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Total Synthesis of Cyclictetrapeptide Analogues of Apicidin

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Histone deacetylase(HDAC), a nuclear enzyme that regulates gene transcription and the assembly of newly synthesized chromatin, has received much attention in recent literature. The explosion of activity in this field has yielded the cloning of mammalian gene which encode a complementary histone acetyl transferases. Several cyclic tetrapeptide inhibitors of HDAC have been reported to affect the hyperacetylation of mammalian and plant histones.

Apicidin, a natural product HDAC inhibitor recently isolated from *Fusarium sp.* at Merk Research Laboratories, induces therapeutic applications as a broad spectrum antiprotozoal agent to multi-drug resistant malaria and a potential antitumor agent. The biological activity of apicidin appears to be apicocomplexan HDAC at low nanomolar concentrations.

In the present, we have worked about the synthesis and evolution of biological activities of new apicidin derivatives. We have discovered that apicidin and some derivatives have mild antitumor activity, which change the morphology of tumor cells to the one of normal cells.

As part of our program toward the development of new antitumor agents, we synthesized its derivatives systemically, and then studied their structure-activity relationships. In this presentation, we will report the total synthesis of new Apicidin analogues.