

Glucerna[®] 1.5 Cal Monograph

Glucerna

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Glucerna® 1.5 Cal	List #
8 fl oz can	53534
1 L Ready-To-Hang®	53536

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Glucerna

Smart nutrition for people with diabetes.™

Product Description

Glucerna® 1.5 Cal is a calorically dense, diabetes-specific enteral product featuring a unique carbohydrate blend for enhanced glycemic control and assistance with wound healing by providing key levels of calories, protein, vitamins, and minerals. Patients with diabetes are often faced with slow-healing wounds that increase calorie and protein needs. This product is designed to help provide optimal nutrition during this time of healing and increased needs.

- For patients with type 1 or type 2 diabetes
- For patients with impaired glucose tolerance/hyperglycemia resulting from metabolic stress, such as illness, trauma, or infection
- For tube feeding or oral use
- For supplemental or sole-source nutrition
- For use under medical supervision
- Not for parenteral use

Features and Benefits of Glucerna 1.5 Cal

Features	Benefits
Clinically demonstrated benefit	Glucerna 1.5 Cal contains a unique carbohydrate blend clinically shown to blunt postprandial glycemic response and to improve blood glucose control. ^{1,2}
Calorically dense	At 1.5 Cal/mL, patient needs can be met with less volume.
Unique blend of carbohydrates	Contributes to blunted postprandial glucose response due to digestive/metabolic properties of the carbohydrates. ^{1,2}
Optimal fat blend	Provides plant-based omega-3 fatty acids from canola oil (3 g of ALA per 1500 calories) to support circulatory and heart health. ^{3,4} 3% of total calories from saturated fatty acids and rich in monounsaturated fatty acids (29% of total calories), which meets American Heart Association (AHA) and American Diabetes Association (ADA) guidelines ⁵
High in protein	22% of calories from protein to promote anabolism and support wound healing
NutraFlora® scFOS®	Fructooligosaccharides are prebiotics and a source of soluble fiber to help maintain digestive-tract health. NutraFlora scFOS is the only short-chain FOS includes 10 g/L of NutraFlora scFOS (2.4 g/8 fl oz).
Complete and balanced	Macronutrient distribution: 33% carbohydrate, 45% fat, and 22% protein. 1500 Cal provides at least 100% of the RDIs for 24 key vitamins and minerals.
Chromium picolinate	Chromium picolinate is the most bioavailable form of chromium and is clinically shown to lower fasting and postprandial glucose and A1C levels. ⁶
Fortified with conditionally essential nutrients	Supplemented with the conditionally essential nutrients carnitine and taurine
Lactose- and gluten-free	Does not contribute to risk of lactose-induced diarrhea in lactose-intolerant patients; may be used by people who are gluten-intolerant

NutraFlora and scFOS are registered trademarks of GTC Nutrition.

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Energy Distribution of Glucerna® 1.5 Cal

Glucerna 1.5 Cal		
Calories	356 Cal/237 mL 1500 Cal/L	
	(g/L)	(% energy)
Protein	82.5	22
Carbohydrate	133.1	33
Fiber	17.0	—
Fat	75	45

Carbohydrate and Fiber Profile of Glucerna® 1.5 Cal

Glucerna 1.5 Cal		
Carbohydrate Content	31.5 g/237 mL 133.1 g/L	
Carbohydrate Sources	Fibersol®, corn maltodextrin, isomaltulose, fructose, sucromalt, glycerine, fiber	
Fiber Content/Sources	4.1 g/237 mL	1.7 g of total dietary fiber from soy, oat, and corn fibers (Fibersol); 2.4 g of scFOS
	17.0 g/L	7.0 g of total dietary fiber from soy, oat, and corn fibers (Fibersol); 10.0 g of scFOS

Fibersol is a registered trademark of Matsutani Chemical Industry Co., Ltd.

Fat Profile of Glucerna® 1.5 Cal

Glucerna 1.5 Cal	
Fat Content	17.8 g/237 mL 75 g/L
Sources of Fat (Listed as % of total fat blend)	
High oleic safflower oil	51.3%
Canola oil	46.3%
Soy lecithin	2.4%
Fatty Acids*	
Monounsaturated Fatty Acids (MUFA)	49 g (29%)†
Polyunsaturated Fatty Acids (PUFA)	16 g (10%)†
Saturated Fatty Acids (SFA)	6 g (3%)†

* Fatty acids equal approximately 95% of total fat.

† Percent of total energy; total energy per liter is 1500 Cal.

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Protein Profile of Glucerna® 1.5 Cal

Glucerna 1.5 Cal	
Protein Content	19.6 g/237 mL 82.5 g/L
Protein Source	Sodium and calcium caseinates, Soy protein isolate
Total Cal/g Nitrogen Ratio	114:1
Nonprotein Cal/g Nitrogen Ratio	88:1

Vitamin and Mineral Profile of Glucerna® 1.5 Cal

Vitamins	8 fl oz	% RDI†	1 L	% RDI†
Total Vitamin A (IU)*	2060	41	8660	175
Vitamin D (IU)	102	26	430	110
Vitamin E (IU)	12	40	48	160
Vitamin K (mcg)	30	38	125	155
Vitamin C (mg)	78	130	325	540
Folic acid (mcg)	95	24	400	100
Thiamin (Vitamin B ¹) (mg)	0.36	24	1.5	100
Riboflavin (Vitamin B ²) (mg)	0.41	24	1.7	100
Vitamin B ⁶ (mg)	0.48	24	2.0	100
Vitamin B ¹² (mcg)	1.5	25	6.0	100
Niacin (mg)	4.8	24	20	100
Choline (mg)	131	‡	550	‡
Biotin (mcg)	75	25	300	100
Pantothenic acid (mg)	2.4	24	10	100
Minerals				
Sodium (mg)	330	‡	1380	‡
Sodium (mEq)	14.3	‡	60	‡
Potassium (mg)	600	‡	2520	‡
Potassium (mEq)	15.4	‡	64.6	‡
Chloride (mg)	380	9	1600	38
Chloride (mEq)	10.9	‡	45.7	‡
Calcium (mg)	240	19	1000	80
Calcium (mEq)	12	‡	50	‡
Phosphorus (mg)	240	19	1000	80
Phosphorus (mEq)	15.5	‡	64.5	‡
Magnesium (mg)	95	19	400	80
Magnesium (mEq)	7.8	‡	32.9	‡
Iodine (mcg)	36	19	150	80
Manganese (mg)	0.48	19	2.0	80
Copper (mcg)	0.48	19	2.0	80
Zinc (mg)	3.6	19	15	80
Iron (mg)	4.3	19	18	83
Selenium (mcg)	17	20	70	80
Chromium (mcg)	48	32	200	135
Molybdenum (mcg)	23	20	95	80
Other				
M-inositol (mg)	205	‡	845	‡
Taurine (mg)	40	‡	165	‡
Carnitine (mg)	51	‡	215	‡

* Includes 1040 IU/8 fl oz of Vitamin A activity supplied by 0.79 mg of beta-carotene.

* Includes 4370 IU/L of Vitamin A activity supplied by 3.3 mg of beta-carotene.

† For adults and children 4 or more years of age.

‡ RDI Not Established.

Ingredient Listings

Glucerna® 1.5 Cal 237 mL/8 fl oz

Water, Sodium and Calcium Caseinates, Corn Maltodextrin, High oleic Safflower Oil, Canola Oil, Isomaltulose, Fructose, Soy Protein Isolate, Sucromalt, Short-chain Fructooligosaccharides, Glycerine, Potassium Citrate, Magnesium Chloride, Oat Fiber, Calcium Phosphate, Soy Fiber, Soy Lecithin, Natural and Artificial Flavor, Sodium Citrate, Inositol, Ascorbic Acid, Choline Chloride, Magnesium Phosphate, Carnitine, Taurine, Sodium Chloride, dl-Alpha-tocopheryl Acetate, Ferrous Sulfate, Gellan Gum, Zinc Sulfate, Niacinamide, Calcium Pantothenate, Manganese Sulfate, Cupric Sulfate, Thiamine Chloride Hydrochloride, Pyridoxine Hydrochloride, Beta-Carotene, Vitamin A Palmitate, Riboflavin, Chromium Picolinate, Folic Acid, Biotin, Sodium Molybdate, Sodium Selenate, Potassium Iodide, Phylloquinone, Cyanocobalamin, and Vitamin D₃.

Contains milk and soy ingredients. Gluten- and lactose-free.

Glucerna 1.5 Cal 1 Liter Ready-To-Hang®

Water, Sodium and Calcium Caseinates, Corn Maltodextrin, High oleic Safflower Oil, Canola Oil, Isomaltulose, Fructose, Soy Protein Isolate, Sucromalt, Short-chain Fructooligosaccharides, Glycerine, Potassium Citrate, Magnesium Chloride, Oat Fiber, Calcium Phosphate, Soy Fiber, Soy Lecithin, Sodium Citrate, Inositol, Ascorbic Acid, Choline Chloride, Magnesium Phosphate, Carnitine, Taurine, Sodium Chloride, dl-Alpha-tocopheryl Acetate, Ferrous Sulfate, Gellan Gum, Zinc Sulfate, Niacinamide, Calcium Pantothenate, Manganese Sulfate, Cupric Sulfate, Thiamine Chloride Hydrochloride, Pyridoxine Hydrochloride, Beta-Carotene, Vitamin A Palmitate, Riboflavin, Chromium Picolinate, Folic Acid, Biotin, Sodium Molybdate, Sodium Selenate, Potassium Iodide, Phylloquinone, Cyanocobalamin, and Vitamin D₃.

Contains milk and soy ingredients. Gluten- and lactose-free.

1.0

1.0 References

1. Data on File. Clinical Study BK06A. Comparison of Nutritional Products for People with Type 2 Diabetes. Abbott Nutrition, Columbus, Ohio, 2008.
2. Data on File. Clinical Study BK06B. Sole Source Bolus Tube Feeding Simulation Pilot Study Using Continuous Glucose Monitoring. Abbott Nutrition, Columbus, Ohio, 2008.
3. Kris-Etherton PM, Harris WS, Appel LJ: Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106:2747-2757.
4. West SG, Hecker KD, Mustad VA, et al: Acute effects of monounsaturated fatty acids with and without omega-3 fatty acids on vascular reactivity in individuals with type 2 diabetes. *Diabetologia* 2005;48:113-122.
5. Buse JB, et al: Primary prevention of cardiovascular disease in people with diabetes mellitus: a scientific statement from the American Heart Association. *Circulation* 2007;115:114-126.
6. Broadhurst CL, Domenico P: Clinical studies on chromium picolinate supplementation in diabetes mellitus—a review. *Diabetes Technol Ther* 2006;8:677-687.

Ingredient Descriptions

Carbohydrates

Hyperglycemia is implicated in both short- and long-term complications of diabetes, and thus, managing postprandial plasma glucose (PPG) is critically important to individuals with diabetes.^{1,2} Postprandial glycemic response can be improved by consuming carbohydrates that are digested relatively slowly, thus releasing glucose over a longer length of the gastrointestinal tract than simpler forms of carbohydrates (Figure 2.1).

Including slowly digested carbohydrates in the diet permits individuals with diabetes to absorb glucose more evenly than when simple carbohydrates are consumed or when the carbohydrate source is rapidly digested and absorbed. The altered linkages of the carbohydrate structure lead to this slowed digestion. The slowly digested carbohydrate sources in Glucerna® 1.5 Cal include Fibersol®, sucromalt, and isomaltulose. These ingredients are described in detail in this section.

Figure 2.1 Points of absorption of rapidly and slowly digested carbohydrate in the gastrointestinal tract

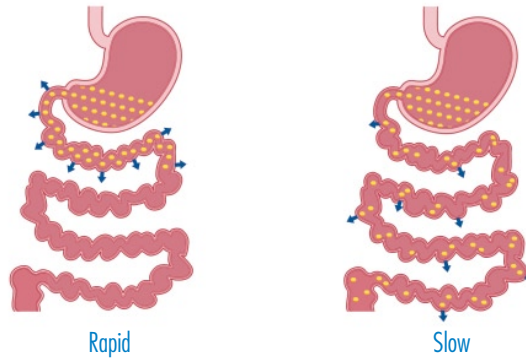
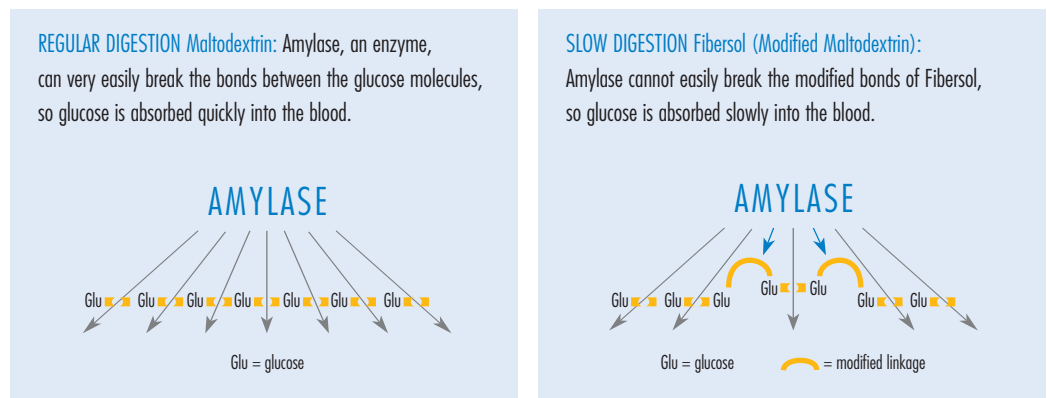


Diagram taken from: Jenkins DJ, Taylor RH, Wolever TM: The diabetic diet, dietary carbohydrate and differences in digestibility. *Diabetologia* 1982;23:477-484.

Fibersol

Fibersol is a modified maltodextrin with glucose linkages that are more resistant to the digestive enzyme amylase than are the glucose linkages of standard maltodextrin (Figure 2.2).³ Because glucose from Fibersol is slowly digested, a portion of Fibersol proceeds to the colon, where it is fermented to short-chain fatty acids, similar to digestion of other soluble fibers. This slowed absorption gives Fibersol a lower glycemic index. Glucerna 1.5 Cal contains 3 g/L.

Figure 2.2 The modified maltodextrin of Fibersol slows its digestion, thus blunting glycemic response



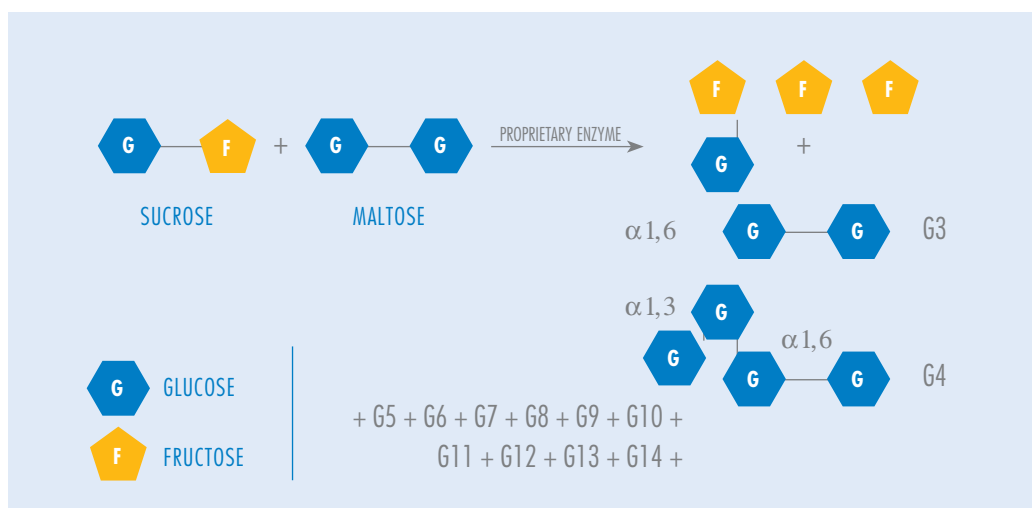
Sucromalt

Origin and Molecular Structure

Sucromalt is a slowly digested carbohydrate that contributes to a lower blood glucose response. Sucromalt is a fully digestible, 4 Cal/g, low-glycemic carbohydrate that provides sweetness and body in one ingredient.

Figure 2.3 below depicts the production of sucromalt. In this process, sucrose (glucose + fructose) and maltose (glucose + glucose) are combined. Sucrose is derived from either sugar cane or sugar beets. Maltose is derived from grains. A proprietary enzyme is added to cleave off fructose and to rearrange the glucose molecules. The glucose molecules are then linked with α -1,3 and α -1,6 linkages. These altered linkages are key to the lower glycemic response because it takes the body more time to identify and break the bonds into individual glucose molecules. As a result, there is less of a rise in blood glucose and eventually, the sucromalt is completely digested. Sucromalt is GRAS (Generally Recognized as Safe) for the general population. Glucerna 1.5 Cal contains 11 g/L.

Figure 2.3 Sucromalt production process



Blood Glucose Response

Glycemic Index Determination of Sucromalt

To date, six studies have been conducted to determine the glycemic index (GI) of sucromalt. The first two studies were conducted at NutriScience Limited (Maastricht University Holding, The Netherlands). The other four studies were conducted at Glycaemic Index Testing, Inc. (Toronto, Ontario).

Overnight-fasted subjects without diabetes were tested on two different occasions, once after ingesting sucromalt and once after ingesting glucose. Blood samples were obtained at baseline, 15, 30, 45, 60, 90, and 120 minutes post-ingestion. Serum levels of glucose were measured and the incremental areas under the response were calculated (any area below baseline was ignored) and used to determine glycemic index. Additional information on the general methods can be found in Wolever TM, et al: The glycemic index: methodology and clinical implications. *AJCN* 1991;54:846-854.

The mean GI of sucromalt from the six different studies was calculated in order to arrive at a value for the GI of sucromalt. The GI of sucromalt is 53.3 ± 4.8 , which is classified as low.⁴

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Isomaltulose

Isomaltulose is a carbohydrate derived from sugar beets (sucrose). Like sucrose, it is fully available to the body but slowly released, thus resulting in a much slower, lower, and longer-lasting blood glucose response compared with sucrose. In other words, isomaltulose provides glucose in a more balanced way. Isomaltulose is GRAS by the FDA. Glucerna® 1.5 Cal contains 29 g/L.

Origin and Molecular Structure

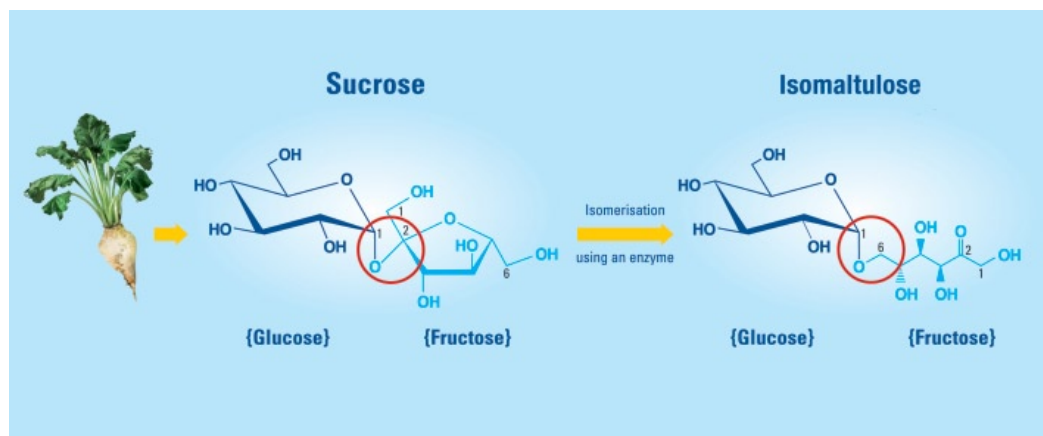
This carbohydrate naturally occurs in foods such as honey and sugar cane juice; however, the amounts are too small to be extracted. Therefore, an enzymatic process was developed by which isomaltulose is made from sucrose from sugar beets. Like sucrose, isomaltulose is a disaccharide carbohydrate consisting of the monosaccharides glucose and fructose. The difference from sucrose lies in the binding between these two monosaccharides, which is an α -1,6 linkage (compared to the α -1,2 linkage in sucrose) and therefore more difficult for gastrointestinal enzymes to split. Further details are summarized in Table 1 and the structure is shown in Figure 2.4.

Table 1: Chemical Description of Isomaltulose

GENERAL OR USUAL NAME:	Isomaltulose
TRADE NAME:	Palatinose™
CHEMICAL CLASSIFICATION:	Carbohydrate (Disaccharide)
TOTAL MOLECULAR FORMULA:	$C_{12}H_{22}O_{11} \times H_2O$

Palatinose™ is not a registered trademark of Abbott Laboratories Inc.

Figure 2.4 Molecular structure of isomaltulose



Physiological Properties

As a result of the stronger bond between the two monosaccharides, isomaltulose distinctly differs in its nutritional and physiological properties from those of sucrose^{5,6}:

Digestion and absorption. Isomaltulose is slowly hydrolyzed in the small intestine, about 4 to 5 times more slowly than sucrose, as demonstrated by enzyme kinetic studies.⁷ The same enzyme system as for other carbohydrates is used to hydrolyze isomaltulose (sucrase-isomaltase complex). Absorption does not only take place in the upper parts of the small intestine (as is the case for quickly absorbed sugars), but along the entire small intestine. This means that isomaltulose still supplies glucose (thus fuel or energy) for the body at a time when the digestion and absorption of sucrose is already completed.⁶

It has been demonstrated, as well, that the overall digestion of isomaltulose is essentially completed in the small intestine, and no significant amounts of isomaltulose reach the large intestine. Thus, isomaltulose provides the same amount of calories as all digestible carbohydrates (sugars and starches: 4 Cal/g) and is equally well tolerated.

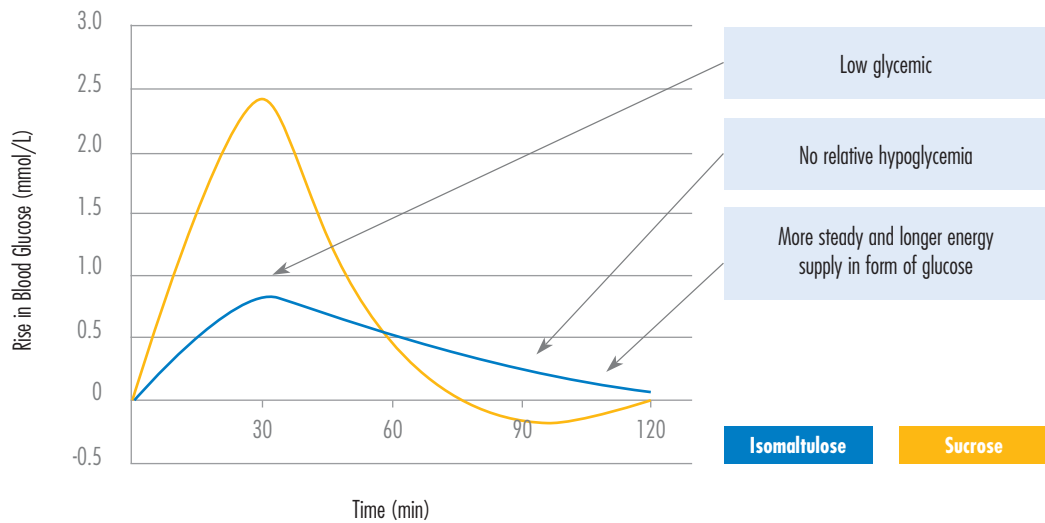
Blood glucose response and prolonged energy release. The slow, but complete, hydrolysis and absorption of isomaltulose is reflected in its characteristic blood glucose response with a slow, low, and sustained rise in blood glucose levels (Figure 2.5) and a correspondingly low insulin demand. The Glycemic Index of isomaltulose has been determined at Sydney University's Glycemic Research Service according to internationally recognized standard methodology, which yielded a GI of 32.⁸ In comparison, a GI of 68 has been determined for sucrose, and glucose has a GI of 100.

Insulin response and fat oxidation. The hormone insulin plays a key role in the regulation of metabolism. Among others, it down-regulates high blood glucose levels by "opening the door" for glucose uptake into cells. At the same time, it promotes the utilization of carbohydrates and the storage of fat and inhibits fat burning. High levels of insulin over a longer period of time are thought to contribute to obesity and the development of diabetes. Isomaltulose with its lower effect on blood glucose levels and subsequent lower insulin release thus shows increased fat oxidation (demonstrated by measurements of the respiratory quotient).^{9,11} A study with metabolic syndrome subjects and studies with active sportsmen showed an increase in fat oxidation of as much as 28%.^{10,11}

Effect on long-term parameters of blood glucose control. A human intervention study over 12 weeks suggests that the regular intake of a liquid formula with isomaltulose by persons with impaired glucose tolerance would have beneficial effects on metabolic-syndrome-related parameters: In this long-term study with persons with impaired glucose tolerance, the intake of an isomaltulose-based formula as part of breakfast was associated with improvements in 2h plasma glucose after an oral glucose tolerance test (OGTT) and serum-free fatty acid levels; moreover, in viscerally obese persons, the visceral fat accumulation was decreased ($P < .05$).¹²

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Figure 2.5 Characteristics of the glycemic response of isomaltulose in comparison to sucrose



Fructose

Fructose is a simple sugar, (4 Cal/g), that occurs naturally in fruits and honey. Glucerna® 1.5 Cal contains 25 g/L of fructose. The fructose in Glucerna 1.5 Cal facilitates hepatic glucose clearance and thus helps blunt a postprandial blood glucose rise.¹³

When fructose is metabolized in the liver, glucokinase is activated, which allows more glucose to enter the liver from the blood, thus lowering blood glucose levels (Figure 2.6). Normally, glucose is taken up by the liver and converted to glucose-6-phosphate by the enzyme glucokinase; glucose-6-phosphate is further metabolized or stored in the liver as glycogen. Glucose-6-phosphate is isomerized to fructose-6-phosphate, which in turn provides normal feedback deactivation of glucokinase.

In people with type 2 diabetes, glucokinase activity is inhibited; glucose uptake by the liver is reduced, and blood glucose levels are increased.¹⁴ However, when dietary fructose is consumed, liver uptake of fructose results in formation of fructose-1-phosphate, a metabolite that reduces the inhibition of glucokinase caused by fructose-6-phosphate (Figure 2.7). Thus, in the presence of dietary fructose, glucokinase activity can be at least partly restored to facilitate further uptake of glucose from the blood.

Glycerine

Glycerine (sometimes called glycerol) is a low-glycemic carbohydrate that functions as a sweetener. Glycerine is classified as a sugar alcohol. However, unlike other sugar alcohols such as maltitol and sorbitol, which are only partially metabolized and provide 2 Cal/g, glycerine is completely metabolized like a carbohydrate and provides 4.3 Cal/g. This difference in metabolism is key to minimizing the risk for GI side effects. The GI tolerance of sugar alcohols depends on how they are digested. The more completely a sugar alcohol is digested (like glycerine), the less potential there is for GI side effects.

Glycerine is listed as GRAS by the FDA and has an upper threshold of 125 g/day. Glycerine is listed with the ingredients on Glucerna products. The amount of glycerine in Glucerna is included in the total carbohydrate grams claimed on the product label. Glucerna 1.5 Cal contains 12 g/L.

Figure 2.6 Glucose metabolism without dietary fructose

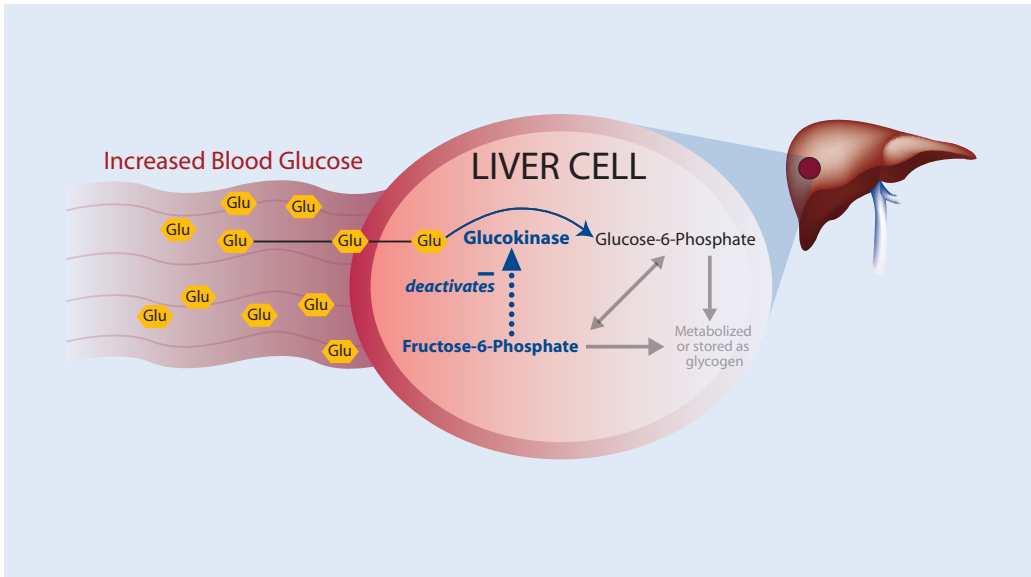
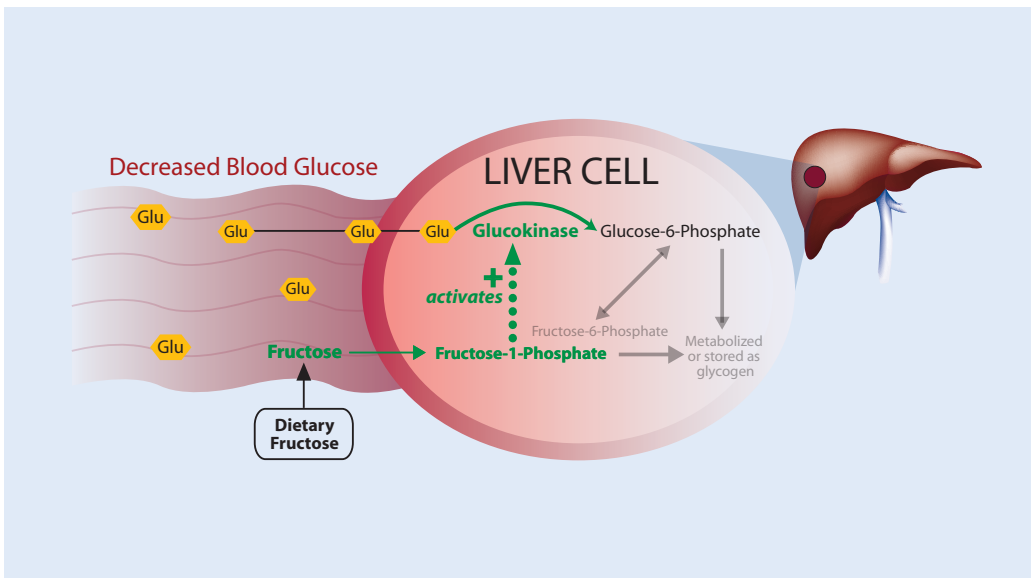


Figure 2.7 Glucose metabolism with dietary fructose



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Role of Fat Intake and Diabetes

Patients with diabetes are at an increased risk for dyslipidemia (abnormal lipid levels, eg, high triglycerides and LDL cholesterol and low HDL cholesterol levels) and macro- and micro-vascular disease. Type 2 diabetes and chronic hyperglycemia increases the risk of cardiovascular disease (CVD) mortality between 40% and 200%.¹⁵ Individuals with diabetes have a threefold to fourfold increase in CVD risk compared with the general population.¹⁶ It is known that dietary fat composition plays an important role in the prevention and treatment of CVD and influences glucose metabolism. Therefore, the composition of the fat blend in nutritional products designed for people with diabetes is key to providing optimal metabolic control in patients with diabetes to reduce the risk for CVD or slow the progression of diabetes- and CVD-related complications.

Fat Profile of Glucerna® 1.5 Cal

Glucerna 1.5 Cal	
Fat Content	17.8 g/237 mL 75 g/L
Sources of Fat (Listed as % of total fat blend)	
High oleic safflower oil	51.3%
Canola oil	46.3%
Soy lecithin	2.4%
Fatty Acids*	
Monounsaturated Fatty Acids (MUFA)	49 g (29%) [†]
Polyunsaturated Fatty Acids (PUFA)	16 g (10%) [†]
Saturated Fatty Acids (SFA)	6 g (3%) [†]
per 1500 kcal	
Total Fat, % of energy	45
Saturated, %	3
Trans-Fatty Acids	0
MUFA %	29
PUFA, n6, %	8
LA, g	13
PUFA, n3, %	2
ALA, g	3
LA/ALA ratio	5.0:1
Total n6:n3 ratio	5.0:1

* Fatty acids equal approximately 95% of total fat.

† Percent of total energy in parentheses; total energy per liter is 1500 Cal.

Overview of the Fat Blend in Glucerna® 1.5 Cal

The fat blend in Glucerna 1.5 Cal was developed with the goal of facilitating metabolic control in patients with diabetes, specifically, improved glycemic and lipidemic profiles.

Saturated Fatty Acids

Saturated fatty acids (SFAs) are composed of carbons with no double bonds between adjacent carbon molecules (-C-C-). Glucerna 1.5 Cal is low in SFAs by providing just 3% of the total energy. SFAs are naturally occurring in the product's high oleic safflower oil and canola oil. The American Diabetes Association (ADA) and American Heart Association (AHA) recommend that less than 7% of calories should come from SFAs.^{17,18}

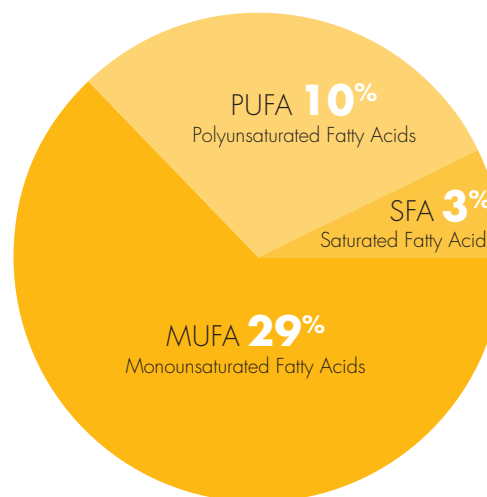
Monounsaturated Fatty Acids

Monounsaturated fatty acids (MUFAs) are fatty acids made up of a carbon chain of varying lengths that contains a single double bond (-C=C-). Glucerna 1.5 Cal is high in MUFAs, which contribute 29% of the total calories. The MUFAs in Glucerna 1.5 Cal are provided from canola oil and high oleic safflower oil and make up 65% of the total fat grams for improved glycemic control and blood lipid profiles.¹⁹⁻²¹

Dietary intakes low in SFAs and rich in MUFAs favorably influence blood lipid levels, specifically plasma triglycerides. Early clinical studies that examined the effect of MUFAs on lipid parameters have shown that a high MUFA intake lowers total cholesterol and triglycerides and can raise HDL cholesterol and, therefore, favorably affect CVD risk in healthy individuals.^{22,23} Significant reductions were demonstrated in plasma triglyceride levels in subjects with type 2 diabetes.²⁴ A meta-analysis of ten, long-term, controlled clinical studies demonstrated that high MUFA intakes (22-32% of the total energy from MUFAs and 37-50% of the total calories from fat) reduced fasting plasma triglycerides and VLDL cholesterol concentrations by 19% and 22%, respectively, compared with lower fat intakes (20-32% of the total calories from fat) in patients with type 2 diabetes.²⁰

In addition to lowering triglycerides in patients with diabetes, a high MUFA intake can improve glycemic control. Consuming a high MUFA intake can lower fasting plasma glucose levels, as well as postprandial and mean 24-h plasma glucose concentrations compared with a high-carbohydrate, low-fat intake.²⁰ Postprandial hyperglycemia is associated with outcomes such as increased risks for cardiovascular disease and thrombosis, and dyslipidemia. A high MUFA intake may help minimize postprandial hyperglycemia and, in turn, reduce the risk for CVD and thrombosis (blood clot formation).^{22,23}

Fat Blend Distribution*



*Fatty acids equal approx. 95% of total fat.

2.0

n-3 (EPA + DHA and ALA) and n-6 Polyunsaturated Fatty Acids

Polyunsaturated fatty acids are fatty acids made up of a chain of carbon atoms with more than one double bond between adjacent carbons. The AHA recommends 1.5 to 3 g per day of plant-based alpha-linolenic omega-3 fatty acids (ALA).²⁵ Glucerna® 1.5 Cal provides approximately 3 g ALA per 1500 Calories.

The two subgroups of n-3 PUFA are ALA, found in plant sources such as canola and walnut oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are found in oils from fatty fish. Linoleic acid (LA) is an n-6 fatty acid found in many types of vegetable oils. ALA and LA are essential fatty acids, meaning that because the body is unable to produce them, they must be consumed in the diet. In the body, LA is elongated to arachidonic acid (AA), a metabolic precursor to eicosanoids, which are signaling compounds that can affect inflammation, platelet aggregation (involved in formation of blood clots), and vascular blood flow.

The eicosanoids produced from LA have greater proinflammatory and prothrombotic (blood clot formation) activity than those made from ALA or EPA. Increasing the intake of n-3 PUFA can partially substitute n-6 PUFA to interfere with the production of eicosanoids from AA and favor the production of weaker eicosanoids made from n-3 PUFA. The benefits of n-3 fatty acids are reduced inflammation, vasoconstriction, and platelet aggregation.

n-6:n-3 Ratio

The n-6:n-3 fatty acid ratio has received a lot of attention lately. Historically, n-3 fatty acids have been part of our diet since the dawn of humankind. The ratio of n-6 to n-3 fatty acids in the diet of humans back then has been estimated to be 1:1.²⁶ Today, that ratio has risen to 10:1 in the United States due to an increased use of n-6-rich vegetable oils along with a reduced intake of n-3 fatty-acid-rich foods. The n-6:n-3 ratio reflects the conversion efficiency of ALA to EPA + DHA in the body. The higher the LA content of the diet, the less the rise in EPA + DHA levels; the lower the ratio, the greater the rise in EPA + DHA levels. The Institute of Medicine has recommended a range of this ratio between 5:1 and 10:1.²⁷ The LA: ALA ratio of Glucerna 1.5 Cal is 5:1.

Reduced CVD risk and related complications, including improved lipid profile, reduced clot formations, and improved circulation, have been demonstrated in people with and without diabetes following diets rich in n-3 fatty acids.^{16,25} The main impact of n-3 fatty acids on improving dyslipidemia is a reduction in plasma triglycerides by 20-50% in healthy individuals, and more in patients with hypertriglyceridemia, including patients with diabetes.^{28,29} A second impact of n-3 fatty acids is on reducing LDL oxidation, a key factor in the early stages of atherosclerosis.³⁰ These fatty acids have also been shown to decrease platelet activity and reduce platelet aggregation and the production of thromboxane A₂, a potent inducer of platelet aggregation and vasoconstriction.¹⁶ In addition to reducing triglycerides and platelet aggregation, n-3 fatty acids in combination with MUFAs have been clinically shown to improve circulation in people with diabetes.³¹

Chromium Picolinate

Mechanism of Action

Chromium is an essential trace mineral required by the body for normal carbohydrate metabolism. Chromium is considered essential because it is not made in the body and a certain level is needed in the diet to maintain health. Dietary form of chromium, also known as chromium III, is found in foods and supplements. Chromium enhances the biological action of insulin, the hormone that is critical for the normal regulation of carbohydrate, lipid, and protein metabolism. Chromium helps insulin work more efficiently to allow blood sugar to move from the blood into the cells.³² The effectiveness of insulin is greater in the presence of chromium than in its absence.

The most bioavailable form of chromium is called chromium picolinate (CrPic).^{33,34} Chromium picolinate is the most efficacious form to use for chromium supplementation. During digestion, carbohydrates are normally broken down to glucose, the body's main source of energy. Glucose is then released into the bloodstream. A rise in blood glucose causes the pancreas to release insulin. Healthy insulin function requires adequate chromium levels. Chromium is also needed for normal insulin function, and insulin is the key metabolic hormone that influences carbohydrate metabolism.

Chromium helps insulin bind to the insulin receptors that line cell membranes. These bonds stimulate glucose transporters, which move to the surface of the cell and allow glucose to enter the cell to be converted into energy.

Daily chromium levels are often compromised, due to consumption of highly processed foods and generally suboptimal nutrition, especially with age. The American diet contains small to moderate amounts of chromium, and a high intake of sugars is correlated to an increase in urinary excretion of chromium and decreased chromium bioavailability.^{31,33} Without supplementation, it is difficult to get enough chromium, and inadequate chromium levels contribute to decreased stimulation of glucose transporters. Therefore, this can be a factor in glucose not entering cells as readily and rising to unhealthy levels in the bloodstream.

The RDI for chromium is 120 mcg and there is no established Upper Limit.

2.0

Clinical Studies

Chromium picolinate was added to Glucerna® 1.5 Cal due to the body of literature supporting the effects of chromium picolinate in people with diabetes.

Amounts of 200-1000 mcg of chromium/day as chromium picolinate have been found to improve blood sugar control in people with diabetes. In 2006, Broadhurst and Domenico conducted a review of 15 studies with results supporting the safety and therapeutic value of CrPic for the management of hyperglycemia in subjects with diabetes.³⁴ The chart on page 21 outlines these 15 studies, and Figure 2.9 outlines studies showing a difference in A1C.

Figure 2.9 The mean difference in A1C from baseline for the chromium picolinate arm in each clinical study (nine studies total) is shown

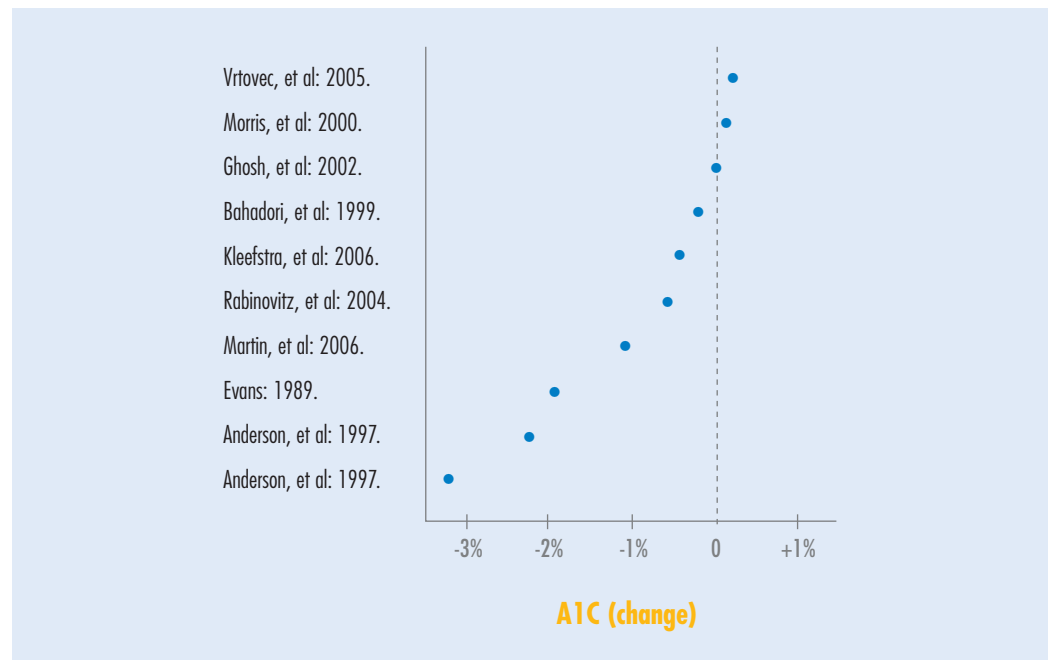


Diagram taken from: Broadhurst CL and Domenico P: Clinical studies on chromium picolinate supplementation in diabetes mellitus—a review. *Diabetes Technol Ther* 2006;8:677-687.³⁴

The chart below outlines studies that have investigated the role of chromium picolinate^{33,35-48}

All results listed were statistically significant unless noted otherwise.

Primary Author	Year	Study Design	Subject Char.	N	Amount per day (mcg)	Study Duration	Results	Concomitant Medications
Ravina	1995	Open label	Types 1 and 2	162	200	3 months	↓ fasting blood glucose levels and insulin ↑ sensitivity	Insulin sulfonylurea or metformin
Anderson	1997	RCT	Type 2	105	200/1000	4 months	↓ fasting blood glucose, postprandial glucose, insulin, and A1C	Glibendamide or glipizide
Lee	1994	RCT	Type 2	28	200	2 months	↓ triglycerides	Insulin, oral meds, diet
Evans	1989	RCT	Type 2	6	200	1.5 months	↓ fasting blood glucose and A1C	Hypoglycemic meds
Jovanovic–Peterson	1999	RCT	Gestational diabetes	20	300-800	2 months	↓ fasting and postprandial blood glucose, insulin ↓ A1C	8 women on insulin
Rabinovitz	2004	RCT	Type 2	39	400	3 weeks	↓ fasting blood glucose ↓ A1C	Insulin/oral hypoglycemic meds
Ghosh	2002	RCT	Type 2	43	400	3 months	↓ fasting and postprandial blood glucose, insulin ↓ A1C	Hypoglycemic meds
Morris	2000	Open label	Type 2	5	400	3 months	↑ insulin sensitivity ↓ A1C (not significant)	None
Feng	2002	RCT	Type 2	136	500	3 months	↓ fasting and 2-hour glucose	Insulin
Cheng	1999	Open label	Type 2	833	500	9 months	↓ fasting blood glucose	Hypoglycemic meds
Kleefstra	2006	RCT	Type 2	29	500/1000	6 months	↓ A1C (not significant)	Oral insulin/oral hypoglycemic meds
Martin	2006	RCT	Type 2	16	1000	6 months	↑ insulin sensitivity ↓ A1C	Sulfonylurea
Vrtovec	2005	RCT	Type 2	56	1000	3 weeks-9 months	↓ fasting insulin levels ↓ A1C (not significant)	ACE inhibitors, A2 antagonists, loop diuretics, statins, aspirin
Bahadori	1999	Open label	Type 2	16	1000	4 months	↑ fasting insulin	Sulfonylurea and metformin
Cefalu	1999	RCT	Insulin resistance	29	1000	8 months	↑ insulin sensitivity	None

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Conditionally Essential Nutrients

Taurine

Taurine is a conditionally essential amino acid made from cysteine and methionine. It is an abundant free amino acid in the body but is not incorporated into body proteins. It possesses antioxidant properties and is important in bile-acid conjugation, cell-volume regulation, neural and retinal function, platelet aggregation, membrane stabilization, calcium homeostasis, and neuromodulation.

Taurine is present in low but adequate levels in the diet. Supplemental taurine may be required in patients being fed a defined formula diet when fed as a sole source of nutrition for prolonged periods of time. The mean daily intake is 58 mg but varies widely (17-1000 mg/d).

Low urinary and plasma taurine levels are found in adults in catabolic states (eg, cancer, chemo/radiation therapies, inflammatory processes, trauma, sepsis, burns, etc.); plasma levels are elevated in renal failure.

No studies have identified any beneficial effects of taurine supplementation for adult patients. Standard enteral formulas contain 0-211 mg taurine/1000 Cal.⁴⁹ Glucerna® 1.5 Cal contains 40 mg/8 fl oz and 165 mg/L.

Carnitine

Carnitine and taurine are present in low but adequate levels in a normal diet. Supplementation with these conditionally essential nutrients may be required under some circumstances, especially if a defined formula diet is consumed for prolonged periods.

Carnitine deficiency has been observed in patients with sepsis and trauma, during long-term total parenteral nutrition, and with long-term enteral nutritional support. Evidence of taurine depletion has been demonstrated after surgical trauma, during prolonged total parenteral nutrition, and in healthy adults fed taurine-free enteral diets.²³⁻²⁵ Glucerna products are fortified with carnitine and taurine.

Carnitine is an amine synthesized in the body from lysine and S-adenosylmethionine and is found in diets containing animal products. The typical Western diet provides 100-300 mg carnitine/day. Carnitine functions to transfer long-chain fatty acids into mitochondria for β -oxidation. It also transports other acyl groups and coenzyme A in many biochemical/metabolic reactions.

Carnitine deficiency can be caused by an inadequate intake, accelerated losses (eg, as in renal failure), and reduced synthesis (eg, in hepatic or renal failure). Carnitine needs are increased during critical illness or hemodialysis. The optimal level of carnitine in these states has not been identified, but many enteral products provide between 0-150 mg carnitine/1000 Cal.⁶ Glucerna 1.5 Cal contains 51 mg/8 fl oz and 215 mg/L.

M-inositol (myoinositol, inositol)

M-inositol, the most abundant stereoisomer of inositol, is an intracellular component of most plant and animal cells. M-inositol is the major nutritionally active form of inositol. M-inositol functions in nerve conduction by modulating the enzyme sodium-potassium-ATPase. Humans can make myoinositol from glucose. Dietary intake can influence the levels of circulation and bound m-inositol in the body, and intake from an average diet is approximately 1 gram daily.⁵⁰ The major dietary sources include cereals and legumes.⁵¹

Because glucose and m-inositol are similar in structure, the two substances compete for transport into tissues, resulting in m-inositol depletion in peripheral nerves and renal glomeruli. Additionally, people with diabetes have been found to lose excessive amounts of m-inositol in their urine.⁵² Deficiency has been proposed to play a role in the pathogenesis of diabetic neuropathy.⁵³

More specifically, in the nerve, glucose is metabolized through the polyol pathway to sorbitol via the enzyme aldose reductase (AR). There is a strong relationship between AR levels and neuropathy. Sorbitol can cause osmotic stress and can lower nerve myoinositol and taurine levels, which decreases sodium-potassium-ATPase.⁵⁴ Furthermore, the hyperglycemia of diabetes leads to an increased flux through the polyol pathway, resulting in elevated levels of sorbitol. Glucerna® 1.5 Cal contains m-inositol at 205 mg/8 fl oz and 845 mg/L.

Other Characteristics of Glucerna 1.5 Cal

Glucerna 1.5 Cal		
Osmolality	875 mOsm/kg water	
Osmolarity	663 mOsm/L	
Viscosity	Nectar-like (room temperature), nectar-like (chilled) Not Low-Residue	
Minimum Tube Size for Gravity/ Pump Feeding, FR	12/10	
Exchanges* (per 8 fl oz)	2 starches, 3 medium-fat meats	
Carbohydrate Choices	2	
Renal Solute Load	643 mOsm/L Renal solute load (RSL) represents the solutes excreted per liter of product consumed. The major determinants of renal solute load are dietary protein and electrolytes. Each milliequivalent (mEq) of sodium, potassium, and chloride contributes approximately 1 mOsm to the renal solute load; in adults, each gram of protein contributes approximately 5.7 mOsm.	
Water	8 fl oz: 180 g/mL/cc, 1 L: 759 g/mL/cc	
	Electrolyte Content (per Liter)	Contribution to RSL (mOsm/L)
Sodium	60 mEq	60
Potassium	64.6 mEq	64.7
Chloride	45.7 mEq	45.7
Protein Content	82.5 g	473
Total RSL		643

*Calculated using Exchange lists for Diabetes, American Diabetes Assn, American Diabetic Assn, 2008.

2.0

Osmolality

Background

Osmolality is a measure of the concentration of particles/solutes in solution.⁴⁹ Osmolality is defined as milliosmoles per kilogram of solvent (ie, mOsm/kg). Osmolality is the appropriate term for describing solutes in enteral formulas. The major contributors to osmolality in enteral formulas are electrolytes, minerals, and organic compounds, such as protein and carbohydrate. The higher the caloric density, the less water in the formula, therefore the higher the osmolality. Smaller molecules contribute to osmolality, so products with hydrolyzed macronutrients tend to have the highest osmolality. For example, the carbohydrates in Glucerna® 1.5 Cal contribute to the higher osmolality. Enteral products available have osmolalities ranging from 270 mOsm/kg H₂O to about 875 mOsm/kg H₂O, depending on the concentration of water-soluble components.

Clinical Application

Osmolality was once considered to be a major factor in gastrointestinal intolerance to enteral feeding.⁵⁵ An isotonic formula has the same osmolality of blood (~300 mOsm/kg), which leads to the assumption that less water will be drawn from the body into the gut lumen and not cause diarrhea. High-osmolality formulas are sometimes diluted in the belief that the GI tract needs to reacclimate to luminal nutrients after a period of receiving nothing by mouth. This practice is not supported to date and can lead to bacterial contamination through manipulation of the formula as well as inadequate nutrient intake. However, in some patients, a period of adaptation (slow rate of delivery) of an enteral formula may be considered to reacclimate the GI tract. When chyme (stomach content) is released from the stomach, bile salts, pancreatic enzymes, bicarbonate, and water are secreted to increase the pH and to make the solution isoosmolar. This function, referred to as “autoisotonicity,” is a function of the small bowel.

Although osmolality has been shown to slow gastric emptying in various subject populations, clinically, it is insignificant.⁵⁶ For comparison and perspective purposes, Table 2 lists the osmolalities of common foods/liquids used in the hospital setting. Consider that a clear liquid diet, with an osmolality of greater than 1200 mOsm/kg, is the first post-op diet initiated when the stomach is first reacclimating. Other examples include sherbet, with an osmolality of approximately 1225 mOsm/kg, and juices, which are 990 mOsm/kg (see Table 2). Patients are rarely intolerant to these fluids. Furthermore, many medications have an osmolality higher than any food or beverage, but the volume of these medications is generally small. For example, metoclopramide, a commonly used agent for gut motility, has an osmolality of 8350 mOsm/kg (see Table 3 for additional values of common medications).

Table 2: Osmolality of Select Liquids Frequently Used in the Hospital Setting

Typical Liquids	mOsm/kg
Milk	275
Gelatin	535
Broth	445
Sodas	695
Ice Pops	720
Juices	990
Ice Cream	1150
Sherbet	1225

Table 3: Osmolality of Common Medications⁵⁷

Drug	Common Single Dosage (mL)	Osmolality (mOsm/kg)
Acetaminophen elixir	15	5400
Diphenoxylate suspension	10-20	8800
Chloral hydrate syrup	2.5-10	4400
Furosemide (oral liquid)	2-8	3938
Metoclopramide liquid	5-15	8350
Cimetidine liquid	5-10	4035

Zarling, et al, fed one of two hypertonic formulas (650 and 690 mOsm/kg H₂O) over 8 hours for four consecutive days.⁵⁷ The aims of this study were to assess the effect of flow rate, osmolality, and composition of tube feedings on clinical tolerance. Ten normal subjects received full-strength enteral nutrition at 50 mL/hr on day 1, 100 mL/hr on day 2, and 150 mL/hr on day 3. The subjects were given half-strength formula at 100 mL/hr on day 4. Another ten normal subjects received the same regimen but in the reverse order, starting at 150 mL/hr and ending with the same half-strength formula at 100 mL/hr. There was no significant difference in tolerance found between subjects or approaches. Even at the maximal flow rate and osmolality, the result demonstrated that both types of enteral formulas were well tolerated as assessed by frequency of abdominal pain, bloating, passage of rectal gas, and stooling.

More specifically, two studies have shown that hypertonic formulas (ranging from 503 to 620 mOsm/kg H₂O) infused either into the stomach or at the ligament of Treitz achieve isotonicity or near isotonicity by the time they reached the ligament of Treitz⁵⁸ or 35 cm farther down into the jejunum.⁵⁹ [note: The ligament of Treitz marks the point where the duodenum and jejunum meet.] Rees, et al, studied the delivery of undiluted, hypertonic (630 mOsm/kg H₂O) elemental enteral nutrition by continuous nasogastric infusion (87 mL/hr) over 24 hours in twelve patients with impaired gastrointestinal function due to inflammatory bowel disease and short-bowel syndrome.⁶⁰ All received standard medical treatment in addition to enteral nutrition. The delivery of nutrition was well tolerated, and a slower rate of administration was not necessary, based on patients' symptoms.

Table 4: Osmolality of Some Abbott Nutrition Tube-Feeding Products

Formula	mOsm/kg H ₂ O
Jevity [®] 1.2	450
Jevity [®] 1.5	525
Nepro [®]	600
TwoCal [®] HN	725
Vital [®] HN	500
Glucerna [®]	355
Glucerna [®] Select	470
Glucerna [®] 1.2 Cal	720
Glucerna [®] 1.5 Cal	875
Pulmocare [®]	475

Conclusion

Osmolality is just one minor characteristic of enteral formulas. Tolerance to tube-feeding delivery is dependent on a variety of other factors, including, but not limited to, the following which must be taken into consideration: overall clinical status of the patient; gastrointestinal function; mode of delivery (tube placement/location); appropriate feeding regimen for patient needs (continuous, nocturnal, bolus, intermittent); infusion rate; formula composition, concurrent medications; and proper, safe delivery of product to avoid contamination. Abbott Laboratories does have a system in place to monitor the safety of all products on the market to collect information related to gastrointestinal issues.

“Hypertonic enteral formulations have frequently been blamed for formula intolerance (eg, diarrhea). However, the osmolality of an enteral formulation has little to do with formula tolerance. Formula tolerance or diarrhea is most often related to severity of illness, comorbid conditions, enteric pathogens, or the concomitant use of medications administered through the enteral access device. In addition, the osmolality of several items on a clear liquid diet and many medications given via the enteral route is much higher than the osmolality of enteral formulations.”⁶¹

–The A.S.P.E.N Nutrition Support Core Curriculum. 2007, p. 212

“The success of enteral tube feeding very much depends on the engagement of the person who delivers the nutrition.”⁶²

–Stephen McClave, MD

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2.0 References

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Clinical Management of Diabetes

Glycemic Control as It Relates to In-Hospital Management

Diabetes is the fourth most-common comorbid condition complicating all hospital discharges. In 1997, diabetes was present in 9.5% of all hospital discharges and 29% of patients undergoing cardiac surgery. Diabetes causes a twofold to fourfold increase in rates of hospitalizations and increases hospital lengths of stay by 1 to 3 days, depending on the admitting diagnosis. Studies have clearly shown that hyperglycemia in hospitalized patients complicates numerous illnesses and is an independent risk factor for adverse outcomes. More intense effort at managing glycemic control may improve short-, intermediate-, and long-term outcomes in patients with diabetes or impaired glucose tolerance in the hospital for therapeutic procedures, as well as for treatment of the complications of this disease.¹

Fortunately, the risk of developing chronic microvascular and neuropathic complications, as well as acute complications such as immune dysfunction, cardiovascular changes (eg, increased blood pressure), thrombosis, inflammation, and oxidative stress, can be dramatically reduced through improved glycemic control.^{2,5} In general, for every percentage reduction in A1C, the risk of chronic complications can be expected to decrease by 40%.⁶ The benefits of tight glycemic control extend to the acute-care setting, where hyperglycemia is common, secondary to metabolic stress or diabetes. Studies have demonstrated improved outcomes in medical and surgical intensive care unit (ICU) patients treated with intensive insulin therapy to attain tight glycemic control, specifically reductions in risk for multisystem organ failure, postoperative length of stay in the ICU, and infection.⁶⁻⁸ Although intensive treatment with insulin or oral glucose-lowering agents can be of great benefit to the patient, these therapies have been associated with an increased risk of hypoglycemia and related outcomes.^{3,4,9} The concomitant use of medical nutrition therapy (MNT) as adjunctive therapy for glycemic control may further enhance the quality of life and reduce risk of hypoglycemia in patients with diabetes. Within MNT, the development of diabetes-specific products designed to attenuate postprandial glycemic excursions should enhance the use of nutrition to achieve glucose control in people with diabetes mellitus.

Medical Nutrition Therapy

Nutrition therapy for people with diabetes is aimed at improving health with healthful food choices, while also meeting individual needs. Individual needs are based on disease state, physical status, personal and cultural food preferences, lifestyle, and attitude.¹⁰ Specific goals of nutrition are to prevent or treat chronic complications by attaining and maintaining optimal metabolic outcomes.

Goals of Medical Nutrition Therapy for Best Possible Metabolic Outcomes

- Improve overall health through optimal nutrition
- Maintain blood glucose levels that are as near normal as possible by balancing food intake with medication (if applicable) and physical activity levels
- Achieve optimal blood lipid levels
- Provide appropriate amounts of calories to achieve and maintain reasonable body weight

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Nutritional Needs

Enteral nutrition support is recommended for patients who are unable to meet their nutritional needs through voluntary oral intake, but have a functioning, intact gastrointestinal tract. There are two schools of thought surrounding the choice of enteral products for patients with diabetes. For some clinicians, the use of a standard enteral product coupled with close blood glucose monitoring and adjustments of exogenous insulin is sufficient to provide acceptable glycemic control.¹¹ Standard enteral products are generally high in low-molecular-weight carbohydrates and low in fat and contain moderate amounts of protein. When ingested, the carbohydrate is rapidly absorbed, which raises blood glucose levels. Diabetes-specific enteral products, on the other hand, possess macronutrient profiles designed to provide better glycemic control. They have lower levels of carbohydrate, are higher in fat, and contain between 16% and 22% of calories from protein. The carbohydrates found in diabetes-specific products are a blend of slowly digested carbohydrates, including fiber, to help modulate the glycemic response. The fat is a lipid blend rich in monounsaturated fatty acids. Because of this macronutrient profile, some clinicians prefer to use diabetes-specific enteral products for their patients with diabetes to circumvent concerns that standard products may compromise glycemic control.

A prospective, randomized, crossover meal tolerance test designed to simulate tube feeding compared the effects of a standard product to a diabetes-specific product in 10 subjects with type 1 diabetes consuming 20 mL of product every 15 minutes while receiving continuous intravenous insulin over 4 hours. Serum glucose levels were consistently lower and total urinary glucose excretion was significantly lower after consuming the diabetes-specific product compared with the standard product.¹²

A study by Sanz-Paris, et al, compared the 2-hour postprandial effects of a low-carbohydrate formula (LCF) and a high-carbohydrate, low-fat formula (HCF), both designed for patients with diabetes.¹³ Fifty-two patients with type 2 diabetes were randomly assigned to consume one of the two products after taking their diabetes medications (either insulin or sulfonylureas). The glycemic response to the HCF was significantly greater than that of the LCF. In addition, insulin and C-peptide levels were greater with the HCF than the LCF products. The researchers concluded that partial replacement of complex digestible carbohydrates with monounsaturated fatty acids in the lower-carbohydrate product may improve glycemic control better than the HCF diabetes product in patients with type 2 diabetes.

Another study compared the glucose and insulin responses of a standard and diabetes-specific product in 48 subjects with type 2 diabetes. The subjects were fed a bolus of each product on separate occasions following an overnight fast. Postprandial glucose and insulin levels were measured for 4 hours following consumption of the product. Results showed that glucose and insulin levels were significantly lower following consumption of the diabetes-specific product.¹⁴

In a study evaluating long-term glycemic control, lipid responses, and clinical outcomes, elderly, tube-fed, long-term-care patients with type 2 diabetes (n=27) were randomized to receive either a standard, high-carbohydrate product or a reduced-carbohydrate, diabetes-specific product for three months. Differences in fasting and serum glucose and capillary glucose levels demonstrated better control with the diabetes-specific product. In addition, the amount of insulin administered was consistently higher in the group fed the standard formula. The group who were fed the diabetes-specific product were reported to have improved clinical outcomes of reductions in the incidence of fevers, pneumonia, and urinary tract infections.¹⁵

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McCargar, et al, assessed the long-term effect of a standard or diabetes-specific product enriched with monounsaturated fatty acids on carbohydrate and lipid metabolism in 32 patients with type 2 diabetes.¹⁶ The products were consumed for 28 days at > 80% of daily energy intake, with subjects self-monitoring their blood glucose levels before and 2 hours after each meal. The postprandial rise in capillary blood glucose was significantly lower in the group fed the diabetes-specific product than the standard product. Trends of clinical interest, but not statistical significance, were greater decreases in fructosamine and insulin observed with consumption of the diabetes-specific product. There were no differences in triglycerides and cholesterol between the two groups, leading the authors to conclude that monounsaturated fatty acids do not present any risk to lipoprotein metabolism in patients with type 2 diabetes.

A randomized, double-blind, prospective study investigated the long-term effects of a low-carbohydrate, high-monounsaturated-fatty-acid diabetes product and a standard enteral product on fasting and postprandial blood glucose, total daily insulin, A1C, and lipid profile in 78 insulin-treated, tube-fed patients with type 2 diabetes over a 12-week period. The results demonstrated significantly lower levels of fasting blood glucose, total daily insulin requirements, and A1C levels in patients receiving the diabetes-specific product compared with the standard product. There was no difference in postprandial glucose or lipid levels between the groups.¹⁷

A recent meta-analysis of 23 studies was conducted to determine whether diabetes-specific products are superior to standard products by comparing their effects on glycemia, lipidemia, medication requirements, and complications.¹⁸ Sixteen of the studies involved oral supplementation and seven involved tube feeding. Following their analysis, the authors concluded that, whether consumed orally or tube-fed, diabetes-specific products improve glycemic control. In addition, the longer-term feeding studies reported a reduced requirement for insulin and fewer complications with diabetes-specific products compared with standard nutritional products.

Management Strategies and Treatment Goals

The complexities of diabetes mean differences in management for each individual with the disease, but the overriding goals are to prevent or delay microvascular and macrovascular complications and to improve overall health. Reaching these broad goals requires meeting and maintaining specific targets—normal plasma glucose, A1C, and lipid levels; a normal range of blood pressure; and appropriate body weight.

Major Goals for Diabetes Management

- Achieve glycemic control to prevent or limit microvascular complications
- Control lipid metabolism and blood pressure to prevent or limit macrovascular complications
- Balance food intake with energy output to control weight and improve overall health

Glycemic Control

Glycemic control for people with diabetes is targeted to specific measurable goals, although certain goals are adjusted to meet specific individual needs.¹⁹ A1C is the preferred measure of long-term glycemic control and the primary management target. A1C testing one to four times per year, depending on the individual's medical condition, is recommended for persons with any type of diabetes. Routine self-monitoring of blood glucose (SMBG), three or more times per day, is recommended for persons with type 1 diabetes; the frequency of testing may be less in type 2 patients on oral antihyperglycemic therapy, but more for those who take insulin with or without oral agents.^{19,20} Glycemic goals should be individualized appropriately for the age, gender, and health status of the patient; certain populations (children, pregnant women, and the elderly) require special considerations. Less-intensive glycemic goals may be indicated in patients who experience severe or frequent hypoglycemia, while more-stringent glycemic goals (eg, A1C \leq 6%; fasting plasma glucose of 70-130 mg/dL; 2-hr postprandial plasma glucose of 90-140 mg/dL) may further reduce complications in some patients.^{20,21}

A1C, the primary target for glycemic control, is a test measuring the amount of glycosylated hemoglobin in the blood. Hemoglobin becomes glycosylated when glucose molecules bond with hemoglobin molecules of the red blood cells. Because the glucose remains attached for the life of the cell (ie, about 120 days), a test to measure A1C shows the person's average blood glucose level for that period of time. Test results reflect the sum of the fasting and postprandial blood glucose measurements.

Correlation Between A1C Level and Mean Plasma Glucose Levels on Multiple Testing Over 2-3 Months

A1C (%)	Mean Plasma Glucose (mg/dL)
6	135
7	170
8	205
9	240
10	275
11	310
12	345

These estimates are based on DCCT data. An updated version of this table, based on final results of the ADAGE Trial, will be available at www.diabetes.org after publication of the study's findings in 2008.

Diagram taken from: American Diabetes Association: Standards of Medical Care in Diabetes. *Diabetes Care* 2008;31(suppl 1):512-554.

Targets for Glycemic Control^{19*}

Parameter	Target
A1C	< 7.0%*
Preprandial capillary plasma glucose	70-130 mg/dL
Peak postprandial capillary plasma glucose [†]	< 180 mg/dL

* These goals are for nonpregnant individuals and are referenced to a nondiabetic range of 4.0-6.0% using a DCCT-based assay.

† Postprandial glucose measurements should be made 1-2 h after the beginning of the meal, generally peak levels in patients with diabetes.

3.0

American Diabetes Association Recommendations for Inpatient Glucose Targets¹⁹:

Critically ill: Close to 110 mg/dL as possible; generally < 140 mg/dL

Noncritically ill: Fasting < 126 mg/dL; all random blood glucose < 180 -200 mg/dL

AACE/ACE Recommendations for Inpatient Glucose Targets¹:

Intensive care units: Maintain blood glucose <110 mg/dL

Noncritical care units: Maintain premeal blood glucose <110 mg/dL and peak postprandial blood glucose < 180 mg/dL

Blood Lipid Control

Lipid management aimed at lowering LDL cholesterol, raising HDL cholesterol, and lowering triglycerides is important for type 2 diabetes (see table below).¹⁹ Effective lipid control has been shown to reduce macrovascular disease and mortality in patients with a history that includes cardiovascular events.²² Diabetes specialists advise testing adult diabetes patients for lipid disorders at least once each year and more often if needed to achieve goals.¹⁹ The recommended initial therapy for managing lipid levels is behavioral modification, including diet modification, weight loss, and increased exercise.¹⁹ The addition of lipid-lowering agents may be necessary to achieve lipid targets.¹⁹

Recommended Blood Lipid Levels^{19*}

Recommended Lipid Levels	
Total cholesterol	< 200 mg/dL
LDL cholesterol	< 100 mg/dL [†]
HDL cholesterol	> 40 mg/dL for men > 50 mg/dL for women
Triglycerides	< 150 mg/dL

* Current NCEP/ATP III guidelines suggest that in patients with triglycerides \geq 200 mg/dL, the “non-HDL cholesterol” (total cholesterol minus HDL) be used. The goal is \leq 130 mg/dL.

† This is the goal for individuals with diabetes aged > 40 years with a total cholesterol \geq 135 mg/dL without overt cardiovascular disease. An LDL cholesterol level of < 70 mg/dL (1.8 mmol/L) is recommended by the ADA for persons with diabetes and overt cardiovascular disease who are at very high risk for further events.

Summary

Clinical management of diabetes requires a multifaceted approach that makes use of pharmacotherapy (oral anti-diabetic agents and insulin), medical nutrition therapy, and lifestyle modification (physical activity and weight management), along with patient education and ongoing support.

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Wound Healing

Introduction

Hyperglycemia is the underlying metabolic impairment that directly and indirectly causes acute, subacute, and chronic complications in patients with diabetes. Over the long term, chronic hyperglycemia damages multiple organs, especially eyes, kidneys, nerves, heart, and blood vessels. Diabetes/hyperglycemia increases the risk of negative clinical outcomes specifically related to patients with wounds, eg, foot ulcers, pressure ulcers, and surgical wounds.

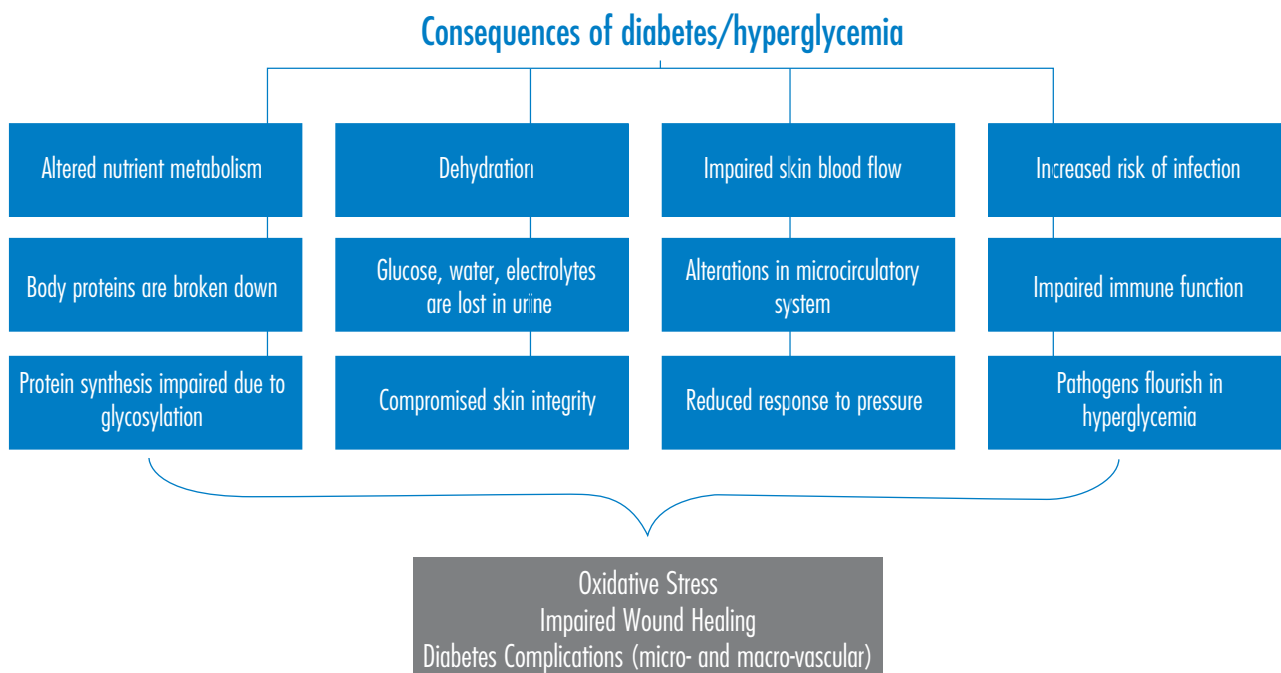
The mnemonic “**DIDN’T HEAL**” as identified by Marsha Steiber, MSA, RD, CNSD, is helpful to understand the various issues that may affect the formation and healing of wounds.¹ Steiber defines “DIDN’T HEAL” as follows:

- D = Diabetes
- I = Infection
- D = Drugs
- N = Nutritional problems
- T = Tissue necrosis

- H = Hypoxia
- E = Excessive tension on wound edges
- A = Another wound
- L = Low temperature

4.0

The diagram below illustrates the links between diabetes/hyperglycemia and impaired wound healing¹⁻³:



Altered Metabolism of Nutrients

Protein is required to build the structures that heal wounds, such as collagen, and insulin is the hormone that stimulates protein synthesis. Deficiencies of protein and insulin inhibit protein metabolism. People with diabetes experience insulin resistance, in which the body is producing insulin, but the cells are resistant to its activity. Insulin resistance is also linked with metabolically inactive fat mass around the abdomen that replaces lean body mass. These changes in body composition are an additional consideration in wound healing.^{2,4}

Lipid metabolism is also altered with diabetes. When blood glucose levels drop and cells do not have proper glucose for energy, stored triglycerides are broken down into glycerol saturated fatty acids for energy. If fats are being used for energy, they are not available for healing. Without the availability of fatty acids to form cell membranes, the cell structure is compromised.

Glycosylation

Chronic hyperglycemia contributes to a metabolic process called *glycosylation*. Glycosylation is the linking of glucose molecules with various proteins. Glucose molecules can bind to most types of protein, including hemoglobin, which is the oxygen-carrying protein in red blood cells. In people without diabetes, the percentage of these glucose-hemoglobin links is low—about 4.5% to 6%—but the percentage can be elevated in people with hyperglycemia. This value is called *glycosylated hemoglobin*, or *hemoglobin A1C* (A1C). The values reflect total *accumulation* of linked glucose and red blood cells over their lifespan of approximately 120 days. In other words, the values are a measure of a person's average blood glucose level over the past 3-4 months. Hyperglycemia at fasting and during postprandial periods activates the process of glycosylation.⁵

Chronically elevated blood glucose levels can lead to glycosylation of other proteins, as well. For example, proteins associated with blood lipids such as low-density lipoproteins (LDLs) can be glycosylated. Glycosylated lipoproteins in arteries can result in the formation of vessel-clogging plaque, helping to explain why people with diabetes are at increased risk for cardiovascular disease. Glycosylated proteins such as collagen alter their normal functioning, thus impairing wound-healing ability.

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Dehydration

Water is essential for normal cell function. Uncontrolled hyperglycemia increases urinary losses of water and electrolytes, increasing risk for dehydration. Glycemic control improves fluid balance, which is necessary for both skin integrity and efficient wound healing. With hyperglycemia, the kidneys cannot reabsorb the large quantities of glucose from the blood. As a result, glucose spills into the urine, pulling water and electrolytes along with it.

Dehydration is a risk factor for pressure-ulcer development because blood volume is reduced, interfering with peripheral circulation and decreasing the nutrient and oxygen supplies to tissues.⁶ Also, in patients who develop a wound such as a pressure ulcer, drainage from the wound can exacerbate dehydration. Optimal glycemic control can help reduce the combined risk for hyperglycemia and dehydration.

Impaired Skin Blood Flow

Small-blood-vessel damage due to hyperglycemia impairs blood flow, decreasing oxygen supply to tissues. This can contribute to the development of pressure ulcers and slow healing. Hyperglycemia impacts wound healing: chronically elevated blood sugar levels can lead to micro- and macro-vascular damage. As a result, blood flow is restricted, which can inhibit pressure, pain sensitivity, and/or temperature sensitivity, and contribute to new tissue damage to a current wound or initiate damage at another location.¹

More specifically, diabetes disturbs the normal regulation of skin circulation even in the absence of neuropathy.³ In the presence of neuropathy, vasodilation is impaired. This inability of the skin to normally respond to injury is an important factor in the development of skin ulceration.

Peripheral and autonomic neuropathies interrupt the pain feedback loop that signals the presence of injury or infection. Peripheral neuropathy causes loss of sensation, which can increase the risk of ulceration, infection, and in some patients, amputation. Autonomic neuropathy may result in decreased perspiration, causing dry, cracked skin, which serves as an entryway for bacteria and infection.⁷

The importance of A1C levels goes beyond being a measure of glucose control. The glycosylation of hemoglobin alters its chemical structure such that it does not release oxygen as easily as nonglycosylated hemoglobin does. Therefore, tissues have less oxygen, a condition known as hypoxia. Because oxygen is needed for the health of cells and synthesis of protein, tissue hypoxia leads to many of the complications of diabetes, including susceptibility to bacterial infection and decreased ability to heal wounds such as foot and pressure ulcers or surgically induced wounds. The dual effects of hyperglycemia and excessive protein glycosylation on protein synthesis can have far-ranging negative implications, including impairment of wound healing. The resulting complications are especially significant for people such as the elderly, who are at risk for pressure ulcers.

Increased Risk of Infection

Several mechanisms of immune defense are impaired, increasing risk of infection. Some common pathogens flourish in the hyperglycemic environment, such as *candida albicans* (yeast).⁸ The metabolic abnormalities of diabetes impair immune response, increasing risk for systemic and localized infections, especially infections of the foot. People with diabetes are more likely to be hospitalized for serious and life-threatening infections than people without the condition.

Infection can be a major complication in long-term tube-fed patients, and rates of infection increase with poor glycemic control. Foot infections are among the most frequent and serious infectious problems in patients with diabetes. Impaired immune response, along with impaired wound healing, predisposes these patients to infectious complications.

Oxidative Stress

Oxidative stress by hyperglycemia plays a major role in the pathogenesis of diabetic complications.⁹ Patients with diabetes have a higher level of oxidative damage to their cells than people without diabetes. Oxidative stress is activated by three main glycemic disorders: hyperglycemia at fasting, hyperglycemia during postprandial periods, and acute glucose fluctuations.⁵

The resulting effect is the risk of complications. This is because biochemical processes associated with hyperglycemia increase the production of free radicals.^{5,10}

More specifically, research has demonstrated that the production of free radicals increased during the postprandial period, and this increase was directly correlated to the rise in postprandial glucose levels. Free radicals are molecules with unpaired electrons in their structures. As a result, they are unstable and “steal” electrons from surrounding cells, damaging those cells in the process. When cells are damaged, tissue function and integrity are impaired. When the body is in a state of oxidative stress, its ability to heal wounds and carry out other normal functions is impaired.

Impaired Wound Healing

In the presence of hyperglycemia, body proteins such as collagen can become glycosylated, which alters their normal functioning, impairing wound-healing ability. Glycosylation also affects the ability of hemoglobin to carry oxygen. The result is that insufficient oxygen is carried to tissues for synthesis of proteins, which also slows wound healing. Poorly controlled diabetes leads to increased protein breakdown and decreased synthesis of body proteins such as collagen, impairing the body’s ability to heal wounds, eg, foot ulcers, pressure ulcers, and surgical wounds. Glycemic control may help avoid the complications of diabetes that are secondary to glycosylation, including impaired protein synthesis and wound healing.

Complications

Chronic complications often are related to the damage done by prolonged, uncontrolled hyperglycemia. These complications result primarily from micro- and macro-vascular damage and from lipid deposits that harden and narrow the blood vessels. These complications may be classified into several categories, as shown below:

- Cardiovascular disease (CVD): People with diabetes are two to four times more likely to develop CVD; more than half the deaths attributed to diabetes complications are caused by coronary heart disease.
- Peripheral vascular disease (PVD): PVD is a condition that results in reduced flow of blood and oxygen to lower extremities, which can cause tissue “death” (gangrene) and result in amputation of a foot or leg.
- Stroke: People with diabetes are two to four times more likely to have a stroke than those without.¹¹
- Retinopathy: Damage to retinal blood vessels can impair vision. Diabetes is the leading cause of new cases of blindness among adults aged 20-74 years. Diabetic retinopathy causes 12,000 to 24,000 new cases of blindness each year.¹¹
- Kidney disease: Kidney disease resulting from diabetes is a significant cause of early death and is the leading cause of kidney failure requiring dialysis.¹¹
- Neuropathy: Neuropathy—damage to nerves—is a chronic complication of diabetes, affecting 60% to 70% of people with type 1 or type 2 diabetes.¹¹

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Role of Nutrition in Wound Healing

Subacute complications of diabetes such as impaired wound healing, dehydration, and impaired immune function are common conditions in acute and long-term care, especially among tube-fed patients. Although these conditions are not always associated with blood-glucose control, they can result from, or are exacerbated by, ongoing hyperglycemia. Therefore, two important nutrition care goals for acute and long-term patients with elevated blood glucose levels are to achieve and maintain glycemic control.

The Role of Specific Nutrients in Skin Integrity and Healing

The presence of certain diseases or conditions, such as diabetes, can influence wound-healing outcomes. Increased protein intake is often emphasized in patients with nonhealing wounds. However, adequate intake of one nutrient alone does not prevent pressure ulcer formation or facilitate healing. Sufficient calories, protein, fluid, and essential vitamins and minerals are all required for preventing and treating pressure ulcers and other wounds.

Calories

Calories provide the body with energy. If sufficient calories are not consumed, weight loss occurs in the form of adipose tissue and lean body mass loss. Weight loss is associated with an increased risk of pressure ulcers.¹²

If the body does not have the sufficient calories it needs, it will use protein and lean body mass for its energy source. Calorie needs should be assessed carefully, and adequate calories should be provided so that protein can be used for tissue maintenance and repair, and not for energy. The Agency for Health Care Policy and Research (AHCPR), now known as The Agency for Health Care Research and Quality (AHRQ), has provided guidelines for determining calorie needs for patients with pressure ulcers. These guidelines recommend providing 30 to 35 kcal/kg body weight per day for malnourished persons who have a pressure ulcer.¹³ It is reasonable for persons with other types of wounds or who are at risk of pressure-ulcer development, but calorie needs should be individualized for each person based on their specific needs and conditions.

Protein

Protein provides amino acids, which are the building blocks of the body. Protein is needed for tissue maintenance and repair. Insufficient intake of protein is associated with pressure-ulcer development,^{12,15} and a high protein intake is important for wound healing.^{13,15}

The AHCPR/AHRQ guidelines recommend 1.25 to 1.5 g/kg body weight per day for malnourished patients with pressure ulcers.¹⁴ As with calories, this protein level may also be used for persons with other types of wounds or who are at risk of pressure-ulcer development. Increasing protein intake beyond 1.5 g/kg per day may not increase protein synthesis and may cause dehydration.¹⁵

Fluid

Fluid is essential for the normal functioning of cells. Dehydration can occur if a person does not consume enough fluid or if fluid losses exceed fluid intake. Wound drainage can be a major source of fluid loss and can lead to dehydration and electrolyte imbalance. Dehydration frequently occurs with malnutrition and is a risk factor for pressure-ulcer development^{16,17} because it can reduce blood volume, thereby interfering with peripheral circulation and decreasing nutrient and oxygen supply to tissues.

Optimal hydration is attained when fluid intake equals fluid output. Current recommendations are that total water intake from all beverages and foods should be 2.7 L (approx. 9 cups) for women more than 19 years old and 3.7 L (approx. 13 cups) for men more than 19 years old.¹⁸ Fluids are particularly important for older adults because they are at increased risk for dehydration as a result of a decreased thirst sensation that occurs with aging. A rule of thumb is to provide 30 to 35 mL of fluid per kg body weight per day, or 1 mL of fluid per calorie fed for persons receiving enteral tube feeding.¹⁹ Patients on air-fluidized beds require an additional 10 to 15 mL fluid/kg body weight to prevent dehydration that can occur from the drying effects of these specialty beds.²⁰

Vitamins and Minerals

Various vitamins and minerals have been studied to examine their effects on wound healing. Nutritional deficiencies have been associated with pressure-ulcer development and impaired wound healing; therefore, clinicians often supplement intake of vitamins and minerals thought to be especially important for wound healing. The AHCPR/AHRQ guidelines recommend a daily multivitamin and mineral supplement if deficiencies are confirmed or suspected.¹³ Additional vitamins and minerals routinely supplemented in persons with wounds or pressure ulcers are vitamins A, C, and E, and zinc. This practice is most beneficial for persons with confirmed or suspected nutritional deficiencies.

Vitamin A

Vitamin A is a fat-soluble vitamin important for cellular differentiation and proliferation. Vitamin A has a role in collagen synthesis, the immune system, and epithelial development.²⁰ Studies indicate that vitamin A plays a role in wound healing by increasing collagen synthesis and epithelialization.²¹ Vitamin A deficiency may result in delayed wound healing and an increased susceptibility to infections.²¹ Studies of vitamin A supplementation for wound healing have been done with doses that range from 25,000 to 50,000 IU (approx. 7500 to 15,000 mcg).^{21,22} However, the research to support vitamin A supplementation for wound healing is lacking.^{23,24} Therefore, vitamin A supplementation appears to be indicated only for patients who are specifically vitamin A-deficient. Vitamin A is stored in the liver, so true deficiency is rare. Clinical vitamin A deficiency is defined as a serum vitamin A level of $<0.35 \mu\text{mol/L}$. The Recommended Dietary Allowance/Adequate Intake (RDA/AI) is 900 mcg/day for males and 700 mcg/day for females.²⁵ The tolerable upper intake level (UL) is 3000 mcg/day.²⁵ Since vitamin A is stored in the liver, high doses can be toxic.

Vitamin C

Vitamin C is a water-soluble vitamin that contributes to the synthesis of connective tissue—in particular, collagen.²⁶ Impaired wound healing resulting from decreased collagen synthesis is associated with vitamin C deficiency and is reversed with adequate supplementation.²⁷ Although vitamin C supplementation has been proven to enhance wound healing in deficient patients, the benefit of supplementation in nondeficient patients remains unclear.²¹ Some studies in nondeficient patients have found no significant improvement in wound healing with vitamin C supplementation.^{28,29} Other research has shown that when vitamin C intake is inadequate, collagen synthesis is reduced,³⁰ and low concentrations of leukocyte vitamin C levels were associated with subsequent pressure-ulcer development in older adults with femoral neck fractures.³¹ Vitamin C supplementation levels reported in the literature range from 120 to 240 mg/day³² and up to 4000 mg/day.²¹ Vitamin C status can be measured by blood, serum, or plasma levels; however, these measurements are expensive. A deficiency is defined as a plasma level of $<0.2 \text{ mg/dL}$.²⁶ The RDA/AI for vitamin C is 75 mg/day for adult women and 90 mg/day for adult men.³³ The UL is 2000 mg/day.³³ Toxic levels are unlikely to occur, but high doses of vitamin C can have adverse effects such as nausea, abdominal pain, and diarrhea. Overall, scientific evidence to support the use of vitamin C supplementation in patients without a deficiency or to accelerate wound healing is lacking and sometimes conflicting, and further research is needed.

4.0

Vitamin E

Vitamin E is a fat-soluble vitamin that acts as an antioxidant that reduces peroxidation of lipids, which in turn helps to stabilize cell membranes. It is also used for skin care to reduce scar formation because it inhibits collagen synthesis and decreases tensile strength of wounds.²¹ Research on the role of vitamin E and wound healing is lacking, and the few studies that have been conducted show conflicting results.²⁴ Excess vitamin E has been found to impair wound healing and inhibit blood-clot formation in animals.²¹ The RDA/AI is 15 mg for adult men and women.³³ The UL is 1000 mg/day.³³ Until more research is conducted on vitamin E and wound healing, supplementation should be used only for patients who are deficient.

Zinc

Zinc is an essential trace mineral required for cellular growth and replication. It is necessary for DNA synthesis, cell division, and protein synthesis, all processes vital for tissue growth and repair. Zinc deficiency affects wound healing by decreasing protein and collagen synthesis.²¹ Chronic, severe zinc deficiency results in abnormal neutrophil and lymphocyte function, delayed wound healing, and an increased susceptibility to infection.³⁴ Zinc deficiency can occur through wound drainage, gastrointestinal losses (such as diarrhea), or a prolonged, low dietary intake. Neither zinc status nor dietary intake of zinc has been shown to be a risk factor for developing pressure ulcers.^{3,12,31,35,36} Amounts of zinc supplementation in studies of wound healing range from 15 to 60 mg/day.^{21,22} Zinc supplementation remains controversial, and there is no significant evidence that routine zinc supplementation promotes pressure-ulcer healing.³⁷ Zinc supplementation should be given only to patients who are deficient, because it does not appear to improve wound healing in nondeficient patients. In addition, excess zinc supplementation can adversely affect wound healing.²¹ The potential toxic effects of zinc include interference with copper metabolism and impaired immune function.²⁰ Zinc levels can be measured by plasma or serum levels, but they are not sensitive nor specific indicators of zinc status.²¹ However, serum zinc levels of <100 mcg/dL are associated with impaired wound healing.²¹ The RDA/AI for zinc is 8 mg/day for adult women and 11 mg/day for adult men.²⁵ The UL is 40 mg/day for adult men and women.²⁵

Table 1 Role of Selected Nutrients

Nutrient	Role	Daily Recommendations	Glucerna 1.5 Cal Contribution
Calories	Energy source Prevents protein and lean body mass from being used for energy	30-35 Cal/kg	1.5 Cal/mL
Protein	Tissue maintenance and repair	0.8 g/kg 1.25-1.5 g/kg (patients with pressure ulcers/malnourished)	22% of calories from high-quality proteins
Fluid	Normal cell function and tissue integrity, adequate blood volume and circulation, and nutrient and oxygen supply to tissues	30-35 mL/kg or 1 mL of fluid per calorie fed for patients receiving enteral tube feeding OR 2.7 L (91 ounces, approx. 9 cups) for women > 19 years old 3.7 L (125 ounces, approx. 13 cups) for men > 19 years old Increase by an additional 10-15 mL/kg if patient is on an air-fluidized bed	180 cc/8 fl oz 759 cc/L Additional fluid requirements should be met by giving water between or after feedings or when flushing the tube
Vitamin C	Connective tissue and collagen synthesis Support wound strength	Supplement if deficient RDA/AI = 90 mg/day for males; 70 mg/day for females UL = 2000 mg/day	78 mg/8 fl oz 325 mg/L
Vitamin A	Cellular differentiation and proliferation Collagen synthesis Immune system Supports wound strength and healthy new tissue	Supplement if deficient RDA/AI = 900 mcg/day (3000 IU) for males; 700 mcg/day (2333 IU) for females UL = 3000 mcg/day (10,000 IU)	2060 IU/8 fl oz (1040 IU of Vitamin A activity supplied by 0.79 mg beta-carotene) 8660 IU/L (4370 IU of Vitamin A activity supplied by 3.3 mg beta-carotene)
Vitamin E	Antioxidant—Quenches free radicals and maintains membrane integrity	Supplement if deficient RDA/AI = 15 mg/day (22.3 IU) for males and females UL = 1000 mg/day (1493 IU)	12 IU/8 fl oz 48 IU/L
Zinc	Supports growth of healthy new tissue	Supplement if deficient RDI/AI: 15 mg for males, 12 mg for females	3.6 mg/8 fl oz 15 mg/L

RDA/AI = Recommended Daily Allowance/Adequate Intake
UL = Tolerable Upper Intake Level

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4.0

Case Examples/Product Application

A 58-year-old woman (Ht: 61" Wt: 250 lb, BMI=47.2 kg/m²) is admitted to a skilled nursing facility from the hospital for rehab and wound care after complicated abdominal surgery. Patient has a PEG tube and arrives at the facility on a 16-hour continuous feed with a standard formula and a mechanical soft diet. After a week at the facility, the wound is not healing and the patient's oral intake is minimal.

Past Medical History: Obesity, Diabetes Mellitus, Hypertension, Hyperlipidemia

Calorie Needs: 1280-1600 (20-25 Cal per kg Adjusted Body Weight)

Protein Needs: 77-96 g (1.2-1.5 g per kg Adjusted Body Weight)

It is decided to change the feeding to a 10-hour nocturnal feed, in hopes of increasing daily oral intake, as the patient stated she was simply not hungry. The standard enteral formula is unable to meet the calorie and high-protein needs within the 10-hour cycle. High blood glucose levels and inadequate protein, calories, and other nutrients are factors that can contribute to a patient's inability to heal. The formula selected should assist in meeting these needs.

At a rate of 100 mL/hr for 10 hr, Glucerna 1.5 Cal provides:

Calories: 1500 Cal

Protein: 82.5 g

This meets the patient's goals without hindering physical therapy during the day.

5.0

Case Examples/Product Application

68-year-old man (Ht: 72", Wt:185 lb, BMI=25.1 kg/m²) is admitted to the ED with traumatic brain injury due to a motor-vehicle accident. Patient is unconscious upon arrival and enteral access is obtained early. The patient exhibits a hypermetabolic response, and a rapid loss of lean body mass is anticipated. Patient has history of uncomplicated diabetes mellitus, but after admission, blood glucose levels have become difficult to control.

Trauma can result in hyperglycemia leading to complications and increased morbidity and mortality. This can be further exacerbated in the patient with diabetes. Therefore, controlling blood glucose in this population is extremely important. In order to preserve glycogen stores, spare protein, and stabilize blood glucose levels, a calorically dense high-protein formula that can help normalize blood glucose is needed.

Calorie Needs: 2100-2520 kcal (25-30 Cal/kg)

Protein Needs: 126-168 g (1.5 -2.0 g/kg)

At a continuous rate of 75 mL/hr for 24 hr, Glucerna 1.5 Cal provides:

Calories: 2475 Cal

Protein: 136 g

Glucerna

Glucerna products are for use under medical supervision as a part of a diabetes management plan.

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