**Supplementary Material**

**Improved solubility, dissolution rate and oral bioavailability of main biflavonoids from *Selaginella doederleini* extractby amorphous solid dispersion**

Bing Chen,1-3,\* Xuewen Wang,2,3,\* Yanyan Zhang,2,3 Kangping Huang,2,3 Hao Liu,2,3 Dafen Xu,2,3 Shaoguang Li,2,3 Qicai Liu,1,2 Jianyong Huang,4 Hong Yao,2,3,5 Xinhua Lin,2,3

1 Nano Medical Technology Research Institute, Fujian Medical University, Fuzhou, Fujian, China, 2 Higher Educational Key Laboratory for Nano Biomedical Technology of Fujian Province, Fujian Medical University, Fuzhou, Fujian, China, 3 Department of Pharmaceutical Analysis, School of Pharmacy, Fujian Medical University, Fuzhou, Fujian, China; 4 Department of Pharmaceutical, Fujian Medical University Union Hospital, Fuzhou, Fujian, China; 5 Fujian Key Laboratory of Drug Target Discovery and Structural and Functional Research, Fujian Medical University, Fuzhou, Fujian, China.

\* Both authors contributed equally to this work.

Correspondence:

**Prof. Xinhua Lin**

Department of Pharmaceutical Analysis, Fujian Medical University, No.1 Xueyuan Road, University Town, Fuzhou, 350122, China

Email 13906939638@163.com

**Prof. Hong Yao**

Department of Pharmaceutical Analysis, Fujian Medical University, No.1 Xueyuan Road, University Town, Fuzhou, 350122, China

Email yauhung@126.com

**Associated Prof. Jianyong Huang**

Department of Pharmaceutics, Fujian Medical University Union Hospital, Fuzhou, 350122, China

Email Hjy8191@163.com

**List of Supplementary Material Captions**

**Table S1.** 1-octanol/water partition coefficients (Mean±SD, n=3)

**Table S2.** Stability test of TBESD-ASD under an accelerated condition (Mean±SD, n=3)

**Table S3.** The average weights and tumor weight-inhibitions of mice before and after treatment (Mean±SD, n=6)

**Table S1.** 1-octanol/water partition coefficients (Mean±SD, n=3)

|  |  |
| --- | --- |
| **Components** | **log Kow** |
| **pH 7.4** |
| **Amentoflavone** | 3.84±0.05 |
| **Robustaflavone** | 3.88±0.06 |
| **2'',3''-Dihydro-3',3'''-biapigenin** | 3.93±0.11 |
| **3',3'''-Binaringenin** | 3.98±0.06 |
| **Delicaflavone** | 4.23±0.11 |

**Table S2.** Stability test of TBESD-ASDs under an accelerated condition (Mean±SD, n=3)

|  |  |
| --- | --- |
| **Content of total biflavonoids**  | **Time** |
| **0 day** | **30 day** | **60 day** | **60 day** |
| **Accelerated condition (25℃/75 % RH)** | 100.00±0.35 | 99.46±0.72 | 99.26±0.86 | 98.85±0.64 |

**Table S3.** The average weights and tumor weight-inhibitions of mice before and after treatment (Mean±SD, n=6)

|  |  |
| --- | --- |
| **Groups** | **MVD** |
|
| **Control** | 96.24 ±6.91 |
| **Dox** | 38.58 ± 6.35\*\* |
| **TBESD** | 72.85 ± 5.35\*\* |
| **TBESD-ASDs** | 46.05 ± 4.66\*\* |

Compared with control: \*p<0.05, \*\*p<0.01.

**Figure legends**

**Fig. S1** Chemical structures of amentoflavone, robustaflavone, 2'',3''-dihydro-3',3'''-biapigenin, 3',3'''-binaringenin, and delicaflavone.



**Fig. S1** Chemical structures of amentoflavone, robustaflavone, 2'',3''-dihydro-3',3'''-biapigenin, 3',3'''-binaringenin, and delicaflavone.