



Virginia Commonwealth University
VCU Scholars Compass

Undergraduate Research Posters

Undergraduate Research Opportunities
Program

2022

The Water Solubility of Ursolic Acid Complexes at Different Choline Concentrations

Sera Lim

Virginia Commonwealth University

Renjie Zhan

Virginia Commonwealth University

Phillip M. Gerk

Virginia Commonwealth University

Follow this and additional works at: <https://scholarscompass.vcu.edu/uresposters>



Part of the [Pharmaceutical Preparations Commons](#), and the [Pharmaceutics and Drug Design Commons](#)

© The Author(s)

Downloaded from

Lim, Sera; Zhan, Renjie; and Gerk, Phillip M., "The Water Solubility of Ursolic Acid Complexes at Different Choline Concentrations" (2022). *Undergraduate Research Posters*. Poster 390.

<https://scholarscompass.vcu.edu/uresposters/390>

This Book is brought to you for free and open access by the Undergraduate Research Opportunities Program at VCU Scholars Compass. It has been accepted for inclusion in Undergraduate Research Posters by an authorized administrator of VCU Scholars Compass. For more information, please contact libcompass@vcu.edu.



The Water Solubility of Ursolic Acid Complexes at Different Choline Concentrations



Sera Lim, Renjie Zhan, Dr. Phillip M. Gerk
VCU School of Pharmacy, Department of Pharmaceutics

Abstract

The purpose of this experiment was to determine whether an aqueous choline complex of ursolic acid will increase its dissolution in water. The dried complexes were combined with water and vortexed in 37°C to allow dissolution. Then, they were centrifuged and analyzed with HPLC-MS. The results helped us identify the optimal choline to ursolic acid complexes and recognize the effectiveness of salt complex formation for the oral bioavailability of ursolic acid.

Introduction

- Ursolic acid (UA) is a natural triterpene acid that can be commonly found in various fruits, plants, herbs, and vegetables^[3].
- UA is known to have numerous pharmacological benefits including anti-inflammatory, anti-viral, antioxidant, and anti-tumor activity as well as liver protection, immune function enhancement, and lowering blood glucose^[1,5].
- Ursolic acid can be taken orally as a currently marketed dietary supplement which would need to dissolve in the gastrointestinal tract, permeate the intestine, and survive metabolic enzymes before reaching the blood^[2,4].
- Unfortunately, ursolic acid is extremely hydrophobic, thus it is poorly soluble in water (with solubility less than 1 µg/mL), giving UA a predicted bioavailability of less than 1%.
- In an attempt to combat the low oral bioavailability of ursolic acid, we used the method of salt complex formation to study and determine whether there was evidence of an increase in dissolution. In this research project, salts of UA at different choline concentrations were prepared and further analyzed to find the optimal choline to UA ratio in terms of highest water solubility.

Methodology

- Varying ratios of choline hydroxide to ursolic acid (UA) were mixed in water to determine the stoichiometry of the complex regarding their water solubility (ratios tested: 1.75, 2, 2.5, 3, 4).
- Those UA salt complexes were dried for 10-14 days at room temperature.
- Approximately 50mg of each UA salt complex was combined with 50µL of water and vortexed for 2 hours at 37°C followed by centrifugation at maximum speed (17000RPM) for 20 minutes to remove undissolved materials..
- Supernatants were then analyzed by performing HPLC-MS on a Cogent bidentate C18 column (with 90% methanol and 10% 5 mM ammonium acetate) and detected by mass spectrometry in negative ion mode ($[M-H]^- = 455$).
- Each UA complex was run in triplicates for greater validity, and samples were quantified by interpolating from the UA standard curve.

Results



Figure 1: An image of the choline to ursolic acid ratios tested for water solubility.

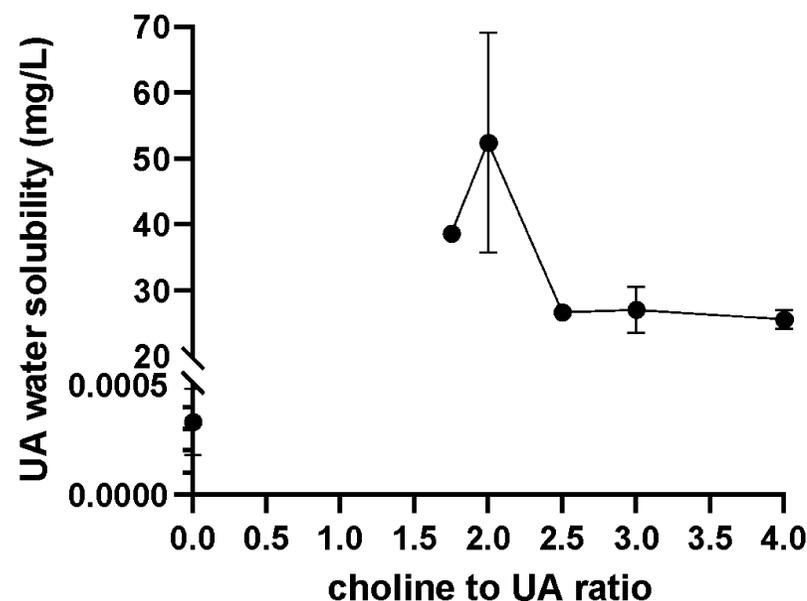


Figure 2: Water Solubility of Ursolic Acid Complexes in Different Choline Concentrations.

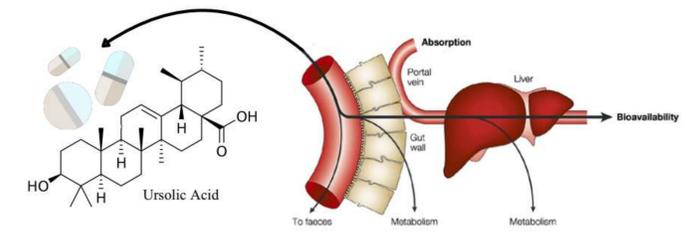
- Water solubility for ursolic acid containing no choline concentration was 0.00034mg/L.
- UA water solubility was highest at a choline:UA ratio of 2
- Higher ratios of choline:UA showed about half the UA solubility
- UA solubility was enhanced by $> 10^5$ fold in the 2:1 choline:UA complex

Discussion

- The data showed that a choline to UA ratio of 2 was optimal. However, the large variability shows that the solubility of UA is a challenging issue.
- Compared to the water solubility value for the control UA, adding choline and making salt complexes did show dramatic improvement in solubility.

Conclusion

Ursolic acid has potential as a treatment for multiple types of conditions and diseases. However, its oral bioavailability is problematic, beginning with its poor aqueous solubility. Therefore, a more novel ursolic acid preparation, having enhanced solubility, is needed. Our choline complex dramatically improved the water solubility of UA. Increasing our understanding of the complex properties of ursolic acid will help us advance towards achieving a positive improvement on its oral bioavailability. Although it will be challenging, we hope to compose an oral dosage form of UA that will efficiently and successfully reach systemic circulation.



Works Cited

- [1] Alfei, S., Schito, A. M., & Zuccari, G. (2021). "Considerable Improvement of Ursolic Acid Water Solubility by Its Encapsulation in Dendrimer Nanoparticles: Design, Synthesis and Physicochemical Characterization." *Nanomaterials (Basel, Switzerland)*, 11(9), 2196. <https://doi.org/10.3390/nano11092196>
- [2] McClements, J. D., & Xiao H. (2014). "Excipient foods: designing food matrices that improve the oral bioavailability of pharmaceuticals and nutraceuticals." *Food Funct.*, 5, 1320-1333. 10.1039/C4FO00100A
- [3] Seo, D. Y., Lee, S. R., Heo, J. W., No, M. H., Rhee, B. D., Ko, K. S., Kwak, H. B., & Han, J. (2018). "Ursolic acid in health and disease." *The Korean journal of physiology & pharmacology: official journal of the Korean Physiological Society and the Korean Society of Pharmacology*, 22(3), 235-248. <https://doi.org/10.4196/kjpp.2018.22.3.235>
- [4] Serajuddin A.T.M. (2007). "Salt formation to improve drug solubility." *Adv. Drug Deliv. Rev.*, 59(7), 603-616, 10.1016/j.addr.2007.05.010
- [5] Woźniak, Ł., Sylwia S., & Krystian M. (2015). "Ursolic Acid—A Pentacyclic Triterpenoid with a Wide Spectrum of Pharmacological Activities" *Molecules* 20, no. 11: 20614-20641. <https://doi.org/10.3390/molecules201119721>
- [6] iStock images

Acknowledgements

Special thanks to Dr. Gerk for his continuous guidance throughout the research process, to Renjie Zhan for the help around the lab, and to the VCU Department of Pharmaceutics for the opportunity.