The sugar everyone would use if they only knew…

The Trehalose Handbook SERIES

A Review of the Science of Trehalose and other Complementary Sugars

Volume One: Chapters 1 through 6

May *The Trehalose Handbook Series* be a beneficial tool for you - be you professor, physician, pharmacist, nurse, research scientist, healthcare professional, politician, or one of the general public who seeks knowledge in the science of sugars and better healthcare. *The Handbook* that reveals pathway for lowering healthcare costs.

An Educational Project of The Endowment for Medical Research
Edited by J. C. Spencer

Intended for educational purposes only

The Trehalose Handbook is written with the intent that my comments are easy to understand by the general public while supported with scientific evidence for the professional. This Handbook contains research data and scientific information for the physician, pharmacist, nurse, research scientist, educator, and healthcare professional.

Additional information can be obtained online at www.endowmentmed.org, in my textbook, ***Expand Your Mind - Improve Your Brain*** and through 14 hours of Continuing Medical Education (CME) and Continuing Educational Credits (CEU) quality Glycomics DVD Series.

- *The Trehalose Handbook* is Interactive -

This Handbook may be downloaded, read offline, printed on 8 ½ x 11 pages, or read online. When read online or offline on a computer open to the internet, there are many hot links that will open to references and additional educational information. These Links are normally highlighted in blue.

- J. C. Spencer

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Volume One
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We welcome Affiliates to help facilitate the education of sugars. It is the intent that when an individual logs onto our website through an Affiliate's Home Page that the Affiliate is credited for all activity of that individual.

Chapter 1

Trehalose, the sugar everyone would use if they only knew.....

This chapter is not as scientific as the other chapters and deal with beneficial information about trehalose.

TREHALOSE is the sugar everyone would use if they only knew...™

* That trehalose is a healthy sugar -- healthier than the refined table sugar that most people use.
* That simply switching table sugars could result in a slowing of premature aging.
* That trehalose is a sugar found in nature. It is NOT a chemical sugar substitute.
* That using trehalose can help lessen brain fog and boost memory.

Changing Your Sugar Can Change Your Life!

Regular table sugar -- the refined, processed kind we typically use every day -- contributes to premature aging, diminished eyesight, and overall weakening of the immune system.

A healthy immune system fights off disease and keeps us healthy when others around us are ill. Regular table sugar has been linked to almost every disease known to man.

Do you really want to get older before your time?

In an attempt to get away from the side effects of regular table sugar, some of you have switched to the “pink stuff” or the “blue stuff” or the “yellow stuff” thinking this may be better for you. All of these alternative sugar substitutes have their own set of side effects.

The majority of people experience little or no health improvement as a

result of using these sugar substitutes. So what are we to do? Try trehalose!

The sugar everyone would use if they only knew...™

* That regulating their blood sugar could contribute to weight loss.

Have you or a loved one been told you must lose weight?

Obesity is an epidemic.

Obesity contributes to many other diseases. Obesity makes even simple tasks difficult and lessens a person's quality of life.

You or a loved one may have been told by the doctor that you must lose weight. If it were that easy, you would have already done it.

One of the greatest contributors to excess weight is consumption of sweets. Cutting the craving for sweets can help you or a loved one lose weight.

Diet pills, extreme diets and extreme measures to lose weight all come with risks. Read on to learn more about trehalose and the potential it has to help you reach your goal of being at your ideal weight. Remember, excessive consumption of even low-calorie foods can lead to weight gain.

Have you cut your calories and still gained weight?

Maybe you have tried chemical sugar substitutes to lose weight. What happened?

In fact, many people gain weight when they start using “low” or “no calorie” sweeteners. If the only cause of weight gain was an increase in the

number of calories consumed, then logic would follow that a decrease in the number of calories consumed would automatically result in weight loss.

Sounds simple, right? Everyone wanting to lose weight would simply need to choose a pink, blue or yellow packet as a substitute for the calories in regular table sugar. And viola! Weight loss! We are thin! However, this is generally not the way it works.

And what is worse, people who gain weight after starting to drink diet sodas and consuming more diet or low-calorie formulated foods may actually damage their metabolic systems more through the use of chemical sugar substitutes.

There are those who use sugar substitutes and have been able to stay thin. However, when discussing the choices they make in order to stay thin, they will usually tell you that they would prefer to use “real” sugar. They miss the satisfaction factor that only comes from using “real” sugar.

Even though they may be happy with their physical appearance as a result of cutting their calorie intake, many sugar substitute users admit that they secretly worry about the long-term health consequences of these chemical sugar substitutes.

This may just be a matter of preference and choice for the reasonably healthy person, but what about someone with health challenges? What is a diabetic or someone with blood sugar problems to do? They have a terrible dilemma. In order to control their blood sugar, they believe that they only have a choice between two undesirable options.

The first option is to go without anything that tastes sweet (boring, miserable, no fun, and have we said YUK!?). The second option is to use one of the sugar substitutes that has other potentially damaging long-term side effects. If they choose to go without anything sweet, they risk hitting a point of desperation and actually going on a sugar binge that could result in

a life-threatening situation.

Trying to use only small amounts of regular table sugar does not seem to work either. Usually the choice most people make is to use some kind of sugar substitute. Talk about being between a rock and a hard place.

TREHALOSE, the sugar everyone would use if they only knew...™

* That trehalose is easy on the body to process.
* That trehalose is pleasant tasting and has no aftertaste.

Prove it to yourself. Take the trehalose taste test challenge:

Rinse the palate with pure water. Put a few grains of trehalose on your tongue. Is there any after taste? Now, rinse the palate again. Put a few grains of regular table sugar on the tongue. Is there any after taste? Most people find that regular table sugar has an aftertaste that they never noticed before. Try it for yourself.

QUIT FEELING GUILTY ABOUT GIVING YOUR CHILDREN SUGARY TREATS.

Parents you now have a choice!

WHAT PARENT WANTS TO PROGRAM THEIR CHILDREN TO BE FAT?

How many parents would love to have a healthy sugar to feed their children without feeling guilty?

Parents love their children, but healthy alternatives are not easy to implement on a long-term practical basis.

How can we raise healthy children?

What can we do so that we are not programming them to be fat?

Today, children are being diagnosed with adult diseases at an alarming rate – and that number is growing. The current generation of children is the first generation not expected to be as healthy as their parents or live as long as their parents.

One of the major contributing factors of poor health is considered to be a lower consumption of fresh fruits and vegetables combined with an increase in the intake of refined sugars and flours. While these things may taste great, they are stealing the health of our children. Childhood obesity is increasing, and regular table sugar is one of the culprits.

What if you could give your children sweet treats that would make them happy without contributing to training (predisposing) them to be sugarholics and likely candidates for future diseases such as diabetes.**

YOU CAN! IT IS CALLED TREHALOSE.

DO YOU OR A LOVED ONE EVER GET BRAIN FOG?

What if a simple change in table sugar could make your brain function more efficiently, and thus you would be able to think more clearly? Alzheimer's and other diseases that affect the ability to think and remember clearly are on the rise.

What is even more alarming is that people are being afflicted younger and younger. Today, there are people in their 50's in nursing homes with diseases that did not touch their parents until their parents were in their 70's or 80's.

More and more baby boomers are actively seeking steps they can take to

assure clear thinking. Maintaining cognitive function is now a concern of baby boomers.

Younger people can derive great benefits from the ability to think more clearly. They will be able to solve problems more quickly. They will be better able to use their critical thinking skills to solve more complex problems.

The income most people earn is relative to the level of problems they are capable of solving, therefore the ability to solve higher-level problems usually results in a higher level of earning ability.

PEOPLE OF ALL AGES WANT TO THINK MORE CLEARLY AND MAKE DECISIONS MORE EASILY.

TREHALOSE CAN HELP!

It is the sugar everyone would use if they only knew...™

> "Consumption of regular table sugar has been shown to result in brain fog, drowsiness, and can reduce learning capacity. It can even lull a person into a state of lethargy. Since trehalose assimilates more slowly, it allows the brain to function at its greatest capacity."
> ***Expand Your Mind - Improve Your Brain***, page 117

And, NOW YOU KNOW!
NOW YOU KNOW - THERE IS A HEALTHY SUGAR THAT'S EASY TO USE!

What is that sugar? IT IS TREHALOSE.

* It is easily processed by the body without contributing to spiking of blood sugar in most people.

* It looks like regular table sugar.
* It pours like regular table sugar.
* It is a sugar found in nature. It is NOT a chemical sugar substitute.
* It leaves no after-taste like regular table sugar.
* It is easy to substitute in many recipes and dissolves adequately in cold drinks like ice tea and lemonade.
* Its use may result in a slowing of premature aging.
* It can be safe for diabetics and hypoglycemics.**
* It may help reduce sugar cravings.

Trehalose is indeed a natural alternative whose time has come.

In fact, you can simply change your sugar and change your future. You may have already received your free article "Change Your Sugar – Change Your Life,™" but if you have not, you will be given an opportunity to order your free downloadable copy on the order form that follows. Make sure you order it and read it today.

CHANGE YOUR SUGAR SO YOU CAN QUIT BEATING YOURSELF UP ABOUT HOW MUCH SUGAR YOU USE.

Changing your sugar is easy and does not require major lifestyle changes. So many of those healthy lifestyle changes we are encouraged to make just seem too hard. You think, "I really want to do that but it is just too much effort." But, changing your sugar is not like that.

Changing your sugar is as easy as using the "turquoise stuff" (trehalose) instead of the white stuff, the pink stuff, the blue stuff or the yellow stuff.

Even if the only change you make is to substitute trehalose (the turquoise stuff) for refined, processed table sugar, you will have taken a positive action toward lifelong health.

You can feel good emotionally about the choice you made, and you can feel better physically because your body won't have to work so hard trying to deal with all of that refined, processed table sugar. You will be able to quit beating yourself up about how much sugar you use.

You can enjoy sweets again when you know that the sugar you are using can make a positive contribution to your overall health instead of breaking down your cells and causing premature aging.

CHANGING YOUR SUGAR IS EASY

Many people with blood sugar challenges have found that switching to the sugar trehalose has been pleasant and painless. They discovered that it is an easy way of making a positive change for long-term better health without unbearable side effects.**

Of course, you should seek the counsel of your personal physician, and no health claims are being made.

> Right now, there may be only one thing standing between you and a step toward improved health and greater energy – your craving for sweets containing regular table sugar or chemical sugar substitutes.
>
> I know, I was exactly where you may be right now. I knew the kind of sugar I was consuming was not good for my body, but I craved sweets all of the time. It seemed that the more sweets I ate, the more I wanted.
>
> Jackie N.
> Fort Worth, Texas

Although your personal physician may not be familiar with trehalose, he or she will find the information that is available to be fascinating. We are

simply asking you to explore the idea that there might be an alternative available to you that you never knew about before.

WHAT IS TREHALOSE?

It is one of the good sugars. Trehalose is a naturally-occurring sugar energy source with forty-five percent (45%) of the sweetness of refined table sugar. So, you may need to use about twice as much as you normally use to get the same sweetness.

Although no medical claims are being made at this time, trehalose may indeed be a brain food. It is a white crystalline powder (trehalose dehydrate) produced from cornstarch by a patented enzymatic Hayashibara process.

For many people, the sugar trehalose has been found to be an easy way of getting their blood sugar more regular.** Of course, no medical claims are being made at this time.

Trehalose is a natural substance found in very small amounts in foods we already eat such as mushrooms, honey, lobster, and foods produced using bakers and brewer's yeast. An independent panel of experts determined trehalose to be generally recognized as safe (GRAS) for use in foods in accordance with current good manufacturing practices.

A clinical study performed in the UK showed that ninety-eight percent (98%) of the population had no problems with trehalose. The other two percent (2%) experienced only a little gas.

A certain enzyme in the body, called trehalase, is used to transport the sugar trehalose to where it is needed in the body or to split the trehalose molecule into two glucose molecules. Research is ongoing to determine the relationship between the metabolism of the body with the potential energy and performance benefits of trehalose.

Energy That Lasts!

In the 1980s scientists learned that certain sugars were good for anything except energy.

Trehalose is a sustained energy food. That means that it has been tested to produce lower insulin and blood glucose responses than regular table sugar.

Athletes Get Sustained Energy From Trehalose.

Athletes like trehalose because it gives them sustained energy. Athletes need sustained energy for increased performance. Sports drinks give quick energy, but then the benefits diminish quickly. Some athletes have found that you can avoid the typical "energy-drink" spike followed by the inevitable low by using trehalose for sustained energy.

For more information about how trehalose and healthy sugars contribute to mental clarity and brain function, see the only easy-to-read book on the subject ***Expand Your Mind -- Improve Your Brain***.

> "Athletes use sports drinks to keep their electrolytes in balance. Electrolytes are responsible for hydration because they direct water-carrying nutrients to every area of the body. The sustained energy provided by trehalose makes this a favorite among informed athletes."
>
> ***Expand Your Mind - Improve Your Brain,*** page 94

It is a unique book that educates, excites, expands the possibilities and challenges you to take a new look at how the seemingly-unconnected connects. While an easy read for the lay person who wants to improve their brain function, it still has extensive scientific proof and references for the aspiring or serious scientist.

Expand Your Mind -- Improve Your Brain is what we call a "multi-book" because it provides information on a variety of subjects and according to where you are in life and your current interests or challenges you will be sure to find vital, life-enhancing discoveries.

Is It Three Books Or Is It One?

The book is so expansive (500 pages) that it is in Two Volumes plus a separate Glossary that is an amazing book by itself. It is one book with three parts. You decide what serves you the best.

In Volume I (includes Chapters 1 through 20) you will discover:

* The basis of brain function (Chapters 1 through 14)
* The difference between the brain and the mind (Chapter 1)
* Steps to diminish addictions (Chapter 10)
* How electrolytes make your brain's "battery" conduct better (Chapter 15)
* How free radicals damage your brain (Chapter 16)
* How to improve the way you think (Chapter 13)

In Volume II (includes Chapters 21 through 37) you will discover:

* How brain neurotransmitters function (Chapter 27)
* How music may help your mind (Chapter 30)
* The connection between your brain, aging and dementia (Chapter 32)
* Insights into reversing brain damage (Chapter 33)
* How the effects of Fetal Alcohol Syndrome can be lessened (Chapter

35)

* How changing your sugar can make your brain work better (Chapter 36)
* Why Americans are becoming more obese and how it can be reversed (Chapter 37)

Did you know your mind turns off information you don't understand?

Whether you enjoy reading the dictionary or not, most of us love understanding the meaning of the words we are reading or hearing. In fact, do you know that your mind just turns off information if you cannot see the words clearly, understand or hear a speaker or understand the meaning of the words you are reading. For you to get the most out of any material you study you need to understand its vocabulary.

The Glossary of ***Expand Your Mind -- Improve Your Brain*** started out simply as a way of serving you, the reader, and helping to assure that you got the most out of its content. Eventually, the Glossary began to take on a life of its own. The Glossary is so powerful that some people may want to buy the Glossary as a stand-alone book.

You will be able to get the Glossary free when you accept both volumes of the "multi-book" ***Expand Your Mind -- Improve Your Brain*** as well as getting a discount on the book itself. With our 180-day money-back guarantee, you will have time to study the book for yourself. We believe so strongly in the impact this book will have on your life that you will want to keep the book as a reference book for the rest of your life.

Start Expanding Your Mind and Improving Your Brain by ordering your copy today. (The book and trehalose are available on the same order page.)

Trehalose may be ordered in quantities from three to fifty pounds. Since it

is only 45% as sweet as sugar, it does require more to get a similar level of sweetness as regular "bad-for-you" table sugar.

Long-term use seems to indicate that sugar cravings will lessen, and a greater level of satisfaction with healthy foods will result.

You owe it to yourself and your family to at least give trehalose a try.

WE ALSO HAVE A GIFT FOR YOU!

We want you to learn more about the benefits of trehalose and the effects healthy sugars can have on your health. Therefore, as promised, your free copy of the article “What Does Your Brain Have to Do with Your Health?” is available by clicking any ORDER NOW button. This free article is a gift, and you have no obligation to order any product.

This article will tell you the power your brain has in affecting your health for good or bad. "Did you know that you can train neurons? This neuron training can be called tracing, or laying down memory, layer upon layer."

Being aware of this connection between your brain and your general health can be a great first step toward taking charge of your health. If you think you are already doing this, then this article will reinforce your positive actions and give you information to share with others who are not so enlightened.

As far as trehalose is concerned, you will never know what trehalose can do for you and your family unless you give it a try. This is your opportunity to improve your health and well being. Take action today. Go ahead and order.

** No medical claims are made by this statement. Blood sugar is fragile, and any change in diet should be preceded by consultation with your personal physician.

Chapter 2

Trehalose Glycolipids have Amazing Function

Trehalose is one of the sugar building blocks that creates great cellular communication. Here is evidence that trehalose is the sugar used to build unique glycolipids. Trehalose is the building block in a number of cell wall glycolipids. Glycoproteins are more on the cell surface while glycolipids do most of their work in the cell wall and within the cell itself.

Sugars are the OPERATING SYSTEM (OS) of the body, processing DNA data, thought, and all cellular communication. Glycomics, the science of sugars, may be thousands of times more complex than the genome project. The eight Royal Sugars used to construct glycoprotein receptor sites that coat every healthy human cell were described by Robert K. Murray, M.D., PhD, in Harper's Biochemistry first in 1996 and then in subsequent editions [and discussed in layman's language in my e-textbook *Expand Your Mind - Improve Your Brain*, foreword by Dr. Murray]. Our dear friend Dr. Rob, as we affectionately call him, is from Scotland and he will be glad to know some of the work you are about to read came out of the Lipid Analysis Unit of the Scottish Crop Research Institute in Dundee.

Ongoing glycoprotein and glycolipid research conducted around the world is getting us closer to understanding the different functions precipitated by the various natural designs. Change one sugar form or fatty acid and you have a whole new functionality and potential health benefit. Glycomics, the science of sugars, is indeed the future of medical science and healthcare.

One of the serendipitous facts about trehalose is not only that it has a hydration factor but that it is part of the construction of a surfactant that may help clean and extract waste from within the cells. That function is discussed in this report which is restricted to natural biosynthesis of trehalose and glycolipids.

Trehalose first esterifies to form monomycolate. Esterify is to form ester which is any of a class of organic compounds corresponding to the inorganic salts and is formed from an organic acid and an alcohol, usually with the elimination of water. Mycolic acids are long fatty acids found in some the cell walls. It is believed that monomycolate is the precursor to dimycolate. We have earlier reported on the Trehalose Dimycolate Project where progress has been made on a drug for treating tuberculosis. Trehalose 6,6'-dimycolate (TDM) is a primary immunostimulatory

component of the cell wall of *Mycobacterium tuberculosis* (TB).

Extra-cellular trehalose lipids contain succinic acid. Succinic acid is a dicarboxylic acid occurring naturally in plant and animal tissues. It plays a significant role in intermediary metabolism (Krebs cycle) in the body. Krebs cycle (also called citric acid cycle or tricarboxylic acid cycle) is a sequence process of enzymatic reaction which a two-carbon acetyl unit is oxidized to carbon dioxide and water to provide energy in the form of high-energy phosphate bonds. The carboxylate anion, succinate, esters from succinic acid called alkyl succinates, powerful surfactants.

The citric acid cycle is the final common pathway for the oxidation to CO_2 of fuel molecules provides intermediates for biosynthetic reactions and generates ATP by providing electrons to the electron transport chain. The citric acid cycle results in a breakdown of glycose during glycolysis in the cytoplasm to fuel the mitochondrion. You may view an interactive graphic of the Krebs cycle designed by John Kyrk at http://www.johnkyrk.com/krebs.html

The Krebs cycle is also known as the citric acid cycle because citric acid is the first sequenced product generated by this chemical conversion. The foods you eat become the fuel supply for the citric acid cycle. How well it processes that food and gets the nutrients to your cells determines your health. The pH factor plays an important role. You can raise your pH by eating less acidic foods, less soft drinks, and less bad sugars while eating more alkaline foods and drinks. The alkaline effect on your body is based upon the mineral content of your food and the ash residue that remains after our foods are consumed. Some foods leave an acid ash and other foods leave an alkaline buffer. The foods that contain alkaline minerals leaving an alkaline buffer are all the foods that really are good for us including fresh vegetables and fruit and good sugars. The foods that leave an acid ash include the bad sugars, alcohol, saturated fats, meats, and dairy.

A higher pH, a more alkaline body, is conducive to better cell function, better cell absorption, cellular communication via better glycolipids and glycoprotein receptor sites, and better health.

More research is needed and much of the activity of trehalose within the human body is yet to be determined. The enzyme trehalase serves as a transporter where trehalose performs different functions. Also, it appears that some of the trehalose is split into two glucose molecules over an extended time which support sustained energy.

Here is the science paper on glycoproteins with references. Trehalose is discussed in #5 with Figures #7 and #8:

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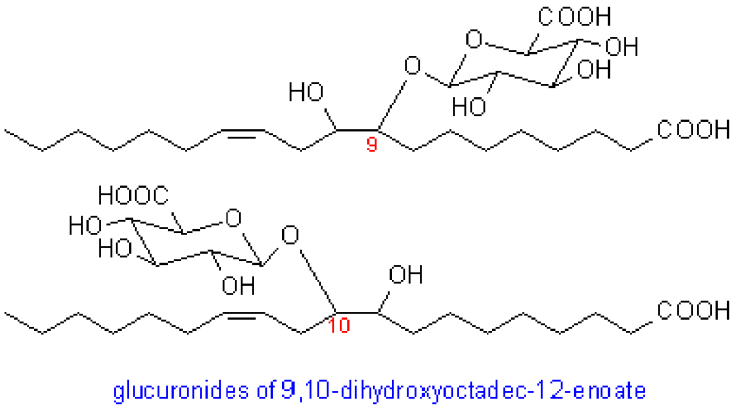
RHAMNOLIPIDS, SOPHOROLIPIDS AND OTHER UNUSUAL GLYCOLIPIDS
STRUCTURES, OCCURRENCE AND BIOLOGY

Innumerable simple glycolipids, comprising simply fatty acids esterified to a carbohydrate moiety have been described in nature, from animals, plants and microorganisms, and it is impossible to discuss more than a few representative examples here. They can vary in structure from monosaccharides with one or more fatty acyl substituents to complex carbohydrates, which can in turn be linked to terpenoids, aromatic compounds or nucleosides, as well as having multiple points of attachment to fatty acids via ester or glycosidic linkages. Some are integral components of tissues, while others produced by microorganisms are secreted into the growth medium. It is only possible to describe a few of the more important of these in this review. Because of their amphipathic nature, simple glycolipids are natural biodegradable detergents. In addition, some are reputed to have valuable pharmaceutical properties, for example as antibiotic, anti-fungal or even anticancer agents. A number of these lipids are major products of certain organisms, and have appreciable commercial importance. Substantial amounts of simple fatty acyl derivatives of sugars, e.g. sucrose esters, are produced in industry by chemical synthesis, but the discussion here is restricted to natural glycolipids.

1. Simple Carbohydrate-Fatty Acid/Alcohol Conjugates

Simple conjugates of mono- and disaccharides with fatty acids via glycosidic or ester bonds (alkyl or acyl glycosides) are common in nature, but especially in marine organisms and in plants. Little or nothing is known of their biological functions or biosynthesis and the reviews by Dembitsky cited below cover the literature thoroughly. In contrast, a glucopyranosyl derivative of tuberonic acid is known to induce tuber formation in potatoes. Mycobacteria produce 6-*O*-acylglucosides of mycolic acids in addition to the more complex trehalose lipids described below.

Linoleic acid is oxidized in the human liver by a P450 mono-oxygenase to a mixture of 9,10 and 12,13 epoxides, which are converted to the corresponding diols, termed leukotoxin and isoleukotoxin, by an epoxide hydrolase. Specific enantiomers of each of the four possible hydroxyl groups can then be converted to glucuronides by the action of a UDP-glucuronosyltransferase. The products from 9,10-dihydroxyoctadec-12-enoate are illustrated.



glucuronides of 9,10-dihydroxyoctadec-12-enoate

Fig. 1: Structure - fattyacid glucuronide

A small proportion of the dihydroxy metabolites are also converted to glucuronide esters. As the precursor monoepoxides of linoleic acid are produced at high levels during acute inflammation, and in patients with adult respiratory distress syndrome or suffering from severe burns, it is believed that glucuronidation may be a detoxification mechanism, facilitating excretion. However, there are also suggestions that some fatty

acid glucuronides, for example of phytanic and docosahexaenoic acids, may be ligands for hormone receptors in the nucleus or have signalling functions.

Many cyanobacterial species contain distinctive organelles termed heterocysts that are capable of fixing nitrogen. The cell walls of these maintain a micro-aerobic environment to enable the reaction to occur, and they consist of three extra layers external to the normal cell envelope, the innermost of which is comprised of unusual glycolipids, i.e. very-long-chain fatty alcohols linked to a carbohydrate moiety, such as the 1-(*O*-α-D-glucopyranosyl)-3*R*,25*R*-hexacosanediol illustrated.

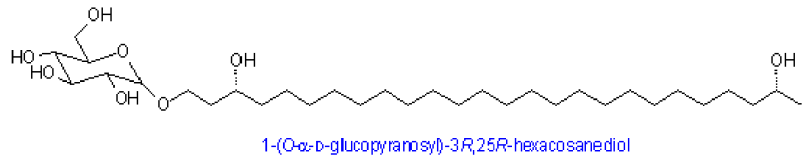


Fig. 2: formula of 1 - (O-alpha-D-glucopyranosyl) - 3R, 25R - hexacosanediol

Other forms exist differing in the number of carbon atoms, and the number and position of hydroxyl and/or keto groups.

Nematodes, including a number of human parasites, contain unusual glycolipids termed ascarosides especially in the eggs and ovaries. These consist of α-L-3,6-dideoxymannose or ascarylose, which occurs in few other organisms, linked glycosidically to the hydroxyl group of a 2-hydroxy alcohol or of an ω-1 hydroxy fatty acid. The free hydroxyl groups of the ascarylose moiety may be acetylated, and the chain-length of the alkyl component can vary from 6 to 29 and can contain further hydroxyl groups or double bonds. For example, the eggs of Ascaris sp. have a four-layer shell, the innermost layer of which consists of 75% of ascarosides and is responsible for the impermeability of the shell. It protect the contents from the harsh conditions in the intestines. Two representative examples are illustrated.

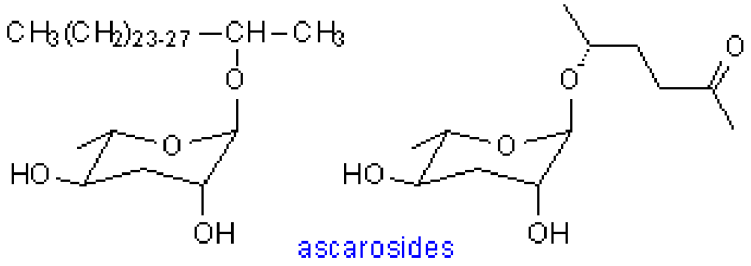


Fig. 3: formula of two representative ascarosides

In addition, certain ascarosides in the nematode *Caenorhabditis elegans* function as pheromones as well as regulating development and behaviour.

2. Rhamnolipids

Pseudomonads are rod-shaped gram-negative bacteria found in soils that produce extracellular lipids known as rhamnolipids. The term is indicative of the fact that these lipids contain one or two rhamnose units, linked glycosidically to a 3-hydroxy acid, thence by an ester bond to a further 3-hydroxy acid as illustrated. Thus, the monorhamnolipid from *Pseudomonas aeruginosa* grown on hydrocarbons is 2-*O*-α-L-rhamnopyranosyl-α-L-3-hydroxydecanoyl-3-hydroxydecanoic acid.

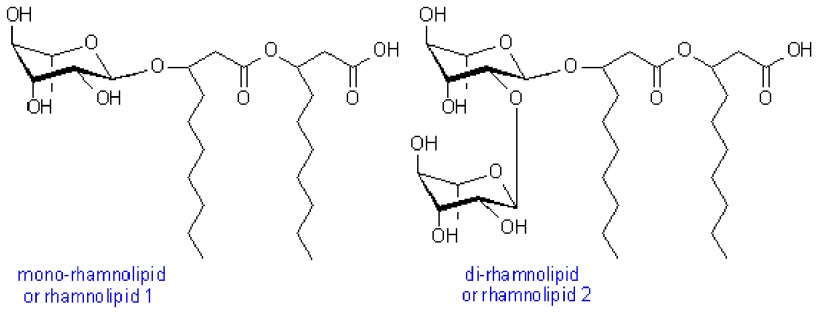


Fig. 4: formula of rhamnolipids

3- or β-Hydroxydecanoic acid is the most common fatty acid constituent, but other fatty acids may be found depending on the *Pseudomonas*

species or growth conditions, including 12:0, 12:1, 12:2 and 8:2 (each with a 3-hydroxyl group), resulting in a number of distinct molecular species. All of these lipids have antifungal and antiviral properties, and they exhibit bactericidal properties to Gram-positive bacteria. On the other hand, they are considered as one of the virulence factors in *Pseudomonas sp*. Because of their potent detergent properties, they are produce commercially as soil remediation agents and to combat marine oil pollution. Although the exact mechanism is not clear, it is evident that rhamnolipids are able to bind to substrates with low degrees of aqueous solubility including hydrophobic pollutants. Rhamnolipids are also used as a source of L-rhamnose. Specific genetically modified *Pseudomonas* species can produce as much as 100g/L of culture medium under optimum conditions. While the wild organisms are pathogenic so must be cultured in a strictly regulated environment, the recombinant Pseudomonads appear to be safe.

Two unusual rhamnolipids, designated myxotyrosides A and B, have been isolated from a *Myxococcus sp* (Myxobacteria are gliding bacteria). These have a rhamnose unit linked to tyrosine and thence to a fatty acid such as (*Z*)-15-methyl-2-hexadecenoic and (*Z*)-2-hexadecenoic acid.

The biosynthesis of monorhamnolipid in *Pseudomonas* species involves two sequential glycosyl-transfer reactions catalysed by specific rhamnosyltransferases, in which 3-hydroxydecanoyl-3-hydroxydecanoate is linked to an activated rhamnose moiety (thymidine diphospho-rhamnose). The lipid intermediate in rhamnolipid biosynthesis has a separate function in the swarming motility of the organisms.

3. Sophorolipids

Some yeast species, and in particular *Candida (Torulopsis) bombicola*, secrete extracellular glycolipids known as sophorolipids (or sophorosides), as they contain the sugar sophorose (β-D-Glc-(1→2)-D-Glc). This is linked glycosidically to the hydroxyl group of a 17-hydroxy-C_{18} saturated or monoenoic (*cis*-9) fatty acid, the carboxyl group of which is usually linked to the 4'-hydroxyl group of the second glucose unit to form a lactone, though it can also remain in free form and then have more powerful detergency properties. One or both of the 6-hydroxyl groups on the

glucose units are acetylated. With the organism *C. bognoriensis*, the fatty acid is 13-hydroxydocosanoate, while in *C. batistae* it is 18-hydroxy-stearic acid (and the acidic form of the lipid predominates).

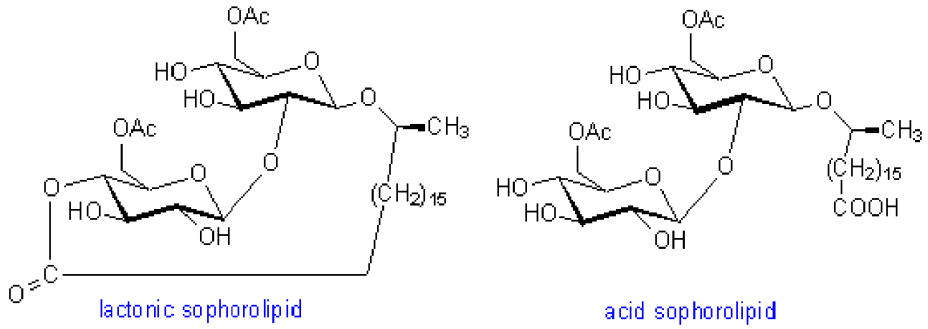


Fig. 5: Formula of sophorolipids

Biosynthesis involves sequential transfer of activated glucose molecules, UDP-glucose (see our webpage on glycosyldiacylglycerols), to a hydroxy acid in processes catalysed by two different glycosyltransferases. Finally, the molecule is acetylated by an acetyltransferase. The fatty acid constituents can be synthesised *de novo* from acetate or by modifying alkanes in the growth medium.

While the physiological role of sophorolipids in yeast species is uncertain, it seems likely that they serve for extracellular carbon storage (reducing the cellular sugar content) and as a defense against competing microorganisms.

These lipids are produced on a commercial scale when the organism is cultured on substrates containing glucose and a source of alkyl moieties, such as alkanes or seed oils, which influence the nature of the fatty acid constituent. Yields can be as much as 300g/L from organisms in the stationary phase. Sophorolipids are used in commerce in cosmetics as deodorant, anti-dandruff and bacteriostatic agents, and they are also known to possess antifungal, antiviral and spermicidal properties. The hydroxy acid constituents are in demand for lactonization for use in perfumes.

4. Mannosylerythritol and Cellobiose Lipids

The yeast *Candida (Pseudozyma) antarctica* secretes an extracellular mannosylerythritol lipid (4-*O*-(2',6'-di-*O*-acyl-β-D-mannopyranosyl)-D-erythritol), with biosurfactant properties, when grown on a vegetable oil substrate. When grown on glucose, the same lipid accumulates intracellularly as an energy store until it amounts to 10% or more of the dry weight of the cell.

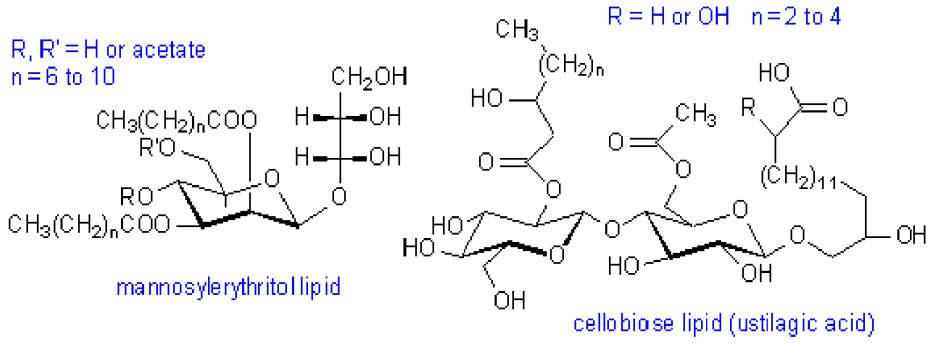


Fig. 6: formula mannosylerythritol and cellobioselipids

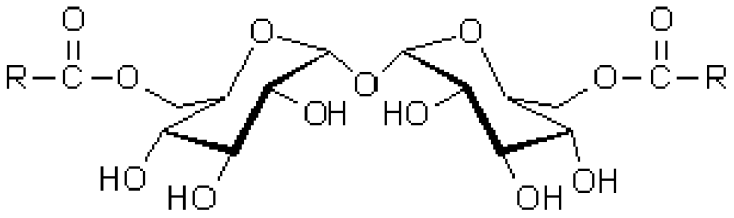
One or two of the hydroxyls on the mannose residue are acetylated, and there are two esterified fatty acids, which are both are odd- and even-numbered from C_8 to C_{12} in chain-length (longer in related species). While this organism gives the greatest yields of these lipids, they were first found in the fungus *Ustilago maydis* and termed 'ustilipids'. In this instance, the 2-hydroxyl group of the mannose residue is esterified with a C_2 to C_8 fatty acid, while the 3-hydroxyl group is esterified by a C_{12} to C_{20} fatty acid. Several other species of the genus *Pseudozyma* are now known to produce similar lipids in which the nature, number and positions of the acyl groups vary. As with other biosurfactants, these compounds are believed to facilitate dissolution of organic hydrophobic compounds so that they can be consumed by the organism. Mannosylerythritol lipids have been shown to have a number of profound biological effects in animals, but especially to induce the differentiation of certain cancer cells.

Ustilago maydis also contains distinctive cellobiose lipids (or 'ustilagic acid'), consisting of the disaccharide cellobiose linked *O*-glycosidically to

the ω-hydroxyl group of the unusual long-chain fatty acid 15,16-dihydroxyhexadecanoic acid or 2,15,16-trihydroxyhexadecanoic acid. Others of the hydroxyl groups are esterified either to acetate or a medium-chain 3-hydroxy fatty acid. A further unusual cellobiose lipid is produced by the fungal biocontrol agent, *Pseudozyma flocculosa*, and has been show to be 2-(2',4'-diacetoxy-5'-carboxy-pentanoyl)octadecyl cellobioside (flocculosin), the compound responsible for the antifungal activities of the organism.

5. Trehalose Lipids

Trehalose is a non-reducing disaccharide in which the two glucose units are linked in an α,α-1,1-glycosidic linkage. It is the basic component of a number of cell wall glycolipids in Mycobacteria and Corynebacteria. Of these trehalose lipids, cord factor is the best known. It is a component of the cell wall lipid of *M. tuberculosis* and comprises a distinctive branched-chain mycolic acid esterified to the 6-hydroxyl group of each glucose to give trehalose 6,6'-dimycolate. In addition to being one of the major toxic components of the cell wall, it is believed to be responsible for the low permeability of the membranes conferring appreciable drug resistance to the organisms.



RCO = mycoloyl
trehalose 6,6'-dimycolate ('cord factor')

Fig. 7: structure-cord factor

During biosynthesis, trehalose is first esterified to form the monomycolate, which is believed to be the precursor to the dimycolate, although via the

action of a mycolyl transferase it also may be the donor of mycolic acid residues to the cell wall arabinogalactan to produce the mycolyl-arabinogalactan-peptidoglycan complex.

Among the other antigenic glycolipids in the mycobacterial cell wall based upon trehalose, there are acylated trehaloses with various fatty acids attached to the 2 and 3 hydroxyl groups of the same glucose. These fatty acids include n-C_{16-19} saturated fatty acids, C_{21-25} α-methyl branched fatty acids, and C_{24-28} α-methyl-branched, β-hydroxy fatty acids. Trehalose lipids produced by Corynebacteria and Nocardia are similar in structure but contain the corynomycolic or nocardomycolic acids, respectively, which are related in structure to the mycolic acids.

A strain of *Rhodococcus erythropolis* produces extra-cellular trehalose lipids containing succinic acid, i.e. 2,3,4,2''-di-*O*-succinoyl-di-*O*-alkanoyl-α,α-trehalose and 2,3,4-mono-*O*-succinoyl-di-*O*-alkanoyl-α,α-trehalose, while 3,4-di-*O*-alkanoyl-2-*O*-succinoyl-α-D-glucopyranosyl-2'-*O*-succinoyl-α-D-glucopyranoside produced by *Rhodococcus* sp. SD-74 is illustrated. They are powerful surfactants. More complex sulfated trehalose lipids are also known.

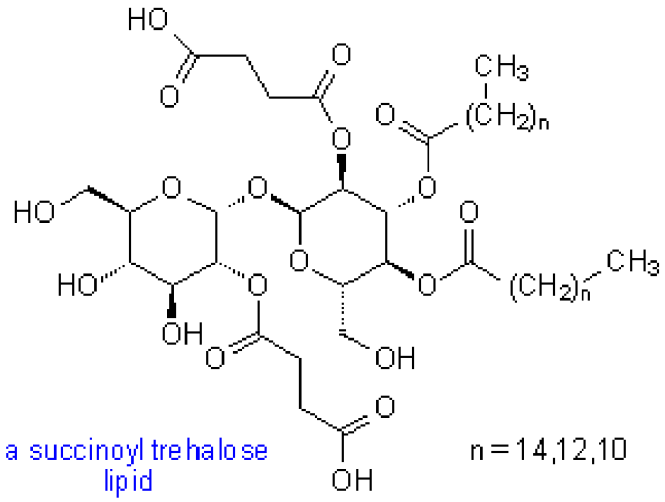


Fig. 8: a succinoyl trehalose lipid

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William W. Christie
Scottish Crop Research Institute (and MRS Lipid Analysis Unit),
Invergowrie, Dundee (DD2 5DA), Scotland.

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www.endowmentmed.org

Chapter

3

New Uses for Trehalose
Add to EVERY Recipe - Here's Why

We have learned of new uses for the healthful sugar trehalose that you can share with your family and friends. The multi-reasons trehalose can be added to almost every dish include 1) trehalose enhances flavor; 2) trehalose increases health benefits; 3) trehalose keeps water pockets from forming when refrigerated or frozen; 4) trehalose helps preserve food and extend life and freshness; 5) trehalose is a simple way to reduce you and your family's use of bad sugars. And, 6) relax in knowing that you need not worried about too much sugar - because trehalose is the GOOD sugar.

Some of the new uses for trehalose include meats in the early stages of preparation, like beef, pork, deer and fowl sausage and hamburger. Sprinkle and mix trehalose throughout the sausage or hamburger meat. Because trehalose is only 45% as sweet as table sugar, you are not as concerned with making the dishes too sweet. With cookies, brownies, pies, and cakes, if you replace table sugar with trehalose, they will not be as sweet but that may be a good thing. An interesting side benefit seems to be that the more trehalose one eats, the more the crave for sugar is removed. Diabetics are encouraged to continue to monitor their sugar load; however, diabetics are indicating that their sugar balance is more normal while using trehalose. More information is available at www.DiabeticHope.com

You are welcome to view recipes and share your recipes with us on **Sugar Science Forum** at www.endowmentmed.org or simply e-mail them to us at jcs@endowmentmed.org. Give trehalose to your friends this Christmas. View the creative ideas on our Home Page.

A number of recipes are posted in the Sugar Science Forum accessible from the top navigation bar on the Home Page os www.endowmentmed.org. Users of trehalose are encouraged to post new recipes for others to enjoy.

Chapter 4

Microarray Technology / Trehalose / NIH / Texas A&M

The world of microarray technology was first introduced to me by Dr. David Busbee of Texas A&M University when he presented two research projects on sugars at our Glycomics Medical Conferences. The study of altered gene expression caused by specific sugars greatly fascinated us and those lessons are available in our Glycomics DVD Training Series at www.endowmentmed.org .

NIH announced a $923,000 grant to upgrade the cell array platform. Barry Bochner, CEO of Biolog told *BioArray News* that the funds will be used to advance the technology working with researchers at Texas A&M. Bochner said. "*They have already presented data on an important gene that they found, using PM technology, to be involved in trehalose metabolism*." Past success with trehalose metabolism has influenced continued research.

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Biolog Nets $923K ARRA Grant to Upgrade Cell Array Platform
November 10, 2009
By Justin Petrone

The National Institutes of Health recently awarded Biolog $923,000 to help it develop a next-generation version of the firm's cell array technology. The grant, called "Phenotype microarray analysis of fastidious pathogens," was awarded under the American Recovery and Reinvestment Act of 2009.

CEO Barry Bochner told *BioArray News* last week that Biolog will use the funds to continue adapting its Phenotype Microarray platform to study *Mycobacterium tuberculosis* and other fastidious pathogens, expand its Microbial Identification System to cover more fastidious species, and work with researchers at Texas A&M University to study gene function in *Mycobacterium*.

Biolog's Phenotype Microarray platform is currently used to study the physiological and metabolic properties of a wide range of microbial cells, according to the grant abstract. Using the PM platform, researchers can scan nearly 2,000 phenotypes of a microbial cell line in a single experiment.

However, a number of fastidious genera are currently not amenable to PM analysis because they are difficult to culture. Biolog intends to enhance its PM technology to study agents of lung, cutaneous, and tissue infections such as *Mycobacterium*, *Nocardia* and *Legionella*; microaerophilic gastrointestinal pathogens, including *Helicobacter*, *Campylobacter*, and *Wolinella*; and colonizers of the colon and vagina, such as *Bacteroides*, *Clostridium*, and *Escherichia*, according to the abstract.

"Part of this has to do with our customer base doing basic research to understand the properties of bacteria that grow on and in the human body," Bochner said of the project. According to Bochner, the new work is being funded to assist the NIH's Human Microbiome Project, part of its Roadmap for Medical Research that funds various studies to determine how microbial cells impact human health.

"The NIH has recognized the importance of understanding the basic biology of these microorganisms and their interaction with the human host," he said. "Biolog technology is being funded in recognition of the utility of our PM testing platform."

As part of that effort, Biolog will seek to lower the cost and increase the throughput of its existing PM platform by developing a new plastic microfluidic device. "This is would be a miniaturized, microfluidic version of our current system," said Bochner. "We would like to have a better piece of hardware to make it easier to put the cells into hundreds of different wells, and we would like to bypass pipetting by developing a better device."

Bochner said Biolog's goal is to get a working prototype developed within the first year of the grant. In terms of price, Bochner added that Phenotype Microarrays currently cost anywhere from between $25 and $500, depending on the array. Biolog hopes to cut the cost of its arrays in half by developing the next-gen platform.

A further goal of Biolog's project is to expand the capabilities of its Microbial Identification System to study fastidious pathogens. Biolog's microplate-based system allows users to identify different species of aerobic and anaerobic bacteria, yeasts, and fungi.

"We want to understand how to test these bacteria so that we can add them to the capability of our GEN III species identification system," Bochner said. Biolog launched the Gen III last year. Using the system, microbiology testing labs can identify 1,044 species.

"We want to continue to push the envelope and add even more species that are important in human health," Bochner said of the project. "We have already added *Nocardia*, which can cause severe respiratory diseases. We also would like to add *Mycobacterium* and perhaps also *Mycoplasma* species."

A final goal of Biolog's project is to work with Texas A&M University researcher Lacy Daniels to study *Mycobacterium*, and use knockout strains with the PM platform to study the function of genes that are unique to the metabolism and drug resistance of the genus, Bochner said. "If successful, this aspect of the project will aid efforts toward the development of new or more effective anti-mycobacterial drug therapies," he added.

Daniels' lab at Texas A&M has expertise in Mycobacterium genetics and metabolism. "They are working to understand genes that are important and unique to making *Mycobacterium* such a difficult pathogen to culture and to kill as well as genes involved in antibiotic drug resistance," Bochner said. "They have already presented data on an important gene that they found, using PM technology, to be involved in trehalose metabolism."

Bochner said that *Mycobacterium* is "unique in having trehalose mycolates in their membrane." He said the "enzymes coded by these unique mycobacterial genes could turn out to be good antibiotic drug targets."

As Biolog's projects are focused on pathogens that affect human health, the company envisions that the projects will also aid researchers that are involved in biodefense-related projects.

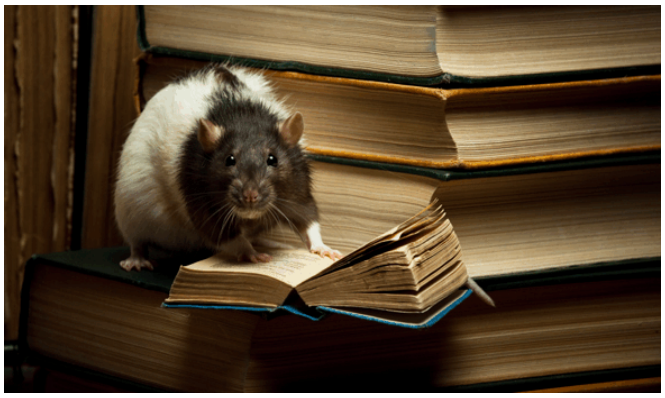
"Some of the biodefense-related bacteria are difficult to culture and researchers would like to understand the properties of these cells in more detail," Bochner said. "Our customers would like to be able to understand how key genes involved in pathogenicity affect a cell. There's a substantial segment of users of our technology that get funded through biodefense

initiatives, either from the NIH or the US Department of Defense."

Chapter 5

Structuring Glycoproteins for Increased Communication

One Smart Rat



Folding proteins properly and structuring glycoproteins for increased communication helps make for one smart rat. This is an update on the work of Joe Z. Tsien that I discussed in my book **Expand Your Mind - Improve Your Brain**. The *Science Daily* reports on how superior brainpower is expressed.

After reading the article, you may enjoy 14 short remarkable graphic video clips that are fascinating lessons about what is required to make all this happen.

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According to *Science Daily*, Hobbie-J was able to remember novel objects, such as a toy she played with, three times longer than the average Long Evans female rat, the smartest rat strain. Hobbie-J was also better at remembering which path she last traveled to find a chocolate treat.

Researchers from the Medical College of Georgia and East China Normal University developed Hobbie-J 's superior brainpower by transgenic over-expression of the NR2B gene, which in turn increased communication between NMDA receptor sites maybe a hundred milliseconds longer than normal, just enough to enhance learning and memory. NMDA receptors (and their NR2B subunits) are the controlling molecular structures for synaptic plasticity and memory.

"This adds to the notion that NR2B is a universal switch for memory formation," says Dr. Joe Z. Tsien, co-director of the MCG Brain & Behavior Discovery Institute and co-corresponding author with Dr. Xiaohua Cao of a paper called “Genetic Enhancement of Memory” published recently in

PLoS One.

Gene expression is translation of information encoded in a gene into protein or RNA. When done to a very high level, it is known as over-expression. The researchers wanted to determine whether the NR2B gene is "a universal genetic factor that acts as a rate-limiting molecule" across species. Here's a short video showing the process of gene expression:

Previous studies of mice suggest a common biochemical mechanism at the root of nearly all learning. Tsien and Cao wanted to show that the brain uses the same basic mechanism in rats when it forms associations. Their research supports the hypothesis that NR2B is a key switch that controls the brain's ability to associate one event with another, critical to learning. Tsien had previously created mice that lacked the gene in a tiny region of the brain and showed that they had impaired learning and memory. Adding new or improved ability, however, is a harder task requiring a more rigorous test of the gene's function.

Joe Tsien: "They're smarter" - Credit: news.bbc.co.uk Charles Stevens, a neuroscientist at the Salk Institute who works on the mechanisms responsible for synaptic transmission, said that Tsien's earlier work with mice helped to answer a hotly debated question in memory research. Many scientists argue that memories are created when two neurons form a strong connection, called long-term potentiation or LTP. Others believe LTP is not necessary for learning. Tsien's work "is one of the best pieces of evidence so far" in favor of the LTP model, Stevens said, because activating the NMDA receptor clearly leads to LTP.

In his earlier research, Tsien developed Doogie –- a "smart" mouse named after the precocious TV character Doogie Howser, M.D. (with a genius intellect and eidetic memory) – by over-expressing the NR2B gene in his hippocampus, a learning and memory center affected in diseases such as Alzheimer's. Hobbie-J-the-rat's memory improvements were very similar to Doogie-the-mouse's. Subsequent testing has demonstrated that Doogie has maintained superior memory as he aged.

Dr. Tsien's work with rats confirms his earlier findings with mice. "We want to make sure this is a real phenomenon," Dr. Tsien says of the connection between higher levels of NR2B and better memory. "You should never

assume that discovery you made in a cell line or a mouse can be translated to other species or systems unless you do the experiments." In one intelligence test, Hobbie-J had to learn to alternate between right and left paths to get a chocolate reward. Both Hobbie-J and a non-enhanced rat did well when they only had to wait a minute to repeat the task. After three minutes only Hobbie-J could remember the path. After five minutes, she forgot as well.

Enhanced intelligence followed by subsequent forgetfulness is the theme of the famous short story, “Flowers for Algernon,” by Daniel Keyes – adapted numerous times for the television and also as the Academy-award winning 1969 film, *Charly*. In the short story, researchers Nemur and Strauss develop a surgical procedure to enhance intelligence. The laboratory mouse Algernon is able to beat the mentally-challenged human, Charlie Gordon, at solving simple mazes. Charlie decides to become the first human to undergo the surgery and ends up with a genius-level IQ – but only temporarily.

Charlie discovers a flaw in Nemur and Strauss’ intelligence-enhancing procedure. Algernon starts behaving erratically, loses his new intelligence, and dies. As Charlie does further research, he determines that he too is at risk. He ends up losing his mental acuity and returning to his former life in a special needs home. In a final postscript, he asks that someone put flowers on Algernon's grave.
This moving little allegory is perhaps a warning to both researchers and potential test subjects to be rigorous in experimental procedures, as it appears that Dr. Tsien is attempting to be with his rat studies. This is not to say that Hobbie-J-the-rat is at risk of dying from NR2B gene over-expression –- it bodes well that Doogie-the-mouse maintained superior memory into old age.

There may not be the need for such caution with nootropics (smart drugs) such as vasopressin, oxiracetam, and *Ginko biloba* that are being used a memory aids (see the h+ article "Tweaking Your Neurons") – the risks are low, although the scientific data to support their effectiveness is largely anecdotal at present. Interestingly, Tsien’s work suggests that magnesium – a mineral found in nuts, legumes and green vegetables such as spinach – may be as effective a memory enhancer as genetic manipulation. The magnesium ion blocks entry to the NMDA receptor so more magnesium

forces brain cells to increase expression levels of the more efficient NR2B to compensate. This is similar to how statin drugs help reduce cholesterol levels in the blood by inhibiting its synthesis in the liver.

So perhaps you should listen to your mother and eat your spinach. Whether it's magnesium biochemical pathways or NR2B gene over-expression in mice and rats, it's clear that further research is warranted with the NR2B gene as a drug target for improving memory in healthy individuals as well as those coping with Alzheimer's or mild dementia.

Hobbie-J may not be smarter than you, but you might be smart to pay attention to Hobbie-J.

Source:
http://www.hplusmagazine.com/articles/neuro/making-smarter-rat

www.endowmentmed.org

Chapter 6

Trehalose pH Fusion

A new all natural composition designed
to absorb into the human cell.

You have learned some of the secrets of trehalose. Now learn the secrets of the active ingredient of Trehalose pH Fusion.

The Secrets of Sodium

This chapter is written by J. C. Spencer and friends (see references). In addition to my comments, this section includes notes of discussions between professors and students.

Sodium is an electrolyte and one of its functions is to pass through the cell membrane. This chapter is about the Structure Function of Minerals in Your Body with the focus on sodium. We will discuss the role trehalose and sodium play with the plasma membrane and mitochondria. The structure function of sodium is the purpose of the lesson.

About 4% of your body mass is composed of 21 different minerals. These inorganic nutrients play a major role as constituents of hormones, enzymes, and vitamins. They (1) regulate cellular metabolism by joining with hormones and enzymes to regulate cellular activity; (2) supply structure in the formation of teeth and bones; and (3) function in the maintenance of muscular contractions, neural activity, heart rhythm, and acid base balance. These minerals roam free in your body fluids as well as combine with other chemicals.

Minerals are divided into two classes: 1) the major class known as macronutrient minerals; and 2) the minor class, known as micronutrient minerals. Macronutrient minerals are required in amounts of more than 100 mg daily, while trace minerals are defined as those required in amounts less than 100 mg daily. There are seven known macronutrient minerals, and 14 trace minerals. Among micronutrient minerals (trace minerals) are iron, fluorine, zinc, copper, selenium, iodide, and chromium. The macronutrient minerals consist of calcium, phosphorous, potassium, sulfur, chloride, magnesium, and our featured subject: sodium.

Sodium plays a deciding role in cellular metabolism. We will see how this inorganic nutrient, unlike other minerals, penetrates the cell membrane and modulates the pH which is vital to all metabolism.

Other inorganic minerals do not easily absorb into the human cell. Sodium is unique and vital. Because sodium is an electrolyte, one of its functions is to pass through cell membranes. About 95% of consumed sodium is absorbed by the body, with the remaining 5% being excreted through the intestines while the excess sodium is excreted by the kidneys.

Several fundamental pathways are used for sodium absorption across the intestinal mucosa (mucosal cells are any membrane or lining, which contain mucus-secreting glands for lubrication).

Sodium (pronounced /ˈsoʊdiəm/) is a metallic element with a symbol Na (from Latin *natrium* or Arabic *natrun*) and atomic number 11. It is a soft, silvery-white, highly reactive metal and is a member of the alkali metals within "group 1". It has only one stable isotope, 23Na.

Elemental sodium was first isolated by Sir Humphry Davy in 1806 by passing an electric current through molten sodium hydroxide. Elemental sodium does not occur naturally on Earth, but quickly oxidizes in air and is violently reactive with water, so it must be stored in an inert medium, such as a liquid hydrocarbon. The free metal is used for some chemical synthesis and heat transfer applications.

Sodium ion is soluble in water in nearly all of its compounds, and is therefore present in great quantities in the Earth's oceans and other stagnant bodies of water. In these bodies it is mostly counterbalanced by the chloride ion, causing evaporated ocean water solids to consist mostly of sodium chloride, or common table salt. Sodium ion is also a component of many minerals.

Sodium is an essential element for all animal life and for some plant species. In animals, **sodium ions are used in opposition to potassium ions, to allow the organism to build up an electrostatic charge on cell membranes, and thus allow transmission of nerve impulses when the charge is allowed to dissipate by a moving wave of voltage change.** Sodium is classified as a “dietary inorganic macro-mineral”. Sodium's relative rarity on land is due to its solubility in water, thus causing it to be leached into bodies of long-standing water by rainfall. Such is its relatively large requirement in animals, in contrast to its relative scarcity in many inland soils, that herbivorous land animals have developed a special taste

receptor for sodium ion.

Sodium (NA) has the atomic number of 11. The atomic number is the number of protons in a particular atom. Each proton has a single positive charge. These eleven protons are equally offset by 11 negatively charged electrons (negative charge of one). To fill its valance shelf, sodium loses an electron. This gives it a charge of +1, making it an ion (atoms with positive or negative charges), more specifically, a cation (a positively charged ion). A synonym for Sodium is therefore, NA+. The most commonly known form of sodium is table salt, or sodium chloride. NA represents 40% of it.

NA+ is very water soluble (can be dissolved/mixed in water, much of this effect is due to its charge, which is attracted to the highly polar H_20 molecule) and highly concentrated in the extracellular fluids (ECF) of the body. Sodium is loosely bound to macromolecules (large molecules, i.e. proteins); one of its functions is to pass through cell membranes. It operates this way in order to enforce nutrient transport mechanisms and signal nerve impulses.

Sodium is an electrolyte because it can dissociate into ions in water. Solutions of electrolytes therefore conduct an electric current and can be decomposed in a solution (electrolysis). Electrolytes are both anions (positively charged ions) and cations (negatively charged ions). The body uses them throughout fluid compartments. The goal is to distribute them in such a way that within a given compartment – the blood plasma for example – electrical neutrality is always maintained with the anion concentration exactly balanced by the cation concentration. Major groups of cations include sodium, potassium, calcium, and magnesium. Their negative counterparts consist of chloride, proteins, and bicarbonate, along with low concentrations of organic acids, sulfate and phosphate. The maintenance of pH (level of acidity, the lower the pH, the more acidic), and electrolyte balance is almost always handled by your kidneys.

Approximately 30% of bodily sodium is located on the surface of bone crystals. The remainder is found in the ECF (extracellular fluids). Lastly, sodium constitutes 93% of the cations in the body, making it by far the most abundant member of this family.

In discussing digestion, keep in mind that trehalose is two glucose molecules. The sodium/glucose co transport system, which transpires throughout the small intestine. The sodium/chloride co transport mechanism is active in both the small intestine and colon.

Electrically silent cotransport on Na+, K+ and 2Cl-.

The mechanisms used for cellular absorption, so that your body can use sodium to properly function, will be discussed subsequently, along with several other fascinating digestive traits.

Before understanding these pathways, it is important to understand the transport system of the Sodium/Potassium Pump which plays a vital role in these functions.

There are two forms of transport process, as follows:

Active transport-assisted transport through the plasma membrane, requiring metabolic energy to “power” the exchange of materials.

Passive transport- the transport of substances through the plasma membrane, requiring no energy.

These transport systems have a tendency to go spontaneously from higher energy concentrations, to lower ones (diffusion). For example, if glucose were to move across the membrane of a cell, it would naturally travel from the higher area of concentration (outside the cell) to the lower area of concentration (inside the cell). This is called passive transport because it naturally occurs, and requires no energy. However, if glucose were to be moved in the opposite direction (from lower to higher concentrations), it would be called active transport because it does not occur naturally, but rather, requires energy.

The NA+ K+ pump is a form of active transport. Here is how it works: ATP pumps ions uphill against their electrochemical gradients through the membrane by a special protein enzyme known as sodium potassium ATPase (remember, ase at the end of a word refers to an enzyme) that serves as a pumping mechanism. Such processes must occur within living cells for optimal distribution of cellular chemicals. Sodium ions normally

stay in the cell, due to its low levels of concentration. As such, sodium outside the cell naturally wants to continue to diffuse into the plasma membrane. Potassium, however, exists in higher levels of concentration and, thus, tends to diffuse into the ECF (extracellular fluids). To counteract this (that is, counteracting a state of equilibrium which would be reached without such pumping mechanisms) and achieve proper sodium and potassium concentrations surrounding the plasma membrane, for the maintenance of muscular and nerve functions, both cations must move against their normal concentration gradients. This leads to higher levels of NA+ in the ECF (extracellular fluids), and higher levels of K+ in the ICF. From this, muscular contractions and nervous functions, among other vital systems, are able to function at a maximal rate.

Gabriel “Venom” Wilson stated, “To make a long story short, in the membrane of both muscle cells and neurons are several complex structures. There are voltage gated channels which allow sodium into the cell, and there are voltage gated channels which let potassium out of the cell. Additionally, there are sodium/potassium pumps, which literally pump three sodiums (against their electrical and chemical gradients) out of the cell, while only pumping two potassiums into the cell. Three positives out and two positives in translates to the inside of the cell being more negative than the outside of the cell. In addition to this, there are also channels in the membrane which allow more potassium to escape than sodium to enter, which means that more positive charge leaves the cell than enters. Finally, negatively charged proteins are manufactured inside of the cell. The point is simple: by complex machinery, both neurons and muscle cells set up what is called a negative membrane potential, which means that the inside of the cell is more negative than the outside. Secondly, the cell has driven sodium outside of the cell, against its chemical and electrical gradient; that is, if you could make the membrane more permeable to sodium, it would rush into the cell like a bullet out of a gun!

This is precisely what occurs in an action potential. Without going into horrid detail, there is a certain threshold for each cell to achieve an action potential. This means that enough positive charge flowing toward negative charge has to occur in order for the entire cell to conduct an electrical impulse. Once this is reached, however, the entire cell will go through an action potential (actually its more similar to tiny action potentials propagating themselves across the cell). Finally, once threshold has been

reached, there is no stopping the action potential from spreading across the entire cell! This is why it is "the all or none principle."

For more information, you may refer to: Is the All or None Applicable to an Entire Muscle?

Sodium/Glucose transport system mechanism was further discussed this mechanism in an earlier issue of JHR, and is quoted here:

Glucose/Sodium transport system

"Earlier in the article I discussed the sodium/glucose co transport mechanism. This concept falls under the heading of secondary active transport. Primary active transport takes place via a pumping system [uses ATP or some other chemical energy source directly to transport substances]. You see, each of your cells contain proteins which break down ATP, into ADP + P + Energy, and use the products to power the pump. The Sodium/Potassium Atpase, pumps three sodiums out of the cell, and only two potassiums into it. This makes sodium's concentration higher on the outside of the cell. Additionally the inside of the cell is more negatively charged than the outside. Sodium is a positively charged ion and is attracted to the negative area. It has been pumped against its electrochemical gradient (concentration is greater outside of the cell and more negative). Thus, Na+ (sodium) will now move back into the cell.

There are proteins within a cell membrane which act to transport glucose. However, the binding site for glucose has a low affinity for it, unless sodium is bound to it. Due to the electrochemical gradient, sodium enters a binding site specific for it on the protein, and when it does so, the protein changes its shape (allosteric reaction), so that sodium can now bind and be transported into the cell. This is called co transport because two substances are transported into the cell together, and secondary active transport because it takes advantage of the concentration gradient set up by the primary mechanism. By taking in the proper amount of sodium, you increase the concentration gradient outside of the cell, and therefore increase sodium's ability to bind to transport proteins. In doing so, you not only increase glucose absorption, but as pointed out, you also further increase water uptake across the luminal membrane of the intestine as well."

In summary, glucose and sodium couple with each other to form a co transport system. This process is mediated by the Sodium Potassium pumping system, which provides the proper energy for this to transpire.

For more on this, study, Dextrose, Maltodextrin, and Sodium an In Depth Analysis.

Electrogenic sodium absorption mechanism

This is called an electrogenic sodium absorption mechanism because the sodium cation is the lone ion moving past cells, and its transport is regulated by several electrical channels. It enters the colon via NA+ conducting pathways called sodium channels. These channels cause diffusion (passive transport) inwardly by the downhill concentration gradient. This reaction is accompanied by anions and water, causing it to flow down the colon lumen (tube) down to its blood stream. Lastly, the sodium potassium system, pumps it across the membrane, on the blood stream side of the cell.

Sodium/Chloride Co Transport

This theory is still being analyzed. But an electro neutral (sodium is positive, and chloride is negative, so they offset each other, becoming electrically neutral) NA+ Cl- system has been suggested. This has been proposed due to the observation that a vast amount of sodium absorption is usually in the presence of Chloride and visa versa [16]. Mechanisms have not been established. One proposed system suggests paired ion exchangers, that is, sodium and hydrogen (H+) exchange with chloride and bicarbonate (HCO3-) [4,22]. This theory states that NA+ and Cl- are allowed into the cell, in exchange for H+ and HCO3-. The sodium is then pumped across the cell membrane by the sodium potassium pump, followed by chloride, which crosses via diffusion.

Contribution includes Bioenergetic Research, The HYPERplasia Magazine, and ABCBodyBuilding

Venom@abcbodybuilding.com

Additional References:
http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/D/Diffusion.html

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This subject is studied in universities in many different countries. The following information is quote from above link and contains discussion notes between professors and students:

Transport Across Cell Membranes

Importance
All cells acquire the molecules and ions they need from their surrounding extracellular fluid (ECF). There is an unceasing traffic of molecules and ions in and out of the cell through its plasma membrane

Examples: glucose, Na^+, Ca^{2+}

In eukaryotic cells, there is also transport in and out of membrane-bounded intracellular compartments such as the nucleus, endoplasmic reticulum, and mitochondria.

Examples: proteins, mRNA, Ca^{2+}, ATP

Two problems to be considered:

1. Relative concentrations

Molecules and ions move spontaneously down their concentration gradient (i.e., from a region of higher to a region of lower concentration) by diffusion.

Molecules and ions can be moved against their concentration gradient, but this process, called active transport, requires the expenditure of energy (usually from ATP).

2. Lipid bilayers are impermeable to most essential molecules and ions.

The lipid bilayer is permeable to water molecules and a few other small, uncharged, molecules like oxygen (O_2) and carbon dioxide (CO_2). These

diffuse freely in and out of the cell. The diffusion of water through the plasma membrane is of such importance to the cell that it is given a special name: osmosis.

Lipid bilayers are not permeable to:

ions such as K^+, Na^+, Ca^{2+} (called cations because when subjected to an electric field they migrate toward the cathode [the negatively-charged electrode])

Cl^-, HCO_3- (called anions because they migrate toward the anode [the positively-charged electrode])

small hydrophilic molecules like glucose

macromolecules like proteins and RNA

This page will examine how ions and small molecules are transported across cell membranes. The transport of macromolecules through membranes is described in Endocytosis.

Solving these problems

Mechanisms by which cells solve the problem of transporting ions and small molecules across their membranes:

Facilitated diffusion

Transmembrane proteins create a water-filled pore through which ions and some small hydrophilic molecules can pass by diffusion. The channels can be opened (or closed) according to the needs of the cell.

Active transport

Transmembrane proteins, called transporters, use the energy of ATP to force ions or small molecules through the membrane against their concentration gradient.

Facilitated Diffusion of Ions

Facilitated diffusion of ions takes place through proteins, or assemblies of proteins, embedded in the plasma membrane. These transmembrane proteins form a water-filled channel through which the ion can pass down its concentration gradient.

The transmembrane channels that permit facilitated diffusion can be opened or closed. They are said to be "gated".

Some types of gated ion channels:

ligand-gated

mechanically-gated

voltage-gated

light-gated

Ligand-gated ion channels.

Many ion channels open or close in response to binding a small signaling molecule or "ligand". Some ion channels are gated by extracellular ligands; some by intracellular ligands. In both cases, the ligand is not the substance that is transported when the channel opens.

External ligands

External ligands (shown here in green) bind to a site on the extracellular side of the channel.

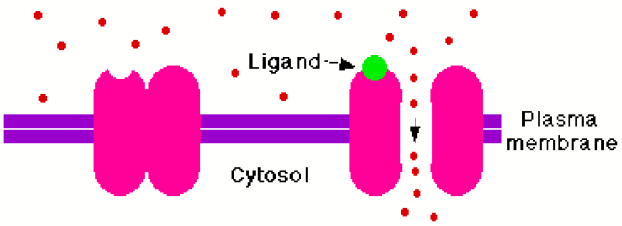

Fig. 1

Examples:

Acetylcholine (Ach). The binding of the neurotransmitter acetylcholine at certain synapses opens channels that admit Na^+ and initiate a nerve impulse or muscle contraction.

Gamma amino butyric acid (GABA). Binding of GABA at certain synapses — designated $GABA_A$ — in the central nervous system admits Cl^- ions into the cell and inhibits the creation of a nerve impulse.

Internal ligands

Internal ligands bind to a site on the channel protein exposed to the cytosol.

Examples:

"Second messengers", like cyclic AMP (cAMP) and cyclic GMP (cGMP), regulate channels involved in the initiation of impulses in neurons responding to odors and light respectively.

ATP is needed to open the channel that allows chloride (Cl^-) and bicarbonate (HCO_3-) ions out of the cell. This channel is defective in patients with cystic fibrosis. Although the energy liberated by the hydrolysis of ATP is needed to open the channel, this is not an example of active transport; the ions diffuse through the open channel following their concentration gradient.

Mechanically-gated ion channels
Examples:

Sound waves bending the cilia-like projections on the hair cells of the inner ear open up ion channels leading to the creation of nerve impulses that the brain interprets as sound.

Mechanical deformation of the cells of stretch receptors opens ion channels leading to the creation of nerve impulses.

Voltage-gated ion channels

In so-called "excitable" cells like neurons and muscle cells, some channels open or close in response to changes in the charge (measured in volts) across the plasma membrane.

Example: As an impulse passes down a neuron, the reduction in the

voltage opens sodium channels in the adjacent portion of the membrane. This allows the influx of Na^+ into the neuron and thus the continuation of the nerve impulse.

Some 7000 sodium ions pass through each channel during the brief period (about 1 millisecond) that it remains open. This was learned by use of the patch clamp technique.

The Patch Clamp Technique

The properties of ion channels can be studied by means of the patch clamp technique.

A very fine pipette (with an opening of about 0.5 μm) is pressed against the plasma membrane of either an intact cell or the plasma membrane can be pulled away from the cell and the preparation placed in a test solution of desired composition.

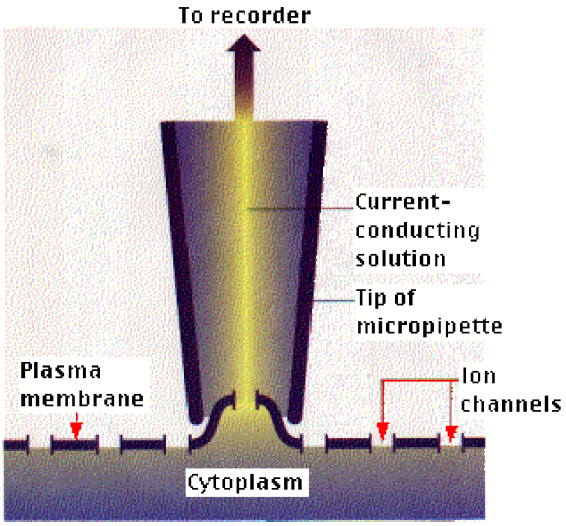

Fig. 2

Current flow through a single ion channel can then be measured.

Such measurements reveal that each channel is either fully open or fully closed; that is, facilitated diffusion through a single channel is "all-or-none".

This technique has provided so much valuable information about ion channels that its inventors, Erwin Neher and Bert Sakmann, were awarded a Nobel Prize in 1991.

Facilitated Diffusion of Molecules

Some small, hydrophilic organic molecules, like sugars, can pass through cell membranes by facilitated diffusion.

Once again, the process requires transmembrane proteins. In some cases, these — like ion channels — form water-filled pores that enable the molecule to pass in (or out) of the membrane following its concentration gradient.

Example: Maltoporin. This homotrimer in the outer membrane of E. coli forms pores that allow the disaccharide maltose and a few related molecules to diffuse into the cell.

In the Trehalose pH Factor, the disaccharide maltose has been replaced with the disaccharide trehalose because of its advance beneficial qualities with neurodegenerative challenges. It appears that after trehalose has performed certain functions that it can, when needed, be broken down into two glucose molecules and be utilized as discussed here and for energy ATP. Some of the study and work accomplished with Maltodextrin and Dextrose as discussed later in this chapter was PRIOR to our having the understanding about trehalose.

Another example: The plasma membrane of human red blood cells contain transmembrane proteins that permit the diffusion of glucose from the blood into the cell.

Note that in all cases of facilitated diffusion through channels, the channels are selective; that is, the structure of the protein admits only certain types of molecules through.

Whether all cases of facilitated diffusion of small molecules use channels is yet to be proven. Perhaps some molecules are passed through the membrane by a conformational change in the shape of the transmembrane protein when it binds the molecule to be transported.

In either case, the interaction between the molecule being transported and its transporter resembles in many ways the interaction between an enzyme and its substrate.

Active Transport

Active transport is the pumping of molecules or ions through a membrane against their concentration gradient. It requires:

a transmembrane protein (usually a complex of them) called a transporter and energy. The source of this energy is ATP.

The energy of ATP may be used directly or indirectly.

Direct Active Transport. Some transporters bind ATP directly and use the energy of its hydrolysis to drive active transport.

Indirect Active Transport. Other transporters use the energy already stored in the gradient of a directly-pumped ion. Direct active transport of the ion establishes a concentration gradient. When this is relieved by facilitated diffusion, the energy released can be harnessed to the pumping of some other ion or molecule.

Direct Active Transport

1. The Na^+/K^+ ATPase

The cytosol of animal cells contains a concentration of potassium ions (K^+) as much as 20 times higher than that in the extracellular fluid. Conversely, the extracellular fluid contains a concentration of sodium ions (Na^+) as much as 10 times greater than that within the cell.

These concentration gradients are established by the active transport of both ions.

The same transporter, called the Na^+/K^+ ATPase, does both jobs. It uses the energy from the hydrolysis of ATP to actively transport 3 Na^+ ions out of the cell for each 2 K^+ ions pumped into the cell.

This accomplishes several vital functions:

It helps establish a net charge across the plasma membrane with the interior of the cell being negatively charged with respect to the exterior. This resting potential prepares nerve and muscle cells for the propagation of action potentials leading to nerve impulses and muscle contraction.

The accumulation of sodium ions outside of the cell draws water out of the cell and thus enables it to maintain osmotic balance (otherwise it would swell and burst from the inward diffusion of water).

The gradient of sodium ions is harnessed to provide the energy to run

several types of indirect pumps.

The crucial roles of the Na^+/K^+ ATPase are reflected in the fact that almost one-third of all the energy generated by the mitochondria in animal cells is used just to run this pump.

2. The H^+/K^+ ATPase

The parietal cells of your stomach use this pump to secrete gastric juice. These cells transport protons (H^+) from a concentration of about 4×10^{-8} M within the cell to a concentration of about 0.15 M in the gastric juice (giving it a pH close to 1). Small wonder that parietal cells are stuffed with mitochondria and uses huge amounts of energy as they carry out this three-million fold concentration of protons.

3. The Ca^{2+} ATPases

A Ca^{2+} ATPase is located in the plasma membrane of all eukaryotic cells. It uses the energy provided by one molecule of ATP to pump one Ca^{2+} ion out of the cell. The activity of these pumps helps to maintain the ~20,000-fold concentration gradient of Ca^{2+} between the cytosol (~ 100 nM) and the ECF (~ 20 mM).

In resting skeletal muscle, there is a much higher concentration of calcium ions (Ca^{2+}) in the sarcoplasmic reticulum than in the cytosol. Activation of the muscle fiber allows some of this Ca^{2+} to pass by facilitated diffusion into the cytosol where it triggers contraction.

After contraction, this Ca^{2+} is pumped back into the sarcoplasmic reticulum. This is done by another Ca^{2+} ATPase that uses the energy from each molecule of ATP to pump 2 Ca^{2+} ions.

Pumps 1. - 3. are designated P-type ion transporters because they use the same basic mechanism: a conformational change in the proteins as they are reversibly phosphorylated by ATP. And all three pumps can be made to run backward. That is, if the pumped ions are allowed to diffuse back through the membrane complex, ATP can be synthesized from ADP and inorganic phosphate.

4. ABC Transporters

ABC ("ATP-Binding Cassette") transporters are transmembrane proteins that expose a ligand-binding domain at one surface and a ATP-binding domain at the other surface.

The ligand-binding domain is usually restricted to a single type of molecule.

The ATP bound to its domain provides the energy to pump the ligand across the membrane.

The human genome contains 48 genes for ABC transporters. Some examples:

CFTR — the cystic fibrosis transmembrane conductance regulator TAP, the transporter associated with antigen processing.

[Discussion]

the transporter that liver cells use to pump the salts of bile acids out into the bile.

ABC transporters that pump chemotherapeutic drugs out of cancer cells thus reducing their effectiveness. The ATP-binding domains in archaea, eubacteria, and eukaryotes all share a homologous structure, the ATP-binding "cassette".

Indirect Active Transport

Indirect active transport uses the downhill flow of an ion to pump some other molecule or ion against its gradient. The driving ion is usually sodium (Na^+) with its gradient established by the Na^+/K^+ ATPase.

Symport Pumps
In this type of indirect active transport, the driving ion (Na^+) and the pumped molecule pass through the membrane pump in the same direction.

Examples:

The Na^+/glucose transporter. This transmembrane protein allows sodium ions and glucose to enter the cell together. The sodium ions flow down their concentration gradient while the glucose molecules are pumped up theirs. Later the sodium is pumped back out of the cell by the Na^+/K^+ ATPase.

The Na^+/glucose transporter is used to actively transport glucose out of the intestine and also out of the kidney tubules and back into the blood.

All the amino acids can be actively transported, for example out of the kidney tubules and into the blood [Example] the reuptake of Glu from the synapse back into the presynaptic neuron by sodium-driven symport pumps.

The Na^+/iodide transporter. This symporter pumps iodide ions into the cells of the thyroid gland (for the manufacture of thyroxine) and also into the cells of the mammary gland (to supply the baby's need for iodide).

The permease encoded by the lac operon of E. coli that transports lactose into the cell.

Antiport Pumps

In antiport pumps, the driving ion (again, usually sodium) diffuses through the pump in one direction providing the energy for the active transport of some other molecule or ion in the opposite direction.

Example: Ca^{2+} ions are pumped out of cells by sodium-driven antiport pumps.

Antiport pumps in the vacuole of some plants harness the outward facilitated diffusion of protons (themselves pumped into the vacuole by a H^+ ATPase) to the active inward transport of sodium ions. This sodium/proton antiport pump enables the plant to sequester sodium ions in its vacuole. Transgenic tomato plants that overexpress this sodium/proton antiport pump are able to thrive in saline soils too salty for conventional

tomatoes.

to the active inward transport of nitrate ions (NO_3^-).

Some inherited ion-channel diseases

A growing number of human diseases have been discovered to be caused by inherited mutations in genes encoding channels.

Some examples:

Chloride-channel diseases

Cystic fibrosis

inherited tendency to kidney stones (caused by a different kind of chloride channel than the one involved in cystic fibrosis)

Potassium-channel diseases

some inherited life-threatening defects in the heartbeat
a rare, inherited tendency to epileptic seizures in the newborn.

several types of inherited deafness [Discussion]

Sodium-channel diseases

inherited tendency to certain types of muscle spasms

Liddle's syndrome. Inadequate sodium transport out of the kidneys, because of a mutant sodium channel, leads to elevated osmotic pressure of the blood and resulting hypertension (high blood pressure).

Osmosis

Osmosis is a special term used for the diffusion of water through cell membranes.

Although water is a polar molecule, it is able to pass through the lipid

bilayer of the plasma membrane. Transmembrane proteins that form hydrophilic channels accelerate the process, but even without these, water is still able to get through.

Water passes by diffusion from a region of higher to a region of lower concentration. Note that this refers to the concentration of water, NOT the concentration of any solutes present in the water.

Water is never transported actively; that is, it never moves against its concentration gradient. However, the concentration of water can be altered by the active transport of solutes and in this way the movement of water in and out of the cell can be controlled.

Example: the reabsorption of water from the kidney tubules back into the blood depends on the water following behind the active transport of Na^+. [Discussion]

Hypotonic solutions

If the concentration of water in the medium surrounding a cell is greater than that of the cytosol, the medium is said to be hypotonic. Water enters the cell by osmosis.

A red blood cell placed in a hypotonic solution (e.g., pure water) bursts immediately ("hemolysis") from the influx of water.

Plant cells and bacterial cells avoid bursting in hypotonic surroundings by their strong cell walls. These allow the buildup of turgor within the cell. When the turgor pressure equals the osmotic pressure, osmosis ceases.

How the kidneys of freshwater fishes and amphibians permit their owners to live in their hypotonic surroundings.

Isotonic solutions

When red blood cells are placed in a 0.9% salt solution, they neither gain nor lose water by osmosis. Such a solution is said to be isotonic.

The extracellular fluid (ECF) of mammalian cells is isotonic to their cytoplasm. This balance must be actively maintained because of the large number of organic molecules dissolved in the cytosol but not present in the ECF. These organic molecules exert an osmotic effect that, if not compensated for, would cause the cell to take in so much water that it would swell and might even burst. This fate is avoided by pumping sodium ions out of the cell with the Na^+/K^+ ATPase.

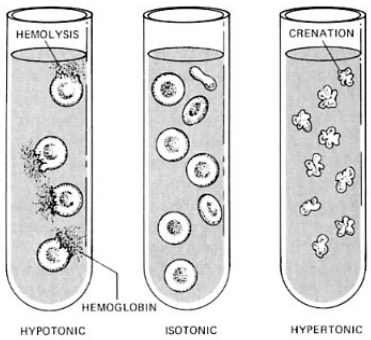

Fig. 3

Hypertonic solutions

If red cells are placed in sea water (about 3% salt), they lose water by osmosis and the cells shrivel up. Sea water is hypertonic to their cytosol.

Similarly, if a plant tissue is placed in sea water, the cell contents shrink away from the rigid cell wall. This is called plasmolysis.

Sea water is also hypertonic to the ECF (extracellular fluid)of most marine vertebrates. To avoid fatal dehydration, these animals (e.g., bony fishes like the cod) must continuously drink sea water and then desalt it by pumping ions out of their gills by active transport.

Marine birds, which may pass long periods of time away from fresh water, and sea turtles use a similar device. They, too, drink salt water to take care of their water needs and use metabolic energy to desalt it. In the herring gull, shown here, the salt is extracted by two glands in the head and released (in a very concentrated solution — it is saltier than the blood) to the outside through the nostrils. Marine snakes use a similar desalting mechanism.

It may be of interest to note here: When a human is lost at sea, *The Rime Of The Ancient Mariner* By Samuel Taylor Coleridge comes to mind, " *Water, water, everywhere and not any drop to drink"*. In fact, this rime is wrong. If you are lost at sea, you can survive by slowly sipping a little seawater every few moments. Your body will expel the salt and retain survival amounts of water in your system. Of course, you cannot drink very much at a time.

Slowly continuing to sip small amounts is the key.

Exercise causes large losses of sodium--every liter of sweat contains .6 grams of NA+. As such, it is prudent to consume sodium post-exercise, and during exercise (if performed long enough).

Drinks absent or containing little amounts of sodium post-exercise dilutes blood plasma, increase urine production (decreased fluid retention), and lower osmolarity. This further inhibits the thirst mechanism, and delays rehydration [8, 26, 32, 21, 22]

For example, an experiment was performed on six men following strenuous exercise in the heat [23]. Within 30 minutes after, they ingested one of four drinks (all with 2045 ml of water) with sodium concentrations of 2, 26, 52, and 100mmol per L of water, respectively. Those who had 2mmol of sodium excreted almost 800 ml of water 1.5 hours later and almost 1400 ml 5.5 hours later. The best results came with 100 mmol of sodium. Only 300 ml of water was excreted in the first 1.5 hours, and 500 in 5.5 hours--which is less than what those who had little sodium excreted in 1.5 hours!

Sweat loss

As mentioned previously, sodium is water soluble. This relates to a large amount of sodium loss through sweat during intense training sessions.

Sweat is produced by specialized sweat glands beneath the skin. Evaporation of sweat's water components results in a refrigeration mechanism to cool the body down. Typically, a well-assimilated athlete will loose .5L - 3L of sweat during each hour of exercise. On average, an athlete looses 1-1.5 liters per hour. Higher intensity results in increased sweat loss. Humidity, heat, and other weather related factors will result in increased sweat secretion as well. Every liter of sweat contains a whopping .6 g of sodium. This is a vital factor in optimal post-workout nutrition.

Osmosis is important!

A report in the 23 April 1998 issue of The New England Journal of

Medicine tells of the life-threatening complications that can be caused by an ignorance of osmosis.

Large volumes of a solution of 5% human albumin are injected into people undergoing a procedure called plasmapheresis.

The albumin is dissolved in physiological saline (0.9% NaCl) and is therefore isotonic to human plasma (the large protein molecules of albumin have only a small osmotic effect).

If 5% solutions are unavailable, pharmacists may substitute a proper dilution of a 25% albumin solution. Mixing 1 part of the 25% solution with 4 parts of diluent results in the correct 5% solution of albumin.

BUT, in several cases, the diluent used was sterile water, not physiological saline.

SO, the resulting solution was strongly hypotonic to human plasma.

Reference Source includes
John Kimball
http://home.comcast.net/~john.kimball1/BiologyPages/D/Diffusion.html

Gabriel “Venom” Wilson
http://www.abcbodybuilding.com/hpresearch.pdf

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The Master Logos

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NOTES:
Dextrose & Maltodextrin an in-depth analysis
Researched and Composed by Gabriel “Venom” Wilson, BSc. (Hons), CSCS

Abstract
It is the intention of the writer to do a comprehensive analysis on the application of dextrose, maltodextrin, water, and sodium for post workout nutrition.

Below is an outline that will allow you to instantaneously access whatever aspect of the article you seek to examine:

Introduction to Gastric emptying and Osmolarity
What is Dextrose
What is Maltodextrin
Hydrogen Bonds/Digestion process
Importance of consuming a combination of Maltodextrin & Dextrose
Importance of water
What Hyponatremia is and how to avoid it
Glucose/Sodium transport system
Measurements

Introduction to Gastric emptying and Osmolarity

In the near future, we will do a complete breakdown on both these important physiological occurrences. But for now, here is a general overview, as it pertains to the article:

• Gastric emptying - the process of digesting and emptying food out of the stomach.

• Osmolarity - the concentration of particles in a solution.
How to speed gastric emptying, and what levels of osmolarity are optimal in a given solution will be discussed. But first, two carbohydrates, dextrose and maltodextrin, will be analyzed.

Dextrose
Dextrose, commonly called glucose, d-glucose, or blood sugar, occurs naturally in food, and is moderately sweet. It is a monosaccharide (basic unit of carbohydrates, C6H1206) and has a high glycemic index (digested carbohydrates ability to raise blood glucose levels, also called GI) ranking at 100.

Maltodextrin

Maltodextrin is a sweat, easily digested carbohydrate made from cornstarch. The starch is cooked, and then acid and/or enzymes (a process similar to that used by the body to digest carbohydrates) are used to break the starch into smaller chains (3-20 chains in maltodextrin).

These chains are composed of several dextrose molecules held together by very weak hydrogen bonds.

WHAT IS TREHALOSE?

It is one of the good sugars. Trehalose is a naturally-occurring sugar energy source with forty-five percent (45%) of the sweetness of refined table sugar. So, you may need to use about twice as much as you normally use to get the same sweetness.

Although no medical claims are being made at this time, trehalose may indeed be a brain food. It is a white crystalline powder (trehalose dehydrate) produced from cornstarch by a patented enzymatic Hayashibara process.

For many people, the sugar trehalose has been found to be an easy way of getting their blood sugar more regular.** Of course, no medical claims are being made at this time.

Trehalose is a natural substance found in very small amounts in foods we already eat such as mushrooms, honey, lobster, and foods produced using bakers and brewer's yeast. An independent panel of experts determined trehalose to be generally recognized as safe (GRAS) for use in foods in accordance with current good manufacturing practices.

A clinical study performed in the UK showed that ninety-eight percent (98%) of the population had no problems with trehalose. The other two percent (2%) experienced only a little gas.

A certain enzyme in the body, called trehalase, is used to transport the sugar trehalose to where it is needed in the body or to split the trehalose molecule into two glucose molecules. Research is ongoing to determine the relationship between the metabolism of the body with the potential energy and performance benefits of trehalose.

Energy That Lasts!

In the 1980s scientists learned that certain sugars had benefits beyond energy.

Trehalose is a sustained energy food. That means that it has been tested to produce lower insulin and blood glucose responses than regular table sugar in most people.

Athletes Get Sustained Energy From Trehalose.

Athletes like trehalose because it gives them sustained energy. Athletes need sustained energy for increased performance. Sports drinks give quick energy, but then the benefits diminish quickly. Some athletes have found that you can avoid the typical "energy-drink" spike followed by the inevitable low by using trehalose for sustained energy.

What are carbohydrates?

Carbohydrates are molecules of carbon, hydrogen, and oxygen produced by plants through photosynthesis. The term saccharide is a synonym for carbohydrate; a monosaccharide (mono=1) is the fundamental unit of carbohydrates. Disaccharides (Di=2) are molecules containing 2 monosaccharide units. Di and monosaccharides are also known as sugars, simple sugars, or simple carbohydrates. Next are oligosaccharides, and polysaccharides. Oligosaccharides are made of 3-9 monosaccharide links. Polysaccharides consist of 10 to thousands of monosaccharide links. A complex carbohydrate refers to many monosaccharide units linked together. In addition, you will often hear the terms “long”, and “short”
carbohydrate chains. Short carbohydrate chains are those under 10 sugar molecules.

And long chains are those over 10 sugar molecules. Which fits in conjunction with the above terms, Oligosaccharides and Polysaccharides. Dextrose is labeled a simple carbohydrate and Maltodextrin complex. And

now this should make perfect sense. But don't be fooled by the word, "complex." The bonds that compose maltodextrin are very weak, and readily broken apart in your stomach; moreover, the chain is extremely minimal in composition. The weak bonds, and fragile composition of maltodextrin cause it to be digested a fraction slower than dextrose. Why this is so and what exactly hydrogen bonds are will be assessed subsequently.

Hydrogen Bonds/Digestion process

A covalent bond is defined as atoms, which are held together by their mutual attraction for sharing electrons. Co is for sharing, and valent refers to valance electrons that are shared. Covalent bonds tend to form from atoms in the upper right of the periodic table, know as *nonmetallic elements* (with the exception of noble gases, which are the last group of the periodic table to the right. These elements are very stable and tend not to form bonds.) Now, electro negativity is an atom's ability to pull electrons toward itself when bonded. Electro negativity is greatest for elements at the upper right of the periodic table, and lowest for elements at the lower left. Noble gases again are not included, because primarily they do not participate in chemical bonding. To represent this, scientists use what is called a dipole (pronounced die-pole) to say a side is slightly negative, or slightly positive, because it has more or less electrons around itself. A bond with a dipole (remember, di=2, 2 poles) is classified as a polar bond. The higher amount of difference in electro negativity in the bonds, the more polar the atom is (greater charge difference).

Electrical attractions are based on polarity between particles; they tend to be very weak. The kind discussed today is called a dipole-dipole attraction, which is defined as an attraction between two polar molecules. In particular, one of the strongest dipole-dipole attractions, known as the hydrogen bond will be analyzed. This attraction occurs between molecules that have a hydrogen atom covalently bonded to a highly electronegative atom--typically nitrogen, oxygen or fluorine. In the case of maltodextrin, this is an H-O bond. The strength of a hydrogen bond is based on two factors:

1. The strength of the dipoles involved (which depends on the difference in

electro negativity for the two atoms in either polar molecule)

2. How strongly nonbonding electrons on one molecule can attract a hydrogen atom on a nearby molecule. Recent research has revealed that a small amount of electron sharing occurs between the hydrogen and the nonbonding pair. Because electron sharing is the definition of covalent bonds, the hydrogen bond is correctly named a covalent bond. However, any hydrogen bond is many times weaker than the typical covalent bond; therefore, it is also appropriate to think of the hydrogen bond not as a bond, but as a very strong dipole-dipole attraction between separate molecules. When confronted with the proper enzymes, this bond has no chance, and is easily separated from the above attractions. Which leads to the next subject, digestion.

Student Editor's Note: I am extremely glad that Venom is covering this subject. Hydrogen bonds are one of the key subjects that one must understand if they are intent on understanding nutrition, and how sizable biological molecules are constructed.

Maltodextrin digestion starts right when it enters the mouth. The salivary glands, located along the base of the jaw (there are actually three specific glands here - parotid, submandibular and sublingual), continually secrete lubricating mucus substances that mingle with food particles during chewing. The enzyme salivary amylase (ptyalin) breaks the hydrogen bonds between the repeating glucose units, beginning the reduction of maltodextrin into smaller linked glucose molecules. When the food-saliva mixture enters the more acidic stomach, breakdowns in the chains from enzymatic action quickly cease because salivary amylase deactivates under conditions of low pH (lower pH means more acidity). After this, food enters the small intestine, and encounters pancreatic amylase, a powerful enzyme released from the pancreas. This enzyme, in conjunction with other enzymes, completes hydrolysis (catabolism of larger molecules into smaller ones the body can absorb. Done by enzymes and water) of maltodextrin into smaller chains of glucose molecules.

Finally, enzyme action on the surfaces of the cells of the intestinal lumen's brush border completes the final stage of carbohydrate digestion to monosaccharides. Due to the weak nature of these hydrogen bonds, this

is a swift process. In addition, the shorter the chains, the quicker these molecules are separated. Therefore, maltodextrin at 3-20 monosaccharide links, is very easily digested. Once absorbed from the small intestines into the bloodstream, the body uses glucose for 3 potential tasks:

1. Given directly to muscle cells for energy.

2. Stored as glycogen in the muscles and liver.

3. Converted to fat for energy storage.

As stated earlier, scientists simply try and mimic this process when breaking down starches to maltodextrin. Actually, as one ventures further in the studies of chemistry, biology, endocrinology, and such like, they will see this is commonly the case.

Importance of consuming a combination of Maltodextrin & Dextrose
After reading Old School's excellent article on post workout nutrition, the reader is now aware of the importance of consuming easily digested, high GI carbohydrates at this time. But the question is, why a combination of dextrose and maltodextrin? Both are high in GI rating, and easily digested right? True, but there is more logic than GI rating to stacking these two powerhouses. Read on for the answer. Beginning with the first concept discussed called, "gastric emptying." Our goal post workout is to maintain a prompt digestion rate so nutrients can transport swiftly and efficiently to our muscles. With that said, it has been shown that this process slows when the ingested fluid contains a high osmolarity concentration (the second concept studied). Osmolarity is dependent on the number of particles in a solution. That is, a100-milliliter solution with 20 glucose molecules will have a higher osmolarity then a100-millileter solution that only contains 10 molecules. The shorter chain length a carbohydrate has, the higher it raises the solution's osmolarity. Therefore, it is no surprise that a pure glucose solution (or dextrose, a monosaccharide) induces very high concentrations of solute (1,3,10).

Fortunately these negative effects become greatly reduced when the drink contains a glucose polymer stacked with dextrose. However, a carbohydrate that is easily digested, and has a high GI is still desired.

Hence, a combination of dextrose and maltodextrin is advised. Osmolarity will be decreased, and glucose will still enter the blood stream at a proficient rate, thus maintaining its anabolic nature (1,3).

A second factor concerning osmolarity must now be examined. From a clinical standpoint, it is vital to take into consideration the fact that plasma (the liquid portion of blood) has an Osmolarity of 300 mOsm. This means that if one were to inject a solution with a greater concentration of solute into their blood, it would cause water from inside their red blood cells to leave by Osmosis (water always travels down its concentration gradient) and move into the plasma, in turn shrinking the erythrocytes (red blood cells). This is because the cells are iso-osmotic to the plasma (both have the same concentration of solute) (11).

A similar concept can be applied to your post workout meal. If a competitor were to consume a solution that was hypertonic or had a higher concentration of solute then 300 mOsm, it could dehydrate them (showing why digestion is rightfully slowed in a high concentrated solution). The addition of maltodextrin once again solves this problem (2,13).

The next question is, why not just use maltodextrin, and eliminate dextrose since it is so proficient? Ah, once again it is not that simple. Shi. X et al. in an outstanding study, tested the digestive effects of two substrates (any substance acted upon by an enzyme) as opposed to only one substrate in the small intestine. What they found was quite fascinating. The solution containing two substrates stimulated the activation of more transport mechanisms in the intestinal lumen, than did its singular counterpart. Therefore, more carbohydrates were transported out of the small intestine (absorbed into the blood), which additionally aided a greater absorption rate of water into the blood stream (by osmosis). Thus, the higher activation rate of transport mechanisms, even with higher osmolarity facilitated faster energy uptake and hydration (12)!

Student Editor's note: Truly Fascinating!

One of these mechanisms is the glucose/Sodium co transport system (discussed in further detail shortly). When a proper amount of sodium and glucose are combined, an even greater amount of glucose is absorbed,

and in turn, a higher rate of H20 is absorbed. Thus, dextrose increases fluid uptake, and contributes to blood glucose maintenance. Which in turn helps spare liver and muscle glycogen from being depleted (4,5,6).

As discussed in the Window of Opportunity, these factors make dextrose and maltodextrin the perfect post workout combo. One can purchase both of these in pure form from a local grocery store, or the Internet.

Importance of water

Gastric emptying is greatly influenced by its volume. Emptying rate decreases exponentially as fluid volume is depleted. Therefore, an effective way to speed gastric emptying is by maintaining high fluid volumes in the stomach. This will also optimize nutrient passage into the intestines. About 500 mL of water immediately before training (spread through a 30 minute time span), and 200 mL every 15-20 minutes (about the rate at which fluids are drained during intense training sessions) of the workout has been recommended to maintain high water levels in your stomach. For optimal hydration, consume a 92% water solution in your post-workout shake. To calculate this, divide the carbohydrate content (in grams) by the fluid volume (in millimeters), and multiply by 100. Thus if you consumed 80 grams of carbohydrates in 1 L of water (1000 mL) you would be having 8% carbohydrates, and 92% H2O (1,3,4,10).

Another reason to frequently drink water is avoidance of dehydration. To name a few reasons why, dehydration reduces circulatory and temperature-regulating capacities, which meet metabolic needs and thermal demands of exercise, and recovery (8,9).

The effects of this can further reduce blood flow to the skin for more effective cooling.

For much more, read, Effect of Plasma Volume on Myofibril Hydration, Nutrient Delivery, and Athletic Performance and Thermoregulation:

Physiological Responses and Adaptations to Exercise in Hot and Cold Environments.

What Hyponatremia is and how to avoid it

Hyponatremia occurs when plasma sodium concentrations fall below normal levels in the body, and severe symptoms are triggered. Lighter symptoms are headaches, nausea, cramping, and confusion. Ultimately, this may lead to seizures, coma, pulmonary edema, and even death! These fatal conditions usually pertain to long distance runners, consuming large amounts of water with little or no sodium contained, and training in stifling heat. Non-the-less, bodybuilders are still at risk, especially during cutting season when cardio and posing hours are at a high point. As such, I would highly recommend using sodium post workout, not only to avoid any minor (much likelier to occur) or major side symptoms, but also for its anabolic effects (5,7,8).

Student Editor's Note: From Venom's description you can see why sodium depletion precontest can be dangerous if not done correctly. Quite frankly it usually is done incorrectly. Such a concept is worthy of a future hyperplasia magazine article.

Sodium is the most abundant ion in the extra cellular space (outside of cells). Adding a small amount has several benefits, such as:

1. Reduces urine output by maintaining osmotic drive (prevents water from leaving, going out, or coming into cell to rapidly, maintaining even flow). Moreover, this will promote thirst, and fluid retention during recovery, further amplifying hydration.

2. Helps prevent hyponatremia by keeping sodium levels stable.

3. Helps maintain proper osmolarity levels.

4. Enhanced co transport efficiency.

In general, it is recommend to have 500-600 mg of sodium per liter of solution after a workout, the solution being the recommended amount of water and carbohydrates to consume at this time (6,7).

For more read, Sodium - A comprehensive Analysis

Glucose/Sodium transport system

Earlier in the article, the sodium/glucose co transport mechanism was discussed. This concept falls under the heading of secondary active transport. Primary active transport takes place via a pumping system. Each cell contains proteins which break down ATP into ADP + P + Energy, and uses the products to power the pump. The Sodium/Potassium Atpase, pumps three sodium's out of the cell, and only two potassium's into it. This makes sodium's concentration higher on the outside of the cell.

Additionally, the inside of the cell is more negatively charged than the outside. Sodium is a positively charged ion, and attracted to the negative area. It has been pumped against its electrochemical gradient (concentration is greater outside of the cell and more negative). Thus, Na+ (sodium) will now move back into the cell.

There are proteins within a cell membrane, which act to transport glucose. However, the binding site for glucose has a low affinity for it, unless sodium is bound to it. Due to the electrochemical gradient, sodium enters a binding site specific for it on the protein, and when it does so, the protein changes its shape (allosteric reaction), so that sodium can now bind, and be transported into the cell. This is called co transport because two substances are transported into the cell together; and secondary active transport because it takes advantage of the concentration gradient set up by the primary mechanism. Therefore, by taking in the proper amount of sodium, one increases the concentration gradient outside of the cell, and therefore, increases sodium's ability to bind to transport proteins. In doing so, one not only increase glucose absorption, but as pointed out, you also further increase water uptake across the luminal membrane of the intestine.

This explains the reasoning and the potential for **Trehalose pH Fusion**. **Trehalose pH Fusion** as recommended is designed to help the cells have a higher pH, to receive better absorption of nutrients and to better hydrate the human body.

Trehalose pH Fusion

Ingredients: Trehalose (Food Grade), sodium bicarbonate Net Wt. 2 lb (907.34g)

Designed to help the cells have a moderately higher pH, to help the cells receive better absorption of nutrients and to better hydrate the human body.

Trehalose pH Fusion is a proprietary nutritional buffer designed to help raise and modulate the human cellular pH level, to lower acid level, and reduce cell stress. **Trehalose pH Fusion** is designed to offset the acid overload without interrupting good digestion. The buffer formulation is designed with the intent of helping fortify the cell membrane and to equip the cell for superior nutrient absorption. One teaspoon of **Trehalose pH Fusion** may be mixed with 4 ounces of clean filtered water and taken between meals. The taste is slightly sweet with a soothing swallow. You may add another teaspoon of trehalose for a sweeter taste. DO NOT add a different sweetener, juice, or other ingredients as that may upset the pH balance.

Trehalose pH Fusion is a specific blend of trehalose and sodium bicarbonate. Trehalose is a naturally occurring sugar about 45% as sweet as sucrose and has a clean profile which means it has no after-taste. Trehalose is a white crystalline dihydrate powder produced from corn starch. It is a non-reducing disaccharide consisting of two glucose molecules bonded by an α,α - 1, 1 glycosidic link which is **stable at low pH (high acid) conditions** and is non-hygroscopic, which results in a free-flowing dry crystal that is stable to 94% humidity. Trehalose has known protein and cell membrane stabilizing capabilities and may preserve and protect multiple normal biological systems by protecting the cell proteins and interfering with the natural cellular processes of protein turnover and reduce neurological cell stress.

The Buffer, sodium bicarbonate, is a naturally occurring substance that is found in all living things, where it helps modulate (regulate) their pH balance. The Buffer is made from soda ash, which is mined in the form of an ore called trona. The soda ash is then dissolved into a solution through which carbon dioxide is bubbled and sodium bicarbonate precipitates out, forming the "Pure, Safe and Natural" Buffer.

Sodium, NA+, is very water soluble (can be dissolved/mixed in water, much of this effect is due to its charge, which is attracted to the highly polar H_20 molecule) and highly concentrated in the extracellular fluids (ECF) of the body. Sodium is loosely bound to macromolecules (large molecules, i.e. proteins); one of its functions is to pass through cell membranes. It operates this way in order to enforce nutrient transport mechanisms and signal nerve impulses.

Trehalose pH Fusion does NOT contain Baking Powder which is a mixture of baking soda and various acidic ingredients. Baking powder contains acidic ingredients which makes a carbon dioxide producing reaction.

Warnings:

Do not use if you are on a sodium restricted diet unless directed by a doctor. Ask a doctor or a pharmacist before use if you are taking a prescription drug. Because **Trehalose pH Fusion** acts as an antacid, it may interact with certain prescription drugs. Do not administer to children under age 5. STOMACH WARNING: TO AVOID SERIOUS INJURY, DO NOT TAKE UNTIL POWDER IS COMPLETELY DISSOLVED. IT IS VERY IMPORTANT NOT TO TAKE THIS PRODUCT WHEN OVERLY FULL FROM FOOD OR DRINK. Consult a doctor if severe stomach pain occurs after taking this product. Stop use and ask a doctor if symptoms last more than 2 weeks. Mix only with clean water. DO NOT add a different sweetener, juice, or other ingredients as that may upset the pH balance.

Directions:

Settling may occur in transport. Measured by weight. Before opening, mix content by turning container end over end and rolling around and around a few times. Add 1 teaspoon to a small glass (4 oz.) of water between meals, or as directed by physician. Cold water may take a moment longer to dissolve. Dissolve completely in water. Accurately measure 1 teaspoon. Do not take more than the following amounts in 24 hours: Twenty eight (28) teaspoons. Twelve (12) teaspoons if you are over 60 years. Do not use the maximum amounts for more than 2 weeks. It is recommended that you monitor your pH level. Monitoring your saliva or urine pH can be accomplished with a pH meter or with pH strips from your local drug store. Saliva and urine should test around 6.4 pH. Further research is needed to verify the overall effect. May be used for baking.

Trehalose pH Fusion in 4 oz of clean filtered water has a factor over 9 pH. The pH factor of the liquid **Trehalose pH Fusion** may vary slightly due to the pH factor of the water.

OPEN SOURCE TECHNOLOGY:

In 2009 The Endowment for Medical Research, developer, formulator, and intellectual technology holder, has chosen to NOT patent or restrict the use of **Trehalose pH Fusion**; rather, to openly supply the formula for private and public use for the benefit of all people.

Trehalose pH Fusion may also be purchased at www.pHmarker.com with the profits going for ongoing glycomics education and research.

Other Information:

Each teaspoon contains 154 mg sodium. When **Trehalose pH Fusion** comes in contact with either an acidic or an alkaline substance, it's natural effect is to modulate (neutralize) that extreme pH level. **Trehalose pH Fusion** is designed to help resist further radical changes in the pH balance - this is called buffering. One teaspoon of **Trehalose pH Fusion** in 4 oz of clean filtered water has a factor of over 9 pH. The pH factor of the liquid **Trehalose pH Fusion** may vary slightly due to the pH factor of the water.

Nutrition Facts: Serving Size 1 teaspoon (3g) (3,086mg) (.109oz)
Servings Per 2 lb Container 192

Amount Per Serving	
Calories 5.5 (3.6 calories per g)	
	% Daily Value*
Total Fat 0g	0%
Potassium 0g	0%
Sodium 154mg	6%
Total Carbohydrates 1.4g	0.4%
Sugars 1.5g	
Protein 0g	0%

***Percentage Daily Values are based on a 2000 calorie diet. Your daily value may be higher or lower depending on your calorie needs. Caution: Any amount over 34 grams of trehalose per day has not yet been determined safe by the FDA or USDA. Further testing is ongoing to discover the safe upper limits for human consumption, sustained energy, and other possible health benefits.**

Drug Facts

Active ingredients	Purpose
Sodium Bicarbonate 12%	Skin protectant

Uses

- temporarily protects and helps relieve minor skin irritation and itching due to:
- poison ivy, oak, and sumac
- insect bites

Warning

- Do not get in eyes

KEEP OUT OF REACH OF CHILDREN

If swallowed, get medical help or contact a Poison Control Center right away.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevents any disease.

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You may participate in a self funding pH Evaluation Pilot Survey.

Evaluation Forms can be requested or downloaded from www.endowmentmed.org/phforms Each participant, family, or physician will monitor his and her own pH level for one week prior to starting to use **Trehalose pH Buffer**, then for three or six months complete the pH Evaluation Pilot Survey FORMS to determine possible pH improvements and other health benefits or cravings. We welcome physicians, nurses, and researchers to assist in this evaluation process.

This Handbook Series is Volume One in a Review Series on the Science of Trehalose.
Review new information as it is posted at www.endowmentmed.org