Treat Your Supplement Delivery System Like You Do Your Patients... Individually

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It's a common conversation with seemingly many variables and much emotion involved; which supplement delivery system is superior? Capsules, tablets or liquids? Some will argue for the efficacy of liquids, others for the patient compliance of capsules and still others for the dissolution control of tablet formulations. But is this simply assumption or truth? Hearsay or fact?

Dr. David A. Tallman, DC, ND notes in his October 4, 2010 Natural Products Insider article, "Naturopathic physicians .... are arguably the most highly trained physicians with regard to the use of natural products."[1] As naturopathic medicine becomes increasingly more integrated into society's medical system and our practitioners move more frequently into the media spotlight, we need to have this topic down to a science, not an opinion.

The purpose of this article is to lay out the facts on the subject. From there, as I tell my patients, you can decide what to do with the information.

First, just as there is no one treatment best for all patients, there is no one supplement delivery system that is best for all situations. In fact, tablets, capsules, liquids, powders, gels, sprays and topicals all represent effective delivery methods for the supplements you prescribe to your patients. The goal is to prescribe the delivery system which offers the greatest stability, bioavailability, convenience, tolerance and efficacy for the patient for that particular ingredient or combination of ingredients.

Liquids

Liquid delivery systems have a long history of use in medicine and are made using various methods including extraction of key constituents through the use of alcohol, water, honey, glycerin, vinegar or oils. The benefits of a liquid delivery system are multi-dimensional and may depend on the menstruum used for extraction. Liquids are easy to swallow making them particularly useful for the pediatric and geriatric populations as well as for dosing supplements via feeding tubes or supplementing a liquid diet.

Liquid formulations also have the benefit of bringing patients "closer" to their medicine and in certain cases, such as with bitters, will actually start their therapeutic actions as soon as the formulation hits the taste buds. Shelf life is another factor often favoring liquid delivery systems. The shelf life of alcohol tinctures in particular far exceeds the shelf life of other delivery systems making them valuable options for stocking a pharmacy with a slow rate of turnover or for medicines which are dosed only occasionally rather than on a routine basis.

On the other hand, tinctures are often stored in glass bottles which can easily break or leak. More frequent dosing often becomes challenging and if the taste is unpalatable may lead to decreased compliance. Tinctures, however, often come with a higher price tag and are not always financially viable for all patient populations.

Capsules

Capsules are another commonly prescribed supplement delivery system with their own set of pros and cons. For some patients, capsules have the advantage of being easier to swallow than tablets due to their smooth texture as well as being an effective system to conceal offensive odors and tastes. This is also the delivery system of choice for preserving the integrity of sensitive molecules such as CoQ10 and for delivering oil and fat-soluble nutrients to your patients in a convenient, usable form.

Hard shelled capsules are dependent on a patient's internal gastrointestinal environment and thus are restricted to a tight pH range which may differ from patient to patient. Soft gels do not have this constraint. (More discussion on disintegration standards and testing below.)

Moisture is the enemy of both capsules and tablets, while heat can easily lead to melting and sticking together of capsules resulting in damaged product and consequently reduced compliance. Instructing patients on storage instructions is necessary to ensure predictable, effective results, particularly when it comes to temperature related storage directions for capsules.

Tablets

Tablets offer manufacturers the ability to include higher quantities of material per tablet which lowers the number of "pills" required for a certain dose. Since the same quantity of ingredients can be incorporated into a lesser number of tablets than capsules, patients can take fewer tablets for their required dosage as well as pay less. Both characteristics increase compliance of tablet delivery systems

leading to improved effectiveness of your recommendations. This brings up the highly debated and commonly held belief that tablets are often too highly compressed thus inhibiting disintegration of the tablet. If you are recommending supplements from a reputable supplement company you need not be concerned about this. Virtually all reputable supplement companies which NDs do business with are GMP (Good Manufacturing Practices) compliant and will have standard USP designated procedures in place to test each batch of tablets for proper disintegration times; some will even test each batch multiple times throughout the manufacturing process.

USP guidelines state that disintegration of tablets in an aqueous solution should be complete within a certain number of minutes depending on the type of tablet (sublingual, enteric coated etc.) As long as the company you are working with is GMP certified the disintegration time of tablets is a non-issue; the tablets you are buying will break down at the proper place and at the proper time. Finally, tablets can be notched allowing the patient to divide their tablets into smaller sizes for ease of swallowing or for changing dosage without buying a new size.

On the downside, tablets, unlike capsules, cannot hide undesirable odors or tastes potentially lowering patient compliance and can be more difficult to swallow for some. Tablets are susceptible to moisture and need to be stored in a cool, dry place.

Disintegration Testing

The United States Pharmacopeia (USP) outlines the disintegration testing process that companies must follow in order to be GMP compliant. Disintegration is defined by USP as *"that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core"* [2]

Table 1 – USP Disintegration Method and Immersion Media Information

Dosage Form	Form Preparation	Procedure	Immersion Fluid	Media Temp.	Immersion Time
tablet	uncoated, sublingual	standard disintegration	water	37°C ± 2°C (body temperature-BT)	30 minutes
	coated (plain and film)	standard disintegration	water	37°C ± 2°C	5 minutes at RT then 30 minutes at BT
tablet capsule	delayed-release (enteric-coated)	standard disintegration	simulated gastic fluid (SGF), simulated intestinal fluid (SIF)	37°C ± 2°C	1 hr in SGF then in SIF for the allotted time according to form preparation
capsule	hard gelatin, hard shelled	standard disintegration	acetate buffer (pH 4.5 ± 0.05)	37°C ± 2°C	30 minutes
	soft shelled, soft gelatin (softgels)	rupture	water	N/A	15 minutes

**Information in this table was obtained from USP 32. The equipment used was the Hanson Research QC-21, 2 basket test system (6 tablet capacity per basket).

The table above summarizes the USP disintegration testing process.[3] The procedure requires water to be used as the testing solution for disintegration of tablets and soft gel capsules while hard shelled capsules and extended release delivery systems must use an acetate buffer or gastrointestinal simulated environment for testing. This confirms the need for hard shelled capsules to be used cautiously in patients with suspected or confirmed hypochlorhydria, whereas the status of gastrointestinal pH does not necessarily affect the disintegration of other delivery forms. As noted previously, if a company is GMP certified, they will use USP standard testing and their tablets and capsules will disintegrate as necessary for reproducible, effective results in your patients.

Excipients within Capsules and Tablets

Supplement excipients are added to formulations for various reasons such cellulose, a non-reactive plant fiber, to hold a tablet together and regulate the rate at which the tablet disintegrates in the stomach. Hypermellose (HPMC) from cellulose is also an ingredient in vegetarian capsules. Still other ingredients are used to protect fat-soluble ingredients from oxidation or to protect active ingredients during storage; for example silicon dioxide is used to absorb moisture and also doubles as a "space filler" in some capsules.

The majority of pharmaceutical and dietary supplements today contain minute traces of stearates. Stearates, the most common of which is magnesium stearate, are used to ensure that finished products are of uniform size, weight, texture, and shape. These agents are necessary to ensure reproducible and reliable results dose after dose in both capsules and tablets.

Magnesium stearate is widely used for pill manufacturing both in the pharmaceutical and nutraceutical worlds, and consequently is one of the most studied excipients used today with a long and recorded safety track record. Magnesium stearate, the salt of stearic acid, has been granted GRAS (generally recognized as safe) status whereas other less frequently used excipients may not have a similar safety track record.

Concerns over whether excipients such as magnesium stearate inhibit the body's ability to absorb the nutrients are grossly misunderstood. Stearic acid is one of the most common long-chain fatty acids found in a large number of animal and vegetable fats including olives, beef, and chocolate (see Table 2) and is extremely well-absorbed. In fact, the absorption of stearic acid is comparable to palmitic acid and oleic acid (the major constituent of olive oil).[4]

Table 2 – Stearic Acid Content of Common Foods[5]

Food	Stearic Acid Content
Fish oil, cod liver (1 oz.)	784 mg
Fish oil, salmon (1 oz.)	1,176 mg
Olive oil (1 oz.)	700 mg
Sesame oil (1 oz.)	1,344 mg
Soybean lecithin (1 oz.)	812 mg
Soybean oil (1 oz.)	1,064 mg
Sunflower oil, linoleic (1 oz.)	1,260 mg
½ chicken breast (w/out skin)	100 mg
Cheddar cheese (1 oz.)	1,120 mg
Butter (1 pat)	500 mg
Semi-sweet chocolate (1.45 oz.)	4,800 mg

To help put it into proper perspective, a high quality tablet may contain 20 mg of stearic acid which means that a daily recommendation of six (6) tablets would contain approximately 120 mg of stearic acid. In comparison, mean stearic acid intake from food sources is 5.7 g per day (5700 mg or 2.3% of calories) for women and 8.2 g per day (8200 mg or 2.8% of calories) for men, 20 years of age and older, based on data from the National Health and Nutrition Examination Survey (NHANES), 2001-2002.[6]

The average patient will receive far more stearic acid from their diet than from their supplements. And, unlike other long chain saturated fatty acids (lauric, myristic, and palmitic acids) stearic acid has not been shown to raise both total and LDL cholesterol levels.[7,8,9]

In Summary

There are several key takeaways from this article:

Be sure to do business with reputable companies who are cGMP compliant (via third party inspection and certification) and using USP standards where applicable. Recall that GMPs are guidelines that outline the aspects of production and testing that can impact the quality of the products you are recommending.

Ensure the company you are working with has efficacy and safety data for the supplements and protocols they are recommending. When considering which supplement delivery systems to prescribe consider stability, bioavailability, convenience, tolerance and efficacy.

A company that has a "one size fits all" philosophy in regards to ingredient delivery system may not be giving your patients the best delivery form for each of the different formulations.

In conclusion, do your homework, work with reputable companies and treat your supplement delivery systems like you do your patients - individually.

About the Author

Dr. Garilli is a former U.S. Marine turned Naturopathic Doctor, graduate of Bastyr. Currently, Dr. Garilli lives and practices in Northern California specializing in the treatment of obesity and other lifestyle related chronic diseases through FLT as well as seeing children with autism, ADHD/ADD and congenital heart conditions. Additionally, she consults with Metagenics to support the ND specific educational platform, speaking events and clinical support.

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References

1. Tallman, D. A., Berry-Tallman, R. Naturopathic Market Offers Opportunity. *Natural Products Insider*. Oct. 2, 2010. http://www.naturalproductsinsider.com/articles/2010/10/naturopathic-market-offers-opportunity.aspx?pg=3
2. USP Guidelines, Dietary Supplements/(2040) Disintegration and Dissolution of Dietary Supplements. http://www.usp.org/pdf/EN/USPNF/genChapter2040.pdf
3. Middleton, A., Holden, J., et. al. Preliminary Disintegration Analysis of Commercially Available Multivitamin/Mineral Dietary Supplements in the Adult US Market. United States Department of Agriculture – ARS – Beltsville Human Nutrition Research Center, Nutrient Data Laboratory, NIH – Office Of Dietary Supplements. Beltsville, MD. http://www.ars.usda.gov/SP2UserFiles/Place/12354500/Articles/AOAC09_Disintegration.pdf
4. Bonanome, A., Grundy S.M. Intestinal Absorption of Stearic Acid after consumption of High Fat Meals in Humans. *J. Nutrition*. Nov. 1989;Vol. 119 no. 11, 1556-1560.
5. Metagenics Educational Document, Tablet Delivery & Stearic Acid.
6. What We Eat in America, NHANES, 2001-2002. Nutrient Intakes: Mean Amount Consumed per Individual, One Day, 2001-2002. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/Table_1_BIA.pdf
7. Yu S, Derr J, Etherton TD, et al. Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic. *Am J Clin Nutr*. 1995;61:1129-1139.
8. Bonanome A, Grundy SM. Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. *N Engl J Med*. 1988;318:1244-1248.
9. Stearic Acid Monograph. Beef Facts, Human Nutrition Research, 2008. http://www.beefresearch.org/CMDocs/BeefResearch/Stearic%20Acid.pdf