Response to the Letter to the Editor for “Management of Osteoarthritis with Avocado/Soybean Unsaponifiables”

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The Changes in the Text

On page 34, we state “Clinical trial testing short-term efficacy of SierraSil at doses of 2 and 3 g per day failed to show sustained benefits over placebo, and iron toxicity has been reported.⁷⁴” In fact, although this formulation contains a warning about iron toxicity in children younger than 6 years, we are unaware of studies that have reported iron toxicity in adult subjects. The reference (Miller et al.) makes no mention of iron toxicity.

On page 37, we state “Avoca ASU (ASU-NMX1000, Nutramax Laboratories Inc., Edgewood, MD, USA)”. In fact, this should state “Avoca ASU (ASU-**OptiMSM**, Nutramax Laboratories Inc., Edgewood, MD, USA).”

On page 37, we state “Avoca ASU, a combination of ASU and glucosamine sulfate, has been shown to suppress TNF α , IL1 β , COX2, iNOS, PGE2, NF κ B activation and nitrite production in articular chondrocytes and monocytes/macrophages, reducing pain and inflammation in OA patients.^{115,116,124}” In fact, this should state “Avoca ASU, a combination of ASU and glucosamine **hydrochloride**, has been shown to suppress TNF α , IL1 β , COX2, iNOS, PGE2, NF κ B activation and nitrite production in articular chondrocytes and monocytes/macrophages, reducing pain and inflammation in OA patients.^{115,116,124}”

On page 37, we state “Avoca ASU that contains glucosamine can induce allergic reaction in people with shellfish allergy. Even in very small quantities, these people may experience mild symptoms, such as hives or nasal congestion, or more-severe, even life-threatening symptoms.” In fact, Avoca ASU contains non-shellfish glucosamine

hydrochloride. The glucosamine hydrochloride in Avoca ASU is plant based, and therefore would have no risk of side effects in people with shellfish allergy.

On page 38, Table 3, “Nutramax” has been misspelled as “Nuramax.”

On page 39, Table 4, we state “references 106, 129, 130.” In fact, references are 106, 128, 130.

On page 37, we state, “Further prospective multicenter studies are warranted to investigate whether other microscopic colitis cases¹²⁹ are observed in patients treated with Piascledine.” In fact, we conclude that further prospective multicenter studies are warranted to investigate microscopic colitis cases; however, this is not specific to the use of Piascledine.

On page 39, in the Declaration of Conflicting Interests, we state “Simrit Bhatti and Dr. Ramin Goudarzi are employees of Formulation Technology Inc. and Pharmin USA, LLC, respectively.” In fact, Simrit Bhatti is an employee of Formulation Technology Inc.; however, Dr. Ramin Goudarzi is the **Principal** of Pharmin USA, LLC.”

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The changes in Table 3, page 39, are as follows:

Table 3. Content Analysis of Supplements Containing Avocado Soybean Unsaponifiable.

Company/Manufacturer	Brand name	Dosage form	Other ingredients	Excipients on the label
Dr. Theo's Official	Avosoy	ASU	Vitamin C, vitamin E	c, croscarmellose, SDO, gum acacia, vegetable SA
Dr. Theo's Official	Avosoy Complete	ASU, glucosamine	Manganese Vitamin C, vitamin E	c, gum Arabic, SDO, SA, shellfish-free
Helseudsalg Faaborg Denmark	Avosol	HCl, porcine chondroitin sulfate ASU	Manganese, calcium Vitamin C	Glucose syrup, oxgelatin, SPI, extract rich in tocopherol, SDO, Mg salts from fatty acids
Laboratoires Expanscience, Pharmascience, Pharma Investi, Solvay Farma, Siegfried Rhein, SAdeCV	Piascledine 300	ASU	BHT, CAS	Gelatin, polysorbate 80, TDO, erythrosine, yellow iron oxide
Maximum International	Maximize, ASU	SierraSil, iron, CC, DCP	MCC, maltodextrin, croscarmellose Na	SDO, SA, HPMC, HPC, MS, PEG
Nutramax Laboratories, Inc.	Avoca ASU	Glucosamine HCl, ASU, DCP MSM	Decaffeinated green tea leaf extract	SPI, tocopherols, MCC, MS, SDO, non-shellfish, gluten-free
Nutramax Laboratories, Inc.	Cosamin ASU	Glucosamine HCl, Na chondroitin sulfate, ASU	Decaffeinated green tea leaf extract	Gelatin, SPI, tocopherols, SDO, gum resin, MS, TDO, yellow 5 and blue 1
Pharmin, USA, LLC.	Arthrocen	ASU	Persea gratissima, Glycine max, preservative free, gelatin fines,	Silica, magnesium stearate (E470b from vegetable oil)
Swanson Health Products	AvoVida	ASU	Phytosterols (β -sitosterol, campesterol, stigmasterol)	SPI, mixed tocopherols, silica, MCC, gelatin, MS, rice flour

Abbreviations: ASU = avocado/soybean unsaponifiable; BHT = butylated hydroxytoluene; CC = calcium carbonate; c = cellulose; CAS = colloidal anhydrous silica; DCP = dicalcium phosphate; HPC = hydroxypropyl cellulose; HPMC = hydroxypropyl methylcellulose; MS = magnesium stearate; Mg = magnesium; MSM = methylsulfonylmethane; MCC = microcrystalline cellulose; PEG = polyethylene glycol; SDO = silicon dioxide; Na = sodium; SPI = soy protein isolate; SA = stearic acid; TDO = titanium dioxide.

The authors acknowledge the above factual errors and misspellings.