## Introduction

Throughout the history of traditional medicine, plants have consistently played a vital role in providing therapeutic remedies. Even amidst the rapid advancement of synthetic medicinal chemistry and biotechnology, screening for bioactive compounds from plant sources remains one of the most significant and effective strategies for identifying lead compounds for new drugs. Statistics from the FDA and international health organizations indicate that a substantial proportion of drugs approved in recent decades are derived-either directly or indirectly-from natural sources, particularly in the treatment of cancer and inflammatory diseases. As one of the world's sixteen most biodiverse nations, Vietnam faces both significant opportunities and challenges in harnessing this wealth of indigenous knowledge and valuable genetic resources. Consequently, systematic phytochemical research holds not only fundamental scientific significance but also immense practical value, contributing to the affirmation of national sovereignty over medicinal resources.

The genus *Asarum* L., belonging to the family Aristolochiaceae, is a large genus comprising over 100 species distributed primarily across the temperate regions of the Northern Hemisphere and East Asia. In the traditional medicine systems of countries such as China, Japan, and Vietnam, species of this genus are widely utilized as valuable medicinal agents for treating rheumatism, joint and bone pain, toothache, bronchitis, and various infectious diseases. Modern global research has demonstrated that the *Asarum* genus is a rich source of diverse secondary metabolites. Notable constituents include essential oils (containing phenylpropanoid and monoterpene derivatives), lignans, flavonoids, and phenanthrenes. These compounds exhibit a broad spectrum of biological activities-including antibacterial, antifungal, antioxidant, and anti-inflammatory effects-and, notably, demonstrate cytotoxic activity against various human cancer cell lines. In Vietnam, the *Asarum* genus is relatively diverse, comprising approximately 11 species concentrated mainly in high-mountain regions.

Despite this immense potential, the chemical and biological profiles of Vietnamese *Asarum* species have not yet been comprehensively or systematically investigated. Previous studies have largely been limited to analyzing the chemical composition of essential oils or isolating simple compound groups from common species. Endemic or rare species-such as *Asarum yentuense*, *Asarum cordifolium*, and *Asarum geophilum* have not yet undergone in-depth study regarding the non-volatile constituents present in their extracts. Furthermore, data regarding the antibacterial and antifungal properties at the molecular level, as well as the cytotoxic mechanisms of these species in Vietnam, remain very limited. In particular, many species face the risk of severe population decline due to overexploitation and habitat loss.

Based on the reasons mentioned above, the thesis topic "Research on the chemical composition and biological activity of *Asarum cordifolium*, *Asarum yentuense*, and *Asarum geophilum* species in Vietnam" was chosen for implementation. This is a timely and essential undertaking aimed at providing reliable scientific data to help guide the conservation and effective utilization of these valuable medicinal plant resources.

## Chapter 1: OVERVIEW

This chapter synthesizes domestic and international research on the genus *Asarum* L., focusing on the following key aspects:

Botany: An overview of the morphological characteristics, taxonomic classification, and distribution of the genus *Asarum* (family Aristolochiaceae). Approximately 11 species of this genus have been recorded in Vietnam, including rare and endemic species such as *A. yentuense* and *A. cordifolium*.

Regarding chemical composition: Studies indicate that *Asarum* possesses a diverse chemical profile, comprising two main groups: volatile compounds (rich in phenylpropanoids and monoterpenes) and non-volatile compounds (primarily lignans, flavonoids, phenanthrenes, and aristolactam derivatives).

Regarding biological activity: The review summarizes traditional medicinal uses (such as alleviating rheumatic conditions, relieving pain, and treating the common cold) alongside proven modern pharmacological activities, including antibacterial, antifungal, anti-inflammatory, and cytotoxic effects against cancer cells. Additionally, the chapter addresses the potential toxicity associated with aristolochic acids, compounds commonly found in this genus.

Conclusion drawn from the review: Although the genus *Asarum* has been extensively studied globally, data regarding the chemical composition (particularly compounds derived from extracts) and the mechanisms of action of *Asarum* species distributed in Vietnam remain very limited. This provides the practical basis for the selection of the research topic for this thesis.

## Chapter 2. RESEARCH OBJECTS AND METHODS

### 2.1 Research object

Plant samples: Three species of the genus *Asarum* collected in Vietnam between 2020 and 2021: *Asarum cordifolium* (collected in Sa Pa, Lao Cai), *Asarum yentuense* (collected in Uong Bi, Quang Ninh), and *Asarum geophilum* (collected in Trung Khanh, Cao Bang). Identification was performed by Dr. Nguyen Anh Tuan (Indochina Institute of Biology and Environment) and Dr. Nguyen Quoc Binh (Vietnam National Museum of Nature). Voucher specimens are deposited at the Institute of Chemistry of Natural Products (currently the Institute of Chemistry), Vietnam Academy of Science and Technology.

### 2.2 Research methods

#### 2.2.1 Chemical method

Essential oil extraction: Steam distillation using a Clevenger apparatus.

Compound extraction: Extraction with methanol, followed by liquid-liquid partitioning using solvents of increasing polarity (n-hexane, ethyl acetate).

Isolation: Separation via column chromatography (CC) using silica gel/RP-18 stationary phases and thin-layer chromatography (TLC).

Structure determination: Mass spectrometry (ESI-MS, HR-ESI-MS) and nuclear magnetic resonance spectroscopy (1D & 2D NMR) measured on a Bruker 500/600 MHz instrument.

Essential oil analysis: GC-MS system combined with GC-FID.

### 2.2.2 Biological methods

Antimicrobial activity: Determination of minimum inhibitory concentration (MIC).

Antioxidant activity: DPPH radical scavenging assay.

Anti-inflammatory activity: Evaluation of NO production inhibition in RAW 264.7 cells.

Cytotoxicity: MTT assay on liver cancer cells (Hep-G2).

### 2.2.3. Simulation method (in silico)

Molecular docking software is used to predict the interaction between the active compound and the target protein JAK2.

## Chapter 3. EXPERIMENT

This chapter describes in detail the experimental procedure for extracting and isolating compounds from three main Asarum species.

### 3.1 Asarum geophilum

#### *3.1.1. Extraction*

The dried sample (3 kg) was extracted with methanol and fractionated with n-hexane and ethyl acetate to yield the corresponding extracts.

#### *3.1.2. Isolation*

From the ethyl acetate (ACE) and aqueous (ACW) extracts, different chromatographic methods were used. Eighteen compounds (designated AG1 through AG18) were isolated, including two new compounds: chalcononaringenin 2′,4-di-O-*β*-D-glucopyranoside (AG1) and asageoside (AG2).

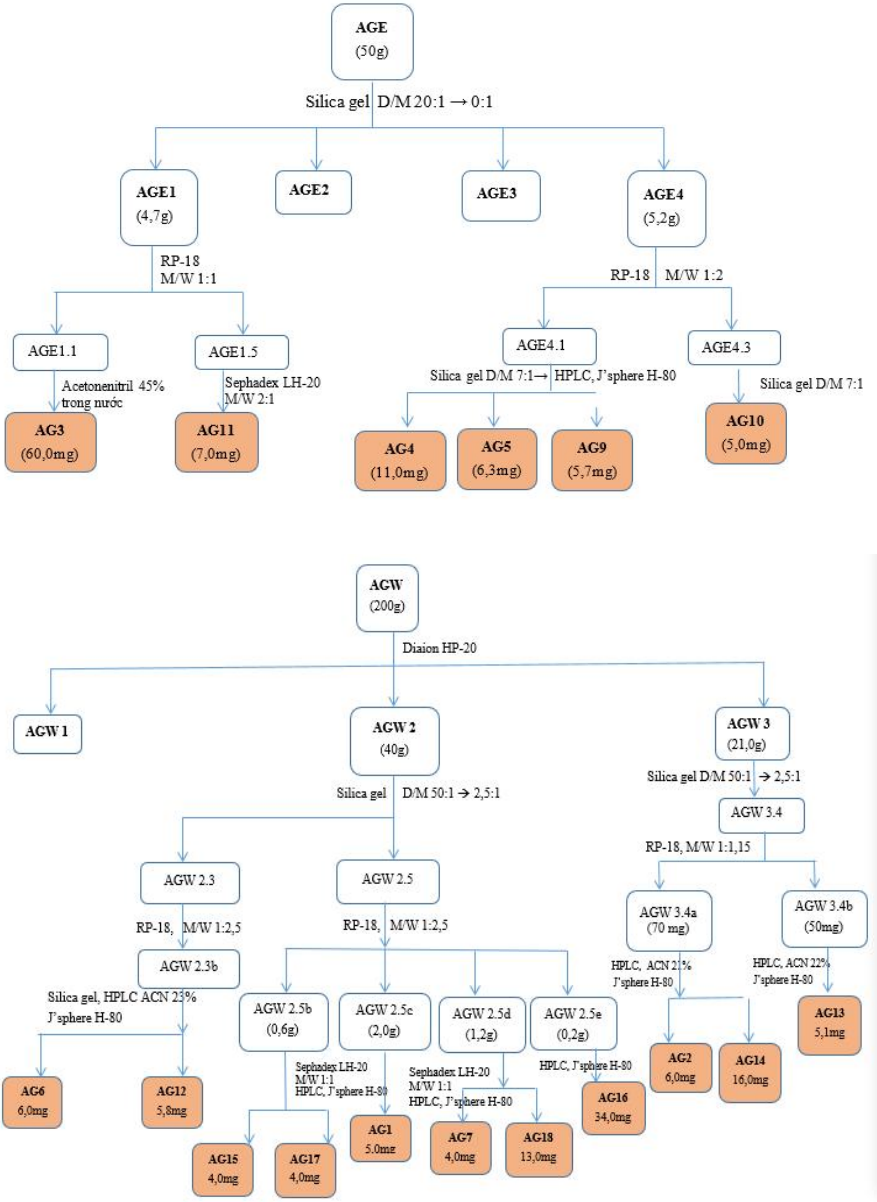



*Figure 3.1*. Scheme for the isolation of compounds from *A. geophilum*

### 3.2. Asarum cordifolium

#### *3.2.1. Extraction*

From the dried sample (1.2 kg), the corresponding extract fractions were obtained.

#### *3.2.2. Isolation*

Focus was placed on the n-hexane and ethyl acetate extracts.

Eight compounds were isolated, primarily phenylpropanoid derivatives (such as elemicin and methyl eugenol) and flavonoids.

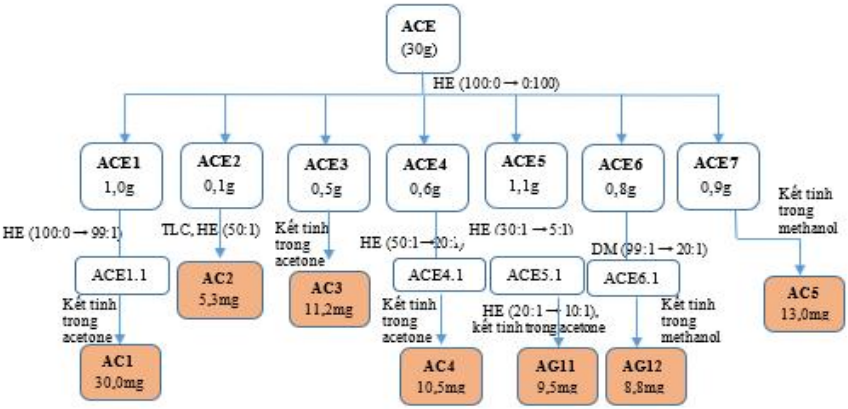



*Figure 3.2*. Scheme for the isolation of compounds from *A. cordifolium*

### 3.3. Asarum yentuense

#### *3.3.1. Extraction*

The dried sample (2.5 kg) was processed to obtain the extract residue.

#### 3.3.2. Isolation

Chromatography was performed on the n-hexane and ethyl acetate fractions.

Eight compounds were isolated, including characteristic flavonoids such as acacetin and cynaroside.

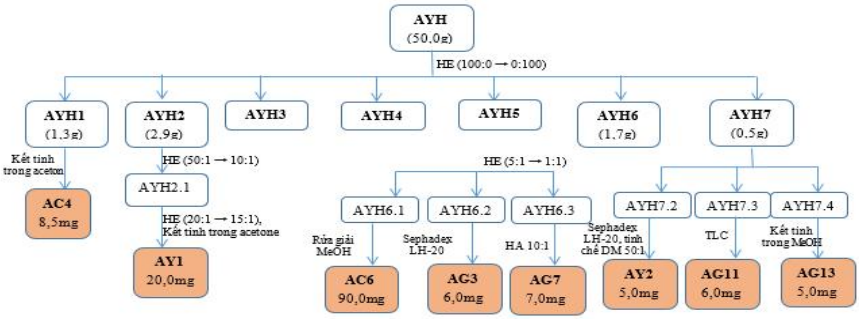



*Figure 3.3*. Scheme for the isolation of compounds from *A. yentuense*

### 3.4. Determination of essential oil composition of A. cordifolium, A. geophilum, and A. yentuense

The determination of the chemical composition of the essential oils from the three species *A. cordifolium, A. geophilum, and A. yentuense* was conducted as described in section 2.2.1.

### 3.5. Evaluation of biological activity

The biological activities of the essential oils (antimicrobial, antioxidant, and anti-inflammatory activities) and the cytotoxicity against cancer cell lines (Hep-G2, JAK2) of the extracts and certain isolated compounds from the three studied species were evaluated.

## Chapter 4. RESULTS AND DISCUSSION

### 4.1. Chemical composition of essential oils from three *Asarum* species in Vietnam

Essential oils from the aerial parts (leaves and stems) of three Asarum species (*A. geophilum, A. yentuense, and A. cordifolium*) were obtained via steam distillation. The chemical composition of these oils was

analyzed using gas chromatography-mass spectrometry (GC-MS).

In summary, the research results on the chemical composition of essential oils from three *Asarum* species in Vietnam have contributed to supplementing the database on essential oils of the *Asarum* genus. Notably, the chemical composition of the essential oil from *A. yentuense* was comprehensively analyzed, revealing significant chemical diversity. Regarding *A. geophilum*, the study identified 9-epi-(*E*)-caryophyllene (18.43%) as the major constituent, whereas the essential oil of *A. cordifolium* was characterized by a high content of elemicin (77.20%).

The value of this research lies in its initial assessment of establishing a chemical basis for classification. Regarding essential oil composition, the results provide scientific insight by revealing a clear division into two groups: one dominated by benzenoid derivatives (e.g., *A. yentuense, A. cordifolium*) and another dominated by sesquiterpenes (e.g., *A. geophilum*). This provides precise scientific data to distinguish between *Asarum* species, which are otherwise easily confused due to their similar morphological characteristics in the wild. Furthermore, the detection of safrole and elemicin present at specific levels in the essential oils holds practical value for pharmacological safety; it aids in standardizing dosages for traditional medicinal use, thereby helping to prevent toxicity. These chemical findings have served as a guiding framework for selecting appropriate bioactivity testing models, establishing a coherent link between chemistry and biology.

Consequently, based on the identification and characterization of novel chemical structures, the study established a scientific rationale for selecting appropriate biological targets, thereby confirming that the medicinal potential of Vietnamese *Asarum* species extends beyond oral tradition and rests on a clear molecular foundation.

Based on the research findings of the thesis, the biological activities of the essential oils from three *Asarum* species (*A. geophilum, A. yentuense,* and *A. cordifolium*) are summarized as follows:

The essential oil of *A. yentuense* strongly inhibits S*taphylococcus aureus*. The essential oil of *A. cordifolium* strongly inhibits *Bacillus subtilis*.

Beneficial activity (MIC 200 µg/ml): All the essential oils exhibited activity against *Escherichia coli*, the yeast *Saccharomyces cerevisiae*, and the mold *Fusarium oxysporum*.

- Antioxidant activity: The essential oil of *A. geophilum* exhibited the strongest antioxidant activity ($SC_{50}$ = 28.57 µg/mL), followed by the essential oil of *A. cordifolium* ($SC_{50}$ = 39.62 µg/mL).

- Anti-inflammatory activity: The essential oils exhibited moderate to weak activity.

Table 4.1. Chemical composition of essential oils from three species of the genus *Asarum*

| STT | Tên | Công thức | RI | *A. geophilum* | | | *A. yentuense* | | | *A. cordifolium* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Time | RI | %FID | Time | RI | %FID | Time | RI | %FID |
| 1 | *β*-pinene | $C_{10}H_{16}$ | 932 | 10,01 | 938 | 0,33 | 10,37 | 939 | 0,84 | 10,70 | 939 | 0,56 |
| 2 | camphenen | $C_{10}H_{16}$ | 946 | - | - | - | 10,87 | 955 | 0,39 | 11,21 | 956 | 0,38 |
| 3 | *β*-pinene | $C_{10}H_{16}$ | 986 | 11,36 | 983 | 1,45 | 11,74 | 984 | 0,91 | 12,11 | 985 | 0,96 |
| 4 | myrcene | $C_{10}H_{16}$ | 988 | - | - | - | - | - | - | 12,32 | 992 | 0,21 |
| 5 | *β*-phelandren | $C_{10}H_{16}$ | 1010 | 12,17 | 1009 | 0,13 | - | - | - | 12,93 | 1010 | 0,79 |
| 6 | *δ*-3-carene | $C_{10}H_{16}$ | 1015 | - | - | - | 12,77 | 1016 | 0,39 | 13,15 | 1017 | 0,83 |
| 7 | o-cymene | $C_{10}H_{14}$ | 1022 | 12,82 | 1028 | 0,17 | - | - | - | 13,60 | 1030 | 1,80 |
| 8 | Limonene | $C_{10}H_{16}$ | 1030 | 12,97 | 1033 | 0,18 | - | - | - | 13,75 | 1034 | 1,87 |
| 9 | *β*-phelandrene | $C_{10}H_{16}$ | 1031 | - | - | - | - | - | - | 13,82 | 1036 | 0,31 |
| 10 | eucalyptol | $C_{10}H_{18}O$ | 1032 | - | - | - | - | - | - | - | - | - |
| 11 | (Z)-*β*-ocimene | $C_{10}H_{16}$ | 1039 | - | - | - | 13,49 | 1038 | 0,13 | 13,88 | 1038 | 1,33 |
| 12 | (E)-*β*-ocimene | $C_{10}H_{16}$ | 1050 | - | - | - | 13,87 | 1049 | 0,42 | 14,26 | 1049 | 0,34 |
| 13 | terpinolene | $C_{10}H_{16}$ | 1094 | 15,02 | 1093 | 0,20 | 15,43 | 1094 | 0,13 | | | |
| 14 | linalool | $C_{10}H_{18}O$ | 1095 | 15,27 | 1101 | 0,18 | 15,67 | 1101 | 3,19 | 16,10 | 1102 | 0,20 |
| 15 | Exo-fenchol | $C_{10}H_{18}O$ | 1118 | 15,95 | 1120 | 0,13 | - | - | - | - | - | - |
| 16 | borneol | $C_{10}H_{18}O$ | 1171 | 17,84 | 1174 | 0,15 | 18,25 | 1175 | 0,31 | - | - | - |
| 17 | Terpinen-4-ol | $C_{10}H_{18}O$ | 1184 | 18,20 | 1184 | 0,30 | - | - | - | - | - | - |
| 18 | *β*-terpineol | $C_{10}H_{18}O$ | 1195 | 18,65 | 1197 | 4,07 | - | - | - | - | - | - |
| 19 | Thymol methyl ether | $C_{11}H_{16}O$ | 1232 | - | - | - | - | - | - | - | - | - |
| 20 | geranial | $C_{10}H_{16}O$ | 1271 | - | - | - | - | - | - | - | - | - |
| 21 | Bornyl acetate | $C_{12}H_{20}O_2$ | 1289 | 21,94 | 1293 | 0,23 | - | - | - | 22,85 | 1295 | 0,23 |
| 22 | safrole | $C_{12}H_{20}O_2$ | 1293 | - | - | - | 22,59 | 1300 | 64,74 | - | - | - |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23 | *n*-tridecane | $C_{13}H_{28}$ | 1300 | 22,14 | 1299 | 0,18 | - | - | - | - | - | - |
| 24 | *δ*-elemene | $C_{15}H_{24}$ | 1343 | 23,72 | 1347 | 0,81 | - | - | - | - | - | - |
| 25 | *β*-terpinyl acetate | $C_{12}H_{20}O_2$ | 1349 | 24,00 | 1355 | 0,35 | - | - | - | - | - | - |
| 26 | Endo-isocamphanyl acetate | $C_{11}H_{18}O_2$ | 1350 | - | - | - | - | - | - | - | - | - |
| 27 | Geranyl acetate | $C_{12}H_{20}O_2$ | 1379 | - | - | - | - | - | - | - | - | - |
| 28 | *β*-copaene | $C_{15}H_{24}$ | 1394 | 25,07 | 1388 | 0,42 | - | - | - | 26,00 | 1390 | 0,50 |
| 29 | *cis*-*β*-elemene | $C_{15}H_{24}$ | 1396 | 25,54 | 1402 | 2,75 | - | - | - | 26,45 | 1404 | 1,84 |
| 30 | Methyl eugenol | $C_{11}H_{14}O_2$ | 1403 | - | - | - | 26,09 | 1407 | 1,22 | 26,58 | 1408 | 2,16 |
| 31 | *β* -caryophyllene | $C_{15}H_{24}$ | 1434 | 26,60 | 1436 | 8,05 | 27,03 | 1437 | 0,29 | | | |
| 32 | γ-elemene | $C_{15}H_{24}$ | 1440 | 26,84 | 1444 | 0,68 | - | - | - | - | - | - |
| 33 | *β*-*trans*-bergamotene | $C_{15}H_{24}$ | 1443 | - | - | - | 27,31 | 1446 | 0,67 | - | - | - |
| 34 | *β*-gurjunene | $C_{15}H_{24}$ | 1446 | 27,01 | 1449 | 1,66 | - | - | - | - | - | - |
| 35 | aromadendrene | $C_{15}H_{24}$ | 1449 | 27,20 | 1455 | 0,61 | - | - | - | - | - | - |
| 36 | (Z)-*β*-farmesene | $C_{15}H_{24}$ | 1451 | - | - | - | 27,78 | 1461 | 2,81 | - | - | - |
| 37 | (E)-methyl isoeugenol | $C_{15}H_{24}$ | 1460 | - | - | - | 27,92 | 1465 | 0,19 | - | - | - |
| 38 | *β*-humulene | $C_{15}H_{24}$ | 1471 | 27,67 | 1470 | 3,87 | 28,11 | 1471 | 0,55 | - | - | - |
| 39 | 9-epi-(E)-caryophyllene | $C_{15}H_{24}$ | 1474 | 2795 | 1479 | 18,43 | - | - | - | - | - | - |
| 40 | γ-curcumene | $C_{15}H_{24}$ | 1481 | - | - | - | 28,66 | 1488 | 0,24 | - | - | - |
| 41 | γ-muurolene | $C_{15}H_{24}$ | 1483 | - | - | - | - | - | - | - | - | - |
| 42 | Ar-curcumene | $C_{15}H_{24}$ | 1484 | - | - | - | - | - | - | - | - | - |
| 43 | Germacrene D | $C_{15}H_{24}$ | 1496 | 28,49 | 1496 | 0,56 | - | - | - | 29,44 | 1499 | 1,00 |
| 44 | *n*-pentadecane | $C_{15}H_{32}$ | 1500 | 28,58 | 1499 | 1,10 | - | - | - | - | - | - |
| 45 | (E)-methyl isoeugenol | $C_{11}H_{14}O_2$ | 1501 | - | - | - | 29,05 | 1501 | 0,27 | - | - | - |
| 46 | *β*-selinene | $C_{15}H_{24}$ | 1502 | 28,69 | 1503 | 0,60 | - | - | - | 29,62 | 1505 | 0,17 |
| 47 | *δ*-selinene | $C_{15}H_{24}$ | 1503 | - | - | - | - | - | - | 29,65 | 1507 | 0,17 |
| 48 | *trans*-muurola-4(14),5-diene | $C_{15}H_{24}$ | 1503 | - | - | - | - | - | - | - | - | - |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 49 | viridiflorene | $C_{15}H_{24}$ | 1505 | 28,93 | 1511 | 0,60 | - | - | - | 29,62 | 1505 | 0,17 |
| 50 | γ-amorphene | $C_{15}H_{24}$ | 1508 | - | - | - | - | - | - | 29,65 | 1507 | 0,17 |
| 51 | *cis*-bicyclogermacene | $C_{15}H_{24}$ | 1510 | 28,98 | 1512 | 4,46 | - | - | - | 29,91 | 1515 | 0,73 |
| 52 | (E,E)-a-farnesene | $C_{15}H_{24}$ | 1511 | - | - | - | 29,39 | 1512 | 0,36 | - | - | - |
| 53 | *trans*-bicyclogermacrene | $C_{15}H_{24}$ | 1512 | - | - | - | 29,42 | 1513 | 0,73 | - | - | - |
| 54 | *β*-bisabolene | $C_{15}H_{24}$ | 1514 | - | - | - | - | - | - | - | - | - |
| 55 | *β*-bulnesene | $C_{15}H_{24}$ | 1517 | - | - | - | - | - | - | 30,13 | 1522 | 0,20 |
| 56 | Cuparene | $C_{15}H_{22}$ | 1518 | - | - | - | - | - | - | - | - | - |
| 57 | Sesquicinene | $C_{15}H_{26}O$ | 1521 | - | - | - | 29,80 | 1526 | 15,34 | - | - | - |
| 58 | γ-cadinene | $C_{15}H_{24}$ | 1524 | - | - | - | - | - | - | 30,44 | 1533 | 0,27 |
| 59 | Myristicin | $C_{11}H_{14}O_2$ | 1529 | - | - | - | 29,95 | 1531 | 0,31 | - | - | - |
| 60 | *β*-sequiphellandrene | $C_{15}H_{24}$ | 1531 | - | - | - | 30,03 | 1534 | 0,16 | - | - | - |
| 61 | *δ*-cadinene | $C_{15}H_{24}$ | 1533 | 29,65 | 1535 | 0,60 | - | - | - | 30,58 | 1538 | 0,41 |
| 62 | Zonarene | $C_{15}H_{24}$ | 1537 | - | - | - | - | - | - | - | - | - |
| 63 | *β*-bisabolene | $C_{15}H_{24}$ | 1544 | - | - | - | - | - | - | 31,00 | 1552 | 1,81 |
| 64 | Selina-4(15),7(11)-diene | $C_{15}H_{24}$ | 1545 | 30,15 | 1552 | 1,02 | - | - | - | - | - | - |
| 65 | Selina-3,7(11)-diene | $C_{15}H_{24}$ | 1560 | 30,36 | 1559 | 0,41 | - | - | - | - | - | - |
| 66 | elemol | $C_{15}H_{26}O$ | 1562 | 30,43 | 1561 | 0,41 | - | - | - | - | - | - |
| 67 | elemicin | $C_{12}H_{16}O_2$ | 1565 | - | - | - | - | - | - | 31,43 | 1566 | 77,20 |
| 68 | (E)-nerolidol | $C_{15}H_{26}O$ | 1569 | 30,64 | 1568 | 0,47 | 31,07 | 1569 | 0,41 | 31,60 | 1572 | 0,32 |
| 69 | Germacrene B | $C_{15}H_{24}$ | 1572 | 30,86 | 1575 | 0,43 | - | - | - | - | - | - |
| 70 | isoelemicin | $C_{12}H_{16}O_2$ | 1577 | - | - | - | 31,33 | 1578 | 0,32 | - | - | - |
| 71 | 4-epi-maaliol | $C_{15}H_{26}O$ | 1577 | 31,17 | 1586 | 0,67 | - | - | - | - | - | - |
| 72 | scapanol | $C_{15}H_{26}O$ | 1580 | - | - | - | - | - | - | 32,32 | 1596 | 0,33 |
| 73 | spathulenol | $C_{15}H_{24}O$ | 1593 | 31,44 | 1595 | 1,24 | - | - | - | - | - | - |
| 74 | viridiflorol | $C_{15}H_{26}O$ | 1595 | 31,65 | 1602 | 2,16 | - | - | - | - | - | - |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 75 | Caryophyllene oxide | $C_{15}H_{24}O$ | 1599 | - | - | - | - | - | - | 32,65 | 1607 | 0,23 |
| 76 | Cubeban-11-ol | $C_{15}H_{26}O$ | 1601 | 31,91 | 1611 | 2,27 | - | - | - | - | - | - |
| 77 | rosifoliol | $C_{15}H_{26}O$ | 1615 | 32,14 | 1620 | 0,62 | - | - | - | - | - | - |
| 78 | humulene epoxidell | $C_{15}H_{24}O$ | 1520 | - | - | - | - | - | - | - | - | - |
| 79 | γ-eudesmol | $C_{15}H_{26}O$ | 1646 | 32,96 | 1648 | 0,29 | - | - | - | - | - | - |
| 80 | *β*-asarone | $C_{12}H_{16}O_3$ | 1650 | - | - | - | - | - | - | 34,09 | 1658 | 0,73 |
| 81 | *β*-muurolol | $C_{15}H_{26}O$ | 1654 | - | - | - | - | - | - | 34,18 | 1661 | 0,24 |
| 82 | *β*-cadinol | $C_{15}H_{26}O$ | 1665 | 33,58 | 1670 | 0,74 | - | - | - | 34,55 | 1674 | 0,84 |
| 83 | Neo-intermedeol | $C_{15}H_{26}O$ | 1670 | 33,67 | 1674 | 1,01 | - | - | - | - | - | - |
| 84 | *β*-asarone | $C_{12}H_{16}O_3$ | 1678 | - | - | - | 34,38 | 1684 | 0,98 | 34,88 | 1686 | 0,14 |
| 85 | Eudesm-7(11)-en-4-ol | $C_{15}H_{26}O$ | 1709 | 34,90 | 1718 | 13,41 | - | - | - | - | - | - |
| 86 | (Z)-ligustilide | $C_{12}H_{14}O_2$ | 1741 | - | - | - | - | - | - | - | - | - |
| 87 | n-tetradecanoic acid | $C_{14}H_{28}O$ | 1759 | 35,97 | 1758 | 0,18 | - | - | - | - | - | - |
| 88 | isophytol | $C_{20}H_{40}O$ | 1946 | 40,86 | 1949 | 0,12 | - | - | - | - | - | - |
| 89 | n-hexadecanoic acid | $C_{16}H_{32}O_2$ | 1959 | 41,17 | 1962 | 1,31 | - | - | - | - | - | - |
| 90 | phytol | $C_{20}H_{40}O$ | 2122 | 44,81 | 2117 | 7,23 | - | - | - | - | - | - |
| 91 | Linoleic acid | $C_{18}H_{32}O$ | 2132 | 45,30 | 2139 | 2,45 | - | - | - | - | - | - |
| 92 | Linolenic acid | $C_{18}H_{32}O$ | 2143 | 45,44 | 2145 | 2,31 | - | - | - | - | - | - |
| | Monoterpene hydrocarbon | | | 5 (2,46%) | | | 7 (3,21%) | | | 10 (7,58%) | | |
| | Oxigenated monoterpene | | | 7 (5,41%) | | | 2 (3,5%) | | | 2 (0,43%) | | |
| | Sesquiterpene hydrocarbon | | | 17 (46,84%) | | | 9 (6,0%) | | | 11 (6,53%) | | |
| | Oxigenated sesquiterpene | | | 11 (23,29%) | | | 2 (15,75%) | | | 5 (1,96%) | | |
| | Benzenoid | | | 1 (0,17%) | | | 6 (67,84%) | | | 5 (82,03%) | | |
| | Khác | | | 8 (14,88%) | | | - | | | - | | |
| | **Total** | | | **93,05%** | | | **96,30%** | | | **98,78%** | | |

### 4.2. Compounds isolated from Asarum species

Thirty-four compounds isolated from *Asarum* species are listed in Table 4.25. Among them, two are new compounds.

*Table 4.25. Compounds isolated from the studied species*

| Tên hợp chất | Lớp chất | Loài phân lập | KL (mg) | Tính mới |
|---|---|---|---|---|
| Chalcononaringenin 2′,4-di-O-*β*-D-glucopyranoside | Flavonoid | *A. geophilum* | 5,0 | M |
| Asageoside | Alkaloid | *A. geophilum* | 6,0 | M |
| Naringenin | Flavonoid | *A. geophilum*<br>*A. yentuense* | 60<br>6,0 | L |
| Naringenin 5-O-*β*-glucopyranoside | Flavonoid | *A. geophilum* | 11,0 | L |
| Naringenin 7-O-*β*-glucopyranoside | Flavonoid | *A. geophilum* | 6,3 | L |
| Naringenin 5,7-di-O-*β*-glucopyranoside | Flavonoid | *A. geophilum* | 6,0 | L |
| Vitexin | Flavonoid | *A. geophilum*<br>*A. yentuense* | 4,0<br>7,0 | L |
| Isorhamnetin 3-O-[*β*-rhamnopyranosyl-(1→6)-*β*-D glucopyranoside] | Flavonoid | *A. geophilum* | 5,8 | L |
| Isorhamnetin 3-O-*β*-D-glucopyranoside | Flavonoid | *A. geophilum* | 5,7 | L |
| Cacticin | Flavonoid | *A. geophilum* | 5,0 | L |
| Kaempferol | Flavonoid | *A. geophilum*<br>*A. yentuense*<br>*A. cordifolium* | 7,0<br>6,0<br>9,5 | L |
| Kaempferol 3-O-*β*-rhamnopyranosyl-(1→6)-*β*-galactopyranoside | Flavonoid | *A. geophilum*<br>*A. cordifolium* | 5,8<br>8,8 | L |
| Luteoside | Flavonoid | *A. geophilum*<br>*A. yentuense* | 5,1<br>5,0 | L |
| Kaempferol 3-O-(2,6-di-*β*-L-rhamnopyranosyl)-*β*-D-galactopyranoside | Flavonoid | *A. geophilum* | 16,0 | L |
| Alangiflavoside | Flavonoid | *A. geophilum* | 4,0 | L |
| Quercetin 3-O-(2,6-di-*β*-L-rhamnopyranosyl)-*β*-D-galactopyranoside | Flavonoid | *A. geophilum* | 34,0 | L |
| Quercetin 3-O-*β*-L-rhamnopyranosyl-(1→2)- [*β*-rhamnopyranosyl-(1→6)]-*β*-galactopyranosyl-7-O-*β*-glucopyranoside | Flavonoid | *A. geophilum* | 4,0 | L |
| Aureusidin 4,6-di-O-glucoside | Flavonoid | *A. geophilum* | 13,0 | L |
| Elemicin | Phenylpropanoid | *A. cordifolium* | 30,0 | |
| Methyl eugenol | Phenylpropanoid | *A. cordifolium* | 25,3 | L |
| *β*-sitosterol | Steroid (Phytosterol) | *A. cordifolium* | 11,2 | L |
| Quercetin | Flavonoid | *A. cordifolium* | 10,5 | L |

| | | | | |
|---|---|---|---|---|
| Daucosterol | Steroid (Phytosterol) | *A. cordifolium*<br>*A. yentuense* | 13,0<br>90,0 | L |
| 5,4'-dihydroxy-7-methoxyflavone | Flavonoid | *A. yentuense* | 20,0 | L |
| Luteolin -7-O-*β*-D-glucopyranoside | Flavonoid | *A. yentuense* | 5,0 | L |

M: Hợp chất mới L: lần đầu tiên phân lập từ loài

### *4.2.1. New Chalcone glycoside: chalcononaringenin 2',4-di-O- β -glucopyranoside (AG1)*

The obtained compound **AG1** was a white powder. The HR-ESI-MS spectrum showed a quasi-molecular ion peak $[M+H]^+$ at m/z 597.1810 amu (calculated value for $[C_{27}H_{32}O_{15}]^+$: 597.1814). Consequently, the molecular formula of **AG1** was determined to be $C_{27}H_{32}O_{15}$.

The $^1$H-NMR spectrum of **AG1** showed signals for two trans-oriented olefinic protons at $\delta_H$ 7.73 (1H, d, J = 15.6 Hz, H-β) and 7.98 (1H, d, J = 15.6 Hz, H-β), characteristic of the chalcone skeleton. In the downfield region, proton signals characteristic of a para-substituted benzene ring (AA'BB' spin system) appear at $\delta_H$ 6.86 (2H, d, J = 8.4 Hz) and 7.64 (2H, d, J = 8.4 Hz). Additionally, two doublet signals at $\delta_H$ 6.30 and 6.53 with a small coupling constant (J = 2.4 Hz) are assigned to two protons at the meta positions of a tetrasubstituted aromatic ring. Furthermore, the spectrum exhibits two anomeric proton signals at $\delta_H$ 5.06 (1H, d, J = 7.2 Hz) and 5.22 (1H, d, J = 7.8 Hz), suggesting the presence of two sugar units.

Analysis of $^{13}$C-NMR and HSQC spectral data reveals that the **AG1** molecule contains 27 carbon atoms, comprising: one carbonyl carbon at $\delta_C$ 195.0 ppm; six side-chain carbons ($\delta_C$ 109.3, 128.3, 161.1, 161.4, 164.4, and 166.5); 18 methine carbons (including those belonging to the sugar moiety and aromatic ring, in the range of $\delta_C$ 71.5–145.2); and two sugar-derived methylene groups at $\delta_C$ 62.7 ppm and 62.8 ppm (Table 10).

A comparison of the $^1$H- and $^{13}$C-NMR spectral data of **AG1** with literature values reveals that the structure of **AG1** is similar to that of the previously reported compound chalcononaringenin 2′,4′-di-O-*β*-D-glucopyranoside [44], although there is a difference regarding the attachment sites of the sugar units. This is demonstrated by the HMBC

spectrum of AG1, which shows interactions between H-β ($\delta_H$ 7.98)/H-β ($\delta_H$ 7.73) and C-β′ ($\delta_C$ 195.0), confirming the presence of the enone bridge characteristic of chalcones. Interactions from H-2/H-6 to C-4/C-β, from H-3′ to C-1′/C-2′/C-5′, and from H-5′ to C-1′/C-3′/C-4′/C-6′ facilitate the determination of the positions of the four oxygenated substituents at C-4, C-2′, C-4′, and C-6′.

The presence of two D-glucopyranosyl moieties was established by the chemical shifts of the sugar carbons, and the *β*-glycosidic configuration was determined based on the coupling constants of the two anomeric protons (J = 7.2 and 7.8 Hz). The linkage positions of these two sugar units were precisely identified through carbon-proton interactions observed in the HMBC spectrum: the anomeric proton of the first sugar unit (GlcI H-1, $\delta_H$ 5.22) showed a correlation with C-4 ($\delta_C$ 161.4), while the anomeric proton of the second sugar unit (GlcII H-1, $\delta_H$ 5.06) correlated with C-2′ ($\delta_C$ 164.4). Based on these analyses, the structure of compound AG1 was identified as a new compound named chalcononaringenin 2′,4-di-O-*β*-D-glucopyranoside.

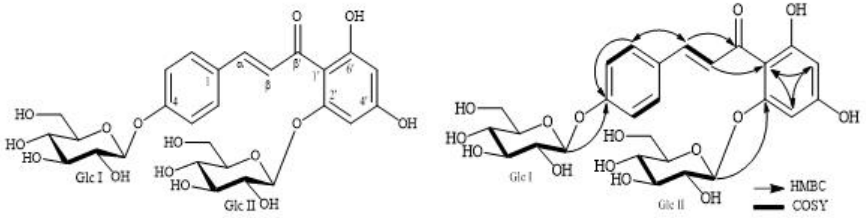



*Figure 4.2.* Chemical structure and key HMBC (H–C) correlations of **AG1.**

Table 4.2. $^{1}$H- and $^{13}$C-NMR spectral data of AG1 (1H: 600 MHz, $^{13}$C: 125 MHz, $CD_3OD$) and reference

| **C** | **AG1** | | **[44]** chalcononaringenin 2′,4′-di-*O*-*β*-D-glucopyranoside | |
|---|---|---|---|---|
| | **$\delta_C$** | **$\delta_H$ (mult., *J* in Hz)** | **#$\delta_C$** | **#$\delta_H$ (mult., *J* in Hz)** |
| *β* | 145,2 | 7,73 (d; 15,6) | 125,2 | 8,66 (d; 15,3) |
| *β* | 125,6 | 7,98 (d; 15,6) | 144,4 | 8,17 (d; 15,3 ) |

| | | | | |
|---|---|---|---|---|
| *β′* | 195,0 | - | 193,9 | - |
| 1 | 128,3 | - | 127,3 | - |
| 2, 6 | 132,0 | 7,64 (d; 8,4) | 131,7 | 7,96 (d; 8,6) |
| 3, 5 | 117,0 | 6,86 (d; 8,4) | 116,9 | 7,06 (d; 8,6) |
| 4 | 161,4 | - | 161,0 | - |
| 1′ | 109,3 | - | 108,4 | - |
| 2′ | 164,4 | - | 164,2 | - |
| 3′ | 99,7 | 6,30 (d; 2,4) | 98,9 | 7,19 (d; 2,1) |
| 4′ | 166,5 | - | 166,7 | - |
| 5′ | 95,8 | 6,53 (d; 2,4) | 95,7 | 6,66 (d; 2,1) |
| 6′ | 161,1 | - | 161,6 | - |
| **Glc I** | | | | |
| 1 | 101,7 | 5,22 (d; 7,8) | 102,0 | 5,93 (d; 7,6) |
| 2 | 75,0 | 3,58 (dd; 7,8; 9,0) | 75,1 | |
| 3 | 78,4 | 3,53 (t; 9,0) | 79,0 | |
| 4 | 71,6 | 3,37 (t; 9,0) | 71,6 | |
| 5 | 78,9 | 3,63 (m) | 79,1 | |
| 6 | 62,8 | 3,70 (dd; 6,6; 12,0)<br>3,95 (dd; 2,4; 12,0) | 62,5 | |
| **Glc II** | | | | |
| 1 | 101,1 | 5,06 (d; 7,2) | 101,1 | 5,90 (d; 7,9) |
| 2 | 74,7 | 3,47 (dd; 7,2; 9,0) | 74,8 | |
| 3 | 77,9 | 3,49 (t; 9,0) | 78,5 | |
| 4 | 71,5 | 3,39 (t; 9,0) | 71,7 | |
| 5 | 78,5 | 3,64 (m) | 79,0 | |
| 6 | 62,7 | 3,72 (dd; 6,6; 12,0)<br>3,97 (dd; 2,4; 12,0) | 62,7 | |

#$\delta_H$ và #$\delta_C$ của chalcononaringenin 2′,4′-di-O-*β*-D-glucopyranoside ($^1$H: 500 MHz, $^{13}$C: 125 MHz, pyridine-$d_5$) [44]

### *4.2.2. New Alkaloid: asageoside (AG2)*

The isolated compound **AG2** is amorphous. High-resolution ESI-MS (HR-ESI-MS) analysis revealed a quasi-molecular ion peak $[M+H]^+$ at m/z 666.2033, corresponding to the calculated molecular formula $C_{30}H_{36}O_{15}N$.

The $^1$H-NMR spectrum of **AG2** displayed three singlet signals at $\delta_H$ 7.40 ppm (H-9), 8.12 ppm (H-2), and 8.93 ppm (H-5), characteristic of a phenanthrene skeleton. Additionally, the spectrum showed signals for three methoxy groups (singlets at $\delta_H$ 3.99, 4.01, and 4.09; 3H each) and two

anomeric protons at $\delta_H$ 5.06 (1H, d, J = 7.8 Hz) and 5.79 (1H, d, J = 7.8 Hz), suggesting the presence of two sugar units in the molecule.

Combining the $^{13}$C-NMR and HSQC spectral data for **AG2** confirms the presence of 30 carbon atoms, comprising: one carbonyl carbon, 11 side-chain carbons, three aromatic methine (CH) carbons, 10 methine carbons (belonging to the sugar moiety), two methylene ($CH_2$) carbons, and three methoxy ($OCH_3$) groups. This is fully consistent with the proton signals observed in the $^1$H-NMR spectrum. The distribution of these carbon signals aligns with the structure of a glycoside derivative featuring a nitrogen-containing phenanthrene aglycone scaffold (specifically, an aristolochic acid or aristolactam derivative) [127].

The positions of the substituents on the phenanthrene skeleton were precisely determined based on long-range correlations in the HMBC spectrum and spatial correlations in the NOESY spectrum. HMBC correlations were observed between the methoxy groups at $\delta_H$ 4.09, 3.99, and 4.01 and carbons C-6 ($\delta_C$ 152.5), C-7 ($\delta_C$ 143.2), and C-8 ($\delta_C$ 150.2), confirming their attachment at positions C-6, C-7, and C-8. This conclusion was further supported by the NOESY spectrum, which showed spatial correlations between the 6-methoxy group protons ($\delta_H$ 4.09) and H-5 ($\delta_H$ 8.93), as well as between the 8-methoxy group protons ($\delta_H$ 4.01) and H-9 ($\delta_H$ 7.40).

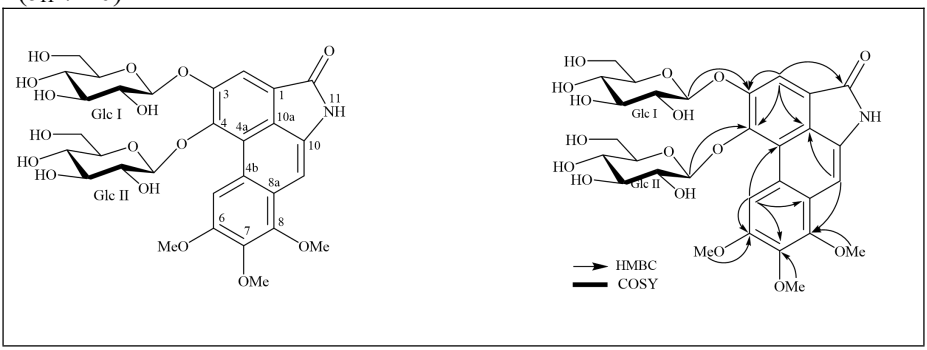



*Figure 4.3*. Chemical structure and key HMBC (H–C) interactions of **AG2**.

Regarding the sugar moieties, the $^{13}$C-NMR chemical shifts and the large coupling constants (J = 7.8 Hz) of the two anomeric protons indicate

that both sugar units are β-D-glucopyranosyl; the key to elucidating the structure lies in determining the linkage sites of these sugar chains. HMBC spectra revealed correlations between the anomeric proton of the first sugar unit (GlcI H-1, $\delta_H$ 5.06) and carbon C-3 ($\delta_C$ 152.7), as well as between the anomeric proton of the second sugar unit (GlcII H-1, $\delta_H$ 5.79) and carbon C-4 ($\delta_C$ 149.3) of the phenanthrene skeleton. Thus, the two Glc units are attached to C-3 and C-4.

Based on the combined experimental spectroscopic data, the chemical structure of compound **AG2** was identified as a new compound and named asageoside.

*Table 4.3*. $^{1}$H- and $^{13}$C-NMR spectral data of AG2 ($^{1}$H: 600 MHz, $^{13}$C: 125 MHz, $CD_3OD$) and reference compound.

| | **AG2** | | **[127]** | |
|---|---|---|---|---|
| **C** | **$\delta_C$** | **$\delta_H$ (mult., *J* in Hz)** | **#$\delta_C$** | **#$\delta_H$ (mult., *J* in Hz)** |
| 1 | 123,0 | - | 121,7 | - |
| 2 | 115,9 | 8,12 (s) | 110,8 | 7,84 (s) |
| 3 | 152,7 | - | 155,3 | - |
| 4 | 149,3 | - | 150,7 | - |
| 4a | 123,5 | - | 135,2 | - |
| 4b | 124,9 | - | 120,2 | - |
| 5 | 108,3 | 8,93 (s) | 127,7 | 9,11 (dd; 1,1; 5,2; 7,8) |
| 6 | 152,5 | - | 125,7 | 7,55 (ddd;1,2;7,2;6,0; 8,4) |
| 7 | 143,2 | - | 127,1 | 7,55 (dd;1,2; 7,2; 6,0; 8,4) |
| 8 | 150,2 | - | 129,3 | 7,92 (d; 0,6; 8,4; 7,8) |
| 8a | 126,0 | - | 126,2 | - |
| 9 | 101,8 | 7,40 (s) | 104,9 | 7,12 (s) |
| 10 | 134,2 | - | 135,1 | - |
| 10a | 125,6 | - | 123,5 | - |
| 11 | 171,1 | - | 168,6 | - |
| 6-$OCH_3$ | 56,8 | 4,09 (s) | - | - |
| 7-$OCH_3$ | 61,5 | 3,99 (s) | - | - |
| 8-$OCH_3$ | 62,1 | 4,01 (s) | - | - |
| **Glc I** | | | - | - |
| 1 | 104,7 | 5,06 (d, 7,8) | - | - |
| 2 | 75,1 | 3,72 (dd, 7,8; 9,0) | - | - |
| 3 | 77,4 | 3,57 (m) | - | - |
| 4 | 71,2 | 3,55 (m) | - | - |

| | | | | |
|---|---|---|---|---|
| 5 | 78,5 | 3,57 (m) | - | - |
| 6 | 62,4 | 3,83 (dd, 4,8; 12,0)<br>4,00 (dd, 2,4; 12,0) | - | - |
| **Glc II** | | | - | - |
| 1 | 105,1 | 5,79 (d, 7,8) | - | - |
| 2 | 76,6 | 3,81 (dd, 7,8; 9,0) | - | - |
| 3 | 78,2 | 3,58 (m) | - | - |
| 4 | 71,6 | 3,42 (t, 9,0) | - | - |
| 5 | 78,6 | 3,27 (m) | - | - |
| 6 | 62,4 | 3,52 (dd, 5,4; 12,0)<br>3,63 (dd, 2,4; 12,0) | - | - |
| 3-$OCH_3$ | - | - | 57,0 | 4,03 (s) |
| 4-$OCH_3$ | - | - | 60,1 | 4,02 (s) |

#$\delta_H$ và #$\delta_C$ của aristolactam BII ($^1$H: 500 MHz, $^{13}$C: 125 MHz, DMSO-$d_6$) [127]

## 4.3. Biological activity of isolated compounds

### *4.3.1. Antimicrobial activity*

Based on the preliminary screening results of the crude extracts, pure compounds isolated from A. *cordifolium* and *A. geophilum* were selected to evaluate their ability to inhibit the growth of test microbial strains. Experimental results revealed a distinct variation in activity among the groups of compounds:

Among the phenylpropanoid compounds isolated from *A. cordifolium*, elemicin (**AC1**) exhibited the broadest antimicrobial spectrum, inhibiting the growth of 7 out of the 11 tested microbial strains (including Gram-negative bacteria, Gram-positive bacteria, and fungi) with an MIC value of 200 µg/mL. In contrast, methyl eugenol (**AC2**) demonstrated specific activity against three fungal strains: *Aspergillus niger, Fusarium oxysporum,* and *Phytophthora infestans* (MIC = 200 µg/mL). These results suggest that phenylpropanoids play a significant role in the plant's self-defense mechanism against fungal pathogens.

Regarding the flavonoid glycosides isolated from *A. geophilum*, derivatives of quercetin, kaempferol, and naringenin exhibited potent and specific antimicrobial activity. Most notably, naringenin (**AG3**)

demonstrated superior inhibitory activity against *Vibrio cholerae* and the fungus *Cryptococcus neoformans*, with very low MIC values of 16–32 µg/mL and 32 µg/mL, respectively. Other compounds—such as isorhamnetin 3-O-*β*-D-glucopyranoside (**AG2**), cacticin (**AG4**), and alangiflavoside (**AG8**) also displayed significant inhibitory activity (MIC 50–200 µg/mL) against strains of *Escherichia coli, Pseudomonas aeruginosa,* and *Bacillus subtilis.*

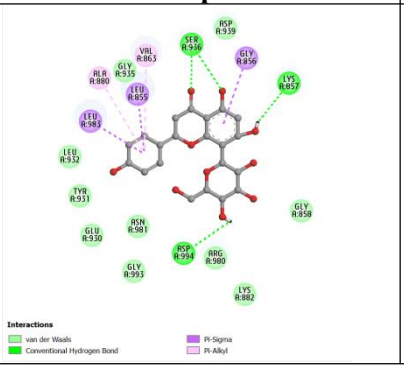
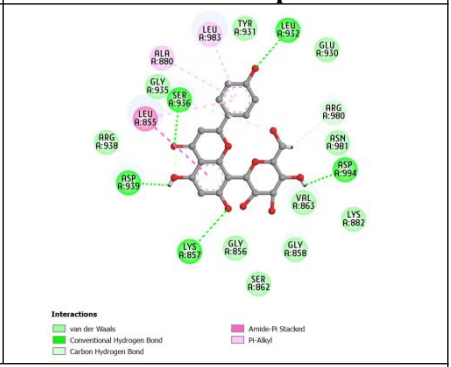
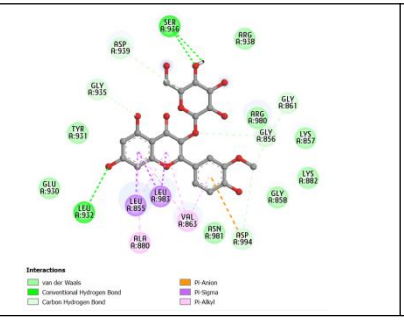
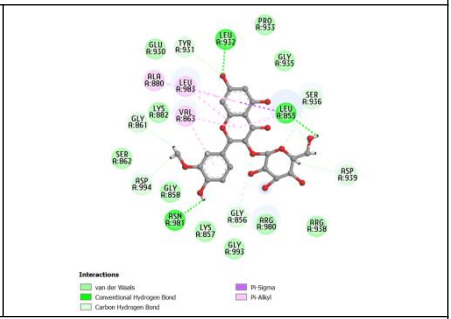
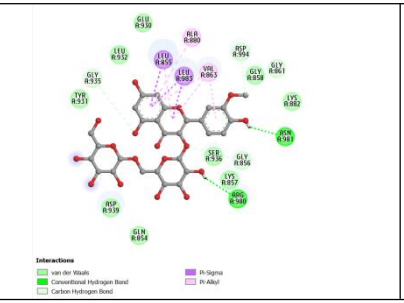
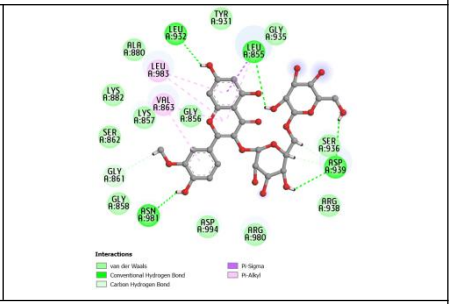
***4.3.2. Hepatoprotective and cytotoxic activities***

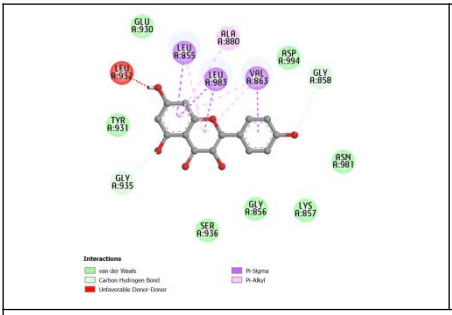
The hepatoprotective activity of the isolated compounds was evaluated using a human liver cancer cell line (Hep-G2) under CCl4-induced toxicity. The results revealed a strong correlation between chemical structure and biological activity:

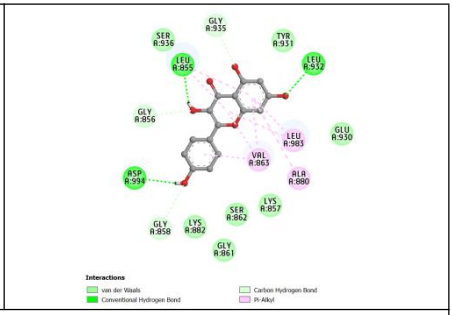
Among the tested compounds, kaempferol (**AG11**) exhibited the strongest hepatoprotective activity, with an $IC_{50}$ value of 13.4 ± 1.2 µg/mL. Its mechanism of action is attributed to its compact aglycone structure, which facilitates easy penetration of the cell membrane to scavenge intracellular free radicals. In contrast, the bulkier glycoside derivative quercetin 3-O-glycoside (AG16) showed only moderate activity ($IC_{50}$ = 73.6 ± 9.1 µg/mL). This underscores the critical role of the sugar moiety in modulating the pharmacological activity of the flavonoid scaffold.

***4.3.3. In silico screening study targeting JAK2***

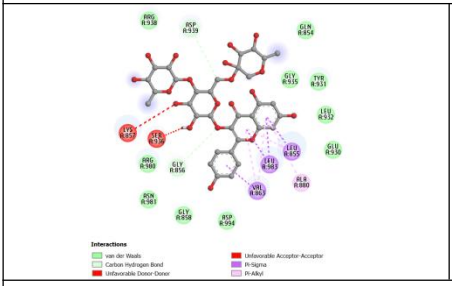
To elucidate the potential molecular mechanisms underlying anti-inflammatory and cancer-supportive effects, 18 compounds isolated from *A. geophilum* were investigated using molecular docking simulations against the Janus Kinase 2 (JAK2) target protein. The 2D interaction diagrams of the structures docked with potential compounds within the active site of the JAK2 protein are presented below:

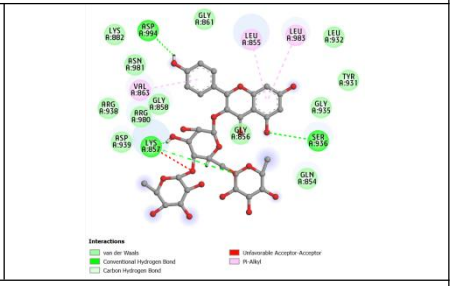
| Docked pose | MD-refined pose |
| --- | --- |
|  |  |
| **AG7** | |
|  |  |
| **AG8** | |
|  |  |
| **AG9** | |



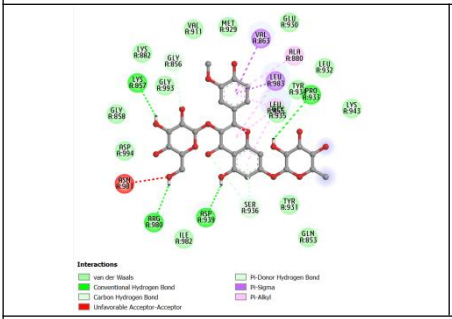


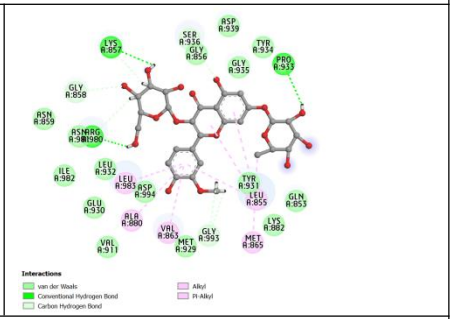
**AG11**



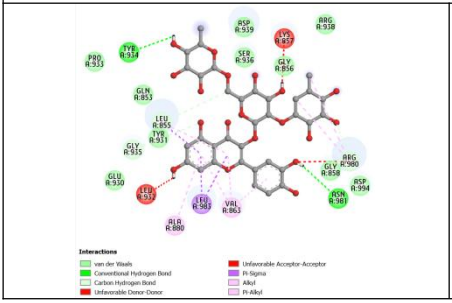


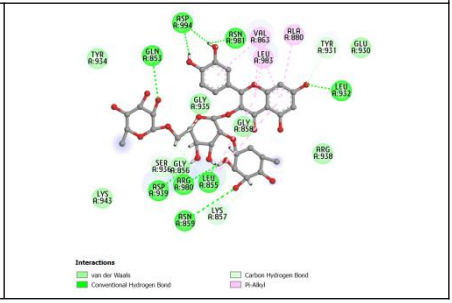
**AG12**

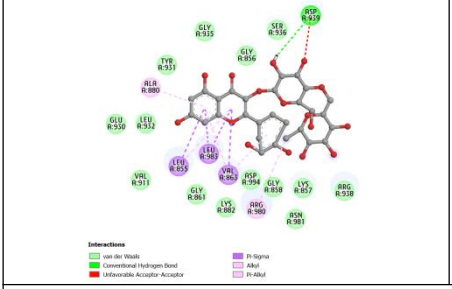
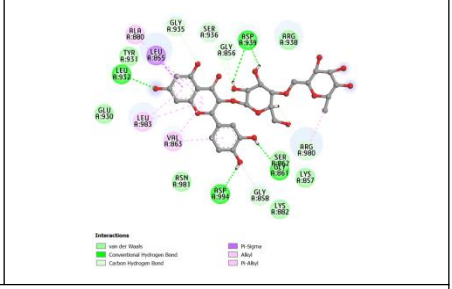
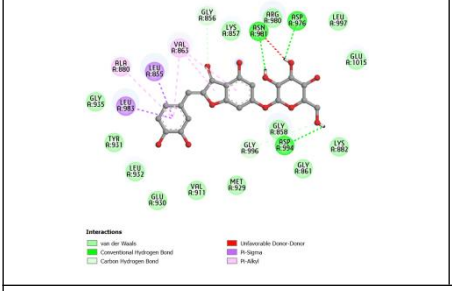
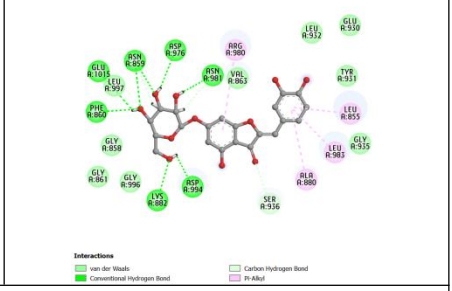




**AG13**





| AG14 | |
|---|---|
|  |  |
| **AG16** | |
|  |  |
| **AG18** | |

## CONCLUSION

This thesis has systematically investigated the chemical constituents and biological activities of three species of the genus *Asarum* found in Vietnam: *A. cordifolium, A. yentuense, and A. geophilum*. The key results obtained are as follows:

1. Regarding the chemical composition of the isolated pure substances: By combining chromatographic methods and modern spectroscopic techniques (1D and 2D NMR, MS), a total of 34 compounds (including 6 duplicates) were isolated and structurally elucidated from the aerial parts of the three studied species:

From *A. cordifolium*: Eight compounds were isolated and structurally elucidated, primarily belonging to the flavonoid and terpenoid

groups.

From *A. geophilum*: Eighteen compounds were isolated and structurally elucidated. Notably, two new compounds were discovered: chalcononaringenin 2′,4-di-O-*β*-D-glucopyranoside (**AG1**) and asageoside (**AG2**).

From A. yentuense: Eight compounds were isolated and structurally elucidated, with flavonoids constituting the main components.

2. Regarding essential oil chemical composition: The chemical composition of the essential oils from three species was determined, with data on *A. yentuense* being reported for the first time. *β*-Pinene and (*E*)-nerolidol were present in all three species. Additionally, distinct differences were observed:

*A. geophilum*: Dominated by sesquiterpenes, with 9-epi-(*E*)-caryophyllene and eudesm-7(11)-en-4-ol as the major constituents.

*A. yentuense*: Elemicin (77.20%) was the major constituent.

*A. cordifolium*: Safrole (64.74%) was the major constituent.

***3. Regarding biological activity:***

Regarding the activity of the essential oils:

Antibacterial and antifungal: All four essential oils demonstrated significant inhibitory activity (MIC 100–200 µg/mL) against test strains such as *E. coli, S. aureus,* and *C. albicans*.

Antioxidant activity: *A. geophilum* essential oil exhibited the strongest activity ($SC_{50}$ = 28.57 µg/ml), followed by *A. cordifolium*.

Flavonol glycoside compounds (such as **AG3, AG4, AG8, AG9**) demonstrated strong antimicrobial activity (MIC 50–200 µg/ml) against various bacterial and fungal strains. Notably, compound **AG3** effectively inhibited *Vibrio cholerae* and *Cryptococcus neoformans* (MIC 16–32

μg/ml).

Hepatoprotection: Kaempferol and quercetin glycoside (**AG17**) demonstrated significant hepatoprotective activity, with $IC_{50}$ values of 13.4 and 73.6 μg/mL, respectively.

4. Molecular docking results: In silico studies targeting the JAK2 protein revealed that compound **AG14** exhibited the strongest binding affinity (ΔGLIE = -21.7751 kcal/mol), surpassing that of the reference inhibitors. These findings suggest the potential of compounds derived from *Asarum* in the development of new anti-inflammatory drugs and agents for cancer treatment support.

## RECOMMENDATIONS

Based on the promising results regarding chemical composition and biological activity, the thesis proposes further research in the future: Conducting in-depth research: It is necessary to expand the study of the molecular mechanisms of action of the potential compounds that have been isolated.

## NEW CONTRIBUTIONS OF THE THESIS

This is the first study in Vietnam to conduct a comprehensive analysis of the essential oil composition of three *Asarum* species, as well as the compounds derived from the extracts of two endemic and under-studied species: *Asarum yentuense* and *Asarum cordifolium*.

The content and chemical composition of the essential oils from the three studied species (*A. cordifolium, A. geophilum, and A. yentuense)* have been determined in detail, identifying characteristic chemical markers (such as elemicin, safrole, and 9-epi-(E)-caryophyllene) that help distinguish between these Vietnamese *Asarum* species.

This study marks the first time a series of pure compounds has been isolated and structurally characterized from these species in Vietnam. Notably, the thesis determined the structures of two new compounds, thereby contributing to the global repository of natural products: chalcononaringenin 2′,4-di-O-$\beta$-D-glucopyranoside (AG1)-a chalcone glycoside-and asageoside (AG2)-a novel alkaloid (specifically, an aristolactam glycoside).

Provided the first scientific data on the cytotoxicity against the human liver cancer cell line Hep-G2, as well as the antibacterial and antifungal activities, of extract fractions and pure compounds derived from the three studied *Asarum* species.

Molecular docking simulation results have initially elucidated the interaction mechanism between the isolated key active compounds and the target protein Janus kinase 2 (JAK2), providing an important theoretical basis for subsequent pharmacological studies.