**Supplementary materials**

**A review of Viticis Fructus: botany, historical records, phytochemistry, pharmacology, toxicity, quality control, pharmacokinetics and comprehensive applications**

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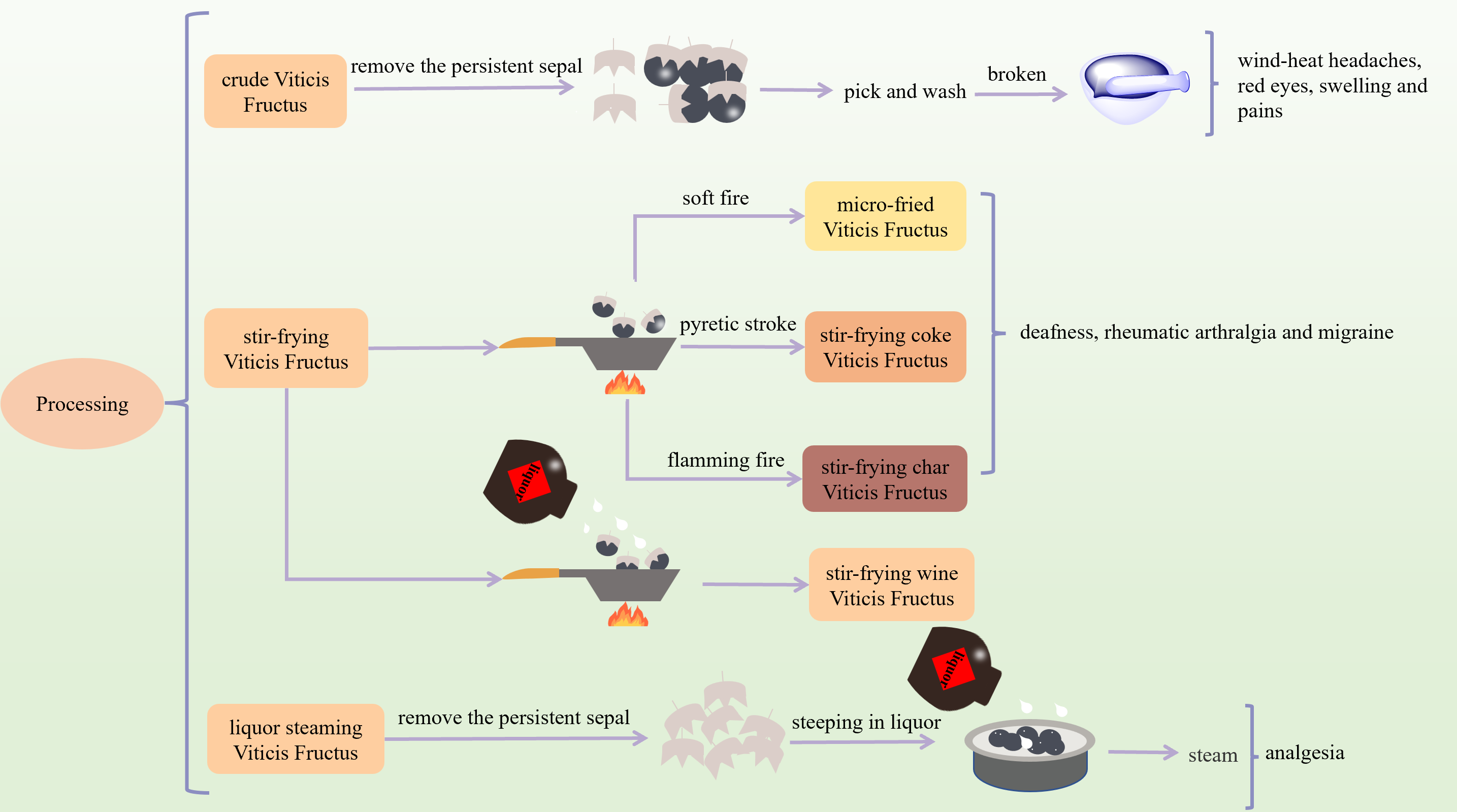
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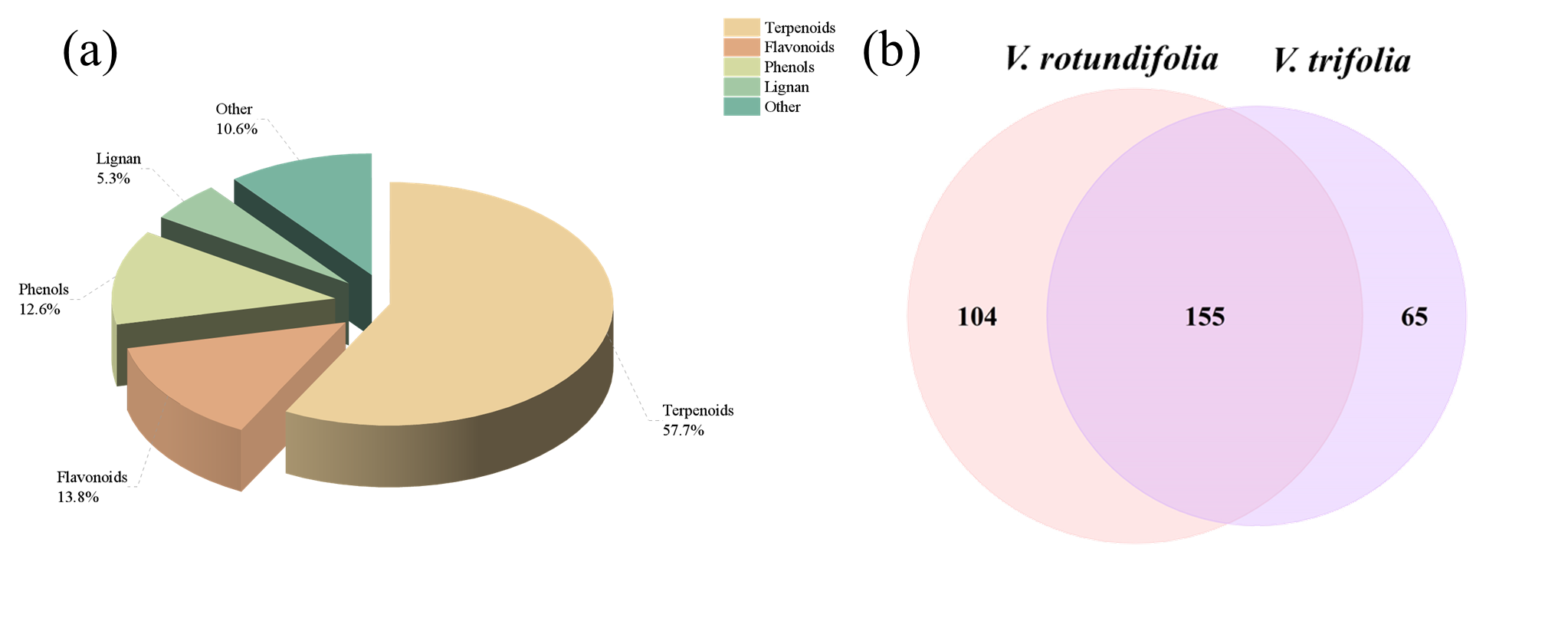
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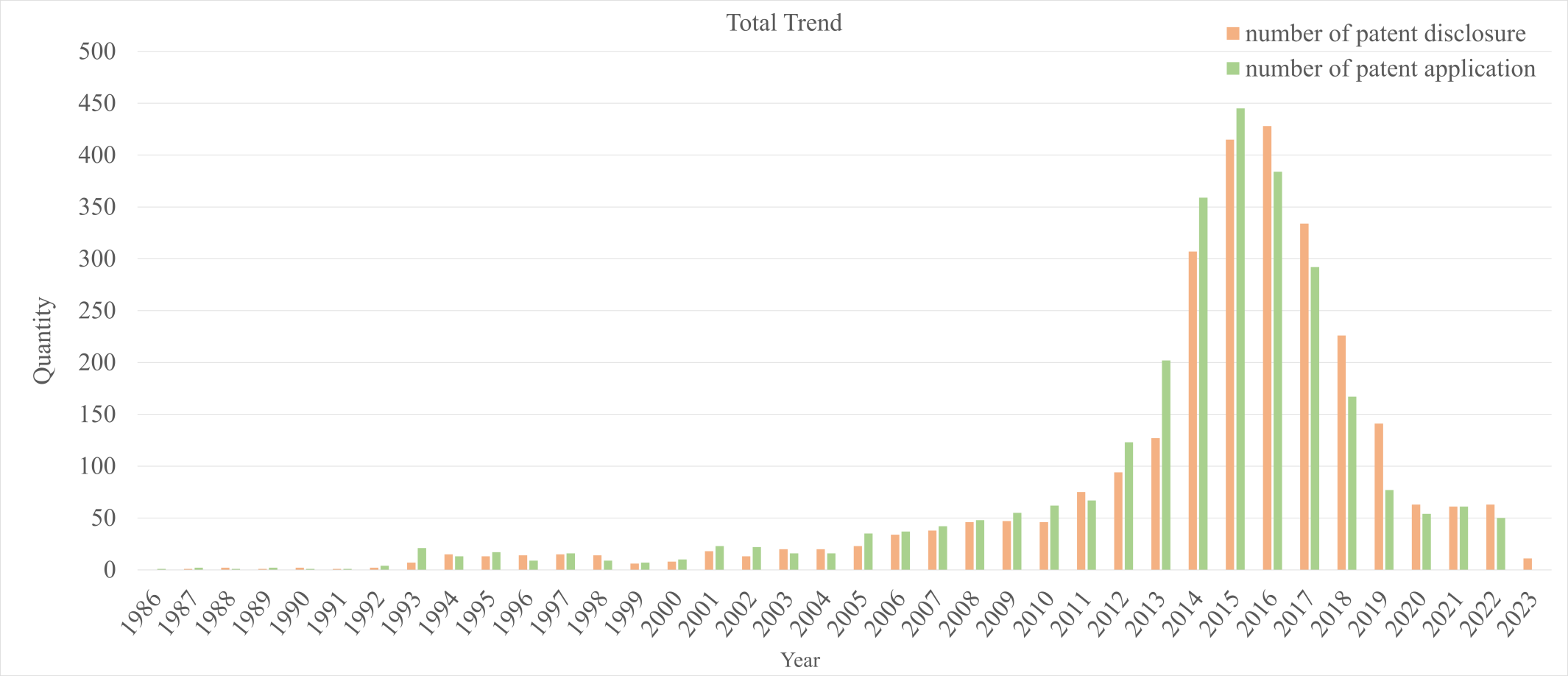
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**Figure S1.** Different processing methods of Viticis Fructus*.*

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**Figure S2.** The proportion of various types of compounds in Viticis Fructus (a) and the Venn diagram of the compound number in the two origins (b).



**Figure S3.** The trend of patent application and disclosure of Viticis Fructus.

Table S1. The origins records of Viticis Fructus in the ancient books

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Origin | Descriptions | Reference |
| Qin-Han Dynasty | *Shennong Bencao Jing* | N/A | *V. negundo* var. *cannabifolia* was not distinguished from *V. trifolia*. | Viticis Fructus was bitter and slightly cold. It could be used to treat rheumatism, remove tapeworms and had the health care effects of bright eyes, firmed teeth and anti-aging, Xiao Jingshi, too. | (Zhang et al., 2018) |
| N/A | *Guangzhi* | Guo YiGong | *V. negundo* var. *cannabifolia* was not distinguished from *V. trifolia*. | *V. negundo* var. *cannabifolia* was *V. trifolia.* | (Zhang et al., 2019) |
| N/A | *Guangya* | Zhang Ji | *V. negundo* var. *cannabifolia* was not distinguished from *V. trifolia*. | *V. negundo* var. *cannabifolia* was *V. trifolia.* | (Zhang et al., 2019) |
| Southern and Northern Dynasties | *Bencao Jingjizhu* | Tao HongJing | The fruit of *V.negundo* var.*cannabifolia* was not used asViticis Fructus*.* | Viticis Fructus was larger than the fruit of *V. negundo* var. *cannabifolia.* | (Tao, 1994) |
| Tang Dynasty | *Xinxiu Bencao* | Su Jing | *V. rotundifolia* | *V. rotundifolia* was a characteristic of creeping and grew on the waterfront. | (Su, 1981) |

Table S1 (*continued*)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Origin | Descriptions | Reference |
| Tang Dynasty | *Shu Bencao* | Han BaoSheng | The fruit of *V. negundo* var. *cannabifolia* was not used asViticis Fructus*.* | *V. trifolia* was *vine*, *V. negundo* var. *cannabifolia* was *tree*,the fruit of *V. negundo* var. *cannabifolia* was larger than Viticis Fructus*.* | (Han, 2005) |
| Song Dynasty | *Bencao Tujing* | N/A | *V. quinata* var*. quinata*, *V. negundo* var*. negundo* and *V. negundo* var*. cannabifolia.* | The pictures in the book were similar to *V. quinata* var*. quinata*, *V. negundo* var*. negundo* and *V. negundo* var*. cannabifolia.* | (Su, 2017) |
| Song Dynasty | *Bencao Yanyi* | Kou ZongShi | The fruit of *V. negundo* var. *cannabifolia* was not used asViticis Fructus*.* | *V. trifolia* was vine, *V. negundo* var. *cannabifolia* was tree. What was the doubt? | (Kou, 1985) |
| Ming Dynasty | *Bencao Mengquan* | Chen JiaMo | The fruit of *V. negundo* var. *cannabifolia* was not used asViticis Fructus*.* | *V. trifolia* wasvine, *V. negundo* var. *cannabifolia* was tree. | (Chen, 1988) |
| Ming Dynasty | *Bencao Yuanshi* | N/A | N/A | The pictures in the book were similar to *V. quinata* var*. quinata*, *V. negundo* var*. negundo* and *V. negundo* var*. cannabifolia.* | (Li, Z.L., 2011) |

Table S1 (*continued*)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Origin | Descriptions | Reference |
| Qing Dynasty | *Bencao Gangmu* | Li ShiZhen | *V. trifolia* | Its branches were as weak as vines, so it was called *V. trifolia.* The pictures in the book were similar to *V. trifolia.* | (Li, S.Z., 2011) |
| Qing Dynasty | *Bencao Chongyuan* | Zhang ZhiCong | The fruit of *V. negundo* var. *cannabifolia* was not used asViticis Fructus*.* | *V. trifolia* was vine, *V. negundo* var. *cannabifolia* was tree. | (Zhang, 1992) |
| Qing Dynasty | *Zhiwuming Shitukao* | Wu QiJun | *V. quinata* var*. quinata*, *V. negundo* var*. negundo* and *V. negundo* var*. cannabifolia.* | The pictures in the book were similar to *V. quinata* var*. quinata*, *V. negundo* var*. negundo and V. negundo* var*. cannabifolia.* | (Wu, 1957) |
| 1935 | *Chinese Pharmaceutical Dictionary* | Chen CunRen | *V. rotundifolia* | *V. rotundifolia* labeled its Latin name as *V. trifolia* var. *unifoliolata.* (This name has been processed by ' Flora of China ' as *Vitex trifolia* L. var. *simplicifolia* Cham.). | (Chen, 1935) |
| 1955 | *Xin Bencao Beiyao* | Chen BangXian | *V. rotundifolia* | *V. rotundifolia* was the original plant of Viticis Fructus*.* | (Chen, 1955) |

Table S1 (*continued*)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Origin | Descriptions | Reference |
| 2020 | Ch. P of 2020 edition | State Pharmacopoeia Committee | *V. rotundifolia* and *V. trifolia* | Viticis Fructus was the fruit of *Vitex trifolia* L. var. *simplicifolia* Cham. and *Vitex trifolia* L. of the Verbenaceae family. | (Chinese Pharmacopoeia, 2020) |

Table S2. The morphologies and habitats of *V. rotundifolia*, *V. trifolia* and its varieties.

|  |  |  |  |
| --- | --- | --- | --- |
| Species | Source | Morphology | Producing areas |
| 1 | *Vitex trifolia* L. | Shrubs or small trees, 1.5-5 m tall, Leaves 1-3(-5)-foliolate. Fruit black, subglobose, ca. 5 mm in diam. | China, S and SE Asia, Australia, Pacific Islands. |
| 2 | *Vitex rotundifolia* L. | Shrubs, prostrate. Leaves mostly 1(-3)-foliolate. Fruit dark brown when dry, globose. | China, Japan, SE Asia, Pacific Islands. |
| 3 | *Vitex trifolia* var. *taihangensis* | Shrubs, erect, 40-90 cm tall. Leaves simple or rarely compound. | China |
| 4 | *Vitex trifolia* var. *trifolia* | Leaves 3(-5)-foliolate; middle leaflet 5-9×1.7-3 cm. | China, SE Asia, Australia, Pacific Islands. |
| 5 | *Vitex trifolia* var. *subtrisecta* | Shrubs, erect. Leaves were both simple and compound; compound leaves were usually 3-foliolate. | China, S and SE Asia, Australia, Pacific Islands. |

Cited from the website: (http://www.iplant.cn/foc)

**Table S3.** **Historical evolution of traditional medical uses of Viticis Fructusin China.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Efficacy/Indications | Reference |
| Qin-Han Dynasty | *Shennong Bencao Jing* | N/A | treat rheumatism and had the health care effects of bright eyes, firmed teeth and anti-aging | (Zhang et al., 2018) |
| Southern and Northern Dynasties | *Mingyi Bielu* | Tao HongJing | headaches, intracranial tinnitus and benefit qi | (Tao, 1986) |
| Eastern jin Dynasty | *Zhouhou Beiji Fang* | Ge Hong | eye swelling, itching astringent, ulcerous eyelid margin and promote hair growth | (Ge, 1955) |
| Tang Dynasty | *Yaoxing Lun* | N/A | headaches and hair growth | (Zhen, 1983) |
| Tang Dynasty | *Qianjin Yifang* | Shun SiMiao | headaches and hair growth | (Sun, 1982) |
| Tang Dynasty | *Rihuazi Bencao* | Wu Yue | lubricate joints, eye diseases and epilepsy | (Ri, 1983) |
| Song Dynasty | *Taiping Shenghui Fang* | Wang HuaiYin | head wind, skin numbness, headache, heartache and limb weakness | (Wang, H.Y., 1958) |
| Song Dynasty | *BoJi Fang* | Wang Gun | phlegm and dry tongue | (Wang, G., 1958) |
| Song Dynasty | *Shengji Zonglu* | N/A | the head and face wind, headache, fever, aversion to wind and sweats. | (Zhao, 1982) |
| Yuan Dynasty | *Danxi Xinfa* | Zhu DanXi | intermittent headache | (Zhu, 1956) |
| Ming Dynasty | *Bencao Gangmu* | Li ShiZhen | treat rheumatism and had the health care effects of bright eyes, firmed teeth and anti-aging | (Li, S.Z., 2011) |

Table S3 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Dynasty | Classic | Writer | Efficacy/Indications | Reference |
| Qing Dynasty | *Bencao Congxin* | Wu YiLuo | headache, intracranial tinnitus, eye pain and tooth pain, arthralgia caused by the damp pathogen | (Wu, 2013) |
| Qing Dynasty | *Depei Bencao* | Yan Jie | dispel cold-dampness, remove headaches, relieve eye pain, treat damp arthralgia, muscular, intracranial tinnitus and toothache. | (Yan et al., 1997) |
| Qing Dynasty | *Bencao Shuzheng* | Peng Shu | treat rheumatism and had the health care effects of bright eyes, firmed teeth and anti-aging | (Zou, 1959) |
| Qing Dynasty | *Bencao Shugou Yuan* | Yang ShiTai | treat rheumatism and has the health care effects of bright eyes, firmed teeth and anti-aging. Additionally, the effect of dispelling wind pathogens, treating solar wind headache (migraine), vertigo, eye pain and tears. | (Yang, 1958) |

**Table S4.** **Viticis Fructus prescription in ancient books.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| **Benefiting effect** | | | | |
| *Study on TCM Treatment of Ocular Fundus Disease* | Yi-Qi-Sheng-Yang-Tong-Luo Prescription | N/A | Strengthening spleen and replenishing qi | *Ginseng Radix et rhizoma*, *Astragali Radix*, *Paeoniae Radix Alba*, Viticis Fructus, *etc*. |
| *Dongyuan Shixiao Fang* | Yi-Qi-Cong-Ming Decoction | 9 g | Dizziness, tinnitus and deafness. | *Astragali radix*, *Codonopsis* R*adix*, Viticis Fructus, *Paeoniae Radix Alba* and so on. |
| *Piwei Lun* | Zhu-Yang-Huo-Xue-Bu-Qi Decoction | 9 g | Reinforcing yang, activating blood circulation and benefiting qi. | *Angelicae Dahuricae Radix*, Viticis Fructus, Glycyrrhizae R*adix et Rhizoma Praeparata Cum Melle* and so on. |
| The 2020 edition of Ch. P | Fu-Ke-Yang-Kun Pill | 119 g | Irregular menstruation, dysmenorrhea and menstrual headache caused by blood deficiency and liver depression. | *Rehmanniae* *Radix* *Praeparata*, *Glycyrrhizae Radix et Rhizoma*, *Chuanxiong Rhizoma*, *Rehmanniae Radix*, *Angelicae Sinensis Radix*, wine steamed Viticis Fructus, *etc*. |

Table S4 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| **The effect of heat clearing** | | | | |
| *Yuan Ji Qi Wei* | Zhi-Zi-Sheng-Qi San | N/A | Clearing heat | *Serpentis Periostracum*, Cassiae Semen, Chuanxiong *Rhizoma* and so on. |
| *Yuan Ji Qi Wei* | Ju-Hua-Jue-Ming San | N/A | Clearing heat in viscera | *Cassiae Semen*, *Haliotidis Concha*, *Equiseti Hiemalis Herba*, *Saposhnikoviae Radix*, *Notopterygll Radix et Rhizoma*,Viticis Fructus and so on. |
| *Yan Ke Zuan Yao* | Xin-Zhi-Chai-Lian Decoction | 10 g | Eyes swelling, red, itching and pain. | *Bupleuri Radix*, *Coptidis Rhizoma*, *Scutellariae Radix*, *Paeoniae Radix*, Viticis Fructus and so on. |
| *Shen Shi Yao Han*•volume 6 | Bi-Yu San | 9 g | Clearing heat, activating blood circulation and alleviating pain. | *Notopterygii Radix et rhizome*, Chuanxiong *Rhizoma,* Viticis Fructus and so on. |

Table S4 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| **The effect of treating wind pathogen** | | | | |
| *Shen Shi Yao Han* • volume 3 | Chai-Xiong Decoction | N/A | Reconciling shaoyang, alleviating pain. | *Chuanxiong Rhizoma*, *Poria*, *Bupleuri Radix*,Viticis Fructus and so on. |
| *Yuan Ji Qi Wei* | Yi-Yang-Jiu-Lian san addition and subtraction | 1.2 g | Dispersing external wind. | Rehmanniae *Radix*, *Angelicae Pubescentis Radix Saposhnikoviae Radi*,Viticis Fructus, *etc*. |
| *System of Ophthalmology* • volume 5 | Bai-Ji-Li San | N/A | Eye disease | *Leonuri Fructus*, *Atractylodis Rhizoma*, Viticis Fructus and so on. |
| Song • *Taiping Huimin Heji Ju Fang* | Fu-Hu Dan | N/A | Paralysis | Rehmanniae *Radix*, Viticis Fructus, Bombyx Batryticatus and so on. |
| *Yi Fang Lei Ju* | Chu-Shi San | N/A | All wind-toxicity and pruritus. | *Sophorae Flavescentis Radix*, Viticis Fructus, *Saposhnikoviae Radix*, *etc*. |
| *Zhengzhi Zhunsheng* • Leifang • volume 5 | Dang-Gui-Chuan-Xiong San | 1.5 g | Headaches | Angelicae *Sinensis* *Radix*, *Chuanxiong Rhizoma*, *Bupleuri Radix*, Viticis Fructus, *etc*. |

Table S4 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| Song • *Taiping Huimin Heji Ju Fang* | Chan-Hua san | Each equal amount | Eye disease | *Cicadae Periostracum*, *Chrysanthemi Flos*, *Saposhnikoviae Radix*,Viticis Fructus, *etc*. |
| **The effect of improving vision** | | | | |
| *Wai Tai MiYao* | Fang-Feng-Man-Jing-Zi wan | N/A | Improving acuity of vision | *Saposhnikoviae Radix*, Coptidis Rhizoma, Viticis Fructusand so on. |
| The 2020 edition of Ch. P | Bo-Yun-Tui-Yi Pill | 80 g | Blurred vision, eye pain and tears. | *Buddlejae* *Flos*, *Chrysanthemi Flos*, *Equiseti Hiemalis Herba*, Viticis Fructus, *etc*. |
| **The effect of treating cold and dispelling summer heat** | | | | |
| *Yixue Xinwu* (Qing • Cheng Guopeng) | Jia-Wei-Xiang-Su San | 3 g | Exogenous wind-cold and treatment qi stagnation. | *Perillae Folium*, *Citri Reticulatae Pericarpium*, *Cyperi Rhizoma*,Viticis Fructus, *etc.* |

Table S4 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| The 2020 edition of Ch. P | Qi-Wei-Ke-Teng-Zi Pills | 66 g | Dispelling heat, invigorating spleen and stomach, resolving convulsion and relieving pain. | The kernel of *Entadae Semen*, *Ferulae Resina*, *Piperis Fructus*,Viticis Fructus, the leaves of *V. trifolia*, *etc.* |
| **The effect of dissipating phlegm** | | | | |
| *Yixue Xinwu* • volume 3 | Ban-Xia-Bai-Zhu-Tian-Ma Decoction | 3 g | Eliminating dampness and phlegm, suppressing hyperactive liver for calming endogenous wind. | *Pinellie Rhizoma*, *Atractylodis macrocephalae Rhizoma*,Viticis Fructus, *etc*. |
| **Analgesia effect** | | | | |
| The 2020 edition of Ch. P | Qing-Shang-Juan-Tong Decoction | 1.865 g | Intractable pain and trigeminal neuralgia. | *Angelicae Sinensis Radix*, *Angelicae Dahuricae Radix*, *Chuanxiong Rhizoma*, *Angelicae Pubescentis Radix*, *Saposhnikoviae Radix*, Viticis Fructus, *etc.* |

Table S4 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source | Preparation Name | Dosage of Viticis Fructus | Efficacy/Indications | Main Compositions |
| The 2020 edition of Ch. P | Tian-Ju-Nao-An Capsule | 166 g | Migraine, vertigo caused by vertebral-basilar insufficiency. | *Chuanxiong Rhizoma*,*Gastrodiae Rhizoma*, *Chrysanthemi Flos*,Viticis Fructus, *Ligustici Rhizomaet Radix*, *etc.* |
| The 2020 edition of Ch. P | Xiong-Ju-Shang-Qing Pill | 30 g | Migraine | *Chuanxiong Rhizoma*, *Chrysanthemi Flos*,  *Scutellariae* *Radix*, *Gardeniae Fructus*, stir-fried Viticis Fructus, *etc*. |
| **The effect of curing rheumatism** | | | | |
| The 2020 edition of Ch. P | Qiang-Huo-Sheng-Shi Decoction | 2 g | Rheumatism | *Notopterygii Rhizoma et Radix*, *Angelicae Pubescentis Radix*, *Saposhnikoviae Radix*, *Ligustici Rhizomaet Radix*, *Chuanxiong Rhizoma*, *Glycyrrhizae Radix et Rhizoma* and Viticis Fructus*.* |

**Table S5.** **Processing methods of Viticis Fructus in different periods.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Dynasty | Book | Editor | Processing name | Processing method |
| Southern and Northern Dynasties | *Leigong Paozhi Lun* | Lei Xiao | Liquor steaming | Viticis Fructus was removed the persistent calyx and pedicle. After soaking in liquor for ten days, it was steamed for several hours and dried in the sun. |
| Tang Dynasty | *Shiliao Bencao* | Meng Shen | Steaming | Viticis Fructus was steamed and exposed many times, pounded into powder. |
| Tang Dynasty | *Waitai Miyao* | Wang Tao | N/A | Soak in liquor. |
| Song Dynasty | *Taiping Shenghui Fang* | Wang HuaiYin | Boiling | The ratio of medicine to liquor was 1:5, and after the wine was boiled, it was dried in the sun. |
| Song Dynasty | *Boji Fang* | Wang Gun | Micro-frying | Viticis Fructus was washed clean, baked with slight fire and then broke; washed, stir fry. |
| Song Dynasty | *Taiping Huimin Heji Jufang* | N/A | Stir-frying | The persistent sepal removal; stir-fry. |
| Song Dynasty | *Shengji Zonglu* | N/A | Stir-frying | The persistent sepal removal; stir-fry. |
| Yuan Dynasty | *Danxi Xingfa* | Zhu DanXi | Stir-frying char | Fry to black. |

Table S5 (*continued*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Dynasty | Book | Editor | Processing name | Processing method |
| Ming Dynasty | *Bencao Mengjian* | Chen JiaMo | Stir-frying | Harvest according to time, dry in the shade and stir fry to remove non-medicinal parts. |
| Ming Dynasty | *Yixue Rumen* | Li Chan | Liquor steaming | Liquor steamed, dried and mashed. |
| Ming Dynasty | *Bencao Gangmu* | Li ShiZhen | Liquor steaming | Viticis Fructus was used to remove the persistent calyx and pedicle. After soaking in wine for ten days, it was steamed for several hours and dried in the sun. |
| Ming Dynasty | *Bencao Tongxuan* | Li ZhongZi | Liquor stir-frying | Remove the persistent calyx, liquor stir-fried and broken. |
| Ming Dynasty | *Yizong Cuiyan* | N/A | Liquor stir-frying | Crushed, washed with liquor, stir-fried and decocted. |
| Qing Dynasty | *Bencao Beiyao* | Wang Ang | Liquor stir-frying | Liquor steamed and stir-fried. |
| Qing Dynasty | *Xiushi Zhinan* | Zhang ZhongYan | Liquor steaming | Liquor steamed. |
| Qing Dynasty | *Depei Bencao* | Yan Jie | Liquor steaming/Liquor stir-frying | Removed the persistent calyx, steamed with liquor or stir-fried with liquor. |
| Qing Dynasty | *Bencao Qiuzhen* | Huang GongXiu | Liquor steaming and stir-frying | Removed the persistent calyx, steamed with liquor and stir-fried. |

**Table S6. Viticis Fructus patents worldwide**

|  |  |  |  |
| --- | --- | --- | --- |
| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| **China** | | | |
| Health products | 2017-11-17 | Pillow core (Viticis Fructus pillow) | Sleep supplies |
| Health products | 2017-08-11 | Brewing method of Viticis Fructus health wine | Viticis Fructus had the healthcare functions of evacuating wind and heat, relaxing tendons and activating collaterals. |
| Health products | 2016-10-19 | A kind of Viticis Fructus invigorating spleen and kidney granule beverage and its preparation method | Tonify the spleen and kidney, evacuate wind and heat |
| Health products | 2015-11-04 | A hypotensive lipid-lowering Viticis Fructus health oral liquid and its preparation method | Unlike Western medicine, the expansion of blood vessels temporarily lowers blood pressure to improve symptoms. |
| Health products | 2015-08-12 | Viticis Fructus health Chinese medicine tea beverage and preparation method | Dispel wind, relieve pain, bright eyes and stop dizziness. It was used to treat syndrome of liver wind stirring up internally, headache, dizziness, bitter mouth and tinnitus. |

Table S6 (*continued*)

|  |  |  |  |
| --- | --- | --- | --- |
| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Health products | 2014-11-12 | Viticis Fructus Chinese herbal medicine pillow | Clear heat and detoxify, dispel wind and relive exterior and help sleep |
| Health products | 2014-04-16 | A kind of Viticis Fructus epiphora health tea | Dispel wind and relieve pain, detoxify, brighten eyes and relieve the eyes discomfort |
| Health products | 2014-04-16 | A kind of Viticis Fructus epiphora health wine | Tonify the liver and kidneys, dispel wind and brighten eyes |
| Health products | 2014-01-15 | A Viticis Fructus Tongluo beverage | Effectively promote blood circulation to prevent headaches |
| Health products | 2013-10-30 | A Viticis Fructus hypoglycemic beverage and its preparation method | Effectively achieved the effect of controlling blood sugar |
| Health products | 2013-10-30 | A Viticis Fructus hypoglycemic wine and brewing method | Controlling blood sugar |
| Health products | 2013-03-27 | A dizzying Viticis Fructus health wine | Prevent dizzy symptoms |
| Health products | 2013-03-27 | A dizzying Viticis Fructus health tea | Prevent dizzy symptoms |

Table S6 (*continued*)

|  |  |  |  |
| --- | --- | --- | --- |
| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Health products | 1999-02-10 | Viticis Fructus bagged tea | Clear heat and detoxify, remove wind and dampness, remove liver-fire, benefiting intelligence and facilitating urination |
| Cosmetics | 2022-08-05 | A skin care product for skin after-sun repair and its preparation method | Effectively relieve skin sunburn and help skin recover quickly. |
| Cosmetics | 2019-11-22 | Application of casticin as a cosmetic sunscreen ingredient | Casticin with a mass percentage of 1-10% was applied in sunscreen cosmetics. |
| Daily Products | 2022-05-13 | Application of ethanolic extract of Viticis Fructus in the preparation of disinfection products | It was used to disinfect hands and body surface to kill, inhibit or reduce attached bacteria. |
| Daily Products | 2019-03-26 | A kind of hair moisturizing shampoo | Compared with the existing technology, it had better anti-dandruff itching function, safe and non-toxic side effects. |
| Daily Products | 2017-09-29 | A toothpaste containing casticin ingredients | It had significant antibacterial, anti-inflammatory and analgesic effects. |

Table S6 (*continued*)

|  |  |  |  |
| --- | --- | --- | --- |
| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Daily Products | 2017-02-01 | A natural shampoo | It had better anti-dandruff itching function. |
| Daily Products | 2016-03-09 | A kind of nourishing type herbal hair dye | A pure natural plant hair dye. |
| Daily Products | 2015-08-26 | A toothpaste containing casticin ingredients | It could fundamentally reduce oral problems such as gingival swelling, pain and bleeding. |
| Medical use | 2022-10-14 | The use of Viticis Fructus in the preparation of anti-radiation drugs | Viticis Fructus had a protective effect on natural ionizing radiation and artificial radiation. |
| Medical use | 2022-04-29 | Application of ethanol extract of Viticis Fructus in the preparation of antibacterial drugs | Antibacterial drugs |
| Medical use | 2021-12-31 | Application of a Viticis Fructus extract in the preparation of antidepressants | Extracts and active ingredients had a mitigating effect on depression symptoms. |
| Medical use | 2021-12-03 | A clear eye antibacterial eye drops and its preparation method | It had a significant effect on relieving visual fatigue, dry eye and eye astringency and had a good inhibitory effect on Staphylococcus aureus, Escherichia coli and Candida albicans. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Medical use | 2017-09-19 | A hair growth formula containing Viticis Fructus | Hair growth |
| Medical use | 2015-10-07 | A Viticis Fructus oral solution for prevention and treatment of wind-heat attack red swelling and pain and its preparation method | Prevention and treatment of wind-heat attack red swelling. |
| Medical use | 2014-01-15 | Treatment of headache Viticis Fructus Chinese medicine preparation and preparation method | Exogenous headache rheumatism patients had a significant therapeutic effect. |
| Medical use | 2013-02-06 | Casticin as an effective component of anti-angiogenesis drugs | The invention found that casticin had a significant effect on inhibiting the proliferation of vascular endothelial cells and plays a role in the treatment of angiogenesis-related diseases such as tumors and rheumatoid arthritis. |
| Medical use | 2012-10-03 | Treatment of headache Viticis Fructus Chinese medicine preparation and preparation method | Exogenous headache rheumatism patients had a significant therapeutic effect. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Medical use | 2007-02-14 | A new method for the treatment of headaches by Chuanxiong Rhizoma, Viticis Fructus, Bombyx Batryticatus and Shengshi, Jianming | It mainly treated headaches, activated blood, dispelled wind, tranquilized and relieved pain. Suitable for vascular migraine. |
| Medical use/health products | 2021-07-30 | Application of bergapten and/or vitexin products and their products | It had a good effect on the prevention and treatment of trachovirus infection. |
| Technical Methods | 2022-09-02 | A method for determining the content of components in Fructus Viticis formula granules by quantitative analysis of multicomponents by single-marker | This method could realize the simultaneous determination of protocatechuic acid, 4-Hydroxybenzoic acid, Luteolin-6-*O*-glucoside, agnuside and casticin in Viticis Fructus formula granules. |
| Technical Methods | 2022-08-09 | The fingerprint construction method and multi-index content detection method of Viticis Fructus | It had many characteristic peaks, especially the characteristic peaks of flavonoids, which could quickly and comprehensively reflect the quality of Viticis Fructus. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Technical Methods | 2021-12-14 | A method for quality detection of fried Viticis Fructus standard decoction | It was possible to establish a feasible quality standard Viticis Fructus decoction and realized the effective control of the quality of fried Viticis Fructus standard decoction. |
| Technical Methods | 2021-07-09 | A method for simultaneous preparation of Viticis Fructus oil and flavonoid extract | The simultaneous preparation of Viticis Fructus oil and Viticis Fructus flavonoids extract was realized, which further improved the content of flavonoids and the utilization rate of raw materials. |
| Technical Methods | 2019-10-08 | The method of extracting rotundifuran by Viticis Fructus | Extracting rotundifuran |
| Technical Methods | 2019-01-18 | A Viticis Fructus graded polysaccharide and its application in pharmaceutical industry | A graded polysaccharide of Viticis Fructus and its application in pharmaceutical industry |
| Technical Methods | 2016-02-03 | A preparation method of casticin | The preparation of casticin had high purity and good quality. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Technical Methods | 2015-03-25 | A method for extracting total flavonoids from Viticis Fructus | The total flavonoids extracted from Viticis Fructus by this method were brown powder. |
| Technical Methods | 2011-01-12 | A method for purifying casticin from Viticis Fructus | The products produced by this process had high content, low cost and simple operation. |
| Technical Methods | 2009-06-24 | Viticis Fructus extract and its preparation method and use | Viticis Fructus-1 (rich in flavonoids) and Viticis Fructus-2 (containing flavonoids and terpenoids) had therapeutic and closely related diseases such as periodic breast pain and dysmenorrhea, and could be used to prepare drugs and foods for the prevention and treatment of premenstrual syndrome and its closely related diseases. |
| Technical Methods | 2010-12-08 | A Viticis Fructus extract and its supercritical preparation process | The extract of Chinese medicine Viticis Fructus prepared by the method of the invention had active components such as volatile oil and flavonoids. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Others | 2023-01-06 | A high-quality seedling device for Viticis Fructus planting | It solved the problem that the current seedling raising device for Viticis Fructus planting only had a single function. |
| Others | 2020-08-04 | Special standard planting equipment for Viticis Fructus | It solved a series of problems, such as uneven seeding, waste of resources, time-consuming and labor-intensive manual seeding. |
| Others | 2018-04-20 | Standardized high quality and high yield cultivation techniques of Viticis Fructus | The standardized high-quality and high-yield cultivation techniques of Viticis Fructus |
| Others | 2017-01-04 | A planting method of Viticis Fructus | A planting method of Viticis Fructus |
| Others | 2016-04-13 | A cultivation method of Viticis Fructus | A cultivation method of Viticis Fructus |
| Others | 2012-05-30 | A method for quickly relieving seed dormancy of Viticis Fructus | Quickly relieving seed dormancy of Viticis Fructus |
| Others | 2015-08-26 | A method of Viticis Fructus cutting seedling | It could provide sufficient high-quality clonal seedlings for large-scale artificial cultivation of Viticis Fructus. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| **Other countries** | | | |
| Health products | 2006-11-30 | Universal detoxifying composition | Universal detoxifying composition |
| Health products/Drugs | 1999-10-07 | Topical liquid composition for promoting hair growth and process of manufacturing thereof | It could effectively promote hair growth and prevent hair loss. |
| Health products/Drugs | 2022-01-21 | A composition for preventing or improving or treating menopausal syndrome, including vitexin extract as an active ingredient | It could be used as health care products or drugs to prevent, improve or treat male climacteric syndrome. |
| Cosmetics | 2021-03-26 | Cosmetic compositions comprising extracts from fruits of *V. rotundifolia* | Cosmetic compositions had strong bactericidal power. |
| Cosmetics | 2018-08-09 | Cosmetic composition comprising extract of medicinal herbs as active ingredient | It had excellent collagen synthesis promotion, elastase activity inhibition and excellent anti-inflammatory and moisturizing effects. |
| Cosmetics | 2018-07-12 | Composition for anti-obesity and skin-whitening comprising *Vitex rotundifolia* extract as practical component | Pure Viticis Fructus extract had anti-obesity and skin-whitening functions. |

Table S6 (*continued*)

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| --- | --- | --- | --- |
| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Cosmetics | 2018-06-25 | Cosmetic composition for skin moisturizing comprising *Vitex rotundifolia* Linne fil. Fruit extracts | It was excellent in moisturizing effect and could be used as a skin moisturizing cosmetic composition |
| Daily Products | 2011-06-22 | External compositions for preventing loss of hair and promoting growth | It could effectively promote hair growth and prevent hair loss. |
| Daily Products | 2006-10-19 | A traditional Chinese medicinal formulation of antidandruff and degreasing and its preparation | The formulation could be prepared into antidandruff shampoo or other hair preparation. |
| Medical use | 2022-01-14 | Pharmaceutical composition for the prevention or treatment of asthma comprising essential oil extract derived from *Vitex rotundifolia* L. f. | A medicinal composition effective for asthma in which an essential oil extract derived from Viticis Fructus had the effect of reducing IL-1*β* expression. |
| Medical use | 2007-06-29 | Extracts of Viticis Fructusforthe prevention or treatment of hepatic diseases and/or method for the production and use thereof | Its extract had the ability to scavenge free radicals, inhibited liver damage such as inflammatory cell infiltration and hepatocyte vacuolar degeneration so as to protect the liver, prevent and treat liver diseases. |

Table S6 (*continued*)

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| Category | Authorization Announcement Date | Patent Name | Functions/Features |
| Medical use | 2004-08-04 | Furanic labdane diterpene compounds extracted from Viticis Fructus were found to inhibit ACAT activity. | It could effectively reduce the cholesterol level in the blood and could be effectively used to prevent and treat cardiovascular diseases caused by hypercholesterolemia. |

Cited from the website: (https://www.cnki.net/)

# References

Chen, C.Z., 1935. Chinese Pharmaceutical Dictionary. Universal book company, Shanghai.

Chen, J.M., 1988. Bencao Mengquan. People's health publishing house, Beijing.

Chinese Pharmacopoeia, C., 2020. Pharmacopoeia of the People's Republic of China, 2020ed. Chinese Pharmacopoeia Commission, China.

Ge, H., 1955. Zhouhou Beiji Fang. People's Medical Publishing House, Beijing.

Han, B.S., 2005. Shu Bencao. Anhui Science&Technology Publishing House, Hefei.

Kou, Z.S., 1985. Bencao Yanyi. Zhonghua Book Co., Ltd., Beijing.

Li, S.Z., 2011. Bencao Gangmu. Huaxia Publishing House, Beijing.

Li, Z.L., 2011. Bencao Yuanshi. Xueyuan publishing house, Beijing.

Ri, H.Z., 1983. Rihuazi Bencao. Wannan Medical College, Wuhu.

Su, J., 1981. Xinxiu Bencao. Anhui Science&Technology Publishing House, Hefei.

Su, S., 2017. Bencao Tujing. Xueyuan publishing house, Beijing.

Sun, S.M., 1982. Qianjin Yifang People's Medical Publishing House, Beijing.

Tao, H.J., 1986. Mingyi Bielu People's Medical Publishing House, Beijing.

Tao, H.J., 1994. Bencao Jingji Zhu. People's Medical Publishing House, Beijing.

Wang, H.Y., 1958. Taiping Shenghui Fang. People's health publishing house, Beijing.

Wang, G., 1958. Boji Fang. the commercial press, Beijing.

Wu, Q.J., 1957. Zhiwuming Shitukao. The commercial press, Shanghai.

Wu, Y.L., 2013. Bencao Congxin. China traditional Chinese medicine publishing house, Beijing.

Yan, J., Shi, W., Hong, W., 1997. Depei Bencao. China traditional Chinese medicine publishing house, Beijing.

Yang, S.T., 1958. Bencao Shugou Yuan. Science and technology health publishing house, Beijing.

Zhang, R.X., Zhang, W., Liu, G.S., 2018. Shennong Bencao Jing. Guangxi Science&Technology Publishing, Nanning.

Zhang, W., Wang, J.L., Tang, L.Y., Zhan, Z.L., Peng, H.S., Yang, H.J., 2019. Herbal textual research on Chinese medicine "Manjingzi" (Viticis Fructus) China. J. Chin. Mater. Med. 44(24), 5503-5507. https://doi.org/ 10.19540/j.cnki.cjcmm.20191009.102.

Zhang, Z.C., 1992. Bencao Chongyuan. Huaxia Publishing House, Beijing.

Zhao, J., 1982. Shengji Zonglu. People's Medical Publishing House, Beijing.

Zhen, Q., 1983. Yaoxing Lun. Wannan Medical College, Wuhu.

Zhu, Z.H., 1956. Danxi Xinfa. Shanghai scientific and technical publishers, Shanghai.

Zou, S., 1959. Bencao Shuzheng. Shanghai scientific and technical publishers, Shanghai.