# การประเมินคุณภาพสมุนไพรบัวบกจากแหล่งจัดหาวัตถุดิบในประเทศไทย
# Quality Assessment of *Centella asiatica* (L.) Urban from Herbal Suppliers in Thailand

**นิพนธ์ต้นฉบับ** **Original Article**


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## บทคัดย่อ

**วัตถุประสงค์:** เพื่อศึกษาคุณภาพของวัตถุดิบสมุนไพรบัวบกจากร้านจำหน่ายสมุนไพรและพื้นที่แหล่งปลูกในประเทศไทย **วิธีการศึกษา:** รวบรวมวัตถุดิบสมุนไพรบัวบก 12 ตัวอย่าง (จากร้านจำหน่ายในกรุงเทพมหานคร 4 ตัวอย่าง และแหล่งปลูกสมุนไพร 8 ตัวอย่าง) จากจังหวัดบุรีรัมย์ หนองบัวลำภู มหาสารคาม และปราจีนบุรี เมินเปรียบเทียบปริมาณร้อยละสารสกัดและปริมาณสารสำคัญ ได้แก่ มาเดคาสโซไซด์ เอเชียติโคไซด์ กรดมาเดคาสซิก กรดเอเชียติก และสารไทรเทอร์พีนอยด์รวม **ผลการศึกษา:** พบปริมาณสารสกัดด้วยเอทานอลจากตัวอย่างบัวบกทั้งหมดเป็นไปตามเกณฑ์ของตำรามาตรฐานยาสมุนไพรไทย คือ ไม่น้อยกว่าร้อยละ 15.0 โดยน้ำหนัก เมื่อเปรียบเทียบวัตถุดิบสมุนไพรบัวบกจากร้านสมุนไพรและแหล่งปลูก พบว่าค่าเฉลี่ยร้อยละสารสกัดไม่ต่างกัน (ร้อยละ 23.54 ± 4.35 และ 23.78 ± 5.04 โดยน้ำหนัก ตามลำดับ P-value = 0.990) และสารไทรเทอร์พีนอยด์รวม (ร้อยละ 1.20 ± 0.53 และ 1.98 ± 0.59 โดยน้ำหนัก ตามลำดับ P-value = 0.346) วัตถุดิบสมุนไพรบัวบกที่ซื้อจากแหล่งเดียวกันในช่วงเวลาที่ต่างกันพบความแปรผันของร้อยละสารสกัด (ร้อยละ 16.06 ± 0.22 และ 25.20 ± 1.31 โดยน้ำหนัก P-value < 0.01) และสารไทรเทอร์พีนอยด์รวม (ร้อยละ 1.98 ± 0.20 และ 1.04 ± 0.07 โดยน้ำหนัก P-value = 0.010) พบปริมาณสารไทรเทอร์พีนอยด์แต่ละชนิดต่างกัน โดยสัดส่วนของสารกลุ่มไกลโคไซด์ (มาเดคาสโซไซด์และเอเชียติโคไซด์) ต่อสารกลุ่มอะไกลโคน (กรดมาเดคาสซิกและกรดเอเชียติก) อยู่ในช่วงตั้งแต่ 0.4: 1 ถึง 36.9: 1 ซึ่งแบ่งเป็น 2 กลุ่ม คือ กลุ่มที่สารหลักเป็นไกลโคไซด์และอะไกลโคน **สรุป:** วัตถุดิบสมุนไพรบัวบกมีความไม่คงที่ของคุณภาพวัตถุดิบจากตลาดจำหน่าย และแหล่งปลูกที่ต่างกันทั้งสารไทรเทอร์พีนอยด์และสารกลุ่มไกลโคไซด์ และแหล่งปลูกเดียวกันยังมีปริมาณสารสำคัญแต่ละชนิดต่างกัน



**คำสำคัญ:** บัวบก; สารไทรเทอร์พีนอยด์; คุณภาพวัตถุดิบสมุนไพร; ปริมาณสารสกัดด้วยเอทานอล



## Abstract

**Objective:** To investigate the quality of *C. asiatica* raw material obtained from Thai herbal stores and cultivation sites. **Methods:** Twelve *C. asiatica* raw material samples were obtained, 4 from stores in Bangkok and 8 from cultivation sites samples from Buri Ram, Nong Bua Lamphu, Maha Sarakham and Prachin Buri. These samples were investigated for extract yields and active compound contents (madecassoside, asiaticoside, madecassic acid, asiatic acid and total triterpenoids). **Results:** All the ethanol-soluble extracts met the Thai herbal pharmacopoeia (THP) criteria (i.e., ≥ 15.0% w/w). Between herbal stores and plantation sites, there were no differences of the average extract yields (23.54 ± 4.35 and 23.78 ± 5.04% w/w, respectively, P-value = 0.990) or total triterpenoid contents (1.20±0.53 and 1.98±0.59% w/w, respectively, P-value = 0.346). Nevertheless, variability of the yields (16.06 ± 0.22 and 25.20 ± 1.31% w/w, respectively, P-value < 0.01) and triterpenoid contents (1.98 ± 0.20 and 1.04 ± 0.07% w/w, respectively, P-value = 0.010) was found among the raw materials purchased from the same store at different times. The ratios of the triterpenoids (madecassoside and asiaticoside) to the aglycones (madecassic acid and asiatic acid) varied from 0.4:1 to 36.9:1, and the ratios could be divided into two groups: glycoside-dominant and aglycone-dominant groups. **Conclusion:** The variation in the quality of *C. asiatica* from the same herbal store indicated that it is an unstable herbal material on the market. *C. asiatica* from different plantation sites contained different triterpenoids, mostly glycosides in various amounts. Plants in the same site also had different patterns of active compounds.



**Keywords:** *Centella asiatica*; triterpenoids; herbal material quality; ethanol-soluble extractive

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## Introduction

*Centella asiatica* (L.) Urban is a medicinal plant that is widely used as food, drug and cosmetic, especially for dermatological purposes such as wound healing[1-3], anti-inflammatory activity[4], and venous insufficiency treatment.[5] The major triterpenoids are madecassoside, asiaticoside, madecassic acid and asiatic acid[6], which are used to indicate the quality of raw materials in global regulations. The World Health Organization (WHO) monograph[7] recommends that the madecassoside and asiaticoside contents be greater than 2%, and the United States Pharmacopoeia (USP) shows this value for determining the content of triterpene derivatives.[8] In Thailand, the Thai Herbal Pharmacopoeia (THP) indicates that ethanol-soluble extracts should be greater than or equal to 15% or 24% for water-soluble extracts.[9] According to the

National List of Essential Medicines of Thailand, *C. asiatica* products are categorized into three forms including: herbal tea, capsules and cream, and leaf extract preparations which are recommended for wound healing.[10] The use of *C. asiatica* as a cosmetic and pharmaceutical ingredient is increasing. The raw material supply is derived from two main sources, the herbal market and cultivation sites. The largest trading place is in Bangkok, where the raw material originates from domestic farms and imported material. For cultivation sites, the major cultivation site of this plant is in the northeastern region of Thailand, which supplies *C. asiatica* raw material to the herbal industry. This study aimed to investigate the quality of *C. asiatica* raw material obtained from Thai herbal stores and cultivation sites.

## Materials and Methods

### Plant material sources

Twelve *C. asiatica* samples were obtained from two sources: four dried whole plant materials were purchased from three herbal stores in Bangkok (CA1 to CA4), and CA3 and CA4 were obtained from different batches of the same store. There was no information from sellers about plant origin, accession or age. The dried whole plant materials were initially organoleptic evaluated. For cultivated plant samples, eight samples were harvested from 4 provinces of Thailand specifically Buri Ram (CA5: Na Pho District), Prachin Buri (CA6: Na Di District, and CA12: Noen Hom District), Nong Bua Lamphu (CA7: Na Klang District) and Maha Sarakham (CA8, CA9, CA10 and CA11). The CA8 to CA11 samples were cultivated in the Na Dun District, Maha Sarakham, and were collected from different plots. The aerial parts were washed and dried in a hot air oven at 50 °C for 48 hours, after which the dry biomass was recorded. Their chemical characteristics were evaluated by thin layer chromatography (TLC), and the chemical characteristics of all the materials were compared with those of authentic *C. asiatica* plants according to the Thai Herbal Pharmacopoeia (THP) procedure.[9] The plant material sources are summarized in Table 1.

### Methods

### Plant sample extraction

Each dried plant samples was homogenized into powder, passed through a No. 40 sieve and then extracted by maceration according to the Thai herbal pharmacopoeia (THP) procedure.[9] Fifty grams of powder was macerated with 100 ml of ethanol by shaking for 8 hours and incubated at room temperature for 16 hours. The extracted solutions were filtered through filter paper (Whatman no. 1), evaporated until dryness, kept at 4 - 6 °C and protected from light before analysis. The extract yields (% w/w) from three replications were recorded.

**Table 1** Sources of plant materials.

| Plant material No. | Source |
|---|---|
| CA1 | Herbal store 1, Bangkok |
| CA2 | Herbal store 2, Bangkok |
| CA3* | Herbal store 3, Bangkok |
| CA4* | Herbal store 3, Bangkok |
| CA5 | Plantation site 1, Na Pho District, Buri Ram |
| CA6** | Plantation site 2, Na Di District, Prachin Buri |
| CA7 | Plantation site 3, Na Klang District, Nong Bua Lamphu |
| CA8*** | Plantation site 4, Na Dun District, Maha Sarakham |
| CA9*** | Plantation site 4, Na Dun District, Maha Sarakham |
| CA10*** | Plantation site 4, Na Dun District, Maha Sarakham |
| CA11*** | Plantation site 4, Na Dun District, Maha Sarakham |
| CA12** | Plantation site 5, Noen Hom District, Prachin Buri |

* same store ** different accession *** same plantation

### Triterpenoid content analysis

All sample extracts were diluted with methanol to a concentration of 5,000 µg/ml and filtered through a 0.45 µm filter for triterpenoid content analysis by a Thermo® HPLC model Ultimate 3000. The protocol followed the validated criteria of the Association of Official Analytical Chemists (AOAC) guidelines.[11] A LiChroCART® column (LiChrospher® 100 RP-18, 250 mm × 4 mm I.D., particle size 5 µm), an acetonitrile gradient (solvent A) and 0.1% $H_3PO_4$ (solvent B) were used. The mobile phase of solvent A was varied as follows: 20 – 35% (10 min), 35 – 65% (15 min), 65 – 80% (5 min), 80 – 20% (5 min) and 20% (10 min). The injection volume was 20 µl, the flow rate was 1 ml/min, and detection was performed at 206 nm. Four reference standards, asiaticoside, madecassoside, asiatic acid and madecassic acid, were prepared at five concentrations: 12.5, 25.0, 50.0, 100.0 and 200.0 µg/ml. The validated method of Thong-on et al[12] was applied to estimate the amounts of four triterpenoids in *C. asiatica* samples. Figure 1 and Figure 2 show HPLC chromatograms of four reference standards at 100.0 µg/ml and *C. asiatica* extract at 5,000 µg/ml, respectively.

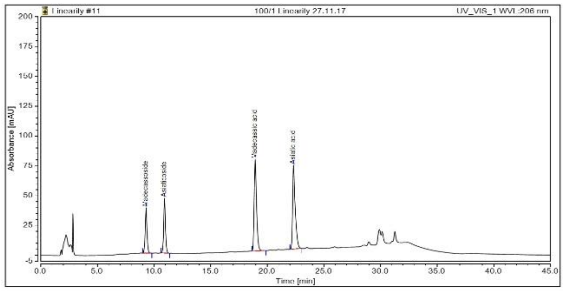


**Figure 1** HPLC chromatogram of madecassoside, asiaticoside, madecassic acid and asiatic acid at 100.0 µg/ml.

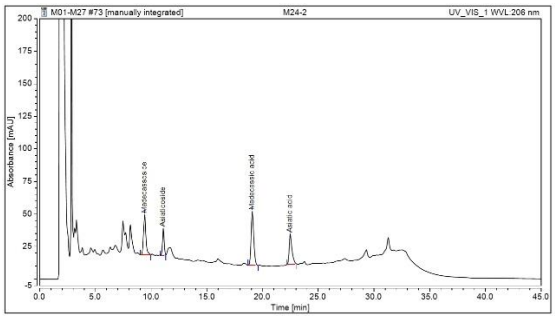


**Figure 2** HPLC chromatogram of C. asiatica extract at 5,000 µg/ml.

**Statistical analysis**

The data were analyzed using PASW ver. 18.0. Significant differences were determined using ANOVA, and multiple pairwise comparisons of means were carried out using Duncan's multiple range test (DMRT) at a 95% confidence level (P-value < 0.05).

# Results

***Centella asiatica* yields and triterpenoid contents from herbal stores and plantation sites**

*C. asiatica* plant materials from 12 sources in Thailand exhibited variations in yield and triterpenoid content (Table 2). The highest extract yield was obtained from CA8 (27.79±0.38% w/w). All extract yields were within the Thai herbal pharmacopoeia (THP) criteria, which indicated that the ethanol-soluble extract of the dried aerial part should be greater than or equal to 15.0% w/w. When comparing plant material sources, herbal stores (CA1 to CA4) and plantation sites (CA5 to CA12), there were no significant differences in average extract yields (23.54±4.35 and 23.78±5.04% w/w, respectively, $p$ = 0.990) or total triterpenoid contents (1.20±0.53 and 1.98±0.59% w/w, respectively, $p$ = 0.346). Among the raw materials purchased from the same store at different times, CA3 and CA4 had different yields (16.06±0.22 and 25.20±1.31% w/w, respectively, $p$ < 0.01) and triterpenoid contents (1.98±0.20 and 1.04±0.07% w/w, respectively, $p$ = 0.010), which indicated unstable herbal material quality in the herbal market. Moreover, the storage conditions (temperature, humidity, and light protection) of plant materials may be the main factors affecting yields and active ingredient contents and may directly affect product quality.

**Table 2** Yield in dry plants (%w/w) and triterpenoid ratio of *C. asiatica* samples from herbal stores and plantation sites.

| Plant material number | Yield in dry plant (%w/w) | | | | | |
|---|---|---|---|---|---|---|
| | Extract yield | Glycosides | | Aglycones | | TT |
| | | MS | AS | MA | AA | |
| CA1 | 27.02 ± 0.30$^{b}$ | 0.31 ± 0.01$^{gh}$ | 0.22 ± 0.02$^{e}$ | 0.16 ± 0.08$^{ef}$ | 0.11 ± 0.06$^{efg}$ | 0.80 ± 0.17$^{g}$ |
| CA2 | 25.89 ± 0.10$^{b}$ | 0.19 ± 0.03$^{h}$ | 0.16 ± 0.03$^{e}$ | 0.36 ± 0.21$^{c}$ | 0.27 ± 0.17$^{c}$ | 0.98 ± 0.43$^{fg}$ |
| CA3 | 16.06 ± 0.22$^{e}$ | 1.03 ± 0.06$^{c}$ | 0.49 ± 0.06$^{cd}$ | 0.30 ± 0.05$^{cde}$ | 0.14 ± 0.02$^{def}$ | 1.98 ± 0.20$^{bc}$ |
| CA4 | 25.20 ± 1.31$^{cb}$ | 0.27 ± 0.02$^{gh}$ | 0.21 ± 0.02$^{e}$ | 0.32 ± 0.01$^{cd}$ | 0.24 ± 0.01$^{cd}$ | 1.04 ± 0.07$^{efg}$ |
| CA5 | 22.81 ± 1.77$^{cd}$ | 0.70 ± 0.36$^{de}$ | 0.51 ± 0.22$^{cd}$ | 0.21 ± 0.03$^{de}$ | 0.16 ± 0.02$^{de}$ | 1.57 ± 0.63$^{cde}$ |
| CA6 | 25.47 ± 0.23$^{b}$ | 0.61 ± 0.04$^{ef}$ | 0.69 ± 0.02$^{b}$ | 0.05 ± 0.00$^{f}$ | 0.04 ± 0.00$^{fg}$ | 1.39 ± 0.07$^{def}$ |
| CA7 | 20.62 ± 0.51$^{d}$ | 1.51 ± 0.04$^{b}$ | 0.65 ± 0.03$^{bc}$ | 0.65 ± 0.03$^{b}$ | 0.02 ± 0.00$^{g}$ | 2.83 ± 0.10$^{a}$ |
| CA8 | 29.79 ± 0.38$^{a}$ | 0.51 ± 0.08$^{efg}$ | 0.27 ± 0.04$^{e}$ | 0.70 ± 0.09$^{b}$ | 0.44 ± 0.03$^{b}$ | 1.93 ± 0.24$^{bcd}$ |
| CA9 | 27.02 ± 0.09$^{b}$ | 0.38 ± 0.03$^{fgh}$ | 0.24 ± 0.02$^{e}$ | 0.98 ± 0.10$^{a}$ | 0.67 ± 0.08$^{a}$ | 2.27 ± 0.23$^{b}$ |
| CA10 | 26.31 ± 0.83$^{b}$ | 0.46 ± 0.01$^{efgh}$ | 0.34 ± 0.01$^{de}$ | 0.41 ± 0.04$^{c}$ | 0.28 ± 0.03$^{c}$ | 1.49 ± 0.09$^{cdef}$ |
| CA11 | 15.79 ± 0.94$^{e}$ | 0.93 ± 0.11$^{cd}$ | 0.55 ± 0.09$^{bc}$ | 0.04 ± 0.02$^{f}$ | 0.02 ± 0.00$^{g}$ | 1.54 ± 0.21$^{cde}$ |
| CA12 | 22.45 ± 4.35$^{d}$ | 1.82 ± 0.38$^{a}$ | 0.93 ± 0.02$^{a}$ | 0.05 ± 0.01$^{f}$ | 0.03 ± 0.00$^{g}$ | 2.82 ± 0.61$^{a}$ |

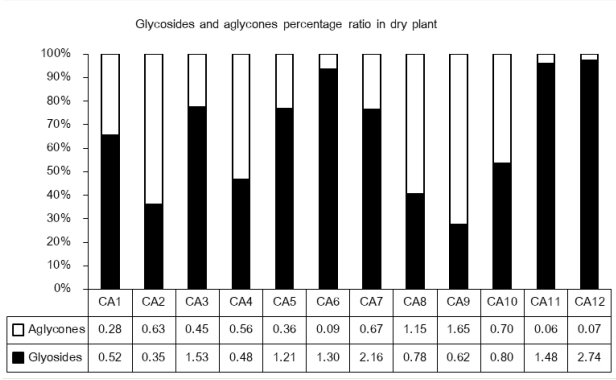
**Note:** MS = Madecassoside; AS = Asiaticoside; MA = Madecassic acid; AA = Asiatic acid; TT = Total triterpenoids. The data are presented as the mean ± standard deviation (SD) (n=3). Different letters within the same column indicate significantly different samples (DMRT, ANOVA p < 0.05).

***Centella asiatica* yields and triterpenoid contents at different plantation sites**

To avoid the degradation of active compounds in medicinal plant materials during the postharvesting process[13], we contacted five plantation sites to obtain eight fresh *C. asiatica* materials (CA5 to CA12). Plant materials from different plantation sites, CA5 to CA12, had extraction yields ranging from 15.79-29.79% w/w, and total triterpenoid contents ranging from 1.39-2.83% w/w. In the sample from plantation site 4 at Maha Sarakham, CA8 to CA10 had the highest yields, ranging from 26.31-29.79% w/w, except for CA11, which had lower yields, at 15.79±0.94% w/w. CA9 had the greatest content of the aglycones madecassic acid (0.98 ± 0.10% w/w) and asiatic acid (0.67 ± 0.08% w/w), whereas CA12 had the greatest content of the glycosides madecassoside (1.82 ± 0.38% w/w) and asiaticoside (0.93 ± 0.02% w/w), which were significantly different from those at the other plantation sites. Moreover, CA12 and CA7 had the highest triterpenoid contents, at 2.83±0.10 and 2.82±0.61% w/w, respectively, and contained more than 2% w/w

asiaticoside and madecassoside, respectively, following the acceptable WHO and USP criteria.

Figure 3 shows that the ratios of glycosides to aglycones in the plant materials varied widely from 0.4:1 (CA9) to 36.9:1 (CA12). These ratios could be divided into two groups: a glycoside-dominant group (CA1, CA3, CA5, CA6, CA7, CA10, CA11 and CA12) and an aglycone-dominant group (CA2, CA4, CA8 and CA9).




| | CA1 | CA2 | CA3 | CA4 | CA5 | CA6 | CA7 | CA8 | CA9 | CA10 | CA11 | CA12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aglycones | 0.28 | 0.63 | 0.45 | 0.56 | 0.36 | 0.09 | 0.67 | 1.15 | 1.65 | 0.70 | 0.06 | 0.07 |
| Glyosides | 0.52 | 0.35 | 1.53 | 0.48 | 1.21 | 1.30 | 2.16 | 0.78 | 0.62 | 0.80 | 1.48 | 2.74 |

**Figure 3** The percentage ratio of glycosides to aglycones in dry plants.

## Discussion and Conclusion

This investigation revealed variations in the yield, triterpenoid content and composition of the extracts of *C. asiatica* raw materials from 2 supplier groups, 3 herbal stores and 5 plantation sites in Thailand. Plants collected from different plantation sites tended to produce more triterpenoids than did those from purchased sites. The variation from the same herbal store indicated the unstable quality of the herbal materials on the market. Plants grown at different plantation sites exhibited different yields and active compound patterns. Previous reports of *C. asiatica* triterpenoids have shown that the ratios of these triterpenoids vary widely. In Madagascar, the ratios ranged from 5:1 to 30:114, whereas in South Africa, the ratio was 2.5:115. The factors affecting the chemical composition of *C. asiatica* have been reported previously. Genetics essentially influence the triterpenoid content; madecassoside, asiaticoside, madecassic acid and asiatic acid of *C. asiatica*. Similar to those in other plants, the synthesis and accumulation of secondary metabolites are controlled by individual plant genetics.[16-18] In Thailand, Thong-on et al investigated the effects of *C. asiatica* genetics and harvesting time on yield and triterpenoid content. The tetraploid plants, which are *C. asiatica* raw materials with double chromosome sets, demonstrated greater yields and active compound contents than did the diploid mother plants. Moreover, four-month-old plants, as the optimal harvesting time for producing the highest biomass and triterpenoid content, grew longer (five or six months), turned yellow and wilted, and a new growth cycle started.[19] With respect to the effect of light intensity reported by Sritongkul et al, higher light intensity (0% shading) had the greatest effect on madecassoside and asiaticoside[20], similar to the results of a study in Nepal in which plants grown under light conditions produced more asiaticoside than those grown under shading conditions, whereas less asiatic acid was produced.[21] For the effect of season, Alqahtani et al reported that the total content of four triterpenoids reached its highest levels in the summer season and lowest in the winter.[22] Similar results in India showed that a humid and warm climate generally supported improved biomass and triterpenoid productivity.[23] Therefore, the major factors that directly affect the growth and triterpenoid content of *C. asiatica* can be divided into two main groups: intrinsic (i.e., genetics) and extrinsic factors (i.e., cultivation conditions). Moreover, post-harvesting and storage conditions could affect the stability of triterpenoids and the ratio of glycosides to aglycones in plant materials. The amounts of active compounds in medicinal plants are related to their pharmacological action. We observed the variation in the proportions of glycosides and aglycones (C8 - C11), even when the plant grown in the same plantation site. *C. asiatica*, glycosides and aglycones have different pharmacological effects. For example, several *in vivo* models have reported that asiaticoside and madecassoside have major effects on wound healing, especially burn wounds[24-27], while recent studies of asiatic acid have demonstrated neuroprotective properties and cognitive benefits, such as the prevention of Alzheimer's disease.[28-30] The impact of different proportions of glycosides (asiaticoside and madecassoside) and aglycones (asiatic acid and madecassic acid) in *C. asiatica* raw materials affected pharmacological activities, bioavailability, and therapeutic applications. The consistent proportions of glycosides and aglycones are beneficial for use as quality raw materials for pharmaceutical or cosmeceutical purposes. Measuring the ratio of glycosides to aglycones is important in the standardization and quality control of *C. asiatica* raw materials.

Therefore, the quality control of seedling genetics by using micropropagation could be developed to produce consistent plantlets before planting. Agricultural practices, cultivation conditions (i.e., soil type, irrigation, light intensity), harvesting protocols, postharvest processes and storage conditions should be controlled to produce a chemical composition consistent with that of *C. asiatica* as a high-quality raw material for cosmetic, cosmeceutical and pharmaceutical applications.

In summary, the findings of this study suggest that the cultivation of *C. asiatica* under controlled conditions, post-harvesing processes and storage conditions should be optimized to produce raw material with the desired amounts of each group of active compounds.

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