Agonists

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We began the research of the subtype 2 selective agonists of the somatostatin receptor (SSTR), which is a significant modulator for various endocrine systems as the new antidiabetic agents. A tetralin compound **A** was found to possess moderate affinity to SSTRs by randomized screening of Takeda compounds library. After overlapping study of **A** with Octreotide, which was peptide ligand to SSTRs, we designed and synthesized the 1-acylsubstituted tetrahydroquinoline derivative **B**. We found that incorporation of the nitrogen atom of **B** and incorporation of the substituent at 6-position of tetrahydroquinoline ring to develop potent SSTR2 affinity (derivative **C**). After various modification of acyl grup of **C**, compound **D** was found to potent and selective affinity to SSTR2 in vitro (IC_{50}:0.3 nM). In this symposium, it reports on the design, the synthesis and the SAR of the tetrahydroquinoline derivatives.