Review on Corosolic Acid: Based on Various Pharmaceutical Effects

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ABSTRACT

Corosolic acid is a pentacyclic triterpene acid found in banaba leaves, Lagerstroemia speciosa which is similar in structure to useful pharmaceutical material such as ursolic acid and has been reported to have beneficial activities, as found in in vitro and several animal studies including human studies, particularly due to its effects on lowering of blood sugar. This review paper is focused on various pharmaceutical effects including decreasing of blood sugar of corosolic acid from published articles and can be helpful on the understanding of those effects which can be appliable on maintenance and treatment against several disease.

Keywords: corosolic acid, banaba, Lagerstroemia speciosa, pharmaceutical effects

INTRODUCTION

Banaba is the best source of corosolic acid, a known agent that helps absorb glucose into blood cells according to several studies. Several of the active components (extracts) included in banaba leaf are corosolic acid and tannins, including lagerstroemia. There are two possible mechanisms of action for corosolic acid. The first is that it may improve the sensitivity of the insulin receptor on all cells of the body. Insulin has to bind to this receptor to allow blood glucose to enter the cells. If it does not bind to the receptor, this results in increased levels of insulin, which can damage the nerves, brain, eyes, and any other part of the body that is vulnerable to insulin damage. It is called insulin resistance which can be important factor to bring metabolic syndrome. Corosolic acid improves the sensitivity of the insulin receptor by inhibiting a protein in the body called tyrosine phosphates, which reduces insulin receptor site activity. The second path of action for corosolic acid involves its ability to open an entirely new path in cells for insulin to enter the cell. This is called the GLUT4 glucose transporter, which actions the taking-up of glucose into the muscles of the body which means a good effect on controlling of blood glucose levels. Besides these mechanisms, there are also studies that show corosolic acid can inhibit our own body’s manufacture of glucose in a process called gluconeogenesis. This can have a important effect on lowering of blood glucose levels in the body.

Effects of corosolic acid

Corosolic acid (Figure 1) has been reported various biological properties including antidiabetic, anti-inflammatory, antiproliferative, and protein kinase C inhibition activity.1,2 It is found in numerous plants species, particularly Lagerstroemia speciosa called banaba as local name3.

Figure 1: Structure of corosolic acid
**Diabetes**

The most published articles about the function of corosolic acid is lowering blood sugar level in human and animal. It was first reported in 2006 that corosolic acid has a lowering effect on postprandial blood sugar levels in vivo from human studies. Corosolic acid may improve the insulin resistance conditions. The work of insulin is controlled by tyrosine phosphorylation and initiated by the binding of insulin to the insulin receptor. Corosolic acid may act as an insulin sensitizer, enhancing insulin receptor B phosphorylation indirectly by inhibiting certain nonreceptor protein tyrosine phosphatases. Corosolic acid may also stimulate GLUT4 glucose transporter course of glucose taking-up into muscle cells. Another study reported that corosolic acid inhibited gluconeogenesis by increasing the production of the gluconeogenic intermediate fructose-2,6-bisphosphate in isolated hepatocytes, which can be corosolic acid may promote glycolysis. Triterpene acids including corosolic acid isolated from Lagerstroemia speciosa leaves acts alpha-glucosidase inhibitors.

**Cancer**

Corosolic acid has toxic to cells' activity against several cancer cell lines of humans. The regulation may be associated with suppression of protein kinase C activity. In addition, cytotxic activity has been reported against HL-60 (leukemia carcinoma), MCF-7 (breast carcinoma), and Hep-G2 (hepatic carcinoma) from several human cell lines. Corosolic acid exerts their antineoplasticroles against colorectal cancer cells by encouraging the N-terminal phosphorylation and subsequent proteasomal degradation of β-catenin. Corosolic acid also isolated from the fruit of *Crataegus pinnatifida* presumed and mimiced a protein kinase C inhibitor as well as a cytotoxic agent.

Corosolic acid was able to reverse the chemoresistance of epithelial ovarian cancer cells and suppress the cell-cell interaction with tumorigenic macrophages. It is suggested that corosolic acid may be useful as an adjuvant treatment to patients with advanced ovarian and other types of cancer due to the multiple anticancer effects.

Corosolic acid impedes VEGFR2 kinase activity from hepatocellular carcinoma cell by direct interaction with the ATP binding pocket. Corosolic acid regulates the decrease of VEGFR2/Src/FAK/cdc42 axis, subsequently preventing F-actin formation and migratory activity in vitro.

**Inflammation**

The complement plays an pivotal role in immune defense against infection and inflammation. Activation of the complement system provides efficient means for protecting the host from the actions of invading antigens. Several ursane-type triterpenoids from including corosolic acid show anti-complementary activity. Corosolic acid also blocks oxidative stress, inflammation and high blood pressure in SHR/NDmcr-cp rats.

**Obesity**

There is in vitro research result for corosolic acid hindering protein tyrosine phosphatase 1B; inhibition of this phosphatase is suggested as for an obesity treatment. Corosolic acid presumes also a pancreatic lipase inhibitor, the essential enzyme for lipid consumption. From an animal study, corosolic acid acted as a peroxisome proliferator-activated receptor alpha agonist, modulating lipid metabolism process and augmenting fatty acid beta-oxidation in the liver.

**HIV**

Ellagic acid and gallic acid from *Lagerstroemia speciosa* inhibit HIV-1 infection through inhibition of HIV-1 protease & reverse transcriptase activity. The purpose of this study was to appraise the anti-HIV characteristics of the extracts from the leaves of banaba, and further purification and characterization of the active components. The active elements for anti-HIV activity were gallic acid and ellagic acid, through inhibition of reverse transcriptase and HIV protease, respectively and so could be regarded as favorable candidates for the improvement of anti-HIV-1 materials.

**Metabolic syndrome**

Metabolic syndrome means a condition in which several risk factors for cardiovascular disease and type II diabetes, abdominal obesity, hypertension, bad lipid metabolism and insulin resistance are occurred together. In an animal study for metabolic syndrome, corosolic acid had antihypertensive, lipid-lowering, antioxidative, and anti-inflammatory effects on rats. In a similar animal study, corosolic acid also reduced blood pressure and serum-free fatty acid levels.

**Cholesterol**

In patients with type II diabetes mellitus intestinal cholesterol synthesis and cholesterol esterification is increased. This is very important stuff because diabetes coupled with high blood cholesterol increases the risk of cardiovascular disease (CVD). Corosolic acid has been show to reduce cholesterol absorption process in the small intestine via inhibition of activity of cholesterol acyltransferase.

**Side effects of corosolic acid**

Some side effects of corosolic acid include skin rashes, headaches and fatigue. According to research, these side effects will most likely be experienced by individuals who exceed the optimal dosage. It is not recommended for consumption by children or during pregnancy.

No adverse effects about corosolic acid or banaba did not reported in clinical trials. Contrary to the logical expectation that the blood sugar-lowering capacity of banaba would cause low blood sugar (hypoglycemia), 6 clinical human trials did not lead to any such effect.

Another human study showed that Glucosol (soft capsule form of brand name containing 15% corosolic acid from banaba leaves, *Lagerstroemia speciosa*) had been applied and checked the blood sugar levels and side effects of 56 subjects. This group concluded that corosolic acid had a lowering blood sugar levels but no adverse effects such as rash, nausea and others.

**CONCLUSION**

Corosolic acid (CRA), one of components of banaba leaves, has been reported to have anti-inflammatory and...
Corosolic acid has antidiabetic effects (especially type 2 diabetes) which can improve glucose metabolism by decreasing insulin resistance; it prevents the enzymatic activities of several diabetes-related non-receptor protein tyrosine phosphatases (PTPs) in vitro\(^9\), \(^30\).

Corosolic acid has antitumor effects in sarcoma rat model through importantly impairing subcutaneous tumor development and lung metastasis and targeting the immunosuppressive activity of myeloid-derived suppressor cells (MDSC), and can aggrandize the antitumor effects of adriamycin and cisplatin in vitro\(^11\). Corosolic acid reduces 5-Fluorouracil (5-FU) chemo resistance, which is one of the most commonly used chemo therapeutic agents by activating AMPK from human gastric cancer cells\(^32\).

Corosolic acid which is isolated from *Eriobotrya japonica* (loquat) reveals anti-melanogenesis, anti-acne, anti-allergy and anti-aging activities\(^33\).

Corosolic acid as a pentacyclic triterpenes significantly inhibited osteosarcoma of MG-63 cells in a dose-and time-dependent manner and this provides that corosolic acid may be useful chemotherapeutic material for osteosarcoma\(^34\).

Corosolic acid exerts anti-inflammatory effects by regulating phosphorylation of interleukin receptor-associated kinase (IRAK-2) via the NF-kB cascade in mouse BMDMs and may be useful as a pharmacological agent to prevent acute inflammation\(^35\).

Besides these various effects, there are lots of studies about valuable effects on different human disease but it still has limitation to develop the powerful and effective pharmacological effects. Consequently, corosolic acid isolated from banana leaves and other herbs have future possible applications on clinical treatment as ingredients of drugs, functional foods for health benefits.


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