Innophos®

Whitepaper

Co-Processed Multifunctional Excipients in Tableting

Simplify Labels and Enhance Compressibility

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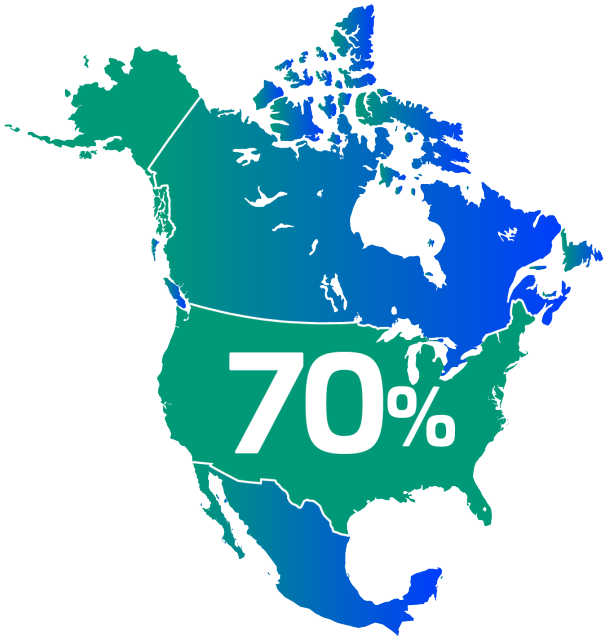
Overview

The global dietary supplement industry is experiencing unprecedented growth in product development from existing players as well as new entrants. To gain a competitive edge, many supplement makers formulate with multiple ingredients, including minerals, amino acids, herbals, and vitamins in a single tablet. Doing so allows these companies to position their products with additional benefits compared to other delivery systems in the same category. However, multi-ingredient formulations also create marketing and operational challenges for manufacturers.

A trend dominating the supplement market is the clean label movement. This trend is increasing pressure on manufacturers to simplify labels by reducing the number of ingredients. Additionally, consumers desire smaller, easier-to-swallow tablets for children and senior citizens. To meet these consumer trends, dietary supplement manufacturers should consider CPMEs as a key solution.



In 2019, 70% of all supplement introductions in North America had at least one clean label claim[1]

In this paper, you will learn:

- What CPMEs are
- Advantages of CPMEs
- How CPMEs enable manufacturers to reduce ingredients
- Why CPMEs deliver more in a smaller pill
- Comparison of Innophos CPMEs vs. conventional excipients

What CPMEs are

The International Pharmaceutical Excipients Council (IPEC) defines excipient as substance other than the Active Pharmaceutical Ingredient (API) which have been appropriately evaluated for safety and are intentionally included in a drug delivery system.

Dietary supplement manufacturers should consider CPMEs as a key solution

Methods of CPME manufacture may include standard unit operations such as granulation, spray drying, melt extrusion, milling etc. The methods of manufacture and ratios of components depend on the materials used, their form (e.g. whether powders or liquid), specific physical properties desired, and performance goals.

Excipients are divided into 4 major types:

I. Single-entity excipients are one component ingredients usually listed in the FDA's dietary supplement database.

II. Mixtures (or blends of multiple excipients) are simple blends of single entities using various low-energy blenders.

III. Chemically-modified excipients which form new/novel excipients.

IV. Co-processed multifunctional excipients (CPMEs) are a combination of two or more compendial or non-compendial excipients designed to physically modify their properties in a manner not achievable by simple physical mixing, and without significant chemical change.

Advantages of CPMEs

For Consumers

Tablets made with CPMEs vs. conventional excipients offer many advantages for consumers. The tablets are smaller due to fewer ingredients and higher compressibility, which makes them easier to swallow. Additionally, tablets made with CPMEs may have fewer ingredients resulting in a simpler label. Finally, supplements made with CPMEs may include a greater variety of active nutrients and therefore can provide improved efficacy and convenience, as one tablet can take the place of many.

For Supplement Manufacturers

CPMEs provide formulation and operational benefits. They also provide flexibility to formulators by reducing the number of excipients required and thereby “making room” for additional active ingredients.

From an operational standpoint, CPMEs decrease production time due to the reduced complexity in the procurement, testing, QC, and manufacturing process. The improved compressibility of some CPMEs allows manufacturers to run their tablet presses with lower pressure, which extends the life of the equipment. CPMEs also help to improve overall yield and reduce waste through enhanced tablet integrity.

Study of A-TAB® MD vs. Conventional Excipients

A-TAB® MD is a co-processed excipient consisting of anhydrous dicalcium phosphate and maltodextrin. This product is used as a diluent, binder, and flow agent and is a source of both calcium and phosphorus.

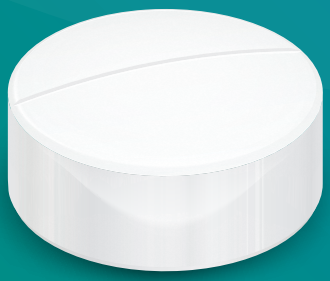
Dicalcium phosphate and maltodextrin are two of the most commonly used excipients in nutraceutical applications, which means that when supplement producers use A-TAB® MD, they do not need to add additional excipients to the label such as: microcrystalline cellulose, calcium carbonate and silicon dioxide. In addition, dicalcium phosphate is compliant with USP (United States Pharmacopoeia) and maltodextrin is NF (National Formulary) compliant and both are non-GMO, Kosher, and Halal certified.

In this study, we compared A-TAB® MD to conventional excipients in the production of a commercially available greens herbal blend tablet. The conventional excipient batch used microcrystalline cellulose as a diluent source, maltodextrin as the binder, and silicon dioxide as the flow agent. Dicalcium phosphate and calcium carbonate were included as calcium/phosphorus sources.

Greens herbal blend tablet formulations made with conventional excipients vs. A-TAB® MD

8 INGREDIENTS reduced to 4 INGREDIENTS using A-TAB® MD

TABLETS MADE USING CONVENTIONAL EXCIPIENTS



Greens Herbal Blend* (33.57%)
Silicon Dioxide (0.84%)
Dicalcium Phosphate (12.11%)
Calcium Carbonate (27.27%)
Maltodextrin (6.71%)
Microcrystalline Cellulose (16.98%)
Croscarmellose Sodium (1.68%)
Magnesium Stearate (0.84%)

TABLETS MADE USING A-TAB® MD

Greens Herbal Blend* (55.94%)
A-TAB® MD (39.86%)
Croscarmellose Sodium (2.80%)
Magnesium Stearate (1.40%)

*Greens Herbal Blend: Organic Wheat Grass Powder, Organic Barley Grass Powder, Organic Parsley Leaf Powder, Organic Kale Powder, Organic Broccoli Powder, Organic Spinach Powder, Organic Chlorella Powder, Organic Spirulina Powder, Organic Alfalfa Powder and Organic Beet Root Powder

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Results from A-TAB® MD Study

50% **Reduction** in number of ingredients

50% **Increase** in average hardness

25% **Decrease** in average thickness

34% **Reduction** in tablet weight

50% **Reduction** in processing time

Benefits of A-TAB® MD

Our study findings confirm that A-TAB® MD replaces the functionality of microcrystalline cellulose, dicalcium phosphate, calcium carbonate, silicon dioxide, and maltodextrin.

- Simplifies label
- Improves manufacturing efficiency
- Results in smaller tablet size

Physicochemical properties of tablets made with conventional excipients vs. A-TAB® MD[2]

	TABLETS MADE USING CONVENTIONAL EXCIPIENTS	TABLETS MADE USING A-TAB® MD
Total Number of Ingredients	**8**	**4**
Average Hardness (KP)	23.01	34.55
Average Thickness (mm)	7.59	5.72
Average Weight (mg)	1185	788
Processing Time (mm:ss)	23:04	11:46
Average Friability (%)	0.037	0.036
Bulk Density (g/ml)	0.56	0.51
Tapped Density (g/ml)	0.80	0.71

Study of NUTRA-TAB® vs. Conventional Excipients

NUTRA-TAB®, a co-processed excipient, uses tricalcium phosphate and guar gum as a diluent, binder, and flow agent, and provides calcium and phosphorus.

This study tested NUTRA-TAB® against conventional excipients in the production of a commercially available multivitamin. In the conventional excipients batch, microcrystalline cellulose is the diluent source, maltodextrin is the binder, and silicon dioxide is the flow agent. Dicalcium phosphate and calcium carbonate are the calcium/phosphorus sources.

Multivitamin tablet formulation made with conventional excipients vs. NUTRA-TAB®

8 INGREDIENTS reduced to 4 INGREDIENTS using NUTRA-TAB®

TABLETS MADE USING CONVENTIONAL EXCIPIENTS

Multivitamin Blend* (30.77%)
Colloidal Silicon Dioxide (0.77%)
Dicalcium Phosphate (13.85%)
Calcium Carbonate (30.77%)

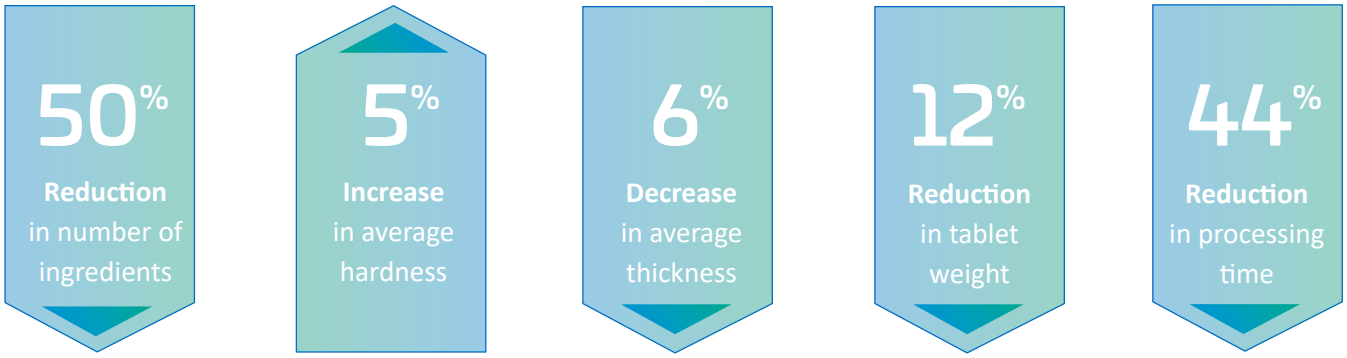
Maltodextrin (6.15%)
Microcrystalline Cellulose (15.38%)
Croscarmellose Sodium (1.54%)
Magnesium Stearate (0.77%)

TABLETS MADE USING NUTRA-TAB®

Multivitamin Blend* (40.00%)
NUTRA-TAB® (57.00%)
Magnesium Stearate (1.00%)
Croscarmellose Sodium (2.00%)

*Multivitamin Blend: Vitamin A, Vitamin C, Vitamin E, Vitamin K, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B6, Vitamin B9, Vitamin B12 and Vitamin B5

Results from NUTRA-TAB® Study



Benefits of NUTRA-TAB®

Tablets made with NUTRA-TAB® excipients have the same level of calcium as those made with conventional excipients but 3X more phosphorus content. Lighter in weight than those made with conventional excipients, NUTRA-TAB® tablets have the potential to contain higher dosage levels of active ingredients. What's more, NUTRA-TAB® can help to reduce production time, increase efficiency and save money improving manufacturing efficiency.

Physicochemical properties of tablets made with conventional excipients vs. NUTRA-TAB® MD[2]

	TABLETS MADE USING CONVENTIONAL EXCIPIENTS	TABLETS MADE USING NUTRA-TAB®
Total Number of Ingredients	**8**	**4**
Average Hardness (KP)	15.24	16.07
Average Thickness (mm)	6.75	6.33
Average Weight (mg)	1180.50	1034.50
Processing Time (mm:ss)	46:13	25:42
Average Friability (%)	0.18	0.32
Bulk Density (g/ml)	0.74	0.71
Tapped Density (g/ml)	0.95	0.90

Conclusion

Co-processed excipients have gained popularity in recent years due to their many advantages over conventional directly compressible excipient sources. Tablets made with CPMEs can be made with about half the number of ingredients as those with conventional excipients leading to a simpler label. By replacing several conventional excipients with a single CPME, manufacturers can reduce inventory and complexity. Equally as important, the greater compressibility achieved with a CPME enables smaller and lighter tablets with no reduction in dosages of active ingredients. As a result, more actives can be added to the CPME tablet, enabling less frequent dosing. From a manufacturing standpoint, CPMEs can reduce production time, and improve efficiency by as much as 40%. Plus, CPMEs display better physicochemical characteristics indicating superior tablet integrity with improved performance and robustness.

In the highly competitive generic and branded nutritional supplements industry, CPMEs provide a solution for creating more label-friendly tablets with more active ingredients while supporting lean manufacturing and faster speed to market.

Reach out to our technology team to learn how CPMEs can be a key solution for you.

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[1.] Innova Market Insights, Clean Label Supplements in North America 2020

[2.] Physiochemical Properties of Tablets Containing Excipients:

- Friability testing is a laboratory technique used by the pharmaceutical industry to determine the durability of tablets during transit. This testing involves repeatedly dropping a sample of tablets over a fixed time, using a rotating wheel with a baffle.
- Hardness testing, also known as diametric compression testing, is the measurement of compression force or breaking force at failure to determine the tensile strength of a tablet.
- Thickness is simply the diameter of the tablet, and thickness testing is an important QC procedure for tablet packaging.
- Density is weight of material per unit of volume. You can gain information about inter-particulate interactions that influence the bulking properties of a powder and interfere with powder flow by comparing the bulk and tapped densities; such a comparison can be used to index the ability of the powder to flow.