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Review

Research and Application of Adlay in Medicinal Field

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ABSTRACT

The traditional Chinese medicine (TCM) adlay has been used as a dietary supplement to promote health and treat various ailments for thousands of years. The effective and safe ingredients of TCM could be used as sources for developing new drugs. This paper reviews the main research and application of adlay seed in medicinal field in the following aspects: botanical resource, ethnopharmacological function, chemical constituents, pharmacology and pharmacokinetics, safety evaluation and toxicity, and clinical application. We hope that the review could help researchers mine the scientific values of adlay seed, innovative drug design, provide the guidance for the application in clinical therapy, and enhance the academic level and clinical efficacy of adlay seed.

Key words

botanical resource; clinical application of adlay seed; ethno-pharmacology; pharmacology

1. Introduction

Over thousands of years, food materials have been continuously studied for their health benefits, while a wide range of Chinese herbal medicines have also been investigated and incorporated into the daily diet for maintaining general wellness or prevention of certain diseases in China. The effective and safe ingredients of natural materials could be used as sources for developing new drugs.

The adlay seed (*Coix lacryma-jobi* L. var. *ma-yuen* Stapf) is a medicinal material listed in *Bencao Gangmu* edited by Shi-zhen Li (Li, 1596) and in the 2015 edition of *Chinese Pharmacopoeia*. The seed has been widely used in Asian countries for the treatment of rheumatism, warts, neuralgia, and female endocrine disorder from ancient times. Recent studies have demonstrated that the adlay seed exhibits anti-inflammatory, anti-obesity, anti-hyperlipidemia, anti-tumor (Xu et al, 2012; Liu et al, 2015), anti-allergic, and anti-microbial effects (Ukiya and Tanimura 1961; Seo et al, 2000; Hung and Change, 2003; Kim et al, 2004; 2007; Yu et al, 2008; 2014). In this review paper, authors introduced the botanical resource, chemistry, ethnopharmacology and pharmacology, and clinical application of adlay seed.

2. Botanical resource

Adlay (*Coix lacryma-jobi* var. *ma-yuen*) is an annual or perennial herb in the family of Cramineae (Figures 1 and 2). Its seed has now become one of the most popular Chinese herbal medicines. Although frequently used as a dietary

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supplement there is still controversy in terms of its classification in China and globally. The medicinal part is mainly the seeds of adlay. It is considered to be 7−10 different species overall. Of them, four species (*C. lacryma-jobi* L., *C. puellarum* Balansa, *C. agrestis* L., and *C. aguatica* Roxb), and one varietie (*C. lacryma-jobi* L. var. *ma-yuen*) are the main and legal source recorded in *Chinese Pharmacopoeia* and other historical records of Chinese herbal medicine (Pharmacopoeia Committee of P. R. China, 2015). Traditionally wild *Coix* seeds were harvested, but now cultivation has become the main source of supply. As an increasing amount of *Coix* seed derivative commercial products are on the market, there has been shortage of wild seeds. Generally, *Coix* seeds are mainly produced in Fujian, Jiangsu, Hebei, and Liaoning provinces in China.

Figure 1 Plants of *C. lachryma-jobi* var. *ma-yuen*
(http://image.haosou.com/v/q=Coix+lacryma-jobi+L.var.ma-yuen)

Figure 2 Seeds of *C. lachryma-jobi* var. *ma-yuen*
(http://image.baidu.com/search/detail?ct=503316480&z=0&ipn=d&word)

3. Ethnopharmacological function

According to the ethnopharmacological theory, *Coix* seeds stimulate the functions of spleen, stomach, and lung, remit fever (which helps in the drainage of pus), and induce diuresis. They have long been used in China to treat warts, chapped skin, rheumatism, and neuralgia (Li, 1596). Recent studies showed that *Coix* seeds presented antiproliferative, antitumor,r and various immunomodulatory activities, for instance, anti-complementary, anti-inflammatory, and anti-allergic effects. In addition, modern research found that *Coix* seed oil could prevent or reduce the contracture action of striated muscle and stimulate action on uterus (Liu et al, 2000).

In folk medicine, the fruits are used in folk remedies for various tumors, such as abdominal, esophageal, gastro-intestinal, and lung cancers, as well as excrescences, warts, and whitlows (Hartwell, 1968). This folk reputation is more interesting when reading that coixenolide has antitumor activity (List and Horhammer, 1979). Job's tear is also a folk remedy for abscess, anodyne, anthrax, appendicitis, arthritis, beriberi, bronchitis, catarrh, diabetes, dysentery, dysuria, edema, fever, gotter, halitosis, headache, hydrothorax, metroxenia, phthisis, pleurisy, pneumonia, puerperium, rheumatism, small-pox, splenitis, strangury, tenesmus, and worms (Duke and Wain, 1981). Walker cites other medicinal uses (Walker, 1971)

4. Chemical constituents

Adlay is widely planted in China and Japan, where it is considered as a healthy food supplement. *Coix* seeds contain a large number of nutrients, for instance, proteins, superior amino acids, and carbohydrates. Additionally several major classes of bioactive ingredients were identified in *Coix* seeds with many beneficial functions to human health, particularly coixenolide, triglyceride, fatty acids, and triterpenes. Nutritional and bioactive ingredients are presented in *Coix* seeds (Yu et al, 2014).

4.1 Nutritional ingredients

As a nourishing grain, *Coix* seeds contain 14% protein, 5% fat, 65% carbohydrates, 3% crude fiber, 0.07% calcium, 0.242% phosphorus, and 0.001% iron. The levels of all nutrients in *Coix* seeds are higher than those in rice. It also contains mineral substances and essential amino acids, for example, leucine, arginine, lysine, and tyrosine. Due to high content of unsaturated fatty acids and extremely low levels of heavy metals and toxic residues in *Coix* seeds, it has become a typical "green food" (Yu et al, 2014).

4.2 Bioactive ingredients

Up until now, more than 41 chemical ingredients have been isolated and identified in *Coix* seeds, including coixenolide, triglyceride, fatty acids, lactams, coixol, saccharides, sterols, and triterpenes (Huc et al, 2007; Du et al, 2012; Lu et al, 2010). *Coix* seeds mainly contain abundant amounts of coixenolide, coixan, and total triterpenes. Their contents on average are 44.60, 59.03, and 22.83 mg/g, respectively. As two major bioactive ingredients identified in *Coix* seeds, fatty acids and coixenolide were reported to present significant antitumor activity. In *Coix* seed oil the content of triglyceride is up to 87%, and unsaturated fatty acid residues in all triglyceride fatty acid residues are over 84%, mainly including oleic acid (31.42%) and linoleic acid (47.38%). Three active polysaccharides were also obtained and they are able to regulate blood glucose levels. After purification, polysaccharide A consists of rhamnose, arabinose, xylose, mannose, and galactose (1:1:1:11:10);

polysaccharide B consists of rhamnose, arabinose, xylose, mannose, galactose, and glucose (3:18:13:3:10:5); polysaccharide C is glucan (Yu et al, 2014).

Yang et al investigated the effect of adlay on osteoporosis using an ovariectomized mouse model. The adlay diet (10% and 30% adlay in mouse diet) or water extract of adlay (0.3 g/kg/day) was given to ovariectomized mice for 4 weeks. The findings indicate that adlay is capable of increasing the proliferation of osteoblast cells via an ERK-regulated signaling pathway. Adlay may be a helpful healthy food for osteoporosis prevention (Yang et al, 2013). Choi et al isolated and identificated two new stereoisomers, (+)-(7'*S*,8'*R*,7″*S*,8″*R*)-guaiacylglycerol β-*O*-4'-dihydrodisinapyl ether and (+)-(7'*S*,8'*R*,7″*R*,8″*R*)-guaiacylglycerol β-*O*-4'-dihydrodisinapyl ether) from *Coicis Semen* (Choi et al, 2015).

Li et al suggested the possibility that adlay bran and its ethanolic extract and residue inhibit colonic preneoplastic lesions in an early stage. Adlay and its fractions may have the potential to be developed as chemopreventive cereal products (Li et al, 2011). Jia et al studied the EtOAc extract of *G. moniliformis* AH13 in adlay, and the extract showed strong antitumor activity against four types of tumor cells (A549, HCT116, MDA-MB-231, and SW1990). The results studied by Jia et al suggest that *G. moniliformis* AH13 has significant scientific and industrial potential to meet the pharmaceutical demands and sustainable energy requirements for TAGs in a cost-effective, easily accessible, and reproducible way and is also a potential novel source of natural antitumor bioactive agents (Jia et al, 2014).

5. Pharmacology and pharmacokinetics

5.1 Pharmacology

As a tasty food, *Coix* seeds were commonly seen on dinner tables. Most importantly it is widely used as a traditional Chinese medicine (TCM) over thousands of years in treatment of diseases such as cancer, metastasis, hypertension, arthritis, asthma, and immunological disorders (Normile, 2003; Woo et al, 2007).

The fatty oil is also able to reduce serum calcium and blood glucose levels. *Coix* seed oil also exerts beneficial effects on cancer with multiple mechanisms as seen in clinical trials. It presented activities of blood lipid-reducing and anti-oxidant effects, and could be used as a supplementary in healthcare food products and drugs for prevention of chronic diseases (particularly arthrosclerosis and coronary artery disease) (Yu et al, 2008; 2011; Kim et al, 2012). While the active component of *Coix* seed, coixenolide, promotes cellular immunity and humoral immunity; coixans A, B, and C significantly reduce the blood glucose level (Zhang and Shen, 2007; Zhao et al, 2004). Moreover, the consumption of *Coix* seed extracts can increase the activities of cytotoxic T cells and natural killer (NK) cells. The methanol extract of *Coix* seeds inhibits production of NO and O_2-byactivating macrophages (Chen et al, 2012).

The Nrf2/ARE pathway plays an important role in inducing phase II detoxifying enzymes and anti-oxidant proteins and the considered potential target for cancer chemoprevention. Chen et al established to screen a potentially cytoprotective compound, 4-ketopinoresinol (4-KPR), the (α-γ) double-cyclized type of lignan obtained from adlay (*C. lachryma-jobi* var. *ma-yuen*). They observed and suggested that 4-KPR was a novel Nrf2/ARE-mediated transcription activator, activated the Nrf2/HO-1 axis, and protected against oxidative stress-induced cell injury via activation of PI3K/AKT signaling in an ARE-regulated gene system (Chen et al, 2012).

5.2 Anti-inflammatory and anti-allergic effects

In a paper titled "Anti-inflammatory effects and chemical study of a flavonoid-enriched fraction from adlay bran" by Chen HJ et al, their study results suggest that flavonoids in adlay bran, partially at least, contribute to its anti-inflammatory effect. Thus, adlay bran may be beneficial to the health of consumers (Chen et al, 2011). In 2012, Chen et al investigated the anti-allergic effects of adlay bran on rat basophilic leukemia (RBL)-2H3 cells. Their study suggested that adlay bran extract reduced the release of histamines and cytokines and suppressed the production of Akt. These combined effects influenced the signal transduction in RBL-2H3 cells, thereby revealing the mechanisms of the anti-allergic effects of adlay (Chen et al, 2012).

5.3 Chemopreventive action

In cancer therapy, adlay can be used as a chemopreventive agent. The chemoprevention refers to the use of natural or synthetic, non-toxic chemical substances to reverse, repress, or prevent carcinogenesis. The chemopreventive agents can be broadly categorized into two types: blocking agents and suppressing agents (Figure 3) (Wattenberg, 1985; Manson et al, 2000).

In 2007, Woo et al at School of Medicine, Johns Hopkins University, USA reported the research result that *Coix* seed extract inhibits NFκB and protein kinase C signaling (Woo et al, 2007). Using oligonucleotide microarrays, we determined that *Coix* seed extract also significantly affects gene expression in these cells, including downregulation of genes. They first evaluated the anti-neoplastic activity of a *Coix* extract emulsion in xenografts of MDA-MB-231 breast cancer cells and found that the extract significantly inhibited growth of MDA-MB-231 xenografts in athymic nude mice. The specific gene expression changes noted after *Coix* seed extract treatment are characteristic of inhibition of NFκB-dependent transcription, leading us to evaluate how the treatment affects that pathway. An NFκB-dependent reporter assay demonstrated dose-dependant inhibition of NFκB signaling by treatment of cultures with the extract, and immunofluorescent microscopy found that these effects are associated with reduced translocation of the Rel-A/p65 subunit of NFκB to the nucleus. *Coix* extract also inhibits activity of protein kinase C, a major mediator of signal

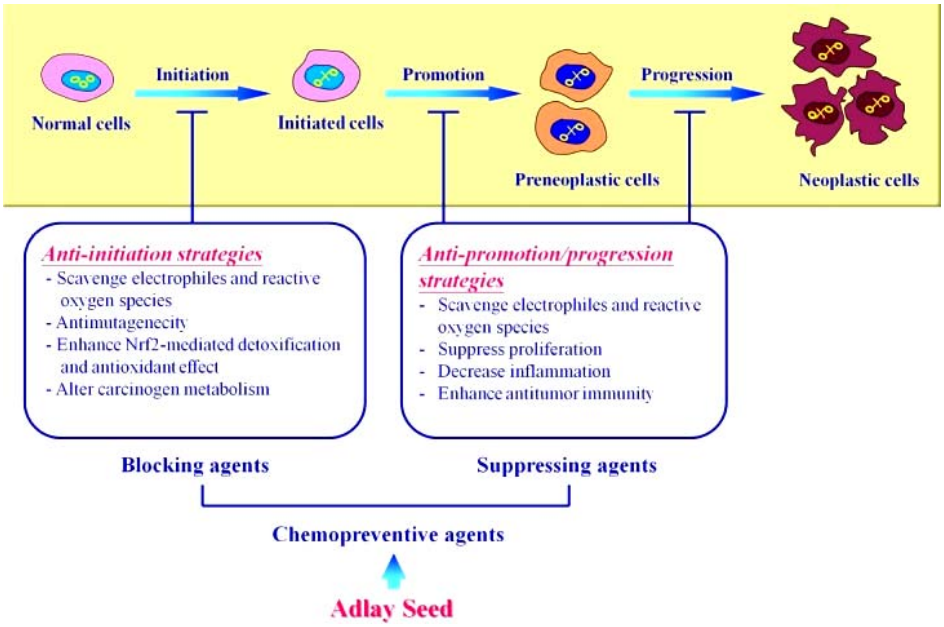

Figure 3 Multistage carcinogenesis and strategies for cancer chemoprevention (Kou et al, 2012)

transduction and activator of NFκB. Thus, they suggested that this TCM-based cancer treatment affects cellular pathways of recognized importance in neoplasia.

Kuo et al summarized recent researches attempting to study the chemopreventive blocking and suppressing potential of adlay and its active components in scavenging electrophiles and reactive oxygen species, antimutagenicity, enhancing Nrf2-mediated detoxification and antioxidant effect, altering carcinogen metabolism, suppressing proliferation, decreasing inflammation, and enhancing antitumor immunity (Kuo et al, 2012). The chemopreventive functionality of adlay involving in scavenging electrophiles and reactive oxygen species, antimutagenicity, enhancing Nrf2-mediated detoxification and anti-oxidant effect, altering carcinogen metabolism, suppressing proliferation, decreasing inflammation, and enhancing antitumor immunity. Oil extracts, especially KLT injection, have been proved therapeutic efficacy in clinical application (Kuo et al, 2012).

5.4 Antioxidant capacity

In a study on the effect of polyphenol extract of adlay (APE) in hypercholesterolemia-induced oxidative stress rats, authors found the serum triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C), and markers of oxidative stress, malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) in the serum and liver of HCD and normal rats were assessed and compared at the end of four weeks. Their results exhibited that APE was significantly effective in decreasing the serum levels of TC, LDL-C, and MDA, increasing the serum level of HDL-C and anti-oxidant capacity. In addition, oral gavage of APE could also increase the anti-oxidant capacity, CAT and GSH-Px activities in the liver. Therefore, it is suggested that APE exerted a high hypocholesterolemic and anti-oxidant activities. The results might be characterized by a protective effect on cardiovascular health (Wang et al, 2012).

5.5 Mechanism of action for cancer therapy

Pre-clinical studies have found that KLT may block the tumor cell cycle at the G_2/M phase, and induce tumor cell apoptosis (Wu et al, 2004; Lu et al, 2008; 2009). In the examination of the effects of KLT on PI3K/Akt/mTOR pathway in pancreatic cancer xenografts in mice (Liu et al, 2014), Liu et al suggested that KLT could suppress the growth and induce apoptosis of pancreatic cancer xenografts. Moreover, KLT can downregulate the expression of phospho-Akt and phospho-mTOR to modulate the PI3K/Akt/mTOR signaling pathway.

In vivo experiments showed that *Coix* seed extract inhibited FAS activity in the liver, elevated LPL and HL activity in the plasma, and effected G-6-PD activity, thereby inhibited fatty acid synthesis and reduced the components and forms of energy for tumor cell growth (Yu et al, 2008).

Fatty-acid synthesis (FAS) is now regarded as the key process for tumor cell growth than survival. The inhibition of FAS activity should inhibit tumor cell growth, and finally realize the objective of cancer therapy. The mechanisms of action of *Coix* seed extract of KLT are as follows: The drug (1) inhibits the mitosis of tumor cells during G_2/M phases; (2) induces apoptosis of tumor cells; (3) affects the genetic expression of tumor cells by up-regulating FAS/Apo-1 gene expression and down-regulating Bc1-2 gene expression; (4) inhibits tumor angiogenesis; (5) counteracts the cachexia of cancers; and (6) reverses the multi-resistance of tumor cells to anticancer drugs and the resistance modification in some chemotherapeutic agents (Li, 2006). All the above mechanisms of action of *Coix* seed extract reflect the multiple targets of action of *Coix* seed extract (Figure 4).

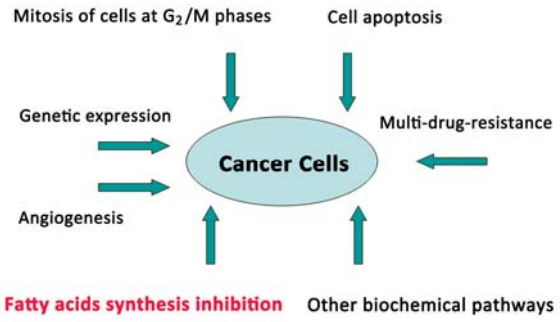

Figure 4 A new target for active component of *Coix* seed (Yu et al, 2008)

This is the first time to describe a new action mechanism of *Coix* seed extract through the inhibition of FAS. Further experiments *in vitro* showed that the inhibition of *Coix* seed extract on FAS activity was significant and dose dependent. *Coix* seed extract inhibited two active sites such as KR and ER (Figure 5). Continued studies are required to explain whether *Coix* seed extract inhibits other active sites.

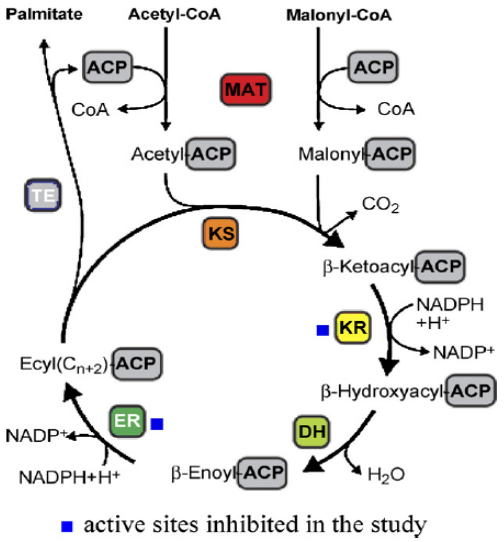

Figure 5 Catalytic cycle and domain organization of FAS (Yu et al, 2008)

5.6 Pharmacokinerics

Yu et al carried out a study on the *in vivo* pharmacokinetics of KLT injection in rats. The concentration change of exogenous triglyceride (TG) in rat serum was detected by TG Kit after iv administration of KLT injection (Yu et al, 2009). At the dosages of 10 and 5 mL/kg, the main pharmacokinetic parameters of KLT injection were as follows: C_{max} = (8.532 ± 1.031) and (5.418 ± 0.764) mmol/L, $AUC_{0\text{-}t}$ = (13.248 ± 3.692) and (5.339 ± 1.219) mmol/(L·h), Vc = (1.030 ± 0.131) and (0.756± 0.150) L^2/(kg·mol), CLs = (0.838 ± 0.319) and (0.975 ± 0.330) L^2/(kg·mol·h), $t_{1/2\,\alpha}$ = (0.481 ± 0.168) and (0.322 ± 0.109) h, $t_{1/2\,\beta}$ = (1.452 ± 0.776) and (1.384 ± 0.404) h (Figure 6).

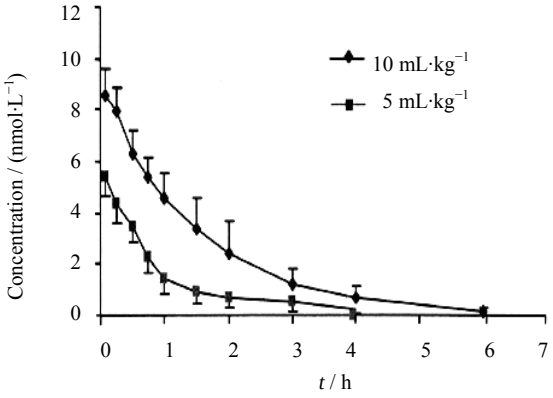

Figure 6 Curves of blood concentration in rat after iv injection with KLT

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6. Safety and toxicity evaluation

Clinical studies on the toxicity or side effects that could be directly related to the use of *Coix* seeds remain limited. Currently, pre-clinical studies have not shown toxicity for various organs through iv drip or oral administration. The maximal oral dose of *Coix* seed oil in mice was 40 mL/kg or 32.8 g/kg, there was no irritation in rectum and normal or damaged skin of rabbits observed. It is considered safe for both routine oral administration and external use of *Coix* seeds.

It was reported that LD_{50} (per oral administration) was higher than 20 g/kg. Ames test, micronucleus test of bone marrow cells in mice, and shape abnormality test in mice were negative and less toxic (Li, 2006; Tao et al, 2013). There were no adverse actions when people took decocted *Coix* seeds at the normal dose (no more than 30 g). As reported, gastrointestinal reactions and bone marrow suppression in the experimental group receiving KLT injection combined with chemotherapy were significantly lower than that in the control group with chemotherapy alone ($P < 0.05$). KLT injection enhanced efficacy and reduced the side effects of chemotherapy, and improved quality of life of gastric cancer patients (Zhan et al, 2012).

7. Clinical application

7.1 TCM application to therapeutics

Pharmacological studies and clinical investigation suggest that *Coix* seed oil has certain anti-hepatoma effects. It exerts anti-hepatoma activity by inhibiting hepatoma cells proliferation via inducing apoptosis and reducing nutritive supplies for growing tumors. This is done through inhibiting angiopoiesis in tumor tissue, as well as by increasing immunologic function against tumors. In the treatment of primary liver carcinoma, either single *Coix* seed oil or *Coix* seed oil in combination with other medicines can be used. When combined with chemotherapeutic drugs, it can reduce the occurrence of immune degeneration and bone marrow inhibition. Therefore, it has great potential for further development (Zhang and Shen, 2010).

7.2 Cancer therapy

In clinical practice, *Coix* seed has been used in patients with verruca vulgaris and verruca planae juveniles, which have been considered to be induced by viral infection. However, KLT injection is mainly made of *Coix* seed oil, which was extracted from *Coix* seeds through supercritical CO_2 extraction. KLT injection has been successfully applied in the treatment of a variety of malignant tumors, such as carcinomas of the lung, liver, stomach, esophagus, colon, pancreas, kidney, ovaries, malignant lymphoma, and leukemiain over 200 000 cases in China and Russia. When combined with chemotherapy, radiotherapy, and surgery, it could improve the response rate, regulate the energy of advanced patients, and improve life quality and prolong survival time. A Phase II clinical trial has been approved by FDA to evaluate its efficacy in treating non-small-cell lung cancer in 2003. It is the first drug derived from a traditional Chinese herbal remedy that has entered into clinical trials in the United States (Normile, 2003; Li, 2006).

Coix seed is one of the most common herbs traditionally used in herbal medicines and healthcare products. In terms of classification of TCM, the herb is sweet and tasteless in flavour, slightly cold in nature. Tasteless flavour is for removing dampness; sweet flavour is for tonifying the spleen; and slight coldness is for clearing heat. *Coix* seed is neutral, neither oily nor drastic (Liu and Xiao, 2009). The herb exerts therapeutic healthcare actions in the following aspects: inducing diuresis, excreting dampness, strengthening spleen, arresting diarrhea, clearing heat and pus, antitumor and enhancing immunologic function. *Coix* seeds could be used alone or jointly with other herbs based on TCM theory (Liu et al, 2000; Chen et al, 2012). The amount of *Coix* seeds needed to be taken depends on its usage. Generally, the daily dosage recommendation is 9−30 g, while the dosage in clinical use is 12−30 g with the highest dosage being up to 30−60 g. *Coix* seeds are either mixed with water for a decoction or grounded into powder to make pills; It also can be mixed with wine or rice porridge (Zhuo, 2009).

Clinically, *Coix* seeds are used in the following preparations: (1) *Coix* seed extract and its powder are convenient for administration, which can be made from either only *Coix* seeds or mixed with other herbs. The significant advantage of this form is ease of use and absorption; (2) KLT injection, a lipid emulsion for iv and intra-arterial injection containing 10% oil (a triglyceride containing four fatty acids) extracted from *Coix* seeds. The injection was approved by SFDA for manufacturing and marketing in 1997, and it has been successfully applied in the treatment of a variety of malignant tumor such as carcinomas of the lung, liver, stomach, esophagus, colon, pancreas, kidney, ovaries, malignant lymphoma, and leukemia for more than 200 000 cases with no obvious toxicity or side effect (Li, 2006).

7.3 Dietary usages

As a nourishing food and one of the most valuable dietary botanical materials, it was the tribute for imperial palace known as “Yiyi Pearl” in ancient China. Adlay was also called “Gramineae of Life and Health” in Europe. The grain is prepared by roasting and may be eaten dry, used as porridge, or processed into flour (Jideani and Jideani, 2011). *Coix* seeds have always been considered very precious for nourishment, healthcare, bath and skin moisturizer in Japan. Historically, *Coix* seeds have been widely used for its beneficial components, especially its high protein content and superior amino acid composition. These products are *Coix* seed tea, health care wine, yoghurt, porridge, pastry, powder, and extract. Some of the following dietary forms can be easily made at home, others are more difficult and some have been industrialized for sale (Normile, 2003).

7.3.1 Coix seed tea

Herbal tea made of *Coix* seeds mixed with other herbs is the most common way to use *Coix* seeds. Here are several examples: *Coix* seed tea composed of fried *Coix* seeds (10 g), hawthorn (5 g) and fresh lotus leaf (5 g); *Coix* seed jasmine tea composed of *Coix* seeds (10 g), jasmine tea (3 g), etc. To make the herbal tea, hot water is used to freshly brew all raw materials. Softened water or natural spring water with less mineral and alkaline is recommended in order to reduce the loss of nutrients.

7.3.2 Coix seed health care wine

Coix seed either on its own or combined with other herbs are used to prepare herbal wine for health care. Different from the conventional method of wine making, the 39 *Coix lacryma-jobi* L. var. *ma-yuen* nutrition and health-care *Coix* seed wine is produced by direct fermentation with *Coix* seeds as raw materials followed by distillation. Components with high boiling point (coixenolide and specific triterpenoids) in *Coix* seed are distilled into the wine.

Another example is the half solid state fermentation process which was used for making fermented glutinous wine from *Coix* seed. Taking *Coix* seeds and the glutinous rice as the starting stock, the sweet wine tune and the white sugar as the supplementary materials, the best fermentation process for fermented glutinous wine was when *Coix* seeds were fermented for 48 h at 33 °C, liquor tune recruitment 1%. The ratio of *Coix* seed to the glutinous rice was 1.4:1; the mixture was cooked for 60 min, boiled for 25 min, and then steamed for 30 min. The ratio of material to water was 1:2.5; the final sweetness was 12%. The fermented glutinous wine from *Coix* seeds under these conditions described presented white color, rich in pure liquor, rice wine unique fragrance, mellow liquor body, suitable crisp, sour and sweet (Wu, 2010). *Coix* seed can also be used to make herbal wines in combination with many other herbs depending on the specific needs of functions. Daily intake amount will vary depending on the content of *Coix* seed, other herbs, and alcohol.

7.3.3 Coix seed used in medicated foods

In general, *Coix* seed is used to make porridge with lily, yam, red beans, rice, and sticky rice. A typical way is to boil 30

g of *Coix* seed with other herbs, such as 30 g of Shanyao (rhizome of *Dioscorea opposita*), 15 g of Lianzi (seed of *Nelumbo nucifera*), 50 g of millet, and 10 Dazao (fruit of *Ziziphus jujuba*). This rice porridge was recommended to be taken twice daily for prevention of cancer, weak the spleen and stomach, or related diseases. Epidemiologists have long suspected that the low cancer rate in Southeast China might be related to *Coix* seeds because it is a dietary staple in the region.

Mutton, carp, spareribs, Chinese cabbage, peanuts, corn, and most of cereals can be boiled with *Coix* seed. Nutrients and the health-maintaining effect of *Coix* seed can be utilized simultaneously. The taste of foods that contain *Coix* seed can be adjusted according to personal preferences.

In addition, extracted juice of *Coix* seed and fresh milk were mixed together and fermented into yogurt. It was rich in nutrients with a good taste. It also exerted many healthcare functions such as anticancer, blood sugar reduction, pain relief, enhancement of body immunity system, cosmetic functions and so on.

8. Conclusion

As one of the most popular Chinese herbal medicines, *Coix* seed is a healthcare fruit with rich experience over thousands of years of continuous practice and refinement. It contains a large number of nutrients and bioactive ingredients. Ethnopharmacologically *Coix* seeds which were used in many folk remedies for various tumors and warts stimulate functions of the spleen, stomach, and lung, remit fever, and induce diuresis. Since ancient times, *Coix* seeds alone or jointly with other herbs have been used as both food and medicine in prevention or treatment of diseases such as cancer, metastasis, hypertension, arthritis, asthma, and immunological disorders. Clinically, KLT injection, a lipid emulsion for iv and intra-arterial injection containing 10% oil, has been successfully applied in the treatment of a variety of malignant tumor such as carcinomas of the lung, liver, stomach, esophagus, colon, pancreas, kidney, ovaries, malignant lymphoma, leukemia for more than 200 000 cases with no obvious toxicity or side effect in China and Russia. As a nourishing food and one of the most valuable dietary botanical materials, in daily life *Coix* seeds are commonly prepared into tea, health care wine, yoghurt, porridge, pastry, powder, and extract. At present, though the applications of adlay seeds are much less popular than modern medicine, preclinical and clinical studies have achieved some great successes, especially the success of KLT. We outline the current research progress of adlay seeds and sincerely hope that could be helpful for mining the scientific values of the adlay seed, and provide more data for the daily use and clinical efficacy of TCM adlay.

Conflict of interest statement

The authors declare no conflict of interest.

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