

ON THE VALUE OF APRICOT KERNEL IN MODERN MEDICINE AND ITS FUTURE DEVELOPMENT

QIAN HU¹, YING-YING CHEN¹, GAO-YING ZHU^{1,2}, HAN ZHAO³, LIN WANG³, HUI-MIN LIU³,
TANA WUYUN³, FANG-DONG LI³ AND GAO-PU ZHU^{1,3*}

¹Zhengzhou Railway Vocational and Technical College, Zhengzhou 451460, P. R. China

²Xiangcheng County People's Hospital, Xuchang, 452670, P. R. China

³Research Institute of Non-timber Forestry, Chinese Academy of Forestry, Kernel-Apricot Engineering and Technology Research Center of National Forestry and Grassland Administration, and Key Laboratory of Non-timber Forest Germplasm Enhancement & Utilization of National Forestry and Grassland Administration, Zhengzhou 450003, P.R. China

*Corresponding author's email: poog502@hotmail.com

Abstract

Apricot kernels are one of the most regularly used traditional Chinese medicinal ingredients in Asia. The medical significance of apricot kernels is highlighted since Traditional Chinese Medicine (TCM) demonstrated its favourable impact when apricot kernels were used in the prevention and treatment of Corona Virus Disease 2019 (COVID-19). Furthermore, apricot kernels are high in fat, protein, dietary fibre, and specific amygdalin, making them a new form of dried fruit in comparison to almond kernels, with a bigger market opportunity. This paper systematically reviewed the active components of apricot kernels and their application in medicine, especially for molecular mechanisms of anti-tumors of amygdalin, providing scientific theoretical foundations for modern medicine treatment with COVID-19-induced lung disease, and for the development of high value-added apricot kernels.

Key words: Apricot kernel; Amygdalin; Corona virus disease 2019 (COVID-19); Modern medicine.

Introduction

The apricot is one of the most important fruit species in the world, belonging to the Armeniaca, Prunoideae Focke, Rosaceae family (Li *et al.*, 2019). According to Food and Agriculture Organization (FAO) statistics, the world's total harvest area of edible fresh apricots reached 586,000 hm² in 2019, with a total output of 4.153 million tonnes. With more than 3,500 years of apricot growing history, China is the world's cradleland (Sun *et al.*, 2019). However, unlike other nations, China divides apricots into two categories: edible fresh apricots and kernel-apricots, based on their use and edible sections. Among them, edible fresh apricots, such as *A. vulgaris*, are mostly used for eating the pulp section, with large fruit, soft pulp, less fibre, more juice, and palatability. And kernel-apricot is a generic word for dried fruits with the kernel as their primary usage, such as *A. sibirica*, *A. sibirica*, *A. zhidanensis* and *A. zhidanensis* etc. Thin pulp and acerbity, coarse fibre, thin seed sheer, and a big kernel are its key qualities. Others, like *A. holosericea*, *A. dasycarpa*, *A. mandshurica*, *A. aune*, *A. limeixing* and *A. zhengheensis* is still exclusively grown in the wild, with little development, use, and commercial worth (Li *et al.*, 2019).

According to the amount of amygdalin in kernels, sweet kernels and bitter kernels are produced in the kernel-apricot industry. *A. cathayana*, for example, comprises around 0.23‰~1.89‰ amygdalin and has a thin seed sheer, a large and tasty kernel. While amygdalin levels in *A. sibirica* range from 27.0% to 77.7%, the seed sheath is thick, the kernel is tiny and bitter, but the seed is full (Xu *et al.*, 2016; Li *et al.*, 2019).

The kernel-apricot has gained drought resistance, barren resistance, and sand resistance during a long

period of biological evolution, making it suited for cultivation in arid and semi-arid locations between 33° N and 43° N (Yue *et al.*, 2022). The cultivation area of kernel-apricot in China is currently at 1.35 million hm², making it the world's largest kernel-apricot grower, with an annual output of about 250,000 to 300,000 tonnes (Xu *et al.*, 2016; Sun *et al.*, 2019). The sweet kernel is mostly used for making nuts, pastries, flavour masking agents, meal protein powder, and high-grade edible oil, all of which are transported to Europe, southeast Asia, and other nations. While the bitter kernel is mostly used in TCM to treat lung disease, influenza, and other illnesses, it can also be processed into a protein drink or used for cooking after the laetrile has been removed. In general, most people are unaware of the importance of kernels, resulting in a low utilisation rate and low economic value. After more investigation, scientists have discovered that the kernel has considerable effects on COVID-19 treatment (Chu *et al.*, 2021; Liu *et al.*, 2021) and anti-tumor treatment (Jaswal *et al.*, 2018; Arshi *et al.*, 2019; Pan *et al.*, 2021). Hands and feet can be treated with the kernel oil. The kernel protein can be used as a vegetarian meal replacement as well as a whitening agent. The kernel is also high in selenium and calcium, making it useful in the prevention and treatment of growth retardation in children.

Apricots have up to 3.82 mg/100g of carotenoid, which is 22.4 times that of an apple, and up to 19.0 mg/100g of flavonoid, which is the most of any fruit (Li *et al.*, 2019; Shi *et al.*, 2019). This paper reviewed the functions of the main active ingredients of apricot kernel in modern medicine in recent years, providing theoretical support for the directional cultivation of new varieties with high amygdalin, high fatty acid, high protein, and other active ingredients, increasing the added value of products and enhancing industrial vitality.

Medical value of amygdalin: Bitter apricots contain between 2% and 4% of amygdalin, which is distributed properly. In the natural population of siberian apricots in Inner Mongolia (Li *et al.*, 2019), we found an excellent single plant with a content of 7.77 percent. The chemical formula of amygdalin is $C_{20}H_{27}NO_{11}$, and the structural formula is (2R)-[6-O-(D-glucopyranosyl) D-glucopyranosyl]oxy (phenyl) acetonitril, with an average mass of 457.428 Da, a melting point at 200~220°C, and a solubility of 1g amygdalin in 12 mL water or 900 mL ethanol or 11 mL boiling ethanol (Shi *et al.*, 2019). Amygdalin has considerable effects in treating cough and asthma, as well as preventing gastric ulcers, hepatic fibrosis, atherosclerosis, oxidation, and tumours (Bolarinwa *et al.*, 2014; Reck *et al.*, 2014; Xu and Song, 2014; Li *et*

al., 2019; Shi *et al.*, 2019) (Fig. 1), and it has not exhibit side effects to animal physiology (Halenar *et al.*, 2017), but excessive use can cause human body poisoning. Since amygdalin is hydrolyzed into cymatin and cyanide under the action of glucoside enzymes such as amygdalase and cymatin, which is unstable and easily decomposed to benzaldehyde and hydrogen cyanide (HCN) when heated, excessive use can cause human body poisoning, since HCN is highly toxic and can inhibit the cytopigment C oxidase in the respiratory chain of mitochondria (Shi *et al.*, 2019). The lethal dose 50 (LD50) of amygdalin for the human body, and 1g bitter kernel can create roughly 2.5mg HCN under normal circumstances. Adults can die from 50~60 bitter kernels, whereas children can die from 7~10 bitter kernels (Fu and Ye, 2015).

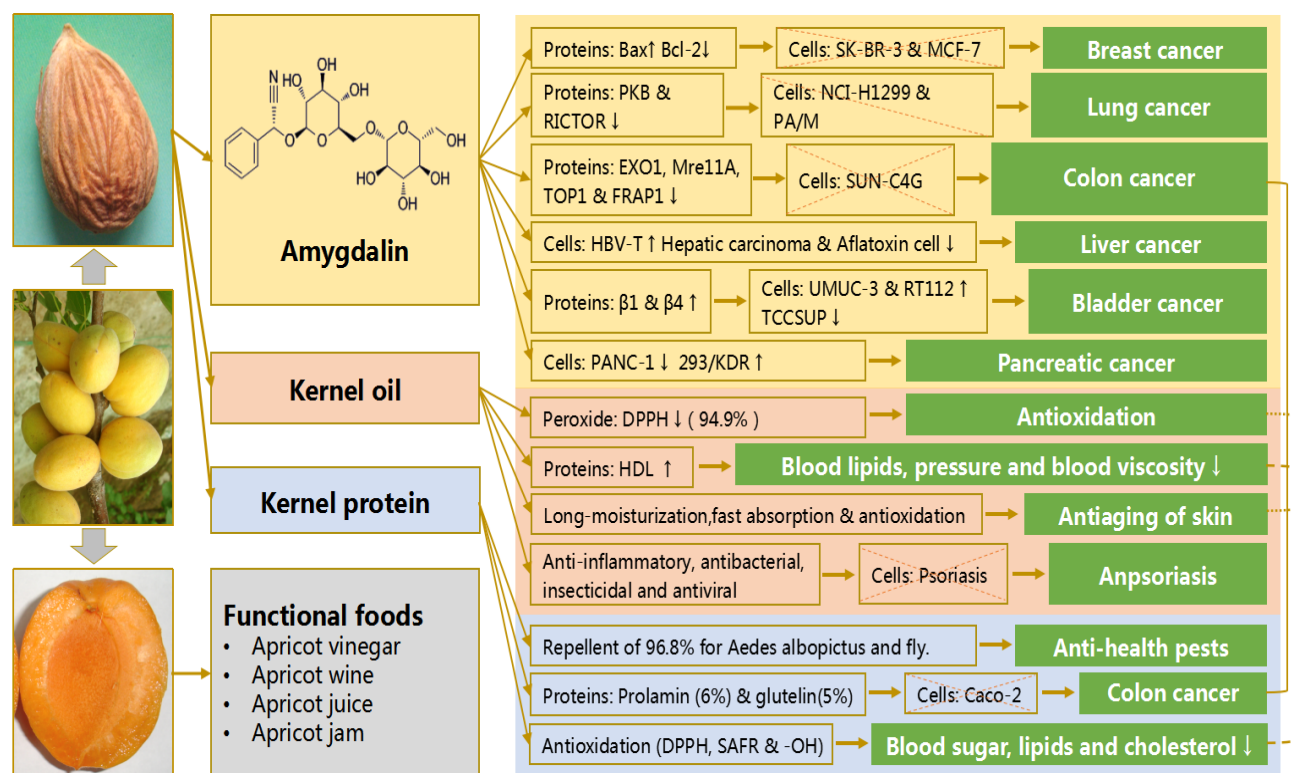


Fig. 1. The function of main ingredients of kernel-apricot.

Anti-tumor studies: One of the primary causes of death in humans is malignant tumours. Cancer patients are still treated with surgery and chemotherapy. However, neither approach is helpful in the late stages of cancer. Natural anticancer substances have become more popular in recent years. Amygdalin, which is abundant in the kernel, has received a lot of interest for its anti-tumor adjuvant therapy, preventive, and rehabilitation properties.

In 2020, there were 2.3 million female breast cancer patients, accounting for 11.7 percent of the 19.3 million new cancer cases reported worldwide. Breast cancer has surpassed lung cancer as the most frequent cancer worldwide, with a death rate of 6.9%, placing it sixth globally (Sung *et al.*, 2021). It is one of the most serious disorders that endanger the health of women. Amygdalin can induce apoptosis in SK-Br-3 and McF-7 breast cancer cells by increasing the expression of pro-apoptotic Bax

protein and decreasing the expression of anti-apoptotic Bcl-2 protein, especially the death-positive cells human epidermal receptor 2 (HER2) (Moradipoodeh *et al.*, 2019; Moradipoodeh *et al.*, 2020) (Fig. 1), indicating a positive effect in breast cancer treatment.

Lung cancer is the world's second most common cancer, after breast cancer, with a rate of 11.4 percent, but it has the highest mortality rate. Lung cancer claimed the lives of approximately 1.8 million people in 2020. Lung cancer incidence and death rates in China were the highest in the world, at 37.0 percent and 39.8 percent, respectively (Sung *et al.*, 2021). According to TCM thought, it affects mostly the lungs. In 2,100 anti-lung cancer prescriptions from TCM clinics, the frequency of kernel appears as high as 29.1 percent, ranking in the top 30 TCM commonly used for lung cancer (Cai, 2021; Yuan *et al.*, 2021). Sun *et al.*, (2016) found that the

amygdalin can significantly reduce the phosphorylation levels of protein kinase B and rapamycin-insensitive companion of mTOR (RICTOR) (Fig. 1). As a result, it dramatically reduced the proliferation of human lung cancer cells nCI-H1299 and PA/M in vitro, generated a considerable drop in tumour cell invasion and migratory abilities, and significantly ($p \leq 0.05$) reduced the development of non-small cell lung cancer. Bufeixiaowei Decoction is a traditional Chinese medication, in patients with late-stage lung cancer, the decoction containing kernel combined with apatinib can effectively reduce the marker levels of Carcino-embryonic Antigen (CEA), Squamous cell carcinoma antigen (SCC), and Carbohydrate antigen 125 (CA125), improving the curative effect, reducing adverse reactions, and improving patient quality of life (Pan *et al.*, 2021).

Colorectal cancer, which includes both colorectal and colon cancers, is the third most frequent disease worldwide, accounting for roughly 10% of cancer cases and 9.4% of deaths in 2020 (Sung *et al.*, 2020). Park *et al.*, (2005) discovered that 5g/L amygdalin might diminish the expression abundance of human cell cycle-related protein components Exonuclease-1, Mre11A, topoisomerase, and FRAP1 in the prevention of bowel cancer (Fig. 1). After 24 hours, sun-C4G causes substantial apoptosis in colon cancer cells. Furthermore, β -glucosidase conjugated to CEA (carcino embryonic antigen) could effectively activate the amygdalin's inhibitory effect on the weight and volume of transplanted nude mice tumours (Lian *et al.*, 2005), as well as significantly improve the ability to induce apoptosis in colorectal cancer LoVo cells (Zhou *et al.*, 2012), indicating that it could be used therapeutically.

In 2020, 8.3% of patients died of liver cancer, making it the third fatal cancer in the world (Sung *et al.*, 2020). One of the leading causes of liver cancer is the hepatitis B virus (HBV). Amygdalin can increase the activity of HBV-T cells, regulate CD4⁺/CD8⁺ T cells through the JAK2-STAT3 pathway, weaken the immunosuppressive effect of HBV-T cells, increase secretion of lethal cytokines, enhance the inhibitory effect on cell viability, invasion, and migration of hepatocarcinoma (HCC) cells (Wu, 2019; Zhou *et al.*, 2012) (Fig. 1), and enhance the catalytic effect of amygdalin via in vitro investigations also revealed that amygdalin inhibited the growth of *Aspergillus* and tremycin, indicating that it may play a role in anti-hepatocellular carcinoma therapy.

After prostate cancer, Human bladder cancer is the second most prevalent tumour of the urinary tract (Cheng *et al.*, 2016). In the treatment of bladder cancer, amygdalin activated by β -glucosidase can significantly reduce the adhesion and migration ability of UMUC-3 and RT112 cells by regulating β 1 and β 4 proteins (Zhen *et al.*, 2013) (Fig. 1), possibly because amygdalin can significantly reduce the adhesion and migration ability of UMUC-3 and RT112 cells. The improved migratory potential of TCCSUP cells caused bladder cancer cells to become stuck in the G0/G1 (Makarević *et al.*, 2014a; Makarević *et al.*, 2014b) or S phase (Liu *et al.*, 2017) (Fig. 1), resulting in their death.

One of the most common malignant tumours in the digestive tract is pancreatic cancer. According to the journal Lancet, pancreatic cancer is one of the least curable cancers, with a five-year survival rate of about 10% following diagnosis. Amygdalin can cause apoptosis in PANC-1 tumour cells via a mitochondrial-dependent mechanism, but not in non-cancerous 293/KDR cells, suggesting that it could have a role in pancreatic cancer prevention (Aamazadeh *et al.*, 2020) (Fig. 1).

Finally, the effect of amygdalin on the prevention and treatment of human malignancies can be summarised in three ways: First, it inhibits tumour cell development (before S phase) by down-regulating cell cycle-related proteins, resulting in tumour cell apoptosis. Second, it suppresses the production of antiapoptotic genes (*Survivin*; X-linked inhibitor of apoptosis protein, *XIAP*) and other genes in tumour cells, causing tumour cells to die (Arshi *et al.*, 2019). Third, it inhibits tumour cell proliferation, migration, and invasion in vitro by regulating the expression of relevant proteins in tumour cell-related signalling pathways (Akt and RICTOR).

Prevention and treatment of fibrosis disease: Fibrosis is a big health threat in today's world. Pathological fibrous hyperplasia caused by a metabolic imbalance of extracellular matrix (ECM) is thought to be the origin of organ fibrosis, which can occur in the liver, pancreas, kidney, lung, and other organs, resulting in organ failure (Zhao *et al.*, 2020). As a result, the major objective of clinical treatment for fibrosis disease is to stop the fibrosis process as soon as possible. Studies have demonstrated that a certain concentration of kernel extract can effectively suppress liver fibrosis caused by dimethylnitrosamine (DMN) by improving liver function, improving liver lipid peroxides, and increasing liver superoxide dismutase (SOD) enzyme activity, so as to effectively inhibit liver fibrosis induced by DMN (Abdel-Rahman, 2011). At the same time, amygdalin can reduce the amount of malondialdehyde produced by CCl₄ in rats, boost the activity of SOD and other enzymes, and lower the level of monocyte chemotactic protein 1 (MCP-1) expression in blood. It can reduce CCl₄-induced liver fibrosis by inhibiting oxidative stress and inflammatory responses (Wang *et al.*, 2020). Multi-component medications containing amygdalin, *Cordyceps sinensis mycelium*, and *Gynostemma pentaphyllum* glycoside can suppress hepatic stellate cell activation and minimise hepatocyte death (Tian *et al.*, 2019), which is one of the most effective treatments and preventative strategies for hepatic fibrosis.

Appropriate concentration of amygdalin can also improve the activity of type I collagenase secreted by human kidney fibroblasts (KFB), inhibit the proliferation of KFB and the expression of type I collagen, inducing apoptosis in KFB, preventing and curing renal fibrosis (Qu *et al.*, 2000), or reduce the secretion of transforming growth factor 1 (TGF- β 1) by human renal interstitial fibroblasts (Guo *et al.*, 2013).

Amygdalin could improve pancreatic microcirculation by down-regulating diastin-1 expression and up-regulating the expression of the calcitonin gene, reducing the activation of pancreatic stellate cells and the secretion of

pro-inflammatory cytokines such as platelet-derived growth factor-BB and TGF- β 1, and thus alleviating pancreatic fibrosis (Zhang *et al.*, 2018).

In addition, amygdalin inhibits the epithelial-mesenchymal transition and reduces TGF- β 1 and phosphorylated Smad 2/3 expression in mice with chronic obstructive pulmonary disease, which helps to minimise pulmonary fibrosis and achieve respiratory tract reconstruction (Wang *et al.*, 2019).

Finally, amygdalin can inhibit the activation of fibroblasts and induce the apoptosis of activated fibroblasts in organs by improving the microcirculation of the viscera, regulating the extracellular matrix ECM, participating in the growth of anti-fibrotic cytokines, regulating key genes and protein synthesis networks, reducing the release of inflammatory cytokines, and other mechanisms. This impact was especially noticeable in compound formulations containing amygdalin (Li *et al.*, 2016b; Tian *et al.*, 2019).

Prevention and treatment of other diseases: Amygdalin has been shown to improve macrophage phagocytosis, increase death in atherosclerotic plaque cells to reduce plaque area and coverage, and have a role in anti-atherosclerosis (Deng *et al.*, 2011). Amygdalin can also improve cytochrome oxidase activity in the presence of cerebral ischemia and has a considerable anti-cerebral ischemia impact (Yang *et al.*, 2006). Furthermore, amygdalin can considerably stimulate the proliferation of human T lymphocytes' precocious agglutination chromosome, and it has antioxidant, anti-inflammatory, anti-ulcer (Zheng *et al.*, 2009), and analgesic properties, as well as being effective in preventing and treating chronic gastritis and stomach ulcer. In mice, a combination of atorvastatin and amygdalin can dramatically reduce lipid peroxidation, boost the amount of SOD and other antioxidant enzymes by more than 40%, and significantly reduce leukocyte infiltration and fibrosis, all of which can help with endometriosis symptoms (Hu *et al.*, 2019). Furthermore, the tumour medicine alloxan can cause diabetes, although it has a protective effect when used with amygdalin. Through the benzoin condensation enzyme, the benzaldehyde produced by the decomposition of amygdalin can form benzoin, which has an anti-inflammatory analgesic effect and can be used to replace painkillers in patients with liver cancer (Yang & Chen, 2005).

Medical value of apricot kernel oil: Oil, unsaturated fatty acids, oleic acid and linoleic acid make up 42.6 ~ 61.07 percent, 94 percent, 62.8 percent, and 24 percent, respectively, in the apricot kernel (Li *et al.*, 2019), indicating great medical value. Bitter apricot kernel oil has a moistening and relaxing effect on the intestines, and it may also be used as a raw material for external medication to heal skin burns. Because apricot kernel oil contains unsaturated fatty acids that can lower bad cholesterol and triglycerides in the blood while also protecting the liver (Zhang *et al.*, 2011), it can be used as a health food to treat and prevent liver disease. The scavenging rate can reach 94.9 percent for 2,2-diphenyl-1-picrylhydrazyl (DPPH) using kernel oil (Wang *et al.*, 2014) (Fig. 1). Apricot kernel

oil can also effectively control blood lipid concentrations in humans, improve the content of high-density lipoprotein (HDL) (Fig. 1), promote the metabolism of saturated fatty acids in the body, reduce and eliminate the harm of animal fat in food, prevent fat deposition, inhibit atherosclerosis, and improve the elasticity and toughness of blood vessels. It also improves the ability of red blood cells to carry oxygen by lowering blood viscosity (Esfahlan *et al.*, 2010).

Apricot kernel oil has a high affinity for the skin, is easily absorbed by the skin, and moisturises, beautifies, and prevents wrinkles. Apricot kernel oil is soft and non-greasy, and it can be blended with vegetable oil and essential oils to form a variety of skin masks and massage incense, which is the best product for skin care. Hair quality can be improved and hair sparseness can be solved by using apricot kernel oil on a regular basis (Li *et al.*, 2019).

The anti-inflammatory, antibacterial, insecticidal, and antiviral activities of apricot kernel essential oil can also trigger apoptosis in psoriasis cells, resulting in a considerable therapeutic benefit (Li *et al.*, 2016). At the same time, apricot kernel essential oil has a 96.8% avoidance impact on health pests like *Aedes albopictus* and *Musca domestica* (Fig. 1), with a duration of more than 6 hours (Ma, 2007), indicating a broad potential in health pest integrated control.

Medical value of apricot kernel protein: The protein level of an apricot kernel is 25%~27%, whereas skimmed apricot kernel meal has a protein content of up to 55%. The protein composition is similar to that of the FAO/WHO (Yue, 2020). The protein has a molecular weight of 2263 kD and is made up of 17 different amino acids, including 26.5 percent glutamate, 11.3 percent aspartic acid, and 10% arginine (Yin *et al.*, 2020). The essential amino acid to total amino acid ratio is approximately 28.37 percent (Li *et al.*, 2019), which is close to the international standard (FAO/WHO). It is a high-quality plant protein with a wide range of applications in the field of healthy food preparation. Prolamin and glutelin make up about 6% and 5% of the apricot kernel protein (Fig. 1), respectively, and have been shown to suppress the growth of human colon cancer cells (Zhang, 2011). The process can be deduced from the fact that 89.5 percent of Caco-2 human colon cancer cells die 48 hours after ingesting apricot kernel protein (Hui *et al.*, 2014).

Functional peptides with molecular weights in the range of 400~3000 Da can be generated during the enzymatic hydrolysis of apricot kernel protein, which are simpler to absorb by the human body and demonstrate actions such as decreasing blood lipids, lowering cholesterol, and anti-aging. The bitter apricot kernel peptide produced by alcalase protease hydrolysis has an antihypertensive effect by inhibiting the angiotensin converting enzyme (Zhu *et al.*, 2010; García *et al.*, 2016). The amygdalus peptide with significant antioxidant activity can be obtained using the α -glucosidase inhibitory peptidolytic technique, and the IC₅₀ cleaned by DPPH free radical, superoxide anion free radical (SAFR), and hydroxyl radical is in the range of 1.43 to 15.6 mg/mL, indicating a significant hypoglycemic effect (Wang, 2014) (Fig. 1). The serum total cholesterol, triglyceride, and high

density lipoprotein cholesterol content were reduced by 19.21 percent (0.73 mmol/L), 42.42 percent (0.28 mmol/L), and 78.90 percent (0.86mmol/L), respectively, when rats were fed apricot kernel protein digested by trypsin. It had a greater impact in lowering blood lipid levels than apricot kernel protein (Lai *et al.*, 2011).

Medical value of vitamins, minerals and other nutrients in apricot kernels: V_C 26.0 mg, V_E 27.4 mg, V_{B1} 0.14 mg, V_{B2} 0.65 mg and niacin 2.30 mg per 100g, especially V_{D3} 5.01 mg/100g, which is uncommon in vegetable oil. V_{D3} has an impact on calcium and phosphorus intake and storage in the human body, as well as the mineralization of human bone (Li *et al.*, 2019). V_E has a content of 5.58 mg per 100 g, which can help the human body improve immunity, resist oxidation, and protect the body's cells from free radicals, as well as reduce speckle organisation, protect skin from ultraviolet rays and pollution damage, reduce scarring with pigment deposition, delay ageing, and reduce wrinkles, as well as aid digestion, prevent constipation, and contribute to significant weight loss (Tian *et al.*, 2016).

129.8 mg of calcium, phosphorus 352.0 mg, magnesium 2927.0 mg, sodium 7.1 mg, microelement iron 5.1 mg and zinc 3.64.1 mg are all present in 100g of sweet apricot kernels, with a selenium level of 27.6 mg, which is 6.3 times that of walnuts. Selenium has high antioxidant activity, and supplementing with it can help to prevent organ ageing. Apricot kernels have the highest quantities of calcium and selenium, both of which are good for memory (Li *et al.*, 2019).

Discussion

After thousand years of medical practice in China, it has been proved that apricot kernels can treat cough and asthma as well as have anti-oxidation, anti-tumor, and other properties. Apricot kernels have become a major ingredient in Chinese herbal prescriptions for COVID-19 treatment, particularly after Severe Acute Respiratory Syndrome (SARS), Middle East Re-spiratory Syndrome (MERS), and other viruses, demonstrating a significant therapeutic effect (Wang *et al.*, 2019) and demonstrating the great potential of Chinese medicine in the treatment of COVID-19 (Zhang *et al.*, 2021). The method for preventing and curing COVID-19-induced lung illness should be studied further in the future.

Apricot kernels are processed into cans, drinks and daily cooking in China, and eating them has been shown to increase biological immunity, promote the creation of immunoglobulin and lymphocyte cytokines, and have a positive effect on the growth and destruction of human organs. It can be used as an energy and nutrition supplement as well as a meal replacement for every day and physical activity, and it can assist in overcoming the negative effects of immunological suppression caused by surgery, chemotherapy, life and job stress, exercise, physiological ageing and obesity (Tian *et al.*, 2016). Furthermore, the apricot pulp can be used to make functional apricot vinegar, which has a natural pH of 3.14 to 3.25 and calcium and magnesium contents of 150.0 mg/L and 85.4 mg/L, sodium 280.0 mg/L, phosphorus

123.0 mg/L, and amino acid 200.1 mg/L, respectively, which are obviously higher than persimmon vinegar. Proline has a concentration of 93.1 mg/L, which is 180 times that of apple cider vinegar (0.50 mg/L) (Zhao *et al.*, 2017). Furthermore, apricot kernel oil has unique qualities such as remaining clear at -10°C and solidifying at -20°C (Ma *et al.*, 2020), which allows for a large market opportunity. It should be noted, however, that apricot kernels contain an allergen component called amandin, which might trigger allergic reactions in some people (Zhu *et al.*, 2020). As a result, the only way to extend the market for apricot kernels is to look into cost-effective ways to diminish or eliminate allergies.

Two breeding directions should be determined in the future. The first step is to develop superior hyper amygdalin-producing cultivars. It is feasible to produce exceptional super kinds of bitter apricot kernels with an amygdalin concentration of more than 7% using human-selection breeding, distant hybridization breeding, and marker-assisted selective breeding procedures. Furthermore, it is necessary to investigate the efficient amygdalin accumulation rule, to conduct molecular design breeding, to accelerate the process of breeding improved varieties, and to offer plenty of natural amygdalin raw materials for modern medications. Second, the production of sweet apricot kernels with excellent yield and cold resistance to lower the cost of bitter removal, cultivate high-sweet apricot kernel cultivars with amygdarin content below 0.18 percent, protein content above 25 percent, or fatty acid content above 45 percent, and immature fruit resistant to freezing below -2°C. As a result, it is possible to increase the output of sweet apricot kernels while making them affordable enough to be included in customers' daily consumption lists. It can also be used to bridge the consumption gap, pique the interest of fruit growers, and promote the industry's healthy and long-term development.

Acknowledgments

This work was supported by the National Key R&D Program of China (2019YFD1001200).

References

- Aamazadeh, F., A. Ostadrahimi, Y.R. Saadat and J. Barar. 2020. Bitter apricot ethanolic extract induces apoptosis through increasing expression of Bax/Bcl-2 ratio and caspase-3 in PANC-1 pancreatic cancer cells. *Mol. Biol. Rep.*, 47(3): 1895-1904.
- Abdel-Rahman, M.K. 2011. Can apricot kernels fatty acids delay the atrophied hepatocytes from progression to fibrosis in dimethylnitrosamine (DMN)-induced liver injury in rats? *Lipids Health Dis.*, 10(1): 1-10.
- Arshi, A., S.M. Hosseini, F.K. Hosseini, Z.Y. Amiri, F.S. Hosseini, M.S. Lavasani, H. Kerdarian and M.S. Dehkordi. 2019. The anti-cancer effect of amygdalin on human cancer cell lines. *Mol. Biol. Rep.*, 46(2): 2059-2066.
- Bolarinwa, I.F., C. Orfila and M.R. Morgan. 2014. Amygdalin content of seeds, kernels and food products commercially-available in the UK. *Food Chem.*, 152(2): 133-139.
- Cai, K. 2021. Analysis and management suggestions for anti-lung cancer in outpatient department based on 1800 TCM prescriptions. *J. Trad. Chin. Med. Manage.*, 29(1): 117-119.

- Cheng, P., Y. Guan, H. Li, W. Chen and Z. Gang. 2016. Urologic cancer in China. *Jpn. J. Clin. Oncol.*, 46(6): 497-501.
- Chu, L., F. Huang, M.D. Zhang, B. Huang and Y.G. Wang. 2021. Current status of traditional Chinese medicine for the treatment of COVID-19 in China. *Chin. Med.*, 16: 63.
- Deng, J.G., C.Y. Li, H.L. Wang, E.W. Hao, Z.C. Du, C.H. Bao, J.Z. Lv and Y. Wang. 2011. Amygdalin mediates relieved atherosclerosis in apolipoprotein E deficient mice through the induction of regulatory T cells. *Biochem. Bioph. Res. Co.*, 411(3): 523-529.
- Esfahlan, A.J., R. Jamei and R.J. Esfahlan. 2010. The importance of almond (*Prunus amygdalus* L.) and its by-products. *Food Chem.*, 120: 349-360.
- Fu, M. and J. Ye. 2015. Analysis on exotoxicity of *Armeniacae amarum*. *Liaoning J. Tradit. Chin. Med.*, 42(2): 384-384.
- García, M.C., E. González-García, R. Vázquez-Villanueva and M.L. Marina. 2016. Apricot and other seed stones: amygdalin content and the potential to obtain antioxidant, angiotensin I converting enzyme inhibitor and hypocholesterolemic peptides. *Food Funct.*, 7(11): 4693-4701.
- Guo, J.Q., W.Z. Wu, M.X. Sheng, S.L. Yang and J.M. Tan. 2013. Amygdalin inhibits renal fibrosis in chronic kidney disease. *Mol. Med. Rep.*, 7(5): 1453-1457.
- Halenar, M., L. Chrastinova, L. Ondruska, R. Jurcik, K. Zbynovska, E. Tusimova, A. Kovacik and A. Kolesarova. 2017. The evaluation of endocrine regulators after intramuscular and oral application of cyanogenic glycoside amygdalin in rabbits. *Biologia*, 72(4): 468-474.
- Hu, F., Y.C. Hu and F. Peng. 2019. Synergistic and protective effect of atorvastatin and amygdalin against histopathological and biochemical alterations in Sprague-Dawley rats with experimental endometriosis. *Amb. Express*, 9(1): 37.
- Hui, Q., Y. Lai, Y.T. Zhang, X.L. He and M.Y. Xu. 2014. Caco-2 human colon carcinoma cell death induced by apricot kernel protein. *Food Sci. Tech.*, 39(5): 203-207.
- Jaswal, V., J. Palanivelu and C. Ramalingam. 2018. Effects of the gut microbiota on amygdalin and its use as an anti-cancer therapy: substantial review on the key components involved in altering dose efficacy and toxicity. *Biochem. Biophys. Rep.*, 14(C): 125-132.
- Lai, Y., W. Xia, Y. Yuan, X. Wen, W.Y. Liu and M.Y. Xu. 2011. Study on reducing serum lipid function of apricot kernel protein. *Food Nutr. Chin.*, 17(4): 66-68.
- Li, F.D., T.N. Wuyun and G.P. Zhu. 2019. *Cultivation operative technology of kernel-apricot*. Vol: 1. China Forestry Publishing House, China.
- Li, K.Y., W.H. Yang, Z. Li, W.W. Jia, J.Z. Li, P.F. Zhang and T.C. Xiao. 2016a. Bitter apricot essential oil induces apoptosis of human HaCaT keratinocytes. *Int. Immunopharmacol.*, 34: 189-198.
- Li, X., J. Peng, Z. Sun, H.J. Tian, X.H. Duan, L. Liu, X. Ma, Q. Feng, P. Liu and Y.L. Hu. 2016b. Chinese medicine CGA formula ameliorates DMN-induced liver fibrosis in rats via inhibiting MMP2/9, TIMP1/2 and the TGF- β /Smad signaling pathways. *Acta pharm. Acologica Sinica*, 37(6): 783-793.
- Lian, Y.J., T.W. Xu, Y.B. Zheng, M.L. Ke, Z. Li, T. Huang and D.D. Chen. 2005. The therapeutic effect of anti-CEA McAb- β -glucosidase conjugate/amygdalin system on colorectal cancer xenografts in nude mice. *Central Chin. Med. J.*, 29(1): 49-51.
- Liu, Q.Q., C. Li, J. Zhou, T.T. Sun, Z.B. Di, Y. Li, Y. Liu and H. Zhang. 2021. Study on potential pharmacodynamic substances of Qingwen Hufei granules for prevention and treatment of COVID-19 based on network pharmacology and molecular docking. *Nat. Prod. Res. Dev.*, 33: 500-509.
- Liu, S., X.Q. Wang, G.H. Liao and W. Xu. 2017. Research progress on antitumor activity and mechanism of amygdalin. *Sh. J. Tcm. Jul.*, 51(7): 99-101.
- Ma, Y., S. Wang, X. Liu, H. Yu, D. Yu, G. Li and L. Wang. 2020. Oil content, fatty acid composition and biodiesel properties among natural provenances of Siberian apricot (*Prunus sibirica* L.) from China. *GCB Bioenergy*, 00: 1-21.
- Ma, Y.H. 2007. Extraction and application of bitter apricot-kernel oil in insecticide. Doctor degree Thesis of Northwest Agriculture and Forestry University, China.
- Makarević, J., J. Rutz, E. Juenge, S. Kaulfuss, I. Tsauro, K. Nelson, J. Pfitzenmaier, A. Haferkamp and R.A. Blaheta. 2014a. Amygdalin influences bladder cancer cell adhesion and invasion in vitro. *Plos One*, 9(10): e110244.
- Makarević, J., J. Rutz, E. Juenge, S. Kaulfuss, M. Reiter, I. Tsauro, G. Bartsch, A. Haferkamp and R.A. Blaheta. 2014b. Amygdalin blocks bladder cancer cell growth in vitro by diminishing cyclin A and cdk2. *Plos One*, 9(8): e105590.
- Moradipoodeh, B., M. Jamalan, M. Zeinali, M. Fereidoonhezahad and G. Mohammadzadeh. 2019. *In vitro* and in silico anticancer activity of amygdalin on the SK-BR-3 human breast cancer cell line. *Mol. Biol. Rep.*, 46(6): 6361-6370.
- Moradipoodeh, B., M. Jamalan, M. Zeinali, M. Fereidoonhezahad and G. Mohammadzadeh. 2020. Specific targeting of HER2-positive human breast carcinoma SK-BR-3 cells by amygdaline-Z_{HER2} affibody conjugate. *Mol. Biol. Rep.*, 47: 7139-7151.
- Pan, S.J., J. Yang and R. Ma. 2021. Clinical effect of bufei xiaowei decoction combined with apatinib on advanced lung cancer and its effect on CEA, SCC and CA125. *Chin. Arch. Tradit. Chin. Med.*, 39(7): 181-183.
- Park, H.J., S.H. Yoon, L.S. Han, L.T. Zheng, K.H. Jung, Y.K. Uhm, J.H. Lee, J.S. Jeong, W.S. Joo, S.V. Yim, J.H. Chung and S.P. Hong. 2005. Amygdalin inhibits genes related to cell cycle in SNU-C4 human colon cancer cells. *World J. Gastroentero.*, 11(33): 72-77.
- Qu S.L., Q. Fang and G. Chen. 2000. Effects of tetrandrine, tetramethylpyrazine and amygdalin on human kidney fibroblast. *Chin. J. Nephrol.*, 16(3): 186-191.
- Reck, M., S. Popat, N. Reinmuth, D.D. Ruysscher, K.M. Kerr and S. Peters. 2014. Metastatic non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann. Oncol.*, 25(Suppl 3): 27-39.
- Shi, J., Q. Chen, M. Xu, Q. Xia, T. Zheng, J. Teng, M. Li and L. Fan. 2019. Recent updates and future perspectives about amygdalin as a potential anticancer agent: a review. *Cancer Med.*, 8(6): 3004-3011.
- Sun, H.Y., J.H. Zhang, L. Yang, F.C. Jiang, M.L. Zhang and Y.Z. Wang. 2019. Fruit scientific research in New China in the past 70 years: Apricot. *J. Fruit Sci.*, 36(10): 1302-1319.
- Sun, Z.L., J.W. Liu and C.C. Kuang. 2016. Inhibitions and mechanisms of amygdalin in non-small cell lung cancer NCI-H1299. *J. Chin. Pharm Univ.*, 47(4): 479-482.
- Sung, H., J. Ferlay, R.L. Siegel and M. Laversanne. 2021. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer J. Clin.*, 71(3). DOI: 10.3322/caac.21660.
- Tian, H., H. Yan, S. Tan, P. Zhan, X.Y. Mao, P. Wang and Z.P. Wang. 2016. Apricot kernel oil ameliorates cyclophosphamide-associated immunosuppression in rats. *Lipids*, 51(8): 1-9.
- Tian, H., L. Liu, Z. Li, W. Liu, Z. Sun, Y. Xu, S. Wang, C. Liang, Y. Hai, Q. Feng, Y. Zhao, Y. Hu and J. Peng. 2019. Chinese medicine CGA formula ameliorates liver fibrosis induced by carbon tetrachloride involving inhibition of hepatic apoptosis in rats. *J. Ethnopharmacol*, 232: 227-235.

- Wang, S. 2014. Development of antidiabetic beverage from apricot (*Armeniaca sibirica*) kernel protein. Master Degree Thesis of Beijing Forestry University, China.
- Wang, S.Y., X. Wang, Z.Q. Xu, Y. Liu and F.L. Kong. 2020. Amygdalin alleviates carbon tetrachloride induced hepatic fibrosis in rats by inhibiting oxidative stress and inflammatory response. *Curr. Immunol.*, 40(6): 471-475.
- Wang, Y., B. Zhou and H.Y. Zhong. 2014. Content of phenol and antioxidant ability of apricot kernel oil under different pretreatment. *Food Mach.*, 30(6): 149-152.
- Wang, Z., K. Fang, G. Wang, X. Guan, Z. Pang, Y. Guo, Y.Z. Yuan, N. Ran, Y. Liu and F. Wang. 2019. Protective effect of amygdalin on epithelial-mesenchymal transformation in experimental chronic obstructive pulmonary disease mice: protective effect of amygdalin on emt *In vivo* and *In vitro*. *Phytother. Res.*, 33(3): 808-817.
- Wu, Y.N. 2019. Amygdalin promotes the activity of T cells to suppress the progression of HBV-related hepatocellular carcinoma via JAK2/STAT3 signaling pathway. Doctor Degree Thesis of Hunan University of Chinese Medicine, China.
- Xu, M.S., H. Zhao, X.X. Zhou, T.N. Wuyun, F.D. Li and G.P. Zhu. 2016. The responses of photosynthetic physiology and biomass accumulation of sweet-kernel apricot (*Prunus armeniaca* × *sibirica*) seedling to soil water stress, *Taiwan J. For. Res.*, 31(4): 271-284.
- Xu, X. and Z. Song. 2014. Advanced research on anti-tumor effects of amygdalin. *J. Cancer Res. Ther.*, 10(Supplement): C3-C7.
- Yang, X.P., C.M. Zhang, X. Feng and J.H. 2006. Yang. Preliminary study on clinical efficacy of amygdalin oral preparation. *J. Chin. Med. Mater.*, 29(6): 636-637.
- Yang, X.Y. and J.P. Chen. 2005. Nutritional and healthy function of apricot kernel and its application in food industry. *Food Sci.*, 26(9): 629-631.
- Yin, M., T. Wuyun, Z. Jiang and J. Zeng. 2020. Amino acid profiles and protein quality of Siberian apricot (*Prunus sibirica* L.) kernels from Inner Mongolia. *J. Forestry Res.*, 31: 1391-1397.
- Yuan, L., S.M. Ruan and M.H. Shen. 2021. Experience summary of Shen Minhe treating lung cancer based on syndrome differentiation based on cluster analysis of 1300 prescriptions. *J. New Chin. Med.*, 53(2): 87-92.
- Yue, H.F., M. Zhou, X.K. Hou, X. Yang, H. Zhao, M.S. Xu, L. Wang, H.M. Liu, T.N. Wuyun, G.P. Zhu and F.D. Li. 2022. Effect of elements nitrogen, phosphorus and potassium on phenotype, photosynthesis and biomass accumulation in juvenile phase of *Prunus armeniaca* × *Sibirica*. *Pak. J. Bot.*, 54(2): 577-588.
- Yue, H.H. 2020. Determination, analysis and evaluation of nutritional quality of major apricot varieties in Xinjiang. Master Degree Thesis of Kashi University, China.
- Zhang, F. 2011. Extraction and effect on human colon adenocarcinoma cell growth of apricot kernel protein. Master Degree Thesis of Beijing Forestry University, China.
- Zhang, J., H.D. Gu, L. Zhang, Z.J. Tian, Z.Q. Zhang, X.C. Shi and W.H. Ma. 2011. Protective effects of apricot kernel oil on myocardium against ischemia-reperfusion injury in rats. *Food Chem. Toxicol.*, 49(12): 3136-3141.
- Zhang, J.G., B. Yang and T.M. Gao. 2021. Advances in treatment of coronavirus disease 2019 (COVID19). *Chin. J. Virol.*, 37(1): 201-210.
- Zhang, X., J. Hu, Y. Zhuo, L. Cui, C. Li, N. Cui and S. Zhang. 2018. Amygdalin improves microcirculatory disturbance and attenuates pancreatic fibrosis by regulating the expression of endothelin-1 and calcitonin gene-related peptide in rats. *J. Chin. Med. Assoc.*, 81(5): 437-443.
- Zhao, H., X. Zhou, L. Ying, Y.L. Huang, T.N. Wuyun, F.D. Li and G.P. Zhu. 2017. Two types of new natural materials for fruit vinegar in *Prunus* plants. *MATEC Web of Conferences*, 100:04006.
- Zhao, X., W.L. Lv, J.M. Li, Y.M. Ni, Y.T. Liu and Z. Cao. 2020. Research progress on anti-fibrosis mechanism of amygdalin. *Chin. Arch. Tradit. Chin. Med.*, 38(10): 109-112.
- Zhen, N., J. Zhou, Q.H. Wang and G.H. Wang. 2013. Bladder cancer cells apoptosis induced by amygdalin following specific activation by β -glucosidase. *J. Modern Urol.*, 18(3): 113-116.
- Zheng, Q.L., Y.C. Guo, J. Sun, G.Q. Xie, X.N. Li and G.L. Liao. 2009. An experiment of amygdalin induced premature chromosome condensation in human blood T lymphocytes. *J. Environ. Occup. Med.*, 26(6): 572-574.
- Zhou, C., L. Qian, H. Ma, X. Yu, Y. Zhang, W. Qu, W. Xia, X. Zhang and W. Xia. 2012. Enhancement of amygdalin activated with β -D-glucosidase on Hep G2 cells proliferation and apoptosis. *Carbohydr. Polym.*, 90(1): 516-523.
- Zhu, Q.Q., J.J. Chen, T. Zhang and B. Jiang. 2020. Effect of ultra-high pressure on structure and immunoreactivity of bitter apricot kernel protein isolate. *J. Food Sci. Biotechnol.*, 39(10): 34-39.
- Zhu, Z., N. Qiu and J. Yi. 2010. Production and characterization of angiotensin converting enzyme (ACE) inhibitory peptides from apricot (*Prunus armeniaca* L.) kernel protein hydrolysate. *Eur. Food Res. Technol.*, 231(1):13-19.

(Received for publication 23 August 2021)