PROFESSIONAL LITERATURE

Sambucus nigra (elderberry) * Andrographis paniculata (king of bitters) * Allium sativum (garlic) * Marrubium vulgare (white horehound) * Curcuma longa (turmeric) + Piperine * Bile Acids

The Importance and Physiological Effects of the Active Ingredients Mainly in Scientific Literature on product website:
www.antibacvir.eu

The purpose of this document is to provide customers, by summarizing the contents of relevant scientific literature, with appropriate and comprehensive information prior to purchase in order to assist them in making an informed decision. This fact sheet thus addresses the basic requirement of ensuring consumer satisfaction, with special emphasis on customers'/consumers' rights to life and health, through providing clear and unambiguous information as to what purposes the various ingredients serve.

In compiling this document, we have fully observed the intention expressed in relevant legislation to provide consumers with the most comprehensive and most detailed information possible on the effects of the ingredients in the product to be purchased.

The details provided with regards to the active substances of the ingredients are for information only, they do not indicate synergistic effects of the ingredients, these are referred to in the product claims.

The various areas of effectiveness contributed to the below ingredients do not guarantee, either individually or collectively, that they are equally effective in every case with every person.

1. BLACK ELDERBERRY supports the immune system that protects the human body:

Elderflower has been part of European folk medicine for centuries: it is used primarily for inducing sweating and in cases of fever and cold. More recently, the squeezed juice and extract of its berries have also been used in colds.

These compounds have an antiviral effect against respiratory viruses (influenza, rhino and coronavirus). They also support the immune system and thus contribute to the protection against viruses. [1] [2].

HUMAN STUDIES: Traditional studies of elderberry extract have shown that elderberry accelerates recovery and reduces symptoms in people with influenza. [3] A similar effect was observed for colds[4]. A re-analysis (meta-analysis) of the results of the clinical trials confirmed the above findings.

2. GARLIC contributes to maintaining intestinal microbiological balance and protection against harmful bacteria and microorganisms:

In the Middle Ages garlic was used to prevent contagious diseases. According to several accounts, it could be successfully used in preventing the plague.

The *efficacy of its active agents against pathogens*[5] has been proven in several experiments. Due to the proven antibacterial effect of sulphur-containing compounds, in theory, it could be used in *the eradication of Helicobacter pylori infections*.[6] [7]

HUMAN STUDIES
Among the cardiovascular effects of garlic, *the slowing of atherosclerosis, the lowering of cholesterol level and blood pressure*[8] have been supported by clinical trials.

The regular, scheduled intake of garlic *reduces the level of LDL cholesterol in the blood responsible for the damage of blood vessel walls*[9] [10] and is thus used to slow down the development of *atherosclerosis.*

Taking garlic also slowed down the growth of plaques typical in atherosclerosis.

The risk of developing stomach and colon tumours is lower[11] in people who consume a high amount of garlic.

It also has a positive effect in the supplementary treatment of gastrointestinal ulcers.

Efficacy against respiratory infections has been proven in a modern clinical trial[12]. According to a study, the prolonged preventive intake of garlic significantly reduced the risk of respiratory infections.

The severity of the infection caused by the 2019 coronavirus (COVID-19) varies within a wide range, from an asymptomatic course of the disease to the development of a severe acute respiratory infection. A fever, a dry cough, shortness of breath, muscle pain, fatigue, the loss of appetite, disturbances in smell and taste are the most common general symptoms. This condition is characterized by a reduction in the number of immune cells and an increase of inflammatory cytokines. The compounds in Allium sativum (garlic) are capable of diminishing the impact of inflammatory cytokines and bringing

immunological disorders to a more acceptable level. Allium sativum is a beneficial preventive measure prior to SARS-CoV-2 infection. Allium sativum is a functional food that is well known for its immunological, anti-pathogenic, anti-inflammatory, antimutagenic and antineoplastic qualities. Its antiviral effect has also been proven. Certain parts of this plant have been found to be effective against unicellular parasites. It appears to restore most of the immune system disfunctions observed in patients with COVID-19 infection and stops the cytokine storm.

In conclusion, it can be stated that *Allium sativum may be an acceptable preventive measure against COVID-19 infection by boosting immune system cells and suppressing the production and secretion of inflammatory cytokines and the inflammatory adipose-derived leptin hormone*. [13]

3. KING OF BITTERS supports the body's natural defences, especially in the upper respiratory tract:

The efficacy of the plant's extract against various pathogens (*E. coli, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, B. subtilis, Candida albicans) and its anti-inflammatory, immunomodulant*[14] [15] and antispasmodic qualities have been experimentally proven.

It has also been proven to have a hepatoprotective and antioxidant[16] *function internally*, while local application has demonstrated wound healing qualities.

Computer modelling has shown that the andrographolide of the plant is able to bind to the protease of the Sars-Cov-2 virus, thereby inhibiting its growth[17] [18]. *Andrographolide enhances T cell cytotoxicity, NK cell function, phagocytosis, and antibody-dependent cellular* cytotoxicity[19]. *Through these bioactivities it is able to inhibit the growth of several viruses (hepatitis C and B, HIV, EBV, CHIKV)*[20].

HUMAN STUDIES:
In a meta-analysis the efficacy of Andrographis *in treating colds*[21] was analysed based on data from over 7000 patients. The results indicate that it *relieves cough, soreness of the throat, the symptoms of cold and accelerates recovery* when compared to a placebo. [22] [23]

Andrographis has been clinically proven to *reduce the pain caused by the arthritis of the knee*[24] compared to placebo.

As a supplementary treatment, it *alleviates the symptoms of colitis ulcerosa.*[25] [26]

Its prolonged use, according to a study, reduces high blood fat level.[27]

It displays significant potential in the treatment of diseases affecting the central nervous system, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, chronic stress disorders, anxiety and depression.[28]

The anti-inflammatory effects of the active agents of Andrographis (andrographolide, a diterpenoid) has been tested under various conditions, for example in cases of ischemia, pyrogenesis, arthritis, liver or nerve toxicity, *malignancies and oxidative stress. It inhibits the growth of viruses and diseases caused by viruses.* [29]

4. WHITE HOREHOUND supports the intestinal tract, contributes to healthy digestion and to proper liver and bile function:

Its *appetite enhancing and digestion stimulating effect*[30] is related to its bitter substance content. Bitter taste improves appetite reflexively and supports digestion by increasing the secretion of digestive fluids.

Its anti-inflammatory, antispasmodic, hypotensive and hypoglycaemic effects[31] [32] [33] [34] *are supported by animal experiment data.*

Its efficacy as an immunomodulant has been demonstrated on animals infected by *Salmonella typhimurium.*[35]

It has shown an antimicrobial effect against several pathogens (Gram + bacteria, fungi, parasites such as Toxoplasma gondii, Trichomonas vaginalis and Plasmodium berghei, E. Coli)[36] [37] *under laboratory conditions.*

It has showed an antiviral effect against the herpes virus. [38] [39]

HUMAN STUDIES
No modern clinical trials have been done with white horehound, *its main areas of application (alleviation of cough and digestive complaints, improvement of appetite) are supported by experience gained through traditional use.* [40]

5. **TURMERIC + PIPERINE supports the immune system, lung and respiratory health. It provides protection against allergies and has a significant antioxidant function.**

Turmeric also has an effect of increasing bile production and contracting the gallbladder. [41] The antispasmodic effect of its extract contributes to its efficacy in alleviating digestive disorders. [42] Turmeric extract decreases triglyceride levels, which can be partly explained by increased bile production. [43]

The cholesterol-reducing effect of turmeric has been proven in several clinical trials and in their meta-analysis. [44]

The anti-inflammatory effect of curcuminoids has been confirmed by the positive results of several human trials, their consumption alleviated joint pains. [45] Several clinical trials have indicated that curcumin – presumably due to its anti-inflammatory function – relieves the symptoms of ulcerative colitis. [46]

Curcumin, the active substance in turmeric*, displayed an antiviral effect against various viruses (hepatitis, Zika, Chikungunya, HIV, HPV, herpes and influenza viruses). In experiments it inhibited the growth of the SARS-CoV corona virus (by inhibiting DNA polymerase and protein kinase).* [47] [48] Furthermore, it modulates the inflammatory process triggered by the virus infection and by inhibiting ACE2, it impedes the entrance of the viruses into the cells. Through its immunomodulant and anti-inflammatory effect, it can theoretically be useful in cases of cytokine storm and may reduce damage to the cells. Its impact on coagulation, theoretically, may also prove useful as in some Covid patients disseminated coagulation occurs. *[49]*

6. **BILE ACIDS reduce digestive and biliary complaints caused by bile deficiency thus significantly supporting the weakened immune system. They also neutralize endotoxins released from the necrosed cell walls of Gram-negative bacteria that are the cause of numerous diseases. Bile acids inhibit the spread of several strains of viruses (influenza, corona, hepatitis, herpes/Epstein-Barr[50], HIV, EBOLA) by preventing virions from biding to the membrane of host cells, thus impeding the production of viruses, but they also break down the virion-host cell bond in viruses already produced:**

6.1. **THE ROLE OF BILE ACIDS IN DIGESTION AND THE LACK OF THEM AFTER GALL BLADDER SURGERY (bile deficiency states)**

If bile secretion, bile production or the enterohepatic circulation are insufficient **(resulting in bile deficiency that occurs in 25 % of people**), then the breakdown and the digestion of fats will not be correct. ***This can be favourably influenced by the administration of bile acids at mealtimes.***

After cholecystectomy, storage function of the gall bladder is lost. The bile continuously trickles, so, <u>if there is a higher demand for bile (when having a meal containing a larger amount of fat), there is not any bile to release because of the lack of the bladder. So, the fats are not completely digested (fat metabolism disorder)</u>, and when it is getting into the colon, the intestinal flora eliminates the indigestible parts along with gas formation, causing abdominal bloating, possibly diarrhoea. Occasionally occurring meal-related bile deficiency, caused by gall bladder surgery, can favourably influenced by administration of bile acids.

6.2. **NATURAL IMMUNITY. „The Role of Bile Acids in Physico-Chemical Host Defence"**[51,52]. Bile acids regulate immunity, according to the latest international research, immunity depends on bile acids.

„The important effect of bile acids, what we have discovered (since then others have confirmed the results of our studies) is the special protection of the human body, expressing itself in the bowel system.

In connection with this investigation, we found out in 1969 that the absorption (translocation) of endotoxins from the intestinal tract is caused by bile acid deficiency. However, in natural conditions, bile acids protect the human body against endotoxins that are always present in the intestines, because they split them into nontoxic parts. It turned out that this defence protects against all agents with lipoid (lipoproteid) structure (e.g. enveloped viruses, so called large viruses). The virus of yellow fever and other athropod borne viruses (Flaviviridae-family according to present taxonomy) are inactivated.

We named this protection system, based on the surfactant (detergent) effect of bile acids „physico-chemical host defence" (Bertók, 2002). Weaker or stronger endotoxemia due to bile deficiency may play a role in several forms of the disease, such as septic shock, renal insufficiency in patients with jaundice due to bile duct obstruction, intestinal ischemia, burn shock, radiation sickness, certain endocrine disorders, psoriasis, or the development of atherosclerosis. All of the effects that damage the intestinal mucosa have been shown to reduce or prevent altogether the production of a peptide, cholecystokinin (CCK), in the absence of which the gallbladder cannot empty the bile into the gut and, in its partial absence, endotoxins produced by the disintegration of bacteria may be "absorbed" and reach the circulation causing endotoxemia, or – in more severe cases – shock.

It can be concluded that „physico-chemical host defence", that based on the surface-active property of bile acids is a general defence mechanism of the human body, which is not confined to bacterial endotoxins but refers to all the "agents" (such as some viruses) having lipoid (peplos) or lipoprotein structure on their surface. Therefore, we can add „physico-chemical host

defence" to the line-up of general defence mechanisms of the human body, which trustees are bile acids, produced in the liver and taking part in the enterohepatic circulation."

6.3. **STRESS: The negative effects of stress on bile production and on bile secretion can be reduced by bile acids** [53]

„Stress is a characteristic group of symptoms manifested by the body's response to any harmful (physical or psychological) stimuli, especially in women with more sensitive nervous systems.

It cannot be ignored that **stress is a major influence on the whole digestive system, so that on bile production and secretion too (the muscular valve controlling the flow of bile, the so called sphincter of Oddi, does not open) Disorders of bile production and secretion reduce or suspend one of the important protective mechanisms of the human body, the "physico-chemical host defence" based on the surface-active (detergent) effect of bile acids, without which the body will become exposed to the attack of some of the toxins in the gut (e.g. endotoxins) and to so-called large viruses (such as the herpes family)"**

6.4. **Chenodeoxycholic Acid from Bile Inhibits Influenza A Virus Replication** via Blocking Nuclear Export of Viral Ribonucleoprotein Complexes[54]

ABSTRACT: Influenza A virus (IAV) infection is still a major global threat for humans, especially for the risk groups: young children and the elderly. **Chenodeoxycholic acid (CDCA), one of the main primary bile acids, is synthesized from cholesterol in the liver and classically functions in emulsification and absorption of dietary fats. Clinically, CDCA has been used in the treatment of patients with cholesterol gallstones for more than five decades. In this study, we showed that CDCA attenuated the replication of three subtypes of influenza A virus, including a highly pathogenic H5N1 strain. Mechanistically, CDCA effectively restrained the nuclear export of viral ribonucleoprotein (vRNP) complexes. In conclusion, as an endogenous physiological small molecule, CDCA can inhibit IAV replication in vitro, at least in part, by blocking vRNP nuclear export, and affords further studies for development as a potential antiviral agent against IAV infections.**

6.5. **Natural small molecules as inhibitors of coronavirus lipid-dependent attachment to host cells: a possible strategy for reducing SARS-COV-2 infectivity**[55]

Viral infectivity depends on interactions between components of the host cell plasma membrane and the virus envelope.

Methods and Results: We focus on the role of lipid structures, such as lipid rafts and cholesterol, involved in the process, mediated by endocytosis, by which viruses attach to and infect cells. Previous studies have shown that many naturally derived substances, such as cyclodextrin and sterols, could reduce the infectivity of many types of viruses, including the coronavirus family, through interference with lipid-dependent attachment to human host cells.

Conclusion: Certain molecules prove able to reduce the infectivity of some coronaviruses, possibly by inhibiting viral lipid-dependent attachment to host cells.

6.6. **Can natural detergent properties of bile acids be used beneficially in tackling coronavirus disease-19?**

The virus usually affects the respiratory tract, causing an illness that may range from mild affection to severe acute respiratory symptoms leading to death.

The lipid layer in enveloped viruses is believed not only to protect its genome but also, help in its invasion into the cell. Also, these viruses are believed to be more sensitive to environmental stressors like high temperature (>70°C), extremes of pH, etc. Their nucleic acid, proteins and lipids are supposed to be held together by non-covalent interactions that are broken by soap or detergent thus destroying the virus.

While high concentrations of bile acids can cause lysis of the cell membrane, at lower doses, they have been found to facilitate delivery of drugs (Amphotericin B and Resveratrol) into the cells. Due to their potential pharmaceutical applications, extensive efforts are being directed into synthesis of bile acids and their derivatives with improved carrier properties. Nowadays, cholic acid obtained from bovine source is used as a precursor for its synthesis.

6.6.1. The following attributes may make bile acids suitable for SARS-CoV-2 targeting[56]:

First, the bile acids have been proposed to possess anti-inflammatory properties that may prove beneficial in curbing the cytokine storm believed to be involved in the pathogenicity of the virus.

Previous studies have shown that bile acids can incorporate themselves in between the membrane lipids thus altering their distribution and also the function of proteins attached to them. In our preliminary work on chenodeoxycholic and ursodeoxycholic acid, the above bile acids were found to bind with receptor binding domain of S-glycoprotein of SARS-CoV-2. This shows that bile acids have the potential to bind to SARS-CoV-2.

Whether or not the bile acids can strip SARS-CoV-2 of its envelope by targeting its lipoprotein components, thus, destroying it completely remains interesting (though wishful thinking as of now) arena to explore. A possible, although weak clue in favour of their protective role in SARS-CoV-2 infection may be that in the intestine the virus is less active due to the presence of bile acids.

Thus, whether naturally acting detergents like bile acids/salts can help in stripping off the envelope of SARS-CoV-2 thereby disrupting its assembly is a million-dollar question.

6.7. **A Viral Entry of Hepatitis B and D Viruses and Bile Salts Transportation Share Common Molecular Determinants on Sodium Taurocholate Cotransporting Polypeptide**[57]

ABSTRACT: The liver bile acids transporter sodium taurocholate co-transporting polypeptide (NTCP) is responsible for the majority of sodium-dependent bile salts uptake by hepatocytes. NTCP also functions as a cellular receptor for viral entry of hepatitis B virus (HBV) and hepatitis D virus (HDV) through a specific interaction between NTCP and the pre-S1 domain of HBV large envelope protein. **Mutations of NTCP residues critical for bile salts binding severely impair viral infection by HDV and HBV; to a lesser extent, the residues important for sodium binding also inhibit viral infection.** These results demonstrate that molecular determinants critical for HBV and HDV entry overlap with that for bile salts uptake by NTCP, indicating that viral infection may interfere with the normal function of NTCP, and **bile acids and their derivatives hold the potential for further development into antiviral drugs.**

6.8. **A large-scale, multicentre, double-blind study of ursodeoxycholic acid in patients with chronic hepatitis C**[58]

Background: **We assessed oral ursodeoxycholic acid (UDCA) on serum biomarkers as a possible treatment for interferon non-responders.**

Methods: CH-C patients with elevated alanine aminotransferase (ALT) were assigned randomly to 150 (n=199), 600 (n=200) or 900 mg/day (n=197) UDCA intake for 24 weeks.

Conclusions: **Although changes in ALT and AST did not differ between the 600 and 900 mg/day groups, GGT was significantly lower in the 900 mg/day group.**

6.9. **Inhibitory Effects of Bile Acids and Synthetic Farnesoid X Receptor Agonists on Rotavirus Replication**[59]

ABSTRACT: Rotaviruses (group A rotaviruses) are the most important cause of severe gastroenteritis in infants and children worldwide. Currently, an antiviral drug is not available and information on therapeutic targets for antiviral development is limited for rotavirus infection. **Previously, it was shown that lipid homeostasis is important in rotavirus replication. Farnesoid X receptor (FXR) and its natural ligands bile acids (such as chenodeoxycholic acid [CDCA]) play major roles in cholesterol and lipid homeostasis. The results demonstrate the following.** First, the intracellular contents of triglycerides were significantly increased by rotavirus infection. **Second, CDCA, deoxycholic acid (DCA) significantly reduced rotavirus replication in cell culture in a dose-dependent manner. We conclude that bile acids play important roles in the suppression of rotavirus replication.** The inhibition mechanism is proposed to be the downregulation of lipid synthesis induced by rotavirus infection.

6.10. **Bile Acids Act as Soluble Host Restriction Factors Limiting Cytomegalovirus Replication in Hepatocytes**[60]

ABSTRACT: The liver constitutes a prime site of cytomegalovirus (CMV) replication and latency. Hepatocytes produce, secrete, and recycle a chemically diverse set of bile acids, with the result that interactions between bile acids and cytomegalovirus inevitably occur.

IMPORTANCE: Cytomegaloviruses are members of the Betaherpesvirinae subfamily. Primary infection leads to latency, from which cytomegaloviruses can reactivate under immunocompromised conditions and cause severe disease manifestations, including hepatitis. **The present study describes an unanticipated antiviral activity of conjugated bile acids on MCMV replication in hepatocytes. Bile acids negatively influence viral transcription and exhibit a global effect on translation. Our data identify bile acids as site-specific soluble host restriction factors against MCMV**, which may allow rational design of anti-cytomegalovirus drugs using bile acids as lead compounds.

6.11. **Bile Acid Metabolism and Signalling**[61]

ABSTRACT: Bile acids are important physiological agents for intestinal nutrient absorption and biliary secretion of lipids, toxic metabolites, and xenobiotics. Enterohepatic circulation of bile acids from the liver to intestine and back to the liver plays a central role in nutrient absorption and distribution, and metabolic regulation and homeostasis. **Disorders in bile acid metabolism cause cholestatic liver diseases, dyslipidaemia, fatty liver diseases, cardiovascular diseases, and diabetes. Bile acids, bile acid derivatives, and bile acid sequestrants are therapeutic agents for treating chronic liver diseases, obesity, and diabetes in humans.**

6.12. **New directions in the treatment of bile acid disorders: New directions in the treatment of bile acid disorders, including acute pancreatitis, Barrett's oesophagus and colon cancer, were presented by dr. Professor Péter Hegyi, who recently reported on this with his fellow researchers in the journal Physiological Reviews.**[62]

If the composition, microbiology or route of bile changes, it can lead to the development of serious diseases.

The scientific article also identified about ten drug "points of attack" to which the development of drugs can restore the normal circulation and composition of bile acids. This can reduce the chances of developing the disease and the severity of the pre-existing condition.

6.13. **Antiviral immunity: a link to bile acids**[63]

A recent study describes a novel function of intracellular bile acids (BAs), a class of cholesterol-derived metabolites, which activate several key innate antiviral signalling components through the TGR5-β-arrestin-SRC pathway to potentiate antiviral immunity. This finding adds a new metabolic regulatory dimension of innate antiviral response and provides a new antiviral strategy by supplementing BAs.

6.14. **The Immunomodulatory Role of Bile Acids**[64]

ABSTRACT: Enzymatic oxidation of cholesterol generates numerous distinct bile acids which function both as detergents that facilitate the digestion and absorption of dietary lipids and as hormones that activate five distinct receptors. Activation of these receptors alters gene expression in multiple tissues, leading to changes not only in bile acid metabolism but also in glucose homeostasis, lipid and lipoprotein metabolism, energy expenditure, intestinal motility, bacterial growth, inflammation, and in the liver-gut axis. This review focuses on the present knowledge regarding the physiologic and pathologic role of bile acids and their immunomodulatory role, with particular attention to bacterial lipopolysaccharides (endotoxins) and bile acid and immunological disorders. The specific role that bile acids play in the regulation of innate immunity, various systemic inflammations, inflammatory bowel diseases, allergy, psoriasis, cholestasis, obesity, metabolic syndrome, alcoholic liver disease, and colon cancer will be reviewed.

6.15. **Bile acids against Herpes/Epstein-Barr (EBV) virus**[65]

In the United States, about half of all five-year-old children and about 90% of adults have evidence of previous infection.[66] It is also associated with various non-malignant, premalignant, and malignant lymphoproliferative diseases. The EBV surrounded by an envelope containing lipids and surface projections of glycoproteins. The detergent effect of bile acids in the digestion tract and blood circulation helps in stripping off the envelope by preventing virions from biding to the membrane of host cells, thus impeding the production of viruses, but they also break down the virion-host cell bond in viruses already produced [67, 68].

6.16. **Gram negative sepsis and shock**[69]

In the modern hospital gram negative bacteraemia and the associated condition of septic shock are common occurrences. In the United States the estimated incidence of gram-negative bacteraemia ranges from 71,000 to 330,000 cases annually. Fatalities attributed to this disease are between 18,000 and 132,000 each year. Sepsis is defined as a systemic disease caused by microorganisms or their products in the blood. Gram negative bacteraemia in the critically ill patient is synonymous with gram negative sepsis. Septic shock is a clinical syndrome characterized by circulatory insufficiency and inadequate tissue perfusion. **Septic shock is associated primarily although not exclusively with gram negative bacilli. The underlying illness of the patient is the primary factor determining the outcome of an episode of gram-negative bacteraemia.** Patients with a life-threatening disorder have a very poor prognosis, while sepsis in a previously healthy person carries a good prognosis. **The overall mortality in gram negative bacteraemia is 25%. When septic shock develops, the mortality increases to 50-60%.**

In addition, the authors found that the mortality of multi-resistant Gram-negative blood-stream infections was higher compared to that caused by non-multi-resistant bacteria. The active agents in garlic, white horehound and bile acids, due to their antibacterial effect, can be used effectively against Gram-negative bacteria that cause the majority of nosocomial infections!

6.17. **COVID-19: Is There Evidence for the Use of Herbal Medicines as Adjuvant Symptomatic Therapy?**[70]

Background: Current recommendations for the self-management of SARS-Cov-2 disease (COVID-19) include self-isolation, rest, hydration, and the use of NSAID in case of high fever only. It is expected that many patients will add other symptomatic/adjuvant treatments, such as herbal medicines.

Aims: To provide a benefits/risks assessment of selected herbal medicines traditionally indicated for “respiratory diseases” within the current frame of the COVID-19 pandemic as an adjuvant treatment.

Method: The plant selection was primarily based on species listed by the WHO and EMA, but some other herbal remedies were considered due to their widespread use in respiratory conditions. These were evaluated according to a modified PrOACT-URL method with paracetamol, ibuprofen, and codeine as reference drugs. The benefits/risks balance of the treatments was classified as positive, promising, negative, and unknown.

Results: A total of 39 herbal medicines were identified as very likely to appeal to the COVID-19 patient. According to our method, the benefits/risks assessment of the herbal medicines was found to be positive in 5 cases (Althaea officinalis, Commiphora molmol, Glycyrrhiza glabra, Hedera helix, and Sambucus nigra), promising in 12 cases (Allium sativum, Andrographis paniculata, Echinacea angustifolia, Echinacea purpurea, Eucalyptus globulus essential oil, Justicia pectoralis, Magnolia officinalis, Mikania glomerata, Pelargonium sidoides, Pimpinella anisum, Salix sp, Zingiber officinale), and unknown for the rest.

Conclusions: Our work suggests that several herbal medicines have safety margins superior to those of reference drugs and enough levels of evidence to start a clinical discussion about their potential use as adjuvants in the treatment of early/mild common flu in otherwise healthy adults within the context of COVID-19. While these herbal medicines will not cure or prevent the flu, they may both improve general patient well-being and offer them an opportunity to personalize the therapeutic approaches.

This document can also be found on the next link available on the product website with nearly 70 references: www.professional-literature.antibacvir.eu

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