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Comment on "Clinical Significance of the Water Retention and Barrier Function-Improving Capabilities of Ceramide-Containing Formulations: A Qualitative Review"

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Abstract:	

Comment on "Clinical Significance of the Water Retention and Barrier Function-Improving Capabilities of Ceramide-Containing Formulations: A Qualitative Review"

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Dear Editor,

We support the analysis of Kono *et al*. the publication of *'Clinical significance of the water retention and barrier function-improving capabilities of ceramide-containing formulations'* recently published in the Journal of Dermatology [1]. ~~Kono *et al.*~~ We especially applaud the authors on their conclusion for the need to determine the efficacy of different ceramides used in dermatological products and also for greater clarity of the particular ceramides used. Here we are not addressing efficacy but the importance of declaring the precise molecular structures of the ceramides used. In our opinions there is confusion in the literature of the definition of ceramides versus other molecules (pseudoceramides) that mimic some of their physiochemical and biological behaviour with the result that some formulations containing so called physiological lipids actually contain molecules that are not skin-identical ceramides. Moreover, usually the concentrations of ceramides used in products is not always disclosed.

The generalised structures of ceramides used in skin care products are shown in Figure 1A. Many studies have been conducted using these ceramides but not all publications use the correct International Nomenclature of Cosmetic Ingredients (INCI) nomenclature [~~1~~2]. It is important to correctly classify these lipids as they possess different physical characteristics especially the acylceramides CER EOS & EOP [~~2~~3]. Moreover, we have called for even greater clarity on the types of omega-esterified fatty acids within these molecules as these also dictate their behaviour [~~1~~2, ~~3~~4]. It is also important to note that in some cases racemic rather than stereospecific ceramides are used in skin care products. The effects of using the stereospecific and nature-identical sphingoid bases (2S, 3R-sphingosine and 2S, 3S, 4R-phytosphingosine etc.) together with R-α-hydroxy fatty acids have recently been studied [~~4~~5,~~5~~6]. For at least one marketed Ceramide AP the α-hydroxy fatty acid component consists of the two diastereomers of which the natural R-isomer promotes tighter lipid packing and the authors conclude that it should be preferred compared with the unnatural S-isomer or the racemic version [~~5~~6].

The representative structures of other types of molecules (pseudoceramides) that are used in skin care products are shown in Figure 1B. Moreover, in comparison to skin ceramides none of these contain intricate esters of long chain omega-hydroxy fatty acids like those in acylceramides or N-acylated α-hydroxy fatty acids or multiple sphingoid-like base mimics. Only one contains multiple chain length species but it is still not as complex as the ceramides found in skin [Figure 1B (vii)] and none possess the heterogenous diversity of the natural molecular species. Although these retain some, but not all, of the characteristics of skin-identical ceramides their correct chemical classification needs to be recorded and labelled as pseudoceramides or as ceramide-mimics rather than ceramides in ceramide-dominant/pseudoceramide-dominant formulations.

In conclusion, in order to compare efficacy of ceramides there needs to be greater scientific clarity of the chemistry of ceramides and/or ceramide mimics used together with precise concentrations. The INCI nomenclature is insufficient for scientific scrutiny of the data and precise molecular and stereochemical details of the ceramides/pseudoceramides used should be reported.

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Legend.

Figure 1. A Representation of the most common ceramides used in skin care products. Ceramide EOS (R=linoleate, oleate stearate etc.) (i), EOP (ii), NS (iii), NP (iv), AP (v). B. Representation of the most common pseudoceramides used in skin care products. Pseudoceramide: Cetyl-PG hydroxyethyl palmitamide (Sphingolipid E, SLC66) (vi). Pseudoceramide: myristyl/palmityl-oxo-stearamide/ arachimide MEA is a mixture of myristyl-oxostearamide MEA, palmityl-oxostearamide MEA, myristyl-oxoarachamide and palmityl-oxoarachamide MEA. (vii). N-palmitoyl-4-hydroxy-L-Proline Palmitoyl Ester (Bio391) (viii). Pseudoceramide PC-104, 1,3-bis(N-2-(hydroxyethyl)palmitoylamino)-2-hydroxypropane (ix).

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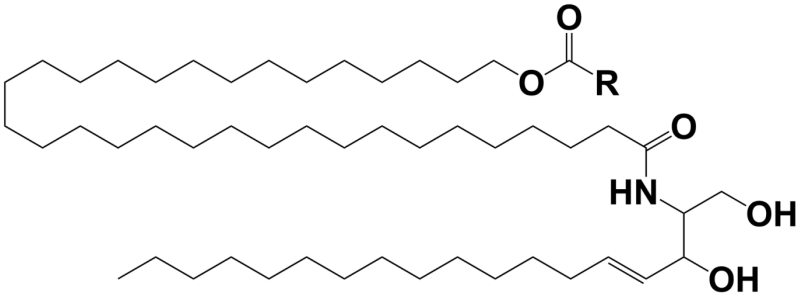
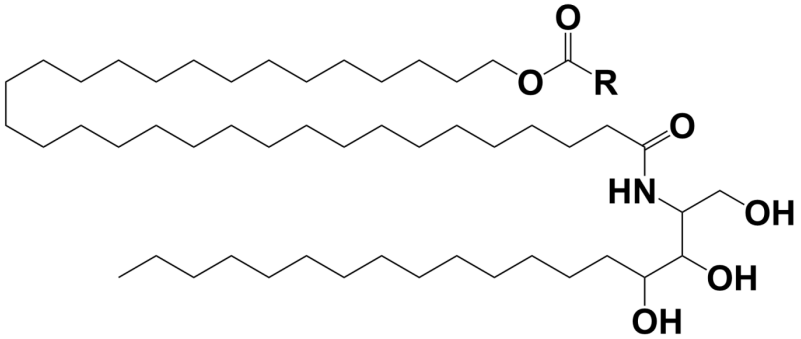
Figure 1: Common ceramides found in skincare products

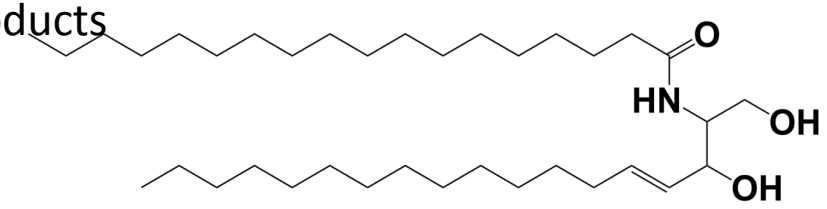


(i) Ceramide EOS

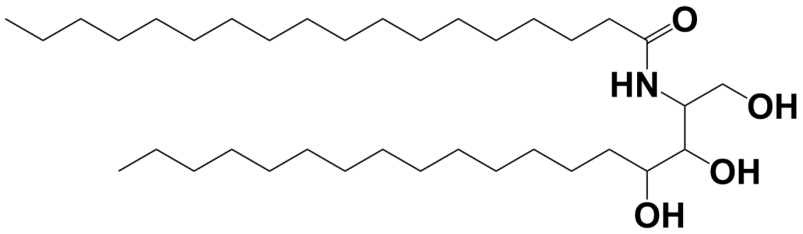


(ii) Ceramide EOP

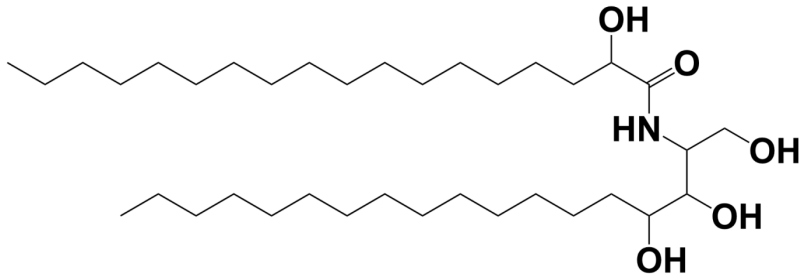
R= Linoleate, Oleate, Stearate etc.



(iii) Ceramide NS

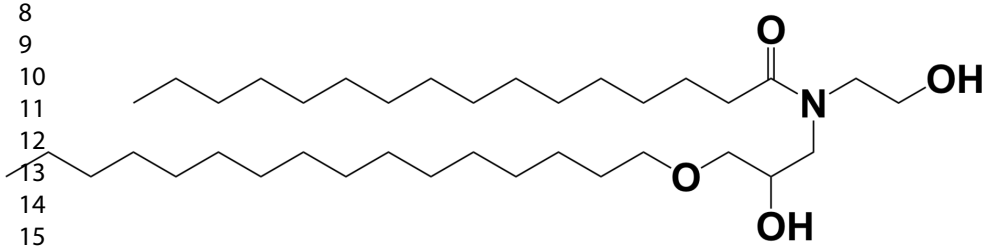


(iv) Ceramide NP

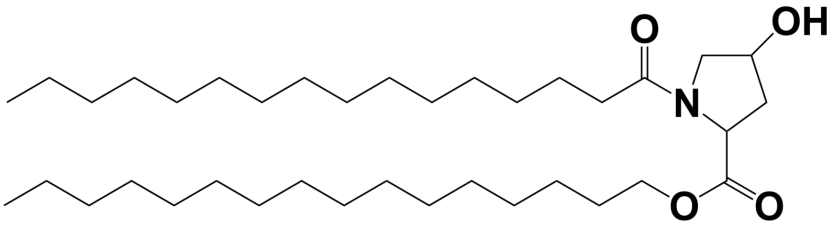


(v) Ceramide AP

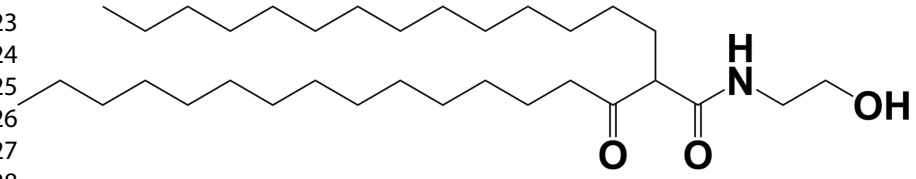
Figure 1: Common pseudoceramides found in skincare products



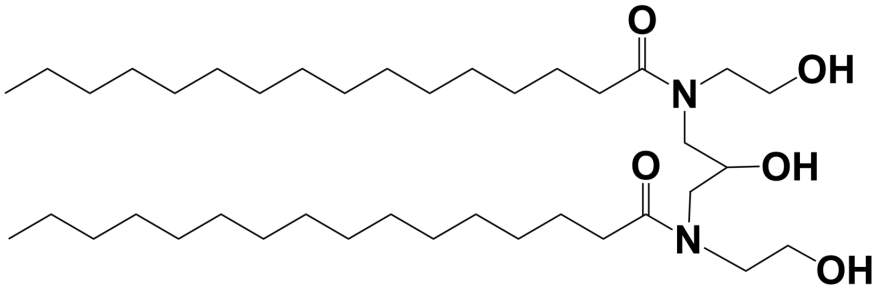
(vi) Sphingolipid E (SLC66) (Cetyl-PG Hydroxyethyl Palmitamide)



(viii) N-palmitoyl-4-hydroxy-L-Proline Palmitoyl



(vii) Myristyl/palmityl-oxo-stearamide/arachimide MEA



(ix) 1,3-bis(N-2-(hydroxyethyl)palmitoylamino)-2-hydroxypropane (Ceramide PC104)