Journal of Pharmacy and Pharmacology 9 (2021) 313-319
doi: 10.17265/2328-2150/2021.10.001

Immunostimulator Api-phytotherapy for the Treatment of Upper Respiratory Tract Infection and Chronic Bronchitis

Dr. Elnur Eldaroglu Rahimov and Dr. Zumrud Alasgar Ahmedova
Apimed Natural Methods Centre, Baku 3137, Azerbaijan

Abstract: Throughout history, respiratory tract infections due to viruses, especially influenza viruses, continue to cause serious diseases, up to death, all over the world, as a result of the inability to develop effective treatment methods or vaccines. Due to changes in the antigenic structures of respiratory viruses, especially RNA viruses, there are difficulties in the production of effective vaccines. The World Health Organization estimates 150,000 hospitalizations and 30,000 to 40,000 deaths due to the flu epidemic in the United States alone, with a total of 25 to 50 million cases each year. Respiratory viruses are a major cause of influenza-like illness symptoms in children and adults, causing significant illness and death each year. Various herbal remedies have been used for the prevention and treatment of viral respiratory diseases in many parts of the world. Among those found to be effective are propolis, licorice root, ginger, black cumin, carob, but there is also scientific evidence for the effectiveness of several complementary treatments for the common cold. For example, oral zinc intake can reduce the severity of the common cold. Regular intake of vitamin C supplements can reduce the duration and severity of viral infections. Various herbs are widely used as medicine to clear viral respiratory infections. Influenza control and treatment mainly depend on chemical or biochemical agents isolated from plants. These agents include various polyphenols, flavonoids, saponins, glucosides, and alkaloids. We added such plants, propolis, and licorice honey to the content of bronxbal paste, which is a combination of supportive therapy, bronchial dilator, immunomodulator, mucolytic, and born antiviral and antibacterial effects during coronavirus and other bacterial-virus-caused pneumonia. We prepared it as a paste and used it in patients who do not have allergies. The plant and bee products in the bronxbal content we have prepared are natural pastes to solve problems that need ongoing rehabilitation, such as coronavirus pneumonia and chronic bronchitis caused by other viruses and bacteria, or Covid-19.

Key words: Phytotherapy, apitherapy, integrative medicine, pneumonia, herbal immunotherapy, coronavirus, Azerbaijan, Bronxbal paste.

1. Literature Review and Methods

Glycyrrhizin is an active component of licorice root. An influenza virus investigated in mice infected with influenza virus A2 (H2N2) revealed that glycyrrhizin can protect mice exposed to influenza virus through stimulation of interferon-gamma production produced by T cells. Besides, glycyrrhizin is a candidate drug for immunomodulatory and anti-inflammatory control. The researchers found that the antiviral activity of glycyrrhizin prevented the virus from entering the cell, causing a decrease in the viral effect. Licorice root extract has a steroid effect over glucorticoid by acting on the adrenal glands according to the substance containing carbenexelone. It is used in the treatment of asthma and chronic bronchitis with its steroid effect, spasmolytic and expectorant activity [1].

DGL (deglycyrrhizinated) is a safer form of licorice root with a reduced amount of glycyrrhizin. In some studies, it has been stated that licorice plant has antimicrobial effects. It has been reported that the extract prepared from the roots of Glandulifera varieties showed antibacterial activity against *E. coli*, *S. aureus* and Mycobacterium smegrnatis.

The growth of *B. cereus*, one of the microorganisms used in this study, was inhibited by ethyl alcohol and

Corresponding authors: Elnur Eldaroglu Rahimov, Ph.D., research fields: phytotherapy, apitherapy.

water extracts. Among the plant samples, the maximum inhibition zone against *B. cereus* was 14 mm, formed by ethanol extracts, and the inhibition zone formed by water extracts was 2.7 mm. Other microorganism species did not show any sensitivity to these plant extracts. The inhibitory effect of licorice plant extracts on *Salmonella* Typhi, S. Paratyphi B, *Shigella sonnei*, *S. flexneri* and *E. coli* was investigated, and reported that no inhibition was observed at low concentrations, and all microorganisms showed sensitivity to high concentrations. In this study, it is thought that the lack of sensitivity of most microorganisms may be due to the low concentration of the extract used. The total antioxidant values of the plant samples were measured according to the trolox equivalent antioxidant capacity (TEAC) method, and ethanol and water extracts of the plant samples were prepared in order to investigate the effect of the extraction process.

Nigella sativa is an annual herbaceous plant from the Ranunculaceae family. The genus Nigella is generally widespread in Mediterranean countries and includes a total of 20 species. Of these, 12 species are found in our country and *N. sativa* species is widely grown. In our country where plant diversity is rich, black cumin is known as, grain of abundance and black seed (Figure 1). Boiled seed extract of black cumin improved asthma symptoms in one study (15 mL/kg of 0.1 g boiled extract per day) of 29 asthmatic patients. Frequency of asthma symptoms, wheezing and lung function decreased within 3 months. The need for additional medications and inhalers decreased in patients taking black cumin seed extract. Similar results were obtained in another placebo-controlled study of 80 patients with asthma. In the study, black seed oil taken by mouth for 4 weeks improved asthma control. Scientists have also observed a trend towards improvement in lung function. A meta-analysis of 4 clinical trials concluded that black seed oil may be helpful as an addition to conventional treatments for asthma. Black cumin seed extract has also shown anti-inflammatory effects in rats and mice with asthma. The anti-inflammatory effects of black cumin seeds have been useful in clinical studies of asthma [2].

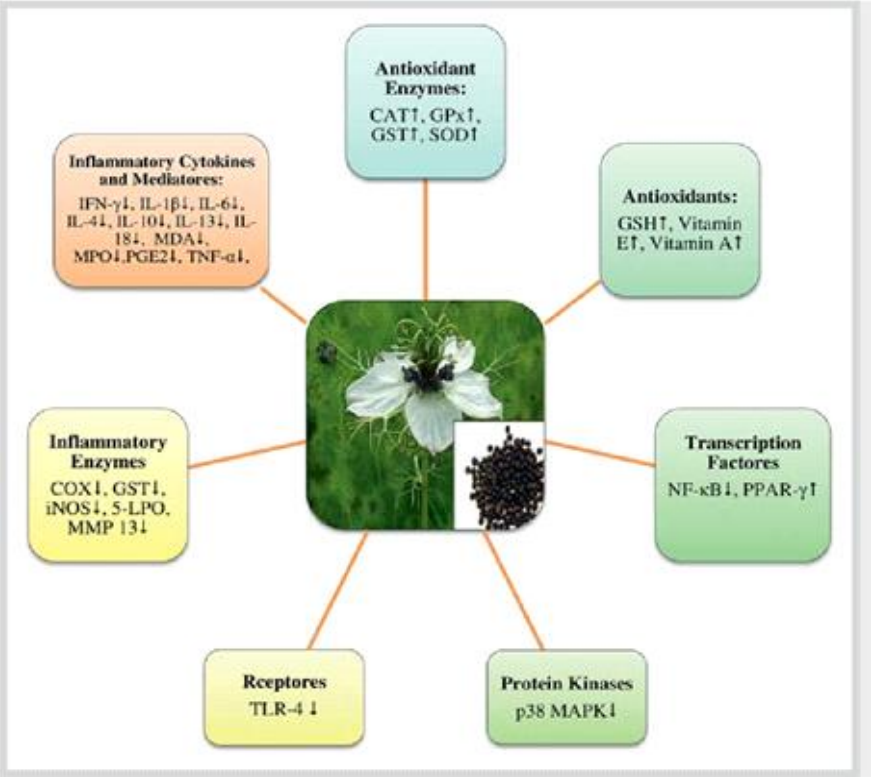

Fig. 1 The effect of *Nigella sativa*.

The nigericin substance in the composition of black cumin has anti-inflammatory, antiseptic and bronchodilator effects. According to 19 preclinical and 7 clinical studies, it has been proven to reduce asthma attacks with the active substance thymoquinolone in asthma [3].

Defined as a "natural antibiotic", propolis has an inhibitory effect on 21 bacteria, 9 fungi, 3 protozoa and many virus species. It is known to be used in the treatment of various diseases due to its strong antioxidant, antiseptic, antibacterial, antiviral, antifungal, anticancer and anti-inflammatory effects.

Poplar propolis, the bee product with the highest antifungal activity, has been tested against 40 fungi containing strains of Candida albicans, Candida glabrata, Candida krusei and Trichosporon spp and has been found to have fungicidal effects on Candida famata, C. glabrata, C. kefyr, C. pelliculosa, C. parapsilosis and Pichia ohmeri, a type of fungus that causes spoilage in juices [4].

Many researchers have reported the anti-tumor effect of propolis in vitro and in vivo. Propolis has been found to have an inhibitory effect on tumor cells and some compounds responsible for this have been isolated. The synergy between propolis and anti-cancer agents is particularly interesting. In a trial on mice, the flavonoids in propolis played a protective role against the toxic effects of chemotherapeutic agents or radiation, raising the hope that this protective effect would have similar results in humans. When propolis is used together with an auxiliary combination to antioxidant therapy, it increases the effectiveness of chemotherapy, provides elimination of side effects on leukocytes, liver and kidneys, and allows high dose administration. Active compounds isolated from Brazilian propolis have been shown to inhibit the growth of liver tumor cells and arrest tumor cells in S phase. A compound (PRF1) obtained from aqueous solutions of propolis was found to exhibit antioxidant activity and have a cytotoxic effect on human liver cancer cells and human lung cancer cells HLC-2.

It has been reported that propolis is effective against various bacterial strains in the laboratory environment. Many researchers have examined the antibacterial effect of propolis and its extract against gram-positive and gram-negative bacteria, and found that it has a broad effect against gram-positive rod bacteria, but has limited activity against gram-negative bacilli [5]. In addition to aerobic bacteria, the antimicrobial effect of ethanol extract of propolis against 267 anaerobic bacteria strains was investigated.

Propolis has a lethal effect against influenza virus (type A) in vitro, while aqueous propolis extract greatly reduces the effect of smallpox virus within 15 minutes. It has been reported that propolis is effective in vitro against various DNA and RNA viruses, including herpes simplex virus (type 1 and 2), adenovirus type 2, pharyngitis virus and poliovirus (type 2).

In a study conducted on propolis with different geographical and botanical origins, it was found that antioxidant activity was directly proportional to the total polyphenol concentration. It was determined that the antioxidant activity of poplar propolis, which has higher polyphenol content, is higher than Caucasian propolis, which has less polyphenol content.

Clinical studies have shown that propolis has been effective on respiratory system infections (bronchitis, COPD, influenza), skin diseases (herpes, skin fungi, allergies, burns, skin ulcers, abscesses), dental and gingival disorders (gingival recession, mouth sores), ear, nose, throat infections, digestive system diseases (parasite, colitis, stomach ulcer, reflux), gynecological diseases (vaginal and cervical disorders) and urinary system diseases (urinary tract inflammation)[6]. Propolis occurs in the shoots and buds of plants and trees. It softens in the heat, solidifies in the cold, the melting point is below the wax.

Propolis can be yellow, gray, brown and red in color. It melts in hot weather and becomes sticky. Bees collect propolis when necessary and carry it to the hive to use it for a variety of reasons. They use

pollen baskets to transport propolis. It is very difficult to collect and empty because it is a sticky substance. The bee collecting propolis can transfer its load to the domestic bee in about 30 minutes. The bee does not store propolis, it collects it as needed. Scientific research and technology have revealed that this substance, which is used in many different places in the world of bees, is also very important for humans.

It has been determined that propolis has a strong antibacterial effect against microbial diseases of the respiratory system (Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenza, Moraxella catarrhalis and Streptococcus pyogenes, Mycobacterium humanus). In this respect, it is extremely effective in respiratory diseases such as influenza, pneumonia, bronchitis, and tuberculosis [7]. Propolis has achieved promising results in the treatment of acute and chronic rhinopharyngitis, pharyngitis, pharyngolaryngitis and otorhinolaryngologic diseases, and it has been reported to have positive effects in upper respiratory tract infections. It has been determined that inhalation of propolis ethanol extract, especially by dripping into water, relieves the upper respiratory tract and bronchi, and gives positive results in the treatment of asthma, bronchitis, pneumonia and allergy. It has been shown that the regular administration of echinacea (50 mg/mL), propolis (50 mg/mL) and vitamin C (10 mg/mL) to children for 12 weeks during the winter period significantly reduces upper respiratory tract infections [8].

Ginger rhizomes contain 4.7-7.5% oleoresin. In the non-volatile part; 1- gingerols ([6]-gingerol, [8]-gingerol, [10]-gingerol), dehydration products, shogaols ([6]-shogaol, [10]-shogaol), 2-fixed oils, 3-waxes. It contains 1-3.3% essential oil. Sesquiterpenes constitute 30-70% of this essential oil. Among the sesquiterpenes, f3-bisabolene, (-) zingiberene, f3-seskifellandrene (+)-ar-curcumen, monoterpenes have geranial and neral. Other compounds include carbohydrates, starch (40-60%), proteins (9-10%), lipids (6-10), lecithin, vitamins (niacin, vit A), minerals, amino acids.

Today, ginger, which is recommended by modern western medicine as well as traditional eastern medicine, contains many vitamins and minerals, as well as essential healing oils. This medicinal plant, which has antioxidant properties, is appetizing, and it is used for the treatment of inflammatory diseases and for strengthening the immune system, as well as digestive system problems such as nausea, diarrhea and stomach pain, especially colds [9].

Ginger has a B2 agonist effect thanks to the antioxidants and gingerol it contains. Good results were obtained in 40% of patients who used the time of asthma attacks. It has LTB4 antagonizing effects that will provide bronchial dilatation and relaxation of the bronchial muscle. It activates its anti-inflammatory receptors [10].

Licorice honey is an interesting type of honey, but it is very rare honey as well. It is common in the districts of Azerbaijan. It is known as Azerbaijan ginseng. Its active ingredients are glycirizzin and carbenexolone. Like other kinds of filtered honey, it is easier to be absorbed by the body and has an agonist effect with other plants [11].

Licorice Root Honey, Licorice plant has been used since 2000 years BC. Research related to it is still ongoing today. It is used in medicine because it is a very powerful nutrient. Licorice honey is a type of honey that is obtained by processing fresh or dried licorice roots in boiling water and then condensing them under low pressure. It is shiny and black in color. It is a special substance that dissolves easily in water and is very sweet.

It is very good for cough and wheezing in the chest. It is also very effective in healing wounds. It is an extract obtained by processing the roots of the licorice plant in boiling water and condensing the licorice water. It is commercially available in powder, cylindrical rods or square pieces. It is a specific sweet mass with glossy black color. It dissolves easily in

water. Its composition is the same as licorice, but the proportion of glycyrrhizin is higher (20%). It has a chest softener, cough suppressant, mucous protection and wound-healing effect. Therefore, it is included in the composition of some lozenges [12].

The uses of carob are quite diverse. It occupies an important place in traditional flavors in different cultures and is the biggest rival of cocoa with its taste. Today, after consumption as a snack, it is used in bakery products, chocolate milk production, foodstuffs such as confectionery and alcohol industry, since it is the most common consumption area as cocoa alternative; It is important that carob does not contain as much fat as cocoa in the preference of cocoa as an alternative. Carob flour is also a natural sweetener due to its high content of sugar (32-38% sucrose, 5-7% fructose, 5-6% glucose). Before the refined sugar used today, carob was used as a natural sweetener. The fact that the fruit contains a high amount of sugar does not increase the blood sugar in the abdomen, because it contains sugar-stabilizing active substances.

Carob is used to relax the upper respiratory tract during asthma and bronchitis. Carob reduces the risk of disease by increasing the activation and synthesis of the OGG1 (8-Oxo Guanine DNA Glycosylase) ferment, which is one of the factors that prevent lung cancer. It has an antioxidant effect and gives an antiallergic effect by inhibiting the synthesis of cytokines and histamine, which are inflammatory mediators [13]. Carob is a nutritious food with its rich vitamins and minerals, and it heals diseases by helping to strengthen many parts of the body from the immune system to the digestive system, from the musculoskeletal system to the reproductive system. The diseases in which carob is most effective are; especially chest diseases such as cough, shortness of breath and cold. It is described as a miraculous food for shortness of breath, bronchitis, asthma and allergic asthma, as it provides very effective protection against lung health.

Asthma and allergic asthma diseases increase by being triggered by caffeine, theobromine and theophylline, which are called phytochemicals. However, carob is a very effective herb in the treatment of asthma because it does not contain these herbal chemicals that trigger asthma. Carob is the most effective treatment method, especially if asthma has developed against allergies. In addition, cold allergy, which has no medical treatment and occurs when cold air triggers an allergy in the body, can also be treated with carob [14].

White-colored locust bean gum with galactomannan structure obtained from seeds is used in foods such as ice creams, sauces, jelly products, condensed fruit juices, meat and fish preserves, as a strength-enhancing and thickening agent with the code E410 among nutritional additives in the food industry. However, the fruit parts that increase during the production of gum from seed cannot be used industrially. The largest producer of carob products in the world is Spain, with 36 percent of fruit pulp production and 28 percent of seed production being produced here. Unfortunately, our country comes after Morocco, Italy, Portugal and Greece with a low rate of 4% and 6%.

Information on the use of carob fruits for therapeutic purposes among regional peoples is quite limited. It is registered that the fruit is recommended as a sore throat and cough syrup in Malta. In general, it is known that fresh fruits have diuretic and intestinal softening effects. However, it is reported to be useful in the treatment of diarrhea, especially in infants, in relation to its tannin content. As a matter of fact, a formula containing carob fibers has been patented as an antidiarrheal in bedridden patients.

Due to the polyphenolic components found in fruits, it has been observed that it has a higher antioxidant and free radical scavenging effect than some known antioxidants. The patented aqueous extract prepared by boiling and straining the fruits in water showed an antioxidant effect equivalent to green tea.

Thanks to the experimental and clinical studies carried out, it is thought that carob fruits may be beneficial in lowering cholesterol and triglycerides and reducing the risk of colon cancer due to their rich polyphenol and fiber content. It was observed that fruit fibers reduced total cholesterol and LDL-cholesterol levels when administered before breakfast for 6 weeks in 49 mild and moderately high cholesterol patients. In another study, carob fruit (4 g twice a day) was administered to one group of 88 high cholesterol patients for 4 weeks, and a similar ineffective product (placebo) was administered to the other group. In the blood samples taken at the beginning and end of the experiment, carob fruit showed a statistically significant change in the observed cholesterol parameters; It has been observed that while it lowers total cholesterol by 17-18%, LDL cholesterol by 14-30%, it increases HDL cholesterol (good cholesterol) by 12-40%. There was no significant change in the values of the placebo group during this period.

It is stated that the fruit extract has some effects on the nervous system. The fruit extract showed sedative, tension-relieving and anti-depression effects in experimental animals. It has been reported that the effect of carob on depression is provided by neuromediators (substances that provide neural communication in the body), such as dopamine and noradrenaline, and therefore may be beneficial in patients with depression [15].

2. Results

In recent years, medicinal plants have gained increasing importance due to the interest in herbal medicines. As it is known, based on the historical and public uses of medicinal plants, first their bioactivity and then their phytochemical analysis are carried out. Especially in Europe, some herbal medicines have more sales than their synthetic counterparts. The use of medicinal plants among people is increasing day by day. Of course, it is the pharmacological studies on this subject that shed light on these uses.

When used together with the LTB4 antagonist drug, it took away the side effects of the drug. When used with antihistamine (Loratadine) drugs, it gave a synergistic effect and no contraindications were observed. It caused tachycardia when combined with B2 mimetics.

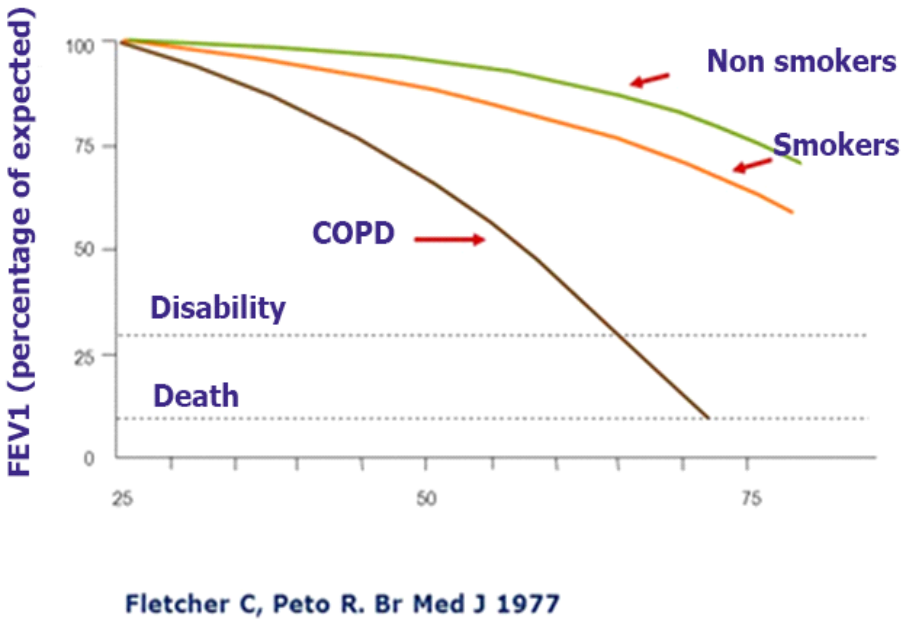

Fig. 1 The relationship between smoking, lung function and age.

References

[1] Kim, K. R., et al. 2010. "Anti-Inflammatory Effects of Licorice and Roasted Licorice Extracts on TPA-Induced Acute Inflammation and Collagen-Induced Arthritis in Mice." *J Biomed Biotechnol* doi: 10.1155/2010/709378.

[2] He, T., and Xu, X. 2020. "The Influence of *Nigella sativa* for Asthma Control: A Meta-analysis." *Am J Emerg Med* 38 (3): 589-593.

[3] Koshak, A., Koshak, E., and Heinrich, M. 2017. "Medicinal Benefits of *Nigella sativa* in Bronchial Asthma: A Literature Review." *Saudi Pharm J* 25 (8): 1130-1136.

[4] Bogdanov, S. 2012. "Propolis: Composition, Health, Medicine: A Review." *Bee Product Science* Available in: https://www.bee-hexagon.net/.

[5] Hegazi, A. G. 1998. "Propolis an overview." *Congreso Internacional de Propóleos, Buenos Aires* 1-2nd, September 2000.

[6] Yücel, B., Topal, E., Akçiçek, E., & Köseoğlu, M. 2014. "Effect of Propolis on Human Health." (Turkish into English) *Anadolu, J. of Aarı* 24 (2): 41-49.

[7] B. Yucel, E. Topal, E. Akcicek, M. Koseoglu, 2014. Effects of Propolis on Human Health, 46.

[8] Cohen, H. A., et al. 2004. "Effectiveness of an herbal preparation containing echinacea, propolis, and vitamin C in preventing respiratory tract infections in children: a randomized, double-blind, placebo-controlled, multicenter study." *Arch Pediatr Adolesc Med* 158 (3): 217-21.

[9] Blumenthal, M., Goldberg, A., Brincmann, J., Herbal Medicine. Expanded Conımission E Monographs, United States of America: Integrative Medicine Communications 2000.

[10] Townsend, E. A., et al. 2013. "Effects of Ginger and Its Constituents on Airway Smooth Muscle Relaxation and Calcium Regulation." *Am J Respir Cell Mol Biol* 48 (2): 157-163.

[11] Rahimov, E. E., and Ahmedova, Z. A. 2021. "An Example of Apiphytotherapy Studies in Azerbaijan: Herbal." *Journal of Pharmacy and Pharmacology* 9 (1): 28-33.

[12] Wang, M., et al. 2012. "Influence of Honey-Roasting on the Main Pharmacological Activities and the Water-Soluble Active Glycosides of Licorice." *Afr J Tradit Complement Altern Med* 9 (2): 189-196.

[13] Colom, M. F., et al. 2012. "*Ceratonia siliqua* (carob) trees as natural habitat and source of infection by *Cryptococcus gattii* in the Mediterranean environment." *Med Mycol* 50 (1): 67-73.

[14] Corsi, L., et al. 2002. "Antiproliferative Effects of *Ceratonia siliqua* L. on Mouse Hepatocellular Carcinoma Cell Line." *Fitoterapia* 73 (7-8): 674-84.

[15] Available from: https://www.erdemyesilada.com/tr/keciboynuzu-meyvesinin-oneminin-yeterince-farkinda-miyiz-a.