Natural Solutions for Lung Diseases

Dr. Bryan Ardis D.C.

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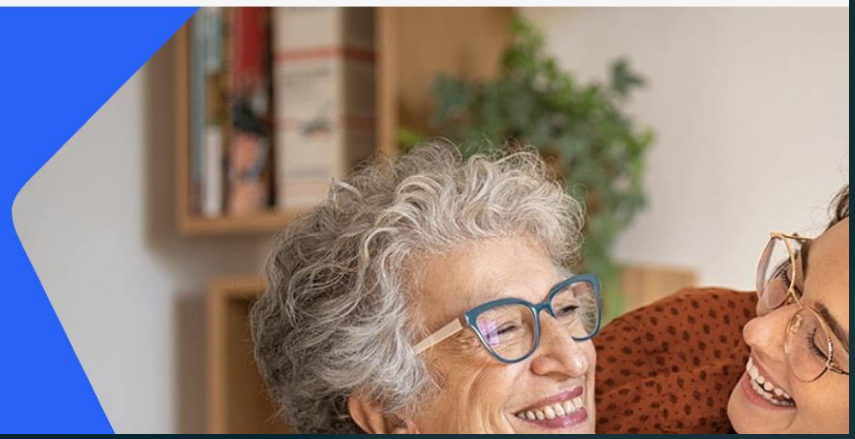
Lung Health & Diseases | Quit Smoking | Clean Air | Research & Reports | Policy & Advocacy | Get Involved | Ways to Give | DONATE

Home > Lung Health & Diseases > Lung Disease Lookup > COPD > Learn About COPD > COPD Awareness Month

COPD Awareness Month

November is COPD Awareness Month. This month is dedicated to raising awareness about chronic obstructive pulmonary disease, a leading cause of death and disability in the United States. You can help.



https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/learn-about-copd/copd-awareness-month

AACR American Association for Cancer Research®

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NOVEMBER IS LUNG CANCER AWARENESS MONTH

JOIN WITH THE AACR TO FIND BETTER WAYS TO PREVENT AND TREAT LUNG CANCER

Lung cancer is the most common cause of cancer death in the United States for both men and women. About 64,190 men and 60,540 women are estimated to die from lung cancer in 2025.

SUPPORT CANCER RESEARCH

https://www.aacr.org/patients-caregivers/awareness-months/lung-cancer-awareness-month/

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American Association for Respiratory Care

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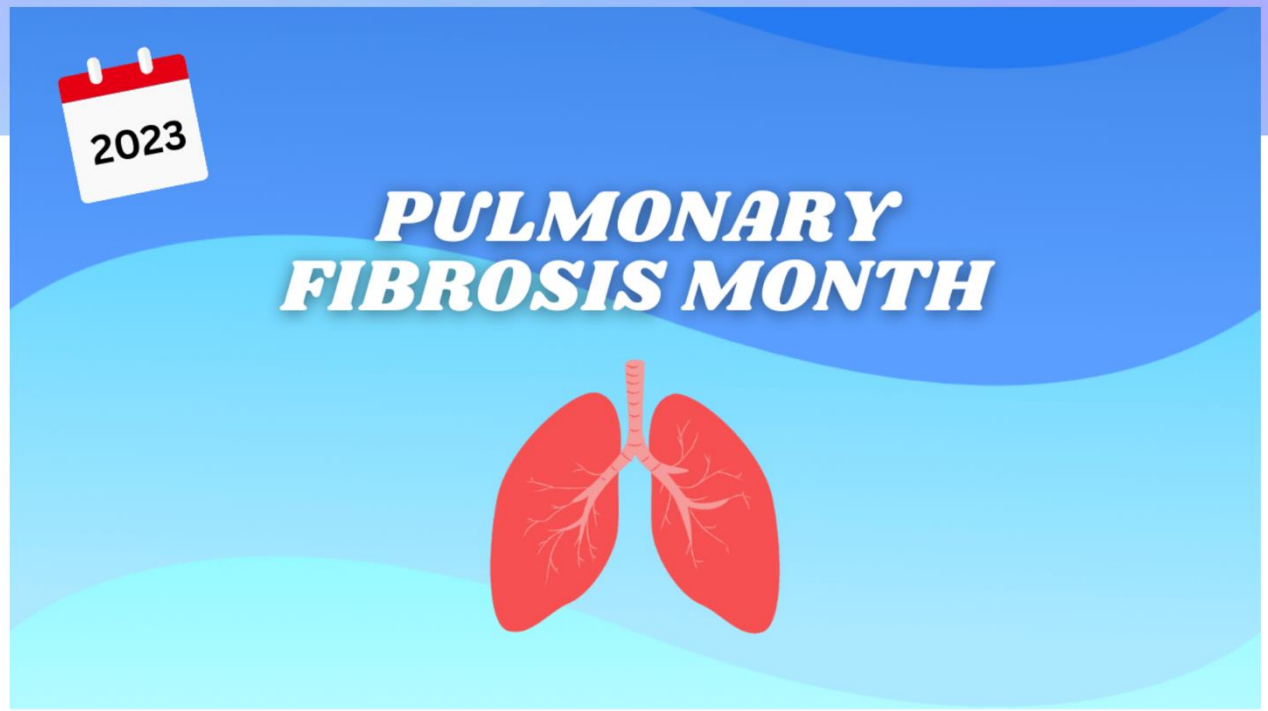
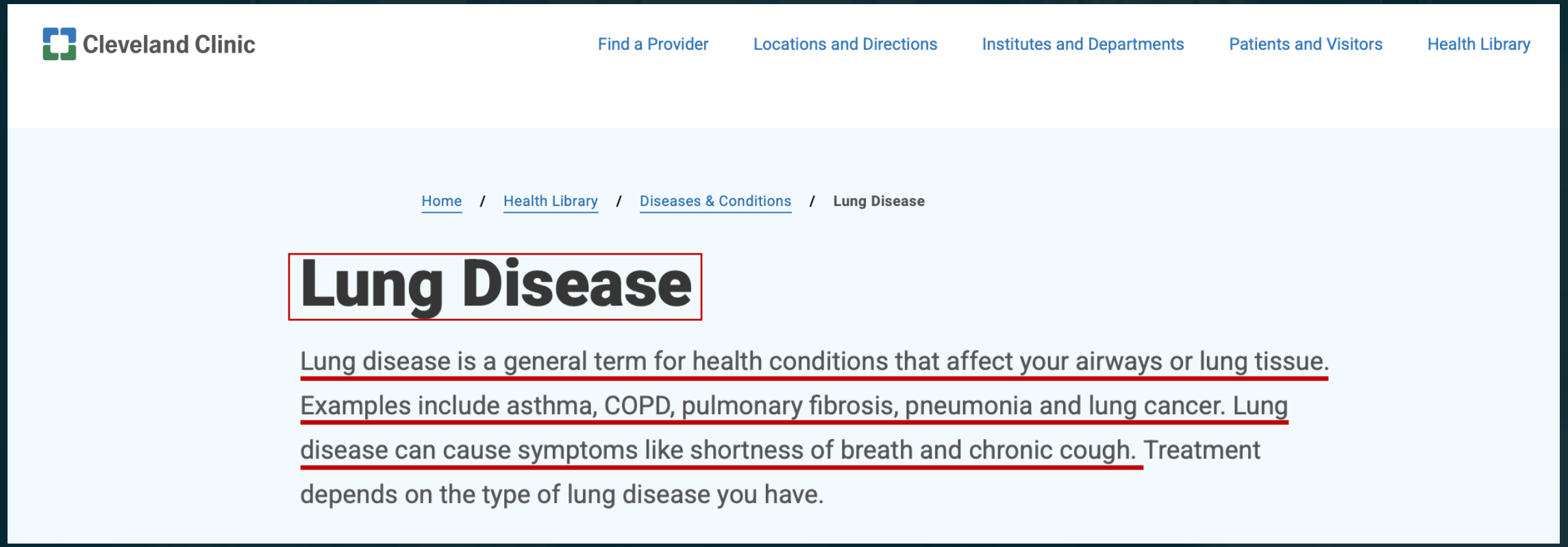
September is Pulmonary Fibrosis Month



PUBLISHED
08/30/2023

https://www.aarc.org/news/an23-september-is-pulmonary-fibrosis-month/ /



https://my.clevelandclinic.org/health/diseases/lung-disease

What Is Lung Disease?

Lung disease is a general term for health conditions that affect your airways (tubes leading into your lungs) or tissue that makes up your lungs. Common lung diseases include asthma and COPD (chronic obstructive pulmonary disease). Cardiovascular diseases that affect your lungs — like pulmonary hypertension and pulmonary embolism — are also sometimes considered lung diseases.

Most lung diseases are long-term (chronic). You may be born with one (like cystic fibrosis) or you might develop one later in life (like COPD). A few lung diseases, like infections, are short-term and can be cured.

https://my.clevelandclinic.org/health/diseases/lung-disease

Types of lung disease

Examples of lung diseases include:

- Asthma, a condition that causes inflammation and narrows your airways
- Bronchiectasis, a condition where your airways widen and form pouches
- COPD (including emphysema), airway damage that makes it hard to breathe
- Cystic fibrosis, a pancreatic disease that affects your lungs
- Infections, like pneumonia and tuberculosis
- Pulmonary fibrosis and other types of interstitial lung disease, conditions that damage your lung tissue and can get worse over time
- Lung cancers, like non-small cell lung cancer, small cell lung cancer and mesothelioma
- Lymphangioleiomyomatosis (LAM), a disease that causes cysts in your lungs

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Lung disease causes

Some causes of lung disease include:

- Smoking
- Germs, like viruses, bacteria and fungi
- Connective tissue and inflammatory diseases, like rheumatoid arthritis (RA), lupus, scleroderma and sarcoidosis
- Inhaling harmful substances, like asbestos and radon
- Allergic reactions to something you inhale (hypersensitivity pneumonitis)
- Certain medications or treatments
- Genetic changes — either that you're born with or that you acquire as you get older

https://my.clevelandclinic.org/health/diseases/lung-disease

Treatments for lung disease

Treatment depends on what type of lung disease you have. Some options could include:

- **Corticosteroids**: Drugs like prednisone can help reduce inflammation in your airways.
- **Inhaled medications**: Bronchodilators and inhaled steroids can reduce inflammation and open your airways.
- **Oxygen therapy**: Your provider will prescribe extra oxygen if you don't have enough getting to your blood or tissues.
- **Smoking cessation programs**: If you smoke, quitting can sometimes slow down the progression of some lung diseases.
- **Anti-fibrotic and cytotoxic drugs**: Medications that can slow down lung scarring caused by certain types of lung disease.
- **Biologic drugs**: Medications like rituximab are sometimes used to treat autoimmune diseases and other causes of lung disease.
- **Clinical trials**: Clinical trials are tests of new treatments to see if they're safe and effective. Your provider might recommend one if a new treatment could be a good fit.
- **Positive airway pressure**: Your provider might have you use a BiPAP machine to help you breathe.
- **Pulmonary rehabilitation**: An exercise and education program can strengthen your lungs and help you manage certain lung diseases.

https://my.clevelandclinic.org/health/diseases/lung-disease

The Health Policy Partnership

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THE HEALTH POLICY PARTNERSHIP TEAM

Lung health now: a global call to action

14 MAY 2025

https://www.healthpolicypartnership.com/lung-health-now-a-global-call-to-action/

The global impact of lung ill health

Diseases of the lungs include communicable diseases (e.g. tuberculosis) and non-communicable diseases (NCDs), which include chronic respiratory diseases (CRDs, such as chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, occupational lung diseases and pulmonary hypertension) and lung cancer. Their collective burden is huge. In 2021, lung conditions caused almost 17.7 million deaths globally. Even just looking at CRDs, together they affect almost 470 million people and caused almost 4.5 million deaths in 2021; and globally, of all cancers, lung cancer has both the highest incidence rate and the highest mortality rate.

https://www.healthpolicypartnership.com/lung-health-now-a-global-call-to-action/

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https://www.healthpolicypartnership.com/lung-health-now-a-global-call-to-action/

What Do These Prescribed Medications Actually Do??

Home > Prednisone

Prednisone

Pronunciation: *PRED-ni-sone*
Generic name: prednisone
Brand names: Rayos, Sterapred, Deltasone
Drug class: Glucocorticoids

Medically reviewed by Melisa Puckey, BPharm. Last updated on May 13, 2025.

Uses | Warnings | Before taking | Dosage | Side effects | Interactions | FAQ

What is prednisone?

Prednisone is a corticosteroid medicine used to decrease inflammation and keep your immune system in check, if it is overactive. Prednisone is used to treat allergic disorders, skin conditions, ulcerative colitis, Crohn's disease, arthritis, lupus, psoriasis, asthma, chronic obstructive pulmonary disease (COPD) and many more conditions.

https://www.drugs.com/prednisone.html

Official Answer by Drugs.com 18 April 2024

If a side effect has the words "frequency not reported" then this means that neither the product information nor clinical trials have specified exactly how many people have experienced this side effect for this particular medicine.

Sometimes side effects are not reported until after a drug goes to market. When this happens, there is no way to know how many people have experienced this side effect reliably, and the side effect will usually always state "frequency not reported". This is because you would have to ask every single person taking that medicine in the world if they have experienced this side effect.

This type of data is not collected unless it has emerged that this is a side effect of concern and the medicine is being monitored by the FDA Adverse Event Reporting System (FAERS). Even then it will only be an estimate.

https://www.drugs.com/answers/what-mean-when-you-frequency-reported-under-side-3576854.html

Prednisone Side Effects

Medically reviewed by Drugs.com. Last updated on Feb 17, 2025.

Metabolic

- **Frequency not reported**: Decreased carbohydrate and glucose tolerance, increased requirements for insulin or oral hypoglycemic agents in diabetics, lipid abnormal, negative nitrogen balance caused by protein catabolism, hypokalemia, hypokalemic alkalosis, metabolic alkalosis, potassium loss, sodium retention with resulting edema, increased appetite and weight gain, anorexia and weight loss, hypertriglyceridemia, hypercholesterolemia[Ref]

https://www.drugs.com/prednisone.html

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Cardiovascular

- **Frequency not reported**: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, ECG changes caused by potassium deficiency, edema, fat embolism, hypotension, hypertension or aggravation of hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, necrotizing angiitis, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis[Ref]

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Ocular

- **Frequency not reported**: Blurred vision, cataracts (including posterior subcapsular cataracts) central serous chorioretinopathy, secondary bacterial, fungal, and viral infections, exophthalmos, glaucoma, increased intraocular pressure[Ref]

https://www.drugs.com/prednisone.html

Endocrine

- **Frequency not reported**: Adrenal insufficiency associated symptoms including arthralgias, buffalo hump, amenorrhea, postmenopausal bleeding or menstrual irregularities, development of cushingoid state, hyperthyroidism, hypothyroidism, moon face, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress as in trauma, surgery, or illness), increased or decreased motility and number of spermatozoa[Ref]

Gastrointestinal

- **Frequency not reported**: Abdominal distention, abdominal pain, constipation, diarrhea, gastric irritation, nausea, oropharyngeal candidiasis, pancreatitis, peptic ulcer with possible perforation and hemorrhage, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), ulcerative esophagitis, vomiting[Ref]

Musculoskeletal

- **Frequency not reported**: Arthralgia, aseptic necrosis of femoral and humeral heads, increased risk of fracture, loss of muscle mass, muscle weakness, myalgias, osteopenia, osteoporosis, pathologic fracture of long bones, steroid myopathy, tendon rupture (particularly of the Achilles tendon), vertebral compression fractures, suppression of growth in pediatric patients[Ref]

Nervous system

- **Frequency not reported**: Arachnoiditis, benign intracranial hypertension, convulsions, dementia, dizziness, EEG abnormalities, impaired cognition, increased intracranial pressure with papilledema, increased motor activity, ischemic neuropathy, severe tiredness or weakness, meningitis, neuritis, neuropathy, paraparesis/paraplegia, sensory disturbances[Ref]

https://www.drugs.com/prednisone.html

Psychiatric

- **Frequency not reported**: Amnesia, anxiety, delirium, depression, emotional instability and irritability, euphoria, hallucinations, severe psychiatric symptoms, insomnia, long-term memory loss, mania, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychiatric disorders including steroid psychoses or aggravation of preexisting psychiatric conditions, restlessness, schizophrenia, verbal memory loss, withdrawn behavior[Ref]

Hematologic

- **Frequency not reported**: Anemia, neutropenia, febrile neutropenia, moderate leukocytosis, lymphopenia, eosinopenia, polycythemia[Ref]

Dermatologic

- **Frequency not reported**: Acne, acneiform eruptions, allergic dermatitis, alopecia, angioedema, angioneurotic edema, atrophy and thinning of skin, dry scaly skin, ecchymosis and petechiae (bruising), erythema, facial edema, hirsutism, impaired wound healing, increased sweating, lupus erythematosus-like lesions, perineal irritation, purpura, rash, striae, subcutaneous fat atrophy, suppression of reactions to skin tests, telangiectasis, thin fragile skin, thinning scalp hair, urticaria, hypertrichosis[Ref]

Hepatic

- **Frequency not reported**: ALT, AST and alkaline phosphatase elevations (usually reversible upon discontinuation), hepatomegaly[Ref]

https://www.drugs.com/prednisone.html

Trelegy Ellipta

Pronunciation: *TREL-e-ge e-LIP-ta*

Generic name: fluticasone, umeclidinium, and vilanterol

Dosage forms: oral inhalation device (100 mcg fluticasone furoate, 62.5 mcg umeclidinium, and 25 mcg vilanterol per actuation), ... show all 2 dosage forms

Drug class: Bronchodilator combinations

Medically reviewed by Melisa Puckey, BPharm. Last updated on July 7, 2025.

Uses | Side effects | Warnings | Before taking | Dosage | Interactions | FAQ

What is Trelegy Ellipta?

Trelegy Ellipta is used to treat COPD (chronic obstructive pulmonary disease), including bronchitis and emphysema, and is also used for asthma in adults as a maintenance treatment. Trelegy Ellipta is used daily to improve symptoms and prevent bronchospasm in adults with COPD, and for adults with asthma, it is used daily to prevent and control symptoms of asthma.

https://www.drugs.com/trelegy-ellipta.html

Home > Trelegy Ellipta

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https://www.drugs.com/trelegy-ellipta.html

Trelegy Ellipta Side Effects

Generic name: *fluticasone / umeclidinium / vilanterol*

Medically reviewed by Philip Thornton, DipPharm. Last updated on Sep 22, 2025.

★ This medicine should not be used if you are having an asthma or COPD attack, or if symptoms of an asthma or COPD attack has already started. Your doctor will prescribe another medicine for you to use in case of an acute attack. If the other medicine does not work as well, tell your doctor right away.

★ This medicine may increase the chance of asthma-related problems. Be sure to read about these risks in the Medication Guide and talk to your doctor or pharmacist about any questions or concerns that you have.

★ This medicine may increase the risk of worsening asthma, which may lead to hospitalization, intubation, and death in patients with asthma. Talk to your doctor if you have concerns about this.

This medicine may weaken your immune system and increase your risk for infections. Tell your doctor about any immune system problems or infections, including tuberculosis or herpes infection in your eye. Tell your doctor right away if you have been exposed to chickenpox or measles.

This medicine may cause a fungus infection of the mouth or throat (thrush). Tell your doctor right away if you have white patches in the mouth or throat, or pain when eating or swallowing.

https://www.drugs.com/trelegy-ellipta.html

This medicine may cause paradoxical bronchospasm, which means your breathing or wheezing will get worse. This may be life-threatening. Check with your doctor right away if you have coughing, or difficulty breathing after using this medicine.

Using too much of this medicine or using it for a long time may cause may increase your risk of having adrenal gland problems. Talk to your doctor if you have darkening of the skin, diarrhea, lightheadedness, dizziness, or fainting, loss of appetite, mental depression, muscle pain or weakness, nausea, skin rash, unusual tiredness or weakness, or vomiting.

This medicine may cause serious allergic reactions, including anaphylaxis and angioedema, which can be life-threatening and require immediate medical attention. Tell your doctor right away if you have a rash, itching, hoarseness, trouble breathing, trouble swallowing, or any swelling of your hands, face, or mouth after using this medicine.

This medicine may increase your risk for heart and blood vessel problems, including changes in heart rhythm. Check with your doctor right away if you have dizziness, fainting spells, severe tiredness, chest pain, trouble with breathing, sudden or severe headache, or fast or irregular heartbeat.

Check with your doctor right away if blurred vision, difficulty in reading, or any other change in vision occurs during or after treatment. Your doctor may want your eyes be checked by an ophthalmologist (eye doctor).

This medicine may decrease bone mineral density when used for a long time. A low bone mineral density can cause weak bones or osteoporosis. If you have any questions about this, ask your doctor.

https://www.drugs.com/trelegy-ellipta.html

Rituximab

Pronunciation: *ri-TUX-i-mab*
Generic name: rituximab
Brand names: Rituxan, Riabni, Ruxience, Truxima
Dosage form: injection for intravenous infusion (100 mg/10 mL, 500 mg/50 mL)
Drug classes: Antirheumatics, CD20 monoclonal antibodies

Medically reviewed by Carmen Pope, BPharm. Last updated on May 2, 2025.

Uses | Side effects | Before taking | Dosage | What to avoid | Interactions | FAQ

What is rituximab?

Rituximab infusion is used to treat certain leukemias and lymphomas and some non-cancer conditions, such as rheumatoid arthritis, polyangiitis, and pemphigus vulgaris, depending on the brand. Brand names include Rituxan, Riabni, Ruxience, and Truxima. Rituximab is given by IV infusion (an infusion into a vein) by a healthcare provider.

https://www.drugs.com/rituximab.html

Home > Rituximab

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https://www.drugs.com/rituximab.html

Home > Rituximab

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Rituximab

Important warnings

This medicine can cause some serious health issues

Intravenous route (solution)

Fatal infusion-related reactions may occur within 24 hours of rituximab infusion; approximately 80% of fatal reactions occurred with the first infusion.

Monitor patients and discontinue rituximab infusion after severe reactions.

Severe and potentially fatal mucocutaneous reactions can occur.

Reactivation of hepatitis B virus (HBV) may occur; in some cases, it results in fulminant hepatitis, hepatic failure, or death.

Screen patients for HBV infection prior to treatment.

Progressive multifocal leukoencephalopathy (PML) and death can also occur.

https://www.drugs.com/rituximab.html

Rituximab Side Effects

Medically reviewed by Philip Thornton, DipPharm. Last updated on Aug 31, 2025.

This medicine may cause infusion-related reactions, which can be life-threatening and require immediate medical attention. Tell your doctor right away if you start to have a fever, chills or shaking, dizziness, trouble breathing, itching or rash, lightheadedness or fainting after receiving this medicine.

This medicine can cause a hepatitis B infection to come back. Check with your doctor right away if you have any symptoms of liver problems, including skin and eyes turning yellow, dark brown-colored urine, right-sided abdominal or stomach pain, fever, or severe tiredness.

Serious skin and mouth reactions (eg, paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis) can occur during treatment with this medicine. Check with your doctor right away if you have blistering, peeling, or loosening of the skin, chills, cough, diarrhea, itching, joint or muscle pain, red irritated eyes, red skin lesions, often with a purple center, sore throat, sores, ulcers, or white spots in the mouth or on the lips, or unusual tiredness or weakness while you are receiving this medicine.

This medicine may cause a serious type of reaction called tumor lysis syndrome (TLS). Your doctor may give you a medicine to help prevent this. Call your doctor right away if you have a decrease or change in urine amount, joint pain, stiffness, or swelling, lower back, side, or stomach pain, a rapid weight gain, swelling of the feet or lower legs, or unusual tiredness or weakness.

https://www.drugs.com/rituximab.html

This medicine may cause a rare and serious brain infection called progressive multifocal leukoencephalopathy (PML). The risk for getting this infection is higher if you have rheumatoid arthritis. Talk to your doctor about the benefits of receiving this medicine and the risk for this infection. Check with your doctor right away if you have vision changes, loss of coordination, clumsiness, memory loss, difficulty speaking or understanding what others say, and weakness in the legs.

This medicine may increase your risk of developing infections (eg, viral, bacterial, or fungal) during or after treatment with this medicine. Avoid being near people who are sick or have infections while you are using this medicine. Wash your hands often. Tell your doctor if you have lupus or if you have any kind of infection before you start using this medicine. Also tell your doctor if you have ever had an infection that would not go away or an infection that kept coming back.

This medicine may cause heart and heart rhythm problems (eg, heart attack, arrhythmia, cardiogenic shock). Check with your doctor if you have chest pain or discomfort, pain or discomfort in the arms, jaw, back, or neck, dizziness, fainting, fast, slow, or irregular heartbeat, cool, sweaty skin, or trouble breathing.

Check with your doctor right away if you have bloody urine, a decrease in frequency or amount of urine, an increase in blood pressure, increased thirst, loss of appetite, lower back or side pain, nausea, swelling of the face, fingers, or lower legs, trouble breathing, unusual tiredness or weakness, vomiting, or weight gain. These could be symptoms of a serious kidney problem.

This medicine may cause serious stomach and bowel problems, especially when used with other cancer medicines. Check with your doctor right away if you start having stomach pain while being treated with this medicine.

https://www.drugs.com/rituximab.html

Home > Methotrexate

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Methotrexate

Generic name: methotrexate (oral) [*meth-oh-TREX-ate*]
Brand names: Trexall, Xatmep Jylamvo
Drug classes: Antimetabolites, Antipsoriatics, Antirheumatics, Other immunosuppressants

Medically reviewed by Sophia Entringer, PharmD. Last updated on Oct 31, 2024.

Uses | Side effects | Warnings | Before taking | Dosage | Interactions | FAQ

What is methotrexate?

Methotrexate interferes with the growth of certain cells of the body, especially cells that reproduce quickly, such as cancer cells, bone marrow cells, and skin cells.

Methotrexate is used to treat leukemia and certain types of cancer of the breast, skin, head and neck, lung, or uterus.

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https://www.drugs.com/methotrexate.html

Methotrexate

Important warnings

This medicine can cause some serious health issues

Oral route (solution)

Severe Toxic Reactions, Including Embryo-Fetal Toxicity. Methotrexate can cause severe or fatal toxicities.

Monitor closely and modify dose or discontinue for the following toxicities: bone marrow suppression, infection, renal, gastrointestinal, hepatic, pulmonary, hypersensitivity and dermatologic.Methotrexate can cause embryo-fetal toxicity and fetal death.

Use in polyarticular juvenile idiopathic arthritis is contraindicated in pregnancy.

Consider the benefits and risks of methotrexate and risks to the fetus when prescribing methotrexate to a pregnant patient with a neoplastic disease.

Advise patients to use effective contraception during and after treatment with methotrexate.

https://www.drugs.com/methotrexate.html

Methotrexate Side Effects

Medically reviewed by Philip Thornton, DipPharm. Last updated on Feb 23, 2024.

This medicine may cause serious allergic reactions, including anaphylaxis, which may be life-threatening and require immediate medical attention. Check with your doctor right away if you have a rash, itching, dizziness, fainting, fast heartbeat, trouble breathing or swallowing, or chest tightness while you are using this medicine.

Check with your doctor right away if you have pain or tenderness in the upper stomach, pale stools, dark urine, loss of appetite, nausea, vomiting, or yellow eyes or skin. These could be symptoms of a serious liver problem.

Methotrexate can lower the number of white blood cells in your blood, which increases the chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting. If this occurs, there are certain precautions you can take, especially when your blood count is low, to reduce the risk of infection or bleeding:

This medicine may cause stomach and bowel problems. Check with your doctor right away if you have stomach pain, black, tarry stools, constipation, diarrhea, loss of appetite, nausea, pain in the back of the throat or chest when swallowing, or vomiting blood or material that looks like coffee grounds.

https://www.drugs.com/methotrexate.html

Serious skin reactions (eg, toxic epidermal necrolysis, Stevens-Johnson syndrome, exfoliative dermatitis, skin necrosis, or erythema multiforme) can occur with this medicine. Check with your doctor right away if you have blistering, peeling, or loosening of the skin, blue-green to black skin discoloration, cough, cracks in the skin, diarrhea, itching, joint or muscle pain, loss of heat from the body, red irritated eyes, red skin lesions, often with a purple center, sore throat, sores, ulcers, or white spots in the mouth or on the lips, fever or chills, or unusual tiredness or weakness while you are using this medicine.

Tell your doctor right away if you have a change in how much or how often you urinate, rapid weight gain, swelling in the legs, ankles, or feet, or trouble breathing. These could be symptoms of a serious kidney problem.

This medicine may cause serious nerve problems. Check with your doctor right away if you have seizures, confusion, tingling or numbness in your hands, feet, or lips, trouble seeing, or headache.

This medicine may increase your risk for other cancers, including blood or skin cancer. The risk for skin cancer may be increased if you take cyclosporine after receiving treatment with methotrexate for psoriasis.

This medicine may cause a serious reaction called tumor lysis syndrome. Your doctor may give you a medicine to help prevent this. Tell your doctor right away if you have a change in urine amount, joint pain, stiffness, or swelling, lower back, side, or stomach pain, rapid weight gain, swelling of the feet or lower legs, or unusual tiredness or weakness.

https://www.drugs.com/methotrexate.html

What Dr. Ardis Recommends for Lung Health!!

Available online at www.annclinlabsci.org

96 *Annals of Clinical & Laboratory Science, vol. 37, no. 1, 2007*

Minireview:
Antioxidant Vitamin Supplementation in Asthma

Graziano Riccioni,[1] Mancini Barbara,[1] Tonino Bucciarelli,[2] Carmine di Ilio,[2] and Nicolantonio D'Orazio[1]

[1] Human Nutrition, Department of Biomedical Sciences, G. D'Annunzio University, and
[2] Biochemical Clinic, Department of Biomedical Sciences, University of Chieti, Chieti, Italy

Abstract. The influence of nutrition on chronic bronchial asthma has an important place in the management of this disease. Evidence suggests that specific inflammatory abnormalities exist in the airways of subjects suffering from mild-to-moderate persistent asthma, in whom an inflammatory state is often associated with increased generation of reactive oxygen species and the damaging effects of free radicals. For this reason oxidant stress may be an important pathogenic factor in the progress of the disease. The role of nutrition in bronchial asthma is related to antioxidant vitamins A, C, and E. By counteracting oxidants and reducing external attacks (bacteria, virus, toxins, xenobiotics) in the lung, antioxidant vitamins modulate the development of asthma and the impairment of pulmonary function. Dietary studies suggest relations

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Antioxidant Vitamins

Many studies have reported increased indices of oxidative stress in the blood and airways of asthmatic subjects [16]. Gilliland et al [2] investigated the relation between pulmonary function and the intake of fruit, vegetables, juices, and vitamins A, C, and E by examining cross-sectional data from a Children's Health Study that involved 2,566 children. Low total intake of vitamins A, C, and E was associated with deficits in spirometric parameters (forced vital capacity [FVC], forced expiratory flow at 1 sec [FEV1], and forced expiratory flow (25-75%) [FEF]) [2]. Other studies have likewise demonstrated lower lung function levels in children with inadequate dietary intake of antioxidant vitamins [17,18].

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Vitamin A. Vitamin A is a fat-soluble vitamin with 3 active forms: retinol, retinal, and retinoic acid, which collectively are called retinoids. In addition, there are provitamin A compounds, defined as carotenoids, the most important being β-carotene, which prevent DNA damage secondary to lipid peroxidation [19]. Studies have shown effects of vitamin A and carotenoids in human diseases such as diarrhea, acute respiratory infections, ischemic heart disease, immunological disorders, and asthma [20-22]. Some authors have reported an association between low levels of serum vitamin A and chronic airway obstruction in adults, even if patients with asthma were not included in these studies [23,24]. Arora et al [25] observed that vitamin A deficiency was 4 times more common in children with asthma compared to controls [25].

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Many hypotheses have been proposed to explain the altered vitamin A status in asthma. Children with asthma have frequent exacerbations of asthmatic symptoms in association with airway inflammation, infection, exertion, or stress. These factors have been shown to decrease serum retinol levels by increasing cellular demand for retinol and increasing its urinary elimination [26,27]. Airway inflammation in asthmatic patients is associated with increased production of ROS (superoxide anion, hydrogen peroxide, and hydroxyl radicals) by peripheral blood eosinophils, neutrophils, and alveolar macrophages [28]. β-Carotene, by quenching singlet oxygen (an antioxidant effect), may reduce airway inflammation in asthma [29].

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Vitamin C. Vitamin C is an important water-soluble vitamin that is present in 2 biologically active forms: ascorbic acid and its oxidized derivative, dehydroascorbic acid. Vitamin C can act as a hydrogen donor to reverse oxidation and therefore functions as an antioxidant that reacts with free radicals (FRs) and deactivates them before they cause damage to proteins or lipids [19]. Oxygen metabolites may play direct and indirect roles in the modulation of airway inflammation. Many studies suggest that SOD and other FR scavengers in blood are significantly lower in patients with asthma. There is correlation between asthmatic severity and ROS products in asthmatic subjects

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Epidemiological studies indicate that elevated dietary intake of vitamin C may be associated with a reduced risk of asthma [35-37]. Furtheremore, vitamin C levels are diminished in mild asthma [38]. A study of 7,505 youths (age 4-16 yr) in the National Health And Nutrition Examination Survey-III (NHANES III) showed an association between antioxidants and the prevalence of asthma; this association was stronger among children exposed to cigarette smoke [2,39]. A study of 4,300 healthy Norwegians (20-44 yr) reported that dietary vitamin C intake reduced coughing and wheezing in smokers having high oxidant stress

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frontiers in Pharmacology

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Googling the Guggul (Commiphora and Boswellia) for Prevention of Chronic Diseases

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Asthma

Asthma is a chronic multifactorial inflammatory disease of the respiratory tract and is one of the major health concern. Notably, *Boswellia* has been found to be effective in the treatment of this disease. In a clinical study, 40 patients having 23 males, and 17 females in the age range of 18–75 years, suffering from bronchial asthma were treated with 300 mg of gum resin thrice daily for a period of 6 weeks. This led to improved prognosis in around 70% of the patients as various signs and symptoms of bronchial asthma like rhonchi, dyspnoea, and attacks disappeared upon treatment (Gupta et al., 1998).

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Protective effect of oleo-gum resin of *Commiphora wightii* against elastase-induced chronic obstructive pulmonary disease-linked lung inflammation and emphysema: Isolation and identification of key bioactive phytoconstituent

Manpreet Kaur [a], Jai Malik [b], Amarjit S. Naura [a]

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Traditionally, oleo-gum resin of *C. wightii* was used for treating chronic bronchitis, acute and nasal congestion, nasal catarrh, laryngitis, and bronchial asthma (Mishra et al., 2001). Accordingly, present work was undertaken to investigate the protective effects of *C. wightii* using bioassay-guided fractionation against elastase-induced pulmonary inflammation, characteristic feature of COPD. In the current study, well-established elastase-induced model was used to identify related mechanisms in the development of COPD *i.e.* lung inflammation and emphysema. Elastase model is widely used amongst the various laboratory models of animal as single dose of elastase leads to rapid inflammatory and histological changes (Ghorani et al., 2017).

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Neutrophilic inflammation is a prominent feature of COPD and is correlated with the enhanced release of pro-inflammatory mediators, ROS, protease/anti-protease imbalance and deterioration of lung function (Hoenderdos and Condliffe, 2013). Therefore, therapies targeting neutrophilic inflammation might help in ameliorating COPD associated features. The anti-inflammatory effect of standardized methanolic *C. wightii* extract in our model was evaluated at three different doses (100, 200, and 400 mg/kg b.*wt.*), and the most effective dose in exerting anti-inflammatory effects was found to be 400 mg/kg b.*wt.*. MPO is a heme containing peroxidase expressed abundantly in azurophilic granules of neutrophil and its activity is major indicator of neutrophilic accumulation (Van der Veen et al., 2009). Further, increased MPO activity is linked with oxidative stress, epithelial damage and thus disease progression (Zhang et al., 2002; Zhu et al., 2014).

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Interestingly, our data reflect that suppression of MPO activity by *C. wightii* correlates well with the reduction in the number of neutrophils in the lungs. Next, to evaluate the severity of lung edema, BALF protein content was measured and elastase instillation increased the BALF protein content whereas *C. wightii* dose dependently reduced the edema. Thus, methanolic *C. wightii* extract was found to be potent in mitigating elastase-induced pulmonary inflammation. Therefore, in order to identify the bioactive principles, solvent partitioning was carried out and various fractions obtained *i.e.* HF, EAF, BF, and AF were evaluated for their respective potential against elastase-induced lung inflammation. The results obtained revealed that amongst various fractions, EAF (200 mg/kg b.*wt.*) attenuated elastase-linked inflammation by potently reducing the number of total cells, neutrophils, MPO activity, and BALF protein content thus indicating the presence of bioactive constituent in this fraction. Before proceeding with bioactivity directed

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(Chung, 2001). GS treatment attenuated elastase-induced increased mRNA expression of TNF-α, IL-1β, IL-6, KC, MIP-2, and G-CSF. Moreover, attenuated mRNA expression of these genes corroborated well with their reduced protein level in BALF. Additionally, GS administration significantly decreased the elevated protein level of MCP-1 in BALF. Altogether, GS was found to exhibit anti-inflammatory potential and it is possible that these suppressed cytokines and chemokines participated in inhibiting the infiltration of neutrophils into the BALF. Further, previous studies suggest critical role of NF-κB activation in the production of inflammatory cytokines and chemokines associated with COPD (Dharwal and Naura, 2018; Singla et al., 2020). Interestingly, earlier reports have shown that guggulsterone significantly suppressed the production of inflammatory mediators by inhibiting NF-κB signalling in various inflammatory diseases (Cheon et al., 2006; Kim et al., 2015; Huang et al., 2016). Our results that GS down-regulates the expression of elastase-induced pro-inflammatory mediators, we speculate that GS might be exerting its anti-inflammatory action through suppression of NF-κB activation.

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Next, we analyzed the effect of guggulsterone on elastase-induced oxidative stress. Our data on oxidative stress markers ROS, MDA, and protein carbonyls along with counter players (GSH, SOD, and Catalase) distinctly indicate the competence of guggulsterone to restore redox imbalance toward normal in lung tissue. Reactive nitrogen species (RNS) are important in pathogenesis of COPD as they have potent inflammatory action (Hirano et al., 2006). Along with ROS, RNS contribute to oxidative stress and GS decreased the elastase-induced increase in nitrite levels. GS has been reported to possess potent anti-oxidant potential, via its free radical scavenging effects, providing additional support to our observations (Chander et al., 2003; Liu et al., 2020; Kumar et al., 2021). Overall, protective effects of guggulsterone observed by us can be linked with its antioxidant capacity.

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Pulmonary emphysema is a main component of COPD and is characterized by destruction and enlargement of the alveolar region through chronic inflammation, oxidative stress, and protease/anti-protease imbalance. MMPs are essential factors involved in the progression of pulmonary emphysema (Singla et al., 2020). Multiple studies report that expression of MMPs, particularly MMP-2 and MMP-9, is increased in patients with COPD (Vernooy et al., 2004; Black et al., 2008; Zhang et al., 2020). In our study, we observed remarkable airspace enlargement after 21 days of elastase instillation and daily GS treatment effectively provides protection against airspace enlargement. Then, to clarify the effect of GS on elastase-induced emphysema development, we examined expression of active matrix degrading factors and their tissue inhibitors post 7 days of elastase instillation, which consequently result in airspace enlargement at later time points. Earlier studies report that Guggulsterone isomers down-regulate MMP-2 and MMP-9 expression *in vitro* in human gall bladder cancer cell lines and breast cancer cells, respectively (Yang et al., 2012; Noh et al., 2013) and in Lewis rats treated with lipopolysaccharide (LPS) (Kalariya et al., 2010). Consistent with these findings, GS administration mitigates the expression of MMP-2/-9 and increased the expression of TIMP-1 in elastase instilled mice. Furthermore, GS treatment markedly diminished the elastase-induced proteolytic activity of MMP-2. Altogether, our data evince that GS treatment can partly protect against the development of elastase-induced emphysema in COPD by inhibiting the expression and activity of MMPs.

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Numerous *in vitro* studies have indicated the efficiency of guggulsterone against different inflammatory conditions. GS protect against IL-1β induced inflammatory response by suppressing NF-κB activation in fibroblast-like synoviocytes (Lee et al., 2008). GS attenuates LPS induced inflammation by down-regulating IL-1β, TNF-α expression and NF-κB transcriptional activity in human Caco-2 cells and middle ear epithelial cells (Cheon et al., 2006; Song et al., 2010). In addition to this, GS anti-inflammatory activity is well proven in *in vivo* studies utilizing animal model of arthritis, colitis, gastritis, IBD, pancreatitis and uveitis (Mencarelli et al., 2009; Kalariya et al., 2010; Kunnumakkara et al., 2018). Furthermore, number of clinical trials investigating the effects of GS provides substantial evidence of its enormous antioxidant and anti-inflammatory potential (Singh et al., 1994, 2003; Szapary et al., 2003). In line with these studies, our findings demonstrate that GS exhibit anti-inflammatory and anti-oxidant action and could protect lungs from elastase-induced damage in the mouse model of COPD.

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5. Conclusion

Collectively, our data demonstrates, for the first time, that the *C. wightii* extract and its ethyl acetate fraction possess beneficial effect against elastase-induced inflammation. Further, guggulsterone, phytosterol isolated from EAF of *C. wightii* significantly ameliorate elastase associated inflammation, oxidative stress and emphysema in our mouse model of COPD. Hence, guggulsterone might be a potential drug candidate for preventive treatment of COPD.

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VITAMIN D EFFECTS ON LUNG IMMUNITY AND RESPIRATORY DISEASES

Sif Hansdottir *, Martha M Monick *

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https://pmc.ncbi.nlm.nih.gov/articles/PMC3559187/

Several different mechanisms have been proposed for how vitamin D may increase antimicrobial actions of monocytes and macrophages. A multiplicity of studies has been published recently indicating that a vitamin D induced antimicrobial peptide, cathelicidin, plays a key role. The first study was a translational study published in 2006 showing that adequate 25D levels are required for TLR2/1 activation (by a mycobacterial ligand) and subsequent 1α-hydroxylase and VDR dependent expression of cathelicidin. This study also revealed increased killing of mycobacteria by macrophages in the presence of 25D (Liu, Stenger et al. 2006). In a subsequent study of peripheral blood monocytes infected with recombinant mycobacteria, vitamin D strongly induced cathelicidin mRNA and reduced the growth of mycobacteria in a dose dependent fashion (Martineau, Wilkinson et al. 2007). Another study showed a direct correlation between serum 25D levels and monocyte expression of cathelicidin following treatment with TLR 2/1 and TLR 4 ligands. In the same study, *in vivo* supplementation of vitamin D enhanced ex vivo innate immune responses by rescuing TLR-mediated suppression of cathelicidin expression (Adams, Ren et al. 2009).

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Cathelicidins: Immunomodulatory Antimicrobials

Roel M van Harten [1], Esther van Woudenbergh [2], Albert van Dijk [3], Henk P Haagsman [4]

Affiliations + expand

PMID: 30223448 PMCID: PMC6161271 DOI: 10.3390/vaccines6030063

Abstract

Cathelicidins are host defense peptides with antimicrobial and immunomodulatory functions. These effector molecules of the innate immune system of many vertebrates are diverse in their amino acid sequence but share physicochemical characteristics like positive charge and amphipathicity. Besides being antimicrobial, cathelicidins have a wide variety in immunomodulatory functions, both boosting and inhibiting inflammation, directing chemotaxis, and effecting cell differentiation, primarily towards type 1 immune responses. In this review, we will examine the biology and various functions of cathelicidins, focusing on putting in vitro results in the context of in vivo situations. The pro-inflammatory and anti-inflammatory functions are highlighted, as well both direct and indirect effects on chemotaxis and cell differentiation. Additionally, we will discuss the potential and limitations of using cathelicidins as immunomodulatory or antimicrobial drugs.

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Abstract

Cathelicidins are host defense peptides with antimicrobial and immunomodulatory functions. These effector molecules of the innate immune system of many vertebrates are diverse in their amino acid sequence but share physicochemical characteristics like positive charge and amphipathicity. Besides being antimicrobial, cathelicidins have a wide variety in immunomodulatory functions, both boosting and inhibiting inflammation, directing chemotaxis, and effecting cell differentiation, primarily towards type 1 immune responses. In this review, we will examine the biology and various functions of cathelicidins, focusing on putting in vitro results in the context of in vivo situations. The pro-inflammatory and anti-inflammatory functions are highlighted, as well both direct and indirect effects on chemotaxis and cell differentiation. Additionally, we will discuss the potential and limitations of using cathelicidins as immunomodulatory or antimicrobial drugs.

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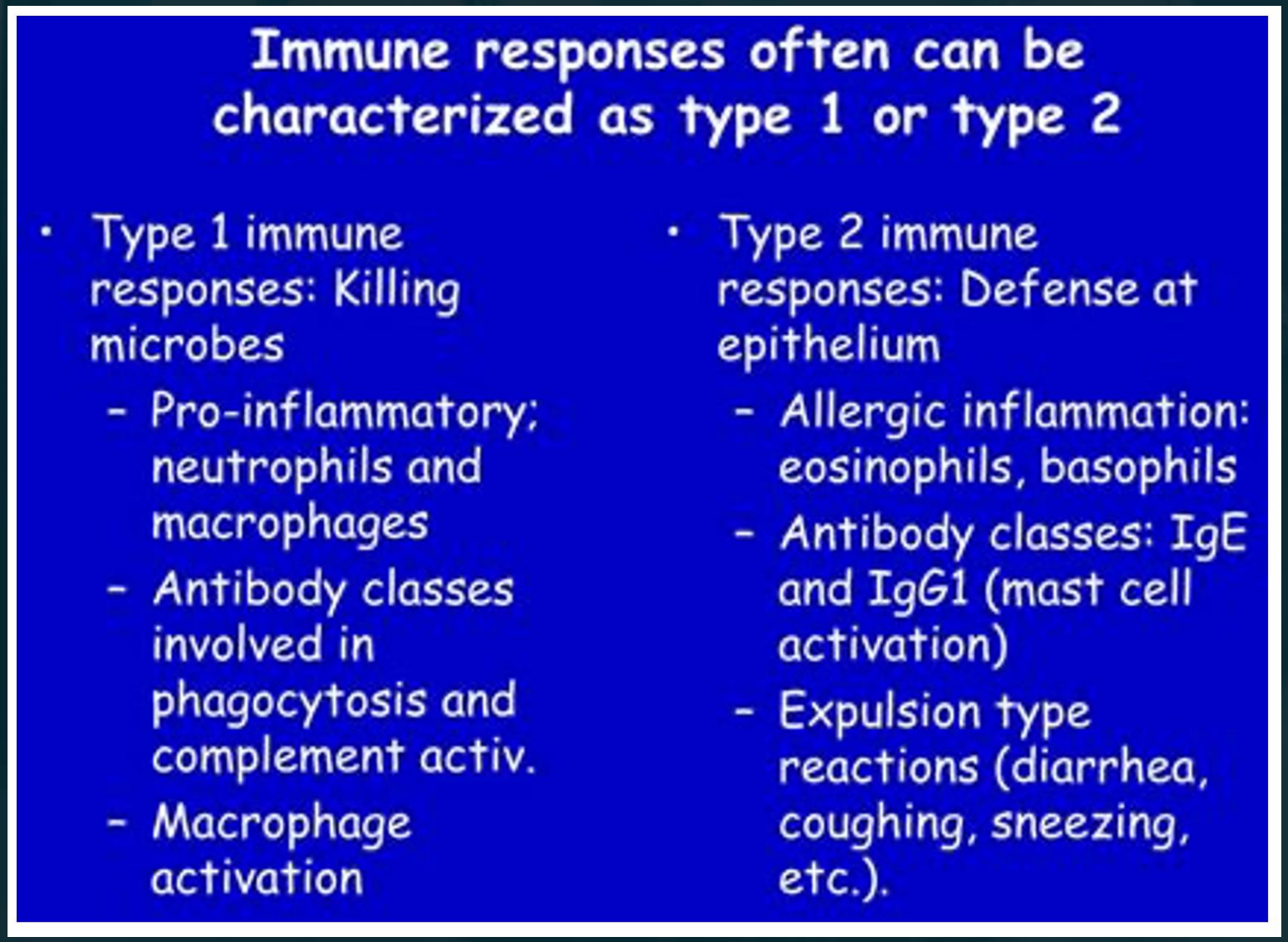

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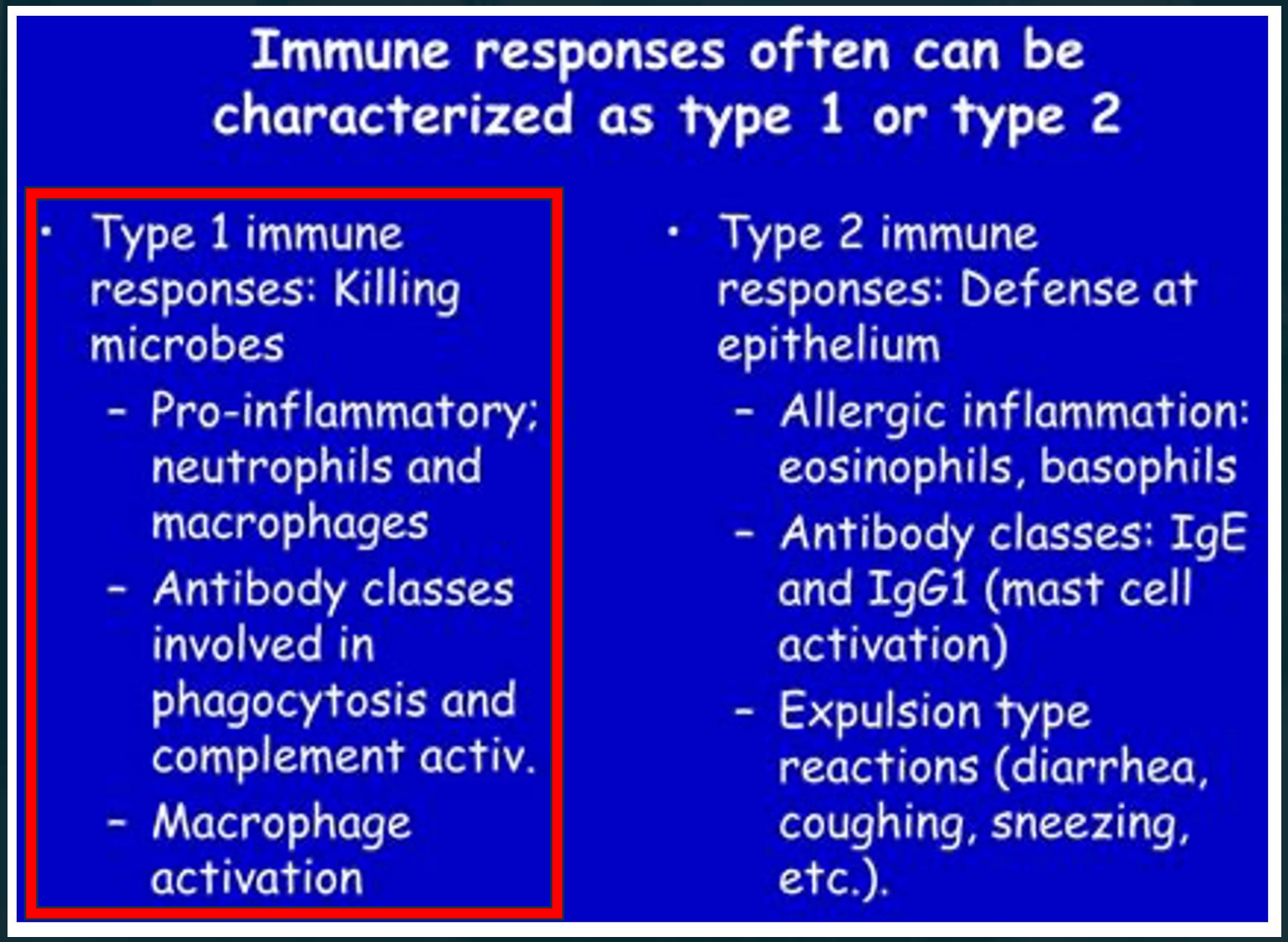

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Several different mechanisms have been proposed for how vitamin D may increase antimicrobial actions of monocytes and macrophages. A multiplicity of studies has been published recently indicating that a vitamin D induced antimicrobial peptide, cathelicidin, plays a key role. The first study was a translational study published in 2006 showing that adequate 25D levels are required for TLR2/1 activation (by a mycobacterial ligand) and subsequent 1α-hydroxylase and VDR dependent expression of cathelicidin. This study also revealed increased killing of mycobacteria by macrophages in the presence of 25D (Liu, Stenger et al. 2006). In a subsequent study of peripheral blood monocytes infected with recombinant mycobacteria, vitamin D strongly induced cathelicidin mRNA and reduced the growth of mycobacteria in a dose dependent fashion (Martineau, Wilkinson et al. 2007). Another study showed a direct correlation between serum 25D levels and monocyte expression of cathelicidin following treatment with TLR 2/1 and TLR 4 ligands. In the same study, *in vivo* supplementation of vitamin D enhanced ex vivo innate immune responses by rescuing TLR-mediated suppression of cathelicidin expression (Adams, Ren et al. 2009).

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The prevalence of asthma has been steadily increasing over the last several decades and over the same period of time vitamin D insufficiency has been on the rise. The prevalence of both conditions have been linked to African American race, obesity and immigration to westernized countries (Litonjua and Weiss 2007). These observations have prompted the hypothesis that vitamin D deficiency is an important contributor to the asthma epidemic. Epidemiological studies have found that vitamin D insufficiency is common in asthmatics and is associated with increased asthma severity and hospitalizations (Brehm, Celedon et al. 2009; Brehm, Schuemann et al. 2010; Freishtat, Iqbal et al. 2010; Sutherland, Goleva et al. 2010). If such an association exists it may be mediated through increased risk of respiratory viral infection in vitamin D deficient individuals or by the effects of vitamin D on adaptive immunity, in particular T regulatory cells (Litonjua 2009).

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To summarize, vitamin D deficiency is common in asthmatic patient and vitamin D supplementation may result in improvement in asthma severity and treatment response to corticosteroids, likely via induction of T_{Regs} and secretion of IL-10. It should be noted that not all the data supports a positive role for vitamin D on the development of asthma. The hypothesis that vitamin D may cause asthma because of inhibition of T_H1 responses also exists (Hypponen, Sovio et al. 2004; Gale, Robinson et al. 2008). Several clinical trials are on going that are looking at vitamin D and asthma, ranging from maternal supplementation during pregnancy and prevention of childhood asthma to the use of vitamin D as a treatment in individuals with asthma (www.clinicaltrials.gov).

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Vitamin D deficiency is on the rise in western countries including the US (Ginde, Liu et al. 2009). Our understanding of vitamin D metabolism and function has grown exponentially over the last decade. It has become clear that vitamin D is not only important for bone and muscle health but has a wide spectrum of biological actions including significant immunomodulatory effects (Holick 2007). The enzyme 1α-hydroxylase is expressed by a variety of cells and the 1,25D that is produced locally in tissues may have direct effects on nearby cells and be responsible for the broad actions of vitamin D.

Epidemiological studies suggest an association between low vitamin D levels and mycobacterial infections, respiratory viral infections and asthma (Figure 1). The enzyme 1α-hydroxylase is expressed by airway epithelium, macrophages, dendritic cells and lymphocytes in the respiratory tract indicating that active vitamin D may be produced locally within the lungs (Table 1). Mechanistic studies have found the 1,25D influences cellular mechanisms that are important for recognition and killing of pathogens, inflammation and control of adaptive immune functions within the lungs (Figure 1).

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Vitamin K2 (MK-7) attenuates LPS-induced acute lung injury via inhibiting inflammation, apoptosis, and ferroptosis

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The inflammatory response is an important defense mechanism induced in the host in response to injury, infection or stimulation [28]. Under LPS induction, the levels of proinflammatory cytokines, including interferons (IFNs), tumor necrosis factors (TNFs), interleukins (ILs), and chemokines [29] were significantly higher than the control group, and the infiltration of inflammatory cells in lung tissue was upregulated as well, which was consistent with our results. However, VK2 pretreatment significantly improved these phenomena and gradually returned to normal levels. VK2 has been investigated as a potential anti-inflammatory and protective drug in several inflammatory diseases including type 2 diabetes mellitus (T2DM) [16], inflammatory bowel disease (IBD) [25], atherosclerosis [30], rheumatoid arthritis (RA) [31], and neurodegenerative diseases, especially Parkinson's and Alzheimer's disease [32, 33].

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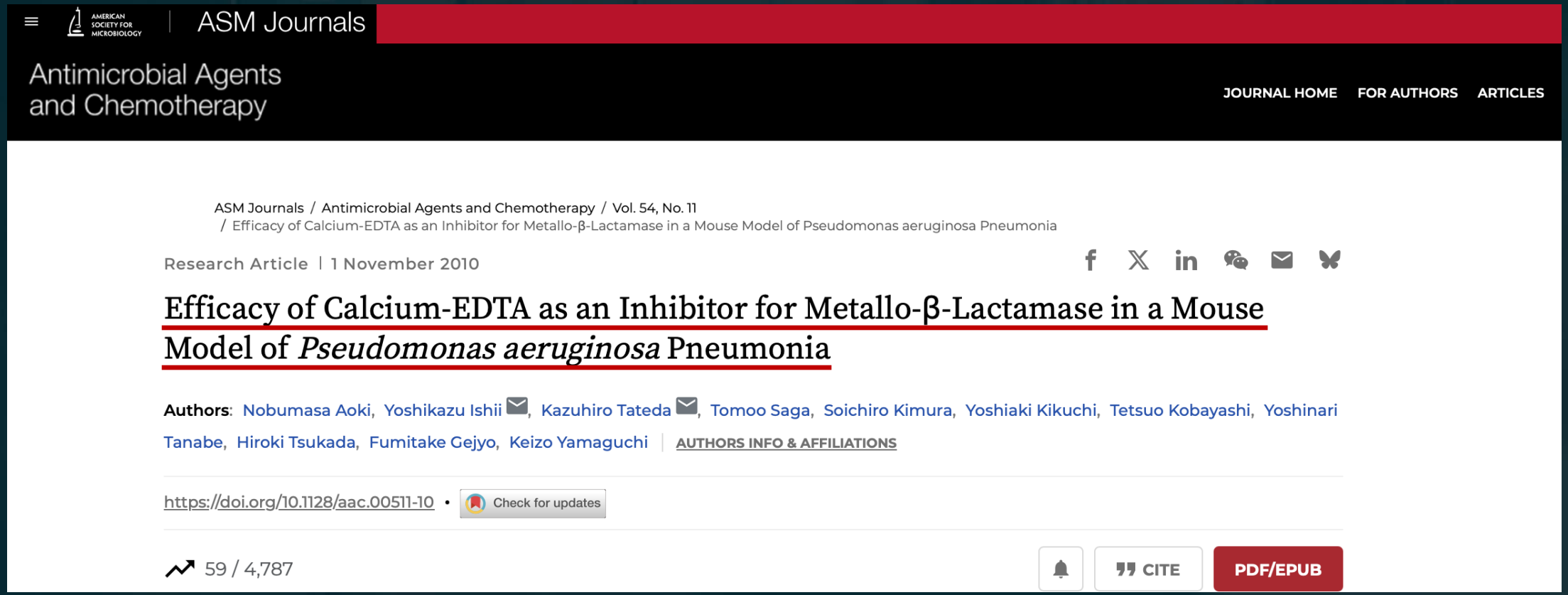

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/ Efficacy of Calcium-EDTA as an Inhibitor for Metallo-β-Lactamase in a Mouse Model of Pseudomonas aeruginosa Pneumonia

Research Article | 1 November 2010

Efficacy of Calcium-EDTA as an Inhibitor for Metallo-β-Lactamase in a Mouse Model of *Pseudomonas aeruginosa* Pneumonia

Authors: Nobumasa Aoki, Yoshikazu Ishii, Kazuhiro Tateda, Tomoo Saga, Soichiro Kimura, Yoshiaki Kikuchi, Tetsuo Kobayashi, Yoshinari Tanabe, Hiroki Tsukada, Fumitake Gejyo, Keizo Yamaguchi | AUTHORS INFO & AFFILIATIONS

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This compound was created for an injectable form of chelator with reduced toxicity, which has been approved for the treatment of lead intoxication (7, 23). Ca-EDTA is used intravenously, and the dose is 1,000 to 1,500 mg/m^2 per day (or 25 to 75 mg/kg of body weight per day) for 5 days. It can be administered continuously or in two to four divided doses. The major potential toxicity with Ca-EDTA is renal nephrotoxicity, neurotoxicity, and hypocalcemia. In this study, we evaluated the efficacy of Ca-EDTA as an inhibitor of bacterial metalloenzymes, such as MBL and other forms of proteases, in a mouse model of *P. aeruginosa* pneumonia. To our knowledge, this is the first report examining the effect of Ca-EDTA on a mouse model of multiple-drug-resistant *P. aeruginosa* pneumonia.

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Effects of Ca-EDTA on survival of mice with *P. aeruginosa* pneumonia.

To assess the effects of Ca-EDTA on the survival of mice, we have applied the *P. aeruginosa* pneumonia model of hyperoxia, which mimics VAP in the clinical setting. As shown in Fig. 1, the control mice started to die at 24 h, and all mice died by 72 to 84 h after the intranasal inoculation of *P. aeruginosa*. Ca-EDTA alone had no effect on survival with either intranasal or subcutaneous administration. IPM treatment delayed the death of mice and increased the survival rate from 0% to approximately 30% at the end of observation, although this was not statistically significant. Importantly, the effects of combining Ca-EDTA with IPM were striking: 100% survival was achieved for this group, regardless of the route of administration of Ca-EDTA. Consistent with the survival data, the bacterial burden was significantly reduced for the combination of IPM and Ca-EDTA (Fig. 2). IPM treatment alone did not induce a significant reduction of bacterial numbers in the lungs. In contrast, the simultaneous administration of Ca-EDTA at both 50 and 100 mg/kg significantly enhanced the clearance of organisms from the lungs. The reduction in the bacterial burden was more than 1 log when the mice were treated with 100 mg/kg of Ca-EDTA subcutaneously in addition to IPM. These results demonstrated the therapeutic efficacy of Ca-EDTA in combination with IPM, which was well correlated with the reduction in the pulmonary bacterial burden.

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The present study demonstrates the effect of combining IPM with Ca-EDTA in the mouse pneumonia model of multiple-drug-resistant *P. aeruginosa*. The presence of Ca-EDTA at 32 μg/ml strikingly reduced the MICs of IPM and CAZ in MBL-producing isolates but not non-MBL-producing isolates. Importantly, we have observed almost the same survival benefits of Ca-EDTA with both intranasal and subcutaneous administrations. Finally, our results indicate that Ca-EDTA also suppressed the protease activity of *P. aeruginosa* culture medium, and these effects may be associated with the protection of alveolar epithelial cells *in vitro* and improvement of survival in the culture supernatant-induced injury model. Together, the present data suggest an application of Ca-EDTA for certain types of infectious diseases caused by MBL and/or tissue-destructive metalloenzyme producers.

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effective and within the accessible range for clinical practice. We also demonstrated the potentiating effects of Ca-EDTA *in vivo*. In a pneumonia model with pneumonia caused by an IMP-1-producing strain, IPM and Ca-EDTA cotherapy resulted in a drastic improvement of the survival rate and reduction of lung bacterial burdens. Additionally, both intranasal and subcutaneous administrations of Ca-EDTA produced similar effects, which suggested a good penetration of this compound into the lungs. These data consistently demonstrate the possibility of Ca-EDTA for clinical applications. Further investigation of Ca-EDTA as a chelating agent against life-threatening infectious diseases by MBL- and/or metalloenzyme-producing organisms, including pharmacokinetic-pharmacodynamic and safety profiles, is warranted.

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Unknown status

Verified **2016-06** by University of Padova

Last known status was: Recruiting

Effect of Magnesium Supplementation in COPD

ClinicalTrials.gov ID NCT02680769

Sponsor University of Padova

Information provided by University of Padova (Responsible Party)

Last Update Posted 2016-06-13

https://www.clinicaltrials.gov/study/NCT02680769

Magnesium (Mg) is involved in several pathways that could be affected in chronic obstructive pulmonary diseases (COPDs), namely in the contractility and excitability of neuro-muscolar endothelial cells and low-grade inflammation, a typical state of COPD. In this sense, several randomized controlled trials (RCTs) confirmed a positive role of Mg in asthma since long-period oral supplementation of Mg leads to a clinical and spirometric improvement.

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Subjects with COPD seem to have a reduced bioavailability of Mg probably due to the use of drugs that may increase Mg losses (e.g. beta-agonists and cortisones), to a reduced dietary Mg intake, and heavy smoking. A recent study showed that the administration of endovenous or aerosol Mg sulphate with beta-agonists acutely improve maximum expiratory flow during COPD relapses as well as the prolonged treatment with endovenous sulphate Mg led to a reduction in pulmonary hyperinflation and increase in muscles involved in respiration, with a consequent clinical and instrumental improvement.

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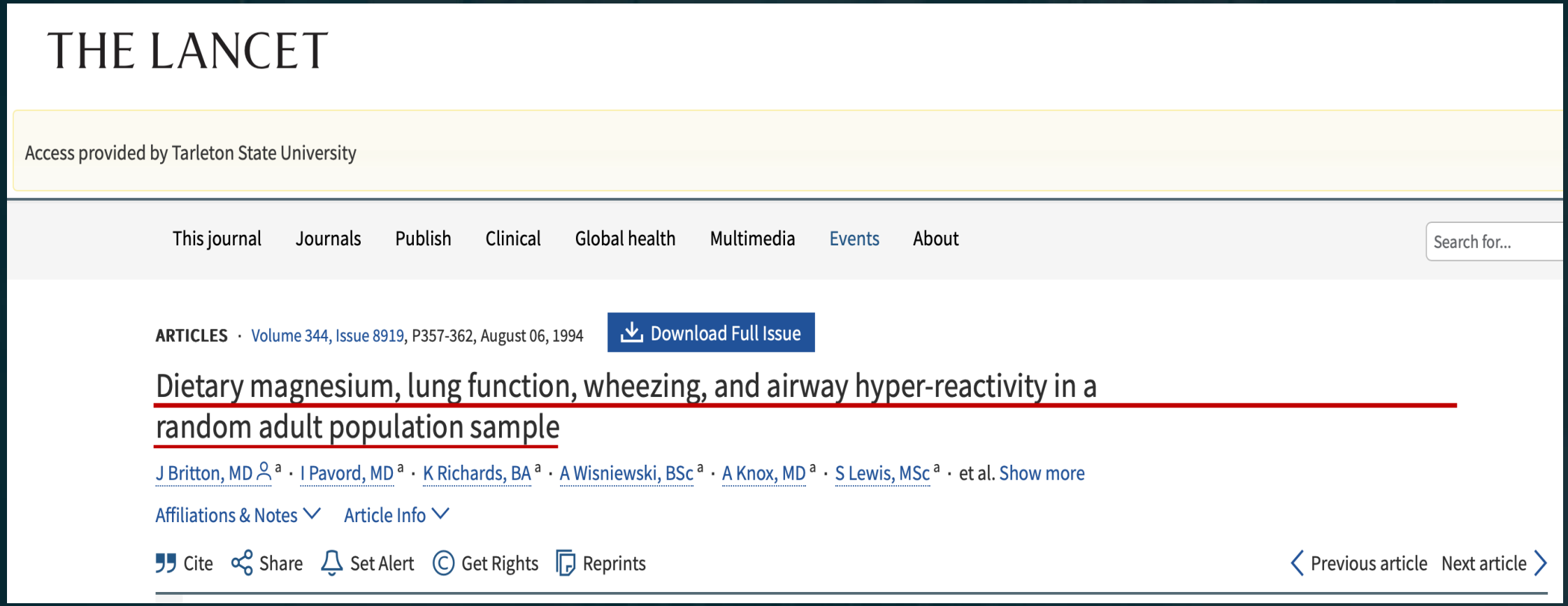

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(94)91399-4/fulltext

Magnesium is involved in a wide range of biological activities, including some that may protect against the development of asthma and chronic airflow obstruction. We tested the hypothesis that high dietary magnesium intake is associated with better lung function, and a reduced risk of airway hyper-reactivity and wheezing in a random sample of adults. In 2633 adults aged 18-70 sampled from the electoral register of an administrative area of Nottingham, UK, we measured dietary magnesium intake by semiquantitative food-frequency questionnaire, lung function as the 1-sec forced expiratory volume (FEV_1), and atopy as the mean skin-prick test response to three common environmental allergens. We measured airway reactivity to methacholine in 2415 individuals, defining hyper-reactivity as a 20% fall in FEV_1 after a cumulative dose of 12 25 µmol or less. Mean (SD) daily intake of magnesium was 380 (114) mg/day. After adjusting for age, sex, and height, and for the effects of atopy and smoking, a 100 mg/day higher magnesium intake was associated with a 27·7 (95% Cl, 11·9-43·5) mL higher FEV_1, and a reduction in the relative odds of hyper-reactivity by a ratio of 0 82 (0·72-0 93). The same incremental difference in magnesium intake was also associated with a reduction in the odds of self-reported wheeze within the past 12 months, adjusted for age, sex, smoking, atopy, and kilojoule intake, by a ratio of 0·85 (0·76-0·95).

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Dietary magnesium intake is independently related to lung function and the occurrence of airway hyper-reactivity and self-reported wheezing in the general population. Low magnesium intake may therefore be involved in the aetiology of asthma and chronic obstructive airways disease.

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The role for N-acetylcysteine in the management of COPD

PNR Dekhuijzen [1,✉], WJC van Beurden [2]

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The efficacy of NAC as a precursor of GSH synthesis has been studied in isolated mouse lungs (Moldeus et al 1986). Cigarette smoke administered directly to the lung through the trachea caused a dose-dependent reduction in total pulmonary GSH. Administering NAC together with cigarette smoke prevented the loss of pulmonary GSH and abolished the effects of cigarette smoke. NAC reduced H_2O_2-induced damage to epithelial cells in vitro (Cotgreave and Moldeus 1987) and NF-kb activation in some cells (Schreck et al 1992). In addition, NAC treatment reduced cigarette smoke-induced abnormalities in polymorphonuclear leukocyte (PMN) (Bridges 1985), alveolar macrophages, fibroblasts, and epithelial cells in vitro (Moldeus et al 1985; Voisin 1987; Linden et al 1988; Drost et al 1991). Treatment with NAC also attenuated rat secretory cell hyperplasia induced by tobacco smoke (Jeffery et al 1985) and prevented hypochlorous acid (HOCl)-mediated inactivation of alpha-1-proteinase inhibitor in vitro (Borregaard 1987). In a rat model of cigarette smoke-induced alterations in small airways, NAC prevented thickening of the airway wall and improved distribution of ventilation (Rubio et al 2000).

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Treatment with NAC in humans alters the pulmonary oxidant–antioxidant imbalance. NAC 600 mg/day given orally increased lung lavage GSH levels (Bridgeman et al 1991), reduced O_2^- production by alveolar macrophages (Linden et al 1988), and decreased bronchoalveolar lavage (BAL) polymorphonuclear leukocyte (PMN) chemiluminescence in vitro (Jankowska et al 1993). NAC 600 mg/day in COPD patients also reduced sputum eosinophilic cation protein (ECP) concentrations and the adhesion of PMNs (Sadowska et al 2005). In vitro, NAC lowered adhesion of *H. influenzae* and *S. pneumoniae* to oropharyngeal epithelial cells (Riise et al 2000).

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It may be questioned if NAC 600 mg once daily is the right dose for an optimal effect in patients with COPD. The abovementioned studies on exhaled biomarkers indicate that NAC in a dose of 1200 mg daily is superior in reducing oxidative stress, measured by the concentration of exhaled H_2O_2. A recent study compared NAC 1200 mg daily, 600 mg daily, and placebo on markers of systemic inflammation and symptoms in patients with COPD GOLD II–III (Zuin et al 2005). NAC 1200 mg daily significantly reduced C-reactive protein and IL-8 levels compared with NAC 600 mg daily and placebo. Both dosages were well tolerated.

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Another indication that NAC in a higher dose might be more effective is provided by the recent data on the IFIGENIA study in patients with idiopathic pulmonary fibrosis (IPF) (Demedts et al 2005). This was a phase III, double-blind, randomised, placebo-controlled study that assessed the effectiveness over 1 year of high-dose NAC (1800 mg daily) on top of the recommended standard therapy of prednisone–azathioprine in 155 IPF patients. The IPF diagnosis was confirmed by independent histology and radiology expert committees.

This study showed that NAC, on top of prednisone–azathioprine, had a significant and clinically relevant effect on VC and diffusion capacity (DLCO test) at 6 and 12 months. NAC was well tolerated and no differences in side-effects were observed between the two groups.

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Oxidative stress is considered to be an important part of the inflammatory response to both environmental and internal signals. Transcription factors like NF-kb and AP-1 are activated by oxidative stress and in turn amplify the inflammatory response to noxious stimuli. In this way, both oxidative stress and inflammation are involved in the complex pathophysiology of COPD, both in terms of pathogenesis and progression of the disease.

In vitro and in vivo data show that NAC protects the lungs against toxic agents by increasing pulmonary defence mechanisms through its direct antioxidant properties and its indirect role as a precursor of GSH synthesis. Indeed, reductions in exhaled biomarkers like H_2O_2 by NAC have been demonstrated in intervention studies with NAC.

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In patients with COPD, treatment with NAC in a dose of 600 mg once daily reduces the risk of exacerbations and improves symptoms compared with placebo. The BRONCUS trial showed that this is especially the case in those COPD patients not using inhaled corticosteroids.

The partial activity of NAC in the BRONCUS trial might be explained by the relatively low dose administered (ie, 600 mg once daily). Data on exhaled biomarkers and markers of systemic inflammation, as well as the recent IFIGENIA study, indicate that higher dosages such as 600 mg twice daily should be administered in patients with COPD.

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Supplement Facts

Serving Size: 1 Capsules Servings Per Container: 90

Amount Per Serving		% Daily Value
Vitamin A (as Vitamin A Palmitate and Beta Carotine)	750mcg	83%*
Vitamin C	90mg	100%*
Raw Bovine Lung Concentrate	200mg	†

*Percent Daily Value (DV) are based on a 2000 calorie diet.
†Daily Value (DV) not established.

OTHER INGREDIENTS: Hydroxypropyl Methylcellulose (HPMC) Capsule, Rice Flour, Vegetable Stearate

Nature Wins Breathe-Free (90 Count)

Nature Wins SKU: BREATHE001--listing

$32.99

★★★★★ (10 reviews) + Write a Review

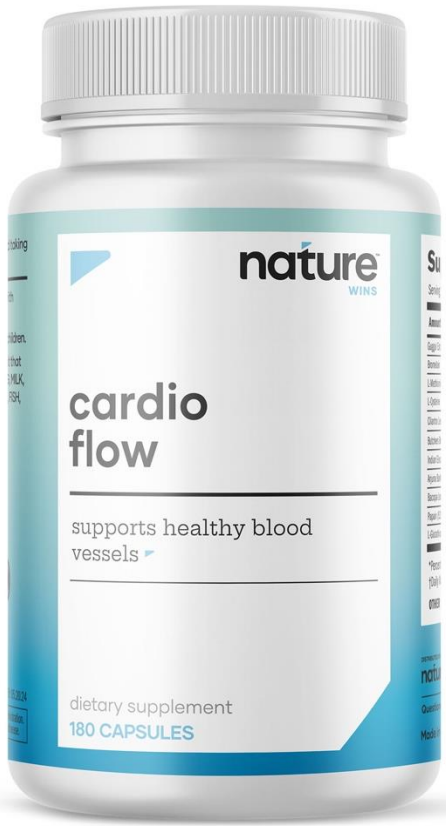
SIZE: *

1 Bottle
$32.99

3.00%
3 Bottles
$96.00

5.00%
6 Bottles
$188.04

https://thedrardisshow.com/



Supplement Facts

Serving Size: 2 Capsules Servings Per Container: 90

Amount Per Serving		% Daily Value
Guggul Extract (Std. to 2.5% Guggulsterones)	300mg	†
Bromelain	200mg	†
L-Methionine	200mg	†
L-Cysteine	200mg	†
Cilantro Leaf Powder	200mg	†
Butchers Broom Extract (Rhizome)	100mg	†
Indian Elecampane Extract 0.5% (Root)	76mg	†
Arjuna Bark Extract (Std. to 0.5% Arjunolic Acid)	50mg	†
Bacopa Leaf Extract (Std. to 20% Bacosides)	50mg	†
Papain (525 TU/mg)	20mg	†
L-Glutathione	14mg	†

*Percent Daily Value (DV) are based on a 2000 calorie diet.
†Daily Value (DV) not established.

OTHER INGREDIENTS: Vegetable Capsule (HPMC).

Nature Wins Cardio-Flow (180 Count)

Nature Wins SKU: CARDIO001--listing

$55.99

★★★★★ (6 reviews) + Write a Review

SIZE: *

1 Bottle
$55.99

3.00%
3 Bottles
$162.93

5.00%
6 Bottles
$319.14

https://thedrardisshow.com/

Supplement Facts

Serving Size: 0.5ml (17 drops)
Servings Per Container: 30

Amount Per Serving		% Daily Value
Vitamin D (as Vitamin D3) 5000IU	125mcg	625%
Vitamin K (as Vitamin K2)	50mcg	42%

Ingredients: Vitamin K2 (menaquione-7 (all-trans)) Vitamin D3-Cholecalciferol, 100% organic MCT oil.

D3+K2 Organic

Nature Wins SKU: D3K2001

$27.99

☆☆☆☆☆ (No reviews yet) + Write a Review

ONE-TIME PURCHASE OR SUBSCRIPTION: *

One Time Purchase	Ships every 30 days
Ships every 90 days	Ships every 180 days

https://thedrardisshow.com/

Supplement Facts

Serving Size: 1 ml Servings Per Container: About 60

Amount Per Serving		% Daily Value
Calcium Disodium EDTA (USP/BP Purity)	225mg	†

†Daily Value (DV) not established.

OTHER INGREDIENTS: Organic Vegetable Gylcerin, Triple-Distilled Biophotonic Structured Water, Organic Extra Virgin Cold Pressed Olive Oil, Organic Extra Virgin Cold Pressed Avocado Oil.

Nature Wins EDTA (2oz)

Nature Wins SKU: EDTA001--listing

$39.99

★★★★★ (37 reviews) + Write a Review

SIZE: *

1 Bottle
$39.99

3.00%
3 Bottles
$116.37

5.00%
6 Bottles
$227.94

https://thedrardisshow.com/

Supplement Facts

Serving Size: 4 Capsules Servings Per Container: 30

Amount Per Serving		% Daily Value
Magnesium (as magnesium citrate, magnesium aspartate, and magnesium malate)	400mg	95%*

*Percent Daily Value (DV) are based on a 2000 calorie diet.
†Daily Value (DV) not established.

OTHER INGREDIENTS: Hydroxypropyl Methylcellulose (Capsule), Vegetable Stearate

Nature Wins Magnesium Complex (120 Count)

Nature Wins SKU: MAGCOMPLEX001--listing

$29.99

★★★★★ (49 reviews) + Write a Review

SIZE: *

1 Bottle	3.00% 3 Bottles
$29.99	$87.27
4.47% 6 Bottles	
$170.94	

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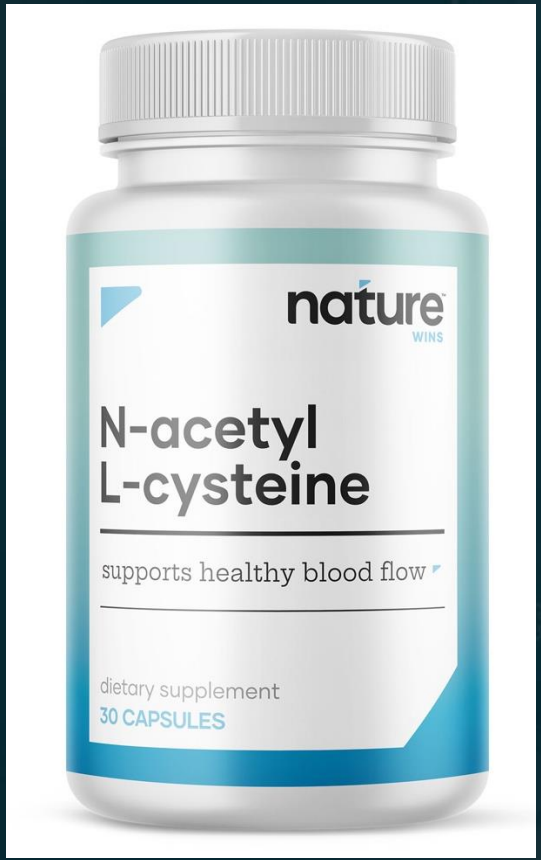

Supplement Facts

Serving Size: 1 Capsule Servings Per Container: 30

Amount Per Serving		% Daily Value
N-Acetyl-L-Cysteine	750mg	†

*Percent Daily Value (DV) are based on a 2000 calorie diet.
†Daily Value (DV) not established.

OTHER INGREDIENTS: Hydroxypropyl Methylcellulose (Vegetable Capsule).

Nature Wins N-acetyl L-cysteine (30 Count)

Nature Wins SKU: NL001--listing

$34.99

~~MSRP $39.99~~

(You save $5.00)

★★★★★ (2 reviews) + Write a Review

SIZE: *

1 Bottle
$34.99

3.00%
3 Bottles
$101.82

5.00%
6 Bottles
$199.44

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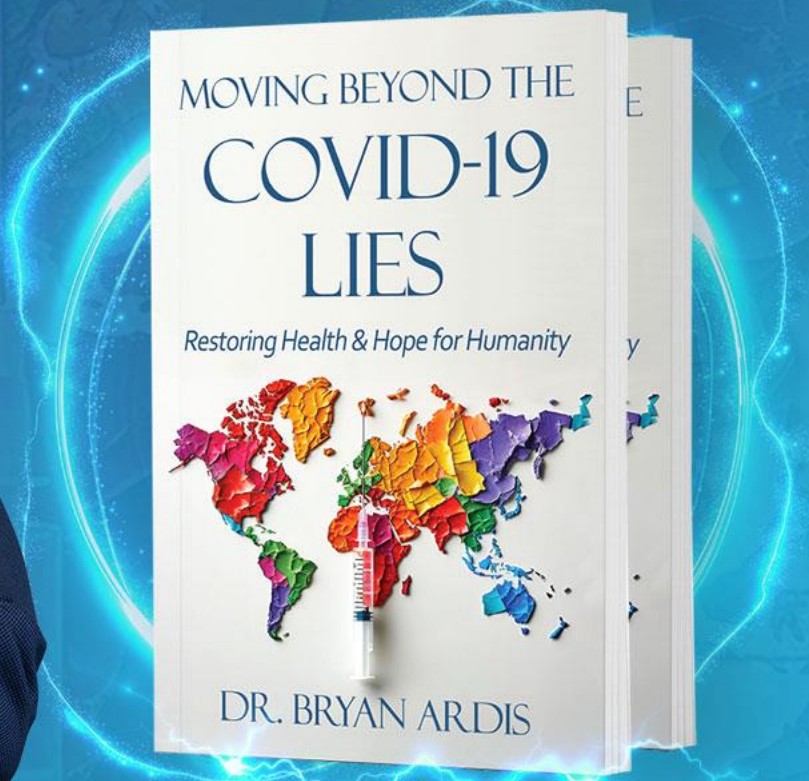

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