

Studies on the tyrosinase inhibitors of cyclic compounds from higher plants

Koichi Takeya

School of Pharmacy, Tokyo University of Pharmacy & Life Science

We have focused our attention on various naturally occurring cyclic peptides with unique structures and biological activities, especially tyrosinase inhibitors, from higher plants. As a part of our continuing studies in search of new bioactive cyclic peptides from higher plants, we have isolated 26 novel cyclic peptides, named pseudostellarins A - H from the roots of *Pseudostellaria heterophylla*, dichotomins A - I from the roots of *Stellaria dichotoma* var. lanceolata, yunnanins A - F from the roots of *Stellaria yunnanensis*, and delavayin from the roots of *Stellaria delavayi*, all of them belonging to Caryophyllaceae family. Some of them showed tyrosinase inhibitory and cell growth inhibitory activities. These structures were elucidated by extensive 2D NMR such as COSY, HOHAHA, HMBC, HMQC, phase sensitive NOESY and ROESY spectra, chemical degradation and ESI MS / MS methods. Also, in order to determine the importance of the specific functional groups for the overall conformation of cyclic heptapeptides, and in an attempt to understand the relationships between chemical composition and three-dimensional structure, conformational analyses of cyclic peptides, pseudostellarin D (**4**), yunnanins A (**18**) and C (**20**) using X-ray crystallography, high field NMR and MD calculations were undertaken. The dominant solution conformations of **4**, **18** and **20** analyzed by high field NMR and MD calculations employing distance constraints were homologous to those observed in the solid state.