

# Eryngium Extracts, Perspective Therapy for Diabetes Mellitus

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## ABSTRACT

Diabetes Mellitus is a group of widespread chronic diseases characterized by sustained high blood sugar known to mankind since ancient times. There were 537 million adults with diabetes in 2021 and projected to rise to 643 million by 2030. Diabetes caused 6.7 million deaths with a health expenditure of USD 966 billion in 2021 globally (IFD report 2022). About 90% of diabetic patients are diabetes type 2 and less than 5% of them are of diabetes type 1. Diabetic complications are considered as strong risk factor for COVID-19 severe illness. As yet there is no definitive or widely accepted cure for diabetes. *Eryngium billardieri* and *E. campestre*, mostly in form of distillates, activate pancreatic cells and stimulate insulin secretion from these cells reducing blood sugar. This presentation is aimed to discuss the perspective on the utilization of *Eryngium* for the treatment of diabetes, particularly for diabetes type 2 and prediabetes.

**Keywords:** *Eryngium*, Diabetes, Insulin, Pancreas, Herbal, Hydrosol, Therapy

## Introduction

The history of diabetes dates back to ancient civilizations, with the first recorded mentions of the disease in Egyptian manuscripts from around 1500 BCE. These texts describe a condition characterized by excessive urination; a symptom of the high blood sugar levels associated with diabetes. Diabetes is a chronic health condition that affects how the body processes glucose (sugar) in the blood. It is an important health concern because it can have serious consequences if not managed properly. There were 537 million adults with diabetes in 2021 and projected to rise to 643 million by 2030. Diabetes caused 6.7 million deaths with a health expenditure of USD 966 billion in 2021 globally [1]. Diabetes Mellitus Type 2 (DMT2) accounts for more than 90% of diabetics worldwide and about 5% are Diabetes Mellitus Type 1 (DMT1). Diabetic complications are considered a strong risk factor for COVID-19 severe illness. As yet there is no definitive or widely accepted cure for diabetes. One of the main risks of diabetes is damage to blood vessels and nerves, which can lead to a range of health complications such as heart disease, stroke, kidney disease, blindness, and nerve damage. Diabetes can also increase

the risk of infections and slow down the healing process of wounds, leading to a higher risk of amputations [2].

Sugar, or glucose, serves as a primary source of energy for the body's cells. In order for the cells to utilize glucose for energy, several steps are involved:

- **Digestion:** When we eat carbohydrates, such as bread, pasta, fruits, and vegetables, our digestive system breaks them down into glucose.
- **Absorption:** The glucose is absorbed into the bloodstream and transported to cells throughout the body.
- **Uptake:** Glucose enters the cells with the help of insulin, a hormone produced in the pancreas. Insulin binds to receptors on the cell surface and triggers a series of chemical reactions that allow glucose to enter the cell.
- **Glycolysis:** Once inside the cell, glucose is broken down into two molecules of pyruvate via a process called glycolysis. This process releases small amounts of energy in the form of Adenosine Triphosphate (ATP) and Nicotinamide Adenine Dinucleotide (NADH).

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- Cellular respiration: Pyruvate is further metabolized inside the cell via cellular respiration. This process produces a large amount of ATP and CO<sub>2</sub> by oxidizing NADH in a series of reactions that occur within the mitochondria. Overall, the energy from the breakdown of glucose is used to power various cellular processes, including muscle contraction, protein synthesis, and nerve transmission. Any excess glucose that is not used right away is stored in the liver and muscles as glycogen, which can be broken down and used for energy during times of fasting or exercise.

Insulin was discovered by F. Banting and C. Best in 1921 a significant breakthrough. Insulin is a hormone produced by the pancreas  $\beta$  cells that helps regulate the amount of glucose (sugar) in the blood. It does this by facilitating the uptake of glucose from the bloodstream into the body's cells, where it can be burned for energy or stored for future use [3]. When blood sugar levels rise after a meal, the pancreas releases insulin into the bloodstream. Insulin works in several ways to reduce blood sugar levels. First, it stimulates the liver and muscles to take up glucose from the blood and store it as glycogen, lowering blood sugar levels. Second, insulin increases the transport of glucose across cell membranes, allowing it to enter cells and be used for energy or storage. Third, insulin inhibits the conversion of stored glycogen back to glucose, which helps prevent excessive release of glucose into the bloodstream. Overall, insulin plays a crucial role in regulating blood sugar levels and preventing high blood sugar (hyperglycemia). In people with type 1 diabetes, the pancreas produces little or no insulin, so they require regular insulin injections to help regulate their blood sugar levels. In people with type 2 diabetes, the body becomes resistant to the effects of insulin, so they may require medication to help improve insulin sensitivity or insulin production.

*Eryngium* is a genus of flowering plants in the family *Apiaceae*. There are about 250 species including 80 poisonous species. The genus has a cosmopolitan distribution, with the center of diversity in South America. Common names include sea holly and eryngo. These are annual and perennial herbs with hairless and usually spiny leaves. This article is about, *Eryngium billardiere* and *Eryngium compestre* along with their medicinal values only. However, *Eryngium compestre*, although some believe that is more

even effective but is not as widely available as *Eryngium billardiere*. Therefore, this article is concentrated on *Eryngium billardiere* F. Delaroche. An herbaceous and stable plant with a height of between 50 cm and 200 cm with an average of one meter, its stem is triangular and covered with bright white and blue cotton webs and has wing-like and prickly sides throughout the length of the main stem and its branches. The leaves of this plant are large, oval and long with edged sides and dents leading to a strong and sharp thorn, at the end of the stem, flowering and its flowers are purple, leading to thorns and in the form of a thick lead. It is extensively used in Persian traditional medicine. The medicinal properties of *Eryngium* is mainly present in the root and fruit of this plant. There is some inulin in the roots and fruits of this plant, which is also called wild artichoke because of its similarity to artichokes. In Iran it grows in Azerbaijan, Hamedan, Isfahan, Kurdistan, Alborz and Zagros slopes at an altitude of 2,600 meters above sea level. Its antidiabetic effect has been found mainly in roots and leaves. Particular process must be applied to obtain *Eryngium distillate* with minimum complications for the patients.

Its chemical composition has not been extensively studied, but some of the compounds identified in its essential oil and extracts include  $\alpha$ -pinene, limonene, sabinene,  $\beta$ -phellandrene, myrcene,  $\alpha$ -terpinolene, caryophyllene, and  $\alpha$ -humulene. There is no comprehensive information available on the chemical composition of *Eryngium billardiere distillate*. The distillate is a product of steam distillation of the plant. The composition of the distillate may vary depending on the distillation process, the part of the plant used, and the geographical location where the plant is cultivated. Generally, *Eryngium billardiere distillate* may contain some of the same compounds as the plant itself. As mentioned before the chemical composition of extracts may vary based on different factors like growing conditions, plant parts, and extraction methods. However, some studies have reported the presence of several bioactive compounds in *Eryngium billardiere* extracts which include:33.

#### ■ Flavonoids

These are a group of polyphenolic compounds that have antioxidant and anti-inflammatory properties. Some of the flavonoids present in *Eryngium billardiere* include apigenin, rutin, kaempferol, quercetin, luteolin, and their

glycosides [4].

- Alkaloids: *Eryngium billardiere* contains alkaloids such as erysimin and erysimoside, eryngionine, erynginidine, and erynginidine N-oxide which have been shown to have hypotensive and cardiotoxic effects. [5, 6].
- Essential oils: The essential oils extracted from *Eryngium billardiere* contain several compounds such as myrcene, limonene, and 1, 8-cineole,  $\alpha$ -pinene, limonene, sabinene,  $\beta$ -phellandrene, myrcene,  $\alpha$ -terpinolene, caryophyllene, and  $\alpha$ -humulene, spathulenol which have antibacterial, antifungal, and anti-inflammatory properties [7]. Zengin, G and colleagues has investigated the essential oil composition of *Eryngium billardiere* and reported the presence of 26 compounds, including germacrene D, caryophyllene, beta-eudesmol, and spathulenol, as the major components of the oil [8]
- Terpenoids: This plant also contains terpenoids such as beta-sitosterol and stigmasterol, which have been shown to exhibit antitumor and cholesterol-lowering effects [9].
- Tannins: *Eryngium billardiere* also contains tannins, which have antiviral and antibacterial properties. Presence of saponins, coumarone, chlorogenic acid, caffeine acid and  $\beta$ -carotene has also been reported in *Eryngium billardiere* [4].

A hydro-distilled oil from the aerial parts of *Eryngium billardiere* F. Delaroche was analyzed by a combination of GC and GC/MS. Forty-two components were identified representing more than 97.2% of the oil. The main constituents of the oil were  $\alpha$ -muurolene (42.0%),  $\beta$ -gurjunene (17.0%),  $\delta$ -cadinene (6.2%) and valencene (5.7%) [10].

Inulin is a type of complex carbohydrate or polysaccharide that belongs to a class of carbohydrates called fructans is present in *Eryngium billardiere*, particularly in roots and fruit base. Inulin is made up of chains of fructose molecules that are linked together by beta (2-1) glycosidic bonds. Inulin is found in many plant-based foods such as chicory roots, onions, garlic, asparagus, artichokes, bananas, Jerusalem artichokes, etc. Inulin is not easily digested by humans and passes through the digestive tract mostly intact without being absorbed. This makes it a type of prebiotic, as it

serves as a food source for beneficial gut bacteria, thereby promoting gut health. Inulin has several potential health benefits, including improving digestion, reducing constipation, aiding in weight loss, supporting healthy blood sugar and cholesterol levels, and promoting bone health. In food, it is commonly used as a natural sweetener, fat replacer, texture modifier, and dietary fiber supplement. Inulin by strengthening the digestive system and improving movement of the intestine makes it easier to excrete and treat constipation. One study found that *Eryngium billardiere* roots contained up to 40% dry weight of inulin and had the highest concentration of inulin among the three *Eryngium* species studied [11]. This compound strengthens the digestive system, relieves constipation, weight loss, stays heart healthy and increases the absorption of minerals. However, further research needs to be conducted to fully understand the chemical composition of *Eryngium billardiere*.

*Eryngium billardiere* is a plant that has been traditionally used in Persian folk medicine for the treatment of diabetes including diabetes type 1 and other ailments as discussed below. One study published in the Journal of Medicinal Plants Research in 2012 investigated the effects of *Eryngium billardiere* on blood glucose levels in diabetic rats. The results showed that the plant extract significantly lowered the blood glucose levels of the rats after 21 days of treatment [12]. Similar results of antidiabetic effects of *Eryngium billardiere* were confirmed by other researchers as well [13]. As for human beings, a study published in the Journal of Ethnopharmacology in 2015 investigated the effects of *Eryngium billardiere* on blood sugar levels in humans with type 2 diabetes. The study found that a 12-week treatment with the plant extract improved fasting blood sugar levels and glycated hemoglobin (HbA1c) levels in the participants. The study also found that the plant extract improved insulin resistance and beta-cell function in the participants [14]. Other studies also confirmed positive effect of *Eryngium billardiere* in diabetic patients [15-17]. A more recently published article showed that the consumption of 50 ml of *Eryngium. Billardiere* hydrosol as a complementary treatment in diabetic patients reduced HbA1C and cholesterol levels without adverse effects on the liver or kidneys functions [18].

While these studies indicate that *Eryngium billardiere* may have antidiabetic effects in

humans, further research is needed to confirm these findings and to determine the safety and efficacy of this plant for the treatment of diabetes.

### Pharmacological and Therapeutic Studies

The pharmacological effects of this plant, which is concentrated in its extract and distillate, were observed by M. Daryayi in 1996 after a series of research and clinical trials on diabetic patients. During his studies, it was found that unlike modern medicine treatments that rely only on lowering blood sugar levels, *Eryngium billardieri* and *E. campestre* hydrosols have the activation and cleansing of the liver and adrenal organs and stimulate insulin secretion from the pancreas. Subsequently, during 17 years of clinical research and investigations conducted by Dr. M. Daryayi, the definitive effect of this drug on the treatment of diabetes was determined and it was recommended to reputable herbal grocers and colleagues of physicians active in the field of traditional medicine and complementary medicine to use *Eryngium billardieri* hydrosol for diabetic patients.

#### ■ Research Background and Successful Statistics

At first, *Eryngium* hydrosol was taken and randomly tested on patients with several incurable diseases, mainly diabetes who had not concluded from modern medicine and other traditional medicine. In a research project for three years, more than 1000 diabetics from different regions of the country were treated with *Eryngium* hydrosol, which in most cases the results of the treatment were positive and diabetes was controlled in these patients. The four-month treatment period was monitored in terms of disease reversal and possible side effects of the drug, in which no severe side effects were observed.

The physicians who cooperated with Dr. Daryayi in this project are Dr. Azizkhani (Tehran), Dr. Navabzadeh (Birjand), Dr. Ramezani (Hamedan), Dr. Rezaei (Behbahan), Dr. Fallah (Amol), Dr. Asgaranfar (Yazd), Dr. Ghaffari (Karaj), Dr. Ghanbarzadeh (Ardabil) and Dr. Akbari (Tehran). According to the patients' statistics, who used this drug extensively the results were satisfactory with over 60% success rate. Thereafter through television interviews, they stated that diabetes can be treated with *Eryngium* hydrosols (provided that they observe the correct principles of nutrition and lifestyle

changes or healthy life style with proper exercise). Patients who were treated in this treatment plan, observed the correct diet in terms of Persian traditional medicine and controlled the nervous stresses by taking herbal teas. This treatment has resulted much better on children. Statistics and records of treatment and phone number of the patients treated in this research project are available in the office of Healthy Food Monthly.

#### ■ “*Eryngium* hydrosols have also been reported useful for”

Preventing and reducing the incidence of stroke and heart attack. Blood diseases (anemia and platelet deficiencies, such as ITP). Shortness of breath. Respiratory diseases such as asthma. Preventing and reducing the incidence of stroke and cardio-myocardial infarction useful for heart muscle weakness. Activate adrenal glands and regulates adrenaline secretion, relieving stress, nervousness and anxiety. Anti-toxin properties and are very useful for clearing the liver of toxins and opening the liver ducts. This hydrosol is useful for better liver enzyme activity, and treatment of fatty liver. The hydrosol is diuretic and treats swelling and stones of kidney and bladder.

To maintain digestive health, relieve gastric bloating, treat constipation and soften the intestines. For treatment of colitis, bile production and shedding it in the duodenum of intestine and breaking down fats [19].

These views are strongly advocated by many traditional practitioners. However, there has not yet been independent scientific study to support these claims to date. Nevertheless, further research needs to be conducted to fully understand the benefits of *Eryngium billardieri* hydrosol.

#### ■ “Precautions and prohibition of *Eryngium billardieri* hydrosol”

Some people show allergic reaction to *Eryngium hydrosol*. Generally, people with allergic reaction to *Apiaceous* family including celery, fennel, and dill must avoid it.

Responsiveness of people to *Eryngium hydrosol* varies. Some show good response while others may not. It is important to determine the optimum dose for each person and timing. Further details are beyond the scope of this paper. Overdose of this medicinal plant causes hypotension. Do not indulge in drinking this hydrosol because excessive drinking reduces your

blood pressure and creates a feeling of lethargy.

*Eryngium billardiere* hydrosol causes drying of breast milk, so should not be taken during lactation, pregnancy, and menstruation cycle. Consumption of *Eryngium billardiere* hydrosol

must be under supervision of a professional healthcare expert taking in account the patient's general conditions, blood sugar level, medical background, drug interactions, and other complications. Self-medication is not recommended.

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