

**Bioactive Natural Products
in the Icelandic *Angelica archangelica*
and other herbs and vegetables**

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Dr. Sigmundur Gudbjarnason is a professor emeritus of biochemistry and former president of the University of Iceland. He has been interested in the effects of bioactive compounds found in fruit and vegetables for many years. In 1992 Dr. Gudbjarnason started research on Icelandic medicinal herbs which led to the founding of SagaMedica in the year 2000.

He earned his doctorate in Munich, Germany and was a professor of medicine and biochemistry for 10 years at Wayne State University in Detroit, Michigan. He has been active in experimental cardiology, studying cardiac metabolism and the biochemical reasons for heart disease.



Health and herbs

- Angelica archangelica and other herbs and vegetables have important bioactive natural products.
- This is an introduction of how bioactive natural products in *Angelica archangelica* and other vegetables support prevention against:
 - a) Cardiovascular diseases
 - b) Dementia and loss of memory, Alzheimer's disease
 - c) Stomach ailments
 - d) Cold and flu
 - e) Prostate problems
 - f) Cancer

Cardiovascular diseases

- Heart attack or coronary artery occlusion occurs most frequently because of atherosclerosis and narrowing of coronary arteries and/or a blood clot in the coronary vessel. Blood flow to a part of the heart muscle is then severely diminished. The ischemia, or lack of blood transporting oxygen and nutrients, leads to myocardial infarction or necrosis and death of muscle cells in the affected area of the heart.
- Atherosclerosis is a complex process which is associated with high blood cholesterol (LDL) and **chronic inflammation of the blood vessel walls**.
- Natural products in vegetables, fruits and medicinal herbs can have important effects in prevention of atherosclerosis and cardiovascular diseases.

Cardiovascular diseases

Bioactivity in *Angelica archangelica* and the heart:

- Relaxes coronary arteries (action of Ca-antagonists).
- Increases blood flow and reduces blood pressure.
- Reduces adhesion of blood platelets and reduces the risk of blood clotting in coronary arteries (antiplatelet activity).
- Reduces the risk of serious irregularities of heartbeat (antiarrhythmic activity).

Cardiovascular diseases

Bioactive natural products responsible for the observed effects:

- *Angelica archangelica* contains many chemical compounds (furanocoumarins) that inhibit the flow of calcium into smooth muscle cells in coronary arterial walls, reduce contraction and relax the vascular wall (Ca-antagonists). Blood flow increases and blood pressure is reduced.
- These compounds also reduce aggregation of blood platelets and prevent formation of blood clots in the coronary arteries of the heart.
- These furanocoumarins also reduce the risk of fatal arrhythmias (VF).

Inflammation and active compounds in Icelandic *Angelica archangelica* seeds

- Chronic inflammation of coronary arteries contribute to development of atherosclerosis.
- Imperatorin prevents prostaglandin E2 production that causes inflammation.
 - Imperatorin acts by preventing production of two enzymes, cyclooxygenase (COX-2) and prostaglandin synthase. Many anti-inflammatory compounds are in *Angelica* and related vegetables and influence either production of enzymes or activities of enzymes that produce inflammatory compounds.
- This anti-inflammatory activity is important for the **prevention of atherosclerosis** and numerous other conditions.

Vegetables and herbs can prevent cardiovascular diseases

a) Vegetables and herbs that can prevent formation of blood clots (antiplatelet activity):

- Angelica archangelica, parsley, celery, onion, lemon, carrots etc.
 - Compounds: bergapten, imperatorin, osthol, allicin, alliin, rutin etc.

b) Vegetables and herbs that can increase blood flow and reduce blood pressure:

- Angelica archangelica, celery, parsley, carrots.
 - Compounds: Calcium-antagonists such as imperatorin, bergapten, iso-imperatorin, isopimpinellin, oxypeucedanin, phellopterin, caffeic acid.

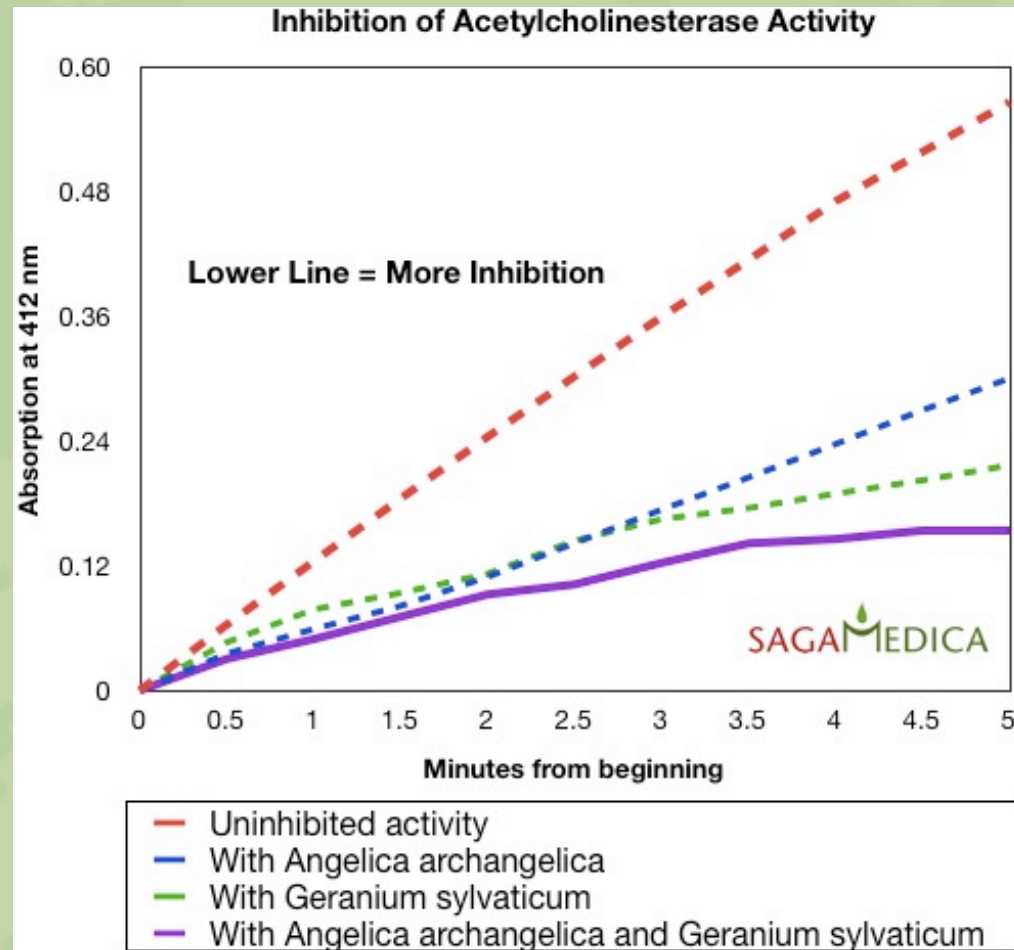
c) Vegetables and herbs that can prevent heartbeat irregularities:

- Angelica archangelica, celery, parsley, salad, white cabbage, spinach, cucumber.
 - Compounds: ferulic acid, magnesium, potassium, furanocoumarins.

Forgetfulness and poor memory Alzheimer's disease

- Various factors cause temporary forgetfulness such as **stress and loss of sleep**.
- **Alzheimer's disease** is the most common cause of dementia in older people. The loss of memory is considered to be the result of shortage of the nerve transmitter acetylcholine. It is possible to increase the level of this transmitter in the brain by inhibiting the activity of the enzyme acetylcholinesterase which splits or breaks down the transmitter substance. Drugs that inhibit the breakdown of the messenger or transmitter acetylcholine delay the development of the disease.
- **Vascular dementia** is due to atherosclerosis in the brain and reduced blood flow to the brain. Transient ischemia and small infarcts in the brain can develop due to occlusion of small blood vessels. These small damaged areas can then accumulate and cause dementia.
- **Side effects of drugs** for various diseases such as high blood pressure, heart disease, sedatives, antibiotics, stomach problems etc. can lead to forgetfulness.

Inhibition of Tinctures on Acetylcholinesterase Activity



Forgetfulness and poor memory Alzheimer's disease

Activity in Angelica :

Angelica archangelica contains several substances that have the same kind of activity as drugs used for Alzheimer's disease. These substances do not cause the side effects observed with the drugs such as nausea, stomach aches, insomnia etc. The same phytochemicals in *Angelica archangelica* can also increase blood flow in the brain.

What are these substances and how do they work?

Many natural products such as imperatorin, isoimperatorin, oxypeucedanin, xanthoxin and isopimpinellin in seeds and limonen in essential oils inhibit the activity of the enzyme acetylcholinesterase. These substances thereby increase the level of acetylcholine in the brain and improve the memory.

These furanocoumarins also serve as Calcium antagonists, reduce Calcium flux in blood vessel walls, relax smooth muscle cells in blood vessels and increase blood flow.

Stomach ailments

- **Activity in herbs** (*Angelica archangelica*, *Cetraria islandica* and Yarrow):
 - Prevent proliferation of *Helicobacter pylori* that cause gastritis and gastric ulcers. Reduce stomach aches and stimulate healing of stomach ulcers.
- **How do the phytochemicals work?**
 - 1. Phytochemicals in *Cetraria islandica* prevent proliferation of the bacteria *Helicobacter pylori* and reduce stomach aches and heal stomach ulcers.
 - 2. Phytochemicals in Yarrow can also prevent proliferation of *Helicobacter pylori* and prevent gastritis and gastric ulcers.
 - 3. Phytochemicals in *Angelica archangelica* inhibit the activity of the enzyme acetylcholinesterase and can thereby reduce stomach aches and dyspepsia.

Antiviral Properties

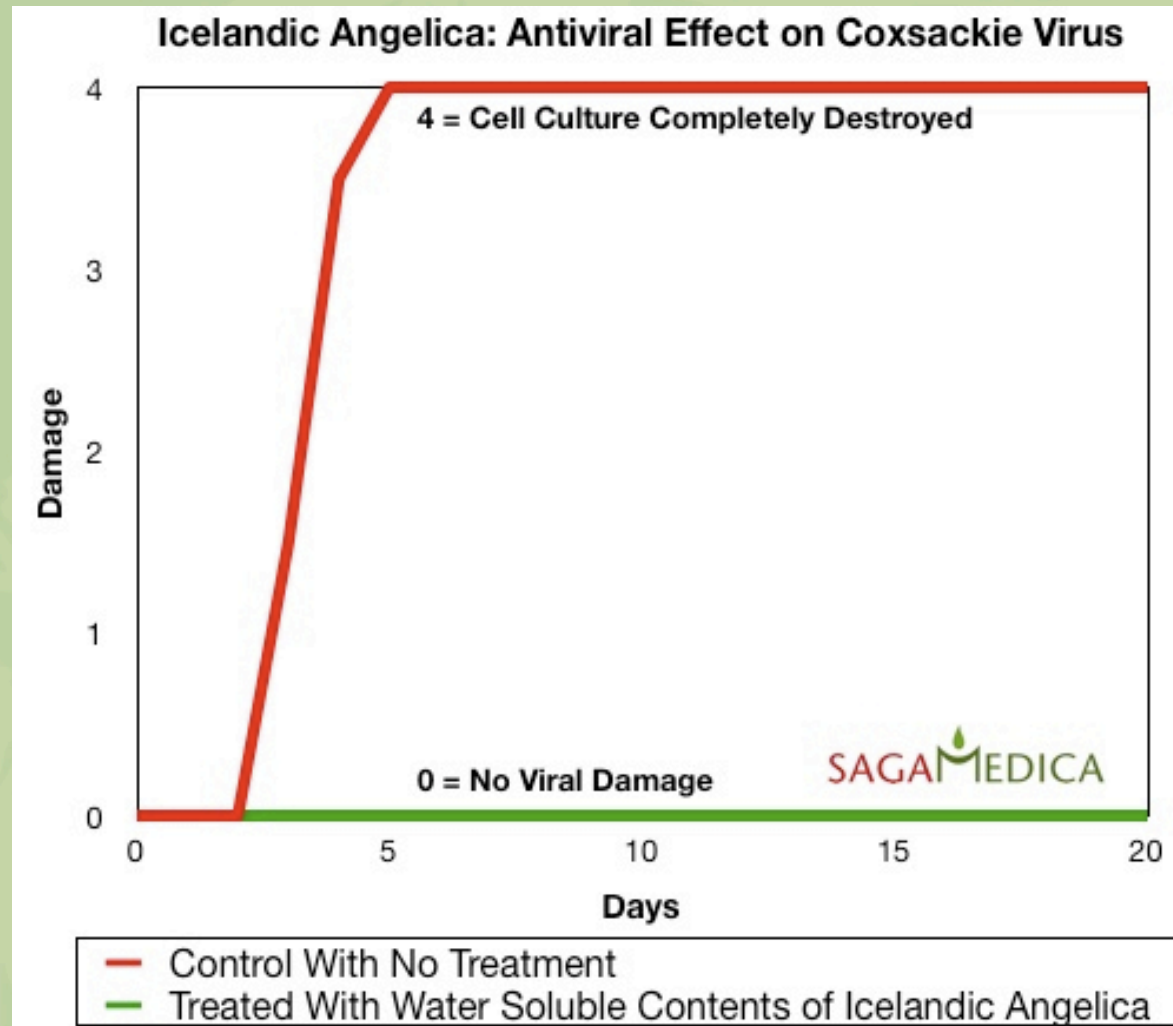
Activity in *Angelica archangelica* (leaves and seeds):

- Prevent proliferation of viruses that cause cold and flu.

Phytochemicals at work:

- Flavonoids in *Angelica* leaves (isoquercitrin, rutin, diosmin and caffeic acid, ferulic acid and chlorogenic acid) prevent proliferation of various viruses i.e. viruses causing cold and flu.
- Furanocoumarins:
 - Imperatorin prevents proliferation of the HIV virus that causes AIDS.
 - Prangenin prevents proliferation of the RS virus that affects small children.

Influence of *Angelica archangelica* Extract on Viral Damage to Cells



Nocturia

Frequent urination at night

Activity in *Angelica archangelica* leaves:

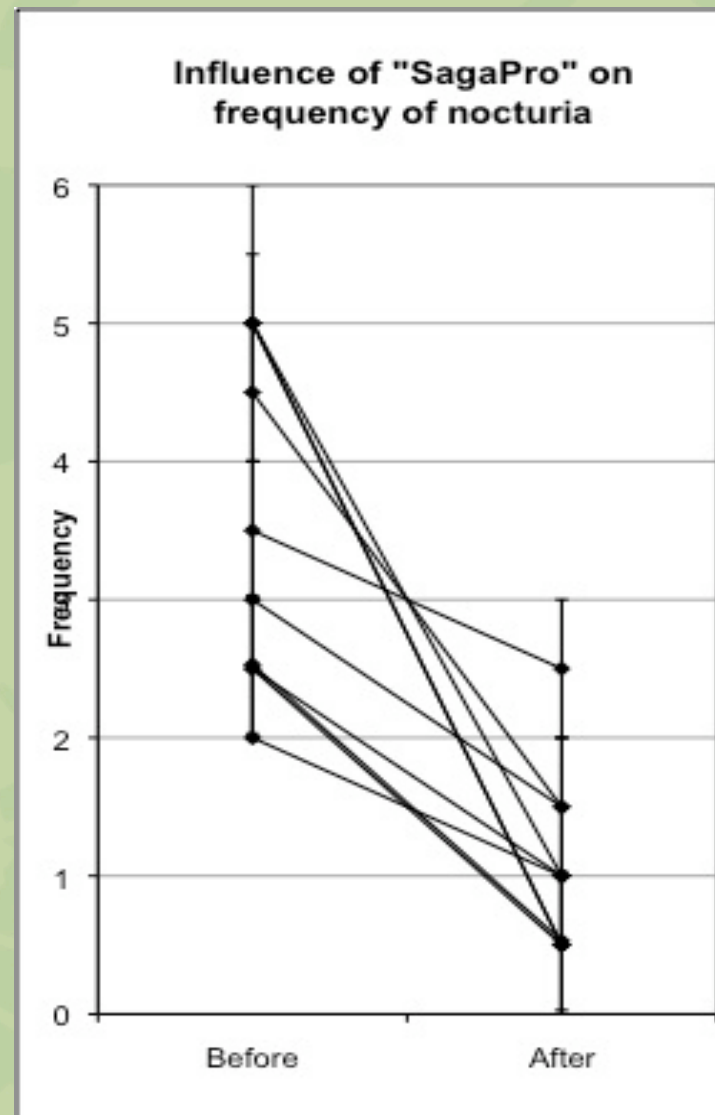
- SagaPro is made from the leaves and reduces nocturia.
 - This is a common problem in men with a benign enlargement of the prostate gland and people of both genders with an overactive bladder.

Phytochemicals and how they work:

- Flavonoids: Isoquercitrin reduces inflammation and prevents contraction in the urinary tract.
 - By inhibiting the production of leukotrien D4 which causes the contraction.
- Prevents formation of new blood vessels or angio-neogenesis.
 - This prevents the growth of tumors since it reduces supply of oxygen and nutrients to the tumor.
- SagaPro can thus reduce nocturia in men and women, reduce inflammation and prevent tumor growth in experimental animals.

Pilot Study on SagaPro

Reduces nocturia in men with a benign enlargement of the prostate gland.



How Does SagaPro Work ?

SagaPro has phytochemicals with many different effects:

- Relaxes contraction in the urinary tract
- Prevents breast cancer cells from developing tumors
 - In experimental animals. Clinical trials have not yet been carried out.
- Relaxes smooth muscle cells in bronchial tubes
- Inhibits proliferation of viruses

Cancer

- Cancer can develop as a result of changes in the genetic material or DNA.
 - Damage to DNA can be caused by chemicals or carcinogens in food, water or air and by sunlight and viruses.
- Changes in DNA or mutations can disturb normal regulation of cellular function
 - This can lead to increased cell division and proliferation of cells which lead to development of tumors.
 - If cellular control mechanisms are normal then cells, damaged by environmental factors or viral infection, are destroyed by a protective mechanism called programmed cell death or apoptosis.

Cancer

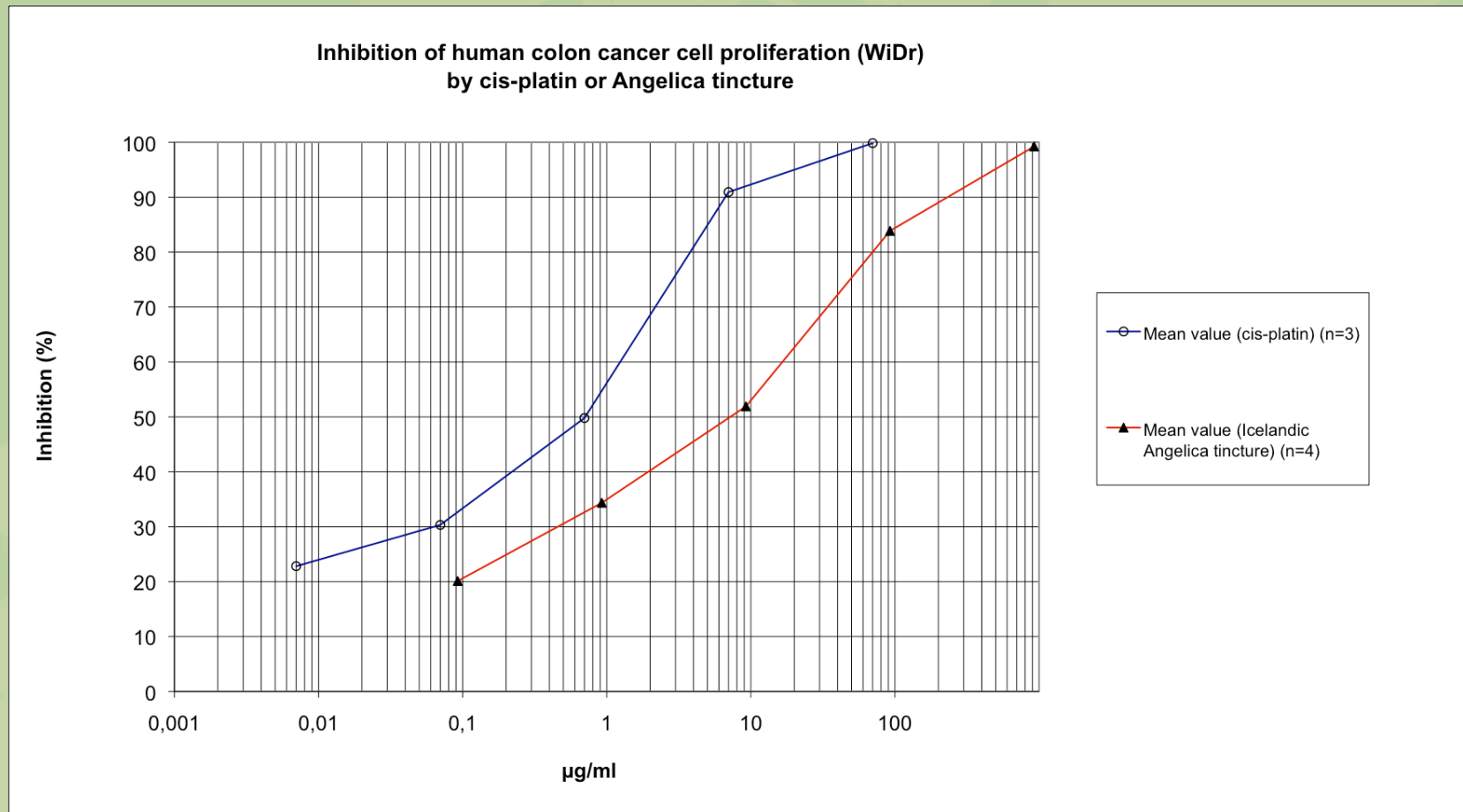
Activity in seeds and leaves of the *Angelica archangelica*:

- Prevents proliferation of cancer cells, prevents cancer cells from developing tumors.

Phytochemicals and how they work:

- Coumarins and furanocoumarins have been used to prevent formation of cancer cells by known carcinogens.
- Imperatorin in Icelandic *Angelica archangelica* seeds stimulates programmed cell death or apoptosis and prevents proliferation of cancer cells.

Influence of Icelandic Angelica Tincture on Proliferation of Cancer Cells in Culture



Cancer

Phytochemicals and their anti-cancer activity:

- Isoquercitrin in *Angelica archangelica* leaves:
 - Inhibits formation of new blood vessels in the tumor
 - Prevents cancer cells from developing cancer
- Diosmin and rutin
 - Flavonoids that can prevent development of tumors and metastasis

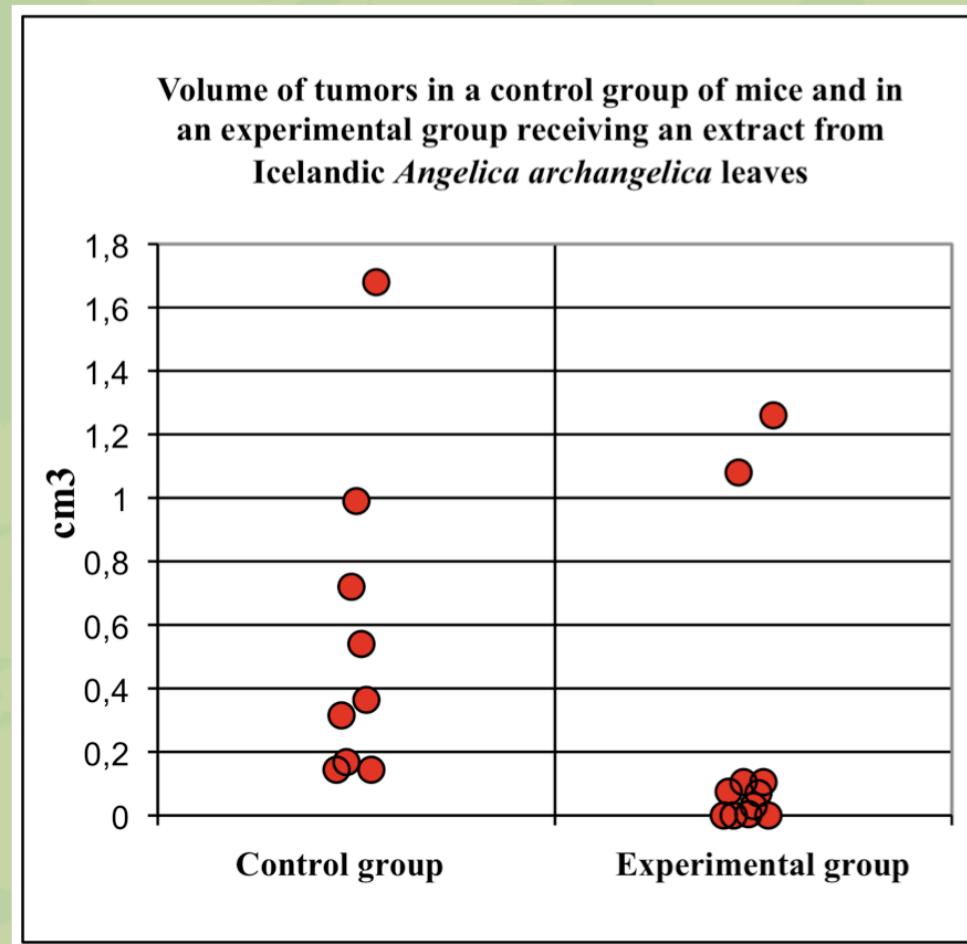
References:

Antitumour activity of Angelica archangelica leaf extract.

Sigurdsson S, Ogmundsdottir HM, Hallgrimsson J. Gudbjarnason S.

In vivo, 2005; 19: 191-194.

Influence of Angelica Leaf Extract (SagaPro) on Development of Tumors in Mice



Influence on Development of Cancer

1. Icelandic Angelica tincture and tablets prevent formation of new cancer cells.
2. Icelandic Angelica tincture and tablets prevent proliferation of cancer cells.
3. Icelandic Angelica tincture and tablets stimulate programmed cell death or apoptosis.
4. SagaPro prevents cancer cells from developing tumors.

Summary

Products from the Icelandic *Angelica archangelica* have been helpful to people in treatment or prevention of:

- Chronic fatigue syndrome
 - Increases energy release from sugars and fat
- Stress, reduces anxiety
 - Phellopterin has anxiolytic effects
- Mild depression
 - Effect of bergapten on mild depression has shown positive effects
- Dementia
 - Decreases the breakdown of neurotransmitter acetylcholine
- Stomach ailments
 - Antiviral and anti-inflammatory properties
- Cold and flu
 - Prevention through antiviral activity

Summary

Products from the Icelandic *Angelica archangelica* have been helpful to people in treatment or prevention of:

- **Cardiovascular diseases**
 - Calcium antagonists reduce hypertension
 - Relaxes blood vessel walls and increased blood flow (vasodilation)
 - Antiarrhythmic
 - Antianginal
 - Antiplatelet (prevents formation of blood clots)

- **Erectile dysfunction**
 - Vasodilation and increased blood flow

- **Nocturia**
 - Reduction in frequency of urination at night in men with prostate problems and in men and women with overactive bladder.

- **Chronic inflammation**
 - a) Prostate problems
 - b) Cardiovascular diseases

Summary

Common bioactive natural products in herbs and vegetables

- Terpens in essential oils, small molecules insoluble in water
 - Anti-proliferative
 - Antibacterial
- Coumarins and furanocoumarins, insoluble in water
 - Anxiolytic effects
 - Vasodilation
 - Anti-inflammatory
 - Anti-tumor
 - Anti-platelet
 - Anti-viral
 - Anti-bacterial
 - Anti-cholinesterase (against Alzheimer's).
- Flavonoids, soluble in water
 - Antioxidants
 - Antiviral
 - Antitumor

Summary

Common bioactive natural products in herbs and vegetables

- Polysaccharides, many soluble in water
- Phytoestrogens, three classes of compounds
- Phytosterols, insoluble in water, similar in structure to cholesterol
- Fibers, vitamins, minerals (Ca, Mg, etc.).

Thank You

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