

University of Groningen

## Exploring natural products: from herbal resources, microbial synthesis to animal models

Guan, Zheng

DOI:  
[10.33612/diss.846916968](https://doi.org/10.33612/diss.846916968)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2024

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
Guan, Z. (2024). *Exploring natural products: from herbal resources, microbial synthesis to animal models*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.  
<https://doi.org/10.33612/diss.846916968>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

# Appendix

**Acknowledgements**

**List of publications**

**About the author**

## Acknowledgments

Firstly, I would like to thank my alma mater, the **University of Groningen**, and my supervisor, Professor **Wim J. Quax**, for their great tolerance that allowed me to come back and complete my doctoral thesis after years of contemplation and confusion that lasted even longer than the Eight-Year of the Anti-Japan War in the Chinese history. If one day I am fortunate enough to make a research breakthrough that can benefit human health, it will undoubtedly be due to your cultivation and guidance, and I will always be grateful!

In the winter of 2013, when I met my mentor, Professor **Wim J. Quax**, at the PhD workshop in Beijing, it was actually the lowest point of my life. At the end of my rope, it was Professor **Quax** and the **University of Groningen** who saved my academic career. If there is anything I want to be most grateful for in this life, besides my parents who gave birth to me, it is dear **Wim** who has always led me, tolerated me, and saved my academic career twice from enrollment to graduation.

Time flies, and during this decade of ups and downs that can be described as a “sea change”, too many things have happened and there are too many people I should be grateful for. At this memorable moment, I want to record them and offer my most sincere thanks to them!

First, I would like to express my thankfulness to my second supervisor Professor **Gerrit J. Polerands**. Dear **Gerrit**, you are so knowledgeable and critical in science and can always find the key points and problems of our projects. I appreciate the suggestions you provided on improving my projects during the Thursday seminars. You are our landmark in pursuing science as your winning projects indicated -- “VENI, VIDI, VICI”. Many thanks also go to Professor **Hidde J. Haisma**, Professor **Frank J. Dekker**, Dr. **Robbert Cool**, and Dr. **Yikelin L. Boersma**, you highly learned and passionate scientists make our group a wonderful department for doing scientific research and a super great family.

I am also very thankful for Prof. **Peter Olinga**, Prof. **Klaas Poelstra** and Prof. **Elfahmi** as the reading committee. Thank you for being interested in my thesis and investing time in evaluating and giving advice to improve it.

I gratefully acknowledge the scholarship from **China Scholarship Council** to support my study and life in the Netherlands. I would also like to thank Prof. **Ailiang Chen** and peer **Wei Li** from the Institute of Quality Standards and Testing Technology for Agro-products, Key Laboratory of Agro-product Quality and Safety, Chinese Academy of Agricultural Sciences, and School of Medicine, Zhejiang University, respectively, for collaborating and encouraging me to carry out multidiscipline research during my PhD period in China.

Besides, many thanks go to our technicians in our department, **Rita**, **Ronald**, and **Pieter** for making our super-large group run smoothly. **Rita**, I still remember the bet between us. You always encourage me and remind me to finish my thesis as soon as I can. Actually, it is one of

the reason that I have not given up to finish my thesis over the decade. I think the beer I own you is enough for you for the next decade. I will wait and keep the unwritten thanks to serve you as my Dutch sister in China. **Ronald**, you are my role model for you know everything in multi-fields, biotech, docking, even computer and internet. Thanks for helping me to finish the CrtM paper, and teaching me the protein separation tech and the AKTA protein purification system. I will remember your intelligent green-blue eyes and your cute daughter. **Pieter**, you helped me a lot in reflux extraction, GC-MS, HPLC and the connection to analyze my samples in MS department. I can never complete my projects without your help. I am happy to work with you, the humorous chemist in the past years.

Dear **Yvonne, Janita, and Eline Kos**, thank you for your professional paper work, which made my study at the university more organized and efficient. I would also like to thank Dr. **Karen Voskamp, Cathy, Ingrid** and Dr. **Anke Schuster-Koster**, for helping me with the registration and graduation issues.

Although the four years in Groningen were a period of confusion for me, I regretted wasting my time in the past. However, the excellent learning and working environment at Groningen has been pushing me forward, as if nothing has been missed. The hospitality, friendliness and diversity of the people and culture, as well as the healthy, exciting and colorful living environment of the Netherlands, have left a deep impression on my memory. From then on, "the elsewhere became another hometown in my dream" that I will never forget.

I remember the impressive biosafety and biotech courses, where I learned to understand the bacteria and proteins. In **Gerrit's** enzyme course, I learned the practical rule that "only the small enzymes, with limited active residues can be well used for directed mutation". I also remember **Rita's** demonstration for cell culture and plasmid transformation.

Next, I would like to thank our "*Bacillus* research group" people: **Yafeng, Hegar, Ingy, Linda and Dan**. **Yafeng**, you helped me so much that I cannot thank you enough. It's really nice experience of traveling to Amsterdam, Lyons, and participate the CHAINS conference with you, jogging and talking in Stadspark and organizing the winter school together. **Hegar**, it's so nice to learn from you about how to construct MVA pathway in *Bacillus*. **Ingy**, I learned a lot from your excellent presentations, writing skills as well as our monthly meetings. **Linda**, I think we had a wonderful experience at the PhD day, your dancing really impressed me. **Dan**, thanks for all the materials you left in the stock and the experience you've taught me. I wish you all be happy and a successful career.

I would like to give my thanks to the Dr. **Ingrid A.M. van Roosmalen**, for your enthusiasm in science, which inspired me a lot, and your consistent help for improving my English. I would like to thank Dr. **Robbert Cool**, for let me know how the academic system runs in the Netherlands, and show diversified happy life, which even can be written down as a wonderful tale, e.g. "how an amphibious scientist find his role in a TV play". I would also

like to thank people in our department, **Baojie, Jielin, Putri, Magda, Christel, Yufeng, TjieKok, Jan-Ytzen, Yizhou, Xinyu, Chao, Haigen, Abel, Lieuwe, Zainal, Jan, Joko, Harsh, Mehran, Martijn, Shanshan, Laura, Hao, Guangcai, Fangyuan, Bin, Olivia, Marie, Saif, Faizan, Zhangping, Alex, Andreas, Sabry, Eman, Saravanan, Michele, Ele, Ting, Siwei, Deng, Hannah, Roberta, Yan, Nikolaos, Petra, Xiaofang, and Nia**. It's nice to know you guys, and thank you for your interesting conversations, nice parties and your assistance.

Thanks also goes to my other friends in Groningen: **Jiaying, Chengtao, Wei, Rui, Xiadong, Chengying, Ji, Yang, Yanjuan, and Yuanze**, thank you for inviting me many times to your places and providing me delicious food and interesting talks. I wish you a happy life.

Besides, I also want to thank the excellent courses and transferable EC system in Groningen and Europe, especially some impressive courses, e.g. Publishing in English for GSMS PhD students (organized by Dr. **Diane Black**), which helped my academic writing a lot; Quantative Bioanalysis (organized by Prof. **N.C. van de Merbel**), which practically shown us how the contract research organization work, and taught us the system/way in industrial and clinical bioanalysis; Good Research Practices: GCP/GLP (Prof. **J.H.G. Jonkman**), which taught us how the European Medicines Agency works and how to apply these rules and regulations in medical Labs and medical activities, such as new drug development. Also, many many thanks goes to the EMBO Practical Course on Metabolomics Bioinformatics for Life Scientists. During the one week course in European Bioinformatics Institute, we 29 students study, talk, eat, and sleep with the 17 teachers in the same building. The exciting discussions always starts from half past 7 and end over 22 everyday, I even reluctant to spend time going to the restroom for people's incisive talks. I can remember Dr. **Reza Salek's** encouragement, Dr. **Pietro Franceschi's** teaching skills especially the use of "Kahoot!". The impact of Dr. **Steffen Neumann's** work in natural products and plant biochemistry, the humorous intruduction of the Galaxy by Dr. **Etienne Thévenot**, and the multi-platform integration strategy from Dr. **Johan Westerhuis** are all affected me a lot. In addigion, I've also learned a motto from Dr. **Ralf Weber** "Good science costs money!", which as a stamp burned into my brain and was been proved in an adverse way in the followling past years that generated my unprecedented strong craving for funds. And I want to thank Prof. **Marta Cascante** and Dr. **Naomi Rankin** in particular, for their amiable and enthusiastic talks to teach and answer my questions in bioflux and NMR techniques. In the end, many thanks for my Chinese friends **Lin** and **Wei**, from Swedish University of Agriculture Sciences and Wageningen University, respectively, for their companion and interesting talks during the whole week in Hinxton.

I would like to continue my thanks to the other teachers of the wonderful programs that I was participated, Prof. **Jan Pieter Abrahams** from Leiden University, for organizing the interesting workshop "Life Sciences with Industry" in Lorenz center; Prof. **Rainer Bischoff**, Professor **Frank J. Dekker**, and Dr. **Hjalmar Permentier** for helping us teach the winter school students. And **Marcel de Vries** from MS department for helping my research.

Furthermore, I would like to acknowledge my former colleagues in Jiangxi Science and Technology Normal University, especially Prof. **Xuemin Duan**, Prof. **Baoyang Lu**, Prof. **Zhenhua Chen**, Prof. **Liang Peng**, Prof. **Jintao Wang**, Prof. **Bin Zhou** and director **Ping Wang** for their trust and help during the past years. Also Dr. **Bubing Xu**, the chairman of

Jiangxi RV Pharmaceutical.,Ltd., for his help and support in my research in the past and the near future.

Last but not least, I would like to thank my beloved family. My dear **father** and **mother**, your unconditional support, help and love are deeply in my heart. I know that whenever and wherever I am, you are firmly standing behind me and give me power to overcome difficulties and to enjoy happy moments. I love you!

亲爱的爸爸、妈妈，感谢你们对我的养育之恩和一直以来的关心鼓励和支持，我永远爱你们。

Zheng (Jane)

Oct. 2023



## List of publications

1. **Guan Z<sup>#</sup>**, Song Y<sup>#</sup>, De Vries M, Permentier H, Tepper P, Van Merkerk R, Setroikromo R, Quax W\*. The promiscuity of squalene synthase-like enzyme: dehydrosqualene synthase, a natural squalene hyperproducer? (manuscript submitted)
2. Zhang K, Fan Y, Zhou L, Li W, Chen Z\*, **Guan Z\***. Construction of mouse model of ankle sprain. *Journal of Jiangxi science & technology normal university*. 2022;78–81.
3. Song Y, **Guan Z**, Van Merkerk R, Pramastya H, Abdallah II, Setroikromo R, Quax W\*. Production of squalene in *Bacillus subtilis* by squalene synthase screening and metabolic engineering. *Journal of agricultural and food chemistry*. 2020;68:4447–4455.
4. Zhou Y, Zhao X, Chen Y, Chen Y, Wang X, Zhao X, **Guan Z\***, Gao J. Research progress on tumor immune checkpoint inhibitors and their combination therapy. *China Pharmacy*. 2020;31:890–896.
5. Zhou Y, Fan Y, Zhang D, **Guan Z**, Wang C\*. Study on the inhibition effects and stability of Gardenia ethanol extract on food-borne bacteria. *China Food Additives*. 2019;30:84–88.
6. **Guan Z**, Song Y, Li W, Chen A, Zhou Y, Shao F, Quax W, Chu X\*, Lv G. Pondering study of traditional Chinese medicine from the perspective of modern patients. *China Journal of Traditional Chinese Medicine and Pharmacy*. 2018;33:4274–4277.
7. Li W, **Guan Z**, Brisset J, Shi Q, Lou Q, Ma Y, Su S, Ying H, Sa X, Chen Z\*, Quax W\*, Chu X\*. A nonalcoholic fatty liver disease cirrhosis model in gerbil: the dynamic relationship between hepatic lipid metabolism and cirrhosis. *International journal of clinical and experimental pathology*. 2018;11:146.
8. **Guan Z<sup>#</sup>**, Xue D<sup>#</sup>, Abdallah II, Dijkshoorn L, Setroikromo R, Lv G, Quax W\*. Metabolic engineering of *Bacillus subtilis* for terpenoid production. *Applied Microbiology and Biotechnology*. 2015;99:9395–9406.
9. **Guan Z**, Li S, Lin Z, Yang R, Zhao Y, Liu J, Yang S, Chen A\*. Identification and quantitation of phenolic compounds from the seed and pomace of *Perilla frutescens* using HPLC/PDA and HPLC–ESI/QTOF/MS/MS. *Phytochemical Analysis*. 2014;25:508–513.
10. **Guan Z**, Liu J, Bai W, Lv Z, Jiang X, Yang S, Chen A\*, Lv G\*. Label-free and sensitive fluorescent detection of sequence-specific single-strand DNA based on S1 nuclease cleavage effects. *PLoS One*. 2014;9:e108401.
11. Liu J, **Guan Z**, Lv Z, Jiang X, Yang S, Chen A\*. Improving sensitivity of gold nanoparticle based fluorescence quenching and colorimetric aptasensor by using water



- resuspended gold nanoparticle. *Biosensors and Bioelectronics*. 2014;52:265–270.
12. Lin Z, Yang R, **Guan Z**, Chen A, Li W\*. Ultra-performance LC separation and quadrupole time-of-flight MS identification of major alkaloids in *Plumula Nelumbinis*. *Phytochemical Analysis*. 2014;25:485–494.
  13. Geng Q, Zheng C, **Guan Z**\*, Zhang X, Zhu C, Yang S, Chen A\*. Protective effect of perilla seed on acute hepatic injury in mice as evaluated by metabolomic analysis. *Food Science*. 2014;35:260–265.
  14. **Guan Z**, Lin Z, Yang R, Chen A. Pharmacological effects of *Fructus Aurantii* and climate effects on its quality. *Food and Nutrition in China*. 2014;20:65–69.
  15. Lv Z, Chen A\*, Liu J, **Guan Z**, Zhou Y, Xu S, Yang S, Li C\*. A simple and sensitive approach for ochratoxin A detection using a label-free fluorescent aptasensor. *PloS one*. 2014;9:e85968.
  16. **Guan Z**<sup>#</sup>, Zhou Y<sup>#</sup>, Liu J, Jiang X, Li S, Yang S, Chen A\*. A simple method to extract DNA from hair shafts using enzymatic laundry powder. *PloS one*. 2013;8:e69588.
  17. **Guan Z**, Liu J, Zhou Y, Jiang X, Yang S, Chen A\*. A fast hair shaft DNA extraction method and its influence on PCR amplification. *Journal of Anhui Agricultural Sciences*. 2013;41:10232–10235.
  18. Lv Z, Liu J, Zhou Y, **Guan Z**, Yang S, Li C, Chen A\*. Highly sensitive fluorescent detection of small molecules, ions, and proteins using a universal label-free aptasensor. *Chemical Communications*. 2013;49:5465–5467.
  19. Chen A, **Guan Z**. Method for extracting perilla seed hydrophilic chemical component from perilla seed oil residue. 2013, Patent Number: CN103099845B
  20. Chen A, **Guan Z**, Bai W, Jiang X, Liu J. Composition with functions of dispelling effects of alcohol and protecting liver and beverage comprising composition. 2014, Patent Number: CN104257788A
  21. **Guan Z**, Chen A\*. Review of different DNA extraction methods in hair shafts. *China Biotechnology*. 2012;32:128–134.
  22. **Guan Z**, Ma X, Lv G\*, Huang W, Qiu S, Chen S, Chen S. Effects of VOM bp on IL-12, IFN- $\gamma$  and histamine levels of rats with allergic rhinitis. *Pharmacology and Clinics of Chinese Materia Medica*. 2011;27:70–72.

<sup>#</sup> Authors contributed equally.

\* Corresponding author.

## About the author

Guan Zheng was born on August 20th, 1980 in Zhejiang, China. Before the college entrance examination, she was blinded by a car accident for half year. After recovering her vision, she became a self-taught student and participated in the Chinese higher education examination program, and worked in the fields of international trade, marketing scheming, and management. In 2000, she became the sole inheritor of the family secret recipes entrusted by her grandmother on her deathbed. In 2002, she quit her job and independently contracted land to engage in the cultivation of tea and herbs. During this period, she worked at the Shanghai Lvgu Pharmaceutical Group, and studied under Professor Song Qiyin at the Medicinal Fungi Research Institute of Changchun University of Traditional Chinese Medicine. In 2006, she began studying science of Chinese traditional medicine at Zhejiang Chinese Medical University, while concurrently auditing courses from two senior grades. From autumn 2007 to spring 2008, she completed a Master course project major in pharmacology at the Peking University Health Science Center. In the spring of 2008, she skipped two grades and graduated with a comprehensive score that placed her ahead of all three grades of self-taught students at Zhejiang Chinese Medical University.

That same year, she was admitted to the master's program in science of Chinese traditional medicine at the university via the national postgraduate entrance examination and served as the class supervisor for new undergraduate students in their first semester. Subsequently, the President Wang Mingliang of the former Xi'an Huaxi University appointed her as the principal in establishing the School of Pharmacy. Soon afterwards, she was selected as a member of the cultural and creative entrepreneurship project jointly held by the Hangzhou Communist Youth League and Zhejiang University. As a master's degree candidate, she conducted her research at the modernization of traditional Chinese medicine pharmacodynamics research center of Ministry of Science and Technology in Zhejiang Chinese Medical University, and Department of Natural Medicine in Peking University, under the guidance of Professors Lv Guiyuan and Chen Shizhong, respectively. In 2011, she obtained a medical master's degree, and her thesis was selected as an outstanding master's thesis and published online on the China National Knowledge Infrastructure.

She subsequently worked at the Institute of Quality Standards and Testing Technology for Agro-products (Key Laboratory of the Ministry of Agriculture), Chinese Academy of Agricultural Sciences with cooperating mentor Researcher Chen Ailiang. In the fall of 2014,

she was admitted to the doctoral program in Chemistry and Pharmaceutical Biology department at the University of Groningen with the support of the China Scholarship Council and Professors Wim J. Quax and Gerrit J. Poelarends as her supervisors. During her time there, she participated in the Life Science with Industry event at the Lorenz Center in Leiden University in the Netherlands and an EMBL metabolomics course at European Bioinformatics Institute in Hinxton, UK. At the end of 2017, she co-organized a winter school for international university students with the support of Professor Quax and professors from the school of medicine, and Chu Kochen Honors College of Zhejiang University, and the Zhejiang Chinese Medical University. At the end of 2018, she qualified as high-level talent introduced by Jiangxi Science and Technology Normal University and began teaching at the School of Pharmacy in 2019.

The sole aim of the author is inheriting and developing traditional Chinese medicine to protect people's health. Her effort is aimed to utilize all possible means and modern scientific techniques to prevent effective treatments from extinction. Her ultimate goal is to develop these undisclosed therapies into drugs that everyone can easily access.