

# ELDERBERRY AND HUMAN HEALTH

## Pharmacological and Clinical Effects of Elderberry Fruit

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In traditional German medicine, the dried ripe or fresh berries of *Sambucus nigra* were used for the treatment of constipation, to increase diuresis, as a diaphoretic in upper respiratory tract infections, for the alleviation of low back and/or neuropathic pain, headache and tooth ache. In the meantime, there are data on the antibacterial, anti-inflammatory, analgesic and antiproliferative effects available, but these need further support. Several *in vitro* studies together with two exploratory studies in humans and one open study in chimpanzees indicate that the aqueous elderberry extract Sambucol<sup>R</sup> may be useful for the treatment of viral influenza infections or other viral infections. The active principle of elderberry, a mixture of procyanidins, anthocyanins and phenolic acids, has a potent antioxidative effect that may be useful for the treatment of the metabolic syndrome (hyperlipidemia, diabetes, hypertonus) associated with obesity. Although the evidence of effectiveness is poor due to the poor quality of the studies, the outcome measures (blood lipids, blood glucose, and blood pressure) provide promising results. Though laboratory and clinical data indicate that elderberry products may be a “functional food” for disorders or diseases related to oxidative stress, these promising indications need to be confirmed in more rigorous studies.

## Usefulness of Elderberry Fruit as Functional Food

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Pharmacological and clinical studies indicate that products from elderberry fruit are useful for the treatment of diseases and the maintenance of health. This, however, requires an adequate daily dose of the active principle of elderberry fruit. Dose-finding studies have not yet been carried out for the different indications. Most promising are elderberry products for viral infections and diseases associated with oxidative stress including arteriosclerosis, diabetes, hyperlipidemia, cancer etc. Temperature, oxygen, and light are destroying the active principle in elderberry juice. This has to be taken into consideration when preparing elderberry functional food. Addition of vitamin C may help to protect from oxidative degradation. The starting material has to be free of leaves and stems because these contain toxic lectins causing intoxications (acute gastrointestinal and neurologic symptoms). Unlike intoxications with solanin, elderberry intoxications had a benign outcome so far, poisoning from cyanide had not

been involved ([www.cdc.gov/mmwr/preview/mmwrhtml/00000311.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/00000311.htm)). For practical reasons, chokeberry (*Aronia*) cultures may replace elderberry cultures, because *Aronia melanocarpa*, for example, is easier to harvest and provides an active principle similar to elderberry but even more potent.

### **Elderberry Juice Prevents Prostate Cancer *In Vitro* and in an *In Vivo* Mouse Model**

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Anti-cancer botanical compounds are proposed to suppress tumor growth by disrupting signaling pathways which are involved with cancer cell growth. Here we investigate the potential for elderberry juice (*Sambucus nigra* L. subsp. *canadensis* (L.) Bolli) to inhibit Gli/hedgehog (Gli/Hh) signaling, a pathway previously found to be important for the growth of many cancers, including prostate cancer. We hypothesized that the claimed anti-cancer effects of elderberry are due to its inhibition of the Gli/Hh signaling and that elderberry would prevent prostate cancer in the TRAMP (Transgenic Adenocarcinoma Mouse Prostate) model. *In vitro*, measuring the Gli/Hh pathway activity, we observe comparable dose-dependent inhibition of the Gli-reporter activity in Shh Light II cells treated with dilutions of either elderberry juice or elderberry pulp extract. Importantly, 100 to 250 fold dilutions of elderberry juice or pulp/pomace extracts are effective at suppressing Gli/Hh signaling by 50%. *In vivo*, diets containing freeze-dried elderberry juice solids at 3 concentrations (low=0.09%, middle=0.45%, and high=2%) were fed to TRAMP mice to determine if elderberry could delay or inhibit prostate cancer progression. [*The Middle elderberry diet in mice is the equivalent dose of a 60-kg human drinking 2 tablespoons of elderberry juice per day.*] In comparison to the control group, fed AIN-93G diet without any freeze-dried elderberry solids, these 3 concentrations of elderberry in the AIN-93G diet exhibited potent dose dependent inhibition of cancer formation with the Middle and High dose elderberry diets being statistically significant at the  $p = 0.03$  and  $p = 0.006$  level, respectively. These results support our hypothesis that elderberry juice is capable of preventing prostate cancer. Additional research is clearly warranted on elderberry's mechanism(s) of action in prostate and other cancers that are potentially dependent upon Gli/Hh signaling.

## Bioactive Compounds of Elder (*Sambucus nigra* L.) with Focus on their Potential Anti-diabetic Effects

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Preparations of elder (*Sambucus nigra*) are used in traditional medicine as diuretics and to treat colds, influenza, inflammation, and diabetes. Elderberries and elderflowers are rich in polyphenols such as phenolic acids, flavonol glycosides, and anthocyanins. Polyphenols are known for their antioxidant activity and are believed to prevent oxidative stress, a condition that may lead to serious diseases such as cancer, cardiovascular diseases, inflammation and type-2 diabetes (T2D). Hence, polyphenols have been pointed out as beneficial agents in both elderflowers and elderberries. Epidemiological investigations tend to confirm the protective effects of polyphenols against cardiovascular diseases and T2D but the mechanisms by which they exert their protective effects are far from understood. The reported beneficial effects of polyphenols against cancers and inflammation are mainly based on *in vitro* studies. The disparity between an excellent *in vitro* activity related to a specific disease(s) and a weaker *in vivo* effect of polyphenols may be due to pharmacokinetic properties such as poor bioavailability, low absorbability, and/or metabolism. Therefore the health effects of elder could be due to (1) polyphenols whose modes of action differ from the traditional one proposed for exogenous antioxidants or (2) other types of biomolecules not identified yet.

Extracts of elderflowers have been found to exert insulin-like and insulin-releasing actions *in vitro* and to activate PPAR $\gamma$  as well as to stimulate insulin-dependent glucose uptake. This indicates that elderflowers may be used in the prevention and/or treatment of insulin resistance. In the search for an explanation of the anti-diabetic effects of elderflowers we undertook an investigation of a methanol extract of elderflowers. A bioassay-guided fractionation of the extract by reverse phase flash column chromatography and semi-preparative HPLC resulted in the isolation of several compounds being able to activate PPAR $\gamma$ , including linoleic acid and linolenic acid, and the flavanone aglycone naringenin. However, major elderflower metabolites such as quercetin-3-O-rutinoside, quercetin-3-O-glucoside, kaempferol-3-O-rutinoside, isorhamnetin-3-O-rutinoside, isorhamnetin-3-O-glucoside, and 5-O-caffeoylquinic acid were unable to activate PPAR $\gamma$  *in vitro*. Several compounds with structures similar to that of naringenin have been identified previously as activators and/or agonists of PPAR $\gamma$ . These include among others the flavonol aglycone kaempferol, which indicates that flavonoid aglycones are relatively good ligands for PPAR $\gamma$  in contrast to their respective glycosides. Further investigations are, however, needed to demonstrate the bioavailability, absorption, and metabolism of elderflower flavonoids in order to determine their potential anti-diabetic or other health-promoting effects.

## Lectins of *Sambucus nigra* as Biologically Active and DNA-protective Substances

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The human genome is affected by diverse environmental pollution factors that are particularly significant for Ukraine, which suffered from Chernobyl radiation disaster. At the same time many natural compounds, especially from medicinal plants, are known as agents preventing DNA lesions which often result in increasing mutagenesis and carcinogenesis. The aim of our work is to present a review of own results and literature data concerning DNA-protective potential of *Sambucus nigra* biologically active compounds named lectins, a very large group of universally occurring proteins that recognize and specifically bind to carbohydrates /glycoconjugates. Various physiological activities of lectins based on protein-carbohydrate interactions have been demonstrated in all living forms. For example, lectins participate in host defense in plants against stress-related conditions, the attack of phytopathogens and phytophagous insects, as well as modulation of immune response, mitogenic stimulation or induction of apoptosis in animals. Antiviral, immunomodulating, antioxidant and insulin-stimulating properties of *S. nigra* fruit and flower extracts have been described in scientific literature. Also, the elderberry lectins were found in roots, leaves, bark, seeds and fruits, with SNA-IV being the predominant protein in the juice. In Ukraine, various parts of the *S. nigra* plant have been used in folk medicine for ages. Using methods of isoelectric focusing and chromatography we succeeded in finding that elderberry flowers and pollen contain rather high levels of lectins agglutinating animal and human erythrocytes (3-4 mg of 100 g dry material), which differ from commercial preparation of *S. nigra* bark lectin (SNA-I). The major lectin found in inflorescences named SNAflu-I is GalNAc specific and is supposed to be a heterotetramer with subunits of about 30 and 33 kDa. *Sambucus nigra* lectins demonstrated the protective and antimutagenic effects against heavy metals (nickel ions) in the soil bacteria *Bacillus subtilis*. Also it was shown that lectins under study can modulate in a concentration-dependent manner the frequency of mutations and genotoxic activity of alkylating agents in eukaryotic cell cultures. Studies focused on elucidation the cell targets sensitive for the *S. nigra* lectins action demonstrated that at least one of the targets in *B. subtilis* may be the DNA-dependent synthesis of RNA – the way to modulate gene expression. The results obtained give the reason to conclude that the protective functions of lectins both in pro- and eukaryotes involve complex mechanisms including components of DNA repair system.

## Lectins of *Sambucus nigra* in Regulation of Cellular DNA-protective Mechanisms

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Genomes of living organisms are constantly affected by exogenous and endogenous factors, which lead to generating cytotoxic, carcinogenic, and/or mutagenic DNA lesions. However cells possess a number of protection mechanisms directed against DNA damage. The repair enzyme O6-methylguanine-DNA methyltransferase (MGMT) plays a key role in the repair of primary damages of DNA caused by alkylating compounds, which are widely used in industry and medicine. In humans MGMT protects the integrity of the genome, but also contributes to the resistance of tumors to DNA-alkylating chemotherapeutic agents. Therefore, modulation of MGMT expression is a possible strategy to improve the efficiency of cancer therapy and defend normal cells from toxicity of alkylating drugs. Development of medicinal plants for this purpose is highly desirable, due to their safety, low toxicity, and ease of oral intake. The aim of our work was to study the potential of *Sambucus nigra* biologically active compounds, such as lectins, in modification of DNA damage repair process and induction of the MGMT expression. *S. nigra* is widely used in Ukrainian folk medicine. It contains a variety of biologically active substances of pharmacological interest and high levels of lectins as well. Lectins are the carbohydrate-recognizing proteins with regulatory function. Protective and antimutagenic activity of *S. nigra* lectins against some DNA-damaging factors with different mechanism of action (nickel ions and alkylating agents) have been studied in mammalian cells *in vitro*. Lectins are known to exhibit no enzymatic activity, but can up- and down-regulate the activity of different enzymes and other regulatory proteins such as cytokines. That is why we have been studying the modulating effect of *S. nigra* lectins on MGMT gene expression in mammalian cell culture. These lectins were shown to be able to affect in concentration-dependent manner the genotoxic activity of damaging agents and to modulate the MGMT gene expression at the protein level. The obtained results give us the reason to assume that one of the protective mechanisms of the lectin acting is stimulating DNA repair in a cell, including direct reversal repair with the help of the MGMT enzyme.

## Health from the Root to the Flower

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Key words: elderberry, essential oil, colors, natural components, medicinal plant

Elderberry (*Sambucus nigra* L.) is one of the oldest medicinal plants. All parts could be usefully applied in phytotherapy. It is usually used as a dried drug and its healing power is enhanced in a mixture of herbs. Leaves (*Folia sambuci*) are collected before flowering. Flowers (*Flores sambuci*), with wonderful fragrance, are collected from May to June. They are the most famous parts of this species for preparing tea. Young sprouts provide the bark (*Cortex sambuci*) for medicinal uses. A toxic substance, sambunigrine, occurs in immature fruits of elderberry, but it is possible to deactivate it by higher temperature. Attention has to be paid in use of extracts from bark and roots of elder. Study of this species is necessary because not all components and their therapeutical effects are known in this modern age.

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## The Effect of Sambucol on the Immune System (Cytokines Production)

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Natural remedies, including *Sambucus nigra*, were shown *in vitro* and *in vivo* to have activating effects on the immune system and to possess anti viral properties, as published in former studies. Sambucol products (Sambucol Black Elderberry Extract, Sambucol Active Defense Formula, and Sambucol for Kids), based on a standardized black elderberry (*Sambucus nigra* L.) extract, were studied in comparison to two other natural products (Protec and Chizukit N) containing Propolis and Echinacea. Those five herbal remedies which are sold as food additives and believed to have immune enhancing properties, have been evaluated for their effects to stimulate production of cytokines - one of the main components of the immune system activation. The production of inflammatory (IL-1 $\beta$ , TNF $\alpha$ , IL-6 and IL-8) and anti-inflammatory (IL-10) cytokines, was tested using blood derived monocytes from 15 healthy donors, as published earlier. The production of all five cytokines was significantly increased by the Sambucol preparations, mostly by the BE type (2 - 45 fold), as compared to controls.

Protec induced only a moderate production of IL-8 (1.6 fold) and of IL-10 (2.3 fold), while Chizukit N caused only a moderate increase in IL-10 (1.4 fold). Both Protec and Chizukit N induced moderate decreases in IL-1 $\beta$ , TNF $\alpha$  and IL-6 production. LPS, a known activator of monocytes, used as a positive control, induced higher levels of cytokine production (3.6 - 10.7 fold), but sometimes even less than Sambucol. Sambucol formulations demonstrated activation of the healthy immune system by increasing inflammatory and anti-inflammatory cytokines production, while the effect of Protec and Chizukit N is much less. Sambucol could therefore have immuno-stimulatory properties when administered to patients suffering from influenza or to immuno depressed cancer / AIDS patients, in conjunction with chemotherapeutic or other treatments.

### **Clinical Studies on the Effects of Sambucol - a Review**

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Sambucol, a standardized elderberry extract, was evaluated in several clinical studies: 1) Reduction of symptoms during an outbreak of influenza B/Panama, 2) Efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections – a randomized study, and 3) Reduction in flu-like symptoms in chimpanzees – prophylactic and symptom-dependent treatment.

1) A placebo-controlled double blind study was carried out on a group of individuals living in an agricultural community (kibbutz) during an outbreak of influenza B/Panama in 1993. Fever, feeling of improvement, and complete cure were recorded during 6 days. Sera obtained in the acute and convalescent phases were tested for the presence of antibodies to influenza A, B, respiratory syncytial and adenoviruses. Convalescent phases serology showed higher mean hemagglutination inhibition (HI) titers to influenza B in the group treated with Sambucol, than in the control group. A significant improvement of the symptoms, including fever, was seen in 93.3% of the cases in the Sambucol treated group within 2 days, whereas in the control group 91.7% of the patients showed an improvement within 6 days ( $p < 0.001$ ). A complete cure was achieved within 2 to 3 days in nearly 90% of the Sambucol-treated group and within at least 6 days in the placebo group ( $p < 0.001$ ). Considering the efficacy of the extract *in vitro* on all strains of influenza virus tested, the clinical results, its low cost, and absence of side effects, this preparation could offer a possibility for safe treatment for influenza A and B.

2) The efficacy and safety of oral elderberry syrup for treating influenza A and B was tested. Sixty patients suffering from influenza-like symptoms for 48 h or less, were enrolled in this randomized double-blind, placebo-controlled study during the influenza season of 1999 – 2000 in Norway. Patients received 15 ml elderberry or placebo syrup four times per day for five days, and recorded their symptoms using a visual analogue scale. Symptoms were relieved on average four days earlier and use of rescue medication was significantly less in those receiving

elderberry extract, compared with placebo. It was concluded that the Elderberry extract offered an efficient, safe and cost-effective treatment for influenza.

3) The effects of Sambucol treatment on flu like symptoms in chimpanzees were evaluated, and a reduction in those symptoms and the duration of illness was reduced in the treated primates.

### **Flowers of Elder (*Sambucus nigra*): Well-established and Traditional Human Disease Claims**

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Key words: elder flowers, WHO monograph, THMP, clinical studies, disease claim, adverse effects

European elder is traditionally used as a medicinal plant by many native peoples and herbalists alike. Stem, bark, leaves, flowers, fruits, and root extracts are used to treat bronchitis, cough, upper respiratory cold infections, and fever. Several pharmacopoeias have for centuries included *Flos Sambuci* or dried flower of elderberry, and even recognized textbooks and monographs have described the medicinal use of elderberry flower. Thus in 2002, WHO (World Health Organization) published a monograph, which stated that although no controlled clinical data are available, the descriptions in pharmacopoeias and traditional systems of medicine justify elder flower herbal preparation being used as a diaphoretic for treatment of fever and chills, and as an expectorant for treatment of mild inflammation of the upper respiratory tract, and also for symptomatic treatment of the common cold. In 2008 EMA (European Medicinal Agency) issued the Community herbal monograph on *Sambucus nigra* L., Flos. With the following approval: Herbal medicinal product traditionally used for the relief of early symptoms of common cold. The product is a traditional herbal medicinal product for use in specified indications exclusively based upon long-standing use.

Elderberry flower is also described in folk medicine, but not supported by experimental or clinical data, for treatment of conjunctivitis, constipation, diabetes, diarrhea, dry skin, headaches and rheumatism. Elderberry flowers are thus sold in Ukrainian and Russian drugstores for relief of congestion, specifically as an expectorant to relieve dry cough and make it productive. The flowers can be used to make an herbal tea as a remedy for inflammation caused by colds and fever. Combination of elderberry flower and four other botanicals (Sinupret®) is approved by national drug authorities according to “well-established medicinal use” based upon pharmacological and clinical literature which suggest that this phytomedicinal preparation has a relatively significant level of safety and efficacy compared to many other botanical or otherwise natural medicinal preparations intended for use in “maintaining the health of sinuses and the upper respiratory tract”. The scientific and clinical literature on Sinupret® supports pharmacological mechanisms of mucolytic, secretolytic, anti-inflammatory,

antibacterial, antiviral, and immunological activity, some of which has been documented in open-label and randomized controlled human clinical trials. The overall safety of Sinupret® has been extensively documented in pharmacovigilance data based on widespread and long-term use in Germany and other European countries, as well as other post-market surveillance safety data, including safety during pregnancy.

### **Elderberries (*Sambucus nigra*): Human Health and Disease Claims**

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Key words: elder berries, syrup, soft, THMP, clinical studies, disease claim, adverse effects

European elder fruit has been used in folk medicine for centuries, but not supported by experimental or clinical data. In recent years, however, dietary supplements, traditional herbal medicinal products (THMP), and other natural health products containing extracts, juices or syrups of European elder berry have become much more popular in the EEC and the US as remedies for treating cold and flu symptoms. They are marketed primarily through natural food stores alongside other popular herbal remedies used for treatment or prevention of upper respiratory tract infections and other symptoms associated with colds and flu. Several small clinical studies have been performed but only results from five small controlled studies on various elder berry preparations that included a total of 144 participants have been published. Two randomized, double-blind, placebo-controlled studies demonstrated that patients having received elder berry syrup (Sambucol®) recovered significantly faster symptoms associated with influenza than patients in the control group. Three other clinical trials investigated the effect on blood lipids like triglyceride and cholesterol levels. No significant effect could be determined.

The biological activity of European elder berry has also been evaluated in experimental laboratory studies. *In vitro* studies have demonstrated a significant antioxidant capacity as determined by oxygen radical absorbing capacity (ORAC). Antiviral capacity is also demonstrated by inhibition of viral replication. Furthermore, immunoprotective and immunostimulatory activity was detected. Elder berry also increased production of inflammatory and anti-inflammatory cytokines. There is no reporting on adverse effects of properly prepared European elder berry preparations at therapeutic dosages. Unripe or insufficiently cooked elder berry preparation can induce toxic effects in humans (e.g., diarrhea, nausea, vomiting) due to content of cyanide-inducing-glycosides. There are reports of poisonings from the fresh juice of other *Sambucus* species like the American (*S. canadensis*) and Mexican elder (*S. mexicana*). Also, very sensitive persons have responded positive in allergy tests. Only few testimonials on drug interactions have been recorded regarding an interaction with diuretics and laxatives. However, there is a preliminary report of a potential beneficial interaction between elder berry preparations and decongestants and antibiotics.

## Does Elderberry Extract Decrease Incidence of Influenza-like Illness? (P)

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Elderberry extract has been shown to be safe and efficacious in the treatment of influenza A and B and to block the ability of H1N1 virions to infect host cells. To our knowledge, no clinical studies have been conducted to test the ability of elderberry to prevent influenza. The purpose of our study was to address this question by comparing the incidence of seasonal influenza during a 12 week period in 3 consecutive years between a treatment group receiving elderberry extract and a control group receiving placebo. A randomized, double-blind, clinical trial was conducted in Hawaii, Washington, Montana, Colorado and North Carolina. Participants were healthy children (aged 2 and older) and adults with no recent history of influenza and no annual influenza vaccination, randomly assigned to take elderberry syrup or placebo for 12 weeks during the flu seasons of 2009-2010, 2010-2011, and 2011-2012. Dosage was 1 teaspoon daily for the first two years and twice daily for the third year. Flu cultures were performed for participants who developed ILI. Over the 3 years, 113 participants were enrolled; 33 taking elderberry completed the trial, and 30 taking placebo. There were 2 cases of influenza reported, both in subjects taking placebo. In those taking placebo who completed the trial, there were 7 reports of other illnesses, and in those taking elderberry, 4 reports of other illnesses. The most common adverse effect reported was dislike for the taste of the placebo, which led to some participants withdrawing. This pilot study lacked power but these results provide some support for prophylaxis of influenza with elderberry extract. A larger trial, sufficiently powered, should be conducted to confirm or reject this finding. A trend was also found suggesting that elderberry may have preventive activity against other viral illnesses as well.

## **In vitro Screening for Anti-inflammatory Bioactivity of Various American Elderberry Genotypes**

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This research sought to characterize the anti-inflammatory bioactivity of various American elderberry genotypes. Elderberries from nine genotypes including Bob Gordon, Dallas, Marge, Ocoee, Ozark, Ozone, Sperandio, Wyldewood and York were harvested from the same location in the year of 2011 at Mt. Vernon, Missouri (USA). The juices were French-pressed, centrifuged, filtered through 0.22-micrometer filters, and stored in a -80°C freezer prior to analysis. Juices were diluted 1:1000 in cell culture medium and then placed on top of THP-1 cells, a human monocytic cell line. After 18 hr. of treatment, cells were exposed to an inflammatory stimulus (i.e., 10 ng/mL LPS) and the activation of the NF-κB signaling pathway was measured using a luciferase reporter construct that contained two NF-κB promoters. Our results showed that juices from different cultivars carry substantially different anti-inflammatory bioactivity. Our chemical analyses of juices suggest that this anti-inflammatory activity correlates ( $r^2=0.605$ ,  $p<0.02$ ) with the concentration of rutin, a major polyphenol present in elderberries. Further research is needed to elucidate the relationship between the chemistry and biological activity of American elderberries.

## **The Revival of the Elderberry**

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Elderberry has been named the “country medicine chest” for its diverse health uses. A wealth of folklore is centered on the black elderberry tree, which is common in England and Northern Europe. From the days of Hippocrates, it has been famous for its medicinal properties. Its uses are manifold and important. Almost from time immemorial, a juice made from elderberries simmered and thickened with sugar formed an invaluable cordial for colds and coughs. It is known as one of the best preventatives against the advance of influenza and the ill effects of a chill. During my Ph.D. research, we isolated active substances from the black elderberry fruit, the AntiVirins®. The mechanism of the antiviral action will be explained. As a result of more than 20 years of research on a standardized extract, laboratory and clinical studies confirmed the activity of elderberry on several viruses as well as its stimulating action on the immune system. Additional studies showed its antioxidant properties. Since the launch of Sambucol in the US in 1995, and its receipt of the Vity Awards in 1997, 1998, 1999, numerous products have appeared and the beneficial properties of elderberry are now known worldwide.

## **The Antiviral Effect of a Standardized Elderberry Extract**

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The mechanism of the antiviral effect of elderberry on different viruses is described. Viruses, unlike bacteria, are unable to replicate themselves on their own. They behave like parasites and must invade a living cell. A very early stage of viral infection is viral entry, when the virus attaches to and enters the host cell, then the virus replicates using the cell machinery. Each invaded cell will release thousands of new viruses that will infect new host cells. In this process the host cell will die. The surface of the influenza virus is covered by tiny protein spikes with H and N antigens. When the H antigen, hemagglutinin, binds to receptors on the surface of our cells, the cells begin to produce new copies of the virus. Elderberry disarms the spikes of hemagglutinin and thus, stops the first step of invasion of the virus by blocking the entry of the virus into the cell. The virus will be eliminated from the body. In laboratory studies using monolayer cell cultures this process can be observed. This test is used to show the antiviral properties of plant extracts or drugs. The virus is pre-incubated with dilutions of the elderberry extract before being added to the cells. The reduction of infectivity in the presence of elderberry is determined. The standardized elderberry extract was shown to inhibit the replication of influenza viruses type A and B, including avian (H5N1) and swine flu (H1N1) viruses. In addition sensitive and Acyclovir-resistant Herpes HSV-1, HIV, Respiratory Syncytial virus (RSV) were found to be sensitive to elderberry.