



# NIAGEN<sup>®</sup>

Nicotinamide Riboside (NR)





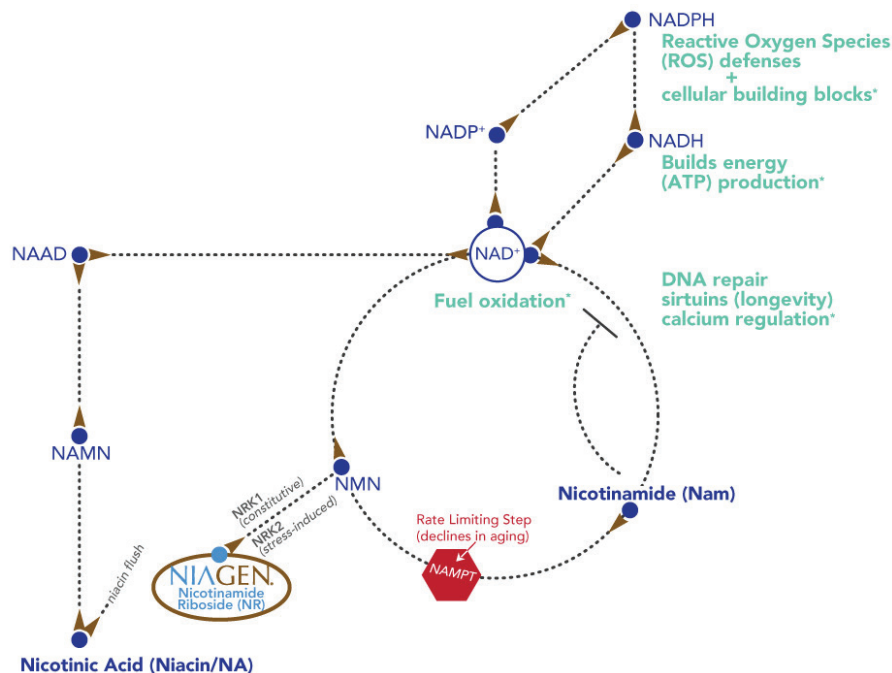
## What is Nicotinamide Riboside (NR)?

NR is a next-generation vitamin B<sub>3</sub> that has been found to be naturally-occurring in milk in trace amounts<sup>1</sup>. The metabolism of NR is unique from that of other more commonly known forms of vitamin B<sub>3</sub>, nicotinamide and nicotinic acid. Specifically, NR has been shown in a pre-clinical study to be the most effective form of vitamin B<sub>3</sub> at increasing nicotinamide adenine dinucleotide (NAD<sup>+</sup>)<sup>2</sup>.

Nicotinic acid (also known as niacin) and nicotinamide (also known as niacinamide) were discovered in the 1930's to be the factors that cured pellagra<sup>3</sup>. Niacin is known to cause severe flushing<sup>4</sup>. In 2004, nicotinamide riboside emerged as a newly discovered NAD<sup>+</sup> precursor<sup>5</sup> and does not bind to the receptor responsible for flushing<sup>6</sup>.

NR has pre-clinically demonstrated that it is superior to both niacin and nicotinamide, both of which are standard forms of vitamin B<sub>3</sub> commonly used in vitamin supplements and foods, at boosting NAD<sup>+</sup><sup>2</sup>. This is due to the fact that NR is not reliant upon a conversion step requiring the enzyme "NAMPT"<sup>7,8</sup>, see Figure below. The activity level of NAMPT determines the amount of nicotinamide that is converted into NAD<sup>+</sup><sup>9</sup>, which is why this particular step in the process is often referred to as the "rate limiting step"<sup>10</sup>. As normal aging occurs, the activity of NAMPT is thought to decrease<sup>11-15</sup>. NR can be used by the cell to make NAD<sup>+</sup> without this enzymatic step.

**Figure – NAD<sup>+</sup> synthesis from nicotinic acid, nicotinamide, and nicotinamide riboside**



## Why is NR Important?

NR is important because it is a potent and bioavailable pre-cursor to NAD<sup>+</sup><sup>2, 5</sup>. NAD<sup>+</sup> is essential to life and is known to be vital to functions that ensure proper cellular and energy metabolism<sup>16</sup>. The most well-known function of NAD<sup>+</sup> is the transferring of electrons to the machinery in the cell that produces ATP, the energy currency of all cells<sup>17, 18</sup>.

NAD<sup>+</sup> is increasingly being shown to have important functions beyond electron transfer. One of the most promising potential roles for NR as a pre-cursor to NAD<sup>+</sup> is activation of sirtuins, enzymes associated with a wide variety of functions related to metabolism and longevity<sup>8, 19-21</sup>.

## Sirtuins – The “Anti-Aging Proteins”

- The sirtuins are proteins that have been shown to perform vital longevity functions in mice and in cellular models <sup>8, 19-21</sup>.
- Increasingly, there is support for the hypothesis that decreased cellular NAD<sup>+</sup> results in a decline in sirtuins activity <sup>11, 22</sup>.
- A pre-clinical study published in 2016 in the journal *Nature Communications*<sup>2</sup> supports the hypothesis<sup>8</sup> that NR is more potent than nicotinamide and nicotinic acid at increasing NAD<sup>+</sup>.

## Human Studies of NR

- The first human study of NIAGEN<sup>®</sup> nicotinamide riboside was published in 2016 in the journal *Nature Communications*<sup>2</sup>. This study reported dose dependent increases in the NAD<sup>+</sup> metabolome following oral administration of 100, 300, and 1000 mg single doses of NIAGEN<sup>®</sup> in adults. There is much interest in the potential for meaningful health benefits of nicotinamide riboside. As a result, human studies are being conducted with NIAGEN<sup>®</sup>.

**Human studies of nicotinamide riboside are registered on the U.S. National Institutes of Health website: [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (search “nicotinamide riboside”).**

Study Title	Research Institution	Trial ID #
Pharmacokinetic Study of Nicotinamide Riboside	University of Washington	NCT02689882
Safety & Efficacy of Nicotinamide Riboside Supplementation for Improving Physiological Function in Middle-Aged and Older Adults	University of Colorado, Boulder	NCT02921659
Nicotinamide Riboside and Metabolic Health	Maastricht University Medical Center	NCT02835664
Pharmacokinetic Analysis of Nicotinamide Riboside	Aarhus University Hospital	NCT02300740
Study to Evaluate the Effect of Nicotinamide Riboside on Immunity	National Heart, Lung, and Blood Institute (NHLBI)	NCT02812238
Use of 31P MRS to Assess Brain NAD <sup>+</sup> in Healthy Collegiate Football Players (TRMC-004)	Mayo Clinic	NCT02721537
Nicotinamide Adenine Dinucleotide and Skeletal Muscle Metabolic Phenotype (NADMmet)	University of Birmingham	NCT02950441
The Effects of Nicotinamide Adenine Dinucleotide (NAD) on Brain Function and Cognition (NAD)	The University of Texas Health Science Center at San Antonio	NCT02942888
The Effect of Vitamin B3 on Substrate Metabolism, Insulin Sensitivity, and Body Composition in Obese Men	Aarhus University Hospital	NCT02303483
A Study Investigating the Effects of Niagen™ in Healthy Adults.	KGK Synergize Inc.	NCT02712593
A Study of the Pharmacokinetics of Three Dosages of Niagen in Healthy Subjects	KGK Synergize Inc.	NCT02191462
A Study to Evaluate Safety and Health Benefits of Basis™ Among Elderly Subjects.	Elysium Health	NCT02678611

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## Claims Supported by Science

- Clinically demonstrated to significantly increase NAD+\*
- Promotes mitochondria health\*
- Promotes healthy cellular metabolism\*
- Promotes healthy aging\*

## Regulatory Status of NIAGEN®

NIAGEN® has a successful New Dietary Ingredient Notification with FDA (NDIN 882) for daily recommended intake of not more than 180 mg/d.

NIAGEN® is generally recognized as safe (FDA GRAS Notice No. 635) for use in vitamin waters, protein shakes, nutrition bars, gum, chews, and powdered beverages. Maximum use level 0.0057% by weight.

## NIAGEN® Patents

NIAGEN® has five issued process and use patents with more pending.

## Potential NIAGEN® Applications

NIAGEN® can be used in capsules, tablets, melts or in powder form as a dietary supplement. It can also be included in functional foods and beverages in the following categories: vitamin waters, protein shakes, nutrition bars, gum, chews, and powdered beverages.

## References

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\* 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.

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