

A Comprehensive Review on Nutraceutical Properties of *Euryale ferox* Salisb

Review Article

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Abstract

The present review aims to highlight the nutraceutical property of *Euryale ferox* Salisb. This plant is also commonly known as prickly waterlily or Gorgon plant or Foxnut. It is an aquatic macrophytic plant that belongs to the Nymphaeaceae family. Nutraceuticals can be defined as substances that are food or part of a food that provides health benefits and are used for the mitigation or treatment of a disease. *Euryale ferox* Salisb seed contains a wide range of nutrients including carbohydrates, protein, minerals, and fats. The protein present in seeds of *Euryale* contains a unique composition of amino acids and also has a high Essential Amino Acid Index (EAAI). Besides the nutritional superior quality, the *Euryale ferox* Salisb whole plant parts have reported for many ethnomedicinal properties. They are being used in the treatment of diseases including chronic diarrhea, kidney problems, excessive leucorrhea, and hypofunction of the spleen in traditional medicine. The pharmaceutical properties of *Euryale ferox* Salisb have been scientifically validated by many researchers. The plants have been reported to have antioxidant, antidiabetic, antidepressant, anticancer, cardioprotective, hepatoprotective, etc. Therefore, *Euryale ferox* Salisb seed will be a potential candidate/ingredient for the formulation of nutraceutical/functional foods. And this present review will be helpful in understanding the economic importance *Euryale ferox* Salisb in the food industry.

Keywords: *Euryale ferox* Salisb; Foxnut; Functional food Nutraceutical; Pharmaceutical

Abbreviations

ABTS- (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); AMPK- adenosine monophosphate-activated protein kinase; BHT- beta-hydroxyl toluene; BUN- blood urea nitrogen; CAGR- Compound Annual Growth Rate; CAT- Catalase; DPPH-2,2-diphenylpicrylhydrazyl; DSHEA- Dietary Supplement Health and Education Act; EAAI- Essential Amino Acid Index; EFx- *E. ferox* Salisb ethanolic extract; FOSHU- Food for Specified Health Uses; GAE- Gallic Acid Equivalent; GSH-Px -Glutathione peroxidase; HP -hepatic glycogen; LDH- lactate dehydrogenase; MDA- Malondialdehyde; NAFLD- non-alcoholic fatty liver disease; ROS- reactive oxygen species; RS- Resistant starch; SOD- Superoxide dismutase.

Introduction

Euryale ferox Salisb also commonly known as prickly waterlily

or Gorgon plant or Foxnut is an aquatic plant that belongs to the Nymphaeaceae family (Figure 1). It is a monotypic species of the genus *Euryale* and native to eastern Asia and distributed in India, Bangladesh, China, Korea, and Japan [1]. Its distribution is also reported in some parts of Holland and Russia. Locally, it is known as Makhana in Hindi, Qianshi in Chinese, and Onibasu in Japanese. The edible part of this plant is the starchy seed kernel. The dried seed is popped like popcorn (known as makhana) and is available commercially worldwide makhana seeds are also known as black diamond's Bihar, a state of India [2], alone contributed 90% of the World's foxnut nut production [3]. Foxnut seed contains a wide range of nutrients including carbohydrates, protein, minerals, and fats. The protein present in seeds of *Euryale* contains a unique composition of amino acids which is rich in arginine, cysteine, glutamine, isoleucine, leucine, and methionine. Among these amino acids, isoleucine, leucine, and methionine are essential amino acids [4]. Recently, some researchers have reported that the starch present in the foxnut kernel

is type 3 resistant starches (RS3). Resistant starches are degraded very slowly by the digestive enzyme and they are more like dietary fibers. It helps to regulate glucose released after a meal, thereby reducing the insulin level in the body which in turn stimulates the body to metabolize the energy stored in fat [5].

Moreover, the *Euryale ferox* Salisb whole plant parts i.e. leaves, rhizome, fruit, and seeds are reported for many ethnomedicinal properties. They are being used in Ayurvedic, traditional Chinese medicines, and other traditional knowledge-based therapy to combat many diseases including chronic diarrhea, kidney problems, excessive leucorrhea, and hypofunction of the spleen [6-8]. From the scientific studies conducted by many researchers, it is established that foxnuts are not only superior in nutrient content but also have diverse pharmaceutical properties such as antidiabetic, antioxidant, anticancer, antimicrobial, antiaging, antidepressant, cardioprotective, hepatoprotective, etc. [6-11].

For the past few decades, human beings are facing many lifestyle-related health problems, especially non-communicable diseases (NCD). Among these, the most prevalent NCDs include cardiovascular, cancers, chronic obstructive pulmonary disease, asthma, and diabetes. Malnutrition and an unhealthy diet are the main cause of NCD [12]. Functional foods and nutraceuticals play a very important role in reducing the risk of noncommunicable diseases. Nutraceuticals can be defined as substances that are food or part of a food that provides health benefits and are used for the mitigation or treatment of a disease [13]. A range of products in the form of dietary supplements, functional food isolated nutrients, processed and fortified products such as cereals/soups, and genetically engineered designer foods are available under the umbrella of nutraceuticals. The global demand for nutraceuticals is increasing and its market size was approximately 454.55 billion USD in 2021 and expected to grow at a compound annual growth rate (CAGR) of 9.0% by 2030 [14]. In this context, foxnut is considered a super food or functional food because of their diverse health-beneficial properties. The aim of this review is to highlight the nutraceutical properties of foxnuts.

Culinary of *Euryale ferox* Salisb

The major edible part of *Euryale ferox* Salisb is its seed kernel. However, other plant parts such as young leaves and stems can also be consumed as vegetables. In the North-Eastern part of India, it is considered more of a vegetable and consumed either raw or cooked. In Manipur, people use tender leaves, seed aril, and fruit skin in the preparation of chutney locally called “eromba” [15]. In the northern and western parts of the country, the popped seed is most common and eaten as a snack. It is also used in making porridge or pudding called *kheer*. In India *Euryale ferox* Salisb seed not only hold significant importance in Indian recipe but is also considered a sacred food and involved in many religious practices. The flour obtained from dry seed has been used in preparing bread and on special religious occasions and the bread prepared with *Euryale ferox* seed is consumed for breaking fasting by some Hindu communities [16]. The flour is used in making delicious dishes such as sweetmeat, vegetable salad, and fried rice. The popped foxnut seed commonly known as makhana is also used as dry fruit and is an important ingredient of the five auspicious dry fruit offered to the deities for religious purposes.

In China, it is popular as a cooling tonic food. In southern China, the seeds are added to soup or porridge.

Nutritional components of *Euryale ferox* Salisb

The major components present in Fox nut are carbohydrates, protein, and fat. The composition of these macromolecules is varied with carbohydrates in the range of 55-80 %, protein, 10-15 %, and fat, 0.2-0.7% (Table 1). It has a high content of phosphorus, potassium, magnesium, calcium, and sodium (Table 2). The protein of foxnut seed has a unique composition of amino acids which is rich in essential amino acids (leucine, isoleucine, methionine, and lysine). Jha et al., revealed that the essential amino acid index (EAAI) and chemical score (CS) of makhana are close to that of fish. The nutritional value of foxnut seed is enhanced when it is roasted. Zhang et al. (2019) have elucidated the structure of polysaccharides extracted from *E. ferox* Salisb seeds.

Pharmaceutical properties of *E. ferox* Salisb

E. ferox Salisb is not only superior in nutritional content but also exerted many medicinal and health beneficial properties. The pharmaceutical properties of *E. ferox* Salisb are presented in Figure 1. And some of the major pharmaceutical properties are discussed below.

Antioxidant activity

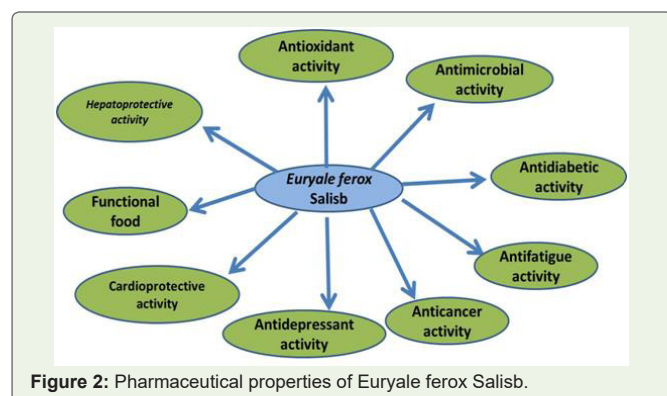
Oxidative stress is the major risk factor for many diseases and is often associated with many lifestyle-oriented pathological conditions like cancer, diabetes cardiovascular diseases. The endogenous and exogenous antioxidants play a vital role in scavenging the reactive oxygen species (ROS). Hence regular consumption of antioxidants as a part of dietary supplements at an appropriate dose helped to encounter and prevent the body from oxidative stress-related diseases. Foods, rich in antioxidant compounds become an indispensable ingredient in modern-day diet. The antioxidant properties of *Euryale ferox* Salisb have been reported by many researchers. Antioxidant activity is displayed by a wide range of compounds so antioxidant activity cannot be determined by a single assay method. There are more than 20 different methods for the determination of antioxidant activities. In a study conducted by Lee et al. [19], *Euryale ferox* Salisb was extracted using two different organic solvents (ethyl acetate and butanol) and fractions were evaluated for antioxidant activities. The fractions enhanced the activities of some antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase) in a dose-dependent manner. The essential oil extracted from *E. ferox* seed showed antioxidant activity in DPPH and ABTS assay [20]. These two assay methods are one of the widely used in-vitro antioxidant assays. Parry, et al. [21] studied the antioxidant activity of leaf and seed extracts of *E. ferox* using three different assay methods viz. DPPH, Deoxyribose assay, and superoxide radical scavenging method. Where they observed that the percentage of inhibition was similar for both seed and leaf extract exhibiting 89.50% and 83.06% respectively and the value was comparable with standard synthetic antioxidant beta-hydroxyl toluene (BHT, 97.0%) at a concentration of 500 µg/ml. Wu et al. [22] conducted *in vitro* and *in vivo* antioxidant assays to examine the antioxidant activity and anti-fatigue effect of phenolic extract of *E. ferox* seed coat. According to the in vitro antioxidant

Table 1: Nutritional composition of *Euryale ferox* Salisb seed.

| Parameters (% by wt.) | Raw Seeds [2] | Raw seeds [9] | Raw seeds Alfasane et al. [23] | Raw seeds [9] | Raw seeds [21] | Popped seeds [2] | Roasted seeds [24] |
|-----------------------|---------------|---------------|--------------------------------|---------------|----------------|------------------|--------------------|
| Moisture | 34.7 | 11.82 | 12.5 | 10.0 | 12.07 | 10.4 | 4.17 |
| Total ash | 0.3 | 0.62 | 1.8 | | 0.58 | 0.4 | 0.66 |
| Fat | 0.3 | 0.51 | 1.3 | 0.5 | 0.63 | 0.5 | 0.68 |
| Protein | 7.2 | 11.16 | 15.6 | 11.2 | 11.4 | 8.7 | 14.57 |
| Crude fiber | 0.5 | - | 7.6 | 0.5 | 0.41 | 0.2 | 0.51 |
| Carbohydrate | 57.0 | 75.04 | 61.2 | 74.9 | 74.9 | 79.8 | 79.4 |

Table 2: Mineral content in *Euryale ferox* Salisb seed.

| Parameters (mg/100g) | Raw Seeds [2] | Raw seeds [9] | Raw seeds [9] | Raw seeds [24] | Popped seeds [2] | Roasted Seeds [24] |
|----------------------|---------------|---------------|---------------|----------------|------------------|--------------------|
| Phosphorus | 66.1 | 28.0 | - | 53.0 | 53.2 | 56.4 |
| Potassium | 35.6 | 37.0 | 260.0 | 45.0 | 42.0 | 47.2 |
| Iron | 0.8 | 6.0 | - | 10.9 | 1.4 | 12.7 |
| Calcium | 9.5 | 27.0 | 50 | 17.9 | 18.5 | 19.2 |
| Magnesium | 11.3 | 6.0 | 60 | 24.4 | 13.9 | 26.3 |
| Sodium | 48.2 | - | 15 | 22.0 | 71.0 | 23.8 |
| Copper | 0.3 | - | - | - | 0.5 | - |
| Manganese | 0.9 | - | - | - | 1.3 | - |
| Zinc | 0.9 | - | - | 1.5 | 1.1 | 1.8 |

**Figure 1:** (a) *Euryale ferox* salisb plant (b) Flower (c) Fruit (d) and seed.**Figure 2:** Pharmaceutical properties of *Euryale ferox* Salisb.

assays, the phenolic extract exhibited scavenging effects on DPPH and hydroxyl radicals and had notable reducing power. The antioxidant activities of the extract were further confirmed by carrying out in vivo assays in mice. The reduction of SOD, CAT, GSH-Px activities and high level of MDA in the liver and kidney of aging mice were observed compared with normal mice. Oral administration of the phenolic extract of *E. ferox* seed coat increased the activities of SOD, CAT, GSH-Px, and decreased the level of MDA in liver and kidney in aging mice compared with the model control group. The antioxidant compounds were extracted and identified from *E. ferox*. The compounds exhibited strong effects against the DPPH assay with SC50 values of 6.8, 10.4, 10.2, and 12.9 μ M, respectively, comparable to that of the positive control gallic acid or ascorbic acid [25].

Antimicrobial activity

The emergence of multidrug-resistant bacteria has been a major challenge in the health sector worldwide. Hence, it dictates the search for novel antimicrobial compounds from plants, animals, and microbial sources. Exploration of antimicrobial activity of *Euryale ferox* has been attempted by some researchers. For instance, Kadu et al. (2020) have reported the antibacterial activity of *E. ferox* seed coat extracted in three different solvents against *Staphylococcus aureus* and *Escherichia coli*. Besides antibacterial activity, *E. ferox* leaf and seed extract exhibited antifungal activity against *Candida albicans* and *Penicillium notatum* [21].

Antidiabetic activity

Diabetic has become one of the most prevalent non-infectious diseases around the globe. The antidiabetic potential of foxnuts is also mentioned in many traditional and ethnomedicinal practices. Recently the antidiabetic property of *E. ferox* Salisb has been proven

scientifically. For example, Song et al. [25] demonstrated that the compounds isolated from *E. ferox* Salisb seeds could inhibit the reactive oxygen species production that is stimulated by high glucose levels. Their study revealed that the diverse compounds present *E. ferox* Salisb seeds have high antioxidant activity and their synergistic effect is responsible for the prevention of in proteinuria, an indicator of diabetic nephropathy. Hence their study suggests that *E. ferox* Salisb seeds will be a potential source of natural antioxidants useful for the treatment of diabetic nephropathy. Similarly, Ahmed et al. [7] have studied the *in vivo* antidiabetic and antihyperlipidemic effect of *E. ferox* Salisb ethanolic extract (EFx) in streptozotocin-induced diabetic rats. They observed that treatment of diabetic rats with EFx resulted in reduced blood glucose level, increased plasma insulin, and stimulation of antioxidant enzyme activity such as superoxide dismutase, catalase, and glutathione peroxidase. It also increases reduced glutathione level significantly and restored the hepatic gluconeogenic enzyme activity to normal. In addition, the microscopic architecture of pancreatic, hepatic, and renal cells was improvised in EFx-treated diabetic rats. Zhang et al. [18] have reported the antidiabetic property of polysaccharides extracted from *E. ferox* Salisb seeds. The study was carried out in insulin resistance HepG2 and 3T3-L1 cell lines. The mechanism of antidiabetic property of polysaccharide fraction of *E. ferox* Salisb underlies the up-regulation of GLUT-4 glucose transporter by activating PI3K/Akt signal pathway, which in turn increases the glucose consumption by insulin-resistant cells.

Antifatigue activity

Wu et al. [22] demonstrated the anti-fatigue property of polyphenols extracted from *E. ferox* Salisb seed coat [29]. Polyphenols are well known for their anti-fatigue activity. The phenolic extract of *E. ferox* Salisb seed coat *E. ferox* Salisb seed coat was recorded as 379.53 mg GAE/g of dry weight which is higher than the green and black teas. The antioxidant activity of polyphenols is closely related to their anti-fatigue property. In physical or emotional fatigue, the reactive oxygen species (ROS) concentration is elevated and causes oxidative damage to the cells. Other important biochemical indicators for fatigue are lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and hepatic glycogen (HG). The level of LDH and BUN are increased while HG level is decreased in fatigue conditions. Treatment of fatigue rats with the *E. ferox* Salisb phenolic extract improved swimming time to exhaustion decreased BUN level and increased HG level. These results suggested that phenolic extract of *E. ferox* Salisb has anti-fatigue properties.

Anticancer activity

The anticancer properties of *E. ferox* Salisb have been reported by some researchers. For instance, Baek et al. [8] studied the antimelanogenesis activity of foxnut seed *in vitro* using melanocyte cells. The ethyl acetate fraction of *E. ferox* Salisb seed inhibited cellular tyrosinase and melanin synthesis in melanocyte cells with an IC_{50} of 25.2 μ g/mL. The extract significantly reduced the levels of melanogenesis-related proteins, such as tyrosinase, tyrosinase-related proteins, and microphthalmia-associated transcription factor. Further, they have investigated the pathway of degradation of these melanogenesis-related proteins and observed that the proteins were

degraded by the lysosomal pathway. Nam et al. [27] investigated both *in vitro* and *in vivo* apoptotic effects of *E. ferox* Salisb extract in A549 lung cancer cells. *In vitro* study results revealed that the apoptotic activity of *E. ferox* Salisb extract was via the inhibition of Akt (protein kinase B) signalling pathway and activation of the p53 protein. Akt protein is a protein kinase involved in many cellular processes. In cancer cells, the level of Akt is increased as compared to normal cells and it inhibits apoptosis. Treatment of lung cancer cell lines with *E. ferox* Salisb extract resulted in Akt signalling pathway suppression and induces apoptosis by p53-dependent manner. Further, they have validated the anticancer property of *E. ferox* Salisb extract *in vivo* using Balb/c *nu/nu* mice transplanted with A549 Human Caucasian lung carcinoma cancer cells. And they observed that the *E. ferox* Salisb extract-treated mice have an increased level of p53 as compared to the control group.

Antidepressant activity

The antidepressant property of *E. ferox* Salisb seed extract has been reported by Huang and his co-workers [10]. During their investigation, it was found that the petroleum ether fraction of *E. ferox* Salisb seed enhanced the autophagy by upregulating the adenosine monophosphate-activated protein kinase (AMPK) and mammalian autophagy-initiating kinase (ULK1) expression in the chronically unpredictable mild stress mouse model. These two kinases are involved in the activation of autophagy in response to starvation stress and maintain cellular energy homeostasis. Autophagy plays a crucial role in maintaining healthy cells by removing damaged cells, proteins, or organelles. Depression is associated with a decline in autophagy. Thus, the study revealed that the antidepressant property of *E. ferox* Salisb is associated with the activation of autophagy by regulating the AMPK pathway.

Cardioprotective activity

From the time immemorial *Euryale ferox* Salisb has been used for the treatment of hypertension and cardiovascular-related diseases. For example, the hot infusion of *Euryale ferox* Salisb flowers and other parts of plants has been used for controlling palpitation, regulating and normalizing heartbeat, and relieving restlessness. All these symptoms are directly or indirectly related to cardiovascular diseases. The cardioprotective property of *Euryale ferox* Salisb has been scientifically confirmed by Das and his co-worker in the year 2006 using two different heart injury rat models viz. acute and chronic heart injury. In the acute model, the isolated heart was preperfused for 15 min with different doses of foxnut prepared in Krebs Henseleit bicarbonate buffer [11]. Then the heart was subjected to global ischemia for 30 min and then 2 h of reperfusion. In the chronic model, the rats were fed with two different doses (250 and 500 mg/kg/day) of foxnut for 21 days. Then the heart was isolated and subjected to 30 min of ischemia followed by 2 h of reperfusion. In both the experimental groups the foxnut-treated hearts were found to show improved post-ischemic ventricular function and reduced myocardial infarct size indicating the resistance of these hearts against ischemic-reperfusion injury. Further, the proteins involved in cardio protection were identified as thioredoxin-1 (Trx-1) and thioredoxin-related protein-32 (TRP32). The hearts treated with *Euryale ferox* Salisb seed were found increased levels of this cardio protective protein than the untreated control

group. Hence the mechanism of cardio protective activity *Euryale ferox* Salisb lies in their ability to induce the expression of cardio protective proteins and in their reactive oxygen scavenging property as evidenced by high antioxidant activity in *in vitro* assays.

Hepatoprotective activity

Jian his colleague [28] demonstrated that ethanolic extract of *Euryale ferox* Salisb seed has hepatoprotective activity against non-alcoholic fatty liver disease (NAFLD) induced by a high-fat diet. Where they observed that the major constituent of the extract were the polyphenols. Treatments of NAFLD mouse model with *Euryale ferox* Salisb seed extract (15 and 30 mg/kg/day) for 4 weeks significantly reduced body weight, and lipid deposition in the liver and blood. The possible mechanism of hepatoprotective activity of the extract is through the inhibition of Cytochrome P450 2E1 (CYP2E1) expression and increased the expression of insulin receptor substrate-1 (IRS-1). CYP2E1 is a member of the oxido reductase cytochrome family which involves the oxidation of fatty acids and the generation of oxidative stress in NAFLD. On the other hand, IRS-1 is involved in the transduction of insulin signalling. It is well established that the insulin signalling pathway is linked with lipid metabolism and insulin resistance is strongly associated with lipid accumulation in the liver.

Euryale ferox Salisbseed as a functional food

The starchy portion of *Euryale ferox* Salisb seed has the potential to formulate as a functional food. Functional foods are simply defined as processed food products that have not only the nutritive value but also have the promoting property. Functional foods can also be considered a healthy diet that has a particular health benefit. Japan is the first country that established the regulatory system for functional foods named "Food for Specified Health Uses" (FOSHU) in the year 1991. Later on, Dietary Supplement Health and Education Act (DSHEA) were established in the USA in the year 1994 [29]. Recently, in 2015 new regulatory system for functional foods was implemented based on DSHEA in the USA. Similarly, India Government passed Food Safety and Standard Act in 2006 to integrate and restructure the many regulations covering nutraceuticals and functional foods [18]. The roasted foxnut seed has a low glycemic index in humans because of the presence of resistant starch. The *Euryale ferox* Type 3 resistant starches (RS3) belonged to B + V type crystal and had high thermal stability and a low glycemic index [5]. These findings suggest that foxnut seeds have the potential for formulation as a functional food for patients with metabolic disorders like obesity and diabetes [22]. Sometimes Foxnut seed is also included in the dry fruit category because of its superior nutritious profile and high Essential Amino Acid Index (EAAI). In general, essential amino acids are obtained from the non-vegetarian diet such as fish, meat, and eggs. Because of its high EAAI, foxnut seed can serve as a good protein source for vegetarian diets. Moreover, foxnut seed is high in magnesium and potassium content. Potassium plays a crucial role in maintaining blood pressure [31]. Hence foods containing high potassium such as foxnut will be a good candidate for the formulation of functional foods for patients having hypertension. In addition, it is believed that consumption of foxnut seed in a daily dietary regime increases humoral as well as cell-mediated immunity to some extent. Vikram

and Mishra [32] have reported the potential of *Euryale ferox* Salisb seed as a functional food for COVID- 19 patients.

Conclusion

In this modern-day society, there is a rapid increase in people's awareness of the importance of diet/food in maintaining a healthy lifestyle. Today food is not only considered a source of nutrition but also a medicine. And this warrants the increased demand for healthy foods such as nutraceutical and functional foods in the global market. In order to meet the demand-supply equilibrium of nutraceutical/functional foods, many countries have established or modified existing laws and standard regulatory systems governing the production and marketing of nutraceutical/functional foods [31,32]. Hence searching for new foods having both superior nutritional quality and health-beneficial activity is the need of the hour. In this context, *Euryale ferox* Salisb seed will be a potential candidate for the formulation and marketing of nutraceutical/functional foods. Although *Euryale ferox* Salisb is distributed in many parts of the world their commercial cultivation is confined to some geographical regions such as China, India, and some other parts of South East Asia. Even in India, the majority of *Euryale ferox* Salisb cultivation is found in Bihar and North-Eastern India. Hence proper awareness and documentation of scientific evidence of the health-promoting effect of this plant are highly essential. Thus, this present review will be helpful in promoting the nutritional and health-beneficial properties of *Euryale ferox* Salisb plan.

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