Trop J Nat Prod Res, October 2023; 7(10):4262-4266 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

A Novel Green Extraction and Molecular Docking Study: Effect of Native Cyclodextrins and Derivatives on the Extraction of Andrographolide from *Andrographis paniculata* (Burm.f.) Nees

Bunleu Sungthong[1], Sirikran Winyupan[1], Nadtanet Nunthaboot[2], Wiraphol Phimarn[3], Ployvadee Sripadung[1]*

[1]*Integrative Pharmaceuticals and Innovation of Pharmaceutical Technology Research Unit, Faculty of Pharmacy, Mahasarakham University, Maha Sarakham, 44150, Thailand*
[2]*Multidisplinary Research Unit of Pure and Applied Chemistry and Supramolecular Chemistry Research Unit, Department of Chemistry and Center of Excellence for Innovation in Chemistry (PERCH-CIC) Faculty of Science, Mahasarakham University, Maha Sarakham, 44150, Thailand*
[3]*Social Pharmacy Research Unit, Faculty of Pharmacy, Mahasarakham University, Maha Sarakham, 44150, Thailand*

ARTICLE INFO

Article history:
Received 18 August 2023
Revised 12 September 2023
Accepted 07 October 2023
Published online 01 November 2023

ABSTRACT

Andrographolide (AP) is a sparingly water solubility bioactive compound from *Andrographis paniculata.* It exhibits several pharmacological activities. With respect to its hydrophobicity, the high-yield extract of AP is primarily obtained from organic solvents, which are considered as environmentally harmful substances. Therefore, the green extraction using an alternative solvent is eventually performed to obtain the highest AP extract. The objectives of this study are to investigate the extraction efficiency of AP using different types of cyclodextrins (CDs) in aqueous media and *in silico* molecular docking study of AP with the corresponding CDs. The cyclodextrin-assisted extraction of AP using alpha cyclodextrin (αCD), beta cyclodextrin (βCD), gamma cyclodextrin (γCD), methyl beta cyclodextrin (MβCD), trimethyl beta cyclodextrin (triMβCD) and hydroxypropyl beta cyclodextrin (HPβCD) at a concentration of 1 mM was investigated in aqueous media comparing with water and methanol by ultrasonication. The amount of AP in each extract was determined by an HPLC method. In screening process, HPβCD exhibited the highest extraction yield of AP compared with the other CDs. However, it was significantly lower than that in the methanolic extract ($P < 0.05$). Subsequently, the extraction of AP was performed as a function of HPβCD concentration. Increasing the concentration of HPβCD resulted to obtain the better extraction yield of AP comparing with a positive control of methanol ($P < 0.05$). In conclusion, the green extraction using HPβCD could be an alternative method to achieve a higher AP in the extract than that in the methanolic extract.

Keywords: cyclodextrin-assisted extraction, host-guest interaction, inclusion complex, labdane diterpenoid, water extraction

Introduction

"King of bitter" or *Andrographis paniculata* (Burm.f.) Nees, a plant in Acanthaceae family, has been included in the National List of Essential Medicine, Herbal Medicinal Product chapter. The plant has been found in tropical countries including India, Sri Lanka, China, Indonesia, Malaysia and Thailand. In traditional medicine, the whole plant and its leaves are commonly used for the treatment of upper respiratory tract infection, antipyretic, skin rashes, malaria and peptic ulcer.[1] Labdane diterpenoids, specifically andrographolide, neoandrographolide, and isoandrographolide, are the primary bioactive components of *A. paniculate*.[2-3] These compounds possess a variety of pharmacological properties, including antibacterial, anti-biofilm formation, anti-HIV, anti-flu, antimalarial, anti-leishmaniasis, and antiviral properties.[4-6]

*Corresponding author. E mail: ployvadee.s@msu.ac.th
Tel: +66 43 754360

Citation: Sungthong B, Winyupan S, Nunthaboot N, Phimarn W, Sripadung P. A Novel Green Extraction and Molecular Docking Study: Effect of Native Cyclodextrins and Derivatives on the Extraction of Andrographolide from *Andrographis paniculata* (Burm.f.) Nees. Trop J Nat Prod Res. 2023; 7(10):4262-4267. http://www.doi.org/10.26538/tjnpr/v7i10.21.

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Extraction of bioactive compounds from medicinal plants is aimed to obtain high yield of active phytochemicals in the extract or to remove fiber and undesired plant materials. The selection of extraction technique is a crucial step, which has to be considered depending on the physicochemical characteristics of the phytochemicals as well as the advantages or disadvantages of that technique. Green extraction is relied on the design of extraction processes such as reductions of energy consumption and organic solvents or using alternative solvents to ensure a safety and environmentally friendly concerns.[7-8] Water is considered as harmless solvent for extraction. However, the extraction efficiency of phytochemicals using water is relatively low due to its high polarity.[9] The use of cyclic oligosaccharides-cyclodextrins in aqueous medium probably improves the extraction efficiency of bioactive compounds such as phenolic compounds, flavonoids and terpenoids.[10] The cyclic oligosaccharides known as cyclodextrins (CDs) are linked by α-1,4 glycosidic bonds and contain *D*-(+)-glucopyranose subunits. Due to the hydroxyl groups of the sugars, the cyclic structure of CDs exhibits external hydrophilic properties, whilst the internal cavity exhibits lipophilic properties.[11] CDs lipophilic internal cavities can encapsulate low- or medium-polar molecules by non-covalent interactions, van der Waal forces, hydrophobic interactions, and hydrogen bonds to generate host-guest inclusion complexes.[12] Native CDs consist of 3 different sizes of macrocyclic oligosaccharides, namely, αCD (6 glucose subunits), βCD (7 glucose subunits) and γCD (8 glucose subunits), which provide different interaction pocket sizes for phytochemicals.[13] CDs are widely used in pharmaceutical-, food-,

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

cosmetics- and chemical industries to improve stability and increase water solubility or mask undesired taste.[14]

Cyclodextrin-assisted extraction (CAE) is one of the green extraction methods. The trend of CAE of plant secondary metabolites has been increasing due to its extraction efficiency and primarily using aqueous medium.[10] Previous researches on CAE of phytochemicals were mostly focused on the extraction of phenolic compounds *e.g.* phenolic acid in Chinese date,[15] anthocyanin in mulberry fruits[16] and mangiferin in mango stem barks.[17] There are various factors influencing the CAE efficiency such as CD types, CD concentration, temperature, extraction time and extraction technique.[18] Additionally, molecular docking of phytochemicals and CDs may be performed to investigate host-guest binding energy and functional group interaction such as CDs and scandenin, a bioactive compound of *Derris* scandens.[19] The objectives of this study were to investigate the extraction efficiency of andrographolide from *A. paniculata* using various types of CDs and binding free energy of andrographolide-CDs complexes using *in silico* molecular docking technique. The results of CAE of andrographolide and molecular docking study were also compared.

Materials and Methods

Chemicals and reagents

Alpha cyclodextrin (αCD) and gamma cyclodextrin (γCD) were purchased from Wako chemicals (Osaka, Japan). Beta cyclodextrin (βCD), methyl beta cyclodextrin (MβCD) and trimethyl beta cyclodextrin (triMβCD) were obtained from Acros Organics (Geel, Begium). Hydroxypropyl beta cyclodextrin (HPβCD) was from CycloLab (Budapest, Hungary). A standard andrographolide (AP, 98%) was from Sigma Aldrich (Saint Louis, MO, USA). Ultra-purified water was generated by Milli-Q academic A10 (Millipore, Darmstadt, Germany). Methanol AR grade was obtained from Labscan (Bangkok, Thailand). All structures of CDs and andrographolide were shown in Figure 1.

Plant materials and HPLC analysis of andrographolide

Andrographis paniculata was harvested in Sakon Nakhon Province (GPS position: 17.537168ºN, 103.729399ºE) in August 2021. The voucher specimen was collected at the herbarium of Faculty of Pharmacy, Mahasarakham University, Thailand (Herbarium Specimen Number: MSU.PH-ACA-AP-1). The whole plant was cleaned with deionized water and dried under 50ºC hot air oven (Model 2000, Contherm Scientific, New Zealand). The dried material was further pulverized (Sunsolid, Samut Prakan, Thailand) and sieved (Retsch GmbH, Haan, Germany) with 60 mesh to obtain fine powder. The powder was then kept under cool condition and protected from light prior to experiment. The analysis of andrographolide was performed under the Thai Herbal pharmacopoeia (THP) monograph.[20] Briefly, the HPLC analytical method of AP was performed on a Primaide 1000 series (Hitachi, Tokyo, Japan). Mobile phase was a mixture of 52 volumes of ultrapure water and 48 volumes of methanol. The separation of andrographolide was carried out using Dr.Maisch Reprosil-Pur C_{18} 5-µm, 150 x 4.6 mm (Ammerbuch-Entringen, Germany) with Luna C_{18} 5-µm guard column, 20 x 3.9 mm (Phenomenex, Torrance, CA, USA) at a flow rate of 1 mL per minute. The analysis of andrographolide was monitored at 224 nm with Primaide 1430 Diode Array Detector (Hitachi, Tokyo, Japan).

Effect of CD and its derivatives on the extraction of andrographolide

The extraction of andrographolide (AP) was performed at 10 minutes using 30% amplitude of 296 W, 40 kHz ultrasonic probe (Sonics & Materials Inc, Newtown, CT, USA). *A. paniculata* was weighed at 300 mg (Sartorius, Goettingen, Germany) in the extraction media of 10 mL. The extraction temperature was set at 25ºC. All CDs were prepared at a concentration of 1 mM to evaluate the extraction efficiency in comparison with water and methanol extracts. After extraction, the samples were centrifuged at 5,000 rpm for 10 minutes (Hettich GmbH, Tuttlingen, Germany). Subsequently, the supernatants were filtered with 0.45 µm PTFE syringe filter prior to injection to the HPLC system. Finally, the CD with highest extraction efficiency was further studied as a function of CD concentration. The extraction yield of AP was calculated using a standard curve of peak areas versus concentrations (y = 89750x – 19007, R^2 = 0.9996).

Molecular docking study

The optimized structures of βCD, MβCD and HPβCD from our prior research was used.[21-23] The triMβCD was created through methyl substitutions at the R1, R2, and R3 positions of the natural βCD. The structural configurations of αCD (PDB: 4FEM) and γCD (PDB: 5E70) were sourced from the Protein Data Bank (https://www.rcsb.org). The two-dimensional (2D) configurations of AP were acquired in SDF format from PubChem Compound (http://pubchem.ncbi.nlm.nih.gov/) using the compound CIDs of 5318517. The preparation of all docking input files was carried out using AutoDockTools (ADT).[24] For the CDs, the Kollman united atom charges were applied[25], while the Gasteiger-Marsili charges[26] were assigned to the partial atomic charges of the AP molecule. The dimensions of 18 x 18 x 18 Å³ was established and centered on the grid box of each CDs molecule. The grid spacing was set to 1.0 Å. Host-guest inclusion structures were generated through molecular docking calculations utilizing AutoDock Vina. Default values were utilized for the other parameters. In the search protocol, the guest molecule had the freedom of unrestricted movement within the CD cavity, while the host molecule remained fixed in a truncated-cone structure. The analysis and visualization of the results of inclusion complexation between AP and various CDs were conducted using Biovia Discovery Studio and ChimeraX software.[27]

Data analysis

All collected data were presented in mean±SD (n=3) using Microsoft Excel. IBM SPSS Statistics Version 29 was used to analyze the statistical difference of the extracted AP among the experimental groups using One-way ANOVA. A Tukey post hoc test was applied to compare the amount of AP in various extraction media with control groups, water- and methanolic extract. Statistically significant difference was considered at p value < 0.05.

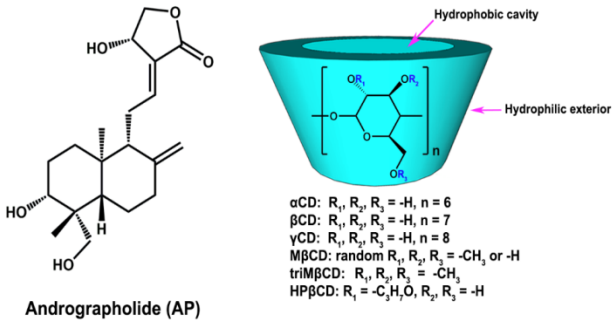

Figure 1: Structures of andrographolide and native CDs and derivatives

Results and Discussion

Cyclodextrin-assisted extraction (CAE) of andrographolide from A. paniculata

AP exhibits a very low solubility in aqueous medium with log P at 2.2.[28] Due to low water solubility, CDs were considered to form host-guest inclusion complexes, which resulted in enhanced water solubility of AP in aqueous media. The amounts of AP extracted from *A. paniculata* using various types of CDs at a concentration of 1 mM in aqueous media were substantially compared with water and methanol as shown in Table 1. The results revealed that γ-, Mβ- and HPβ-CDs exhibited the highest yield at 5.69±0.04, 5.78±0.14 and 5.98±0.17 mg AP/g dried weight, respectively comparing with other CDs and water extract (P < 0.05). However, the highest extraction efficiency at 6.45±0.16 mg AP/g dried weight was observed in methanolic extract. The extraction efficiency is derived from the hydrophobic internal cavity size and molecular interaction of host-guest compounds. In the case of AP containing cyclic moieties, the compound could not form a host-guest inclusion complex with αCD due to its small internal cavity.[10] The low

extraction efficiency of AP was also observed in βCD-assisted extraction. It is probably from a low water solubility of βCD at 18.5 mg/mL which could compete in water solubility with AP. On the other hand, the water solubilities of other CD derivatives range between 145 to more than 2,000 mg/mL, at 25°C. The substitution of native βCD with various functional groups may lead to improve the interaction of the guest compounds as well as the increment of water solubility of CD derivatives.[29] In comparison to other CDs, HPβCD demonstrated the highest extraction efficiency (Table 1).

As shown in Table 1, the extraction using HPβCD exhibited the highest extraction yield. Therefore, HPβCD was considered to perform a further experiment on CAE of AP as a function of the CD concentration. The HPβCD was prepared in different concentrations, *i.e.,* 1%, 2% and 3% w/v in water as extraction media. Our findings revealed that increasing HPβCD concentration tend to enhance the solubility of AP by increasing the chance to encapsulate the compound into the interior cavity. The strong binding affinity of AP and HPβCD could be predominantly from hydrogen bonding interaction.[11,29-30] The solubility enhancement of HPβCD in various concentrations showed a better extraction efficiency than those in water and methanol (Figure 2). The AP extraction yields using 1%, 2% and 3% w/v HPβCD substantially increased from 7.90±0.11 to 9.06±0.01 and 10.27±0.17 mg AP/g dried weight, respectively. The AP extraction yield had linearly complied with the CD concentrations with a correlation coefficient of 0.999, y = 1.181x + 6.7154. As a result of its water solubility at more than 1,200 mg/mL as well as hydroxypropyl groups, increasing the concentration of HPβCD may probably tend to improve the extraction yield of AP.[29] This phenomenon had been observed in CAE using βCD and HPβCD for the extraction of *Hibiscus sabdariffa* anthocyanins.[31] The extraction yield of anthocyanins was comparable to a positive control of 40% ethanol solution ($P > 0.05$), when the concentration of HPβCD had been increased from 1% to 5% w/v. However, increasing the concentration of βCD could not demonstrate the same effect as HPβCD. It is due to the low water solubility of βCD as well as the saturation of internal cavity of βCD at the higher concentration. These could limit further interactions of the compound and βCD.[32] The formation of host-guest inclusion complex is a major role of the extraction which related to the encapsulation of phytochemicals in hydrophobic cavity.[10] The inclusion complexes of CDs and phytochemicals depend on 2 factors *i.e.* (1) size and structure of guest molecules and internal cavity of host CDs, and (2) thermodynamics interaction of CD, guest molecule and solvent.[29,33]

Molecular docking

The modeling results of AP with CDs in all inclusion complexes are shown in Figure 3. The AP molecule was configured to move freely, resulting in the binding of the curved structure between AP and αCD.

Table 1: The CAE of andrographolide (AP) from *A. paniculata* using various CDs at a concentration of 1 mM, water and methanol

Extraction media	Extraction yield of AP (mg/g dried weight)*
αCD	4.32 ± 0.04[a]
βCD	5.25 ± 0.11[c]
γCD	5.69 ± 0.04[d]
MβCD	5.78 ± 0.14[d]
triMβCD	5.16 ± 0.07[c]
HPβCD	5.98 ± 0.17[d]
Water	4.85 ± 0.04[b]
MeOH	6.45 ± 0.16[e]

Different alphabets (a – e) indicate statistically significant differences ($P < 0.05$)
*The result shows in mean ± SD (n=3).

Table 2: The binding free energy (ΔG_{bind}) of andrographolide (AP) encapsulated to different types of CDs

Host-guest inclusion complexes	ΔG_{bind} (kcal/mol)
AP-αCD	-4.3
AP-βCD	-5.5
AP-γCD	-5.5
AP-MβCD	-5.5
AP-triMβCD	-3.6
AP-HPβCD	-6.1

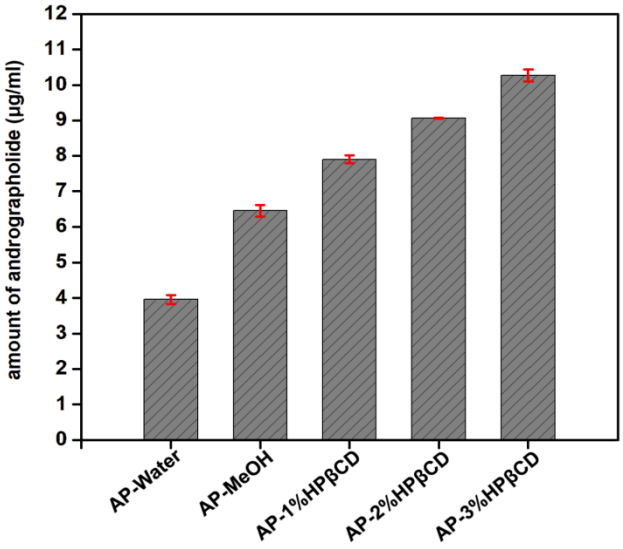

Figure 2: The CAE of andrographolide (AP) from *A. paniculata* as a function of CD concentration comparing with water and methanol, the result shows mean ± SD (n=3)

The decalin rim of the AP molecule was partially enclosed in the fairly hydrophobic cavity of the structure of AP-αCD (Figure 3a), while the lactone group extends beyond the surrounding of αCD. Particularly, AP moving its entire structure into the βCD, γCD, MβCD or HPβCD hydrophobic interior (Figure 3b-d and f) appeared on the CD primary rim. Furthermore, the interaction of AP and hydroxyl groups of native CDs or substituted functional groups was apparently a consequence of either a steric hindrance or inclusion complex forming by non-covalent interaction. In this context, the guest compound could be completely encapsulated into the βCD, γCD, MβCD and HPβCD internal cavity resulting to a low binding free energy. Nevertheless, the methyl substituents on 2,3,6-position of the glucose subunits, triMβCD exhibited more pronounced steric hindrance. Although the hindered AP molecule probably employed a superficial interaction with the CD, it was unable to fully occupy this particular lipophobic cavity of the CD (Figure 3e).

The overall host-guest binding free energy (ΔG_{bind}) of AP-αCD, AP-βCD, AP-γCD, AP-MβCD, AP-triMβCD, and AP-HPβCD are shown in Table 2. The binding energies are found in the range of -3.6 to - 6.1 kcal/mol. The binding strengths relative to binding energies of AP encapsulated into different types of CDs are presented in the order; AP-HPβCD (-6.1 kcal/mol) > AP-βCD (-5.5 kcal/mol) = AP-γCD (-5.5 kcal/mol) = AP-MβCD (-5.5 kcal/mol) > AP-αCD (-4.3 kcal/mol) > AP-triMβCD (-3.6 kcal/mol). The data shows that the AP-HPβCD complex demonstrates the strongest binding interaction between the HPβCD and AP molecules. This ability arises from the capability of the AP structure to completely enter the cavity, preferably by the formation of hydrogen bonds. These binding energies are consistent with previous studies, indicating their favorable energetic agreement.[34] The weakest binding capability was attributed to AP-triMβCD due to the positioning of the

methyl group in triMβCD hindering the AP molecule at the terminal outside the CD hydrophobic cavity, as previously mentioned. Increasing the degree of substitution at a lower range could improve solubility of guest compounds, whereas the very high degree of substitution, as the case of triMβCD, could result to steric hindrance of the guest compounds incorporated to the host molecule.[35]

Conclusion

Among other CDs, the CAE of AP employing HPβCD possessed the highest extraction efficiency. The results from *in silico* molecular docking study mostly complied with the CAE experiment. Therefore, molecular docking can be used for the screening of potential CDs in CAE. The influence of extraction factors *e.g.* liquid-solid ratio, extraction technique, temperature and time should be performed to evaluate the extraction efficiency of AP. Additionally, a study on the optimization of CAE of AP using response surface methodology (RSM) of particular factors would be further investigated.

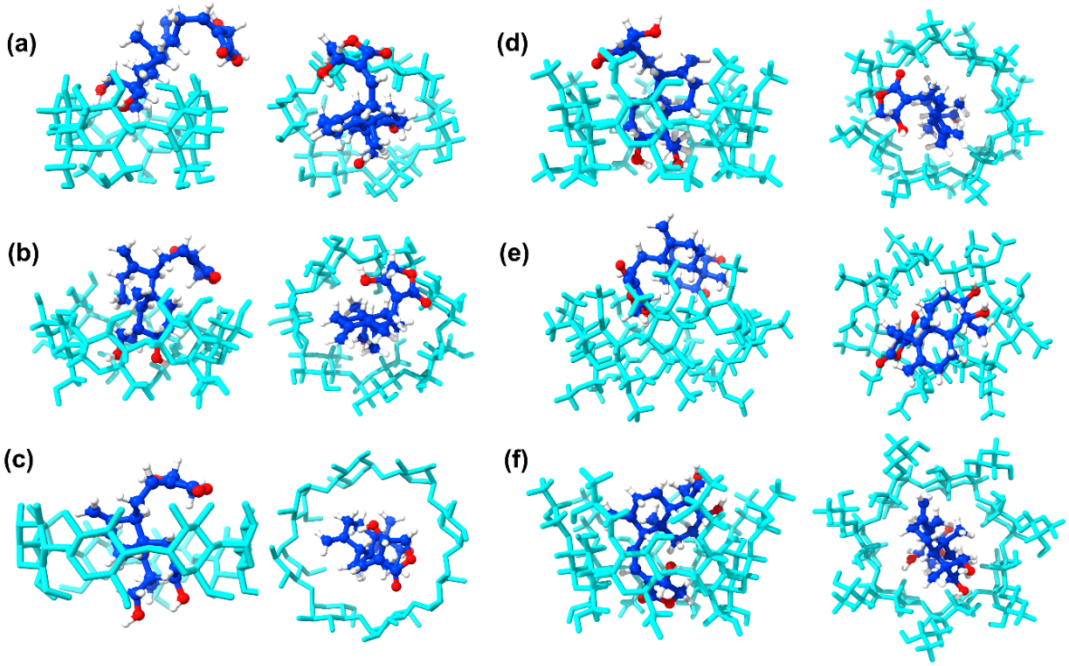

Figure 3: Both front and side view simulations of host-guest inclusion complexes of andrographolide (AP) and CD structures; (a) AP-αCD, (b) AP-βCD, (c) AP-γCD, (d) AP-MβCD, (e) AP-triMβCD and (f) AP-HPβCD.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgments

The authors would like to thank the Faculty of Pharmacy, Mahasarakham University, Thailand for financial support with the grant number RD2/2565. Identification of the plant by Assistant Professor Dr. Wanida Caichompoo, Faculty of Pharmacy, Mahasarakham University, Thailand was gratefully acknowledged.

References

1. Hossain S, Urbi Z, Karuniawati H, Mohiuddin RB, Moh Qrimida A, Allzrag AMM, Ming LC, Pagano E, Capasso R. *Andrographis paniculata* (Burm. f.) Wall. ex Nees: An Updated Review of Phytochemistry, Antimicrobial Pharmacology, and Clinical Safety and Efficacy. Life (Basel). 2021; 11(4): 348.
2. Zhao J, Yang G, Liu H, Wang D, Song X, Chen Y. Determination of andrographolide, deoxyandrographolide and neoandrographolide in the Chinese herb *Andrographis paniculata* by micellar electrokinetic capillary chromatography. Phytochem. Anal. 2002; 13: 222–227.
3. Pramanick S, Banerjee S, Achari B, Das B, Sen Sr AK, Mukhopadhyay S, Neuman A, Prang´e T. Andropanolide and isoandrographolide, minor diterpenoids from Andrographis paniculata: structure and X-ray crystallographic analysis. J Nat Prod. 2006; 69: 403–405.
4. Dai Y, Chen SR, Chai L, Zhao J, Wang Y, Wang Y. Overview of Pharmacological Activities of *Andrographis paniculata* and its Major Compound Andrographolide. Crit Rev Food Sci Nutr. 2019; 59(Sup1): S17-29.
5. Jayakumar T, Hsieh CY, Lee JJ, Sheu JR. Experimental and Clinical Pharmacology of *Andrographis paniculata* and Its Major Bioactive Phytoconstituent Andrographolide. Evid Based Complement Altern Med. 2013; 2013: 846740.
6. Chua LS. Review on liver inflammation and antiinflammatory activity of *Andrographis paniculata* for hepatoprotection. Phytother Res. 2014; 28(11): 1589-1598.
7. Chemat F, Abert-Vian M, Fabiano-Tixier AS, Strube J, Uhlenbrock L, Gunjevic V, Cravotto G. Green extraction of natural products. Origins, current status, and future challenges, TrAC, Trends Anal Chem. 2019; 118: 248-263.
8. Kultys E, Kurek MA. Green Extraction of Carotenoids from Fruit and Vegetable Byproducts: A Review. Molecules. 2022; 27(2): 518.
9. Sixt M, Strube J. Systematic and Model-Assisted Evaluation of Solvent Based- or Pressurized Hot Water Extraction for the Extraction of Artemisinin from *Artemisia annua* L. Processes. 2017; 5(4): 86.

10. Kazlauskaite JA, Ivanauskas L, Bernatoniene J. Cyclodextrin-Assisted Extraction Method as a Green Alternative to Increase the Isoflavone Yield from *Trifolium pratensis* L. Extract. Pharmaceutics. 2021; 13(5): 620.
11. Terekhova IV, Hammitzsch-Wiedemann M, Shi Y, Sungthong B, Scriba GK. Investigation of the pH-dependent complex formation between beta-cyclodextrin and dipeptide enantiomers by capillary electrophoresis and calorimetry. J Sep Sci. 2010; 33(16): 2499-505.
12. Lee JU, Lee SS, Lee S, Oh HB. Noncovalent Complexes of Cyclodextrin with Small Organic Molecules: Applications and Insights into Host-Guest Interactions in the Gas Phase and Condensed Phase. Molecules. 2020; 25(18): 4048.
13. Gidwani B, Vyas A. A Comprehensive Review on Cyclodextrin-Based Carriers for Delivery of Chemotherapeutic Cytotoxic Anticancer Drugs. Biomed Res Int. 2015; 2015: 198268.
14. Jansook P, Ogawa N, Loftsson T. Cyclodextrins: Structure, physicochemical properties and pharmaceutical applications. Int J Pharm. 2018; 535(1-2): 272-284.
15. Zhu QY, Zhang QY, Cao J, Cao W, Xu JJ, Peng LQ. Cyclodextrin-assisted liquid-solid extraction for determination of the composition of jujube fruit using ultrahigh performance liquid chromatography with electrochemical detection and quadrupole time-of-flight tandem mass spectrometry. Food Chem. 2016; 213: 485-493.
16. Xie J, Xu Y, Shishir MR, Zheng X, Chen W. Green extraction of mulberry anthocyanin with improved stability using β-cyclodextrin. J Sci Food Agric. 2019; 99(5): 2494-2503.
17. Mura P. Analytical techniques for characterization of cyclodextrin complexes in the solid state: A review. J Pharm Biomed Anal. 2015; 113: 226-238.
18. Rui C, Yuan Y, Cui L, Wang Z, Yue T. Cyclodextrin-assisted extraction of phenolic compounds: Current research and future prospects. Trends Food Sci Technol. 2018; 79: 19-27.
19. Boonma T, Nutho B, Sungthong B, Sripadung P, Rungrotmongkol T, Nunthaboot N. Molecular insights into complex formation between scandenin and various types of β-cyclodextrin. J Mol Liq. 2021; 344: 117774.
20. Department of Medical Sciences, Ministry of Public Health. Thai Herbal Pharmacopoeia 2016. Nonthaburi: The Agricultural Co-operative Federation of Thailand; 2016. 103-108 p.
21. Wongpituk P, Nutho B, Panman W, Kungwan N, Wolschann P, Rungrotmongkol T, Nunthaboot N. Structural dynamics and binding free energy of neral-cyclodextrins inclusion complexes: Molecular dynamics simulation, Mol. Simul. 2017; 43(13-16): 1356–1363.
22. Frisch A, Nielsen AB, Holder AJ. Gauss View Molecular Visualization Program. User Manual, Gaussian Inc., Pittsburg. 2001.
23. Ulkarni AS, Dias RJ, Ghorpade VS, Mali KK. Freeze-Dried Multicomponent Inclusion Complexes of Curcumin for Enhancement of Solubility and Anti-Inflammatory Activity. Trop J Nat Prod Res. 2020; 4(11): 887–894.
24. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: automated docking with selective receptor flexibility. J Comput Chem. 2009; (30): 2785–2791.
25. Weiner SJ, Kollman PA, Nguyen T, Case DA. An all atom force field for simulations of proteins and nucleic acids. J Comput Chem. 1986; 7(2): 230–252,
26. Gasteiger J, Marsili M. Iterative partial equalization of orbital electronegativity-a rapid access to atomic charges. Tetrahedron. 1980; 36(22): 3219–3228.
27. Pettersen EF, Goddard TD, Huang CC, Meng EC, Couch GS, Croll TI, Morris JH, Ferrin TE. UCSF ChimeraX: Structure visualization for researchers, educators, and developers. Protein Sci. 2021; 30(1): 70-82.
28. PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 5318517, Andrographolide; [Updated 2023 Aug. 18]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Andrographolide
29. Saokham P, Muankaew C, Jansook P, Loftsson T. Solubility of Cyclodextrins and Drug/Cyclodextrin Complexes. Molecules. 2018; 123(5): 1161.
30. Terekhova IV, Scriba GK. Study on complex formation of biologically active pyridine derivatives with cyclodextrins by capillary electrophoresis. J Pharm Biomed Anal. 2007; 45(4): 688-693.
31. Zhang Y, Sang J, Chen Ff, Sang J, Li CQ. β-Cyclodextrin-assisted extraction and green chromatographic analysis of *Hibiscus sabdariffa* L. anthocyanins and the effects of gallic/ferulic/caffeic acids on their stability in beverages. J Food Meas Charact. 2018; 12: 2475–2483.
32. Parmar I., Sharma S, Rupasinghe HPV. Optimization of β-cyclodextrin-based flavonol extraction from apple pomace using response surface methodology. J Food Sci Technol. 2015; 52: 2202–2210.
33. Del Valle EMM. Cyclodextrins and their uses: a review. Process Biochem. 2004; 39(9): 1033-1046.
34. Majumdar M, Misra TK, Roy DN. In vitro anti-biofilm activity of 14-deoxy-11,12-didehydroandrographolide from *Andrographis paniculata* against *Pseudomonas aeruginosa*. Braz J Microbiol. 2020; 51: 15–27.
35. Li Z, Li K, Teng M, Li M, Sui X, Liu B, Tian B, Fu Q. Functionality-related characteristics of hydroxypropyl-β-cyclodextrin for the complexation. J Mol Liq. 2022; 365:120105.