The Chemophylogenetic Taxonomy of the Genus *Aconitum* (Ranunculaceae) in Hokkaido and its neighboring territories

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Abstract The accuracy of the species and its varieties ranking was indicated by the analysis of geohistory (g) on physical (P) and chemical (c) characters. In the genus *Aconitum* distributed in Hokkaido and its neighboring territories, the *A. sachalinense* F. Schmidt group showed all the physical variations [var. (P)]. *A. yesoense* Nakai is the subspecies [var. (P-c)] of the above *A. sachalinense* based on physical and chemical considerations. *A. macroyesoense* Nakai was revealed as a natural mutant [var. (c)] of *A. yesoense* based on chemical consideration. *A. itosiyamum* Miyabe et Tatew. is an independent species [var. (p-c-g)] of *A. sachalinense* from the geohistorical consideration joined with both selections.

Introduction

The tribe Delphinieae is characterized by the zygomorphic flowers in the Ranunculaceae, and includes three genera; i.e., *Aconitum*, *Delphinum* and *Consolida*. *Aconitum* is characterized by having two long stalked calcarate petals, and two unguiculate and ecalcarate petals, and three or more carpels. It is well known that a number of diterpenoidal alkaloids are contained in the above Delphinieae as the characteristic components in the secondary metabolitic products (Tamura 1995).

The genus *Aconitum* is clearly divided into three distinct subgenera; i.e., *Gymnaconitum*, *Aconitum* and *Lycoctonum*.

1) Subgenus *Gymnaconitum* is characterized by annual habit and root without abnormal growth. This is the monotypic subgenus composed of *A. gymnandum* Maxim. which is distributed in the central region of China, the Eurasian Continent.

2) Subgenus *Aconitum* is characterized by leaving the daughter tubes in winter. Furthermore, it includes the species having chain tubes of the daughter as *A. soongaricum* Staph. and *A. karakolicum* Rapaics.

3) Subgenus *Lycoctonum* is characterized by having perennial rhizomes separated into several stands, for example, *A. gigas* Lev. et Van’t.

In the diterpenoidal alkaloids of subgenus *Aconitum* the isolation of C19-protoaconines shows the formation of C19-aconines from it, which is proceeded from Mannich reaction of the C19-protoaconines via the Wagner-Meerwein rearrangement of C20-atisines.

The biosynthesis of subgenus *Lycoctonum* is mainly characterized by the oxygenation of 7.8-double bond of the C19-protoaconines. The phenomenon was also observed in several hybridized species in subgenus *Aconitum*. Further evolution of *Lycoctonum* metabolism occurred to the esterification with anthranilic acid derivatives or Baeyer-Villiger oxidation on 4-hychoxymethyl function of C19-lycoctonums except methylation.

The systematic classification of subgenus *Aconitum* has long been considered quite difficult because its species show high levels of morphological and ecological variability (Nakai 1953). However, Kita et al. (1995) reported recently on the studies of molecular phylogeny of Asian species of subgenus *Aconitum* based on RFLP and sequences of the intergenic spacer between the trn L (UAA) 3’exon and trn F (GAA), and of the trn L intron of the chloroplast DNA.

In this paper, authors describe in detail on the chemophylogenetic taxonomy of subgenera *Aconitum* and *Lycoctonum* in Hokkaido and its neighboring territories based on the above theoretical terms and experimental results. It is concluded that the species and its varieties are expressed by the evolutionary location of three dimensional coordination consisting of physical, chemical and geohistorical selections.

Fundamental unit of organization, the species was distinguished by the research on the history of physical and chemical characters concerning to an individual plant of Aconite.
Consideration and Discussions

1) Morphological consideration

Morphospecies is the orthodox nomenclature for biological species. This is called Linnean species. From particular classification came the term of the biological species for subspecies. Variation, speciation and mutation etc. are generally used (Darwin, 1859; Singh, 1999).

In the twentieth century, the fine words were reported as ecospecies for ecological (Turesson 1922 cited Yasugi et al. 1996, p. 752d), deme for Mendelian (Gilmour 1939 cited Yasugi et al. 1996, p. 963h), and sister species for geographic or sibling species for morphological terms (Mayr 1954 cited Yasugi et al. 1996, p. 597b, 996i). Then, Templeton (1981 cited Yasugi et al. 1996, p. 800g, 1007g) used the expression of evolutionary words, e.g. divergence mode (for adaptation,cline and habitat etc.) and transience mode (for recombined gene, and genetic revolution etc.) (Yasugi et al. 1996). These words are all meaning physical (morphological) observation from the naked eye to electronic microscope.

In the above mentioned category, A. sachalinense F. Schmidt and its allied species are well classified in the previous paper (Ichinohe et al. 2002). From an interest of the island bio-geography, the investigation was first made on the genus Aconitum of Rebun and Rishiri which are isolated from Hokkaido by sea. Specifically, A. sachalinense F. Schmidt var. compactum Miyabe et Tatew. has no opportunity of a hybrid between proper species and the other varieties, because it only propagates by the roots than flowers (Table 1).

Consequently, on the varieties of A. sachalinense F. Schmidt, the sorts of C19-norditerpene alkaloids, jesaconitine, aconitine and mesaconitine, are observed in the quality although they are different in the quantity, respectively. They have in all diversities of the physical (morphological and geographical) selection except A. iio-seiyaman Miyabe et Tatew. as shown in Table 1.

A. gigas Lev. et Van’t of subgenus Lycocotonum is characterized by the pedicles covered with rough-surfaced curved hairs, but this massive collection revealed that most plants had pedicles which were clothed with a mixture of rough-surfaced curved hairs and rough-surface patent hair.

Kadota (2001) reported that the type of intermediate pedicel indumentum suggests putative hybrid derivatives between A. gigas and an unknown species with pedicels villose with rough–surfaced patent hair. Thereupon, Kadota (2001) found A. mashikense Kadota et Umezawa as a new type of species.

A. gigas Lev. et Van’t contains atisine as C20-bases, and so exist lycoctonine, gigacotnine and lycocitnine as C19-bases (Sakai et al. 1978). On the basis of these data and the spectrum of A. umbrosum (Korsch) Korn. (Fig. 3), both are shown as the related species. However, these species are different from A. barbatum Pers. and A. kirinense Nakai which contain C18-bisnor-diterpenoidal alkaloids. Here is shown the skeletal biosynthesis of Aconitum alkaloids is shown in Fig. 1.

2) Chemotaxonomical consideration

The first chemical work was begun by Shimoyama (1881) on Japanese Aconitum plants in 1882. Then, Makoshi (1909) reported on the isolation of jesaconitine from Aconitum species of Hokkaido under the supervision of Schmidt, Marburg University, Germany. In the latter half of the 20th century, the school of Ochiai began the chemical studies on Japanese Aconitum (Ochiai et al. 1955). Jesaconitine is the major alkaloid of the both species, A. sachalinense and A. yessoense. Majima and Morio (1924) purely isolated jesaconitine. The absolute structure of jesaconitine was determined by X-ray crystallographic analysis (Pelletier et al., 1979).

Transplantation of A. grossedentatum Nakai from Mt. Kogosan, Honshu Island to the Botanic Garden of Hokkaido University in Sapporo allowed jesaconitine to produce the variation on the index of leaf form. Thus the above species belonging to the A. japonicum group. Figure 4 shows the LC/MS spectrum of root on wild and native Aconitum japonicum Thunb. (var. subcuneatum Nakai) collected at Kodomari, Aomori Prefecture. An elegant and clear J-pattern appears in the spectrum, but it change to complex and complicated m-pattern spectrum by the hybridization with others.

It is interesting to note the place when and where the specimen of A. japonicum Thunb. was collected, now preserved in Upsala University, Sweden. One of the authors (Y. I.) proposed that it is A. subcuneatum Nakai collected by Tomonoshin Abe at South Hokkaido or Tsugaru Peninsula (e.g. sino surku meaning the true atio in Ainu words) on the basis of the historical and ethical references (Ichinohe 1992). Concerning to cytochemistry, hetero-chromatin is an important factor for the information of the synthetic time or the existence pattern on DNA. The karyomorphological researches were reported by Okada (1979, 1990) and Tamura on A. grossedentatum (2n=32) and A. sanyoense (2n=16).

The investigation of chemical selection proceeded one more step than that of the above mentioned physical selection. Of course, DNA (chloroplast) analysis examines the distribution of nucleic acid in molecular inheritance as the primary metabolic products. This fact is also caused by the results based on a change of the skeletal rearrangement on the secondary metabolites e.g. characteristic components, diterpene alkaloids. The method demonstrated clearly not only the close relationships among A. yuparense Takeda, A. yamazakii Tamura et Namba and A. apoiense Nakai; that is, the alpine type (2n=16) of Hokkaido, but also the relationships among A. tidemontanum Kadota, A. sanyoense Nakai (Kita et al. 1995) and A. tonense Nakai (Kita pers. com.) in Honshu.

In 1940, Suginome and Shimanoouchi (1940) isolated kobusine (German; kobusin'), one of C20-atisine group. : Kobusine was named in comparison with A. sachalinense (small root; Karafuto-kobushi) and A. neosachalinense (large root; Karafuto-ohbushi) in Sakhalin (Karafuto) island of Russia. From either a failure to find older work or neglecting the earlier work, the same nomenclature is observed also in the lignans. (Suginome 2003)
<table>
<thead>
<tr>
<th>Taxa</th>
<th>Inflorescence</th>
<th>Carpel number</th>
<th>Locality</th>
<th>Crude bases (Weak bases)</th>
<th>J</th>
<th>A</th>
<th>M</th>
<th>Voucher specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. sachalinense</em> var. sachalinese (Karafuto-bushi)</td>
<td>dense raceme to corymb</td>
<td>3</td>
<td>no hair</td>
<td>Sakhalin; Poronaisk</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kitami; Yuchi (wet ground)</td>
<td>0.85 ca.9 0.5 0.5</td>
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</tr>
<tr>
<td><em>A. sachalinense</em> var. compactum (Rishiri-bushi)</td>
<td>dense corymb</td>
<td>3</td>
<td>no hair</td>
<td>Rishiri; Mt. Rishiri</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Rebun; Momoiwa (alpine meadow)</td>
<td>1.29 6 2 2</td>
<td></td>
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<tr>
<td><em>A. sachalinense</em> var. lasiocarpum (Kemino-karafuto-bushi)</td>
<td>– (dense corymb)</td>
<td>3</td>
<td>dense hair</td>
<td>Kitami; Yuchi (wet ground)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Kitami; Bakkai (wet ground)</td>
<td>1.59 8 1.5 0.5</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>A. sachalinense</em> var. nemuroense (Kokarafuto-bushi)</td>
<td>corymb to panicle</td>
<td>3–5</td>
<td>no hair or rare hair</td>
<td>Nemuro; Atsuto (wet ground)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Kushiro; Otanoshike (wet ground)</td>
<td>1.10 4 4 trace</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>A. ito-seiyum</em> var. nemuroense</td>
<td>lax panicle to corymb hair</td>
<td>3</td>
<td>dense curled (serpentine zone)</td>
<td>Teshio; Toikanbetsu (wet ground)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Nupromapporo (0.72) (699, 661, 633)</td>
<td>2.81</td>
<td></td>
<td></td>
<td>Ichinohe No.0105-1968</td>
</tr>
</tbody>
</table>

* This is classified as subspecies and the varieties mean each synonymy.
  4. Each population contains ratio 2 of hypaconitine.
  5. Each values are molecular weight.
  6. Herbarium specimen deposited at The Hokkaido University Museum.
<table>
<thead>
<tr>
<th>C20-diterpene alkaloids</th>
<th>C19-norditerpene alkaloids</th>
<th>C18-bisnorditerpene alkaloids</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{C}<em>{20}\text{H}</em>{31}\text{N}$ bases</td>
<td>$\text{C}<em>{20}\text{H}</em>{29}\text{N}$ bases</td>
<td>$\text{C}<em>{19}\text{H}</em>{31}\text{N}$ bases</td>
</tr>
<tr>
<td>napellines</td>
<td>protoaconines</td>
<td>aconines</td>
</tr>
<tr>
<td>atisines</td>
<td>gymnandines (denudatines)</td>
<td>hetidines</td>
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<td>6-oxohetidines</td>
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Figure 1. Skeletal biogenesis of diterpene alkaloids in Delphinieae.
from *A. sachalinense* F. Schmidt.

In 1950, Suginome and Imato reported that *A. kamtchaticum* Wild. et Reichb. contains kobusine as C20-bases and mesaconitine and hypaconitine as C19-bases. *A. neosachalinense* Le’v., which is hybridized with the above *A. kamtchaticum* and *A. fischerii* Reichb., distributes over Sakhalin and was confirmed the existence of miyaconitine as C20-bases (Ichinohe et al. 1970) and sachaconitine, benzoylisodelphonine and isodelphinine as C19 bases (Pelletier et al. 1977). These facts show the predominant course of morphological and biochemical selections. In this case, especially, the absolute structure of proto-aconines becomes a key alkaloids and acts as an important intermediate. From the consideration of the structure on secojesaconitine (Bando et al. 1988), one of us (Y.I.) suggested the existence of the stage of protoaconine group as a determining step, thus proposing a common ionic structure of proto-aconines (Ichinohe 1989, Fig. 1).

Kadota (1987) reported that *A. yesoense* Nakai is the subspecies of *A. sachalinense* F. Schmidt and is also chemically a few steps in the series connection. Moreover, Tamura and Namba (1959) reported already that *A. macroyesoense* Nakai and *A. lucidusclum* Nakai are the ecospecies of *A. yesoense* Nakai as shown in Fig. 5b. It is well known that some toxicaconite plants are mingled with nontoxic ones. Appearance of the instrument on HPL-Lc/Ms using ESI method was achieved at the possibility with super-accuracy of the individual plant in the species population. It is actually observed that the retrogression of aconitines occurs as the biotransformation to lycoctonines via protoaconine skeleton in comparison with *A. yesoense* and *A. macroyesoense*. Consequently, *A. macroyesoense* Nakai

<table>
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<tr>
<th>A. yesoense Nakai</th>
<th>Content*</th>
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<tr>
<td></td>
<td>4.74</td>
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<tr>
<td></td>
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<td></td>
<td>3.65</td>
</tr>
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<td>0.55</td>
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</table>

* The percentage based on Crude base

Table 2a. Isolated alkaloids and their yields from *A. yesoense* Nakai (Takayama et al. 1982).
proves to be a natural mutant of *A. yesoense* and may be called a chemical variation of *A. yesoense* (Table 2-a, b). On the chemical analysis the variation of the diterpenoidal alkaloids was not observed by the transplantation of *A. macroyesoense* from Hokkaido to Kanto region, but it was varied in leave morph (coefficient heterophylly).

It is also observed the impurity in the variety and the metabolism in the structural investigations as well as the case of massive collection of the above mentioned in the morphomic study. The problem was solved by the analysis of the individual body of the plant. Accordingly, *A. macroyesoense* Nakai, a natural mutant, is definitely a chemical variety (var. c) of *A. yesoense* Nakai. On the case of crossbreeding on mutual metabolites of C-20 diterpenoidal alkaloids (e. g. atisines ~ hetidines ~ hetisines ~), the mutation occurred in a new skeletal rearrangement to napellinies via (in situ) an alavistic gymnandine skeleton by the action of potential gene

There are several species in Subgen. *Aconitum* having creeping character although no distributing in Hokkaido. *A. karafutense* Miyabe et Nakai (Nakai 1953), *A. szczukinii* Turcz. (Liao-ning province Institute for Forestry and Soils 1975) and *A. consaguneum* Vorosch. (Charkevicz 1995) are distributed through Provinces Primorskaya to Sakhalin. They contain a trace of gibbererllin-like substances. In comparison with *A. consaguineum* and *A. szczuknii*, the former contains hypaconitine and the latter exists as karakoline in the main C19-norditerpenoidal alkaloids.

3) Geohistorical consideration

It is well known that the Eurasian and North American Continents were connected with the Aleutian Islands like point-bridges. Tsukada (1984) made up a vegetation map of the Japanese Archipelago.
approximately 20,000 years B. P. based on the pollen analysis. *A. delphinifolium* DC is distributed to the Kamchatka Peninsula via the Aleutian Islands from Alaska of the U.S. It contains delphinifoline (lycoctonie skeleton) and 14-acetylsachaconitine (aconitine skeleton) as C19-norditerpenoidal alkaloids. These facts suggest the process to lycoctonies via protoaconines from aconines that is, the evolution of the species is in the direction to Subgen. *Lycoctonum* or *Paraconitium* from *Aconitum*.

Tamura and Namba (1959) classified subgenus *Aconitum* of Hokkaido into four groups (e.g. three as the lowland type and one as the alpine type)

1. *A. japonicum* (*A. subcuneatum*)
2. *A. sachalinense* (*A. yesoense*)
3. *A. maximum*
4. *A. yuparense*

This classification suggests some geohistorical problems before the formation of the Japanese Archipelago as well as the observation of Nakai (1917, 1953).

The treatment of DNA (chloroplast), the analyses of nucleic acid belonging to the primary metabolic products were classified on the relationships of the alpine (2n=16) type in Hokkaido and Honshu although it could not articulate on *A. japonicum* Thunb., and its species (2n=32) (Kita *et al.* 1995) as described in the previous section.

Before the formation of the Japanese Archipelago, the *A. sachalinense* group distributed over northern Hokkaido. Similarly, the *A. japonicum* group was also distributed over southern Hokkaido (Fig. 5a, b).

Then, although the formation of the Soya and Tsugaru straits happened, Hokkaido had been still divided by Ishikari Depression into two islands.

Volcanic eruptions of Mt. Tarumae and Mt. Eniwa were connected with north and south of Hokkaido. Thus *A. yesoense* was occurred as the natural mutant by the spread of the *A. japonicum* group (Fig. 6).

*A. ito-seiyamum* Miyabe et Tatew. grows in the marsh zone on the superbasic serpentinite belt (Mg-Fe exchange reaction system; Mg6SiO14(OH)s-Fe-Ni-Cr redox) particularly geological area (Fig. 6) (Toyokuni 1982; Matsui and Banno 1992). This species shows the difference from p-varieties of other *A. sachalinense* in comparison with Lc/Ms spectra (Ichinohe *et al.*, 2002). According to the consideration of the spectrum, it is possible to describe the physiological course as in Fig. 2 *A. misaoanum* Tamura et Namba, which belongs to *A. maximum* Pall., is distributed over the Kurile Island from the Kamchatka Peninsula, is in progress of the bearing direction.

Consequently, *A. ito-seiyamum* Miyabe et Tatew. is not only p-variety but also chemical and geohistorical varieties of *A. sachalinense* F. Schmidt. The species-level of *A. ito-seiyamum* is confirmed by the results of the analytical considerations.

**Results and Conclusion**

The function of metabolism on the characteristic components, diterpenoidal alkaloids, formulates based on a new direction of the respirative reaction. The phenomenon is caused by a variation of the environments (e. g. meteorological warmth index, the water or soil quality etc).

A sample of the species was obtained in the bloom season. Spectrum of the pure species shows the peaks of brevity on the characteristic alkaloids (Fig. 3). The
cross-pollinated species shows very complex peaks. In the case of mass collection due to the structural determination, frequently, it is observed that an existence of other species is suggested from the description of novel alkaloids (Table 2-a, b).

There are four patterns (J., L., M. and W. types) in pure species and one for hybrid species type (example: m-pattern) in the spectra of Le/Ms.

The authors would like to propose that the species are shown by geohistory of physical and chemical characters on an individual Aconitum plant. They are expressed by the evolitional location of three dimensional coordinations consisting of X-axis (p-selection), Y-axis (c-selection) and Z-axis (g-selection).

1. p-variety; var. (p) (physical selection)
   a) Embryological morphology
   b) Ecological geography
2. c-variety; var. (c) (chemical selection)
   a) Molecular heredity
   b) Physiological chemistry
3. g-variety; var. (g) (geohistorical selection)
   a) Pedological geology
   b) Absolute chronology

The authors would like to name the physiological species to the above biological species.

The chemical investigation of A. miyabei Nakai (a local meaning of Kadohari-bushi distributed in Sakhalin) proved the presence of miyaconitine having α-diketone moiety, the oxidative product of miyaconitine having α-hydroxy-ketone of transannular carbonyl function. This fact means only the substitutional transformation as the chemical selection, and is rather considered by the geological factor. By the use of the above mentioned presentation method, their examples are shown by A. sachalinense F. Schmidt p-var. compactum Miyabe et Tatew., A. yasoeense Nakai, c-var. macroyesoense Nakai and A. sachalinense F. Schmidt g-var. ito-seiyamon Miyabe et Tatew., respectively. However, there are also double and/or triple variety well as the above single selection. Exact species must be uniformed by varieties of the three, and must be exactly distinguished from Linnean species. Then, the origin of new species is the combination of the three varieties [var. (p-c-g)], for example, as in A. ito-seiyamon Miyabe et Tatew.

Acknowledgements

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References


Figure 4. Lc/Ms spectrum of the ethanolic extraction form A. japonicum Thunb. (subcuneatum Nakai).

Orientalis Extremie Sovietici. Tomus 7, 43–68, Nauka, St.-Petersburg.


GILMOUR, G.S.L., 1939. cf. YASUGI et al., 1996, 963h.


KADOTA, Y., 1987. A revision of Aconitum subgenus Aconitum (Ranunculaceae) of East Asia. p 249

Sanwa Shoyaku, Utsunomiya.


MAYR, E.W., 1954. cf. YASUGI et al., 1996, 597b, 996i.


OKADA, H., 1990, Cytological significance of
Figure 5. Geographical distributions of the subgenus *Aconitum* in Hokkaido (cf. Tamura and Namba 1959).


Figure 6. Chemophylogenetic distribution of the subgenus Aconitum, in Hokkaido and its neighboring territories.

TURESSON, G.W., 1922. cf. I.D.B., 751f.