

UNIVERSITI TEKNOLOGI MARA

**ABSOLUTE CONFIGURATION
DETERMINATION OF
ANDROGRAPHOLIDE *VIA*
EXPERIMENTAL AND
THEORETICAL CIRCULAR
DICHROISM SPECTROSCOPIC
TECHNIQUES**

MUHAMAD FAID BIN A KADIR

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ABSTRACT

Chirality is a chemical property that is very important to current pharmaceutical development processes. This study explores the employment of circular dichroism (CD) spectroscopy as a powerful tool for the absolute configuration (AC) assignment of labdane diterpenes which are considered as flexible chiral molecules. *Andrographis paniculata* (Burm. f.) Wall. ex Nees is a medicinal plant whose primary constituent is the labdane diterpene, andrographolide. The first objective of this study was to isolate and characterize andrographolide as the major constituent from *A. paniculata* using various chromatographic and spectroscopic methods. Upon the determination of relative configuration of andrographolide, the second objective was to measure the CD properties of andrographolide *via* experimental ECD and VCD techniques in solution form. The last objective was to determine the AC of andrographolide by the comparison of experimental ECD and VCD spectra to simulated data using TDDFT calculation. The functional theory employed was CAM-B3LYP/6-31+G(d,p) level as implemented in Gaussian 09W software package. From this study, andrographolide (**1**) was successfully isolated and characterized and its initial relative configuration was determined by 1D and 2D NMR spectroscopy. Comparison of the experimental and simulated ECD and VCD data of andrographolide resulted in very good agreement qualitatively leading to the establishment of its absolute configuration (in solution state) as *3R*, *4R*, *5S*, *9R*, *10R*, and *14S*. In conclusion, this work clearly supports the use of CD techniques for the AC determination of naturally occurring labdane-type diterpenes and it may be applied to other structurally complex and flexible natural products. A concerted application of both ECD and VCD techniques should be considered as the main and preferable approach over other chiroptical methods.

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“Hold on to the tiny moments and cherish little snuggles because the future is determined by the past”

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