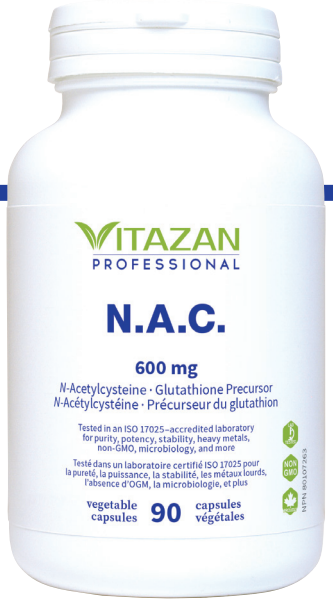
N.A.C.

N-Acetylcysteine
High-Potency Antioxidant



- **Loosens phlegm pockets in the lungs during colds and flu for easier expulsion**
- **Assists reproductive health**
- **Improves nervous-system functioning**
- **600 mg NAC per capsule based on latest clinical trials**

Mechanisms

- Antioxidant: Increase intracellular glutathione (direct precursor), protect against oxidative stress, and maintain redox balance (reacts with highly oxidizing radicals) in a nonenzymatic way.[1][2]
- Anti-inflammatory: Regulates the enzymes inhibitor of nuclear factor κ-B kinase subunit beta (IKKβ) and nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB).[2][3]
- Neurotransmission: Regulates *N*-methyl-D-aspartate (NMDA) receptors and glutamatergic transmission either directly or indirectly (implicated in schizophrenia and addiction).[1][4][5]
- Implicated in the functional pathophysiology of neurodegenerative disease such as Parkinson's and Alzheimer's disease.[2]
- Neuropathic pain: Mechanism unknown, but potentially through the inhibition of nociceptive transmission.[2]
- Addiction: Correction of glutamate (excitatory neurotransmitter) dysregulation via upregulation of the glutamate transporter (GLT-1) that removes glutamate in an area of the brain.[5]

Table 1. Clinical Studies of N.A.C.

Indication	Design	Outcomes	Ref.
Chronic bronchitis and chronic obstructive pulmonary disease (COPD)	Meta-analysis of 13 studies. 4155 COPD patients, NAC $n = 1933$, placebo $n = 2222$. Randomized, double-blind, placebo-controlled trial, 64 patients with COPD.	Patients treated with NAC had statistically fewer exacerbations of chronic bronchitis or COPD. With documented airway obstruction, 1200 mg/d is advised to prevent exacerbation, but without airway obstruction, 600 mg/d can be advised. Post-hoc analysis demonstrated reduced exacerbations (sputum/expectoration and cough) in COPD patients compared to placebo during the winter months. Patients in the NAC group were either asymptomatic or mildly symptomatic compared to placebo by 2–3 months, at NAC 3 × 300 mg/d. Subjective rating was also greater in the NAC group.	[19][20]

Indication	Design	Outcomes	Ref.
Endometriosis-related pain, size reduction of ovarian endometriomas, and fertility outcomes	Prospective observational single-cohort study with 120 patients between 18 and 45 years old with a clinical/histological diagnosis of endometriosis. All patients received quarterly oral NAC 600 mg tid for 3 consecutive days of the week for 3 months.	The intensity of dysmenorrhea, dyspareunia, and chronic pelvic pain significantly improved. NSAIDs use, the size of the endometriomas and the serum levels of CA 125 significantly decreased. Among the 52 patients with reproductive desire, 39 successfully achieved pregnancy within 6 months of starting therapy.	[26]
Improved ovarian response and blastocysts quality in women of advanced age undergoing IVF/ICSI-ET	Prospective randomized controlled study with 200 patients with advanced age undergoing GnRH antagonist protocol. The treatment group (n = 100) received 600 mg NAC tid from the menstrual phase of the previous cycle for about 45 days using the GnRH antagonist protocol. Control group (n = 100) received the same protocol without NAC.	Total doses of Gn in the NAC treatment group were less than those in the control group. Compared with the control, the number of high-quality blastocysts in NAC treatment increased significantly. Clinical pregnancy rates did not differ in both groups. Glutathione content in the follicular fluid increased significantly in the treatment group.	[27]
Adjuvant to clomiphene citrate for induction of ovulation in PCOS patients	Placebo-controlled, double-blind, randomized clinical trial, 180 PCOS infertile patients: group 1 received clomiphene citrate (CC) plus NAC (1.2 g/d); group 2 received CC plus placebo for 5 days starting at cycle day 3. On cycle day 12 in the presence of at least one follicle with an 18–20 mm diameter, hCG was injected intramuscularly, and timed intercourse was advised 36 h after hCG injection.	The number of follicles > 18 mm and the mean endometrial thickness on the day of hCG injection were significantly higher in the CC+NAC group. The ovulation and pregnancy rates were also significantly higher in the CC+NAC group. No adverse side effects and no cases of ovarian hyperstimulation syndrome were observed in the NAC treatment group.	[28]
Sperm parameters in infertile men	Open-label study of 50 infertile men to receive 600 mg/d for 3 months of NAC, followed by semen analysis, oxidative stress markers, and hormones.	Compared to pretreatment levels, NAC demonstrated increased sperm count and motility, while abnormal morphology, DNA fragmentation, and protamine deficiency decreased. Serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) decreased, and testosterone increased. Total antioxidant capacity increased, while malondialdehyde decreased.	[25]
Systemic lupus erythematosus (SLE) disease activity and complications	Randomized, double-blind clinical trial involving 80 SLE patients divided into two groups: 40 patients received NAC (1,800 mg/d, 3 times per day with 8 h intervals) for 3 months, and 40 patients as the control group received normal therapies. Laboratory measurements and disease activity based on the British Isles Lupus Assessment Group (BILAG) and SLE Disease Activity Index (SLEDAI) were assessed before and after the initiation of treatment.	BILAG and SLEDAI scores were significantly decreased after receiving NAC. The disease activity in each organ based on BILAG score after treatment indicated a significant decrease in the NAC group compared to the baseline level in general, mucocutaneous, neurological, musculoskeletal, cardiorespiratory, renal, and vascular complications. Analysis indicated a significant increase in CH50 level in the NAC group.	[29]
Bipolar depression (suicidal ideation)	24-week randomized, multicenter, double-blind, placebo-controlled trial. 2 g/d (n = 75)	According to the scales used in the study, a statistically significant difference was found for reduction in suicidal ideation in bipolar depression with NAC compared to placebo, regardless of age or sex. It may be beneficial for bipolar depression.	[1]

Indication	Design	Outcomes	Ref.
Depression with increased inflammation	Systematic review of 12 randomized controlled trials (RCTs). 12 weeks of NAC or placebo.	A significant decrease in depression symptoms was observed in individuals receiving NAC compared to placebo; however, only in those patients with baseline high-sensitivity C-reactive protein (hs-CRP) > 3 mg/L. CRP levels decreased in the NAC group, in addition to uric acid levels. Weight gain occurred in the placebo group, and no weight change occurred in the NAC group irrespective of baseline hs-CRP compared to placebo.	[3]
Depression	Systematic review and meta-analysis of double-blind, placebo-controlled studies for symptoms of depression regardless of psychiatric condition. Five studies met inclusion out of 38, n = 574, 291 adult patients to receive NAC and 283 adult patients to receive placebo, between 12 and 24 weeks.	NAC significantly improved depression on the Montgomery–Åsberg Depression Rating Scale (MADRS) and global functionality scale compared to placebo. Subjects presented with bipolar depression, major depressive disorder, and other (trichotillomania and smoking).	[6]
Cognitive effects (memory) in psychosis	Adjunctive treatment to standard psychotropic medication using NAC 2 g/d (n = 27) versus placebo (n = 31) for 24 weeks on cognitive functions such as attention, memory, and executive functions.	NAC demonstrated significant increase in working memory at 24 weeks compared to placebo.	[7]
Schizophrenia	[NAC, a neuroprotective agent, improves cognitive impairment and negative symptoms (but not positive symptoms)]. NAC (3600 mg/d) for 52 weeks in a randomized, double-blind, placebo-controlled study (n = 60).	NAC significantly improved Positive and Negative Syndrome Scale (PANSS) negative and disorganized thought symptom scores. This study failed to demonstrate causation to effects on brain morphology, mechanism not elucidated.	[8]
		Earlier studies demonstrate increased brain glutathione, and improvement in brain processing speed and positive symptoms over 12 weeks and 6 months.	[9][10]
		Another study demonstrated that NAC may improve white matter integrity.	[11]
Cocaine addiction	Open-label pilot study, 16 patients completed the study, comparing three doses of NAC; 1200 mg/d, 2400 mg/d, and 3600 mg/d for 4 weeks. Double-blind, placebo-controlled study of 111 cocaine, nonabstinent users, 1200 mg/d, 2400 mg/d NAC for 8 weeks.	All volunteers either stopped using cocaine or significantly reduced during the treatment, at both 2400 mg/d and 3600 mg/d. Did not stop the users from seeking cocaine, but for those who were already abstinent, NAC at 2400 mg/d prevented relapse and reported lowered cravings during trial.	[12][13]
Adolescent cannabis addiction	Double-blind, randomized, controlled trial in adolescents 15–21 years of age to receive 1200 mg/d of NAC or placebo for 8 weeks alongside brief (10 min) weekly consulting sessions.	Doubled odds of cannabis abstinence and verified by urinary cannabinoid test.	[14]

Indication	Design	Outcomes	Ref.
Alcohol use disorder	Double-blind, randomized, placebo-controlled study in veterans with posttraumatic stress disorder (PTSD). 8 weeks of 2400 mg/d or placebo. Randomized trial of NAC 1200 mg/d versus placebo in marijuana-dependent adolescents 15–21 years of age.	NAC combined with cognitive behavioral therapy (CBT) helped reduce cravings, improve depression and PTSD symptoms in veterans compared to placebo. Substance abuse declined in both, but were not significantly different between groups. There was significantly less compensatory alcohol use in the lowered-marijuana-use group compared to placebo, suggesting NAC may be valuable for both substance abuse in adolescents.	[15][16]
Tobacco use	12-week randomized, double-blind, controlled trial, 3 g/d NAC versus placebo ($n = 34$). Randomized, double-blind, placebo-controlled trial, NAC 3600 mg/d ($n = 12$) or placebo ($n = 10$) for 3.5 days, on short-term abstinence (asked to stop smoking).	NAC significantly reduced the number of cigarettes and exhaled carbon monoxide, and improved symptoms of depression. 47.1% in NAC group were able to quit smoking, compared to 21.4% in the placebo group. No differences in cravings was observed; however, there was statistical trend in lowered withdrawal symptoms in the NAC compared to placebo. Additionally, the NAC group expressed less reward sensation when given their first cigarette compared to the placebo group.	[17][18]
Meta-analysis on cravings for substance use disorder	7 RCTs ($n = 245$), small to moderate sample sizes, with primary outcome on the statistical analysis of studies used to compare NAC versus placebo for craving symptoms in substance use disorders.	Compared to placebo, NAC was significantly superior in reducing craving symptoms. Additionally, the meta-analysis demonstrated low risk of bias and study heterogenicity was nonsignificant.	[4]
Compulsive disorder in children and adolescents	Systematic review of pharmacotherapy and NAC in children and adolescents for OCD, autism spectrum disorder (ASD), and attention deficit hyperactivity disorder (ADHD) in 21 trials.	Most studies were of poor quality and/or high degree of heterogeneity. NAC and one other medication were found to be worthwhile to investigate further due to the low risk-to-benefit ratio. NAC, as an augmentation to risperidone, was found superior to placebo in improving irritability in children with ASD.	[21][22]
Obsessive-compulsive disorder (OCD)	Randomized, double-blind, placebo-controlled trial NAC 3000 mg/d versus placebo for 16 weeks, $n = 40$, as augmentation to serotonin reuptake inhibitors. Systematic review: OCD and grooming disorders in adults and children. 4 randomized, double-blind, placebo-controlled studies on the usefulness of NAC.	Both NAC and placebo decreased scores in the Yale–Brown Obsessive Compulsive Scale (Y-BOCS) questionnaire for OCD symptomatology, with no significant differences between groups. NAC was superior to placebo in alleviating anxiety but not depression. NAC was well tolerated, except for increased reporting of abdominal pain. Results are inconclusive; however, it may still be useful. Larger trials are needed.	[23][24]

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Each vegetable capsule contains:

N-Acetyl-L-cysteine. . . . . 600 mg

Nonmedicinal ingredients: Microcrystalline cellulose, vegetable magnesium stearate, and silicon dioxide in a non-GMO vegetable capsule composed of vegetable carbohydrate gum and purified water.

Directions of use: **Adults:** Take 1 capsule twice daily with a meal or as directed by your health-care practitioner.

Cautions and warnings: Consult a health-care practitioner prior to use if you are pregnant or breast-feeding, or if you have kidney stones.

Contraindications: Do not use this product if you are taking antibiotics or nitroglycerin.

Product #0407 · 90 vegetable capsules · NPN 80107263 · V0210-R5