

Antiviral Phytomedicine Elderberry (*Sambucus*) will be Inhibition of 2019-nCoV

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Abstract

There is not any medicine during the emergency of 2019-nCoV has been an outbreak and we have already found antiviral phytomedicine Chinese elderberry will be inhibition of 2019-nCoV. This commentary used to be presented in June of 2013 at the first international symposium for the elderberry, the conference, held in the USA, many scientists were surprised to learn of the 9 native species of elderberry in China. This paper aims to publish our comment on the elderberry, as, since our initial presentation in 2013, no English literature references are present in China. Most Chinese horticulturists and farmers consider the elderberry a wild plant. It is regarded as a plant of little value due to its abundance and ease of harvest. This article contains details of the *Sambucus* species groups, including the botanical names, Chinese common names, geographic distributions, economic uses and full descriptions of the elderberry. In southwest China, where the climate is mildly warm, there are 2 species of elderberries; one, *Sambucus adnata*, is termed the “blood-red herb-elderberry” by local residents as the roots, rhizomes, and branches exude red-juice when broken. The second, named *S. javanica* or *S. chinensis*, is commonly called the “herb-elderberry”. In northeast China where the climate is cold, there are 7 species of elderberry, however, most scientists recognize only 2 main species: *Sambucus williamsii*, commonly called the “woody-elderberry”, and *Sambucus sibirica*, commonly called the “Siberian woody-elderberry”. The other 5 species of elderberry in northern-east of China.

INTRODUCTION

On the 31st December, 2019, the WHO China Country Office was informed of 44 cases of pneumonia of unknown microbial aetiology associated with Wuhan City, Hubei Province, China. (Overview of 2019 novel coronavirus (2019-nCoV). WHO recommends that the interim name of the disease causing the current outbreak should be “2019-nCoV acute respiratory disease” (where ‘n’ is for novel and ‘CoV’ is for coronavirus) (Novel Coronavirus (2019-nCoV) Situation Report – 10). Seasonal outbreaks of the virus affect nearly 10% of the world population and may lead up to a million deaths annually (Layne, Monto, & Taubenberger, 2009).

There is a folk song that highlights the importance of the elderberry, “Skin, leaf, flower and fruit, each piece is a treasure”². (Compendium of Materia Medica). The medicinal plant is used to relieve stress, various stomach ailments, high cholesterol, congestion, and to fight all strains of the flu. Elderberries additionally promote a healthy complexion and strengthen the body’s immune system. The main elderberry species is *Sambucus nigra*, which is native and common in Europe and the UK. It is found wild along hedgerows, edges of woodlands and on waste ground. *Sambucus canadensis*, the American elderberry, originates from northern America, and is similar to *Sambucus nigra*. *Sambucus caerulea*, the blue elderberry and *Sambucus mexicana*, are similar species’, with the latter originating from warmer climates. The fruit may be blue, bright-blue, or red.

Elderberry, or elder, has been applied to the skin and used for centuries to treat wounds. Additionally,

elder is taken orally to treat respiratory illnesses such the cold and flu in countries such as Germany. Evidence (Compendium of Materia Medica)suggests that chemicals in elder flower and the berries may reduce swelling in mucous membranes such as the sinuses, and help relieve nasal congestion. Elder may have anti-inflammatory, antiviral, and anticancer properties(Compendium of Materia Medica). The action of elderberry (*Sambucus nigra*) is both direct – suppressing viral entry, affecting the post-infection phase, and viral transmission from cell to cell, and indirect – by modulating the release of cytokines such as IL-6, IL-8, and TNF. (Golnoosh Torabian et al. 2019)

Since the launch of Sambucol in the US in 1995, and achievement of the Vity Awards in 1997, 1998, 1999, numerous products have appeared and the beneficial properties of elderberry are now known worldwide. Sambucus nigra L. product –Sambucol was shown to be effective in vitro against 10 strains of influenza virus. In a double-blind, placebo-controlled, randomized study, Sambucol reduced the duration of flu symptoms to 3-4 days. (Barak, V., et al. 2001). A standardized elderberry extract, (Sambucus nigra), reduced hemagglutination and inhibited replication of human influenza viruses type A/Shandong 9/93 (H3N2), A/Beijing32/92 (H3N2), A /Texas3 6/91 (H1, N1) A, /Singapore6 /85(H1N1)(Zakay-Rones Z et al. 1995). On influenza A and B viruses, elderberry extract offers an efficient, safe and cost-effective supplement to the present armamentarium of medications for the prophylaxis and treatment of influenza. (Zakay-Rones Z et al. 200). The elderberry extract inhibited Human Influenza A (H1N1) infection in vitro with an IC50 value of 252 ± 34 lg/mL. The Direct Binding Assay established that flavonoids from the elderberry extract bind to H1N1 virions and, when bound, block the ability of the viruses to infect host cells. These flavonoids are the major contributors to the anti-influenza activity of the elderberry extract. The molecular mode-of-action of these flavonoids was determined by demonstrating their direct binding to H1N1 virus particles resulting in the inability of the H1N1 viruses to enter host cells, effectively preventing H1N1 infection in vitro (Roschek B Jr. et al.2009).

Elderberry contains flavonoids, which have antioxidant properties and may help to prevent damage to the body's cells. However, very few studies have been done in humans, so researchers have no exact data about the effectiveness of elderberry. Of the several species of elder,*Sambucus nigra* , the European or black elder, is used the most commonly for medicinal purposes. The dwarf elder (*Sambucus ebulus*) is to be avoided as it is toxic. Recommendations suggest using a trusted preparation of elder, raw or unripe fruit –as well as the leaves, seeds, and rind –contain a chemical related to cyanide, which is poisonous.

Elderberry (*Sambucus nigra* L. **subsp. nigra**) is a European species with an oceanic, sub-oceanic, cool-temperate and west-Mediterranean range. This species is common in western and central Europe as well as North Africa, Scandinavia and Great Britain. Its distribution range reaches 63°N latitude in western Norway (with scattered naturalized shrubs up to at least 68°N) and approximately 55°N in Lithuania (Laivins, 2002; Atkinson and Atkinson, 2002).

SAMBUCUS SPECIES IN CHINA

In the world it is well-known that *Sambucus* elderberry is a genus of flowering plants in the family Adoxaceae. It was formerly placed in the honeysuckle family, Caprifoliaceae, but was reclassified with recent genetic research. It contains between 5 and 30 species of deciduous shrubs, small trees and herbaceous perennial plants. The leaves are pinnate with 5–9 leaflets (rarely 3 or 11). Each leaf is 5–30cm long and the leaflets have serrated margins. They bear large clusters of small white or cream-colored flowers in late spring; these are followed by clusters of small black, blue-black, or red berries (rarely yellow or white). The black-berried elder complex is treated as single species*Sambucus nigra*, found in the warmer parts of Europe and North America with several regional varieties and subspecies. The flowers are in flat corymbs, and the berries range from black to glaucous blue. The plants are larger shrubs, reaching 3–8m tall, and occasionally small trees up to 15m tall with a stem diameter of up to 30-60cm.

Sambucus are deciduous trees or shrubs or perennial herbs; Shoots are smooth, striate, or warty, with stout pith, and stems often lenticel, with well-developed marrow. Leaves have an odd number pinnate, opposite stipules with leafy or degraded glands. Inflorescence by Cymose synthesis is an acrogenous complex umbrella

or cone, leaflets are serrate or divided, opposite or alternate. Flowers are small and white or a yellowish-white color, short calyx tubes, five calyx teeth, a five-lobed corolla rotate, five stamens, shorter filaments, exposed anthers, ovaries, a short style or almost no stigma and lobes between two or three. Berries can be red, yellow or purple with three to five seeds, seed shape is prismatic or oval and embryo length is same as endosperm length.

There may be 11 species of elderberry in China (Flora of China, Flora of Heilongjiang, Flora of Inner-Mongolia) and grow from temperate to subtropical regions and tropical mountains. It is not clear when the *Sambucus Nigra* **Linn** European elderberry and *Sambucus Canadian* **Linn** American elderberry were brought into China (Beijing Shanghai, Shandong and Jiangsu Province).

Pollen morphology is of great significance in taxonomy, phylogeny, and paleobotany. Scanning electron microscopy (SEM) studies on pollen from cultivated fruit trees have been carried out for taxonomic purposes and cultivar identification. A pollen diagnosis for our 3 popular elderberry species investigated, European elderberry (*Sambucus Nigra* **Linn**), American elderberry (*Sambucus Canadian* **Linn**) and Chinese Woody-elderberry (*Sambucus wiliamsii*) been made through scanning electron microscopy, are presented below **Fig 1 and Fig 2** :

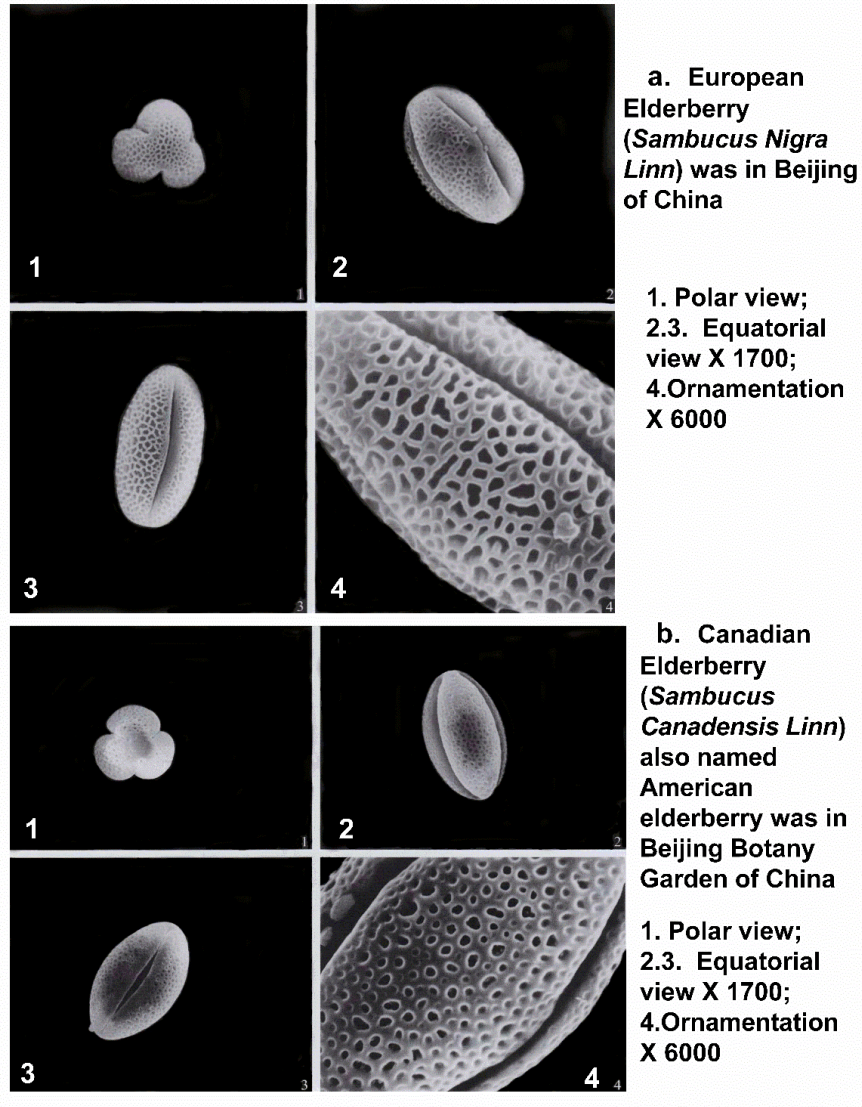


Fig 1. a-1. The pollen has a 3-hole groove; **a-2. and a-3.** The pollen size is about 24 X 14 um, the pollen shape is a long-ball shape with a 3-sided circular shape on the polar surface;**a-4.** The exine surface has a mesh pattern, which is irregularly shaped, and the side of the mesh backbone grain is occasionally seen.

b-1. The pollen has a 3-hole groove, the polar view with 3 parts is round and the polar region is small and raised, and the hole is not obvious; **b-2. and b-3.** The equatorial plane is oblong, the pollen size is about 21X12 um, the pollen shape is long-balloon.**b-4.** The exine surface has a mesh pattern, the mesh backbone is wide, and the mesh circle is irregularly rounded, and there are few particles inside the mesh.



1. Polar view; 2.3. Equatorial view X 1700;
4. Ornamentation X 6000

**The Pollen of Chinese Elderberry named Woody-elderberry
(*Sambucus williamsii* Hance) was in Beijing Xishan, China**

Fig. 2 . 1. The pollen has a 3-hole groove and the polar view is 3-shaped and round; 2. and 3. The shape is a long-ball type and pollen size is about (19-17) X (14-16) um. 4. The exine surface has a mesh pattern. The mesh is round (an irregular polygon) and the base particle is occasionally seen on the side of the mesh backbone.

Chinese Woody-elderberry: *Sambucus williamsii*

This elderberry is a deciduous shrub or small tree, 5-6m high and the old branches are a reddish-brown color with clear oblong lenticels and a pith of hazel color. Pinnate leaves have one to five pairs, the shape is lateral, small and oval, narrowly elliptic to oblong-lanceolate 5-15cm long and 1.2-7cm wide. Leaves have a strong smell if rubbed. Flowers and leaves are growing at the same time with a conical cymes 5-11cm long and 4-14cm wide. With a peduncle, most of the inflorescence branches are at right angles. Fruit is red and rarely blue, violet or black. In the wild, the flowering period is from April to May and the fruit ripening period is from September to October. (**Fig 3 and Fig5-2.**) We have tested the HPLC for Chinese Woody-Elderberry (*Sambucus williamsii*) with standard and tested materials. **Fig 4.**

Geographic Distributions: From Wikipedia, the species is recognized in northeast Asian and from Chinese Words Dictionary the species is recognized in Anhui, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Hebei,

Henan, Heilongjiang, Hubei, Hunan, Liaoning, Jiangsu, Jilin, Shandong, Shanxi, Shaanxi, Sichuan, Yunnan and Zhejiang, The plants are most commonly found under the forest trees, along ditches, among thickets, on valley slopes, in wetlands and among alpine meadows at about 540-1600 meters above sea level.

Medical uses: Whole plant could be used for medicine in curing rheumatism, removing dampness through diuresis, invigorating the circulation of blood, pain relief, treatment of rheumatic arthralgia and myalgia, treatment of lower back pain, treatment of edema, treatment of pruritus, treatment of urticarial, treatment of postpartum ischemia, treatment of traumatic swelling, treatment of bone fractures or the treatment of traumatic hemorrhages (Compendium of Materia Medica).



Fig 3. Image of Chinese woody-Elderberry (*Sambucus williamsii*) in norther China

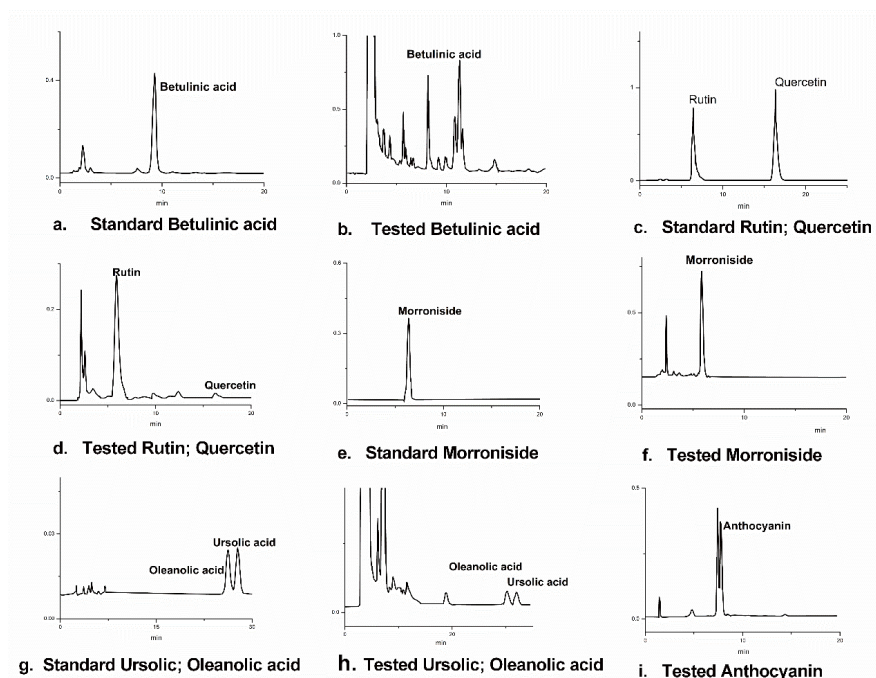


Fig 4. We have tested the HPLC for Chinese Woody-Elderberry (*Sambucus williamsii*) with standard and tested materials.

Chinese Blood-red Herb-elderberry: *Sambucus adnata*

This elderberry is a high perennial herb or soft-wooded shrub, 1-2 meters high. The roots and rhizomes are red, bursting out red juice when broken. The stems are grass-like and have obvious ribs. The leaves are small with three to five pairs and an oblong, ovate or lanceolate shape 4-15 cm long and 1.5-2.5 cm wide. Flowers are small and white with a strong smell and yellow anthers. Fruit is red with wild flowering time between May-July. The elderberry fruit matures between September and October. **Fig 5-1.**

Geographic Distributions: From Wikipedia, species is recognized in the Himalaya's and eastern Asia and from Chinese Words Dictionary the species is recognized in Shanxi, Ningxia, Gansu, Qinghai, Sichuan, Guizhou, Yunnan and Tibet. The plants are most commonly found under the forest trees, along ditches, among thickets, on valley slopes, in wetlands and among alpine meadows at about 1600-3600 meters above sea level. Medical uses: It has been used as a traditional medicine to treat bruises, blood stasis, rheumatism, and diuretic problems.

Chinese Herb-elderberry: *Sambucus chinensis* or *Sambucus javanica*.

This elderberry is a high perennial herb or soft-wooded shrub, 1-2 meters high. The stem has ribs and the pith is white. Leaves are small with two to three pairs and shape is alternate or opposite, narrowly ovate 6-13cm long and 2-3cm wide. New leaves have a hairy surface. Flowers are white, only the base of the joint and anthers are yellow or purple. Fruit is red and wild flowering time is from April to May, ripening between August and September (**Fig 5-3**).

1. Image of Chinese Blood-red Herb-elderberry (*Sambucus adnata*) taken by Yuan. Caixia at Liupanshan, Jingyuan County, Guyuan, Ningxia in China



2. Image of the Chinese Woody-elderberry (*Sambucus williamsii*) taken by Wang. dong in the Garden of Liaoning Normal University, Dalian, Liaoning in China.

3. Image of Chinese Herb-elderberry (*Sambucus chinensis* or *Sambucus javanica*) taken by Wang. Liangcheng at Jiutianfeng, Xuzhou, Anhui in China

Fig 5 . The Imaging of three Chinese Elderberries: 1. Chinese Blood-red Herb-elderberry (*Sambucus adnata*); 2. Chinese Woody-elderberry (*Sambucus williamsii*); 3. Chinese Herb-Elderberry (*Sambucus chinensis* or *Sambucus javanica*).

Geographic Distributions: From Wikipedia, the species is recognized in southeastern Asia and from Chinese Words Dictionary the species is recognized in Anhui, Fujian, Henan, Hubei, Hunan, Gansu, Guangdong, Guangxi, Guizhou, Shanxi, Jiangsu, Jiangxi, Sichuan, Taiwan, Tibet, Yunnan, Zhejiang and Japan. Medical uses: This species is recorded in old Chinese medical books as an herb to treat bruises, rheumatism, help blood circulation, and it is believed to have detoxification anti-inflammatory effect.

Siberian Woody-elderberry: *Sambucus sibirica*

This species is a deciduous shrub, 2-4m high, densely branched with reddish brown skin and vertical cracks. There are oval lenticels, with a light brown pith and twigs with a white papilla. The pinnate usually has two pairs of leaflets, and the rachis and petiole have yellow hirsutes. Small leaves are lanceolate 5-14cm long and 1.6-5.5cm wide. Flowers are light green or yellow with conical cymes. Anthers are ocher yellow and fruit is bright red. Fruit mature period is from July to August.

Geographic Distributions: Xinjiang Fuyun, Fuhai, Siberia and Altai. The plants are most commonly found on stony slopes and beside the stream beds. Medical uses: There are not common uses of this species.

Hairy Woody-elderberry: *Sambucus sieboldiana* or *S. buergeriana*.

This elderberry has new shoots, rachis, pedicels, petioles, and a leaf surface covered by long hair. It is a deciduous shrub or small tree 4-5m high. Small pinnate leaves have two or three pairs, small leaves' main vein and lateral surface contains obvious yellowish-white hair. There is yellow hair on the petiole, rachis and young shoots surface. Fruit is orange-red with two or three seeds. The flowering period is from mid-May to early-June and fruit mature time is July to August.

Geographic Distributions: Inner-Mongolia, Heilongjiang, Jilin, Liaoning as well as Korea and Japan. The plants are most commonly found on valley slopes, forest margins and desert areas at about 540-1600m above sea level. Medical uses: This species can be used for landscaping trees and various medicinal properties,

similar to the Wood Elderberry. New leaves could be consumable and the crushed mixture of shoots and leaves could help in curing injuries of muscles and bones.

6. Hook-tooth Leaf Woody-elderberry: *Sambucus foetidissima*

This species is a deciduous shrub 4-5m high, with an odd number pinnate with five to seven pairs. The leaf shape is oval or slightly oblong, 6-9cm long and 1.5-4cm wide. The leaves have a strong smell and thick, sharp, serrated teeth. The teeth bend inward like hooks. The fruit is red and flowering time is from May to June, fruit mature time is August-September.

Geographic Distributions: Inner-Mongolia only, there is a chance it could be found in Huabei, but no formal record exists. Medical uses: The species is used in landscaping trees and for various medicinal properties.

7. North-Korean Woody-elderberry: *Sambucus coreana*

This elderberry is a deciduous shrub 5m high, with an odd number pinnate with three to five pairs. The leaf shape is lanceolate, 1.5-5cm long and 0.7-2cm wide. The flower is conical inflorescence and light green, the anther is yellow. The fruit is red with three seeds flowering from May to June and maturing in August.

Geographic Distributions: Inner-Mongolia, Heilongjiang, Jilin, Liaoning as well as North-Korea and east of Russia. The plants are most commonly found on the mountain slope and forest margins. Medical uses: The shoots and leaves have medicinal value. The unique seeds contain 18.8% oil which can be used to make soaps and candles. The species may be used in landscaping trees.

8. Latifolia Woody-elderberry: *Sambucus latipinna*

This elderberry is a deciduous shrub, about 3m high, with an odd number of pinnate, opposite with three to five pairs. The leaf shape is oval or oblong, 4-8cm long and 2-3.5cm wide. It called latifolia as the leaflet is 2-3.5cm wide. The flower is conical inflorescence and yellow-green in colour with yellow anthers. The fruit is orange-red flowering in May and maturing in August and September.

Geographic Distributions: Inner-Mongolia, Jilin, Liaoning as well as North-Korea. Shrubs are most commonly found on the mountain slopes, especially along stream beds and in meadowland. Medical uses: There are no common uses of this species.

9. Northern-east Woody-elderberry: *Sambucus mandshurica*

This elderberry is a deciduous shrub about 6m high. The branches grow upright with a reddish grey skin color. There is an odd number of pinnate, opposite with five to seven pairs. The leaf shape is oblong; 2-6cm long and 1-2cm wide. The flower is large conical inflorescence and yellow-green. The anther is yellow and the fruit is red. The flowering period is between May and June and matures in August to September.

Geographic Distributions: Heilongjiang, Jilin, Liaoning, North-Korea, Mongolia, far-east and east-Siberia in Russia. Shrubs are most commonly found on the mountain slopes, especially along stream beds, at bush forest margins, or in low scrub and meadowlands. Medical uses: Shoots and leaves of this species have medicinal value. They are proven to help recover injuries of tendons and muscles. It may also be used in landscaping trees.

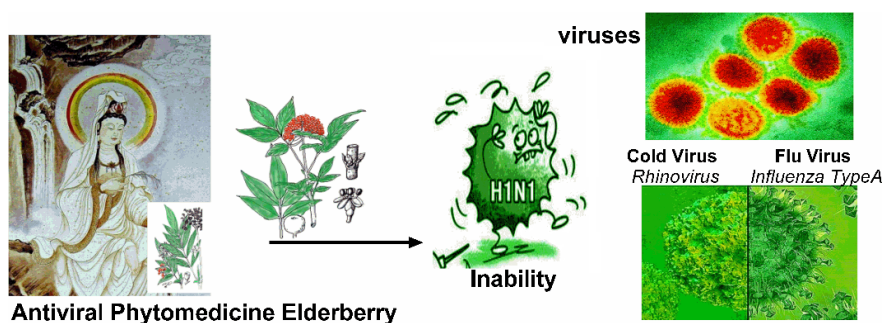
CONCLUSION

It is accepted that there are 11 species of elderberry in China. There is not the evidence about when the *Sambucus nigra* species of elderberry was brought to China (Shanghai, Shandong and Jiangsu Province). In southwest China, where the climate is mildly warm, there are two species of elderberries; *Sambucus adnata*, the “blood-red herb-elderberry” and *S. javanica* or *S. chinensis*, the “herb-elderberry”. There is a significant difference between the herb elderberries and the *Sambucus adnata* elderberry. This is due to the fact that *Sambucus adnata* has a blood-red color in the roots and rhizomes whereas the *S. javanica* or *S. chinensis* elderberry does not.

In northeast China where the climate is cold, there are 7 species of elderberry, however most scientists recognize only 2 species of 7 species: *S. williamsii*, the “woody-elderberry”, and *S. sibirica*, the “Siberian woody-elderberry”. The whole plant of the *S. williamsii* species is able to be used for medicine.

There are an additional 5 species of elderberry in northern-east cold climate of China which is not commonly known to the scientists. *Sambucus sieboldiana* is significantly different from *S. williamsii*, and is commonly called the “hairy woody-elderberry” because its new shoots, rachis, pedicels, petioles, and leaves surface are covered by long hair. The other species are *S. foetidissima*, the “hook-tooth leaf woody-elderberry” as the leaf edge has thick, sharp, serrated teeth that bend inward like hooks. *S. coreana*, the “North-Korean woody-elderberry”, may have originated in North-Korea and whose unique seeds contain 18.8% oil. *S. latipinna*, the “broad-leaf woody-elderberry” is named as it has leaflets 2-3.5cm wide. *S. manshurica*, the “northeast woody-elderberry”, whose leaves and shoots have been used as traditional Chinese medicine to treat human bone fractures.

People have begun to recognize the immense health benefit of elderberry. As a researcher, it is incredibly exciting to be a part of something that has such a positive impact on the world. American elderberry and European elderberry have significantly inability to the flu viruses and cold viruses, we believe that one of 9 Chinese elderberries should be inhibition of the Novel Coronavirus(2019-nCoV).



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Declaration for author contribution statement

Qiang Fu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Mingshu Xu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, Analysis tools or data.

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Declaration of interest

The authors declare that they have no competing interests.