

Polyacetylenic compounds from *Atractylodes* rhizomes

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ABSTRACT

Objectives : *Atractylodes* rhizomes, which have been widely used to treat gastrointestinal disorders, consist of numerous chemical compounds. Polyacetylenes are the parts of characteristic compounds of importance required to understand the therapeutic properties of *Atractylodes* rhizomes. It is necessary to understand the physicochemical and pharmacological properties of polyacetylenes in the *Atractylodes* rhizomes.

Methods : The literatures from 1970 to January 2016 were searched using Korean and international electronic databases. The chemical structures of polyacetylenes were drawn by structure-drawing software.

Results : The reported polyacetylenes were classified by their chemical skeletons and original resources, and their physicochemical and pharmacological features were discussed. Polyacetylenes with skeletal moieties were reported, such as diene-diyne types (two double and two triple carbon-bonds), triene-diyne types (three double carbon bonds and two triple carbon bonds), and monoene-diyne types (one double carbon bonds and two double carbon bonds), with various functional groups. Atractylodin was most frequently reported from many *Atractylodes* species. Atractylodin-related polyacetylenes showed chemical instability in both high and freezing temperatures. Processing of the *Atractylodes* rhizomes by stir-frying with bran could affect the contents of polyacetylenes and their bioavailability *in vivo*. Several polyacetylenes showed structure-related anti-inflammatory activities and gastrointestinal activities.

Conclusion : Polyacetylene compounds in *Atractylodes* rhizomes were based on three chemical backbones and showed diverse physicochemical and pharmacological features. The present study provides structural, physicochemical, and pharmacological information of polyacetylene from *Atractylodes* rhizomes. This information provides fundamental data for further research.

Key words : *Atractylodes* rhizome, polyacetylene, chemical structure, physicochemical properties, pharmacological properties

I . Introduction

The dried rhizomes of genus *Atractylodes* (family: Asteraceae) plants, which have been classified into "Baekchul" and "Changchul", have been used to treat wind-phlegm-caused headache, diarrhea, and phlegm-induced digestive disorders¹⁾. In the Korean pharmacopeia, four species of *Atractylodes* rhizomes are used as Changchul or Baekchul: the rhizomes of *A. lancea* DC. (AL) and *A. chinensis* Koidz. (AC) are registered as Changchul; and those of *A. macrocephala* Koidz. (AM) and *A. japonica* Koidz.(AJ) are registered

as Baekchul²⁾.

Atractylodes rhizomes contain diverse chemical compounds such as polyacetylenes, sesquiterpenes, and essential oils, and those compounds are thought to exert the pharmacological effect of the rhizomes³⁻⁵⁾. Of those compounds, polyacetylenes and sesquiterpenes most occurred in *Atractylodes* rhizomes; however, the occurrences of compounds and the presentation of chemical structures were insufficiently arranged by each *Atractylodes* species⁶⁾.

Polyacetylene (or polyethyne by the IUPAC name) consists of polymerization of acetylene, a alkyne-type

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hydrocarbon, with a chain of olefin groups repeated, and possesses long carbon chains with alternating single and double bonds of either *cis* or *trans* geometry⁷⁾. Hydrogen atoms can be attached at conjugated carbon atoms and they can also be replaced by a functional group⁸⁾.

Therefore, in this study, the chemical structures of polyacetylenes were classified by their chemical backbones and the species of genus *Atractylodes* where the compounds were contained was presented. Additionally, phytochemical characteristics of those compounds were also discussed through extraction or processing. Thereafter, their pharmacological activities could be understood.

II. Materials and methods

1. Paper search

The literatures from 1970 to January 2016 were searched using a variety of electronic bibliographic databases: Korean databases, including the Korea Education and Research Information Service, National Discovery for Science Leaders, the Korean Studies Information Service System, and Korea Institute of Science and Technology Information, Korean Traditional Knowledge Portal, Oriental Medicine Advanced Searching Integrated System, KoreaMed, eArticle, and DBpia; Chinese databases including the China National Knowledge Infrastructure; Japanese databases including Citation Information from the National Institute of Informatics and Japan Science and Technology Information Aggregator, Electronic; and electronic global databases including PubMed, Web of Science, ScienceDirect, and Google Scholar.

2. Search terms and inclusion criteria

The search terms used in the present study were “창출”, “백출”, “蒼朮”, “白朮”, “蒼朮”, “白朮”, “Changchul”, “Baekchul”,

“Changzhu”, “Baizhu”, “Sojutsu”, “Byakujutsu”, “Atractylodes rhizome”, “Atractylodes macrocephala”, “Atractylodes japonica”, “Atractylodes lancea”, “Atractylodes chinensis”, “Atractylodes ovata”, and “Atractylodes koreana”

Studies in accordance with the following criteria were included: 1) original articles (not review articles; 2) medicinal part is the rhizome of *Atractylodes* plant; 3) polyacetylenes were isolated or analyzed using analytical tools from *Atractylodes* rhizomes; 4) chemical names including International Union of Pure and Applied Chemistry (IUPAC) names or chemical structures of polyacetylenes were presented; and 5) no language limitation.

Chemical structures were manually drawn using ChemDraw software (v. Ultra 10.0; Cambridge Soft, Cambridge, MA, USA). If necessary, author amended incorrect chemical structures or names in the studies.

III. Results and discussion

1. Diene-diyne types of *Atractylodes* polyacetylenes

Polyacetylenes of diene-diyne types were classified into furan-ring-attached, alcohol-attached, acetyl-attached, and two more functional groups-attached compounds. Seven atractylodin-related acetylenes, which contained a furan-ring at the terminal carbon, consisted of nine carbons. Another seven polyacetylenes comprised 14 carbons with double bonds at C-6 and C-12, and triple bonds at C-8 and C-10. Diacetyl atractylodiol was acetylene with thirteen carbons and (2E,8E)-decadiene-4,6-diyne-1,10-diol-1-O-β-D-glucopyranoside was the only polyacetylene which consisted of 10 carbons and glucopyranose. Of those compounds, atractylodin was most reported in previous reports and was contained in AL, AC, AJ, and AK (*A. koreana*). However, no diene-diyne types were reported to be contained in AM (Table 1).

Table 1: Polyacetylenes of diene-diyne types.

| Name | Structure | Origin |
|---|-----------|---|
| Atractylodin 2-[(1E,7E)-nona-1,7-dien-3,5-dinylnyl]furan | | AL ⁹⁻³⁶⁾ AC ^{19,20,27,28,31-33,36-49)} AJ ^{28,36)} AK ^{28,34,36,38)} |
| (1Z)-Atractylodin 2-[(1Z,7E)-nona-1,7-dien-3,5-dinylnyl]furan | | AL ^{49,50)} |

| Name | Structure | Origin |
|--|-----------|---|
| 9-Nor-atractylodin | | AL ¹³⁾ |
| Attractylodinol (2E,8E)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne-1-ol | | AL ^{9,17,18,30,31,33)} AC ^{31,33,37,41)} |
| (1Z)-Attractylodinol (2E,8Z)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne-1-ol | | AL ^{50,51)} |
| Acetyltractylodinol [(2E,8E)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne] acetate | | AL ^{12,17,18,30,31,33)} AC ^{31,33,41,47)} |
| (1Z)-Acetyltractylodinol [(2E,8Z)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne] acetate | | AL ⁴⁹⁾ |
| (6E,12E)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵¹⁾ AJ ^{52,53)} Atractylodes rhizomes ⁵⁴⁾ |
| (6E,12Z)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵⁵⁾ |
| (6Z,12Z)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵⁵⁾ |
| (6E,12E)-3-Acetoxytetradeca-6,12-dien-8,10-diyne-1-ol | | AC ⁵¹⁾ |
| (6E,12E)-1-Acetoxytetradeca-6,12-dien-8,10-diyne-3-ol | | AC ⁵¹⁾ |
| 1,4-Acetoxytetradeca-6,12-diene-8,10-diyne | | AJ ⁵⁶⁾ |

| Name | Structure | Origin |
|---|-----------|---|
| 9-Nor-atractylodin | | AL ¹³⁾ |
| Atractylodin (2E,8E)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne-1-ol | | AL ^{9,17,18,30,31,33)} AC ^{31,33,37,41)} |
| (1Z)-Atractylodin (2E,8Z)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne-1-ol | | AL ^{50,51)} |
| Acetyltractylodin [(2E,8E)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne] acetate | | AL ^{12,17,18,30,31,33)} AC ^{31,33,41,47)} |
| (1Z)-Acetyltractylodin [(2E,8Z)-9-(furan-2-yl)nona-2,8-dien-4,6-diyne] acetate | | AL ⁴⁹⁾ |
| (6E,12E)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵¹⁾ AJ ^{52,53)} Atractylodes rhizomes ⁵⁴⁾ |
| (6E,12Z)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵⁵⁾ |
| (6Z,12Z)-Tetradecadiene-8,10-diyne-1,3-diol | | AC ⁵⁵⁾ |
| (6E,12E)-3-Acetoxytetradeca-6,12-dien-8,10-diyne-1-ol | | AC ⁵¹⁾ |
| (6E,12E)-1-Acetoxytetradeca-6,12-dien-8,10-diyne-3-ol | | AC ⁵¹⁾ |
| 1,4-Acetoxytetradeca-6,12-diene-8,10-diyne | | AJ ⁵⁶⁾ |

| Name | Structure | Origin |
|---|-----------|--|
| (6E,12E)-Tetradecadiene-8,10-diyne-1,3-diol diacetate | | AC ⁵¹⁾ AJ ^{35,52-54,57,58)} |
| Diacetyl atractyloidiol [(5E,11E)-3-acetyloxytrideca-5,11-dien-7,9-diyne]acetate | | AJ ^{59,60)} |
| (2E,8E)-Decadiene-4,6-diyne-1,10-diol 1-O-β-D-glucopyranoside | | AL ⁶¹⁾ |

AL, *A. lancea*; AC, *A. chinensis*; AM, *A. macrocephala*; AJ, *A. japonica*; AK, *A. koreana*.

2. Triene-diyne types of *Atractylodes* polyacetylenes

As shown in Table 2, 21 compounds of triene-diyne type polyacetylenes possessed 14 carbons with double bonds at C-2, C-8, and C-12, and triple bonds at C-4 and C-6. Functional groups of these compounds were isovaleryloxy, seneciolyloxy, methylbutyryl, methylpropionyl, and acetoxy, most of which were positioned at C-12 or C-14. Another 14 carbon polyacetylenes showed different positions of double and triple bonds: double bonds at C-4, C-6, and C-12, and triple bonds at C-8 and C-10, also with the functional groups such as

acetoxy, isovaleryloxy, seneciolyloxy, or methylbutyryloxy attachments. Of the nine polyacetylenes with 13 carbons, eight polyacetylenes contained two triple bonds at C-7 and C-9, but double bonds were at different locations: three double bonds at C-1, C-5, and C-11, while at C-3, C-5, and C-11, which were attached by di-acetate, except for one compound with a ferulate. There were three double bonds at C-2, C-4, and C-10, and two triple bonds at C-6 and C-8 with the acetate group attached remaining. Most compounds originated from AM, followed by AL and AO (*A. ovata*), and those from AC or AJ were much less common.

Table 2: Polyacetylenes of triene-diyne types.

| Name | Structure | Origin |
|--|-----------|---|
| Atractyloyne (3S,4E,6E,12E)-1-Isovaleryloxy-tetradeca-4,6,12-triene-8,10-diyne-3,14-diol | | AL ³³⁾ AC ^{33,62)} |
| Atractylodemayne A 14-Seneciolyxytetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol | | AM ⁶³⁾ |
| Atractylodemayne B 14-Methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ⁶³⁾ |
| Atractylodemayne C 12-Seneciolyxytetradeca-2E,8Z,10E-trien-4,6-diyne-1,14-diacetate | | AM ⁶³⁾ |
| Atractylodemayne D 12-Methylbutyryltetradeca-2E,8Z,10E-trien-4,6-diyne-1,14-diacetate | | AM ⁶³⁾ |

| Name | Structure | Origin |
|--|-----------|---------------------------------------|
| Atractylodemayne E 12-Seneciolyxytetradeca-2E,8E,10E-trien-4,6-diyne-1,14-diacetate | | AM ⁽⁶³⁾ |
| Atractylodemayne F 14-Acetoxy-12-methylpropionyltetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁾ |
| Atractylodemayne G 14-Acetoxy-12-methylpropionyltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁾ |
| 14-Acetoxy-12-seneciolyxytetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁻⁶⁵⁾ |
| 14-Acetoxy-12-methylbutyryltetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol 9 | | AM ⁽⁶³⁾ |
| 14-Acetoxy-12-seneciolyxytetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ^(63,65-67) |
| 14-Acetoxy-12-methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ^(63,66,67) |
| 14-Acetoxy-12-methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ^(63,66,67) |
| 14-Methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁾ |
| 14-Methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁾ |
| 12-Seneciolyxytetradeca-2E,8E,10E-trien-4,6-diyne-1-ol | | AM ⁽⁶³⁾ |
| 12,14-Diacetate-2E,8E,10E-trien-4,6-diyne-1-ol | | Atractylodes rhizomes ⁽⁶⁸⁾ |
| 12-Methylbutyryl-14-acetyl-2E,8Z,10E-atractylentriol | | AM ⁽⁶⁹⁾ |

| Name | Structure | Origin |
|---|-----------|--|
| 12-Methylbutyryl-14-acetyl-2E, 8E, 10E-atractylentriol | | AM ⁽⁶⁹⁾ |
| 14-Methylbutyryl-2E, 8Z, 10E-atractylentriol | | AM ⁽⁶⁹⁾ |
| 14-Methylbutyryl-2E, 8E, 10E-atractylentriol | | AM ⁽⁶⁹⁾ |
| (4E, 6E, 12E)-Tetradeca-4, 6, 12-trien-8, 10-diyne-1, 3, 14-triol | | AL ⁽¹⁷⁾ AM ⁽⁷⁰⁻⁷³⁾ |
| (4E, 6E, 12E)-3, 14-Dihydroxytetradeca-4, 6, 12-trien-8, 10-diyne-1-yl acetate | | AM ⁽⁷⁰⁻⁷³⁾ |
| (4E, 6E, 12E)-Tetradecatriene-8, 10-diyne-1, 3-diyl diacetate | | AL ^(49, 50) AJ ^(54, 58) Atractylodes rhizomes ^(63, 74, 75) |
| (4E, 6E, 12E)-3-Isovaleryloxy-tetradeca-4, 6, 12-triene-8, 10-diyne-1, 14-diol | | AL ⁽³³⁾ AC ^(33, 62) |
| (4E, 6E, 12E)-1-Acetoxy-3-seneciolyoxytetradeca-4, 6, 12-triene-8, 10-diyne-14-ol | | AO ^(54, 76-78) |
| (4E, 6E, 12E)-1-Acetoxy-3-isovaleryloxytetradeca-4, 6, 12-trien-8, 10-diyne-14-ol | | AO ⁽⁷⁶⁻⁷⁸⁾ |

| Name | Structure | Origin |
|---|-----------|--------------------------------------|
| (4E, 6E, 12E)-1-Acetoxy-3-(2-methylbutyryloxy) tetradeca-4, 6, 12-trien-8, 10-diyne-14-ol | | AO ⁷⁶⁻⁷⁸⁾ |
| (4E, 6E, 12E)-Tetradecatriene-8, 10-diyne-1, 3-diol | | Atractylodes rhizomes ⁵⁴⁾ |
| (4E, 6E, 12E)-Tetradecatrien-8, 10-diyne-1-ol | | AO ⁵¹⁾ |
| erythro-(1, 3Z, 11E)-Tridecatriene-7, 9-diyne-5, 6-diyl diacetate | | AL ^{14, 49)} |
| erythro-(1, 5E, 11E)-Tridecatriene-7, 9-diyne-3, 4-diacetate | | AL ⁷⁹⁾ |
| threo-(1, 5E, 11E)-Tridecatriene-7, 9-diyne-3, 4-diacetate | | AL ⁷⁹⁾ |
| (1, 5E, 11E)-Trideca-1, 5, 11-trien-7, 9-diyne-3, 4-diacetate | | Atractylodes rhizomes ⁶³⁾ |
| (3Z, 5E, 11E)-Tridecatriene-7, 9-diynyl-1-O-(E)-ferulate | | AL ⁴⁹⁾ |
| (3E, 5E, 11E)-Tridecatriene-7, 9-diyne-1, 2-diacetate | | AL ⁷⁹⁾ |

| Name | Structure | Origin |
|---|-----------|--------------------------------------|
| (3Z,5E,11E)-Tridecatriene-7,9-diyne-1,2-diacetate | | AL ⁷⁹⁾ |
| (3E,5Z,11E)-Tridecatriene-7,9-diyne-1,2-diacetate | | AL ⁷⁹⁾ |
| (2Z,4E,10E)-Trideca-2,4,10-trien-6,8-diynyl acetate | | Atractylodes rhizomes ⁶⁸⁾ |

AL, *A. lancea*; AC, *A. chinensis*; AM, *A. macrocephala*; AJ, *A. japonica*; AO, *A. ovata*.

3. Monoene-diyne types of *Atractylodes* polyacetylenes

Four monoene-diyne type polyacetylenes were reported

to be a single double bond and two triple bonds, consisting of nine, ten, twelve, and thirteen carbons, with furan ring or sugars attached (Table 3).

| Name | Structure | Origin |
|---|-----------|---|
| 1-(2-Furyl)-(7E)-nonene-3,5-diyne-1,2-diacetate | | AL ⁷⁹⁾ Atractylodes rhizomes ⁶⁸⁾ |
| Ethyl-10-methyl-8-dodecene-3,5-diynoate | | AM ⁸⁰⁾ |
| (1,3Z,11E)-Tridecatriene-7,9-diyne-5-hydroxyl-6-O-β-D-glucopyranoside | | AL ⁸¹⁾ |
| (2E)-2-Decene-4,6-diyne-1,8-diol 8-O-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside | | AO ⁸²⁾ |

AL, *A. lancea*; AM, *A. macrocephala*; AO, *A. ovata*.

4. Influence of processing on physicochemical and biological properties of *Atractylodes* polyacetylenes

1) Physicochemical properties

Polyacetylenes experience diverse chemical changes in the process of extraction, especially during boiling with water. Atractylodin (C₁₈H₁₀O), which is the most reported polyacetylene from the essential oil in

Atractylodes rhizomes, is an alkyne-polyacetylene containing a 2-nonyltetrahydrofuran skeleton and it has properties such as instability in the air and light due to an unsaturation structure, which leads it to produce brown insoluble resin rapidly in air at room temperature⁸³. Atractylodin is highly unstable and becomes brown colored when in contact with air, which makes an oil cavity in primitive oil ducts or lysigenous secretory tissues where atractylodin as well as other polyacetylenes are accumulated. This leads to a brown color on a cut surface of the rhizome²⁵. When oxidized at a high temperature (120°C), atractylodin turns to the *cis*-form of atractylodinol, i.e. a H attached to a terminal methyl carbon substituted with OH [13]. Atractylodyne and (4E,6E,12E)-3-isovaleryloxy-tetradeca-4,6,12-triene-8,10-diyne-1,14-diol were converted to (4E,6E,12E)-tetradeca-4,6,12-triene-8,10-diyne-1,3,14-triol, and 14--methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol was deacylated when the rhizomes were extracted by boiling in water⁶².

2) Biological properties

Processing of *Atractylodes* rhizomes also influenced the physicochemical properties and absorption of polyacetylenes. The extraction efficiencies of atractylodin and (4E,6E,12E)-tetradecatriene-8,10-diyne-1,3-diyl diacetate from *Atractylodes* rhizomes were decreased when the rhizomes were stir-fried with bran compared to crude rhizomes⁸⁴⁻⁸⁶. However, processing by stir-frying with bran affected these *in vivo* in different ways. The plasma concentration of atractylodin was increased after *Atractylodes* rhizomes were processed by stir-frying with bran rather than crude rhizomes, which indicated that processing of *Atractylodes* rhizomes can increase the absorption of atractylodin⁸⁷. Stir-frying of *Atractylodes* rhizomes with wheat bran could promote and accelerate the absorption of (4E,6E,12E)-tetradecatriene-8,10-diyne-1,3-diyl diacetate and its concentration was highest in the spleen, possibly increasing the spleen-tonifying effect according to the traditional theory⁷⁴.

5. Chemical stabilities of *Atractylodes* polyacetylenes

Stability is another concerning issue as the occurrences of bioactive polyacetylenes can be changed under certain circumstances, like drying of the rhizomes under the sun. Atractylodin, atractylodinol, and acetyl atractylodinol were reported to have 1-*cis* isomers, (1Z)-attractylodin, (1Z)-attractylodinol, and (1Z)-

acetyl atractylodinol. The proportions of those 1-*cis* isomers were less than 1-*trans* isomers as the 1-*cis* isomers could be formed during drying process of the *Atractylodes* rhizomes under the sun: i.e. (1E)-acetyl atractylodinol is rapidly isomerized to (1Z)-acetyl atractylodinol⁴⁹. On the one hand, the stabilities of 1-*cis* isomers were weaker than those of 1-*trans* isomers: (1Z)-acetyl atractylodinol more expeditiously disappeared in n-hexane solution compared to (1E)-acetyl atractylodinol dissolved in same solvent in the freezer. On the other hand, 1-*cis* isomer of atractylodin was relatively increased up to a similar ratio with its parent compound, atractylodin, in freezer storage, indicating that atractylodin was considerably unstable than its isomer and different from those two polyacetylenes, (1E)-attractylodinol and (1Z)-attractylodinol, which showed the same degree of instability⁴⁹.

6. Pharmacological activities of *Atractylodes* polyacetylenes

In terms of pharmacological activity, polyacetylenes exhibited structure-activity relationships: the introduction of an acyl group into a compound increased the inhibitory effect against NO production; i.e., 14-acetoxy-12-seneciolyloxytetradeca-2E,8E,10E-trien-4,6-diyne-1-ol, 14-acetoxy-12- β -methylbutyryltetra-deca-2E,8E,10E-trien-4,6-diyne-1-ol, and 14-acetoxy-12- β -methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol showed lower IC₅₀ level than 12-seneciolyloxytetradeca-2E,8E,10E-trien-4,6-diyne-1-ol, 14- β -methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol, and 14- β -methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol⁶⁴. Moreover, the compounds with negative specific rotation, 14-acetoxy-12-seneciolyloxytetradeca-2E,8E,10E-trien-4,6-diyne-1-ol and 14-acetoxy-12- β -methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol, showed stronger inhibitory effects against NO production than those with positive rotation, 14-acetoxy-12-seneciolyloxytetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol and 14-acetoxy-12--methylbutyryltetradeca-2E,8Z,10E-trien-4,6-diyne-1-ol⁶³. Deacylated product of 14- β -methylbutyryltetradeca-2E,8E,10E-trien-4,6-diyne-1-ol, due to boiling extraction with water, results in diminished anti-inflammatory activity⁶³.

Other studies also provide us with pharmacologically explainable clues that could be employed to interpret the traditional therapeutic properties of the *Atractylodes* rhizomes. Atractylodiol and diacetyl-attractylodiol from *A. japonica* can stimulate the contractility of the distal colon in rats by inhibiting the

mechanism of nitrenergic-purinergeric relaxation⁵²⁾. Atractylodin, atractylodinol, acetyl atractylodinol, and 4,6,12-tetradecatriene-8,10-diyne-1,3,14-triol from *A. lancea* can promote delayed gastric emptying¹⁷⁾. These acetylenes, even though the traditional therapeutic properties cannot be entirely explained, are considered key elements for pharmacological accounts of the effects of *Atractylodes* rhizomes that have been used to treat gastrointestinal disorders.

IV. Conclusions

Through bibliographical research, polyacetylenes from the *Atractylodes* rhizomes were divided into three categories; diene-diyne types, triene-diyne types, and monoene-diyne types. Those compounds showed a variety of moieties according to diverse functional groups, with following characteristics:

1. Certain polyacetylenes, including atractylodin or atractylodinol, were chemically unstable at a high temperature and even in freezer storage
2. Processing of the *Atractylodes* rhizomes by stir-frying with bran could lower the contents of polyacetylenes in the rhizomes, but improve bioavailability in vivo
3. Structure-related activities of polyacetylenes were shown in pharmacological studies and gastrointestinal activities were also reported.

The present study will help to understand the physicochemical and pharmacological properties of polyacetylene from *Atractylodes* rhizomes.

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References

1. Bensky D, Clavey S, Stöger E. Chinese Herbal Medicine: Materia Medica 3rd Ed. Seattle : Eastland Press, 2004 : 467-470, 726-30.
2. Korea Food and Drug Administration. The Korean Pharmacopeia 10th Ed. The Korea Food and Drug Administration Notification 2013-103, Korea, 2013: 1143, 1202.
3. Murayama C, Wang CC, Michihara S, Norimoto H. Pharmacological effects of "Jutsu" (*Atractylodes* rhizome and *Atractylodes lancea* rhizome) on 1-(2,5-Dimethoxy-4-iodophenyl)-2-aminopropane (DOI)-induced head twitch response in mice (I). *Molecules*, 2014 ; 19 : 14979-86.
4. Koonrungsesomboon N, Na-Bangchang K, Karbwang J. Therapeutic potential and pharmacological activities of *Atractylodes lancea* (Thunb.) DC. *Asian Pac J Trop Med*, 2014 ; 7 : 421-8.
5. Li X, He H, Xiao M, Song L, Liu M, Xie H, Xu Y, Zhou Z, Yu M, Zhou Y. Effect of volatile oil from *Atractylodes ovata* on hypoxia tolerance ability of mice. *J Hunan Norm Univ (Medical Science)*, 2012 ; 9 : 17-20.
6. Meng H, Li G, Dai R, Ma Y, Zhang K, Zhang C, Li X, Wang J. Chemical constituents of *Atractylodes chinensis* (DC.) Koidz. *Biochem Syst Ecol*, 2010 ; 38 : 1220-3.
7. Polyacetylene. Available from URL: <https://en.wikipedia.org/wiki/Polyacetylene> (retrieved March 23, 2016).
8. Gorman CB, Ginsburg EJ, Grubbs RH. Soluble, highly conjugated derivatives of polyacetylene from the ring-opening metathesis polymerization of monosubstituted cyclooctatetraenes: synthesis and the relationship between polymer structure and physical properties. *J Am Chem Soc*, 1993 ; 115 : 1397-409.
9. Chen HP, Zheng LS, Yang K, Lei N, Geng ZF, Ma P, Cai Q, Du SS, Deng ZW. Insecticidal and repellent activities of polyacetylenes and lactones derived from *Atractylodes lancea* rhizomes. *Chem Biodivers*, 2015 ; 12 : 593-8.
10. Ren CG, Dai CC. Nitric oxide and brassinosteroids mediated fungal endophyte-induced volatile oil production through protein phosphorylation pathways in *Atractylodes lancea* plantlets. *J Integr Plant Biol*, 2013 ; 55 : 1136-46.
11. Ren CG, Dai CC. Jasmonic acid is involved in the signaling pathway for fungal endophyte-induced volatile oil accumulation of *Atractylodes lancea* plantlets. *BMC Plant Biol*, 2012 ; 12 : 1-11.
12. Ouyang Z, Zhang L, Zhao M, Wang P, Wei Y, Fang J. Identification and quantification of sesquiterpenes and polyacetylenes in *Atractylodes lancea* from various geographical origins using GC-MS analysis. *Rev Bras Farmacogn*, 2012 ; 22 : 957-63.
13. Chen Y, Wu Y, Wang H, Gao K. A new 9-nor-atractylodin from *Atractylodes lancea* and the

- antibacterial activity of the atractylodin derivatives. *Fitoterapia*, 2012 ; 83 : 199-203.
14. Wang HX, Liu CM, Liu Q, Gao K. Three types of sesquiterpenes from rhizomes of *Atractylodes lancea*. *Phytochemistry*, 2008 ; 69 : 2088-94.
 15. Li N, Deng C, Li Y, Ye H, Zhang X. Gas chromatography-mass spectrometry following microwave distillation and headspace solid-phase microextraction for fast analysis of essential oil in dry traditional Chinese medicine. *J Chromatogr A*, 2006 ; 1133 : 29-34.
 16. Cho H, Kim H, Chon I, Kang I, Ham I, Ze KR, Whang WK. Studies on the crude drugs on *Atractylodes* species. *Kor J Pharmacogn*, 2003 ; 34 : 123-7.
 17. Nakai Y, Kido T, Hashimoto K, Kase Y, Sakakibara I, Higuchi M, Sasaki H. Effect of the rhizomes of *Atractylodes lancea* and its constituents on the delay of gastric emptying. *J Ethnopharmacol*, 2003 ; 84 : 51-5.
 18. Takeda O, Tsuchiya K, Kimura K, Kubo M, Okada M, He SA. Arginine vasopressin and angiotensin II receptor binding inhibition by *Atractylodes* species. *Pharm Biol*, 2001 ; 39 : 191-7.
 19. Takeda O, Miki E, Terabayashi S, Okada M, He SA, Zhu YC. Essential oil components in commercial samples of the Chinese crude drug, “Cangzhu (Soujutsu in Japanese)” and their botanical origins. *Nat Med*, 1997 ; 51 : 499-503.
 20. Kohjyouma M, Nakajima S, Namera A, Shimizu R, Mizukami H, Kohda H. Random amplified polymorphic DNA analysis and variation of essential oil components of *Atractylodes* plants. *Biol Pharm Bull*, 1997 ; 20 : 502-6.
 21. Takeda O, Miki E, Terabayashi S, Okada M, He SA, Sashida Y. Seasonal variation of essential oil components in *Atractylodes lancea* DC. propagated by division of their rhizomes. *Chem Pharm Bull*, 1996 ; 44 : 823-8.
 22. Mizukami H, Shimizu R, Kohda H, Kohjyouma M, Kawanishi F, Hiraoka N. Restriction fragment length polymorphisms of rDNA and variation of essential oil composition in *Atractylodes* plants. *Biol Pharm Bull*, 1996 ; 19 : 577-80.
 23. Takeda O, Miki E, Terabayashi S, Okada M, He HS, He SA. Variation of essential oil components in *Atractylodes lancea* (Thunb.) DC. growing in Shanxi (陝西) and Henan (河南) province, China. *Nat Med*, 1996 ; 50 : 289-95.
 24. Takeda O, Miki E, Terabayashi S, Okada M, Lu Y, He HS, He SA. Variation of essential oil components of *Atractylodes lancea* growing in China. *Nat Med*, 1995 ; 49 : 18-23.
 25. Hiraoka N. Intra-plant distribution of essential oil components and oil accumulation tissues in *Atractylodes lancea*. *Nat Med*, 1995 ; 49 : 168-71.
 26. Takeda O, Miki E, Morita M, Okada M, Lu Y, He HS, He SA. Variation of essential oil components of *Atractylodes lancea* growing in Mt. Maoshan area in Jiangsu province, China. *Nat Med*, 1994 ; 48 : 11-7.
 27. Kohda H, Gotoh K, Anetai M, Yamagishi T. Studies on the botanical origin of *Atractylodes lancea* “Cang Zhu”. *Nat Med*, 1994 ; 48 : 58-62.
 28. Kawanishi F, Takahashi T, Omukai T, Zhang BG, Li ZL, Xiao PG. Comparison of the outer morphologies, growth and the components in the rhizomes of *Atractylodes* plants cultivated in Kyoto and Beijing. *Nat Med*, 1994 ; 48 : 1-10.
 29. Hiraoka N, Kagoshima K. Morphological and chemical evaluation of *Atractylodes lancea* plants raised from refrigerated shoot cultures. *Plant Tissue Culture Letters*, 1993 ; 10 : 169-71.
 30. Sakurai T, Yamada H, Saito KI, Kano Y. Enzyme inhibitory activities of acetylene and sesquiterpene compounds in *Atractylodes* rhizome. *Biol Pharm Bull*, 1993 ; 16 : 142-5.
 31. Nishikawa Y, Yasuda I, Watanabe Y, Seto T. Studies on the evaluation of crude drugs. II. Identification of the ingredients of *Atractylodes* by thin-layer chromatography-gas chromatography and gas chromatography-mass spectrometry and the physical and chemical evaluation. *Shoyakugaku Zasshi*, 1976 ; 30 : 132-7.
 32. Nishikawa Y, Watanabe Y, Seto T. Studies on the evaluation of crude drugs (I). Comparative studies on the components of *Atractylodes* rhizomes. *Shoyakugaku Zasshi*, 1975 ; 29 : 139-46.
 33. Nakai Y, Yano K, Shiba M, Kondo K, Takeda O, Sakakibara I, Terabayashi S, Takeda S, Okada M. Chemical characterization of rhizomes of *Atractylodes lancea* and *A. chinensis* identified by ITS sequences of nrDNA. *Jpn J Bot*, 2006 ; 81 : 63-74.
 34. Takeda O, Miki E, Terabayashi S, Okada M, Lu Y, He HS, He SA. A comparative study on essential oil components of wild and cultivated *Atractylodes lancea* and *A. chinensis*. *Planta Med*, 1996 ; 62 : 444-9.
 35. Sakurai T, Sugawara H, Saito KI, Kano Y. Effects of TDEYA from *Atractylodes* rhizome on experimental gastric ulcer. *Phytother Res*, 1995 ; 9 : 340-5.
 36. 7Nan Y, Jia LY, Li Q, Sun QS. RP-HPLC simultaneous determination of atractylodin and atractylenolide II in *Rhizoma Atractylodis*. *Chinese J Pharm Anal*, 2010 ; 30 : 17-20.

37. Chen HP, Yang K, You CX, Zheng LS, Cai Q, Wang CF, Du SS. Repellency and toxicity of essential Oil from *Atractylodes chinensis* rhizomes against *Liposcelis bostrychophila*. *J Food Process Pres*, 2015 ; 39 : 1913-8.
38. Takeda O, Miki E, Terabayashi S, Okada M, Lu Y, He HS, He SA. Variation of essential oil components of *Atractylodes chinensis* growing in China. *Yakugaku Zasshi*, 1995 ; 115 : 543-52.
39. Yamahara J, Matsuda H, Kobayashi M, Sawada T, Fujimura H. Biologically active principles of crude drugs (2). Pharmacological evaluation of "Baizhu" and "Changzhu" (II). *Shoyakugaku Zasshi*, 1983 ; 37 : 17-20.
40. Yamahara J, Sawada T, Tani T, Nishino T, Kitagawa I, Fujimura H. Biologically active principles of crude drugs. Pharmacological evaluation of the crude drug "Zhu". *Yakugaku Zasshi*, 1977 ; 97 : 873-9.
41. Nishikawa Y, Yasuda I, Watanabe Y, Seto T. Studies on the components of *Atractylodes* II. New polyacetylenic compounds in the rhizome of *Atractylodes lancea* De Candolle var. *chinensis* Kitamura. *Yakugaku Zasshi*, 1976; 96: 1322-6.
42. Yosioka I, Nishino T, Tani T, Kitagawa I. On the constituents of the rhizomes of *Atractylodes lancea* DC. var. *chinensis* Kitamura ("Jin-changzhu) and *Atractylodes ovata* DC ("Chinese baizhu). The gas chromatographic analysis of the crude drug "Zhu". *Yakugaku Zasshi*, 1976 ; 96 : 1229-35.
43. Shan CX, Cui XB, Chai C, Wen HM, Li W, Yu S, Zhang AH. Effect of bran-frying on chemical profile of *Atractylodes chinensis* (DC.) Koidz. by UFLC/Q-TOF-MS. *J Chin Trad Patent Med*, 2013 ; 35 : 2703-7.
44. Yasuda N, Oka Y, Otsuki K, Tsuchihashi H, Katagi M, Nishikawa M. Study of components in crude drugs by headspace gas chromatography II. Components of *Atractylodes*. *Yakugaku Zasshi*, 1996 ; 116 : 728-34.
45. Pan XY. Analysis of the essential oil compositions in *Atractylodes lancea*. *China Pharmacy*, 2008 ; 19 : 2380-1.
46. Ou YZ, Yang L, Su SL, Feng X, Wang M. Fingerprint of volatile oil of *Atractylodes lancea* by GC-MS. *Acta Pharm Sin*, 2007 ; 42 : 968-72.
47. Wang AW, Tian JK, Geng H, Wu LM, Wang M. Study on chemical constituents of the volatile oil from *Atractylodes chinensis* (DC.) Koidz. and its roasted product. *West Chin J Pharm Sci*, 2004 ; 19 : 417-8.
48. Ji L, Ao P, Pan JG, Yang JY, Yang J, Hu SL. GC-MS analysis of essential oils from rhizomes of *Atractylodes lancea* (Thunb.) DC. and *A. chinensis* (DC.) Koidz. *China J Chin Materia Med*, 2001 ; 26 : 182-5.
49. Resch M, Heilmann J, Steigel A, Bauer R. Further phenols and polyacetylenes from the rhizomes of *Atractylodes lancea* and their anti-inflammatory activity. *Planta Med*, 2001 ; 67 : 437-42.
50. Huang Q, Chen YM, Chou GX, Chen J. Chemical fingerprint establishment and stability study of *Atractylodes lancea*. *Shanghai J Tradit Chin Med*, 2012 ; 46 : 76-8.
51. Meng H, Li G, Dai R, Ma Y, Zhang K, Zhang C, Li X, Wang J. Chemical constituents of *Atractylodes chinensis* (DC.) Koidz. *Biochem Syst Ecol*, 2010 ; 38 : 1220-3.
52. Choi KH, Jeong SI, Lee JH, Hwang BS, Lee S, Choi BK, Jung KY. Acetylene compound isolated from *Atractylodes japonica* stimulates the contractility of rat distal colon via inhibiting the nitrenergic-purinernergic relaxation. *J Ethnopharmacol*, 2011 ; 134 : 104-10.
53. Jeong SI, Kim SY, Kim SJ, Hwang BS, Kwon TH, Yu KY, Hang SH, Suzuki K, Kim KJ. Antibacterial activity of phytochemicals isolated from *Atractylodes japonica* against methicillin-resistant *Staphylococcus aureus*. *Molecules*, 2010 ; 15 : 7395-402.
54. Sakurai T, Yamada H, Saito KI, Kano Y. On the evaluation of the preparation of Chinese medicinal prescriptions VIII. Comparative studies on the acetylenes in *Atractylodes* rhizomes by 3D-HPLC. *Nat Med*, 1994 ; 48 : 291-6.
55. Meng H, Li GY, Dai RH, Ma YP, Zhang K, Chang C, Li X, Wang JH. Two new polyacetylenic compounds from *Atractylodes chinensis* (DC.) Koidz. *J Asian Nat Prod Res*, 2011 ; 13 : 346-9.
56. Yim DS, Yu SC, Chi HJ. Phytochemical study on the rhizome of *Atractylodes japonica* from Korea. *Korean J Pharmacogn*, 1988 ; 19 : 228-32.
57. Sakurai T, Sugawara H, Saito KI, Kano Y. Effects of the acetylene compound from *Atractylodes* rhizome on experimental gastric ulcers induced by active oxygen species. *Biol Pharm Bull*, 1994 ; 17 : 1364-8.
58. Kano Y, Komatsu KI, Saito KI, Bando H, Sakurai T. A new polyacetylene compound from *Atractylodes* rhizome. *Chem Pharm Bull*, 1989 ; 37 : 193-4.
59. Lee SO, Seo JH, Lee JW, Yoo MY, Kwon JW, Choi SU, Kang JS, Kwon DY, Kim YK, Kim YS, Ryu SY. Inhibitory effects of the rhizome extract of *Atractylodes japonica* on the proliferation of human tumor cell lines. *Korean J Pharmacogn*, 2005 ; 36 : 201-4.

60. Yosioka I, Tani T, Hirose M, Kitagawa I. Diacetyl-atractylodiol, a new acetylenic compound from *Atractylodes japonica* Koidzumi. *Chem Pharm Bull*, 1974 ; 22 : 1943-5.
61. Kitajima J, Kamoshita A, Ishikawa T, Takano A, Fukuda T, Isoda S, Ida Y. Glycosides of *Atractylodes lancea*. *Chem Pharm Bull*, 2003 ; 51, 673-8.
62. Nakai Y, Sakakibara I, Hirakura K, Terabayashi S, Takeda S. A new acetylenic compound from the rhizomes of *Atractylodes chinensis* and its absolute configuration. *Chem Pharm Bull*, 2005 ; 53 : 1580-1.
63. Yao CM, Yang XW. Bioactivity-guided isolation of polyacetylenes with inhibitory activity against NO production in LPS-activated RAW264.7 macrophages from the rhizomes of *Atractylodes macrocephala*. *J Ethnopharmacol*, 2014 ; 151 : 791-9.
64. Li CQ, He LC, Dong HY, Jin JQ. Screening for the anti-inflammatory activity of fractions and compounds from *Atractylodes macrocephala* koidz. *J Ethnopharmacol*, 2007 ; 114 : 212-7.
65. Chen ZL. The acetylenes from *Atractylodes macrocephala*. *Planta Med*, 1987 ; 53 : 493-4.
66. Dong H, He L, Huang M, Dong Y. Anti-inflammatory components isolated from *Atractylodes macrocephala* Koidz. *Nat Prod Res*, 2008 ; 22 : 1418-27.
67. Dong HY, Dong YL, He LC, Pei WJ. Studies on constituents and anti-inflammatory activity of rhizome *Atractylodes macrocephala*. *Chin Pharm J*, 2007 ; 42 : 1055-9.
68. Zhao J, Deng J, Li X, Qiu B, Li B, Zeng X. Analysis of polyacetylenes from Rhizoma *Atractylodis*. *Tradit Chin Drug Res Clin Pharmacol*, 2015 ; 26 : 525-8.
69. Chen ZL. Chemical constituents of *Atractylodes macrocephala*. *Acta Chim Sin*, 1989 ; 47 : 1022-4.
70. Wang X, Li L, Ran X, Dou D, Li B, Yang B, Li W, Koike K, Kuang H. What caused the changes in the usage of *Atractylodis Macrocephalae* Rhizoma from ancient to current times? *J Nat Med*, 2016 ; 70 : 36-44.
71. Zhao M, Wang Q, Ouyang Z, Han B, Wang W, Wei Y, Wu Y, Yang B. Selective fraction of *Atractylodes lancea* (Thunb.) DC. and its growth inhibitory effect on human gastric cancer cells. *Cytotechnology*, 2014 ; 66 : 201-8.
72. Liu C, Dou D. Chemical constituents of *Atractylodes macrocephala* from Yuqian. *Chin Arch Tradit Chin Med*, 2014 ; 32 : 1615-7.
73. Li LH, Ran XK, Xu YB, Li B, Dou DQ. A method for evaluation of non-similarity degrees between splitting fractions of *Atractylodis Macrocephalae* Rhizoma. *Chin J Anal Chem*, 2014 ; 42 : 343-8.
74. Huo Y, Liu YQ, Bai ZX, Cai Q. Determination of (4E,6E,12E)-tetradecatriene-8,10-diyne-1,3-diyl diacetate in rat plasma and tissues by HPLC-UV method and their application to a pharmacokinetic and tissue distribution study. *J Anal Methods Chem*, 2014 ; 2014 : 1-7.
75. Liu YQ, Cai Q, Jia TZ. Determination of three components in stir-frying *Atractylodis Rhizoma* with and without bran by HPLC. *J Chin Tradit Patent Med*, 2013 ; 35 : 131-5.
76. Fukuda T, Nakajima J, Aragane M, Yoshizawa M, Iwasaki Y, Suzuki Y, Ibuki N. Studies of cultivation of *Atractylodes ovata* VI. Influence of cultivation method on morphology of crude drug and contents of chemical substances of each part of crude drug. *Nat Med*, 1998 ; 52 : 390-5.
77. Fukuda T, Nakajima J, Yasuda I, Aragane M, Yoshizawa M, Suzuki Y, Shimizu T. Studies of cultivation of *Atractylodes ovata* IV. Individual variation of external morphology and individual difference of amount of growth and contents of chemical substances. *Nat Med*, 1998 ; 51 : 420-6.
78. Kano Y, Sakurai T, Komatsu KI, Yamada H, Saito KI. Polyacetylene compounds from *Atractylodes rhizome*. *Chem Pharm Bull*, 1990 ; 38 : 1082-3.
79. Lehner MS, Steigel A, Bauer R. Diacetoxy-substituted polyacetylenes from *Atractylodes lancea*. *Phytochemistry*, 1997 ; 46 : 1023-8.
80. An JS, Lee SW, Seo EH, Ham DG. Volatile organic compounds (VOCs), and acetylenic fragrant component from *Atractylodes Rhizoma alba*. *Korean Society of Odor Research and Engineering Proceedings PA6*, 2002 ; 11 : 141-5.
81. Ji Y, Feng X, Xiao CC, Dong YF, Wang QZ, Wang M, Zhao YY. A new polyacetylene glycoside from the rhizomes of *Atractylodes lancea*. *Chin Chem Lett*, 2010 ; 21 : 850-852.
82. Kitajima J, Kamoshita A, Ishikawa T, Takano A, Fukuda T, Isoda S, Ida Y. Glycosides of *Atractylodes ovata*. *Chem Pharm Bull*, 2003 ; 51 : 1106-8.
83. Yosioka I, Hikino H, Sasaki Y. Studies on the constituents of *Atractylodes* VI: The structure of atractylodin (1): The skeleton. *Chem Pharm Bull*, 1960 ; 8 : 949-51.
84. Zhang JL, Qin KM, Xu ZS, Yao ZQ, Cai BC. Study on specific chromatograms and content of atractylodin between crude and processed *Atractylodes lancea* and *Atractylodes chinensis*. *Sci Technol Eng*, 2011 ; 11 : 4843-7.
85. Liu YQ, Cai Q, Jia TZ. Determination of three components in stir-frying *Atractylodis Rhizoma* with and without bran by HPLC. *J Chin Tradit Patent Med*, 2013 ; 35 : 131-5.

86. Shan CX, Cui XB, Chai C, Wen HM, Li W, Yu S, Zhang AH. Effect of bran-frying on chemical profile of *Atractylodes chinensis* (DC.) Koidz. by UFLC/Q-TOF-MS. *J Chin Tradit Patent Med*. 2013 ; 35 : 2703-7.
87. Xiao-Wen C, Chen-Xi X, Yu-Qiang L, Cai Q. Determination and pharmacokinetic comparisons of atractylodin after oral administration of crude and processed *Atractylodes* rhizoma. *Pharmacogn Mag*. 2016 ; 12 : 80-3.