

Investigation of vitamin and mineral tablets and capsules on the Canadian market

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ABSTRACT PURPOSE: The goal of this study was to investigate the disintegrating properties of tablets and capsules containing minerals and vitamins commercially available on the Canadian market and to review their label information. **METHODS:** The labels were examined for product-related information. The first disintegration test stage was performed using Simulated Intestinal Fluid (SIF) pH 6.8 for 20 minutes. Products which did not disintegrate were further investigated using USP disintegration conditions for dietary supplements. **RESULTS:** The provided label information is difficult to understand and in some cases pseudo-scientific. Thirty out of thirty-nine tablets and six out of ten capsules had a Drug Identification Number (DIN). Twenty-one of thirty-nine tablets and four out of the ten capsules did not disintegrate within 20 minutes. Using the USP disintegration conditions for dietary supplements nine tablet products did not fully disintegrate but all capsules passed the test. None of the three “time-released” products disintegrated under the applied conditions. **CONCLUSIONS:** Industry should follow already existing label recommendations more closely to allow the consumers to make an informed decision on their products by providing only essential information rather than using pseudo-scientific terms. The results of the disintegration study indicated that disintegration, one of the most basic quality control parameters, is still a concern for dietary supplements.

INTRODUCTION

Absorption of minerals, vitamins, drugs or food is a complex process. It can be generalized as passive absorption via a paracellular pathway, facilitated transport through membranes via transporters and active energy consuming transport mechanisms (1, 2). In the case of facilitated and active transport, the uptake mechanism can be specific to individual substances or to substance classes e.g. ions, amino acids, peptides or carbohydrates (3, 4). Absorption of calcium for example depends on the location within

the gut (5). In the duodenum it happens via an active transport mechanism, while in the jejunum and ileum calcium is absorbed via passive diffusion. The extension of the active calcium uptake is greater as compared with the passive diffusion. In the duodenum, calcium enters the cytoplasm of enterocytes through a calcium channel ECaC2 (6). In the cytoplasm, a carrier protein called “calbindin” transports calcium to the basolateral membrane where it is pumped out of the cell via a calcium-ATPase and becomes systemically available. The availability of calbindin depends directly on vitamin D. Another example for partially localized mineral uptake is iron. Efficient absorption of inorganic iron requires an acidic environment due to the pH dependent solubility of iron (7). Drugs, such as antacids, proton inhibitors or excipients, which interfere or neutralize gastric acid secretions, may therefore, interfere with iron absorption. An acetic pH condition is only in the stomach and in the beginning of the duodenum before bile, and pancreatic secretions neutralize gastric fluids (8). Alternatively, organic bound iron is absorbed by endocytosis of hemoglobin or myoglobin by the enterocytes. This process is not limited to acetic environments and can take place throughout the gut. However, available supplements contain inorganic iron. An example of a specialized absorption of vitamins is cobalamin (Vitamin B12). The absorption depends on the availability of an intrinsic factor secreted by the stomach (9). Both molecules bind to each other to form a complex that can bind to specific receptors in the brush border of the intestine and are absorbed (8). The given examples clearly show that the absorption of minerals and vitamins is a complex process which involves in some cases specific transporters. Furthermore, for certain minerals or vitamins the absorption via active transport might be limited to absorption windows, favourable pH values, the presence of transporters or may depend on the availability of co- or intrinsic factors.

Active ingredients can only be absorbed if they are released into solution from the dosage form. Disintegration is the first step in this process for immediate release dosage forms. The goal of this study was to investigate the disintegrating properties of tablets and capsules containing minerals and vitamins commercially available on the Canadian market and to review their label information.

MATERIALS AND METHODS

Products were purchased from commercial outlets or received from professional centers and are listed in Tables 1 and 2.

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Table 1. Tested Mineral and Vitamin Tablets: The front label information is the information which can be seen together with the product name. DIN is the drug identification number, Yes or No indicate if the product had a DIN, Stage 1 and 2 refers to the performed disintegration tests, + fully disintegrated, - not fully disintegrated, +/- not all units disintegrated but test was passed, - & - controlled release dosage form did not disintegrate within 30 minutes or 90 minutes. Other label information refers to additional text which was found on the label to describe the product.

Brand/Product Manufacturer	Front label information	Units DIN	Lot #	Stage 1 Stage 2	Directions	Other information	label
Mel-Vita Melaleuca Inc. Idaho Falls, ID	Multivitamin & Multimineral Supplement	60 Yes	14005	+	For therapeutic use only To be taken as supplement with meals Adult dose above 34 kg 2 tablets per day	This unique formulation has 15 vitamins and minerals with the established Canadian R.D.I. providing the nutrients your body needs for optimum health	
Cell-Wise Melaleuca Inc. Idaho Falls, ID	Vitamin E, C, Zinc Beta Carotene, Selenium	60 Yes	13029	- +	Tablets to be taken with meals For adults only 2 tablets per day	Contains only the finest-quality ingredients in a balanced formula to complement your daily fruit vegetable and whole grain in take Proprietary formula exclusive to Melaleuca	
Right Choice A.M. Multi Formula Body Wise International LLC, Tustin, CA	Now with Pycnogenol Dietary Supplement	90 No	402113	+	Take three tablets with your morning meal	Pycnogenol is registered trademark...	
Right Choice Body Wise International LLC, Tustin, CA	P.M. Multi Formula Now with Pycnogenol Dietary Supplement	90 No	403011	- +	Take three tablets with your evening meal Dietary Supplement	Pycnogenol is registered trademark... Krebs Cycle Chelated Mineral Replenishment factors are uniquely formulated	
Centrum Whitehall-Robison Inc. Mississauga, ON	Centrum Multi Vitamin Multi Mineral Formula New Formula	100 Yes	321461	+	1 tablet daily		
Central-Vite Forte, Safeway Select Safeway Canada Calgary, AB	High potency multivitamins and minerals forte formula, Essential vitamins and minerals, now with lutein	100 Yes	311230CS 6	+	Take one tablet daily with a meal or as directed by a physician or healthcare practitioner For therapeutic use only	Made to US-Pharmacopeia quality, purity and potency standards. Laboratory tested to dissolve within 60 minutes	
one tablet daily Adults Safeway Canada Calgary, AB	24 vitamins and minerals & beta carotene, Scientifically balanced formula	90 Yes	3L0580BY P	+	Take one tablet daily with a meal or as directed by a physician or healthcare practitioner For therapeutic use only	Made to US-Pharmacopeia quality, purity and potency standards Laboratory tested to dissolve within 60 minutes	
One A Day Advance Adults Bayer Inc. Toronto, ON	24 vitamins and Minerals, Feel your best, Advance, Adults Formula	90 Yes	310120A6 Q	+	One tablet daily	Scientifically balanced formula for adults 24 Vitamins and Minerals Advanced formula	
London Naturals Multi Vitamin Iron Free London Drugs Richmond, BC	Multivitamin and mineral complex, with extra Bs and lipotropics one per day	60 No	66901	+	1 tablet per daily, or as directed by professional For therapeutic use only	Certified Guaranteed Excellence	
One Tablet Daily London Drugs Limited Richmond, BC	London Drugs Scientifically balanced formula, Adults,	90	65387	Yes +	Take 1 tablet daily, or as directed by a physician For therapeutic use only		

Basic 3 Atkins Nutritionals Inc. Ronkonkoma, NY	23 vitamins and minerals & Beta Carotene Atkins Essential Nutrients Maintains Normal Blood Sugar Level, Advanced Antioxidants	90 No	0497B4	- +	Take three tablets daily, for adult use only For therapeutic use only	Absorb Best TM
Advanz Holista Health, Burnaby, BC	Most advanced complete daily nutrients from A to Z Extra Strength Daily Multivitamin & Multimineral with iron Holista	90 Yes	60040	+	One Tablet daily or as recommended by a physician	
Usana Health Science Inc. Salt Lake City, UT	Essentials Multi Mineral	84 Yes	9961	+	Information not available	Laboratory tested for guaranteed quality Meets specifications for potency, uniformity, and disintegration, as appropriate
Kirkland Signature Formula Forte Cosco Wholesale Canada, Ottawa	With Lutein 30 essential multivitamins with beta carotene	365	4BA2002	Yes - -	Take one tablet daily with meal For therapeutic use only	Other ingredient: Lutein
Multiple Vitamins Pharmetics Inc. Laval, QC	Plus iron, Tanta	100 Yes	43608A	+/-	As vitamin and iron supplement Take one tablet with a meal or as directed by a health professional	
Ultimate One for Men Active Nu Life, Richmond Hill, ON	Multi vitamin and mineral, Active	60	0045K3	Yes - -	Take 1 caplet daily, with a meal or as directed by a health practitioner For therapeutic use only	In a specially designed base for man
Ultimate One for Women Active Nu Life, Richmond Hill, ON	Multi vitamin and mineral, active	60 Yes	0934A3	- +	Take 1 tablet with a meal or as directed by a health professional For therapeutic use only	In a specially designed base for woman
Wampole Multi Vitamins & Minerals Wampole Brands Inc. Toronto, ON	Fortified with 31 Vitamins Minerals and Nutrients with Lycopene & Lutien	180	566878	No - +	Take 1 tablet with a meal or as directed by a health professional For therapeutic use only	100 % Natural Source
Complete Multi- Adult Tabs Wampole Toronto, ON	Complete Multi- Adult 29 Essential vitamins and minerals	100	539997	Yes - +	One tablet daily with food or after meal For therapeutic use only	Naturally Canadian since 1893
Trophic Trophic Canada LTD Penticton, BC	Multiple Vitamins & Minerals	90 Yes	96905B	- -	Take 1 tablet daily or as directed by physician For therapeutic use only	Purely, Naturally, All Canadian Manufactured under the unique Albion laboratories process

						whereby the minerals are chelated by amino acids, peptides and polypeptides
Sisu Only One Sisu Enterprises Co. Inc. Burnaby, BC	One a day multi vitamin and mineral	60 Yes	40089	- -	Take 1 tablet daily with a meal or as directed by a health professional For therapeutic use only	
Super Multi Plus Iron Natural Factors Coquitlam, BC	All you need is one Multi vitamin and Mineral Complex for Everyone	90 Yes	72290	+	1 tablet daily or as directed by a health practitioner For therapeutic use only	
Multidyn Professional Health Products Innisfail, AB	Professional Health Products	90 Yes	F3942	+	For therapeutic use only One tablet with each meal	
Super Swiss One "50" Swiss Herbal Remedies LTD Richmond Hill	Multi Vitamin & Mineral With Lutein, Natural Sources	60 Yes	2652	- & -	Adults take one caplet daily For therapeutic use only	Time-release caplets are designed to gradually release their contents over a prolonged period of time
Swiss One "80" Swiss Herbal Remedies LTD Richmond Hill	Hi Potency Multivitamin One per day With HVP Chelated minerals, time- release	60 Yes	1741	- & -	Adults take one caplet daily For therapeutic use only	Time-release caplets are designed to gradually release their contents over a prolonged period of time
Quest Exta Once A Day PanGeo Health Brands Inc. Vancouver, BC	Multiple Vitamins & Minerals Premium Quality	60 Yes	517780	- +	One tablet with morning or noon meal For therapeutic use only	Manufactured in Canada according to good manufacturing practices...
Multigenics Without Iron Megagenics Inc. San Clemente, CA	Optimum Multiple Vitamin/Mineral Plan Fast release tablet Dietary Supplement Metagenics: Genetic Potential Through Nutrition	90 No	93072	- +	Servings size 6 tablets with meal	Multigenics without iron is a unique vitamin and mineral formula designed for optimal disintegration and digestibility... Genetic potential through nutrition
Multigenics Megagenics Inc. San Clemente, CA	Optimum Multiple Vitamin/Mineral Plan Fast release tablet Dietary Supplement Metagenics: Genetic Potential Through Nutrition	90 No	103088	- +	Servings size 6 tablets with meal	Selected nutrients to support liver and adrenal function Genetic potential through nutrition
Mega Men General Nutrition Canada, Mississauga, ON	GNC, Multi Vitamin & Mineral, Timed Release	180 Yes	568152	- & -	Take two per day or as directed by your physician For therapeutic use only	Timed Release, multivitamins & Minerals Now with Chloraseal coating

Centrum Forte Whitehall-Robison Inc. Mississauga, ON	High potency Multivitamin Multimineral Formula New Formula	60 Yes	316153	+	1 Tablet daily Therapeutic use only	Complete from A to Zinc
Basic Vita-Vim Jamieson Laboratories, Toronto, ON	20 Minerals, Vitamins & Nutrients Level 1 potency multivitamin	90 Yes	373212	+	Take one caplet daily with a meal For therapeutic use only	No sugar, No Salt, No Starch, No Gluten Guarantee of Absolute Purity & Full Potency
Mega Vita Jamieson Laboratories, Toronto, ON	37 vitamins, Minerals & Nutrients Level 4 Potency Multivitamin	60 Yes	381678	- +	Take one caplet daily with a meal For therapeutic use only	No sugar, No Salt, No Starch, Gluten free
Essential Balance Pharmavite Corp. Thornhill, ON	Nature Made Multivitamin & minerals With selenium & folic acid For adults USP Quality	100 Yes	NK20393	- +/-	As a vitamin and mineral supplement for adults take one tablet daily with a meal , supplying For therapeutic use only	
Ultra Balance III Douglas Labs Pittsburgh, PA	A Vitamin & Mineral Supplement For therapeutic use only	180 Yes	427504	- +/-	Take 6 tablets daily (3 times 2) or as directed by your health care practitioner	
Multi Vite 109 Seroyal Int Inc. Toronto, ON	Multiple Vitamin-Mineral Supplement Genestra Brands	90 Yes	754203	+	For therapeutic use only Take one tablet two times daily with meals or as recommended by your health care practitioner	Hypoallergenic product
Exact Loblaws Inc, Montreal, QC	Multivitamins 8 essential vitamins for adults no preservatives added	250 Yes	F05301	+	Take 1 tablet daily with a meal or as directed by a health professional For therapeutic use only	Trust Exact quality
Exact Essentra Forte Loblaws Inc, Montreal, QC	Vitamins & Multiminerals high potency formula with lutein	100 Yes	F05770	+	Take 1 tablet with a meal or as directed by a health practitioner	
Multi+ Ehn Inc, Toronto, ON	Complete, high potency Multi- Vitamin & Bioactive Mineral Formula	60 DIN pendi ng	30437	- +	Take two to four tablets daily For therapeutic use only	Contains no artificial color, flavours sweeteners or preservatives, corn, diary, egg, whet , soy or animal products
Omnivite Omnivite Nutrition Portland, OR	With iron dietary multi vitamin- mineral supplement	180 No	0652304	+	As a dietary supplement, Adults take 2 tablets 2-3 times per day after meals	2-4 tablets per day provide optimal Daily supplementation to a well rounded whole foods diet and proper lifestyle, 6 tablets provide high level supplementation for chronic malnutrition, high stress or athletes This product is low allergenic

Table 2. Mineral and Vitamin Capsules: The front label information is the information which can be seen together with the product name. DIN is the drug identification number, Yes or No indicate if the product had a DIN, Stage 1 and 2 refers to the performed disintegration tests: + fully disintegrated, - not fully disintegrated, +/- not all units disintegrated but test was passed, - & - controlled release dosage form did not disintegrate within 30 minutes or 90 minutes. Other label information refers to additional text which was found on the label to describe the product.

Brand/Product Name Manufacturer	Front label information	Units DIN Lot # Stage 1 Stage 2	Directions	Other label information
Multi-encap Thorne Research Inc. Dover, IH	Thorne Research without copper and iron	180 Yes 2042040 - +	For Adult therapeutic use only	
Nutri-plex NaturPharm Inc. Toronto	Daily Multi-Vitamin Mineral Formula Hypoallergenic, Iron free Blending tradition with Science	180 Yes D0011 - +	1 capsule 3 times daily with meal or as recommended by a health care practitioner	Contents are free of all artificial ingredients, preservatives, additives and common allergens
Multi IIs Tyler Holdings Surrey, BC	New size, smaller, easier to swallow capsules Selekt	360 Yes 030984 - +	Vitamin and mineral supplement for adults For therapeutic use only Take two capsules three times daily or as recommended by physician	This product is dispensed exclusively by health care professionals Contains no chemical binders, fillers, coatings or allergenic additives
Super Orti Vite Seroyal Int. Inc., Toronto, ON	Vitamin Mineral Supplement 128 Genesta Brands	120 Yes 0122304 - +	For therapeutic use only Take two capsules two times daily with meals or as recommended by your health care practitioner	Quality assurance: Safety-sealed for your protection Hypoallergenic Product Ideal for vegans
Ultra Preventive III Capsules Douglas Laboratories Pittsburgh, PA	A low allergenicity dietary supplement	180 No 0645304 +	As dietary supplement, adults take 6 capsules daily or as directed by physician This product is best taken with meals	Meets Douglas Laboratories Spec [#7564] Conforms to USP<2091> for weight Meets USP<2040> for disintegration
Vital Life Multivitamin Complex	Dietary Supplement	60 No 7430 +	As a dietary supplement; take one capsule daily with food or as directed by a physician	High bioavailability, allergen free; All ingredients are the highest quality and purity available Variation of product color may occur
Mega Multi GNC Pro Performance Elite series Selekt Multis	Superior multivitamin & Mineral Formula, rich in antioxidants, fast absorbing capsules Without copper	180 Yes 577613 + NA NA 030983 +	Adults take 6 capsules daily, for therapeutic use only Information not available	Vitamin and mineral supplement and source of ubiquinone
Ultragenesis	Without iron or copper Comprehensive Multi 180 Vitamin	180 No 03295 +	As a dietary supplement, take 3 capsules two times per day or as directed by your health care practitioner	Comprehensive multivitamin and mineral formula with phosphorylated forms and ratio balanced B vitamins A broad spectrum of essential nutrients, along with fully reacted amino acid chelates
Solaray Spectro Multi- Vita-Min	Natural beta carotene complex in a base of Siberian ginseng Iron Free	100 Yes 082601 +	For therapeutic use only, take 1- 2 capsules 2 time daily take with meals or glass of water	

The disintegration was determined using a disintegration tester ED 2L (Electrolab, Mumbai, India) which complies with USP <701> standards (10). The test units were inserted into the observation cylinder and the basket assembly was attached to the test apparatus. The appropriate immersion medium was filled into each beaker, and the test was started immediately after the basket assembly was attached.

The test was performed using Simulated Intestinal Fluid (SIF) USP 28 pH 6.8 without enzymes and a test time of 20 minutes was applied. Products which did not disintegrate were further investigated using the conditions outlined in chapter <2040> (11). Briefly: for tablets, water was used as an immersion fluid, and the test duration was 30 minutes. If capsules were investigated, 0.05 M acetate buffer pH 4.5 was used as immersion fluid, and the test duration was 45 minutes. Disks were used in these tests. Products which claimed a “time-released” mechanism were included in the disintegration test. Here it was expected that the product will not totally disintegrate within the test duration. Time-release products were then additionally tested for 90 minutes in pH 6.8 without disks.

The acceptance criteria for a successful test are the same for pharmaceutical and nutraceutical preparations. If all six units disintegrate, the test is passed. If one or two units do not fully disintegrate, then twelve additional units are tested. Only two units out of the total of eighteen tested units are allowed to fail complete disintegration.

RESULTS

Thirty out of thirty-nine investigated tablet products had a Drug Identification Number (DIN). Six out of ten capsule preparations investigated had DIN numbers. The DIN number indicates that the product is registered with Health Canada. The product must meet quality and safety requirements set by the regulatory agency. The examination of the product labels showed that thirty-five out of forty-eight products used the term “For therapeutic use only”. These products had a DIN except for two products. Only two products claimed that they meet pharmacopeial quality standards (USP) for disintegration. Two products claimed to meet “US-Pharmacopeia quality, purity and potency standards.” One product claimed “optimal disintegration”, another that it was “manufactured according to Good Manufacturing Practices (GMP).” One product claimed that it “meets specifications for potency,

uniformity and disintegration as appropriate.” However no specifications of “appropriate” were given. Other companies used terms of more general and informative character to describe their product: “New Formula”, “24 Vitamins and Minerals”, “No artificial flavours, no gluten, no lactose, no soy, without beta-carotene”, “time-released”, “Unique formulation”, “...established Canadian R.D.I. providing the nutrients your body needs for optimum health.” Other label claims included: “Scientifically balanced formula – release assured”, “Contains only the finest quality ingredients”, “Purely, Naturally, All Canadian”, “Certified guaranteed excellence”, “Most advanced complete daily nutrient from A to Z...”, “Guarantee of Absolute Purity & Full Potency”; however, there was no additional information available to support such claims. For example, which scientific dietary schedule has to be followed so that the supplement will have a balanced effect? Who certified the excellence? Which method assures the release? How is “Absolute Purity and Potency” defined? Furthermore, we were not able to define the following label statements: “level 4 potency Multivitamin”; the term “level 4 potency” did not produce any results in a Medline search. A “Google” search only brought up WebPages which refer to the manufacturer; however, the scientific meaning of the term could not be clarified. A similarly unclear term was “bioactive mineral.” One product claimed “maintains normal blood sugar level” and this product had no DIN number such that it was not clear how this claim was supported by the product. Another curious claim about the product quality was “High bioavailability, allergen free; all ingredients are the highest quality and purity available. Variation of product color may occur.” If only the highest quality of ingredients is used, then obvious variations in color should not occur. The information “once a day” or “only one” was not considered as a sufficient statement that the product has any kind of time-release mechanism. Such statements were considered to reflect the appropriate daily dose and not any formulation aspects of the product. Only three products clearly stated that they have a time-release mechanism.

The disintegration study was performed in two stages. In stage one; we investigated the disintegration of the tablet products at pH 6.8 in simulated intestinal fluid (SIF) without enzyme for 20 minutes. The test was performed without the use of the disks, eighteen out of thirty-six tablet formulations did not disintegrate according to the test criteria. Three “time-release” products which were

also tested did not disintegrate. Four out of the ten capsule products did not pass the first disintegration test level. In summary, twenty-five products out of forty-six products which should have disintegrated failed the test.

In stage two of our study, we applied the test conditions according to the USP chapter <2040> for minerals. Here the use of a disk in the observation cylinder is allowed. We only investigated products which had failed test stage one. Seven out of the twenty-one tested products did not fully disintegrate. Four products did not pass the test. All capsule products passed the disintegration test.

Five of seven products which failed complete disintegration recommend one tablet daily but none of these products claimed any extended release mechanism. The other two products recommended two and six tablets as daily doses.

The three controlled release products did not disintegrate in stage two and were further investigated by performing an additional test for 90 minutes in SIF without the use of disks. None of the test units disintegrated within 90 minutes. However, it was clearly visible that surface erosion happened under both test conditions, indicating the presence of a time-release mechanism. Both disintegration conditions eroded the tablet surfaces similarly (visual observation).

DISCUSSION

All investigated products were combination products containing a variety of different ingredients. Only in very few cases the combination/formula could be traced to dietary schedule: “This unique formulation has 15 vitamins and minerals with the established Canadian R.D.I. providing the nutrients your body needs for optimum health” However, one has to know that RDI stands for “Recommended Daily Intake”. In many cases it was rather difficult to identify or to differentiate the product name from the brand name. Additional disturbing factors were highlighted “buzz words”, “New Formula”, “Active”. Such information has more advertisement character and should be avoided on the front of the label. The font sizes of some labels were rather small due to the limited space and of the long ingredient lists and other additional information given. Information on quality standards and standardization were only found on four products which used recognized USP standards as reference. However, plenty of self-advertisement and pseudo-standards were found on the product: “Manufactured in Canada according to

good manufacturing practices (GMP)” However, GMP manufacturing does not guarantee drug release or disintegration; it guarantees proper process validation and documentation. Industry should follow already existing label requirements to help consumers to have all required information easily readable on the label. Only this will ensure that consumers can make informed choices.

The USP 28 lists standard test methods for the quality of oral dosage forms. They are divided into different categories: performance test for oral drug products (Pharmaceuticals) (12), and performance test for dietary supplements (13). The different test methods are listed in Table 3.

The characterization and quality control of pharmaceutical dosage forms is much more closely controlled compared to supplements. Drug release or dissolution requirements are core tests for the *in vitro* evaluation of pharmaceutical products. There are no dissolution requirements specified for most minerals and vitamins. Therefore, disintegration was adapted as an easy and cheap test to have at least one quality control parameter for the dosage form. The chapters <701> (10) and <2040> (11) describe the disintegration of tablets and capsules for pharmaceuticals and dietary supplements respectively. The test apparatus is the same. However, different conditions are applied.

Table 3. Comparison of the performance test scheme recommended by the USP 28 for pharmaceuticals and dietary supplements. The <number> indicates the USP general chapter.

Pharmaceuticals	
<301> Acid-Neutralizing capacity	
<701> Disintegration	
<711> Dissolution	
<724> Drug release	
<785>	Osmolarity
<905> Uniformity of Dosage Forms	
<1087> Intrinsic Dissolution	
<1088> In vitro and in vivo Evaluation of Dosage Forms	
<1090> In vivo Bioequivalence Guidance	
<1216> Tablet Friability	
Dietary Supplements	
<1216> Tablet Friability	
<2040> Disintegration and Dissolution of Nutritional Supplements	
<2091> Weight Variation	
<2750> Manufacturing Practices of Dietary Supplements	

The present study showed that the test duration and presumably the use of disks in the observation cylinder had an important impact on the ability of

products to pass the disintegration test. At one test condition eighteen immediate release products failed, at the other only four products failed. The results indicate that disintegration is still a concern for dietary supplements.

However, if a vitamin or mineral is poorly soluble or its dissolution is slow, then dissolution and not disintegration is the most critical parameter. Yet, it has to be pointed out that a product which fails disintegration will presumably fail dissolution criteria. Furthermore, if a mineral has to be absorbed within an absorption window and the dosage form does not release its content in a timely manner, then the therapy might be compromised or fail. An extended release dosage form on the other hand only releases parts of its total content at the absorption window like the duodenum and releases most of its dose in the jejunum, ileum and colon. This might cause a therapeutic failure due to insufficient absorption of some minerals or vitamins in deeper segments of the gut. Consequently, extended release dosage forms must show scientific evidence that the intended mineral or vitamin doses can be absorbed throughout the gastrointestinal passage.

A recent study by Kamba et al. investigated the mechanical forces applied in the disintegration apparatus. (14) A tablet by itself hits the screen of the basket-assembly with a force of 0.19 N. The disk forces on the basket were reported as 0.31 N. This shows that a tablet might undergo two defined impulsive forces in the basket assembly: one when the disk hits and one when it hits the basket screen while the basket-rack assembly is moving up and down. Such forces might apply to the dosage form for each movement cycle of the basket assembly. The disintegration of the time-release products with and without disk showed that fluid forces combined with impact forces of the disks can increase the disintegration.

Motility forces in the human intestine were reported to be up to 1.2 N. (15). The reported motility forces are for healthy humans. Recent studies by Aytug et al. (16) have shown that gender and menstrual cycles have an influence on motility pattern. Furthermore there are several diseases which impact motility like Parkinson's disease, diabetes mellitus and thyroid diseases. (17) Therefore, many patients which have such diseases and take mineral supplements might have compromised motility. This might influence the disintegration of the administered dosage form. The general question which this study cannot answer is how therapeutically relevant are the reported results? However, the results show that there

are products on the market which do not meet basic quality control measurements. Such products, and those needing higher mechanical forces to disintegrate (stage two in the present study), might therapeutically fail in patients due to insufficient motility forces, ultimately this applies to capsules and tablets.

The new Health Canada regulations for Natural Health Products, under which minerals and vitamins are regulated, need to clarify and outline guidance criteria for quality standards of minerals and vitamins. Only recognized test methods should be allowed to be used on the label. Health professionals, the industry and the consumer need to know how to identify a qualitatively acceptable product from a product with unknown quality. Meaningful disintegration standards accompanied with dissolution criteria are needed. Only this will ensure therapeutically efficacious dosage forms.

CONCLUSIONS

This study showed that there are products sold on the Canadian market which use statements on their label which are difficult to define. However, such terms and statements seem to be used to add pseudo-scientific and unjustified value to the product; such statements should be avoided. Only recognized test methods should be used on the labels. Dosage form and active ingredients need to be matched with their intended therapeutic use to ensure that the active is released at its site of absorption. Today's customers cannot assume that the product they buy will have an acceptable quality with regard to the disintegration behaviour.

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