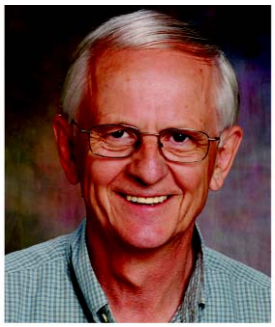

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Structural and biosynthetic studies on the alkaloids from the Australian rainforest tree, *Galbulimima belgraveana*.

The structures have been determined for 22 unique alkaloids isolated from the bark of the rain forest tree *Galbulimima belgraveana* which is the sole surviving species from the relic family Himantandraceae found in Northern Australia, Papua New Guinea and Indonesia. The alkaloids vary considerably in structure and biological activity, but one, namely himbacine, was found to be a potent cardio-selective muscarinic antagonist, due to its ability to bind selectively with M_2/M_4 muscarinic receptors. Thus, himbacine became a lead compound in the search for new drugs for the treatment of neurodegenerative conditions such as Alzheimer's disease. While interest in himbacine has waned, a synthetic analogue has been shown to be a potent orally active thrombin receptor (PAR-1) antagonist and is presently undergoing stage 3 clinical trials for the treatment of acute coronary syndrome and for secondary-prevention in patients who have had a prior myocardial infarct or stroke. In addition to the 22 alkaloids described earlier, we have isolated and determined the structures of a further seven alkaloids with a view to shedding light on their biosynthesis and therapeutic potential.

Biography

Lew Mander was born in Auckland, New Zealand, where he completed his
BSc and MSc (hons.) degrees at the University of Auckland. After moving to Australia, he obtained his Ph.D. in 1964 at the University of Sydney then undertook two years of postdoctoral studies initially at the University of Michigan and then at the California Institute of Technology. He returned to Australia as a lecturer in organic chemistry at the University of Adelaide then moved to the Research School of Chemistry at the Australian National University in 1975. He was appointed Professor in 1980, serving two periods as Dean (1981–85; 1992–95). He was a Nuffield Fellow at Cambridge University in 1972 and a Fulbright Senior Scholar at the California Institute of Technology in 1977 and at Harvard University in 1986. He has been an Eminent Scientist of

RIKEN, Saitama, Japan (1995–96), and a Distinguished Alumnus Professor at the University of Auckland (1992). He has also been a visiting professor at the Universities of Sydney, Cambridge, Alberta, Colorado, and Canterbury (New Zealand). He is a Fellow of the Australian Academy of Science and The Royal Society (London). His research interests are concerned with the development of methods and strategies for the assembly and manipulation of complex natural products with a special interest in the role of gibberellins in plant growth and development.