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Original Article

Investigation and Comparison of Volume and Chemical Compositions of *Ferula assa-foetida* L. Root Essential Oil under Farm and Natural Habitat Conditions

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Abstract

Ferula assa-foetida L. (Apiaceae) (Anguzeh in Farsi) is a medicinal plant which its gum used in medicine. First Agricultural Research, Education, and Natural Resource of Khorasan Razavi Center cultivated seeds of *F.assa-foetida* on the farm in 2002. Then we selected two root samples, one from the farm and the other from the natural habitat of *F.assa-foetida* (Chah-sokhteh, Sabzevar, Iran) in 2020. Then, we extracted essential oil of both root samples using the hydro-distillation method and they were analyzed by capillary gas chromatography and mass spectrometric detections. Result showed that the average volume of E.oil of Anguzeh root (v/w) for nature and farm samples was 0.26% and 0.17%, respectively. Nature and farm E.oils contain 21 and 19 chemical compounds, respectively. Also, the highest percentage of chemical compounds in root E.oil was related to Borneol, which was 37.84% and 33.79%, respectively, for nature and farm samples. In addition, the sum of three chemical compounds including Borneol, P-mentha-1,5-dien-8-ol, and α-guaiene in E.oils of nature and farm accounted for 75.97% and 77.70% respectively. Another result showed that the percentage of p-mentha-1,5-dien-8-ol (3.44%) and α-guaiene (2.34%) in the E.oil of the farm were higher a little bit than the nature sample. Also, 6 chemical compounds such as Camphene, Cis-sabinene hydrate, Cis-carveol, Germacrene B, γ-eudesmol, and 4-cuprenen-1-ol found in root E.oil in nature sample while they were not found in the farm sample. Instead, α-terpinene-7-al, 9-epi-(E)-caryophyllene, and Spathulenol were found in the E.oil of the farm, but they were not in the nature sample E.oil.

Keywords: *Ferula assa-foetida,* Essential oil, GC/MS analysis

Introduction

In many countries, over-exploitation is essentially a local problem, sometimes reaching the national level. One alternative is to domesticate and cultivate medicinal plant species that increasing the supply and potentially helping to reduce pressure on natural habitats [1]. Today, farmers in most countries are taming medicinal plants to protect endangered species [2]. One of the most important goals of taming medicinal plants is easy to access to plant raw materials and reducing the pressure of collecting and exploiting the natural habitats [3]. Most medicinal plants have different production compared with their natural habitat when they grow on the field. In the domestication process of medicinal plants, evaluation of qualitative and quantitative changes of active ingredients is necessary after transfer from nature to farm conditions [4]. One of the endemic plants of Iran whose gum has medicinal and industrial properties is *F.assa-foetida* from Apiaceae family [5]. Other names for *F.assa-foetida* are Anguzeh (Farsi); asafetida (Spanish); awei (Chinese); aza (Greek); ferule persique or merde dudiable (French); haltit or tyib (Arabic); hing (Hindi); stinkasant or teufelsdreck (German) [6].

The genus *Ferula* consists of about 130 species worldwide with thirty species found in Iran, of which fifteen are endemics [5]. Most Ferula species have phytochemical and biological properties [7]. Phytochemical analyses of *Ferula* spp. have confirmed the presence of sesquiterpene coumarins [8,9], sesquiterpenes [10,11], sulfides and volatile oils [12,13]. The exuded substance (gum) by this plant is locally known as "Anguzeh" and it has been traditionally used for the treatment of a vast range of diseases (urinary,

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gasterointestinal and respiratory infections, and epilepsy), as well as an aphrodisiac, an emmenagogue, and also to treat snake and insect bites, with the best-documented folk use being the management of intestinal worm infections [14,15]. There are several reports on the pharmacological activities of *F.assa-foetida* such as antiviral (HSV, HRV, H1N1, HIV), antispasmodic, hypotensive, and antidiabetic [16]. One of the characteristics of its E.oil is the existence of volatile sulfide constituents, a type of non-ubiquitous compounds with significant pharmacological effects [17,18].

Since there was no report about the quality and quality chemical compositions of the E.oil extracted from the root of Anguzeh plant which was grown under field conditions, therefore, we conducted a study to compare the volume and chemical composition of E.oils obtained from the farm and natural habitat.

Material and Methods

Plant Material

In the summer of 2002, Agricultural Research, Education, and Natural Resource of Khorasan Razavi Center collected ripe seeds of *F.assa-foetida* from nature and sowed them in flat furrows in winter of 2002 [19]. The Planting distance and depth of seeds were 50 and 5 cm, respectively, and the seeds were grown under rain-fed conditions. The seeds germinated in April 2003 and seedlings developed and their roots matured sufficiently through these years. For comparison of the quality and quantity of E.oil of Anguzeh root grown in the farm with Anguzeh grown in nature, in April 2020 two samples of the root of *F. assa-foetida* collected. Because *F. assa-foetida* is a perennial hemicryptophyte species, hence we collected two 7-year-old roots of *F.assa-foetida*. One sample from Chah-Sokhteh of Sabsevar city (longitude: 58° 00' 01" E; latitude: 35° 46' 48" N; altitude: 1500 m above sea level), and the other sample from the farm of Khorasan Razavi Agricultural and Natural Resource Research and Education Center (longitude: 59° 38' 22" E; latitude: 36° 13' 21" N; altitude: 990 m above sea level) (Fig. 1). Both areas are in Khorasan Razavi province, Iran. Then the samples were transferred to the medicinal plants laboratory of Khorasan Razavi Agricultural Research Center to extract their E.oils.

Isolation of the Essential Oils

For isolation of the E.oil from root samples, 300 g of Anguzeh fresh root was selected from each sample and milled using a mill (Model PX-MFC90D) according to following analysis [20]. The E.oil extraction operation was performed by a Clevenger-type apparatus based on hydro-distillation (European pharmacopeia, 1998). The duration of the distillation was done for 1.5 hours. This experiment was carried out with three replications and the average weight and volume of E.oils were calculated for each sample (Table 1). Then the E.oils were kept in a dark glass vial at 4 °C for GC–MS examinations.

Gas Chromatography

GC analyses were performed using gas chromatography, Agilent 7890A GC system for identification of the compositions of two E.oil samples. The E.oils were analyzed by GC-MS, Thermo-UFT model, in the central laboratory of Research Institute of Forest and Rangelands, Tehran, Iran. Profile column machine brand HP-5, capillary column, manufactured by Agilent ® J&W™ HP-5 Scientific with Length of 30 m, an inner diameter of 0.25 mm (ID), film thickness: 0.25 µm. The inner surface of the stationary phase material is covered Phenyl Dimethyl Siloxane 5%. Column temperature program: initial temperature 60 °C to start the final temperature of 220 °C. The initial 3 °C per minute to be added and then injected into the chamber to a temperature of 260 °C. Rate: 20 °C/min, hold time: 10 min. Inlet temperature: 260 °C, Split ratio: 40:1. Injection volume: 0.1 µL. Carrier gas: Nitrogen, Flow rate: 0.7 ml/min. Detector (FID) temperature: 260 °C. The carrier gas inlet pressure to the column: helium with a purity of 99/99% of the inlet pressure to the column equal to 5/1 kilogram per square centimeter is set [21].

Gas Chromatography-Mass Spectrometry

GC–MS analysis is performed on an Agilent 7890A/5975C GC-MS system equipped with a DB-5 fused silica column (30 m × 0.25 mm i.d., film thickness 0.25 µm). The oven temperature is programmed as follows: the initial temperature of 60 °C is immediately increased to 220 °C at a rate of 3 °C/min; subsequently the temperature is increased to 260 °C at 20 °C/min and held at this temperature for 3 min. The injector and transfer line temperature are 260 and 280 °C, respectively; carrier gas is helium with a linear velocity of 30.6 cm/s; split ratio 1:100, ionization energy 70 eV, scan time 1s, mass range 30–340 a.m.u. The identity of the volatile oil composition was established from their GC retention indices, relative to C7-C25 n-alkanes standards mixture, and by comparison of their mass spectra and retention indices with those reported in the literature [22, 23] and by computer matching with the Wiley 5 and NIST mass spectra library, whenever possible, by co-injection with standards available in the laboratories. Also, the identified compositions of the E.oils were recorded.

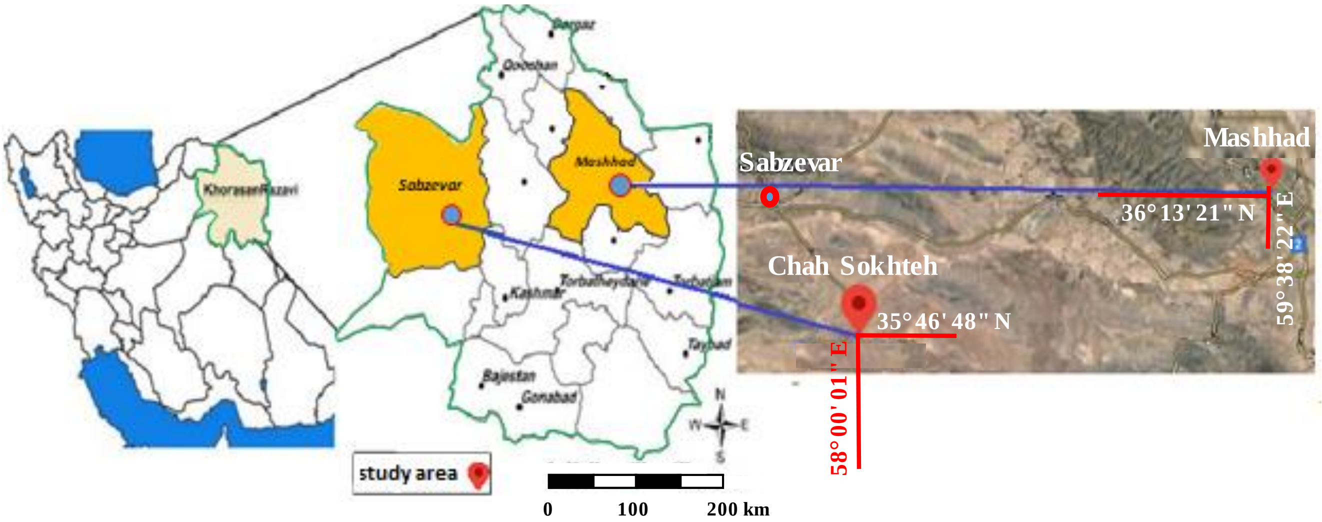


Fig. 1 Sample collection sites

Results

The results showed that *F. assa-foetida* root E.oil has a bright red color and a sulfurous pungent odor. The highest average of weight and volume of the E.oil extracted from the root of *F. assa-foetida* were observed from nature (Table 1).

These compounds belong to four major chemical groups including terpenes, alkanes, ester, and ethers (Table 2). The chemical composition of E.oil from *F.assa-foetida* root for nature and farm samples was identified 99.90% and 99.91% respectively.

The identified compositions and their percentage were shown in Table 2, where the compositions were listed in order of their elution on the HP-5MS column. As it is clarified, the sum of three chemical compound of Borneol, P-mentha-1,5-dien-8-ol, and α-guaiene in Anguzeh root E.oil for nature and farm samples were 75.97% and 77.70 % of E.oil volume, respectively (Fig. 3 and 4).

The highest amount of chemical compound in Anguzeh root E.oil was related to Borneol, which was 37.84% and 33.79%, respectively, for nature and farm samples.

In addition, the amount of p-mentha-1,5-dien-8-ol (3.44%) and α-guaiene (2.34%) in the E.oil of the farm sample were higher a little bit than the nature sample (Fig. 3 and 4).

Also, we found 6 chemical compounds such as Camphene, Cis-sabinene hydrate, Cis-carveol, Germacrene B,γ-eudesmol, and 4-cupreren-1-ol in Anguzeh root E.oil in nature sample, while they were not found in the farm sample (Fig. 5)

Instead α-terpinene-7-al, 9-epi-(E)-caryophyllene, and Spathulenol were found in the E.oil sample of the farm. However, they were not found in the nature sample (Fig. 6).

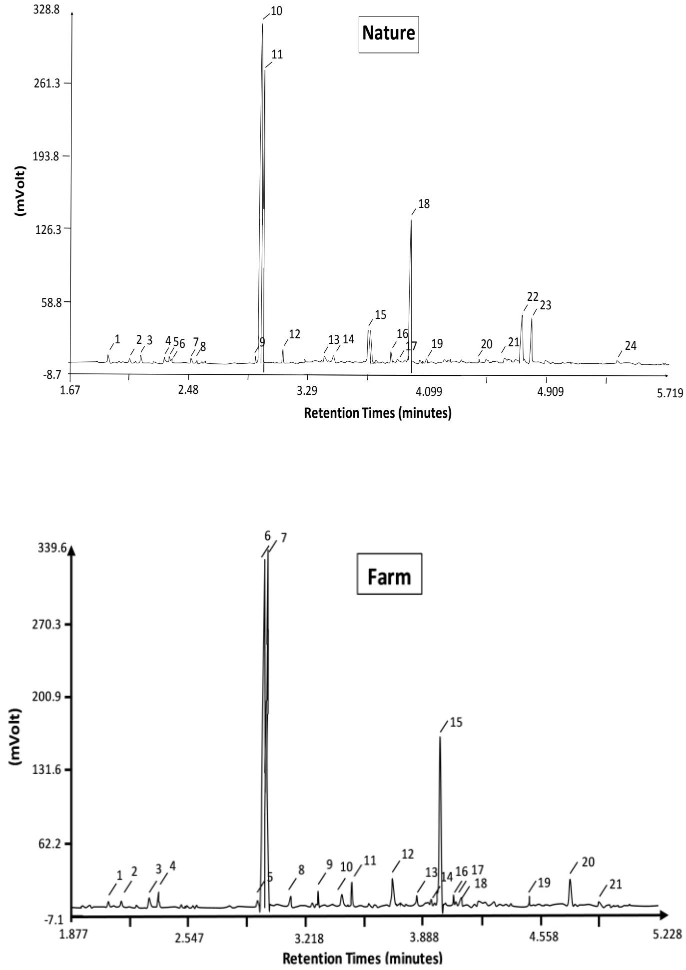


Fig. 2 Gas Cromatogram (GC-MS) of E.oil of *Ferula assa-foetda* L. root (Nature & Farm samples)

Table 1 Weight and volume of E.oil per 300 g of fresh *F. assa-foetda* L. root for samples collected from nature and farm

Sample name	Root wet weight (g)	E. oil weight (g)	Volume of essence (ml)	[E.oil weight (g)/ Root dry weight (g)] * 100 or (v/w)
Nature	300	0.7835	0.80	0.26 %
Farm	300	0.5093	0.52	0.17 %

GC–MS analysis for *F.assa-foetida* root E.oil showed that there are 21 and 19 chemical compounds in nature and farm samples, respectively (Fig. 2).

Table 2 Comparison of percentages and compositions of root E.oils in *F. assa-foetda* L. for natural and field samples

Compounds name	Main chemical compound (%)	Retention index (RI*) (%)	Nature	Farm
Camphene	Terpene	940	0.71	-
Myrcene	Terpene	984	0.55	0.31
γ-terpinene	Terpene	1050	0.37	0.51
Cis-sabinene hydrate	Terpene	1063	0.30	-
Tetra hydro lavandulol	Terpene	1157	0.70	0.74
Borneol	Terpene	1162	37.84	33.79
p-mentha-1,5-dien-8-ol	Terpene	1166	26.49	29.93
Cis-sabinene hydrate acetate	Terpene	1218	0.70	0.76
Cis-carveol	Terpene	1223	0.67	-
α-terpinene-7-al	Terpene	1284	-	0.90
n-tridecane	alkane	1301	0.42	0.94
Dehydro cycloisolongifolene	Terpene	1317	0.63	1.84
α-terpinyl acetate	Terpene	1345	2.48	2.02
α-ubebene	Terpene	1348	1.64	1.67
Geranyl acetate	ester	1379	1.25	0.99
4,8β–epoxy-carophyllene	ether	1426	-	0.63
α-guaiene	Terpene	1437	11.64	13.98
Aromadendrene	Terpene	1439	3.79	5.63
9-epi-(E)-caryophyllene	Terpene	1463	-	1.31
γ-gurjunene	Terpene	1475	0.46	0.77
Germacrene B	Terpene	1559	0.40	-
Spathulenol	Terpene	1576	-	0.80
γ-eudesmol	Terpene	1631	0.51	-
4-cupren-1-ol	Terpene	1691	5.22	-
Germacrone	Terpene	1692	3.14	2.38

*RI, Retention indices relative to C7-C25 *n*-alkanes on a HP-5MS capillary column

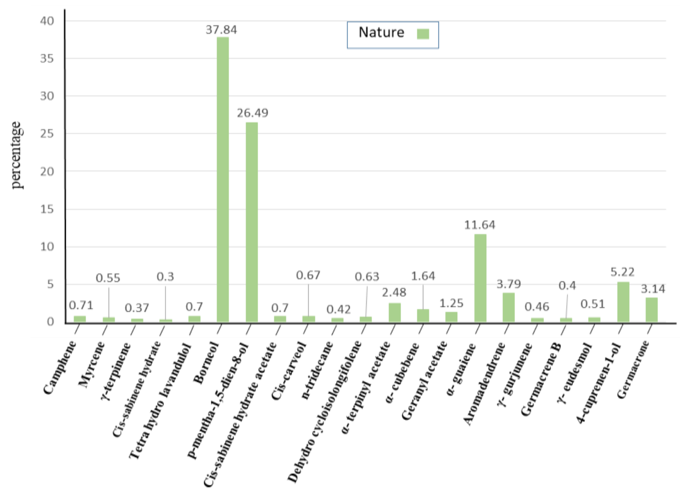


Fig. 3 Identified constituents of root E.oil in the *F. assa-foetda* L. for sample related to nature

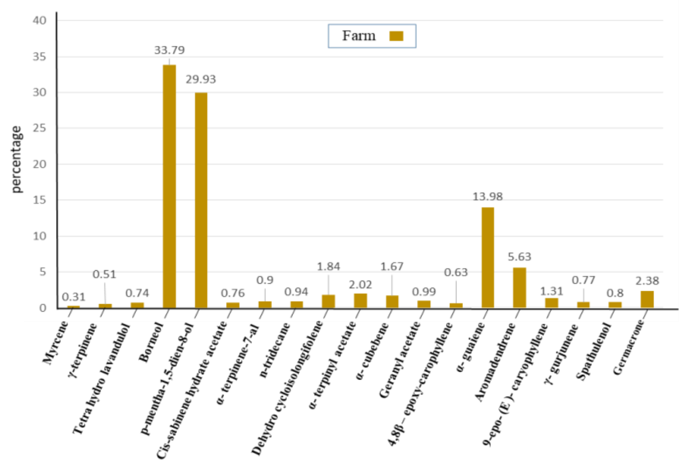
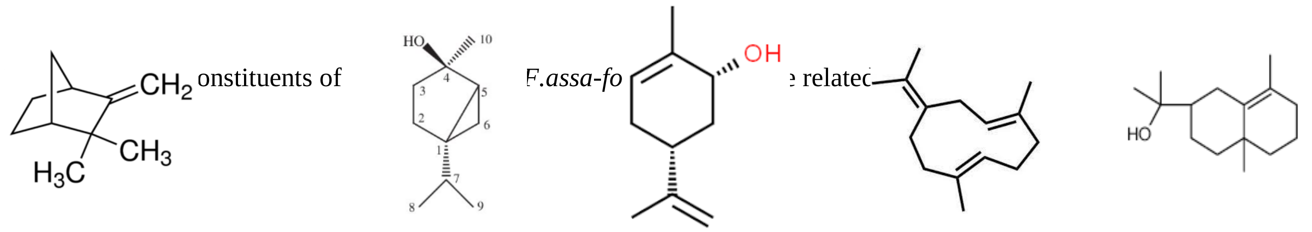
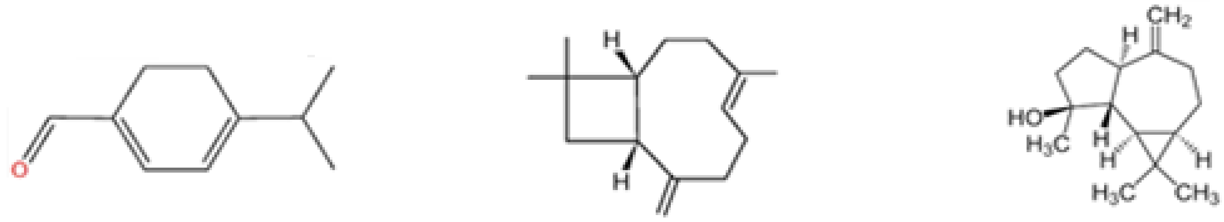


Fig. 4 Identified constituents of root E.oil in the *F. assa-foetda* L. for sample related to farm



Camphene Cis-sabinene hydrate Cis-carveol Germacrene B γ-eudesmol

Fig. 5 The molecular structure of some compounds isolated from the E.oil of *F. assa-foetda* L. root related to the nature sample which was not observed in the farm sample [24].



α-terpinene-7-al 9-epi-(E)-caryophyllene Spathulenol

Fig. 6 Three molecular structures of compounds isolated from the E.oil of *F. assa-foetda* L. root related to the farm sample which were not found in the nature sample [24].

Discussion

The results showed that the E.oil (volatile oils) obtained from *F.assa-foetida* root is an aromatic oily liquid that has a bright red color and a sulfurous pungent odor [25]. In addition, the highest amount and volume of Anguzeh root E.oil was obtained from a sample of nature. Although we found 21 chemical compounds in the sample of natural E.oil and 19 chemical compounds in the sample of E.oil of the farm, some researchers found 30 chemical compounds in *F. Sharifi* E.oil that grows in nature [7]. This difference can be related to edaphic, climatic, and genetic factors. Some researchers reported that percentage of the components of the E.oil varies among species and plants parts which indicated that depending on the species, climate, and altitude, time of collection and growth stage the composition of E.oil might be differed qualitatively and quantitatively [26]. The main chemical compounds of Anguzeh root E.oil consist of four groups including terpenes, alkanes, ester, and ethers [25], while the main chemical groups in *F.Sharifi* E.oil were monoterpene hydrocarbons (43%) including pinene and sabinene [7]. Another result showed that the highest amount of chemical compound in Anguzeh root E.oil in both nature and farm samples is related to Berneol (Fig. 3 & 4). Borneol is a bicyclic organic compound and a terpene derivative that is an expensive compound used in Chinese and Western medicine for many years and it is an ingredient used in 65 traditional Chinese medicinal formulas [27]. In this experiment, another substance that makes up the largest volume of E.oil after borneol is p-mentha-1,5-dien-8-ol. (Fig. 3 & 4). p-mentha-1,5-dien-8-ol is one of the predominant components of monoterpene alcohols, which makes up the volume of E.oil in some Apiaceae plants, such as *F. gummosa* [28]. Our observation showed that Borneol, p-mentha-1,5-dien-8-ol and α-guaiene levels were 37.84%, 26.49%, and 11.64% in the nature sample, respectively, which were slightly different from those obtained in the farm sample. Other researchers reported that the levels of Borneol [29] and α-guaiene [30] in Anguzeh root E.oil are 0.15% and 5.99%, respectively. However, we cannot find "p-mentha-1,5-dien-8-ol" for Anguzeh E.oil in other reports - some researchers, on the other hand, reported that "p-mentha-1,5-dien-8-ol" is found in E.oil of *F.gummusa* (Apiaceae) [31], *Ocimum basilicum* (Lamiaceae) [32], *F. orientalis* (Apiaceae) [33], *Margotia gummiferus* (Apiaceae) [34], and *Heracleum orphanidis* (Apiaceae) [35]. We found "p-mentha-1,5-dien-8-ol" In the essential oil of Anguzeh root grown on the farm which there was not in the essential oil of Anguzeh root grown in nature. On the one hand, we found Camphene, Cis-sabinene hydrate, Cis-carveol, Germacrene B, γ- eudesmol, and 4-cuprenen-1-ol in Anguzeh root E.oil in nature sample and they were not in the farm sample (Fig. 5), but on the other hand, we found α-terpinene-7-al, 9-epi-(E)-caryophyllene, and Spathulenol in the E.oil sample of the farm while they were not found in the nature sample (Fig. 6). This difference may return to interaction among stressors and ecosystem factors or elements of the biotic and abiotic environment [26].

In general, by comparing the amount and composition of E.oil of the field sample with the nature sample, it can be concluded that the cultivation of *F assa-foetida* medicinal plant as a crop to prevent the destruction of Anguzeh habitat seems appropriate. However, it needs to be examined in terms of economy and cost.

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