10.5: Niacin

There are two forms of niacin: nicotinic acid and nicotinamide (aka niacinamide), that have a carboxylic acid group or amide group, respectively. The structure of nicotinic acid and nicotinamide are shown below.

![Structure of nicotinic acid](https://med.libretexts.org/Courses/Kansas_State_University/Book%3A_Human_Nutrition_(Lindshield)/10%3A_Macronutrient_%…)

Figure \(\PageIndex{1}\): Structure of nicotinic acid

![Structure of nicotinamide](https://med.libretexts.org/Courses/Kansas_State_University/Book%3A_Human_Nutrition_(Lindshield)/10%3A_Macronutrient_%…)

Figure \(\PageIndex{2}\): Structure of nicotinamide

Niacin is important for the production of two cofactors: nicotinamide adenine dinucleotide (\(\ce{NAD}\)) and nicotinamide adenine dinucleotide phosphate (\(\ce{NADP^+}\)). The structure of \(\ce{NAD}\) is shown below; you can clearly see the nicotinamide at the top right of the molecule.
\(\text{NAD}\) is reduced to form \(\text{NADH}\), as shown below.

\[
\text{NAD}^+ + H^+ + 2e^- \rightarrow \text{NADH}
\]

The structure of \(\text{NADP}^+\) is exactly the same as \(\text{NAD}\), except it has an extra phosphate group off the bottom of the structure, as shown below.
Like \(\text{NAD}^+\), \(\text{NADP}^+\) can be reduced to \(\text{NADPH}\).

Niacin is unique in that it can be synthesized from the amino acid tryptophan as shown below. An intermediate in this synthesis is kynurenine. Many reactions occur between this compound and niacin, and riboflavin and vitamin \(B_6\) are required for two of these reactions.

To account for niacin synthesis from tryptophan, niacin equivalents (NE) were created by the DRI committee to account for the amount of niacin in foods as well as their tryptophan content. It takes approximately 60 mg of tryptophan to make 1 mg of niacin. Thus, the conversions to niacin equivalents are:

\[
1 \text{ mg Niacin} = 1 \text{ NE} \\
60 \text{ mg Tryptophan} = 1 \text{ NE}
\]

The tryptophan levels of most foods is not known, but a good estimate is that tryptophan is 1% of amino acids in protein. Thus, lets take peanut butter, smooth style, with salt as an example.

The peanut butter contains 13.403 mg of niacin and 25.09 g of protein.

**Step 1:** Calculate the amount of tryptophan:
25.09 g X 0.01 (the numerical value of 1%) = 0.2509g of tryptophan

Step 2: Convert Grams to Milligrams

0.2509 g X 1000 mg/g = 250.9 mg of tryptophan

Step 3: Calculate NE from tryptophan

250.9 mg of tryptophan/(60 mg of tryptophan/1 NE) = 4.182 NE

Step 4: Add NEs together

13.403 NE (from niacin) + 4.182 (from tryptophan) = 17.585 NE

Most niacin we consume is in the form of nicotinamide and nicotinic acid\(^9\), and in general is well absorbed using an unresolved carrier\(^10\). However, in corn, wheat, and certain other cereal products, niacin bioavailability is low. In these foods, some niacin (~70% in corn) is tightly bound, making it unavailable for absorption. Treating the grains with a base frees the niacin and allows it to be absorbed. After absorption nicotinamide is the primary circulating form\(^7,9\).

### Niacin Functions

Approximately 200 enzymes require \(\text{NAD}\) or \(\text{NADP}^+\). We will go through some selected functions of \(\text{NAD}\) and \(\text{NADP}^+\). The following figures and legends show and describe the functions of \(\text{NAD}\) and \(\text{NADP}^+\).
Figure PageIndex(7): \(\text{NAD}\) is required for glycolysis

Figure PageIndex(8): \(\text{NAD}\) is required for the transition reaction and at three different points in the citric acid cycle
Figure \(\PageIndex{9}\): \(\ce{NAD}\) is required for fatty acid oxidation

Figure \(\PageIndex{10}\): Alcohol oxidation; \(\ce{NAD}\) is required by alcohol dehydrogenase, and the MEOS uses \(\ce{NADPH}\)\(^{13,14}\).

Figure \(\PageIndex{11}\): Fatty acid synthesis uses \(\ce{NADPH}\)\(^{15}\).

HMG \(\ce{CoA}\) reductase, the rate-limiting enzyme in cholesterol synthesis, uses \(\ce{NADPH}\). \(\ce{NADPH}\) is also used by the antioxidant enzyme glutathione reductase as shown in the link below\(^{16}\).

Web Link

The Glutathione Oxidation Reduction (Redox) Cycle
Niacin Deficiency & Toxicity

Pellagra is a niacin deficiency. This is no longer a common deficiency in developed countries, but was in the U.S. in the early 1900s. This was because corn was a staple crop, meaning it was what people primarily consumed. The bioavailability of niacin from corn is poor unless treated with a base to release the bound niacin. The symptoms of pellagra are the 3 D's:

- Dementia
- Dermatitis
- Diarrhea

Some refer to 4 D's in which the 4th D is death if the condition is not managed. The following pictures show the symptoms of pellagra.

Figure 12: The 3 D's of pellagra

https://med.libretexts.org/Courses/Kansas_State_University/Book%3A_Human_Nutrition_(Lindshield)/10%3A_Macronutrient_...
Dietary niacin toxicity is rare. However, nicotinic acid (not nicotinamide) can improve people's lipid profiles when consumed at levels far above the RDA. For instance the RDA and upper limit (UL) is 14 or 16 (women & men) and 35 mg (both), respectively. Many people are taking 1-2 grams (up to 6 g/day) to get the benefits in their plasma lipid profiles as shown in the table below.

### Table: Effects of nicotinic acid (>1.5 g/day) on plasma lipid profile

<table>
<thead>
<tr>
<th>Measure</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLDL</td>
<td>↓ 25-40%</td>
</tr>
<tr>
<td>LDL</td>
<td>↓ 6-22%</td>
</tr>
<tr>
<td>HDL</td>
<td>↑ 18-35%</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>↓ 21-44%</td>
</tr>
</tbody>
</table>
Measure | Change
--- | ---
Triglycerides | ↓ 21-44%

It should be pointed out that there are special supplements for this purpose that include a slower release nicotinic acid that helps prevent the toxicity symptoms (nicotinamide is not toxic). A slow (aka long or extended) release form of niacin for people with atherosclerosis is Niaspan®. The link below is to Niaspan’s site.

Web Link

Niaspan®

A study found that Niaspan plus a statin was no better than a statin alone in preventing heart attacks, despite improvements in HDL and triglyceride concentrations. This result challenged the understanding of the importance of HDL and triglyceride concentrations to heart attack risk. The link below explains this study’s results.

Web Link

Niacin Drugs Don’t Reduce Heart Attack Risk

The most well known of the toxicity symptoms is "niacin flush", which is a dilation of capillaries accompanied by tingling that can become painful. This symptom is noted to occur at lower levels than the other toxicity symptoms. Other symptoms include:

- Gastrointestinal Distress
- Liver Damage

A nicotinic acid receptor GPR109A, which is present in adipocytes and immune cells, is believed to mediate niacin flush, but the beneficial effects on lipid profiles do not appear to be mediated by it. It is not clear at this time the mechanism of action for the improvements in lipid profiles. Thus, nicotinic acid supplementation can improve lipid profile and lead to niacin flush, while nicotinamide supplementation does not result in either outcome.

References

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