RU-21: How and Why

By Dr. Kenneth Krul, Ph.D.
Author of "Alcohol Metabolism in Adults"

Kenneth G. Krul, Ph.D., MBA, is a San Diego-based business development and strategic planning consultant with over 30 years of experience in the biomedical industry. He holds a doctorate in biophysical chemistry, an MBA in finance, and certifications in laboratory medicine. Before entering private practice, he served on the staff of Columbia-Presbyterian Medical Center and served in various senior marketing and R&D capacities at some of the world's top diagnostic technology companies, including Dade-Behring, CalBiochem, Technicon, and Beckman-Coulter. Over the past 20 years he has authored over 150 published studies and scores of proprietary studies over a wide range of biomedical and biotechnology subjects, including Diabetes and Diabetic Complications: Major World Markets, The U.S. Market for Molecular Diagnostics, and Nucleic Acid-Based Therapeutics.

Everything of a biochemical nature can be addressed biochemically. This can be something as simple as taking an antacid to deal with the excess stomach acid that gives you heartburn. On the other hand, it can be as complex as the modern psychoactive drugs that correct biochemical imbalances in the brain that cause depression or anxiety. In fact, the whole pharmaceutical industry is based on this one assumption. Preventing or negative effects of alcohol (i.e. morning after) is no different.

When you drink alcoholic beverages, you introduce chemicals into your body that it must process, mostly in the liver. Some of these chemicals are normally found in the body, but others aren't. The body acts to neutralize and eliminate these chemicals.

Some chemicals are found in the body and in the beverages. In the body, however, they are found in much smaller quantities. The body acts to normalize the presence of these chemicals in the body and reduce any potential toxic side effects.

These are two main components of alcoholic beverages that are involved in the development of a negative after effects of alcohol - ethanol, the primary product of fermentation, and byproducts known as aldehydes (mainly acetaldehyde). In addition, there is a mixture of other organic molecules collectively known as “fusile oils,” that have toxic effects. Most of the by-products of the fermentation process, aldehydes and fusile oils, are removed by aging in wooden casks. For this reason, older liquors are said to taste “smoother,” and produce less intense morning after problems.

Acetaldehyde, however, is the major molecular factor in the production of negative after effects of alcohol. It is introduced into the body both from the drink itself and from the metabolism of ethanol in the stomach and liver. These biochemical reactions take place in two steps.

First, ethanol is converted to acetaldehyde by an enzyme known as Alcohol Dehydrogenase (ADH) in the presence of a chemical cofactor, NAD. In the process, NAD is used up and converted to NADH.

Second, the acetaldehyde produced in the breakdown of ethanol is converted to acetic acid by an enzyme known as Aldehyde Dehydrogenase (ALDH). This reaction also uses the chemical cofactor NAD, converting it to NADH in the production of acetic acid. This is where the problem of negative after effects of alcohol begins.

If the quantity of alcohol consumed is large, the ADH uses up the liver’s store of NAD. Not enough NAD is left to convert the acetaldehyde to acetic acid using ALDH. As a result, the acetaldehyde remains in the blood. It can then exert its toxic effects at its increased blood levels.

To make matters worse, blood ethanol levels also rise because there is not enough NAD for ADH to rapidly convert the ethanol to acetaldehyde. It remains in the blood until excreted by the kidneys or converted slowly in the liver. As a result, the toxic effects of acetaldehyde and ethanol produce negative after effects of alcohol, such as what is known as the morning after.

While the entire picture of ethanol metabolism is complex, it is clear that real problem of negative after effects of alcohol is a biochemical depletion of NAD.

Luckily, metabolic cycles - the different biochemical reactions in the body - are linked. While some biochemical reactions deplete NAD and convert it to NADH, others use NADH and convert it to NAD. These reactions occur in the cytosol (the liquid filling the cells) and the cells' factories, intracellular particles known as mitochondria.

Another lucky break is that these reactions can be controlled. For example, enzyme reactions in metabolism are like revolving doors. An enzyme will convert A to B - and B to A. It's a process known as "enzymatic equilibrium." However, if you add a lot more A to the mixture, the enzyme will favor the reaction that converts A to B instead of B to A. Thus, we can control the reaction favoring the conversion of NADH to NAD by adding the necessary materials to the body in the form of a tablet - RU-21.

Several metabolic pathways convert NADH to NAD. For example, the enzyme malate dehydrogenase converts NADH and two other molecules, oxaloacetate and glutamate, to NAD and malate via the Malate/ Aspartate Shuttle reaction. RU-21 contains glutamine - a molecule that is rapidly converted to glutamate to drive the Malate/Aspartate Shuttle in the NADH-to-NAD direction.

In the mitochondria, two reactions are linked to convert NADH to NAD. In this case, NADH oxidase converts NADH to NAD, while succinic acid, in the presence of the enzyme succinic acid dehydrogenase, drives a reaction converting another cofactor, FAD, to $FADH_2$. This is one of the most important reactions of energy production in mitochondria. RU-21 contains succinic acid.

Succinic scid is also a reactant in other metabolic cycles, such as the citric acid cycle. Its presence in excess in these cycles can drive processes that further convert NADH back to NAD.

Succinic acid is closely related to another important metabolite, fumaric acid. In fact, with the exception of two hydrogen atoms, they have the same molecular structure. They are converted to one another in biochemical reactions in the body. The presence of both in excess in the body further drives the conversions of FAD to $FADH_2$ and NADH to NAD. RU-21 contains fumaric acid.

Two other components of RU-21, glucose and ascorbic acid (Vitamin C) are also important in preventing negative after effects of alcohol. Ascorbic acid is a cofactor in several energy-producing (electron transfer) reactions. Similarly, glucose is the primary metabolite in energy production. These components of RU-21 help keep energy levels up and metabolic cycles running properly.

This is a highly simplified view of how and why RU-21 is effective in preventing and/or reducing negative after effects of alcohol. It does show, however, that there is sound biochemical reasoning behind the formulation of RU-21. It’s effectiveness is based on recognized scientific principles and biochemical knowledge.