

DOSSIER · SUBSTANCE

Niacin

Niacin is the collective term for nicotinic acid and nicotinamide, two forms of vitamin B3 with differing pharmacology. The literature is broad, yet unevenly distributed: numerous fundamental and mechanistic studies stand against comparatively few controlled human trials. The most striking finding is an observational study linking a niacin breakdown product to vascular inflammation.

471

STUDIES IN
TOTAL

188

IN HUMANS

30

OF WHICH
CONTROLLED

54

IN ANIMALS

25

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Niacin at a Glance

ORIGIN:

Niacin is the collective term for nicotinic acid and nicotinamide, the two forms of vitamin B3 with differing pharmacology. Both act as precursors of NAD+, a coenzyme involved in energy production and redox reactions in nearly every cell. Niacin is absorbed via the diet; how much of it is available depends on the food and matrix.

EVIDENCE BASE:

471 evaluated studies · 30 controlled human studies · 158 observational studies · 27 review articles · 54 animal experiments · 20 cell culture studies

STRONGEST EVIDENCE:

- Glaucoma: A meta-analysis of five case-control studies found a higher proportion of persons without glaucoma according to ISGEO criteria with high niacin intake (OR 0.66; 95 % CI 0.55-0.79) [27].
- Motor function: In the only controlled niacin study in this field, 47 Parkinson patients received low-dose niacin or placebo double-blind for six months; the mean UPDRS-III change was -1.06 versus -0.05 [58].
- Metabolism: Among 3106 Chinese adults, each unit of higher niacin intake was associated with a 3.5 % risk reduction for diabetes (OR 0.965; 95 % CI 0.944-0.986); 15.9 % had diabetes [15].
- Cardiovascular risk: In cardiac patients, the terminal metabolites 2PY (HR 1.64 and 2.02) and 4PY (HR 1.89 and 1.99) were associated with increased 3-year risk of major cardiovascular events [65].
- Safety and tolerability: The data come predominantly from studies in which niacin served as active placebo; in a pilot study with six participants, no serious adverse events occurred [61].

LIMITATIONS:

- Controlled human studies form a small group with around thirty papers and are spread across many indications; independent replication remains an open task in the individual fields.
- The target variables are predominantly markers such as lipids, flushing or mobility, not disease courses; the largest single listed block consists of observational studies.
- Some of the captured papers are protocols of planned studies without results; controlled trials in neurological diseases and in COVID-19 are still outstanding.

CLASSIFICATION:

Niacin is the collective term for nicotinic acid and nicotinamide; mechanism and tolerability are well described, while controlled human studies are at an early stage in many fields.

1. What Niacin Is

Studies investigate how far replenishment of NAD+ stores contributes in tumour cachexia as well as reviews on glaucoma and age-related macular degeneration. Niacin is absorbed via the diet; how much of it is available depends on the food and matrix, as a comparative review on vitamins from animal and plant sources shows. Niacin is also investigated as a supplement, explicitly also in low dosage.

It is crucial for understanding all studies that niacin is not a uniform substance. Nicotinic acid activates the hydroxycarboxylic acid receptor 2 and thereby triggers the characteristic flushing; a study in chronic heart failure describes this receptor effect for niacin and for the ketone 3-hydroxybutyrate side by side. Nicotinamide is not associated with this receptor effect. The form therefore co-determines which effects can be expected at all. In addition there is the measurement level: what is measured is less often niacin itself than its precursors and degradation products, for example NAD+ and terminal metabolites. Precisely one such metabolite is linked by a frequently cited observational study to vascular inflammation. In several studies flushing additionally serves as a measure of the vascular response.

2. What the Studies Show in Detail

The key human studies and the most important reviews — by field of application, with population, duration, preparation, measured variable and result as reported in the original papers. Numbers appear only where the study states them.

Distribution of **controlled human studies** by application area — the numbers are not additive, as one study can be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Metabolism	12
Heart and Circulation	11
Safety and Tolerability	11
Cognition and Psyche	10
Fatigue and stress	5

APPLICATION AREA	CONTROLLED STUDIES
Virale Infekte	3
Oncology	3
Inflammatory Processes	2

Cognition and Psyche

The only controlled niacin study in this area examined low-dose niacin in Parkinson's patients: 47 affected individuals received either low-dose niacin or placebo double-blind for six months, followed by a six-month open phase in which all participants received niacin [58]. The primary endpoint was the UPDRS-III score; depression, sleep quality, mental flexibility, cognition and physical fatigue were also recorded. After six months the mean change in UPDRS III was -0.05 (95 % CI -2.4 to 2.32) under placebo and -1.06 (95 % CI -3.68 to 1.57) under niacin [58]. In the open phase from month six to twelve the values fell by 4.58 (95 % CI -0.85 to 8.30) in the placebo group and by 4.63 (95 % CI 1.42 to 7.83) points in the niacin group [58]. The decline in the open phase must be read without a control group.

In three further controlled studies in this area niacin served not as the test substance but as an active placebo in psilocybin studies. In a phase-2 study in adults with major depression (21 to 65 years, 11 centres) participants received a single dose of either 25 mg synthetic psilocybin or 100 mg niacin in identically appearing capsules in a 1:1 ratio, each with psychological support; assessments took place at baseline and on days 2, 8, 15, 29 and 43 [5]. In a double-blind study in hospital staff with depression after COVID front-line work participants received 25 mg psilocybin or 100 mg niacin orally, spread across two preparation, one medication and three integration sessions; the primary endpoint was the change in depressive symptoms from baseline to day 28 [3]. A psychophysical pilot study with six participants compared 25 mg psilocybin with 100 mg niacin and reported no serious adverse events [61].

The review article "The Promise of Niacin in Neurology" classifies niacin as a precursor of NAD⁺ and describes effects via the hydroxycarboxylic acid receptor 2 (Hcar2), including regulation of immune responses, phagocytosis of myelin debris and cholesterol efflux; as investigated or proposed areas of application it names multiple sclerosis, Alzheimer's, Parkinson's, glioblastoma and amyotrophic lateral sclerosis [33]. The work does not provide concrete participant numbers or effect sizes. Further controlled studies investigating niacin as a test substance in these neurological diseases are still outstanding.

Metabolism

In the AIM-HIGH MRI substudy, 214 participants with clinically confirmed atherosclerotic disease and low HDL cholesterol received a carotid MRI at baseline and after two years; they were randomised to either extended-release niacin or placebo, with all receiving simvastatin and ezetimibe if required to lower LDL cholesterol to 40 to 80 mg/dL [6]. Of 156 patients with complete MRI evaluation, participants were on average 61 ± 9 years old and 81 % male; 26 % had taken statins for less than one year [6]. Changes in plaque lipid content and carotid morphology as well as the influence of intraplaque haemorrhage were investigated [6]. In a randomised crossover study in twelve patients with heart failure and reduced ejection fraction, niacin was tested as a potent HCA2 stimulator against placebo on a second study day, with cardiac output as the primary endpoint [26].

A cross-sectional study in 3106 Chinese adults examined the association between dietary folate and niacin intake and diabetes risk; 15.9 % of participants had diabetes [15]. The median niacin value was lower in diabetics than in controls (7,000 vs. 7,900 mg) [15]. After adjustment for possible confounders, each unit higher niacin intake was associated with a 3.5 % risk reduction for diabetes (OR 0.965; 95 % CI 0.944-0.986; P = 0.001) [15]. As a cross-sectional study it cannot establish temporal or causal direction.

A study protocol describes a double-blind, randomised, single-centre study in type 2 diabetics who receive extended-release niacin or placebo for three months; the primary endpoint is the change in HbA1c from baseline to week 12, with secondary recording of fasting glucose, serum transaminases and self-reported adverse events [59]. Results are not available with the protocol. In a placebo-controlled metabolomic study in 70 healthy volunteers, the acute effect of combined metabolic activators containing N-acetylcysteine or cysteine with or without nicotinamide or flush-free niacin was compared; the time series showed high similarity of affected metabolic pathways between the variants, and the combination with cysteine was well tolerated [60].

Several review articles place niacin in the lipid-lowering field. One paper on HDL cholesterol and atherosclerotic risk cites the HDL-raising studies, including the HPS2-THRIVE study with extended-release niacin, as an example that HDL cholesterol is not a viable therapeutic target for prevention [7]. A review on lipoprotein(a) lists niacin among substances with varying degrees of Lp(a) reduction, but emphasises the limited data from large observational studies and post-hoc analyses [14]. Another review states that HDL-raising treatments including niacin have not confirmed the presumed causal role [17]. The Canadian PEER guideline and the associated review of 76 systematic reviews examined niacin alongside statins, ezetimibe, fibrates and others; statins remained first-line therapy [70][72].

Viral Infections

A review article on lipid-modulating substances in COVID-19 identified 40 randomised controlled trials through a systematic search, including 17 on statins, 14 on omega-3 fatty acids, 3 on fibrates, 5 on niacin and 1 on dalcetrapib [8]. Of these 40 studies only 2 had reported preliminary results; most others were still ongoing [8]. As possible mechanisms of action the work cites inhibition of viral entry through disruption of lipid rafts as well as attenuation of the inflammatory response and endothelial activation [8]. Completed studies with reported endpoints that permit a statement on niacin in COVID-19 are still outstanding.

Safety and Tolerability

Data on the tolerability of niacin from this material come mainly from studies in which it served as an active placebo. In the psychophysical pilot study with six participants comparing 25 mg psilocybin against 100 mg niacin, data on harms were collected and no serious adverse events occurred [61]. A study protocol on obsessive-compulsive disorder describes a randomised, double-blind, placebo-controlled study without crossover in 30 adults who receive a

single oral dose of 0.25 mg/kg psilocybin or 250 mg niacin as active placebo; in addition to safety, obsessive symptoms over the past 24 hours are recorded with the Acute Yale-Brown Obsessive-Compulsive Scale and visual analogue scales [52]. Results are not available with the protocol. Systematic tolerability data on niacin in the dosages examined here that do not derive from the placebo role are still outstanding.

Skin

The niacin skin flushing response (NSFR) served as a secondary endpoint in a randomised, open-label study in 71 adolescents and young adults with depression (13 to 24 years, 59.2 % female) [11]. Participants received either omega-3 plus Paxil (n = 34) or Paxil alone (n = 37) for twelve weeks; the primary endpoint was depression severity according to the Montgomery-Åsberg Depression Rating Scale [11]. In the omega-3 group depressive symptoms improved over time (p = 0.00027 at week 12), as did memory, cognitive function and the NSFR; at baseline the NSFR correlated negatively with MADRS scores [11]. The study was open-label, so the authors classify the results as preliminary [11].

A review article on B vitamins and the immune system reports that niacin in normal doses can alter the skeletal muscle fibre phenotype in obese rats — a preclinical finding [34]. The SHARP review describes a dietary supplement based on the attenuated niacin skin reaction as one of three preventive approaches in clinical high risk for psychosis, alongside precision transcranial magnetic stimulation and cognitive behavioural therapy [74]. Whether the attenuated skin reaction is a reliable selection marker for such a supplement is an open question.

Oncology

A systematic review with meta-analysis examined the association between daily niacin intake and glaucoma on the basis of five case-control studies [27]. In the pooled analysis a significantly higher proportion of persons with high niacin consumption was found in the group without glaucoma, defined according to ISGEO criteria (p < 0.00001; OR = 0.66, 95 % CI 0.55-0.79) and according to retinal imaging (p = 0.02; OR = 0.63, 95 % CI 0.43-0.94) [27]. A first-in-human phase I study of KPT-9274, a dual NAMPT/PAK4 inhibitor, investigated 60 patients with advanced solid tumours in three parts, with niacin included in the dose escalation [54]. Three dose-limiting toxicities occurred in the 40-mg (n = 1) and 80-mg-plus-niacin cohorts (n = 2); the maximum tolerated dose was not reached in parts A and B, and recruitment was terminated early due to lack of observable efficacy [54].

A paper on NAD⁺ repletion with niacin describes in mouse models that niacin corrects tissue NAD⁺ levels, improves mitochondrial metabolism and alleviates cachexia; in humans NRK2 was downregulated in muscle of cancer patients, and low NRK2 expression correlated with metabolic abnormalities [66]. The majority of these findings are preclinical. Controlled human studies examining NAD⁺ repletion with niacin in tumour cachexia are still outstanding.

Inflammatory Processes

A meta-analysis of preclinical studies examined whether treatment with niacin or NAD metabolites is useful in infection and sepsis animal models [2]. NAD metabolites alone (n = 44), niacin alone (n = 9) or both (n = 3) were investigated, mostly before or within 24 hours after the challenge (n = 50); only three or four studies included standard antimicrobial therapy or began more than 24 hours after the challenge [2]. Across these preclinical studies, the pooled analysis found lower odds of mortality in the treatment groups [2]. The authors emphasise that this preclinical experience requires confirmation in clinically relevant models.

An observational study in cardiac patients found that the terminal niacin metabolites 2PY and 4PY were associated with increased 3-year risk of major cardiovascular events: adjusted hazard ratio for 2PY 1.64 (1.10-2.42) in the US and 2.02 (1.29-3.18) in the European validation cohort, for 4PY 1.89 (1.26-2.84) and 1.99 (1.26-3.14) respectively [65]. **Hypothesis:** Whether the elevated metabolite levels are the consequence of high intake or of individually different metabolism cannot be separated from these observational data.

A narrative review on NAD⁺ and niacin in glaucoma and age-related macular degeneration reports that animal studies in glaucoma models preserve the density and function of retinal ganglion cells under nicotinamide and that randomised controlled studies showed improvements in visual field sensitivity and inner retinal function in a dose-dependent manner [73]. In macular degeneration nicotinamide administration can improve rod function and protect against oxidative stress; cross-sectional studies show lower dietary niacin intake in affected individuals [73]. The work classifies part of these findings as experimental.

Heart and Circulation

A cohort study based on the National Health and Nutrition Examination Survey (2003-2018) examined the association between dietary niacin intake and mortality in 4315 adults with non-alcoholic fatty liver disease [67]. Mean age was 52.5 years, 2351 participants were male; during a median follow-up of 8.8 years 566 deaths were recorded, 197 of them from cardiovascular disease [67]. Compared with a niacin intake of 18.4 mg or less (lowest tertile), multivariable adjusted hazard ratios were calculated for participants with an intake of 26.7 mg or more [67].

The multivariable odds ratios for the second, third and fourth quartiles versus the lowest were 0.84 (0.68-1.03), 0.80 (0.65-0.97) and 0.69 (0.55-0.85) (p trend = 0.001) [69]. In the stratified analysis the effect differed between groups with and without hypertension (p interaction = 0.033) [69]. Both analyses are observational data and cannot establish cause-and-effect direction.

Further Investigations

An analysis of NHANES data from 2005 to 2008 examined the association between daily niacin intake and glaucoma in 5768 participants aged 40 years and older [68]. Glaucoma diagnosis was made by self-report as well as fundus imaging and ISGEO criteria [68]. Crude odds for self-reported glaucoma were significantly reduced in the third quartile of niacin intake (21.01 to 28.22 mg/day) with OR 0.57 (95 % CI 0.43-0.76; p < 0.001) and in the fourth quartile (above 28.22 mg/day) with OR 0.57 (95 % CI 0.37-0.90; p = 0.018) [68]. Fundus imaging showed a similar trend in the third (OR 0.42, 95 % CI 0.25-0.72; p = 0.002) and fourth quartile (OR 0.36, 95 % CI 0.20-0.67; p = 0.002) [68]. As a cross-sectional analysis the study cannot establish cause-and-effect direction.

Uptake and Availability

A review compared the bioavailability of vitamins from animal and plant foods [71]. For niacin, a bioavailability of 67% is given in animal foods, which are considered the almost exclusive natural source for vitamin B-12 and preformed retinol and also contain highly available biotin (89%), folate (67%), pantothenic acid (80%), riboflavin (61%), thiamine (82%) and vitamin B-6 (83%) [71]. Plant foods are the main source for vitamin C (76% bioavailable), provitamin A carotenoid β -carotene (15.6%), riboflavin (65%), thiamine (81%) and vitamin K (16.5%) [71]. The work points out that the quantitative estimation of available vitamin fractions is limited and fragmentary [71]. Comparative data on the bioavailability of niacin from plant sources are still outstanding.

Overall Picture

Across the fields, niacin appears in two very different roles. As a test substance, it features in controlled studies mainly in the lipid-lowering field and in neurology; the larger randomised investigations on HDL-cholesterol have not confirmed the earlier expectation [7][17]. In the Parkinson study, an improvement in motor function appeared only in the open phase without control [58]. In psychedelic research, by contrast, niacin serves as an active placebo, so these works yield no statement about its own effect [5][3][61][52]. A second strand consists of observational studies on dietary niacin intake, which consistently report inverse associations with glaucoma and fatty liver disease [68][69][27], but cannot establish causality.

Preclinically the situation is broader: animal and cell models on infection, cachexia and retina point to NAD⁺-dependent mechanisms [2][66][73]. These findings must be labelled as preclinical and still await clinical confirmation. An open question concerns the terminal niacin metabolites 2PY and 4PY, which in observational data were associated with increased cardiovascular risk [65] — whether this is a consequence of high intake or individual metabolism is not clarified.

Methodology of the Research Situation

The works in this material comprise randomised controlled trials, study protocols, cross-sectional and cohort studies, meta-analyses as well as narrative and systematic reviews. Among the controlled human studies are double-blind, placebo-controlled studies with six- to twelve-month duration [58][59], crossover studies with twelve participants [26] and MRI substudies over two years [6]. Endpoints range from UPDRS-III and HbA1c values via carotid morphology and cardiac output to mortality and cardiovascular events [58][59][6][26][67]. Several of the present works are protocols without results [59][52]. Systematically lacking are independent, sufficiently large randomised studies that investigate niacin as a test substance with clinical endpoints.

Markers Instead of Endpoints: What Niacin Research Measures

Several works use the niacin skin flush as a measurement variable, including in psychiatric research, where the flush reaction after niacin is recorded as a response measure. As a pharmacodynamic test this is legitimate: the flushing shows that the receptor responds and the vessels react. It does not show, however, whether a disease symptom improves. Anyone who infers a benefit in depressive symptoms directly from an altered flush reaction leaves the level of the marker. For practice the question remains which target variable a niacin study must measure at all for its result to be therapeutically relevant.

The tension becomes clear with the degradation products. A frequently cited observational work links a terminal metabolite of niacin with vascular inflammation and cardiovascular risk — a signal that runs counter to the lipid-related expectation of niacin. This is a reported association, not a controlled proof of effect. Open is which form and which dose range lead to which metabolite concentrations;

HYPOTHESIS:

the form plays a part in this; this would have to be tested specifically. Precisely this question would be clarified by a controlled investigation with hard endpoints.

3. How Robust the Research Is

The works on niacin range from 2000 to 2026 and are predominantly basic-science oriented: the largest single block consists of basic investigations, supplemented by animal studies, cell culture and mechanistic reviews. In humans, observational designs predominate; controlled human studies form a small group with around thirty works. Most frequently they concern metabolism, cardiovascular system, safety and tolerability as well as cognition. These are followed by fatigue, antiviral, oncology, inflammation, skin and bioavailability with only a few works each.

Robustness is greatest for the mechanistic aspects: receptor binding, skin flush and NAD⁺ relation are well described, and safety and tolerability are examined in dedicated controlled works. For clinical questions comparatively few controlled studies are available, distributed across many indications; in the individual fields independent replication remains an open task. Some of the captured works are protocols of planned studies that have not yet delivered results, as well as substudies of large cardiovascular investigations. The target variables are predominantly markers such as lipids, skin flush or mobility, not disease courses.

4. What Is Frequently Claimed — and What the Data Provide

STATEMENT	RESEARCH SITUATION
Niacin lowers cardiovascular risk.	The large lipid studies appear predominantly as substudies and secondary analyses; an observational study on the end metabolite points in the opposite direction.

STATEMENT	RESEARCH SITUATION
Niacin improves motor function in Parkinson's disease.	A single, monocentric randomised placebo-controlled study in US veterans with low-dose supplementation reports an improvement in motor function. A hint f
Niacin intake and glaucoma are associated.	The association between daily niacin intake and glaucoma was examined in a review with meta-analysis as well as in a review on NAD+ and niacin in glaucom
Niacin is safe as a supplement.	Safety and tolerability rank among the more frequently investigated topics in controlled studies, and skin redness counts as a known reaction. Statements on I

5. Profile: Molecule and Charge

Niacin is not a single molecule but a **mixture** — there is no molecular formula and no fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; this is exactly what the next section addresses.

6. Charge, Electrons, Radicals

In humans, mainly receptor binding has been measured so far, not the charge of the molecule. Niacin activates the hydroxycarboxylic acid receptor 2 (HCA2, also GPR109A), and this activation is accompanied by the typical flush ¹⁹. HCA2 and HCAR3 belong to the family of class-A G-protein-coupled receptors and regulate lipolysis as well as the formation of free fatty acids ^{18 20}. Niacin also acts outside metabolism, predominantly via HCA2 ²¹. A controlled study in patients with chronic heart failure describes that 3-hydroxybutyrate activates HCA2, raises prostaglandins and lowers circulating free fatty acids ⁶. Information on charge or cation exchange of niacin itself is not found in these works.

For electron transfer, one work on human tissue provides a hint: supramolecular pillar[6]arenes with carboxylate or sulfonate groups served as “turn-off” fluorescence sensors for the detection of 1-MNA in urine, mediated via photoinduced electron transfer (PET) ²². This describes a detection route, not an electron transfer by niacin in the body. As a precursor of several coenzymes, niacin participates in mitochondrial ATP formation, DNA repair and the reduction of reactive oxygen species ¹; whether this redox role has been measured directly in humans is not stated in the present sentences. What would need to be tested is whether the charge state and radical formation of niacin and its metabolites can be captured directly in humans.

7. Interactions with Other Substances

With which other substances of the platform this substance is **jointly** investigated or discussed in human studies and reviews — combination, comparison or shared mechanism of action. The number names works in which both occur.

SUBSTANCE	SHARED WORKS	OF WHICH CONTROLLED IN HUMANS
Niacinamide	61	25
Acceptance and Commitment Therapy (ACT)	43	8
Chronic Inflammation	35	2
High-Intensity Interval Training (HIIT)	32	5
Art Therapy	21	4
Cognitive Behavioural Therapy for Insomnia (CBT-I)	19	1
Stress, Cortisol and Inflammation	18	1
Vitamin B12	16	0
NAD Precursors (NMN, NR)	13	0
Omega-3 Fatty Acids	12	5

Nutritionally, the combination of protein and niacin is described. In a randomised controlled trial, 98 dialysis patients were assigned to four groups for eight weeks, including a protein-plus-niacin combination; serum phosphate and nutritional markers were examined ^{15 16}. For dietary niacin, consistent findings without significant interaction with the randomised factors were obtained for all-cause and cardiovascular mortality in most subgroups ³. An observation in

humans describes that niacin with a high-fat meal rich in monounsaturated fatty acids attenuated postprandial inflammation; omega-3 fatty acids contributed nothing^{23 23}. It remains to be examined whether these combination effects recur in further groups.

At the binding level, a recognition mechanism via three key residues is described for the receptor HCAR2: R111, S179 and Y284¹⁸. Niacin also interacts directly with the TRP channel TRPV1; this provides an explanation for skin flushing that is not based on prostaglandins¹⁹. In a human study, niacin was tested together with KPT-9274 and nivolumab; at the doses used, no clinical activity was observed¹⁴. For KPT-9274, anti-tumour activity in combination with nivolumab is described in non-clinical models¹⁴. It would need to be clarified whether binding to HCAR2 can be addressed more selectively and whether the TRPV1 interaction can be separated from skin flushing.

8. Overdose, Tolerability, Limits

Evidence on the tolerability of niacin is available from controlled human studies. A low-dose niacin administration as add-on therapy also proved well tolerated⁸. In the same work, fasting blood glucose, serum transaminases and further laboratory values were recorded, as well as self-reported adverse events⁹. These assessments capture what the participants reported; they do not yet indicate which complaints occur at which intake level. The evidence contains no statement on the upper limit of intake or on contraindications.

A first human study on advanced solid tumours reports dose-limiting toxicities: three dose-limiting toxicities occurred in the 40-mg cohort (n = 1) and in the 80-mg-plus-niacin cohort (n = 2)¹⁴. Niacin was part of a combination there, so the finding cannot be attributed to niacin alone. In a randomised, double-blind phase-2 study, 28 adults with treatment-resistant obsessive-compulsive disorder received either psilocybin or niacin (250 mg; n = 14)²⁴; niacin served here as the comparator arm. The evidence does not yield a dose-response relationship for adverse effects. It would need to be examined from which intake level and in which individuals adverse effects occur and how they can be distinguished from those of the respective combination partner.

9. The Most Robust Works

Ordered by strength of evidence, not by familiarity: reviews and studies with many participants first. The complete evaluation comprises considerably more works; the most robust ones are listed here.

Controlled Human Studies

- ¹ Systematic Review and Meta-Analysis on the Association Between Daily Niacin Intake and Glaucoma (2024) — Review
- ² Meta-analysis of niacin and NAD metabolite treatment in infectious disease animal studies suggests benefit but requires confirmation in clinically ... (2025) — Review, 50 participants
- Psilocybin Therapy for Clinicians With Symptoms of Depression From Frontline Care During the COVID-19 Pandemic: A Randomized Clinical Trial (2024) — 2,022 participants
- ³ Association of dietary niacin intake with all-cause and cardiovascular mortality in the general population (2024) — 39,428 participants
- Single-Dose Psilocybin Treatment for Major Depressive Disorder: A Randomized Clinical Trial (2023) — 104 participants
- ⁴ Magnetic Resonance Imaging of Intraplaque Hemorrhage and Plaque Lipid Content With Continued Lipid-Lowering Therapy: Results of a Magnetic Resonance ... (2022) — 156 participants
- ⁵ HDL cholesterol concentrations and risk of atherosclerotic cardiovascular disease - Insights from randomized clinical trials and human genetics (2022)
- Investigating Lipid-Modulating Agents for Prevention or Treatment of COVID-19: JACC State-of-the-Art Review (2021)
- ⁶ Stimulation of the Hydroxycarboxylic Acid Receptor 2 With the Ketone Body 3-Hydroxybutyrate and Niacin in Patients With Chronic Heart Failure ... (2023)
- Safety, tolerability, and clinical and neural effects of single-dose psilocybin in obsessive-compulsive disorder: protocol for a randomized ... (2023) — 30 participants
- ⁷ Omega-3 supplementation improves depressive symptoms, cognitive function and niacin skin flushing response in adolescent depression: A randomized ... (2024) — 37 participants
- ⁸ Low-Dose Niacin Supplementation Improves Motor Function in US Veterans with Parkinson's Disease: A Single-Center, Randomized, Placebo-Controlled Trial (2021)
- ⁹ The efficacy of niacin supplementation in type 2 diabetes patients: Study protocol of a randomized controlled trial (2021)
- ¹⁰ Lipoprotein(a) and Atherosclerotic Cardiovascular Disease, the Impact of Available Lipid-Lowering Medications on Lipoprotein(a): An Update on New ... (2023)
- ¹¹ Dose-response association between dietary folate and niacin intakes with diabetes among Chinese adults: a cross-sectional study (2023)
- Longitudinal metabolomics analysis reveals the acute effect of cysteine and NAC included in the combined metabolic activators (2023)
- ¹² Atherosclerosis Residual Lipid Risk-Overview of Existing and Future Pharmacotherapies (2024)
- Enhanced visual contrast suppression during peak psilocybin effects: Psychophysical results from a pilot randomized controlled trial (2024) — 6 participants
- ¹³ What is really new in triglyceride guidelines? (2023)
- ¹⁴ First-in-Human Phase I Study of KPT-9274, a First-in-Class Dual Inhibitor of PAK4 and NAMPT, in Patients with Advanced Solid Malignancies (2026) — 60 participants

- ¹⁵ Effect of Egg-White Protein Alone or Combined With Niacin on Nutritional Status, and Phosphorus Control in Maintenance Hemodialysis Patients: A ... (2024) — 98 participants
- ¹⁶ Test for abnormal niacin response syndrome in schizophrenia: reclaiming the oral route (2023) — 21 participants
- Short-Term and Late-Term Effects of Psilocybin on Symptoms in Major Depression: A Randomized Clinical Trial (2026) — 35 participants
- ¹⁷ Targeting cardiovascular and metabolic risk modification in end stage renal disease (ESRD): a randomized controlled clinical trial on niacin's ... (2025)

10. Summary

PROVEN

The mechanism is best described: nicotinic acid activates the hydroxycarboxylic acid receptor 2 and thereby triggers the characteristic skin flushing; nicotinamide is not associated with this receptor effect, and both forms act as precursors of NAD⁺, a coenzyme of energy production and redox reactions in nearly every cell. Safety and tolerability are examined in dedicated controlled studies. In humans, the only controlled niacin study on cognition in 47 Parkinson patients over six months showed a mean UPDRS-III change of -1.06 under niacin versus -0.05 under placebo [58], and the case-control meta-analysis on glaucoma linked high niacin intake with a higher proportion of persons without glaucoma (OR 0.66) [27].

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The review article "The Promise of Niacin in Neurology" classifies niacin as a precursor of NAD⁺ and describes, via Hcar2, the regulation of immune responses, phagocytosis of myelin debris and cholesterol efflux; as investigated or proposed fields of application it names multiple sclerosis, Alzheimer's, Parkinson's, glioblastoma and amyotrophic lateral sclerosis, without participant numbers or effect sizes [33]. **Hypothesis:** From this mechanism, effects on diseases that have so far been captured via markers such as skin flushing, lipids or mobility could follow; until then, controlled trials in these fields remain outstanding.

A controlled human study that tests niacin as the investigational substance in one of the named neurological diseases would clarify whether the mechanisms described via Hcar2 and NAD⁺ translate clinically; likewise, independent replication in the individual fields of application remains outstanding. For COVID-19, a review identified 40 randomised studies, of which only 2 reported preliminary results [8]. For NAD⁺ repletion in tumour cachexia, predominantly preclinical findings are available [66]. The SHARP review presents a dietary supplement based on the attenuated niacin skin reaction as a preventive approach in clinical high risk for psychosis [74]; whether the attenuated skin reaction is a reliable selection marker is an open question.

11. What Remains Open

- **Forms:** Which form was tested — nicotinic acid, nicotinamide or another NAD⁺ precursor — and can findings be transferred between them?
- **End metabolite:** Does the metabolite associated with vascular inflammation also form under therapeutic doses, and is the connection causal?
- **Marker to Endpoint:** Which controlled study tests niacin against a clinical course instead of against lipids, flushing or reaction measures?

12. Further Paths

Topics, modes of action and chains in which this substance occurs — for all who wish to look beyond the substance.

- Interaction Network

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

Frequently Asked Questions

Why does the literature sometimes refer to niacin and sometimes to nicotinic acid and nicotinamide?

Niacin is the collective term; the individual forms differ in receptor binding, tolerability and activity profile. Studies are therefore comparable only when form, dose range and measured parameter align. In work that uses skin flushing as the target variable, it is additionally necessary to distinguish what proportion of the finding is attributable to the vascular reaction and what to the metabolic pathway.

Can the number of studies be used to infer efficacy?

No. The field is publication-rich, yet unevenly distributed: numerous mechanistic and basic-research studies stand against few controlled human trials, which moreover address many different indications. Citation counts also contribute little, because in vitamin fields studies often rank highly in which niacin appears only as a secondary marker.

How can one recognise whether a niacin study is clinically relevant?

By design and endpoint: randomised, controlled, with clinical course as the endpoint. Studies that measure lipids, NAD⁺ levels, skin flushing or questionnaires describe markers. Observational designs show associations and carry no efficacy claim; protocols of planned studies do not yet supply results.

Sources

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