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When Capsules Aren't Enough

The Growing Trend of Delivering Nutrients in Ready-to-Mix Powder Formulas

Dietary supplements include a wide range of micronutrient ingredients, including vitamins, minerals, essential nutrients (e.g., lutein, CoQ10), antioxidants, and key phytonutrients. For the most part, the doses of these micronutrients can be delivered in reasonable number of capsules or tablets, even when combined. However, the supplementation of macronutrient such as proteins, amino acids, fibers and specialty nutrients that require higher doses (i.e., glutamine) are often best delivered using ready-to-mix powder products that can be combined with a variety of liquids (e.g., water, milk, milk-substitutes, juice, etc.) prior to consumption. Of course, this trend has been around for quite some time in a few basic categories: sports/protein supplements, fiber supplements and ready-to-drink glycemic control shakes. Today, it is quite common for clinicians to recommend ready-to-mix "functional powder" products that can deliver key micronutrients within a macronutrient base of protein and/or fiber. These powder products are designed for a variety of therapeutic outcomes including glycemic control, satiety/weight loss, prebiotic supplementation, inflammation control, hypoallergenic meal replacement, delivery of phytonutrients ("greens"), improved detoxification, and immune system enhancement. In this brief overview, we will discuss some of the potential benefits of using powder-based therapeutic products and discuss some of the reasons this trend is growing.

Therapeutic Powdered Products: Convenience and Control

The use of pre-packaged meals designed to be transportable and convenient has a long history in the military (e.g., C-rations, MREs) and for space travel. Their purpose was to provide the necessary food components packaged in a way that required minimal preparation and maximal nutrient potential. Likewise, there is a long historical use of dried foods designed for travel and storage, some of which can be eaten directly (e.g., jerky, dried fruit) and others that are usually reconstituted with water (i.e., dried milk). Along the way, many products were introduced that have become common household "foods" and it wasn't long before some of these concentrated products were advertised for their healing properties (e.g., Ovaltine), whether there was any data to support them or not.

Ovaltine advertisement in a medical journal, 1909

Today, nearly every store that sells food, including health food stores and supplement retailers, has numerous shelves stocked with "therapeutic foods" of various kinds. These include ready-to-drink (RTD) sports and electrolyte drinks, ready-to-mix (RTM) protein powders, bars, cookies, and sachets of ingredients intended to be added to liquid before consumption. The use of these types of products are a growing trend, due to the increased use of food and dietary supplements overall, the realization that certain ingredients must be consumed at higher doses and the shift away from capsules and tablets toward powders. In fact, "pill fatigue" appears to be responsible for the growth of many non-pill dosage forms including liquids, powders, gummies and chewable tablets.[1,2,3] For clinicians, the use of powdered products offers additional benefits, allowing a patient to take multiple therapeutic ingredients at the same time while controlling for other factors such as caloric intake or allergenic ingredients. In fact, using these types of products to replace a meal for calorie or glycemic control is their most-studied application.

Meal Replacements for Calorie Control

The basic advantage of any meal replacement product is, simply, control. By knowing exactly what a patient is consuming, both the clinician and patient eliminate the ambiguity of implementing a portion of the dietary regimen. For instance, if a patient routinely skips breakfast or often chooses foods with high glycemic impact for breakfast, recommending a high-protein, high-fiber breakfast shake with a known caloric and glycemic impact will allow the patient to control these factors without difficulty. The most common use of meal replacements is for their ability to aid individuals in calorie reduction for weight loss/weight maintenance. Clinical studies in the past several decades have shown that in obese subjects (including type 2 diabetic subjects), those able to use meal replacement products were more likely to reach their daily calorie reduction and weight loss goal than those given only dietary means to restrict calories.

The Look AHEAD trial is a great illustration of this concept.[4] In this trial, a total of 5,145 obese subjects with type 2 diabetes were randomly assigned to an intensive lifestyle intervention or a control Diabetes Support and Education (DSE) group. A more detailed description of these interventions is published elsewhere, but for brevity, the intensive lifestyle intervention (ILI) had a goal of achieving a ≥7% reduction in initial body weight and increasing physical activity to ≥175 minutes/week; patients in the ILI group also received dietary and physical activity counseling in group and individual settings totaling 42 sessions over the course of a year.[5] In order to control calories and macronutrient ratios, patients in the ILI group had the option of using a liquid meal replacement (i.e., SlimFast, Glucerna, OPTIFAST or HMR) to substitute two meals and one snack with a snack-bar during weeks 3 through 9. During months 7 through 12, subjects reduced the frequency of the liquid meal replacement to one meal and one snack-bar. Those in the control DSE group only had three educational sessions and did not receive meal replacements. After one year, those in the ILI group lost 8.6% of initial body weight compared to only 0.7% in the DSE group ($P < 0.001$). Within the ILI group, subjects in the highest quartile of meal replacement use had 4.0 times greater odds of reaching the 7% weight loss goal and 4.1 times better odds of reaching 10% weight loss than those in the lowest quartile. These data suggest that the use of meal replacements greatly increased successful weight loss in obese type 2 diabetic subjects.

Other studies have found similar results to the Look AHEAD trial for the use of meal replacements as a weight loss tool. One retrospective study found over 70% of subjects with type 2 diabetes or high blood sugar (N = 125) lost ≥ 5% of their baseline body weight following a portion-controlled meal replacement program for weight loss with one-on-one behavioral support.[6] A meta-analysis of six studies (N = 454) found the use of a meal replacement diet strategy (structured to replace one or two usual meals/day) compared to a control diet without meal replacement led to significantly greater weight loss at one year of intervention (-3.0 kg for meal replacement versus -1.5 kg for control diet, 95% CI: -2.48 to -0.39).[7] Like the Look AHEAD trial, this meta-analysis found that meal replacement combined with dietary support led to the greater weight loss (compared to the control diet with support, mean difference -2.21 kg, 95% CI: -3.99 to -0.45). Significantly greater improvements in HbA1c were found for those using the meal replacements versus the control diets. Again, these data reinforce the utility in using meal replacement products for those attempting to lose weight.

The Advantage of Whey Protein for Insulin Sensitivity and Diabetes Risk Reduction

Meal replacements and functional powders are often delivered as protein-based, ready-to-mix products. The typical proteins used in these products include various concentrates or isolates of whey, casein, egg, soy, pea, rice, hemp, or even cricket protein. Depending on the source and the method of protein purification, these ingredients can provide up to 90% protein (though some are balanced with naturally occurring fiber, carbohydrates and fat). While each protein source has a different amino acid profile, protein efficiency ratio, utilization and digestibility, and may have slightly different clinical outcomes (based on dose and other factors), most of these protein sources have not been tested in true "head-to-head" comparisons for meaningful clinical endpoints. However, based on the epidemiological data connecting dairy protein consumption and reduced incidence of type 2 diabetes, whey protein products have consistently been associated with clinical trials exploring the benefits of whey protein on glycemic control and biomarkers of insulin resistance.[10]

Several studies have evaluated the effect of supplementation with whey protein (varying doses) as a preload before a test meal (usually meal with high glycemic index [GI]) or whey protein given concomitantly with a similar high GI test meal. These studies have shown a blunting of the glucose area under the curve and a corresponding increase in insulin levels—suggesting whey protein has an insulinemic effect.[8,9,10] Although the relationship between whey protein supplementation, insulin and blood sugar levels appears consistent, the studies measuring these effects have been inconsistent in terms of the whey protein formulation used (e.g., whey protein concentrate, whey protein isolate, reduced lactose whey, partially and extensively hydrolyzed whey and demineralized whey protein), the patient group tested (e.g., healthy subjects of normal weight, overweight/ obese subjects and/or those with type 2 diabetes), the dose of whey protein given and the timing and delivery of the whey protein. Therefore, it is difficult to use these studies to make specific recommendations for the dosing of whey protein with meals for the best glycemic outcomes. However, a linear dose-response relationship for reduction in glucose was reported in two studies of lean, healthy subjects following whey protein supplementation using doses ranging from 5-40 g or 4.5-18.0 g .[11,12]

Mechanistically, whey protein has been suggested to have both an indirect and a direct effect on insulin levels and glycemic control; though it is likely that many mechanisms converge to give whey protein its insulinemic and blood sugar lowering effect.[8,12] One mechanism potentially contributing to whey protein's insulinemic and glucose-lowering effect is its effect on gastric emptying. This concept was illustrated in a study in obese, non-diabetic subjects (N =11) where whey protein isolate (45 g) was found to decrease the rate of gastric emptying compared to other protein sources studied (i.e., casein, gluten and cod, each 45 g) when given with a high fat meal.[13] Additionally, whey protein contains branched chain amino acids (BCAA; i.e., leucine, isoleucine and valine) which have independently been shown to have a stimulatory effect on insulin levels.[14] Since whey protein contains these BCAAs, and whey protein has a rapid rate of digestion (compared to casein), it is suggested that the release of these BCAAs from whey protein may contribute to the increase in insulin secretion.[14,15,16] Additionally, whey protein has been shown to increase the concentrations of the glucose-lowering incretin hormones, gastric inhibitory peptide (GIP, which stimulates insulin release) and glucagon-like peptide 1 (GLP-1, which influences glycemia by slowing gastric emptying), in mouse pancreatic cells incubated with postprandial human serum from subjects who consumed whey protein.[14] The increase in GIP after whey supplementation appears more consistent than whey protein's ability to increase GLP-1, as other studies in human volunteers have not always shown an increase in GLP-1 following whey supplementation.[10,13,16] Another suggested mechanism underlying the insulinemic effect of whey protein is the potential for hydrolyzed whey protein to preserve GIP levels through inactivating the well-studied enzyme dipeptidyl peptidase IV (DPP-IV).[9,17] This enzyme cleaves GIP rendering the incretin hormone inactive thereby reducing the stimulatory effect of GIP on insulin levels. This is a well-understood pathway, as DPP-IV inhibiting drugs are used for glycemic control in subjects with hyperglycemia.[17] Hydrolyzed whey proteins have been shown in some in vitro and in silico studies to have DPP-IV inhibitory activity, but whether this mechanism underlies the attenuation of the AUC for glucose in humans is not well-studied.[17,18,19]

Whey protein has also been researched for its effects on satiety. A meta-analysis of three long-term appetite trials found a significant reduction in long-term appetite with whey protein supplementation (P = 0.001), however, no significant reduction in short-term appetite was seen in the five included trials evaluating this effect (P = 0.63).[20] A significant reduction in prospective food consumption was seen with whey protein consumption. Mechanistically, whey protein (along with other proteins) has been shown to lead to greater increases in several gut hormones involved with regulating satiety including cholecystokinin.[21,22] In addition to whey protein's acute effects on postprandial glucose, one meta-analysis of nine randomized controlled trials found whey supplementation in dosages ranging from 20 g to 70 g/day for durations ranging from 2 weeks to 15 months was associated with significant improvements in fasting glucose compared to control; this study also found a significant reduction in body weight, lean mass and fat mass with whey supplementation.[23] Therefore, while many protein sources are available to the clinician looking to provide a protein-based functional powder to help curb appetite or improve glycemic control, the use of a whey-based product may prove more effective than other animal or plant-sourced proteins.

Challenges and Solutions in the Use of Therapeutic Powder Products

Choosing a protein source is only one of many decisions when using therapeutic powder products. Since additional ingredients are often added to create a therapeutic purpose for the product, these ingredients often alter the taste, color and cost of the product. For instance, a whey-based product designed for glycemic control is likely to contain additional ingredients such as fiber, chromium, and lipoic acid; whereas a rice-based product designed to help improve inflammatory control may include ingredients such as turmeric, curcumin, vitamin D and L-glutamine. These additional ingredients can often be added in doses higher than the dose found in a capsule or tablets, though the challenge of taste and solubility can often limit patient adherence. It is therefore important to allow the patient to try different flavors of the same product to allow them to find a product compatible for their use. In addition to taste and texture, some individuals do not tolerate certain protein sources due to hypersensitivity or allergic reactivity. Most companies provide products using different protein options to accommodate patient preferences and reactivities.

References

1. Haigh L. Consumer interest in liquid nutraceutical delivery forms grow as “pill fatigue” perseveres, says Bormioli Pharma. 2018; https://www.packaginginsights.com/news/consumer-interest-in-liquid-nutraceutical-delivery-forms-grow-as-pill-fatigue-perseveres-says-bormioli-pharma.html. Accessed July 23, 2019.
2. New Hope Network. By the numbers: the state of the supplement industry. 2019; https://www.newhope.com/business-resources/numbers-state-supplement-industry. Accessed July 23, 2019.
3. Watson E. WATCH: GEM tackles pill fatigue with daily bites for the ‘modern millenial woman’. 2019; https://www.foodnavigator-usa.com/Article/2019/04/11/GEM-tackles-pill-fatigue-with-daily-bites-for-the-modern-millennial-woman-at-Foodbytes. Accessed July 23, 2019.
4. Raynor HA, Anderson AM, Miller GD, et al. Partial Meal Replacement Plan and Quality of the Diet at 1 Year: Action for Health in Diabetes (Look AHEAD) Trial. J Acad Nutr Diet. 2015;115(5):731-742.
5. Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. Obesity (Silver Spring, Md). 2009;17(4):713-722.
6. Coleman CD, Kiel JR, Mitola AH, Arterburn LM. Comparative effectiveness of a portion-controlled meal replacement program for weight loss in adults with and without diabetes/high blood sugar. Nutr Diabetes. 2017;7(7):e284.
7. Astbury NM, Piernas C, Hartmann-Boyce J, Lapworth S, Aveyard P, Jebb SA. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. Obes Rev. 2019;20(4):569-587.
8. Stevenson EJ, Allerton DM. The role of whey protein in postprandial glycaemic control. Proc Nutr Soc. 2018;77(1):42-51.
9. Adams RL, Broughton KS. Insulinotropic Effects of Whey: Mechanisms of Action, Recent Clinical Trials, and Clinical Applications. Ann Nutr Metab. 2016;69(1):56-63.
10. Nilsson M, Stenberg M, Frid AH, Holst JJ, Bjorck IM. Glycemia and insulinemia in healthy subjects after lactose-equivalent meals of milk and other food proteins: the role of plasma amino acids and incretins. Am J Clin Nutr. 2004;80(5):1246-1253.
11. Akhavan T, Luhovyy BL, Brown PH, Cho CE, Anderson GH. Effect of premeal consumption of whey protein and its hydrolysate on food intake and postmeal glycemia and insulin responses in young adults. Am J Clin Nutr. 2010;91(4):966-975.
12. Gunnerud UJ, Ostman EM, Bjorck IM. Effects of whey proteins on glycaemia and insulinaemia to an oral glucose load in healthy adults; a dose-response study. Eur J Clin Nutr. 2013;67(7):749-753.
13. Stanstrup J, Schou SS, Holmer-Jensen J, Hermansen K, Dragsted LO. Whey protein delays gastric emptying and suppresses plasma fatty acids and their metabolites compared to casein, gluten, and fish protein. J Proteome Res. 2014;13(5):2396-2408.
14. Salehi A, Gunnerud U, Muhammed SJ, et al. The insulinogenic effect of whey protein is partially mediated by a direct effect of amino acids and GIP on beta-cells. Nutr Metab (Lond). 2012;9(1):48.
15. Boirie Y, Dangin M, Gachon P, Vasson M-P, Maubois J-L, Beaufrère B. Slow and fast dietary proteins differently modulate postprandial protein accretion. Proceedings of the National Academy of Sciences. 1997;94(26):14930-14935.
16. Nilsson M, Holst JJ, Bjorck IM. Metabolic effects of amino acid mixtures and whey protein in healthy subjects: studies using glucose-equivalent drinks. Am J Clin Nutr. 2007;85(4):996-1004.
17. Silveira ST, Martinez-Maqueda D, Recio I, Hernandez-Ledesma B. Dipeptidyl peptidase-IV inhibitory peptides generated by tryptic hydrolysis of a whey protein concentrate rich in beta-lactoglobulin. Food Chem. 2013;141(2):1072-1077.
18. Lacroix IME, Li-Chan ECY. Isolation and characterization of peptides with dipeptidyl peptidase-IV inhibitory activity from pepsin-treated bovine whey proteins. Peptides. 2014;54:39-48.
19. Tulipano G, Sibilia V, Caroli AM, Cocchi D. Whey proteins as source of dipeptidyl dipeptidase IV (dipeptidyl peptidase-4) inhibitors. Peptides. 2011;32(4):835-838.
20. Mollahosseini M, Shab-Bidar S, Rahimi MH, Djafarian K. Effect of whey protein supplementation on long and short term appetite: A meta-analysis of randomized controlled trials. Clinical nutrition ESPEN. 2017;20:34-40.
21. Bowen J, Noakes M, Clifton PM. Appetite Regulatory Hormone Responses to Various Dietary Proteins Differ by Body Mass Index Status Despite Similar Reductions in ad Libitum Energy Intake. The Journal of Clinical Endocrinology & Metabolism. 2006;91(8):2913-2919.
22. Bowen J, Noakes M, Trenerry C, Clifton PM. Energy Intake, Ghrelin, and Cholecystokinin after Different Carbohydrate and Protein Preloads in Overweight Men. The Journal of Clinical Endocrinology & Metabolism. 2006;91(4):1477-1483.
23. Wirunsawanya K, Upala S, Jaruvongvanich V, Sanguankeo A. Whey Protein Supplementation Improves Body Composition and Cardiovascular Risk Factors in Overweight and Obese Patients: A Systematic Review and Meta-Analysis. J Am Coll Nutr. 2018;37(1):60-70.

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