Curcumin

Tian-yi Yuan and Guan-Hua Du

Abstract Curcumin is the principal curcuminoid of turmeric (*Curcuma longa*). It is sold as an herbal supplement, cosmetic ingredient, food flavoring, and food coloring. In China, curcumin is mainly used in food, while in Western countries, it has been regarded as a health-care product. Curcumin has been proved to have multiple pharmacological effects including anti-fibrosis, antitumor, anticancer effects, and so on. As its broad biological activities, it is applied in a lot of diseases such as hyperlipidemia, infection, and cancer. However, curcumin still needs research to confirm its effects and mechanisms and find its exact indications. There is still a long way to go to make curcumin better applied in clinical practice in the future.

Keywords Curcumin · Food additives · Wide application

Alias: curcuma; C.I. 75300; C.I. Natural Yellow 3; diferuloylmethane; curcumin I
Origin: *Curcuma longa* (Fig. 1)
Chemical name (Fig. 2)

1,7-bis(4-Hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione

Molecular formula, $C_{21}H_{20}O_6$; **MW**, 368.38; **CAS**, 458-37-7

Properties

Appearance: orange-brown crystalline powder and tastes a little bitter. It will turn into reddish brown in alkaline solution and yellow in neutral and acidic solution. It has strong stability against the reducing agent. It has excellent pigmentation which

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is not easy to fade. It is sensitive to light, heat, and iron ion. When PH is greater than 8, curcumin turns from yellow to red, which can be used as a pH indicator.

Solubility: insoluble in water or diethyl ether and soluble in ethanol, propylene glycol, acetic acid, and alkali solution.

Melting point: about 183 °C.

Dosage Forms and Indications

This product is contained in the *British Pharmacopoeia* (2017), *United States Pharmacopeia* (40), and *European Pharmacopoeia* (8.7th ed.).

Curcumin is mainly used in food in China at present (E100), such as coloring agent for sausage products, canned food, and pickled products. It is a kind of natural pigment and high-quality food additive. In the United States, curcumin has been listed as the third generation of cancer chemoprevention agent by the US National Cancer Institute and was included in the *United States Pharmacopeia* in 2000. It has been used as a health-care product, including capsules, tablets, and so on. In the treatment of cancer and related diseases, curcumin has been tested in phase I and II clinical trials in several research centers across the world and has been approved by the US FDA into the phase III clinical trial [1].

Literature

The main source of curcumin is the root of Zingiberaceae *Curcuma aromatica*, rhizome of *Curcuma longa* (Jiang Huang), *Curcuma zedoaria*, and *Acorus calamus*. Among them, Jiang Huang contains about 3–6% curcumin. The traditional Chinese medicine, Jiang Huang, is the root tuber of perennial herbaceous plant *Curcuma longa* L. of family Zingiberaceae. It was firstly recorded in the "Tang materia medica" (Xin Xiu Ben Cao). It is pungent, bitter, and warm and enters the liver and spleen meridians. It activates the blood, moves qi, dredges meridians, and alleviates pain. In India and other Asian countries, Jiang Huang has more than 6000 years of application history. In Japan, Jiang Huang has a long history of health care, and the people of Okinawa Island regarded Jiang Huang as a holy tribute to the emperor.

Jiang Huang mainly comes from Taiwan, Fujian, Guangdong, Guangxi, Yunnan, and Tibet of China and other regions in East Asia and Southeast Asia. It grows in warm and humid climate and sunny environment with abundant rainfall and fears cold frost, drought, and flood. At present, *Chinese Pharmacopoeia* only included Jiang Huang and Yu Jin which contains curcumin, while curcumin is not included.

History of R&D

Curcumin is one such agent that was described about two centuries ago as the yellow coloring matter from the rhizomes of *Curcuma longa*. Besides curcumin, more than 300 different components, including phenolics and terpenoids, have been identified in turmeric, but curcumin is one of the most important active components [2]. Pure curcumin was prepared in 1842 by Vogel Jr. After 1870, the possible structure of curcumin was reported by several chemists in the subsequent decades. The chemical structure of curcumin as diferuloylmethane or 1,6-heptadiene-3,5-dione-1,7-bis (4-hydroxy-3-methoxyphenyl)-(1E, 6E) was reported by Milobedzka et al. (1910). Lampe and Milobedzka (1913) reported the synthesis of curcumin. However, Srinivasan (1953) for the first time used chromatography to separate and quantify the components of curcumin [3].

Jiang Huang has been used for more than 6000 years; it is also well known for its medicinal value and active ingredients. But it was not until the middle of the twentieth century that scientists conducted a systematic study on their pharmacological effects. In 1949, Schraufstatter and Bernt found that curcumin has a variety of antibacterial effects against *Streptococcus*, *Salmonella*, *Mucor*, *Mycobacterium* and so on [4]. In the 1970s, the study also found that it has lipid-lowering, anti-inflammatory, antioxidant, and antidiabetic effects. In 1980s, it was found to have antitumor effects. In the last 30 years, there are many reports about the clinical and pharmacological effects of curcumin.

At present, more than 65 human clinical trials have been completed, and more than 35 clinical trials are in progress. In addition, the study of curcumin derivatives has also become a hot topic in recent years.

Pharmacology

1. Anti-fibrosis effects: curcumin has the effect of anti-fibrosis in the lung, liver, kidney, and so on. It could inhibit the release of various inflammatory factors and reduce the expression of collagen, laminin, hyaluronic acid, and other extracellular matrix content. It could also reduce the transforming growth factors such as TGF-β to inhibit cell proliferation [5].
2. Antitumor effects: the antitumor effect of curcumin is currently the most studied pharmacological effects and attracts a lot of attention worldwide. Curcumin has been proved to inhibit the proliferation of a variety of tumor cells through regulating a variety of transcription factors (NF-κB, AP-1, etc.), mitogen-activated protein kinase (MAPK), growth factor receptor kinase (PDGFR, VEGFR, etc.), and cyclooxygenase. It plays an important role in the cell cycle and further to inhibit proliferation. Curcumin can also inhibit the migration of tumor cells by activating caspase and inducing tumor cell apoptosis [6].

3. Anti-inflammatory effects: curcumin has a strong inhibitory effect on different kinds of inflammation. The mechanism might relate to the reduction of the expression of prostaglandins and leukotriene to decrease the release of various inflammatory factors. The anti-inflammatory effect of curcumin is close to that of nonsteroidal anti-inflammatory drugs and glucocorticoids, but it has higher safety and lower side effects [7].
4. Antimicrobial effects: curcumin has a strong inhibitory effect on bacteria, viruses, fungi, and parasites [8]. Researchers believe that curcumin may play a role in inhibiting microbial survival and reproduction by destroying microbial cell membranes, inducing their genetic changes, and so on.
5. Hypolipidemic effect: many researchers believe that curcumin will become a hypolipidemic drug with a good prospect. It can lower the levels of total blood cholesterol and triglyceride levels, increase apolipoprotein A level, promote low-density lipoprotein (LDL) metabolism, and increase LDL excretion to reduce LDL body content [9].
6. Drug metabolism: rats were treated with a single dose of refined curcumin orally, 60–65% of which was absorbed by the gastrointestinal tract. Within 5 days, 40% of curcumin were excreted from the feces. The plasma concentration reached the peak after 3 days. The transformation of curcumin happened in the process of hepato-enteral circulation [10].

Clinical Application

1. Cholagogic effect could promote bile formation and secretion.
2. Hypolipidemic effect could reduce the level of cholesterol in the blood and prevent atherosclerosis.
3. Antibacterial and antiviral effect could inhibit *Staphylococcus aureus* and HIV.
4. Liver protection.
5. Anticancer and antitumor effect.
6. Help with the prevention of dementia.
7. Anti-inflammation and treatment of acne and dermatitis.
8. There are no reports of adverse effect of curcumin till now.

Discussion

As a natural small molecule from plant, curcumin has hypolipidemic, antitumor, anti-inflammation, cholagogic, and antioxidant effects. Curcumin has a wide medicinal resource and it also can be artificially synthesized. Therefore, the price of curcumin is quite low. Although curcumin has a wide range of pharmacological effects

and no obvious side effects and it also has many reports, it still has not become a drug yet on the market. This suggests that curcumin still has great research value and potential. To find the exact indications and related mechanisms of curcumin will be helpful for its better application in clinical practice in the future.

Fig. 1 *Curcuma longa* (Jiang Huang, 姜黄)

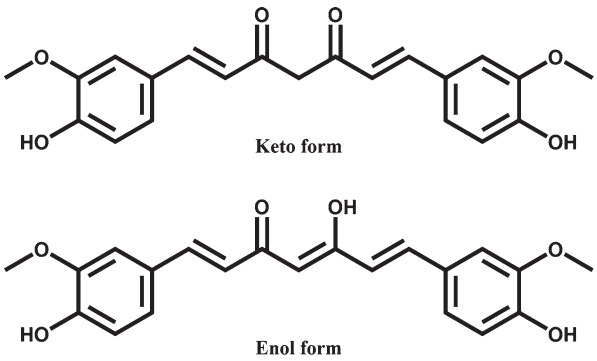

Fig. 2 Chemical structure of curcumin

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