UNIVERSITI TEKNOLOGI MARA

CIRCULAR DICHROISM SPECTRA CALCULATION OF DIASTEREOMERIC C-7 PENTACYCLIC OXINDOLE ALKALOIDS USING DENSITY FUNCTIONAL THEORY AND TIME-DEPENDENT DENSITY FUNCTIONAL THEORY METHODS

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MSc

August 2020

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Density Functional Theory (DFT) and time-dependent density functional theory (TD-DFT) are reliable methods to calculate circular dichroism (CD) spectra in assigning the absolute configuration (AC) of chiral compounds. It requires choosing the correct level of theory that includes basis set, exchange-correlation functional and solvation model. Well established AC of diastereomeric pentacyclic oxindole alkaloids (POAs), isopteropodine and pteropodine were tested to find suitable level of theory. Both isopteropodine and pteropodine were purified by recycling HPLC and the nonempirical correlation between their experimental and computational CD data was studied. A series of Pople's basis set (6-31G, 6-31G*, 6-31+G, 6-31+G*, 6-31+G**, 6-311+G**) exchange-correlation functionals (PBEPBE, MPW1PW91, BVP86, B3LYP, CAM-B3LYP) and polarizable continuum solvation models (IEF-PCM, I-PCM, C-PCM), which are commonly used for natural product, were assessed. It was found that a double zeta basis set with an additional diffuse and polarization functions as 6-31+G** was sufficient for the electronic circular dichroism (ECD) spectra simulation. The calculation inclusive of solvation model is significant to be included and the IEF-PCM is the best solvation model. Although both B3LYP and CAM-B3LYP hybrid functionals could model the ECD data for isopteropodine, however the former functional failed in predicting the critical Cotton effect (CE) of the $n \rightarrow \pi^*$ electronic transition in pteropodine. This was nevertheless solved by the latter long-range correction properties functional. Thus, the suitable level of theory proposed to model the CD data for POAs system is TD-DFT/ CAM-B3LYP/6-31+G**/IEF-PCM with similarity factor of more than 0.9. The reliability on this optimised computational CD method was verified through consistency in simulating ECD data of three new POAs in establishing their AC.

ACKNOWLEDGEMENT

Firstly, I wish to thank Allah for giving me the opportunity to embark on my master's degree and for completing this long and challenging journey successfully. My gratitude and thanks go to my supervisor Dr Fatimah Salim for believing me and never-ending support.

My appreciation goes to my co-supervisors Datin Prof Dr Rohaya Ahmad and Dr Anouar for moral support and fruitful ideas towards this project. I also very thankful for the facilities and assistance from the laboratory staffs. Special thanks to my colleagues and friends for helping me with this project.

Finally, this thesis is dedicated to my very dear father and mother for the vision and determination to educate me. All the prayers from them have success me to complete this project. This piece of victory is dedicated to both of you. Alhamdulillah.

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