



GRAPEFRUIT SEED EXTRACT ANTIBACTERIAL AND ANTIVIRAL ACTIVITY

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Abstract: Corona's misfortune is affecting the whole world. It causes fatal respiratory diseases and threatens public safety and human health. Scientists are scrambling to find effective drugs against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). Dietary supplements to treat coronavirus are a large area of scientific research. Grapefruit (GF) (Rutaceae) A subtropical fruit with strong bioactivity. Natural Grapefruit Seed Extract (GFSE) has proven beneficial healing properties effect. The purpose of this review is to collect published studies demonstrating antibacterial, antifungal, and antiviral activity. GFSE and its bioactive components, and their ability to inhibit SARS-CoV-2 activity. GFSE pair Gram-positive bacteria (Enterococcus and Staphylococcus) and Gram-negative bacteria (Escherichia coli and Pseudomonas) Pseudomonas aeruginosa). In addition, it exhibits a zone of inhibition against multidrug-resistant (MDR) bacteria. The antiviral activity of GFSE Nasal Spray turned out to be resistant to the new coronavirus. the anti-coronavirus potential of key components of GFSE such as naringenin, Resveratrol, limonin, and hesperidin have also been tried. In conclusion, additional clinical and in vivo studies are needed. GFSE (spray or syrup) is effective against SARS-CoV-2.

Keywords: Corona, Anti-viral, grapefruit, seed extract, anti-bacterial

INTRODUCTION

Coronaviruses are a group of different viruses that cause mild severe respiratory infections in humans; cause It is a deadly respiratory disease and a threat to public safety. SARS-CoV-2 impacts global health systems, I've never seen one. search effect Treatments and vaccines against SARS-CoV-2 are essential A challenge for humanity. lots of research going on Identify potential therapies to reduce the SARS-CoV-2 pandemic. natural remedies are safe A low-cost platform to make new and effective medicines Helping treat SARS-CoV-2 while reducing negativity Results.

Grapefruit (GF) Rutaceae (Citrus paradisi) Subtropical fruit. the second most important member of Citrus around the world. In some countries, GF has been used as an antifungal agent in traditional medicine, Antibacterial, antibacterial, antiviral, and anti-inflammatory Agent. cancer prevention, cleanliness, Detoxification and cell regeneration have been demonstrated. Also, grapefruit seed extract (GFSE) has potential. antiviral. Citrus Seed Extract or GFSE is Pulp liquid, seeds and remaining white film After squeezing the grapefruit juice. this fruit is

abundant in Valuable nutrients such as phytochemicals and fibre pectin. that pink and red indicate high levels of Antioxidants such as lycopene. GFSE is rich in ascorbic acid acids, tocopherols, flavonoids, limonin, citric acid, sterols, and many biochemical compounds. mainly flavonoids limonoids such as narirutin, limonin, and naringin Naringenin, hesperidin, resveratrol Grapefruit seeds. These substances help the antioxidant power of GFSE and the Prevention of chronic diseases such as diabetes and heart disease. disease and malignancy. PV consumption It has also been shown to aid weight loss and increase lipid metabolism. In folk medicine, GFSE is used to treat urinary tract disorders. Infections, gastrointestinal disorders, ulcers. Traditionally, grapefruit residue was fed to cattle, pigs, and these animals were found to be less infected. GFSE was developed as a non-toxic antibacterial spray for Fruits and vegetables. In addition, GFSE has Antibacterial against a wide range of foodborne bacteria infections. After being approved as a safe supplement, GFSE was advertised as a disease-modifying diet for Bacterial, viral and fungal infections in humans. This review is GFSE and the antiviral, antifungal and antibacterial effects of Its Active Ingredients, Excluding Compiled Studies on its anti-SARS-CoV-2 activity.

GFSE against bacteria and mushrooms

Multi-resistant (MDR) bacteria are It is believed to be resistant to antibiotics such as penicillin. Bacteria are resistant to cephalosporins and methicillin. In general, if a patient is infected with MDR bacteria, health tends to deteriorate and mortality is higher than that if It infects susceptible bacteria. looking for something new Natural substances targeting MDR bacteria are increasingly important. GFSE antibacterial effect is Shown to exhibit a zone of inhibition against MDR Bacteria that passed the disk diffusion test Contains a lot of naringin flavonoid, sour taste and pH properties of GFSE.

An initial study published in 1990 found 794 commercially available GFSE cash Types of bacteria and 93 strains of fungi. Checked the Antibacterial and antifungal effects of over-the-counter medications GFSE (triclosan, benzethonium chloride, benzalkonium chloride). This article features two open tags Trials in people with gastrointestinal disorders and serious illnesses Atopic eczema. In the first experiment, 10 patients received GFSE. (0.05% aqueous solution 200ml) 2 times a day 1 time Moon. Studies show no big changes in the faecal microbiome test; Furthermore, only 2 out of 10 patients' Gastrointestinal symptoms improved. Existence In a second trial, 15 patients received GFSE 50 mg capsules. 3 times a day for 4 weeks. data visualization GSFE exhibited high antibiotic activity against three drugs Pathogenic intestinal flora (Candida, Geotrichum, hemolytic E. coli) and three others with minimal activity (Lactobacillus, Staphylococcus aureus, aerobic spore-forming bacteria) I found out that GSFE doesn't show anything. Bifidobacterium and Klebsiella spp. Subjectively, all The patient says that their gastrointestinal problems have improved with No side effects.

In 2001, a survey was conducted to measure. Effect of GFSE on the growth of the yeast-like strain Candida albicans. East The study included 200 strains of C. Albicans and 5 subjects isolated from patients with various symptoms of candidiasis Ontogenesis, 12 cases were from patients with Dermatophytes and moulds. Proven Candida susceptibility Use a serial dilution method. GFSE solution 33% seems right for Yeast-like strains, but dermatophytes and Fungi. In 2002, GFSE proved its effectiveness. Targets 67 Gram-negative and Gram-positive biotypes bacteria.

Cvetnić and Vladimir-Knezevic examined alcohol GFSE on 20 bacterial strains and 10 yeast strains using agar Assay and broth dilution test. In the broth dilution test, The extract is effective against all microorganisms. nevertheless, Effective only against yeast and Gram-positive bacteria in the concentration range of 4.13% to 4.13% 16.5% (m/v).

In another study, under electron microscopy, the GFSE is known to disrupt bacterial cell membranes. this is considered Quaternary ammonium salt sterilization technology GFSE composite. In addition, GFSE has Effective against established Borrelia in vitro Systemic Borrelia burgdorferi, the bacterium that causes Lyme

borreliosis illness. The antibacterial effect of GFSE is Due to its active compounds hesperidin, naringenin, etc. Citrus flavonoids.

The antibacterial effect of GFSE aqueous solution in Proteus Staphylococcus Vulgaris, Staphylococcus aureus, Candida albicans, and Klebsiella pneumonia was high, but ethanol GFSE has a low antibacterial effect. In another study, Grapefruit seeds are extracted with 70% ethanol, It is used to produce microbial extract at 33% (p/v) Test. Extract validated against 20 bacteria and yeast by the agar diffusion method. sample Maximum antibacterial activity against Salmonella Enteritidis.

Choi et al. Evaluation of the antibacterial effect of GFSE against a variety of foodborne pathogens, such as Pseudomonas aeruginosa, Candida albicans, and Escherichia coli. East, As a result, the concentrations were found to be 0.1% and 0.2%. GFSE has demonstrated the ability to combat these microbes. East The antibacterial properties of GFSE are due to its Effects on inhibition of active transport and glycolysis, causing inactivation and destruction of microbial growth Bacterial cell membrane.

The inhibitory effect of GFSE nebulization on Salmonella in infants and E. coli was also reviewed. Inactivation of GFSEx1000 Detects salmonella and E. coli in babies in 5 seconds. research GFSE proposed as a promising new disinfectant bacteria.

GFSE demonstrates the antibacterial effect in disk diffusion test Multi-resistant bacteria (vancomycinDrug-resistant Staphylococcus aureus and methicillin-resistant Staphylococcus aureus). Minimum for the microdilution Inhibitory concentration (MIC) test, GFSE showed Antibacterial activity even at the lowest doses.

In their study, Ignacio and Thai investigated. Natural GFSE inhibitor, antifungal activity of tea tree oil, Garlic and probiotic supernatants compared with miconazole Candida albicans nitrate. GFSE had the highest performance Anti-Candida effects on natural inhibitors Tested at 100-120 $\mu\text{g mL}^{-1}$, reducing the Growth rate of less than 0.02 hr⁻¹.

Recently, the antifungal properties of GFSE treatment have been Studied on the structure of fungal spore cells. Transmission electron microscope. GFSEpresents Antifungal action by destroying cell membranes and thick membranes It forms spore cells and loses spore content.

In vitro and in vivo, researchers have the Characterization of Helicobacter pylori with GFSE alone and in combination with Lactobacillus Plantarum (pH 3A) and Glyceryl monolaurate in vitro. According to their results, the monolaurate And GFSE at least suppressed the growth of Helicobacter pylori The inhibitory concentration (MIC) was 62.5 ppm. in vitro, l. plantalum pH 3A reduces Helicobacter pylori infection. Synergistically tested with glyceryl monolaurate, GFSE, but only L. plantalum pH 3A was inhibited in vivo Helicobacter pylori infection.

GFSE antiviral activity

Chinsebu *et al.* reported that 6,7-dihydroxy bergamottin from GF extract improves the bioavailability of HIV protease inhibitors through the 3A4 P450 isoenzyme intestine and liver. The avian influenza virus (AIV) is a pathogen virus. chlorine, basic or cationic The disinfectant is the recommended disinfectant for AIV. However, these medications may not be suitable and may be harmful to human and animal skin and mucous membranes. GFSE is a potentially new and safe virus disinfectant. Previous studies have shown that GFSE does. Newcastle disease virus (NDV) and AIV.

GFSE's antiviral active ingredient is Unconfirmed; however, aglycones such as flavonoid glycosides, limonin, quercetin, naringin, hesperidin, apigenin, Kaempferol and saturated or unsaturated fatty acids are GFSE components with potential antiviral activity.

Another study showed that it contained GFSE. antiviral compounds such as high levels of polyphenols, deacetylnomylin, bioflavonoids, obacnon, deacetylnomylic acid, Tomlin, nomadic acid, 17-βD-glucopyranoside limonoid.

Contains a 0.25% disinfectant spray that kills viruses. GFSE is evaluated against AIV. spray dilution Mix several times and add to the AIV suspension (2.5 mL). return 30 minutes, inactivated fetal calf serum (2.5ml 10%) Add to neutralize the solution. 0.2ml/ Each dilution was injected into the allantoic cavity of 5 chickens. (10 days old). The viability of the AIV in embryos is After 5 days of post-hatch evaluation Hemagglutination titer. In their research, they found AIV pathogen control titer greater than 6.1 log₁₀ EID₅₀/mL does not cause damage to the embryo. these are the result, GFSE has potent virucidal activity against AIV.

Komura et al. We investigated the inhibitory activity of GFSE Spread of Infectious Avian Influenza Virus, Bursal Disease Virus, and Newcastle Disease Virus diseased virus GFSE diluted (100, 500 and 1000 in distillate water) is effective. GFSEx100 reduces 2 birds' Viral titers for influenza and Newcastle disease. The virus is highly resistant to GFSE. This study is based on the GFSE As a promising new antiviral disinfectant, short contact time is effective on contaminated tissue, and spray foam Compared to other disinfectants, GFSE is some advantages GFSE is not volatile or flammable compared to alcohol-based sanitisers. GFSE is also non-toxic on the skin and mucous membranes of humans and animals Countermeasures for dependence on aldehydes, alkalis and phenols disinfectant. GFSE is also low odour and odourless. It is corrosive and does not stain clothes.

Antiviral effects of GFSE against SARS-CoV-2

Human enteroviruses such as Hepatitis A Virus Inc. (HM175) and surrogate viruses (murine norovirus, feline calicivirus and bacteriophage MS2) It is reduced by treatment with GFSE at room temperature. A recently published study found that it has six biological activities GFSE compounds (naringenin, naringin, naringin, citric acid, ascorbic acid, limonin) inhibit the main pathways of SARS-CoV-2. Mpro protease compared to acetoside, remdesivir and gall acid.

Scientists have discovered that the nose may be the main channel main replication site of SARS-CoV-2; In addition, the mode of transport of drops found that it works. The researchers hypothesized including GFSE, Xylitol, known as Xlear nasal spray, can be used as Complementary therapy for Covid-19. In a recently published study, Three symptomatic patients of Covid-19 with mild to moderate risk receiving concomitant intranasal therapy Replenish their current medication. these three patients Take 2 nasal drops every 6 hours. repeat In PCR nasal swab tests, all showed rapid clinical recovery and reduced time to negative. Insecure Problems are discovered during treatment. these results support the idea that the components play an important role in antiviral activity.

Virus-disrupting effect of Xlear nasal spray on SARS CoV-2 is being studied in vitro. two experiments were Implemented to test the effectiveness of Xlear (experimental) a) and reproducible drug inactivation (experiment 2) SARS-CoV-2. SARS-CoV-2, when tested against Xlear Only compounds containing 0.2% GFSE decreased Infectious viruses reach imperceptible levels.

Marano et al. Investigation of the potential impact of GFSE and its main components belonging to the limonoids SARS-CoV-2 infection control classroom with two dual approaches Close to virucidal and antioxidant activity. GCSEs on display Outstanding antioxidant, virucidal and cytoprotective action. Nomilin, obacunone and limenin

work well Against SARS-CoV-2. IC50 between 15 and 31 µg/ml. Limonin GFSE can directly target SARS. It infects CoV-2 and protects host cells from oxidative damage.

Antiviral effects of some active ingredients of GFSE For SARS-Cov-2

Antiviral effects of the grapefruit flavonoid naringenin have been tested against various viruses, including Dengue, Zika, Hepatitis C, Semliki Forest, Chikungunya, yellow fever, herpes simplex 1 and 2, and humans immunodeficiency virus. In vitro studies show Efficacy of naringenin as a pre and post antiviral agent Treatment of infections. Like many natural chemicals, Although naringenin has been extensively studied in vitro, Viral infection models are limited in vivo. one time SARS-CoV-2 infects host cells and is proteolytically processed Release of polypeptides from polyproteins. by proteolysis process, 3-chymotrypsin-like protease (3CLpro) and papain A similar protease (PLpro) is involved. some are unstructured The proteins required for viral replication are 3CLpro when bound to a polyprotein. a possibility Covid-19 treatment may include 3CLpro Inhibitors due to their importance in the viral cycle coronavirus. Studies have shown that flavonoids significantly inhibited the SARS 3CL protease. Naringenin is not a flavonoid, but After investigation, it was found that it can be suppressed through computer analysis. SARS-CoV-2 3CLpro.

According to another study, SARS-CoV-1 and SARS-CoV-2 Show 99.02% genetic similarity to only 12 3CL Promptly modified, Naringenin and many Other flavonoids can inhibit 3CL. Another possibility The approach is to block two ion channels (TPC1 and TPC2). Inhibition of TPC1 and TPC2 reduces intracellular flux. MERS-CoV infection and viral spread. Naringenin is a hydrophilic molecule. Affinity for the plasma membrane, resulting in naringenin It accumulates intracellularly. Consequently, this affinity is In addition to increasing intracellular signalling, Regulation of TPC1 and TPC2.

One of the many active ingredients in GFSE is resveratrol. It is also present in other fruits such as blueberries. Grapes and blueberries. important for resveratrol antiviral properties against RNA viruses, including rhinoviruses; Influenza, Zika virus, Rotavirus, MERS-CoV, and some DNA Viruses such as poxvirus and polyomavirus. Pascual, etc Resveratrol observed in his study shows the antiviral response to SARS-CoV-2, Decrease in HCoV229E (coronavirus family member) cytotoxicity.

Limonoids are tetracyclic triterpenoids that are widely present in plants. citrus. Grapefruit seeds have the highest Large amounts of limonin, limonin, and nomyrin The two most effective components. Another study revealed Possible molecular-based antiviral effects of limonoids Docking and five types of inhibition in silicon ADMET studies SARS-CoV-2 protein. In a recent study, 14 triterpenoids Test compounds for their ability to inhibit the SARS CoV-2 target protein. Limonin was found to inhibit the Transmission and amplification of SARS-CoV-2 primaries Protease (Mpro).

The main functional flavanones identified among the flavonoids are Hesperidin (3,5,7-tri-hydro flavanone 7-rhamnoside). that is Extracted from citrus fruits such as grapefruit and lemon. Hesperidin was confirmed to bind to both cells. protein, angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) Both are necessary for SARS-CoV-2 to enter cells. hesperidin Prevention of SARS-CoV-2 infection by blocking protein S binds to the cell surface receptor ACE2, Expression of ACE2 and TMPRSS2.

CONCLUSION

The antibacterial, antifungal and antiviral properties of GFSE include: This has been established in several previous and current studies. Role of GFSE nose drops in rapid elimination SARS-CoV-2, which has shown a negative rapid PCR test, Recent clinical studies have also shown this. naringenin, resveratrol and hesperidin It

has anti-coronavirus properties. Given the antiviral effects of GFSE, More research is needed to provide more solid information. Evidence of competence in GFSE Treatment against Covid-19.

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