NAC SAP

Science-based glutathione and antioxidant support*

N-Acetylcysteine (NAC) is a precursor to glutathione synthesis and also acts on its own to reduce the effects of reactive oxygen species. NAC has been demonstrated to have antifibrotic activity and may be a useful treatment in disease processes that involve fibrosis.* NAC also has mycolytic properties and decreases viscosity of lung secretions.* Due to its ability to reduce oxidative stress and apoptosis, NAC has shown the ability to restore phospholipids and reduce lipid peroxidation, which in turn can reduce symptoms associated with diabetic neuropathy and encephalopathy.* NAC is also an effective treatment for influenza.* Research has shown NAC treatment can improve recovery from influenza by improving host defense mechanisms and through its antioxidant effect against the oxidative stress associated with viral infections.* NAC has a protective effect on the liver and is the main treatment for acetaminophen overdose, due to its ability to enhance hepatic and mitochondrial levels of glutathione, and by supporting the mitochondrial energy metabolism.*

SUPPLEMENT FACTS

Serving Size: 1 Capsule — **Servings:** 90

	Amount Per Serving	% Daily Value
L-α-Acetamido-β-mercaptopropionic acid (*N*-acetyl-L-cysteine)	500 mg	**

**Daily Value not established

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

NAC SAP contains 90 capsules per bottle.

DIRECTIONS OF USE

Adults: Take 1 capsule daily with meals providing protein or as directed by your healthcare practitioner.

INDICATIONS

NAC SAP:

- Is expected to reduce severity of symptoms of influenza, HIV, and avian flu.*
- Can be used to support glutathione synthesis, thereby increasing the body's total antioxidant capacity.*
- Has mucolytic properties, can reduce the viscosity of lung secretions, and can be used to reduce symptoms in patients with chronic obstructive pulmonary disease (COPD).*
- Has a protective capacity for the liver and is used to treat acute acetaminophen poisoning.*
- Can be used to treat diabetic neuropathy and encephalopathy through its ability to reduce oxidative stress and apoptosis.*
- Can be used to treat symptoms associated with osteoarthritis, as it has the ability to reduce inflammation in synovial fluids.*
- May reduce the smooth muscle–cell proliferation that occurs after venous graft surgery, therefore preventing vessel stenosis.*
- Can be used to treat diseases associated with fibrosis, as it reduces oxidative stress, a major factor in conditions such as Dupuytren's disease.*

FORM AND DOSE TO GUARANTEE EFFICACY AND SAFETY

N-Acetylcysteine in **NAC SAP** is an acetylated form of the amino acid cysteine which is more efficiently absorbed.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **NAC SAP** lot numbers have been validated by a third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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WHAT IS *N*-ACETYLCYSTEINE (NAC)?

NAC is a metabolite of the amino acid cysteine. It is produced within the human body and acts as sulfur donor in the sulfation cycle in phase II detoxification, and as a methyl donor in the conversion of homocysteine to methionine. The addition of the acetyl group to cysteine allows it to be more readily absorbed and distributed in the body. NAC is absorbed by cells and hydrolyzed to cysteine. Cysteine is used for many functions in the body and it is the rate-limiting amino acid in gluthathione production by the body. NAC has also been well documented to reduce viscosity of lung secretions and can help symptoms associated with chronic obstructive pulmonary disease (COPD). NAC has immune-enhancing qualities and can reduce the severity of symptoms associated with viral infections.

NAC AND NUTRITIONAL RESEARCH

Glutathione and NAC

Glutathione is one of the most important antioxidants found in the human body. NAC is a precursor to intracellular cysteine and glutathione (GSH).[1] NAC and GSH have demonstrated the ability to be chemoprotective against lung cancers and colon cancer.[2, 3] A study found that one potential mechanism for cancer prevention by NAC is through its ability to inhibit the growth of cancer cells through modulation of intracellular redox environments.[3] Human colon carcinoma cells were treated with benzyl isothiocyanate, diallyl disulfide, dimethyl fumarate, lycopene, sodium butyrate, or buthione sulfoxamine (a GSH synthesis inhibitor) at concentrations shown to cause oxidation of GSH. A decrease in cell proliferation, as measured by [(3)H]-thymidine incorporation, was observed that could be reversed by pretreatment with the GSH precursor and antioxidant NAC.[3] NAC may be able to assist in prevention of cancer and other mutagenic disease via its antioxidant ability, modulation of DNA repair, regulation of cell survival and apoptosis, its antiangiogenetic activity, and as a precursor to GSH.[2]

Mucolytic Properties

Patients with cystic fibrosis (CF) have a defective chloride transport in the epithelial cells of the lungs which makes the mucous more viscous, leaving patients more prone to developing infections.[4] NAC is well-known for its mucolytic properties and has shown the ability to promote efflux of chloride from the epithelial cells in the lung, thus improving hydration of the mucous and decreasing its viscosity.[4]

COPD leads to irreversible damage of parenchyma and airway walls, and oxidative stress is a major contributor to the pathogenesis and progression of COPD. Placebo-controlled studies in which patients with chronic bronchitis were given maintenance therapy with NAC showed a reduction in the following symptoms: viscosity of sputum, severity of coughing, number of bacteria in the airways, number and severity of influenza-like episodes, and number of exacerbations.[5] It is important to note that the number of exacerbations was only affected in patients not using inhaled corticosteroids.[5]

Immune Modulation

Infection with the influenza virus causes oxidative stress, which can lead to pulmonary damage.[6] NAC had a protective effect in a mice model given a lethal influenza infection. Studies have shown that administration of NAC significantly decreased the mortality in infected mice.[6] NAC has not been demonstrated to have any antiviral activity, so present findings suggest that antioxidant therapy can increase survival either by its direct antioxidant effect against the oxidative stress caused by the viral infection, or by improvement in the host defenses mechanisms.[6]

A study by Dervabin et al. (2008) explored treatment options for avian flu. Using a nutrient mixture containing lysine, proline, ascorbic acid, green tea extract, *N*-acetylcysteine, and selenium, the researchers demonstrated an inhibitory effect on replication of influenza virus and HIV. A significant advantage that this combination had over antivirals, including amantadine and oseltamivir, was that it was still able to affect viral replication during later stages of infection.[7]

Fibrosis

NAC has been shown to have antifibrotic properties; therefore, the effect of NAC on Dupuytren's disease, a benign fibroproliferative disorder of the palmar fascia, was explored.[8] The study involved using varying dosages of NAC on isolated fibroblasts from resected fibrotic palmar tissues. NAC was shown to decrease expression of three major indicators of impaired fibrotic matrix turnover, including α-smooth muscle actin, α-1 type-1 procollagen, and plasminogen activator inhibitor type-1. This would suggest that the signaling and subsequent expression of fibrogenesis-related proteins in Dupuytren's disease or other fibroproliferative disorders may be reduced by NAC.[8]

Smooth Muscle Proliferation

After venous bypass grafting, one important indicator that dictates success versus failure is the formation of neointima, characterized by smooth muscle cell proliferation. A study examined the ability of NAC to attenuate smooth muscle cell proliferation and neointima formation, both in vivo and in vitro.[9] NAC demonstrated the ability to attenuate neointima formation and vein-graft stenosis, by reducing vascular smooth muscle cell (VSMC) proliferation in vivo, and also was able to prevent hyperoxia-induced cytokine production of VSMC proliferation in vitro.[9]

NAC and Chelation Therapy

meso-2,3-Dimercaptosuccinic acid (DMSA) is frequently used as an oral chelator to help remove toxic metals from the body. Studies combining DMSA with NAC for the chelation of lead and arsenic found that the combination of the two substances was more effective at reducing total body burden of these two metals than using DMSA alone.[10, 11] The study also found that there was statistically significant improvement in recovery parameters indicative of oxidative stress with combined administration of NAC with DMSA over monotherapy with DMSA.[10]

Safety of NAC Supplementation

NAC has been studied for over 40 years as both prophylaxis and therapy for a variety of clinical conditions, with the majority involving GSH depletion and alterations of the redox status. These studies have established the safety of NAC, even at very high doses and for long-term treatments.[1] One specific study looking at high dose (2800 mg/d) treatment with NAC for patients with cystic fibrosis demonstrated that NAC is a well-tolerated and safe medication for prolonged therapy for patients with CF.[12]

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INDICATION-SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety has been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc.) assessed and has been rated using a 5-star ★ rating classification.

Indication	Suggested NAC SAP dosage	Supporting evidence and study outcomes	Study design	Outcomes measures	Safety	Evidence quality rating
MENTAL HEALTH						
Schizophrenia [1],[2],[3]	1 to 7 capsules/day	Significant improvement in PANSS score and total score in the supplemented group; also, a substantial improvement in working memory.	7 randomized, controlled studies (*n* = 578; 8 to 52 weeks). 600 to 3,600 mg/d of NAC.	Positive and Negative Syndrome Scale (PANSS), working memory, and total score.	No severe adverse effects reported.	★★★★
	4 capsules/day	Significant improvement in PANSS score and Clinical Global Impression in the supplemented group; also, an improvement in akathisia was noticed.	Randomized, double-blind, placebo-controlled, multicentre study (*n* = 140; 4 weeks). 2 g/d of NAC.	PANSS, Clinical Global Impression (CGI), Severity and Improvement scales, general functioning, and extrapyramidal rating scales.	No severe adverse effects reported (both supplemented and placebo group showed similar adverse effects).	★★★
	2 to 12 capsules/day	Significant improvement in total psychopathology; also, a substantial improvement in lipid metabolic dysregulation in the supplemented group.	6 randomized, controlled studies (*n* = 701; 8 to 24 weeks). 1,000 to 6,000 mg/d of NAC.	PANSS total, negative, general, CGI-S, CGI-I scores, The Longitudinal Interval Follow-Up Evaluation-Range of Impaired Functioning Tool (LIFE-RIFT), and Montgomery–Asberg Depression Rating Scale (MADRS).	No severe adverse effects reported (gastrointestinal, musculoskeletal complaints).	★★★★
Bipolar disorder [4]	2 capsules/day	Significant improvement in overall measures of symptom severity, functioning, and quality of life; and 50% drop in MADRS scores.	Randomized, double-blind, placebo-controlled study (*n* = 17; 24 weeks). 1,000 mg/d of NAC.	MADRS, Bipolar Depression Rating Scale (BDRS), Young Mania Rating Scale (YMRS), measures of symptom severity, functioning, and quality of life.	No severe adverse effects reported (headache, abdominal pain, diarrhea).	★★★
CARDIOVASCULAR AND METABOLIC HEALTH						
Cardiovascular health [5]	2 capsules/day	Significant drop in MMP-2 and MMP-9 levels in the supplemented group; also, a substantial decrease in the length of hospitalizations and creatine kinase-MB, NT-proBNP, and hs-cTnT levels.	Randomized, double-blind, placebo-controlled, prospective study (*n* = 98; 3 days). 1,200 mg/d of NAC.	Serum MMPs levels, creatine kinase-MB, NT-proBNP, hs-cTnT, and occurrence of major adverse cardiac events (MACE) within a year of follow-up.	No severe adverse effects reported.	★★★
Atrial fibrillation [6]	1 to 10 capsules/day	Lower interleukin-6 levels in the supplemented group compared to the baseline; other symptoms did not have statistical significance.	Randomized, double-blind, placebo-controlled study (*n* = 100; 24 hours). 600 mg of NAC plus 150 mg/kg bolus dose.	Postoperative atrial fibrillation, length of hospital stay, and coronary artery bypass grafting.	No severe adverse effects reported.	★★

Blood pressure [7]	12 capsules/day	Significant drop in systolic blood pressure; also, substantial improvement in oxidative stress, glutathione concentration, mitochondrial function, overall physical function, inflammation, and insulin resistance.	Randomized, double-blind, placebo-controlled study (*n* = 36; 2 weeks). 6,000 to 9,000 mg/d of NAC + 100 mg/kg/d of glycine and 200 mg/kg/d of alanine.	Blood pressure, skeletal-muscle intracellular antioxidant glutathione (GSH) concentrations, red blood cell (RBC) total and reduced GSH, mitochondrial fatty-acid oxidation (MFO), insulin resistance (IR), and inflammation markers.	No severe adverse effects reported.	★★★
Oxidative stress [8], [9], [10]	2 capsules/day	Significant net antioxidant capacity of the plasma corresponding to increase in preexercise net peroxyl radical scavenging capacity.	Randomized, controlled study (*n* = 9; 3 days). 800 mg/d of NAC.	Total and oxidized GSH levels, plasma thiobarbituric acid-reactive substances, net peroxyl radical scavenging capacity, and exercise-associated damage in leukocyte DNA.	No severe adverse effects reported.	★★
	2 capsules/day	Significant effect against pro- and anti-inflammatory cytokines; also, substantial prevention of oxidative damage.	Randomized, single-blind, placebo-controlled study (*n* = 29; 21 days). 700 to 800 mg/d of NAC (10 mg/kg body mass).	Measurement of oxidative damage in proteins, muscle soreness levels, carbonyl content, thiobarbituric acid–reactive species, TNF-α, and interleukin-10.	No severe adverse effects reported.	★★★
	2 capsules/day	Significant increase in maximal oxygen uptake in the supplemented group; also, a substantial improvement in muscle fatigue and controlled lactate production.	Randomized controlled study (*n* = 29; 7 days). 1,200 mg/d of NAC.	Muscle fatigue, maximal oxygen uptake ($VO_{2_{max}}$), total antioxidant capacity (TAC), lactate, creatine kinase (CK), and TNF-α.	No severe adverse effects reported.	★★
Exercise performance [11], [12]	4 capsules/day	Significant reduction in respiratory muscle fatigue after heavy exercise; also, lower maximum respiratory pressure (inspiratory).	Randomized, double-blind, placebo-controlled, crossover study (*n* = 8; 4 days). 1,800 mg/d of NAC.	Total lung capacity (TLC), residual volume (RV), peak oxygen uptake, pulmonary function measurements, and plasma total glutathione concentration.	No severe adverse effects reported.	★★★★
	15 capsules/day	Significantly enhanced peak oxygen consumption; also, substantial increase in muscle cysteine in the supplement group.	Randomized, double-blind, placebo-controlled, crossover study (*n* = 8; 24 hours). 9,000 to 11,000 mg/d of NAC.	Measurement of muscle cysteine, cystine, and glutathione and time to fatigue during prolonged, submaximal exercise.	No severe adverse effects reported (flushing, erythema, sweating, itchy skin, coughing, swelling).	★★★★
RESPIRATORY HEALTH						
Bronchitis [13], [14], [15]	1 capsule/day	Significant reduction in risk of exacerbations; also, substantial improvement from bronchitis symptoms.	11 randomized, controlled studies (*n* = 2,011, 12 to 32 weeks). 400 to 600 mg/d of NAC.	Number of participants with "no exacerbation," improvement from symptoms, and number of participants who needed treatment.	No severe adverse effects reported (gastrointestinal disturbance).	★★★★

	2 capsules/day	Significant reduction in risk of exacerbations in chronic bronchitis patients without airway obstruction.	13 randomized, controlled studies (n = 4,155; 5 to 36 months). 260 to 1,200 mg/d of NAC.	Frequency of exacerbations.	No severe adverse effects reported.	★★★★
	1 to 2 capsules/day	Significant reduction of symptoms and risk of exacerbations without increasing risk of adverse effects.	11 randomized, double-blind, placebo-controlled studies (n = 1,564; 3 to 36 months). 400 to 1,200 mg/d of NAC.	Frequency and symptoms of chronic bronchitis exacerbations.	No severe adverse effects reported (nausea, vomiting, dyspepsia, abdominal pain, constipation, and diarrhea).	★★★★
COPD [16], [17], [18]	1 capsule/day	Significant interaction between body mass index and carbohydrate intake of COPD patients; also, substantial improvement in nutritional and antioxidant status.	Randomized, controlled, single-blind, parallel study (n = 79; 6 months). 600 mg/d of NAC, 500 mg/d of vitamin C, or combination of 600 mg/d of NAC and 500 mg/d of vitamin C.	Nutritional and antioxidant status of patients affected by COPD.	No severe adverse effects reported.	★★
	1 to 4 capsules/day	Significant relief in COPD exacerbations observed in long-term–supplemented groups.	12 randomized, controlled studies (n = 2,691; 3 to 36 months). 257 to 1,800 mg/d of NAC.	Rate of COPD exacerbations and lung-function parameters.	No severe adverse effects reported (nausea, vomiting, abdominal pain, indigestion).	★★★★
	2 capsules/day	Significant decrease in COPD exacerbations observed in high-dose–supplemented group; also, a substantial decrease in number of exacerbations.	11 randomized, controlled studies (n = 2,587; 22 weeks to 3 years). 400 to 1,200 mg/d of NAC.	Total number of exacerbations and number of patients with at least one exacerbation.	No severe adverse effects reported (diarrhea, reflux oesophagitis, and gastric complaint).	★★★★
Cystic fibrosis [19], [20]	5 capsules/day	A significant improvement or stable maintenance of lung function was observed in the supplemented group.	Randomized, double-blind, placebo-controlled, multicentre study (n = 70; 24 weeks). 2,700 mg/d of NAC.	Change in $\log_{10}$ HNE activity in sputum from day 0 to day 168, change in spirometry indices, incidence and number of sinus and pulmonary exacerbation, time to first pulmonary and/or sinus exacerbation, time to first new or increased use of antibiotics, change in the neutrophil count, and concentration of interleukin-8.	No severe adverse effects reported.	★★★
	5 capsules/day	Significant decrease in the level of oxidized vitamin C in the supplemented group; also, a substantial increase in vitamin C levels.	Randomized, controlled, open-label study (n = 21; 4 weeks). 2,400 mg/d of NAC.	Level of oxidative stress markers, plasma malondialdehyde (MDA), 8-isoprostane (8-isoP), urinary excretion of 8-oxo-7,8-dihydro-2-deoxyguanosine (8-oxodG), 8-oxo-7,8-dihydroguanosine (8-oxoGuo), lung function, and oxidative burst.	No severe adverse effects reported.	★★

IMMUNE HEALTH						
Antiretroviral [21]	1 capsule/day	Significant increase in the proliferation of CD4 lymphocytes in the supplemented group.	Randomized, double-blind, placebo-controlled study (*n* = 20; 180 days). 600 mg/d of NAC.	Determination of the viral load, quantification of CD4 and CD8 lymphocytes, evaluation of hematocrit, and total lymphocyte count.	No severe adverse effects reported.	★★★
Immunity [22],[23]	4 capsules/day	Significant drop in high-sensitivity C-reactive protein, myeloperoxidase, and Gal-3 levels in the supplemented group.	Randomized, single-blind, controlled study (*n* = 32; 3 days). 1,800 mg/d of NAC.	Quantification of high-sensitivity C-reactive protein (HsCRP), myeloperoxidase (MPO), and galectin-3 (Gal-3).	No severe adverse effects reported.	★★
	2 capsules/day	Significant prevention of increase in transforming growth factor (TGF-β) and improvement in ejection fraction in the supplemented group.	Randomized, double-blind, placebo-controlled study (*n* = 88; 3 days). 1,200 mg/d of NAC.	Quantification of serum levels of TGF-β and TNF-α.	No severe adverse effects reported.	★★★
Rheumatoid arthritis [24]	2 capsules/day	Significant reduction in erythrocyte sedimentation rate, HsCRP, and malondialdehyde levels in the supplemented group; also, a substantial improvement in morning stiffness, fasting blood sugar, and high-density lipoprotein cholesterol (HDL-C) levels.	Randomized, double-blind, placebo-controlled study (*n* = 74; 3 months). 1,200 mg/d of NAC.	Disease activity score-28 (DAS-28), serum malondialdehyde (MDA), total antioxidant capacity (TAC), glutathione peroxidase (GPX) activity, nitric oxide (NO), hs-CRP, fasting blood sugar (FBS), lipid profile, and erythrocyte sedimentation rate (ESR).	No severe adverse effects reported.	★★★
SEXUAL HEALTH						
Sperm quality [25],[26]	1 capsule/day	Significant increase in sperm count and motility in the supplemented group; also, a substantial decrease in abnormal morphology, DNA fragmentation, and protamine deficiency.	Randomized, blind study (*n* = 50; 3 months). 600 mg/d of NAC.	Protamine content, DNA integrity (terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL), total antioxidant capacity (TAC), MDA, LH, FSH, testosterone, and prolactin.	No severe adverse effects reported.	★★
	1 capsule/day	Significant decrease in serum follicle-stimulating hormone in the NAC-plus-selenium supplemented group; also, a substantial improvement in sperm concentration, motility, and morphology.	Randomized, double-blind, placebo-controlled study (*n* = 486; 26 weeks). 600 mg/d of NAC or 200 µg/d selenium plus 600 mg/d NAC.	Quantification of serum testosterone, estradiol, follicle-stimulating hormone, luteinizing hormone, prolactin, inhibin B, selenium, and *N*-acetylcysteine.	No severe adverse effects reported.	★★★

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