



FENACTIVE®



IMMUNITY SUPPORT

ORIGINAL COMPOSITION OF STANDARDISED EXTRACTS

- *Sambucus Nigra L.* | Elderberry
- *Aronia Melanocarpa (Michx.) Elliot* | Aronia berry

— Antiviral activity against respiratory viruses influenza and coronavirus

— Antibacterial and Immunostimulating effect



Sambucus Nigra L.



Aronia Melanocarpa M.

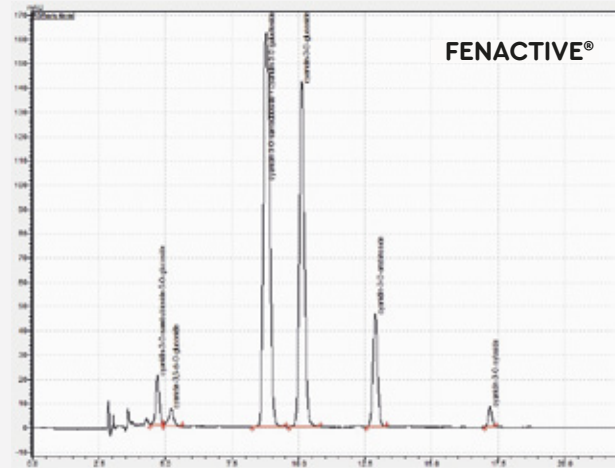
- IMMUNITY
- COLD AND FLU
- INFECTIONS
- ANTIOXIDANT PROTECTION



What is FENACTIVE®

FENACTIVE® is a standardized complex of plant extracts, rich in polyphenols, designed to support and restore the body's immunity, in particular against upper respiratory tract infections (URTI) of viral and bacterial origin. **Aronia melanocarpa (Michaux) + Sambucus nigra L.** have different but complementary anthocyanin fractions in their composition, which is widely proven and brings significant health benefits. As a result of our own laboratory work on the formulation, we have obtained an innovative specific complex with an extended, synergic spectrum of biologically active ingredients.

Plant (fruit)	Dominant anthocyanin fraction
Aronia melanocarpa (chokeberry)	cyanidin-3-O-galactoside cyanidin-3-O-arabinoside cyanidin-3-O-xyloside
Aronia + Elderberry	cyanidin-3-O-glucoside
Sambucus nigra L. (elderberry)	cyanidin-3-O-sambubioside-5-O-glucoside cyanidin-3,5-di-O-glucoside cyanidin-3-O-sambubioside



Specification

The **FENACTIVE®** *Aronia melanocarpa* + *Sambucus nigra* L. complex has been standardised simultaneously regarding the content of:

- anthocyanins (HPLC)
- polyphenols (UV)

It is patented in-house production from selected raw materials. Thanks to contracted, local sources of raw ingredients we guarantee full control over the origins and quality of the extracts. **Reference FENACTIVE® (10) complex contains 10% anthocyanins / 15% polyphenols.**

Recommended use and dosage

FENACTIVE® comes in the form of black powder, with good technological properties. It is convenient to produce formulations, suitable for capsules, tablets, liquid forms. Suggested dosage: 200-250 mg, once daily.

What makes FENACTIVE® unique?

Fusion of the health benefits of two traditionally used fruits with the highest ORAC* scale indices – aronia berry and elderberry – the innovative, standardised composition of **FENACTIVE®** supports the body's natural defensive functions, ensuring i.a.:

- effective prevention and/or treatment of **respiratory infections caused by viruses** (blocking adhesion of the virus to host cells, inhibiting its replication and transmission from cell to cell, and stimulating the response from the immune system) **and/or bacteria**,
- preventing conditions resulting from oxidative stress or supporting their treatment (restoring balance between antioxidative and prooxidative processes; **reducing inflammation in the body**).

* ORAC (Oxygen Radical Absorbance Capacity) – antioxidants' ability to absorb reactive oxygen species

Target Group

The **FENACTIVE®** Complex is recommended for use by the general population. It is particularly beneficial for the population of children (frequent respiratory infections) and seniors (natural aging of the immune system induces chronic inflammatory processes underlying a number of serious diseases). Numerous in vitro and in vivo studies indicate the beneficial effects of *Aronia melanocarpa* and *Sambucus nigra* L.

FENACTIVE® trademark and formulation

The **FENACTIVE®** registered trademark belongs to **GREENVIT®**. Its use is exclusively related to the purchased complex of extracts. The use of the **FENACTIVE®** trademark in finished products containing this complex mixed with other ingredients belonging to the same botanical family is not permitted.

Studies devoted to *Aronia M.* + *Sambucus nigra L.*

There is no fully effective drug or vaccine against viruses causing human respiratory infections, including influenza (1). Moreover, these infections make patients, especially in the high-risk group, more prone to secondary bacterial infections, which often have a much more severe clinical course than the primary viral infection (2). Therefore, efforts are undertaken towards the development of effective, alternative and safe forms of prevention and/or treatment (1,3), which would provide simultaneous, two-way protection against viral and bacterial infections (3).

Elderberry and aronia berry fruits, containing a number of health-promoting ingredients, stand out thanks to their high, multi-directional biological activity. They are an extremely rich source of polyphenols, especially anthocyanins. Due to their strong antioxidant effect, these compounds largely determine the health-promoting properties of these raw materials, including their antiviral, antibacterial, immunomodulating and anti-inflammatory properties (4,5,6).

A metaanalysis of four clinical studies conducted by Hawkins et al. (7) confirmed that supplementation with preparations containing elderberry right after the appearance of upper respiratory tract symptoms has a moderate to large beneficial effect on the duration and intensity of infection.

Antiviral properties of elderberry and chokeberry are most often attributed to the following mechanisms:

- blocking of hemagglutinin (HA), which prevents adhesion (8,9) and penetration (8) of the virus into host cells,
- inhibiting reproduction of the virus (9,10),
- preventing further transmission of the virus from cell to cell (8), by inhibiting neuraminidase (11).

Active antiviral agents include various polyphenolic compounds such as cyanidin-3-glucoside present in both elderberry (8,12) and aronia berry (13), and cyanidin-3-sambubioside present in elderberry (11,13).

An equally important, indirect, mechanism of combatting viral infection – present both in elderberry (8) and aronia berry – is the **stimulation of the immune system response**.

Own studies devoted FENACTIVE®

Studies* to determine antiviral properties of the **FENACTIVE®** complex were conducted in the reference Laboratory of Virology of the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences. The following test viruses were used in the experiments:

A/H1N1 human influenza virus type A, Orthomyxoviridae), **HHV-1** human herpesvirus 1 (Herpesviridae), **HAdV-5** human adenovirus type 5 (Human adenovirus 5; Adenoviridae). Concentrations CC_{50} , IC_{50} were determined and selectivity index was specified.

After establishing non-toxic concentrations of the **FENACTIVE®** composition, antiviral assays (AVAs) for antiviral activity against test viruses were performed on cell cultures of the MDCK and A549 cell lines. Evaluation of antiviral activity was performed in a variant of incubation of cells with Fenactive® composition after viral infection. Positive controls were antiviral drugs appropriate for each virus: ribavirin (RBV), acyclovir (ACV), cidofovir (CDV), oseltamivir (OSV).

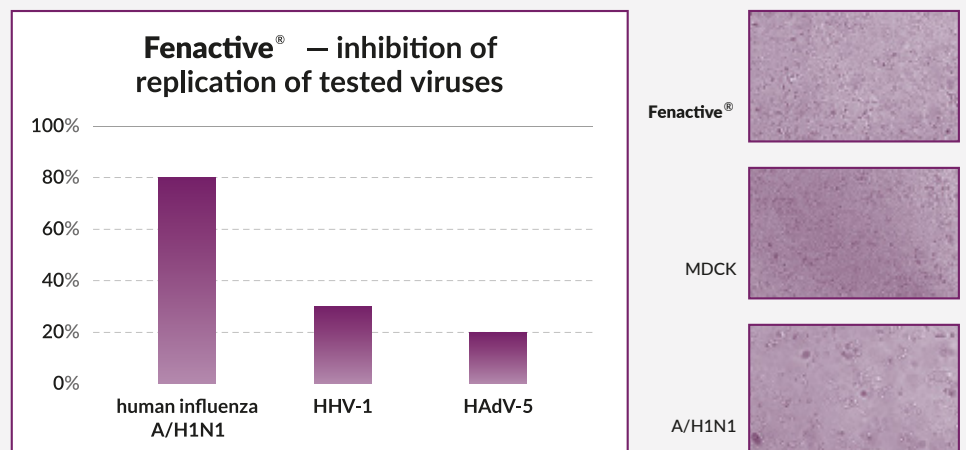


Table. Antiviral activity of the Fenactive® composition

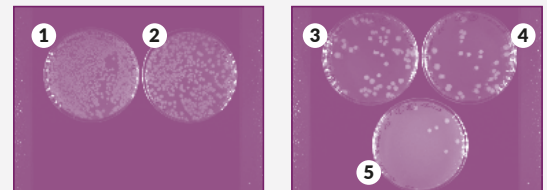
Description: Cytopathic effects of influenza A/H1N1 virus are shown in the images above (A/H1N1) versus control (MDCK). Inhibitory effect of Fenactive® on influenza virus replication is shown for MNCT (Maximum Nontoxic Concentration).

After conducting experiments according to the study protocol, it was found that FENACTIVE® showed significant antiviral activity when administered after infection with the test viruses. The maximum non-toxic concentration (MNCT) of FENACTIVE® inhibited replication (multiplication of influenza A/H1N1 virus) by 80%. Moreover, FENACTIVE® inhibited replication of herpesvirus HHV-1 and adenovirus HAdV-5. The study compared the maximum non-toxic concentration (MNCT) of FENACTIVE®, which inhibited the proliferation of influenza A/H1N1 virus, to single doses of elderberry and chokeberry extracts alone. The results indicate that it is the appropriately selected extract content of the FENACTIVE® composition that allows it to maintain high antiviral activity at generally lower concentrations. The use of single extracts does not bring synergistic effects. This brings a significant clinical benefits to users. In order to confirm immunostimulating effect of the FENACTIVE® composition and to compare the effect of single elderberry and aronia berry extracts, tests were performed on PBMC (peripheral blood mononuclear cells)**. The results indicated a significant increase in IL-6 and TNF- α production in PBMC cells after incubation with FENACTIVE® composition compared to control PBMC cells. Standardized aronia berry extract increased IL-6 and TNF- α production in PBMC cells. On the other hand, cells cultured in the presence of standardized elderberry fruit extract did not show any significant increase in cytokine production. **It has been confirmed that immunostimulating effect of the appropriately selected composition of FENACTIVE® is stronger (more beneficial) than that of the individual elderberry and aronia berry extracts.**

Antibacterial effect of elderberry is attributed to the presence in its composition of flavonoids (5,7,3,4-tetra-O-methyl-quercentin and dihydromyricetin- 3-o 3,4,5-trihydroxy-cyclohexanecarboxylate), triterpenes, lectins, oligosaccharide fragments (15) or ursolic acid (16,17). Available publications demonstrate, among others, the ability of extracts from *S. nigra* gained under laboratory conditions to inhibit the growth of *Staphylococcus aureus* MRSA, *Bacillus cereus* (15), *Escherichia coli* (15,18), *Enterococcus faecalis*, *Pseudomonas fluorescens* (18). **Also aronia berry extracts showed antibacterial effect** against *B. cereus* and *S. aureus*, and also *Pseudomonas aeruginosa* (19). Due to the possibility of synergic interactions between different active substances contained in different raw materials, the activity of standardized mixture of chokeberry and elderberry extracts (FENACTIVE®) was tested in vitro. The combination of extracts from aronia berry and elderberry fruits was tested for their antibacterial activity against pathogenic bacteria: *Staphylococcus aureus* and *Escherichia coli*. In the tests, antibacterial effect of the extracts was observed in different concentrations. The results indicate that inhibition of *S. Aureus* is concentration-dependent.

* ANTIVIRAL ACTIVITY OF FENACTIVE. FINAL REPORT. Study conducted in the R. Hirszfeld Laboratory of Virology of the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences (IPI PAS), Wrocław 2020. Details of the study are available from the manufacturer.

** Evaluation of immunostimulating effect of the Fenactive® composition and single standardized extract of elderberry fruit (*Sambucus nigra*), standardized extract of chokeberry (*Aronia melanocarpa*) in a study on PBMC cells (peripheral blood mononuclear cells). Study conducted at Aronpharma Laboratory, Sopot 2021. Details of the study are available from the manufacturer.



Broth microdilution is used to test the susceptibility of the *S. aureus* bacteria to the tested medium. Concentration of Fenactive® [mg/ml]: 1-50, 2-25, 3-12.5, 4-6.25, 5-3.125

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