

# **Exploring anti-SARS-CoV-2 natural products: dual-viral target inhibition by delphinidin and the anti-coronaviral efficacy of deapio platycodin D**

Jiani Lu<sup>1,2,#</sup>, Yan Tang<sup>3,#</sup>, Hongtao Li<sup>1,2,#</sup>, Saisai Tian<sup>1,4</sup>, Xixiang Chen<sup>1</sup>, Xueyue Song<sup>6</sup>, Pengcheng Qin<sup>1,2,5</sup>, Jiangrong Xu<sup>1</sup>, Haiyan Zhu<sup>6</sup>, Liqiang Ni<sup>7</sup>, Huarong Du<sup>7,\*</sup>, Weidong Zhang<sup>1,4,\*</sup>, Weihua Li<sup>3,\*</sup>, Lili Chen<sup>1,2,\*</sup>

<sup>1</sup>The Research Center for Traditional Chinese Medicine, Shanghai Institute of infectious Diseases and Biosecurity, Shanghai Frontiers Science Center of TCM Chemical Biology, Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine. Shanghai, 201203, China

<sup>2</sup>Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China

<sup>3</sup>Shanghai Frontiers Science Center of Optogenetic Techniques for Cell Metabolism, Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, Shanghai, 200237, China

<sup>4</sup> School of Pharmacy, Second Military Medical University, Shanghai, 200433, China

<sup>5</sup>School of Pharmacy, Henan University, Kaifeng, 475001, China

<sup>6</sup>Department of Biological Medicines & Shanghai Engineering Research Center of ImmunoTherapeutics, School of Pharmacy, Fudan University

<sup>7</sup>Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China

\*Correspondence:

Huarong Du

Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China

E-mail: [huarongdu2017@shutcm.edu.cn](mailto:huarongdu2017@shutcm.edu.cn)

Weidong Zhang, Ph D

School of Pharmacy, Second Military Medical University, Shanghai, 200433, China; School of Pharmacy, Henan University, Kaifeng, 475001, China; Academy of Interdisciplinary Sciences, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China  
E-mail: wdzhangy@hotmail.com

Weihua Li, Ph D

Shanghai Frontiers Science Center of Optogenetic Techniques for Cell Metabolism, Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, Shanghai, 200237, China  
E-mail: whli@ecust.edu.cn

Lili Chen, Ph D

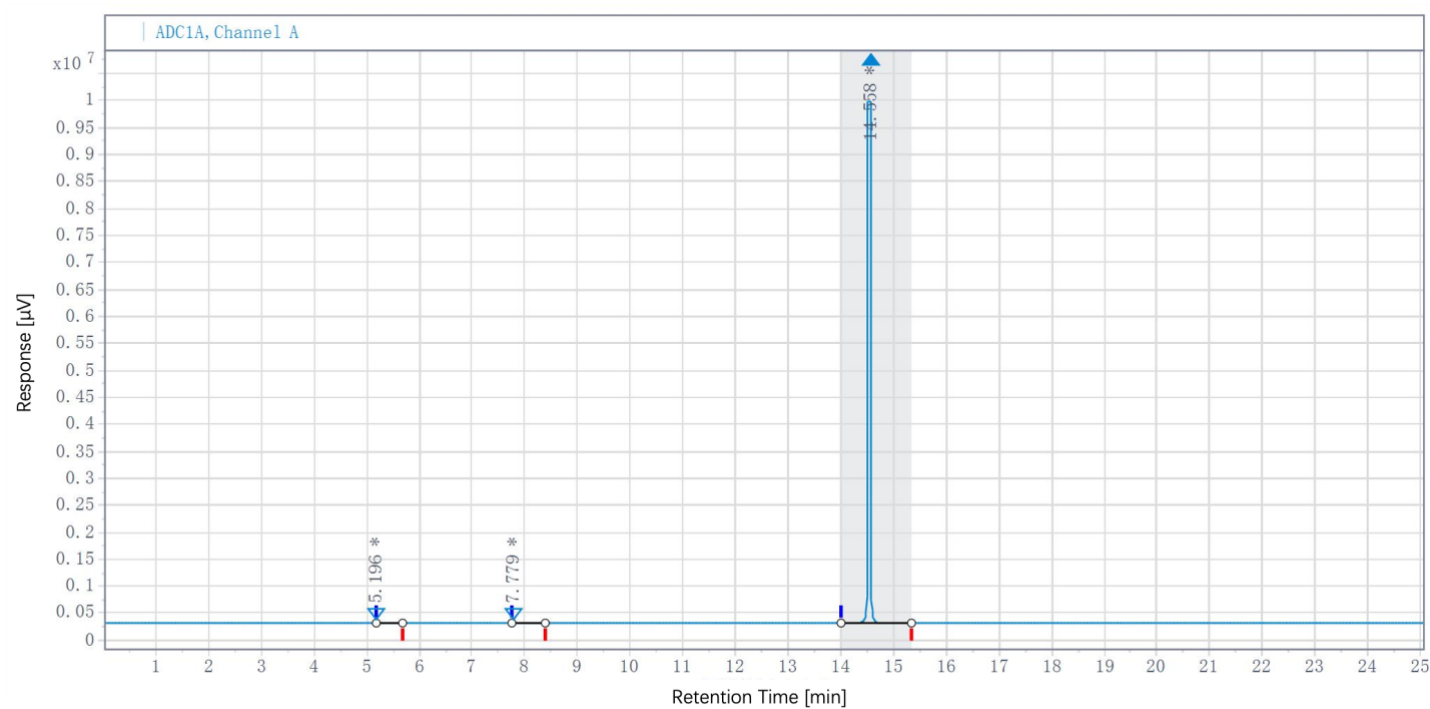
Shanghai Frontiers Science Center of TCM Chemical Biology, Institute of Interdisciplinary Integrative Medicine Research; Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China  
E-mail: [llchen@shutcm.edu.cn](mailto:llchen@shutcm.edu.cn)

# The contribution of these authors to this work is equal.

**Supplementary Table 1 The constituent herbs of QFPDD**

| Chinese Name  | English Name                            | Latin Name                                |
|---------------|-----------------------------------------|-------------------------------------------|
| Bai Zhu       | Atractylodes Macrocephala               | <i>Atractylodis Macrocephalae Rhizoma</i> |
| Chai Hu       | Bupleurum Root                          | <i>Bupleuri Radix</i>                     |
| Chen Pi       | Aged Tangerine Peel                     | <i>Citri Reticulatae Pericarpium</i>      |
| Fu Ling       | Poria Cocos                             | <i>Poria</i>                              |
| Gui Zhi       | Cinnamon Twig                           | <i>Cinnamomi Ramulus</i>                  |
| Huang Qin     | Baikal Skullcap Root                    | <i>Scutellariae Radix</i>                 |
| Huo Xiang     | Patchouli                               | <i>Agastache rugosus</i>                  |
| Jiang Ban Xia | Pinellia Rhizome (prepared with ginger) | <i>Pinelliae Rhizoma</i>                  |
| Kuan Dong Hua | Coltsfoot Flower                        | <i>Farfarae Flos</i>                      |
| Ma Huang      | Ephedra                                 | <i>Ephedrae Herba</i>                     |
| Shan Yao      | Chinese Yam                             | <i>Dioscoreae Rhizoma</i>                 |
| She Gan       | Belamcanda Rhizome                      | <i>Belamcandae Rhizoma</i>                |
| Sheng Jiang   | Fresh Ginger                            | <i>Zingiberis Rhizoma Recens</i>          |
| Sheng Shi Gao | Raw Gypsum                              | <i>Raw Gypsum</i>                         |
| Xing Ren      | Apricot Kernel                          | <i>Armeniaca Semen Amarum</i>             |
| Xi Xin        | Asarum                                  | <i>Asari Radix et Rhizoma</i>             |
| Ze Xie        | Alisma Rhizome                          | <i>Alismatis Rhizoma</i>                  |
| Gan Cao       | Liquorice                               | <i>Glycyrrhizae Radix et Rhizoma</i>      |
| Zhi Shi       | Immature Bitter Orange                  | <i>Fructus Aurantii Immaturus</i>         |
| Zhu Ling      | Polyporus                               | <i>Polyporus</i>                          |
| Zi Wan        | Purple Aster Root                       | <i>Asteris Radix et Rhizoma</i>           |

Supplementary Figure 1. HPLC for deapio platycodin D

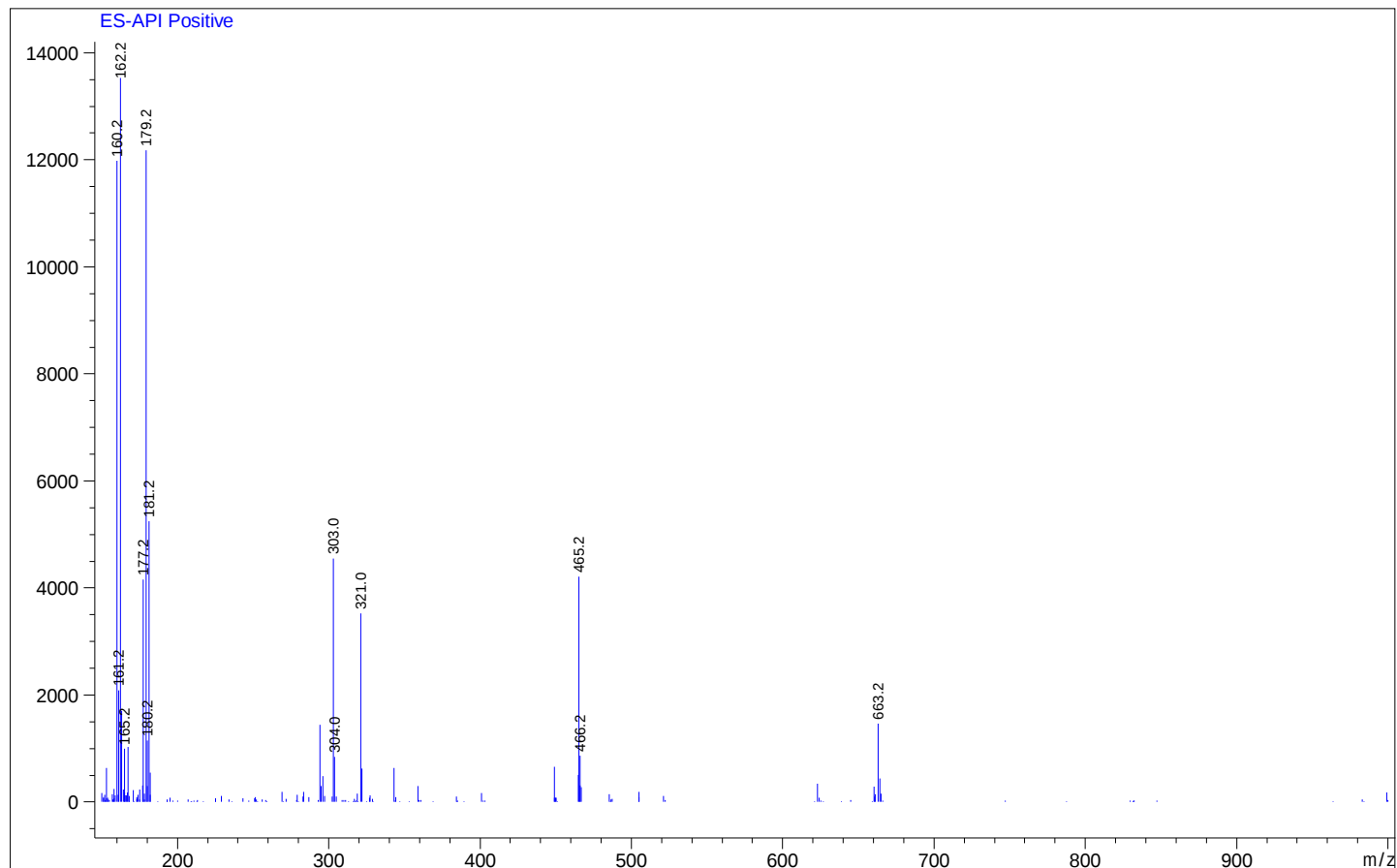


| # | Retention Time (min) | Peak Area   | Peak Area % | Peak Height |
|---|----------------------|-------------|-------------|-------------|
| 1 | 5.196                | 591.716     | 0.001       | 121.9       |
| 2 | 7.779                | 510.882     | 0.001       | 137.827     |
| 3 | 14.558               | 40300713.95 | 99.997      | 10799781.3  |

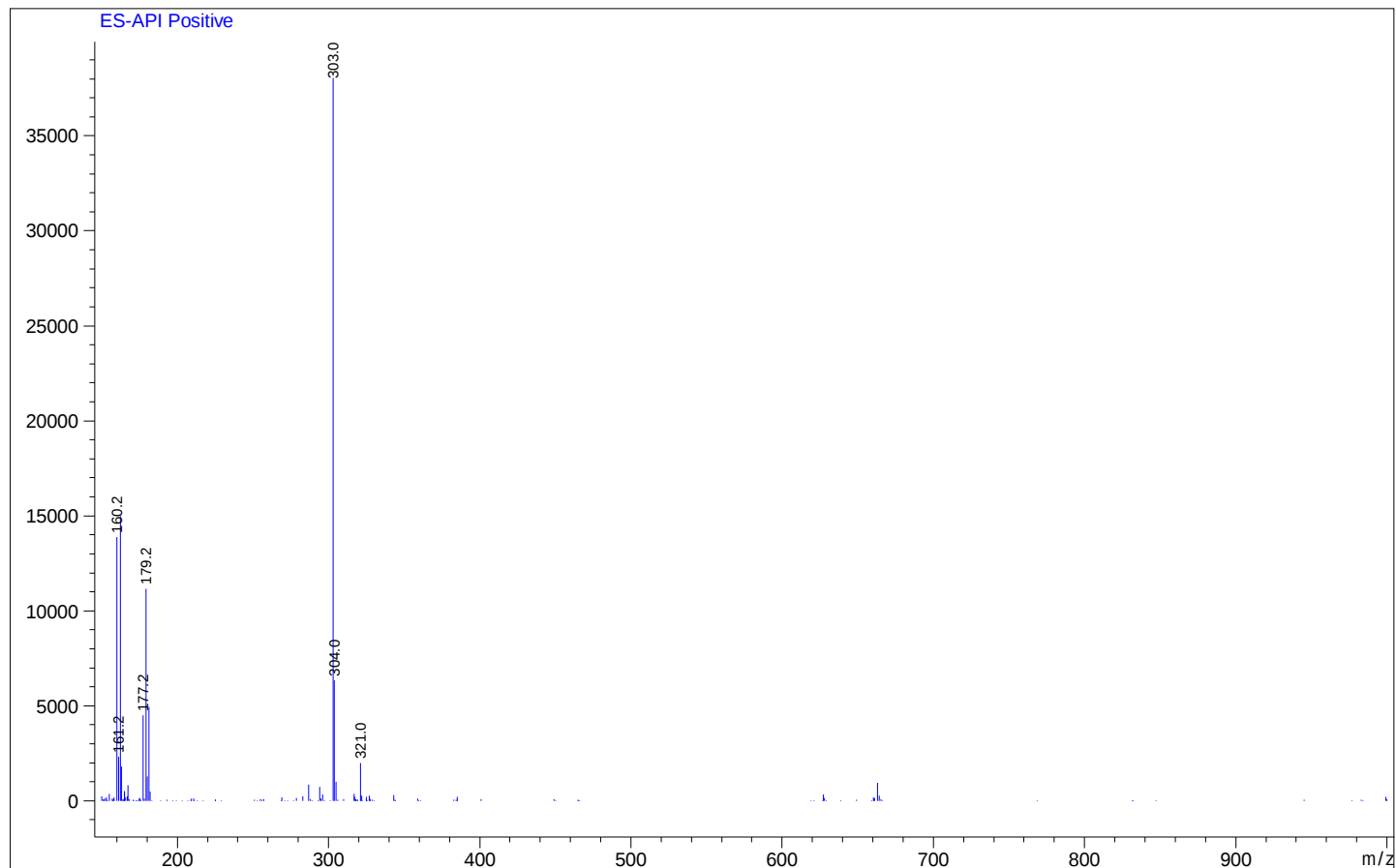
## Supplementary Figure 2. UPLC-MS for delphinidin

Ret. Time: 0.66

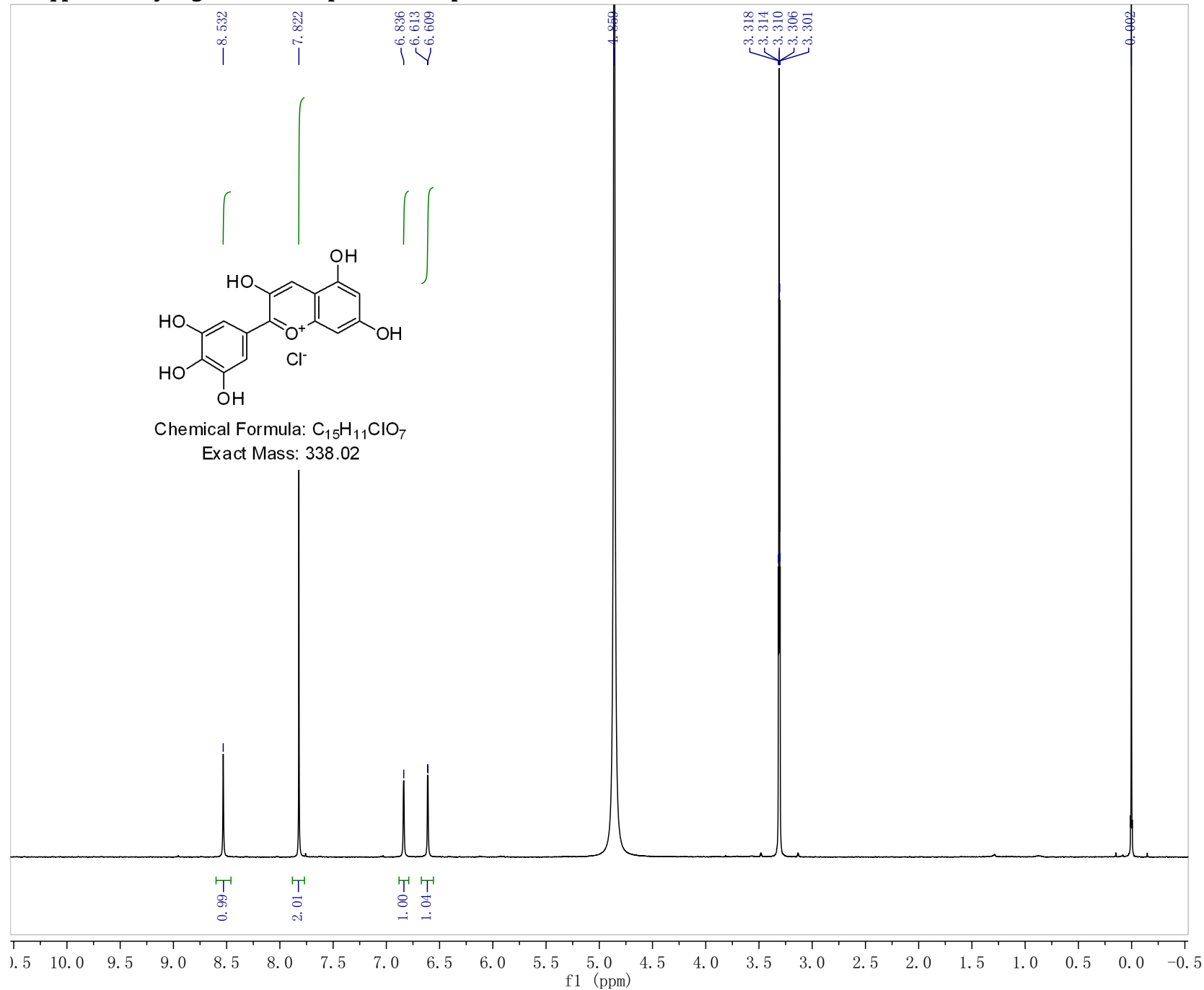
<<<< POSITIVE SPECTRA >>>>



Ret. Time: 0.70



Supplementary Figure 3. NMR spectra for delphinidin



| Parameter                 | Value               |
|---------------------------|---------------------|
| 1 Title                   |                     |
| 2 Origin                  | Bruker BioSpin GmbH |
| 3 Owner                   | nmrsu               |
| 4 Spectrometer            | Avance              |
| 5 Solvent                 | MeOD                |
| 6 Temperature             | 298.2               |
| 7 Pulse Sequence          | zg30                |
| 8 Experiment              | 1D                  |
| 9 Number of Scans         | 8                   |
| 10 Receiver Gain          | 101                 |
| 11 Relaxation Delay       | 1.0000              |
| 12 Pulse Width            | 8.0000              |
| 13 Acquisition Time       | 3.9977              |
| 14 Acquisition Date       | 2023-10-18T17:09:56 |
| 15 Modification Date      | 2023-10-18T17:19:33 |
| 16 Spectrometer Frequency | 400.13              |
| 17 Spectral Width         | 8196.7              |
| 18 Nucleus                | 1H                  |