WOWing the market with a PEG free option: A novel water-in-oil-in-water emulsifier

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Abstract

Consumer demand for high performing, sustainable solutions is higher than ever, and growing rapidly. To meet these demands innovation is needed throughout the Personal Care market including with foundational ingredients like emulsifiers. Emulsifiers are a special class of surfactant that are essential to the formulation of many skin care products. In general, phosphate esters, in particular ethoxylated phosphate esters, commonly serve as excellent emulsifiers in this application. However, the presence of polyethylene glycol (PEG) chains in cosmetic ingredients is viewed negatively by some due to the potential impurities, such as 1,4 dioxane, that are associated with them.

Our research has identified that 1,3 propanediol can be used in place of ethylene oxide and provide similar performance benefits. The emulsifier Cetearyl/Cetearyl Polypropanediol-8 Phosphate has been developed by reacting 1,3 propanediol with fatty alcohol followed by a phosphation reaction. Interestingly, the use of this emulsifier in Personal Care formulations results in the formation of “water-in-oil-in-water” (W/O/W) emulsions.

W/O/W emulsions are known to be high performing emulsions that are often used for improved bioavailability of active ingredients. Indeed, W/O/W emulsions resulting from the use of Cetearyl/Cetearyl Polypropanediol-8 Phosphate as the emulsifier demonstrated several interesting properties such as improving the delivery of water-soluble actives and SPF boost in inorganic sunscreen formulations.

This novel PEG-free W/O/W emulsifier also meets stringent sustainability criteria and thus helps to create the opportunity for more sustainable products in the Personal Care market.

Keywords

Emulsifier; Surfactant; Novel; Bio-based; Sustainability

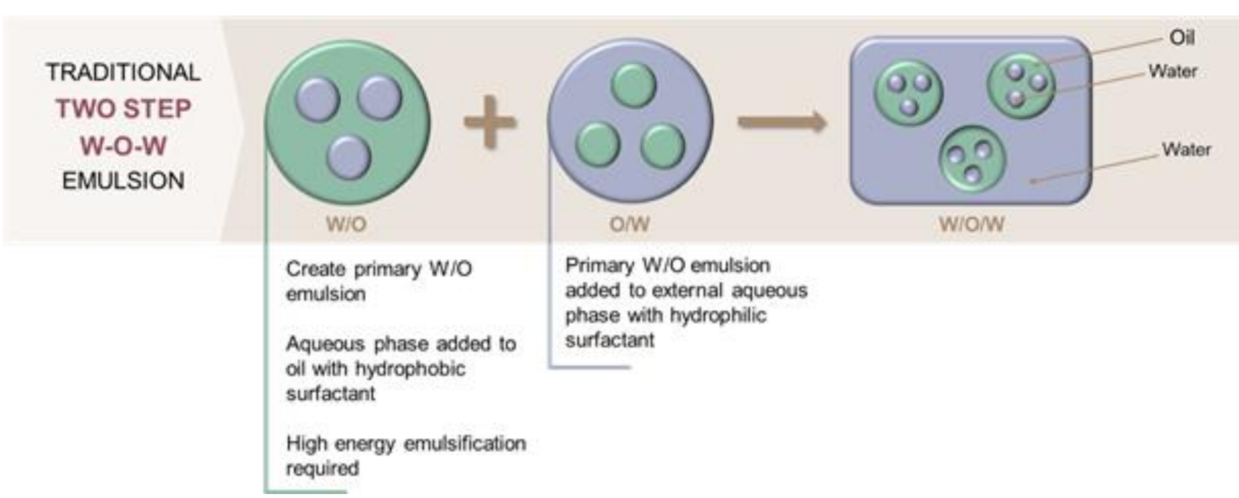
Introduction

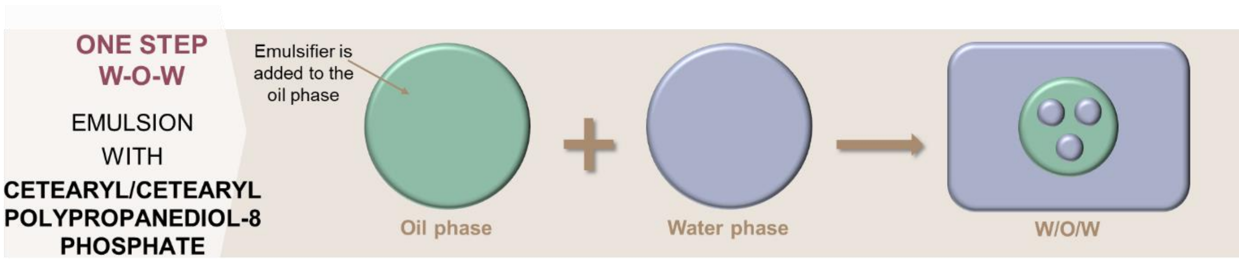
Within the Personal Care industry, consumer demand for high-performing, sustainable solutions is higher than ever, and growing rapidly. Conscious beauty consumers are becoming increasingly educated and driven to purchase purposefully – buying products that align with their personal, environmental, and social motivations. Safe ingredients, bio-based alternatives, and ethical sourcing are all now non-negotiables, with brands and suppliers alike expected to align with the progressing needs of the market [1]. In order to meet the market needs, sustainable innovation of backbone ingredients including emulsifiers is needed.

Phosphate esters are a class of emulsifiers that are used in Personal Care applications to prepare oil-in-water (O/W) emulsions [2]. These anionic surfactants, which often contain PEG chains to improve performance, have good emulsification properties across a wide pH range. However, these PEGylated products often have low biobased content and undesirable by-products such as 1,4 dioxane present. This is of particular concern with ethoxylated phosphate esters as the material's acidic nature makes it difficult to reduce 1,4 dioxane content to the desired level.

Cetearyl/Cetearyl Polypropanediol-8 Phosphate was prepared by reacting 1,3-propanediol with fatty alcohol which was then phosphated yielding a novel emulsifier that contains 100% biobased carbon and does not contain undesirable by-products such as 1,4-dioxane. This emulsifier was found to form a water-in-oil-in-water (W/O/W) emulsion, in a single step. W/O/W emulsions, which are a type of multiple emulsion, are systems "in which the globules of water are dispersed in globule of oil, and the oil globules are themselves dispersed in an aquatic environment." [3]

Traditionally, W/O/W emulsions have been prepared using multiple emulsifiers and multi-step formulation processes. W/O/W emulsions formed using one emulsifier have been reported however, they require arduous processing steps such as passing the formulation numerous times through a high pressure microfluidizer [4]. When compared to O/W emulsions, W/O/W emulsions are traditionally used for encapsulation and sustained/controlled release of active ingredients. These emulsions are known to improve the bioavailability of active ingredients. The novel emulsifier Cetearyl/Cetearyl Polypropanediol-8 Phosphate was compared to Crodafos CES, a traditional O/W emulsifier known to boost SPF and boost the transport of active ingredients and found to have superior performance.





Materials

1,3-propanediol, phosphoric anhydride, polyphosphoric acid, caffeine, Phosphate Buffer Saline pH 7.4, Strat-M membrane were all purchased from Sigma-Aldrich. C16/C18 fatty alcohol was from Croda. The suppliers of the ingredients used in the formulations are listed below each table.

Methods

Synthesis of Cetearyl/Cetearyl Polypropanediol-8 Phosphate

1,3 Propanediol is reacted with a C16/C18 fatty alcohol under acidic conditions at elevated temperatures. Once the reaction is completed the material is neutralized and filtered. The material is then charged back into a reaction vessel and further reacted with phosphoric anhydride or polyphosphoric acid to make the desired phosphate ester.

In Vitro Sunscreen Testing

A sample from both of the sunscreen formulations prepared in Table 3 (0.03 grams, ~ 1.2 mg/cm2) was applied in a series of small dots onto the rough side of a HD6 PMMA plate and spread using a finger clot in two steps according to the 2011 FDS regulations. In the first step, circular motion was used to spread the dots followed by a horizontal sweeping motion to provide an even coating. The plate was then protected from light for 15 minutes before measurements were taken. The UV transmittance of the plate was measured using a LabSphere UV-2000S Transmittance Analyzer. These measurements were run in triplicate.

In Vivo Sunscreen Testing

In-vivo testing was conducted externally through Eurofins CRL, Inc [5]. The test was carried out over three days on three panelists.

Franz Cell Materials and Methods

Caffeine formulations were prepared according to Table 4. Franz diffusion cells (Logan Instruments) were used for Strat-M membrane and the donor compartment was loaded with 1mL of the topical formulation, Table 4. The receptor medium temperature was maintained at 32ºC. The receptor medium was sampled at 4, 7 and 24h. The absorbance of the samples was analyzed at λ_{max} of 270 nm using a UV/Vis spectrophotometer (Cary 60, Agilent Technologies).

Results & Discussion

W/O/W emulsions are a desirable type of multiple emulsion that can be used to deliver both water and oil soluble actives in the same droplet. Unfortunately, they do not form spontaneous emulsions, often requiring multiple steps process and surfactants to form a stable W/O/W emulsion. Typically, these emulsions are created in a multistep process that involves making a primary water-in-oil (W/O) emulsion that is then emulsified in water using a variety of surfactants. Due to the complexity of the process the use of W/O/W emulsions is limited in the industry.

Cetearyl/Cetearyl Polypropanediol-8 Phosphate was screened for its emulsification properties using a simple chassis formulation, Table 1. The properties of this simple formulation containing the novel emulsifier was compared to a traditional W/O/W formulation, Table 2.

Table 1: Simple W/O/W formulation with Cetearyl/Cetearyl Polypropanediol-8 Phosphate

	Wt %
Part A	
Water	82.12
Pricerine 9091 (Glycerin)[1]	2.00
Xanthan Gum[1]	0.25
Sodium Hydroxide (10% solution) [2]	0.63
Part B	
Mineral Oil[2]	10.00
Crodacol 1618 (Cetearyl Alcohol)[3]	2.67
Cetearyl/Cetearyl Polypropanediol-8 Phosphate (and) Cetearyl Alcohol[3]	1.33
Part C	
Euxyl PE9010 (Phenoxyethanol (and) Ethylhexylglycerin)[4]	1.00

Suppliers: 1: CP Kelco 2: Sigma Aldrich 3: Croda 4: Schülke, Inc.

Procedure: Combine ingredients from Part A and heat to 75ºC. In separate beaker, combine ingredients from Part B and heat to 75ºC or until completely melted. Add Part B into Part A and continue mixing for 10 minutes at low to moderate speed while maintaining a temperature of 75ºC. Cool to 60ºC using propeller blade. Change the blade to a side sweep and cool to 40ºC. Add Part C and mix until uniform. Adjust the pH if necessary.

Preparation of the traditional two-step W/O/W emulsion used Crodamol GTCC as the emollient and PEG 30 Dipolyhydroxystearate as the W/O emulsifier in the primary emulsion. The second emulsion was then formed by adding the primary emulsion into the aqueous phase of the secondary emulsion ultimately forming the W/O/W emulsion, Table 2.

Table 2: Traditional two-step W/O/W emulsion formulation.

Ingredient	**%w/w**
Primary Emulsion (W1/O)	
Part A	
Cithrol DPHS (PEG 30 Dipolyhydroxystearate)[1]	4.00
Mineral Oil[2]	20.00
Crodamol GTCC (Caprylic/Capric Triglyceride)[1]	10.00
Part B	
Deionized Water	66.00
Secondary Emulsion (W1/O/W2)	
Ingredient	**%w/w**
Part C	
Primary Emulsion (W1/O)	60.00
Part D	
Deionized Water	22.50
Carbopol Ultrez 20-20% Solution (Acrylates/C10-30 Alkyl Acrylate Crosspolymer)[3]	15.00
Synperonic PE/F127 (Poloxamer 407)[1]	2.00
Euxyl PE9010 (Phenoxyethanol (and) Ethylhexylglycerin)[4]	0.50
Part E	
Triethanolamine[2]	q.s.

Suppliers: 1: Croda 2: Sigma Aldrich 3: Lubrizol : Schülke, Inc.

Procedures for Primary emulsion (W1/O): Combine ingredients of Part A and heat to 75°C while stirring with propeller blade. In a separate beaker, combine ingredients from Part B and heat to 75°C. Once both phases are at 75°C, add Part B into Part A while intensely stirring. Homogenize for 1-2 minutes at 5000rpm. Cool to 40°C with stirring and homogenize for another 1 minute at 5000rpm. ***Note cooling can take 1-2 hours before the primary emulsion can be added into secondary emulsion.***

Procedure for Secondary emulsion (W1/O/W2): Cool deionized water to 5°C and add Synperonic PE/F127 and stir. Once the Synperonic is completely dissolved at temperature, the remaining ingredients are individually added to part D and mixed until uniform. Slowly add Part C “Primary emulsion (W1/O)” into Part D while stirring intensively. The formulation is then neutralized with triethanolamine and stirred slowly until uniform.

The morphology of the emulsions was investigated using microscopy (Dino Lite Edge) which confirmed both formulations create W/O/W emulsions, Figure 1. The simple emulsion containing Cetearyl/Cetearyl Polypropanediol-8 Phosphate clearly shows a uniform W/O/W emulsion with the compartmented structures containing large oil droplets with smaller water droplets inside, Figure 1A.

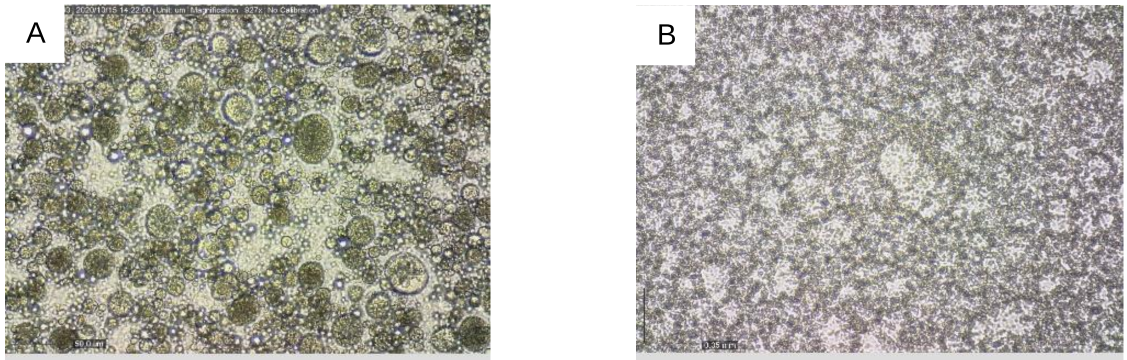


Figure 1: Microscope photos showing the structure of each formulation at a magnification of 927x (Dino-Lite Edge digital microscope). Photo A shows a simple formulation with Cetearyl/Cetearyl Polypropanediol-8 Phosphate and Photo B shows the traditional 2-Step W/O/W emulsion with Cithrol DPHS and Synperonic PE/F127 as the emulsifiers. Multiple emulsion systems have been reported to be beneficial in solar protection technology by reducing photodegradation and boosting SPF in organic and inorganic sunscreens formulations. In this study, a formulation containing the W/O/W emulsifier Cetearyl/Cetearyl Polypropanediol-8 Phosphate was compared to a formulation using the traditional O/W emulsifier, Crodafos CES, Table 3.

Table 3: Two Advanced Comfort Sunscreen formulations. Formulation 1 contains Cetearyl/Cetearyl Polypropanediol-8 Phosphate as the emulsifier and Formulation 2 contains Crodafos CES as the emulsifier.

	Formulation 1	Formulation 2
	Wt %	Wt%
Part A		
Water	39.89	39.89
Pricerine 9091 (Glycerin)[1]	8.00	8.00
Veegum Ultra (Magnesium Aluminum Silicate)[2]	0.80	0.80
Keltrol CG-SFT (Xanthan Gum)[3]	0.20	0.20
Sodium Hydroxide (10% solution)[5]	0.06	0.06
Disodium EDTA[5]	0.05	0.05
Part B		
Crodamol GTCC (Caprylic/Capric Triglyceride)[1]	6.00	6.00
Crodamol CAP (Cetearyl Ethylhexanoate (and) Isopropyl Myristate)[1]	5.00	5.00
Crodamol IPM (Isopropyl Myristate)[1]	4.00	4.00
Crodamol ISIS (Isostearyl Isostearate)[1]	3.00	3.00
Crodacol™ 1618 (Cetearyl Alcohol)[1]	2.67	0.00
Crodafos CES (Cetearyl Alcohol (and) Dicetyl Phosphate (and) Ceteth-10 Phosphate)[1]	---	4.00
Cetearyl/Cetearyl Polypropanediol-8 Phosphate (and) Cetearyl Alcohol)[1]	1.33	---
Solaveil XT-300 (Titanium Dioxide (and) Caprylic/Capric Triglyceride (and) Polyhydroxystearic Acid (and) Stearic Acid (and) Alumina)[1]	28.00	28.00
Part C		
Euxyl PE9010 (Phenoxyethanol (and) Ethylhexylglycerin)[4]	1.00	1.00

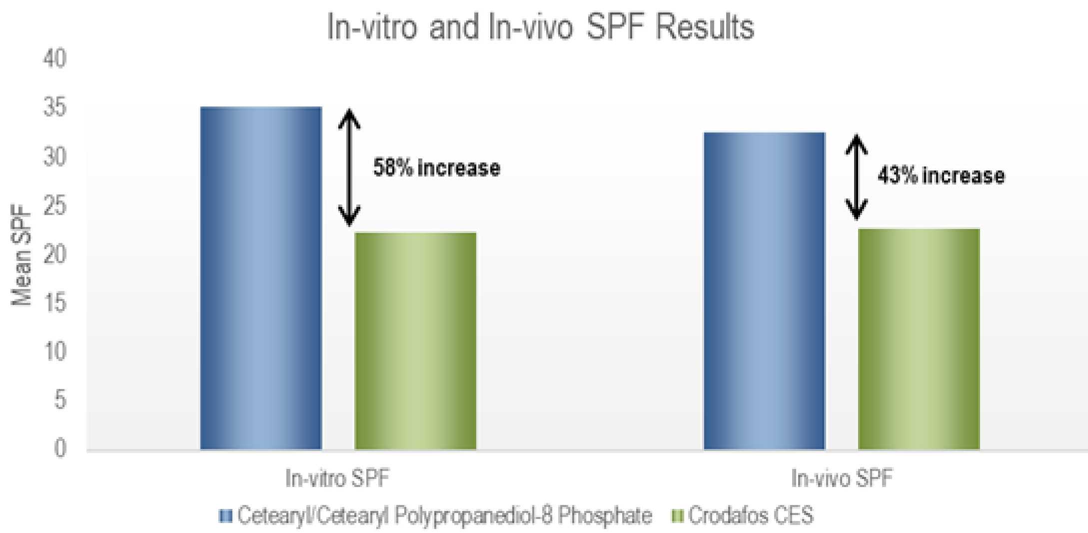
Suppliers: 1: Croda 2: Vanderbilt Minerals, LLC 3: CP Kelco 4: Schülke, Inc. 5 Sigma Aldrich

Procedure: In primary container mix water, sodium hydroxide, and disodium EDTA using a propeller blade. In a weigh boat, combine glycerin, magnesium aluminum silicate, and xanthan gum creating a slurry and add to Part A. Heat Part A to 75 ºC with mixing. In a separate container, combine all ingredients in Part B except Solaveil XT-300 and heat to 75 ºC. Once Part B has reached 75 ºC, Solaveil XT 300 is added and mixed until uniform. Part B is then added into Part A while homogenizing Part A. The batch is then homogenized for 5 minutes at 3000-5000rpm.

Finally, the batch is cooled using a side sweep blade to 40 ºC and Part C is added. Adjust the pH if necessary.

The *in-vitro* SPF results show that the formulation with Cetearyl/Cetearyl Polypropanediol-8 Phosphate had a mean SPF of 35 after radiation, whilst the formulation with Crodafos CES had a mean SPF of 22 after radiation. The *in-vivo* SPF results showed a similar trend in which the Advanced Comfort Sunscreen containing Cetearyl/Cetearyl Polypropanediol-8 Phosphate had a mean SPF of 32, whilst the sunscreen formulation with Crodafos CES had a Mean SPF of 22. The *in-vivo* SPF testing demonstrated that the formulation with Cetearyl/Cetearyl Polypropanediol-8 Phosphate had a 43% (10 units higher) increase in SPF compared to the formulation containing Crodafos CES, Graph 1.

	Formulation 1	Formulation 2
***In-vivo* SPF**	32.6	22.8
In-vitro SPF	35.2	22.3



Graph 1: In-vitro and in-vivo SPF results for the Advanced Comfort Sunscreen with Cetearyl/Cetearyl Polypropanediol-8 Phosphate, Formulation 1 compared to Crodafos CES, Formulation 2.

The novel emulsifier Cetearyl/Cetearyl Polypropanediol-8 Phosphate was shown to substantially increase SPF in a formulation containing titanium dioxide in both *in-vitro* and *in-vivo* testing. By boosting the SPF values of sunscreen formulations this emulsifier can help to reduce the likelihood of sunburn and promote the good health and wellbeing of all. These benefits are achieved while enhancing the sustainability profile of the formulation.

Multiple emulsions such as W/O/W emulsions, are commonly known to protect and control the release of actives in cosmetic applications. The internal water phase of W/O/W emulsions can act as a receptacle to entrap active compounds and protect them from degradation. These emulsions are often used to enhance the solubility and bioavailability of actives over time thereby improving the efficacy of actives in a formulation.

In this study, three simple topical formulations were prepared by varying the emulsifier, Table 4. Formulation 3 used Crodafos CES, a traditional emulsifier used to transport actives, Formulation 4 used Cetearyl/Cetearyl Polypropanediol-8 Phosphate, and Formulation 5 used a combination of two emulsifiers, Cithrol DPHS (W/O) and Arlacel 2121 (O/W), to form a W/O/W emulsion. The total concentration of emulsifier included in all formulations was held constant at 1%.

Table 4: Three topical formulations developed to evaluate the transport of caffeine.

	Formulation 3	**Formulation 4**	**Formulation 5**
Part A			
Water	80.12	81.12	81.75
Pricerine 9091 (Glycerin)[1]	2.00	2.00	2.00
Xanthan Gum[1]	0.25	0.25	0.25
Caffeine[2]	2.00	2.00	2.00
Sodium Hydroxide (10% solution)[2]	0.63	0.63	0.00
Part B			
Mineral Oil[2]	10.00	10.00	10.00
Crodacol 1618 (Cetearyl Alcohol)[3]	---	1.67	2.00
Crodafos CES (Cetearyl Alcohol (and) Dicetyl Phosphate (and) Ceteth-10 Phosphate)[3]	4.00	---	---
Cetearyl/Cetearyl Polypropanediol-8 Phosphate (and) Cetearyl Alcohol[3]	---	1.33	---
Arlacel 2121 (Sorbitan Stearate (and) Sucrose Cocoate)[3]	---	---	0.853
Cithrol DPHS (PEG 30 Dipolyhydroxystearate)[3]	---	---	0.143
Part C			
Euxyl PE9010 (Phenoxyethanol (and) Ethylhexylglycerin)[4]	1.00	1.00	1.00

Suppliers 1: CP Kelco 2: Sigma Aldrich 3: Croda 4: Schülke, Inc.

Procedures: In the main beaker add water and sodium hydroxide then mix using a propeller blade. In a weigh boat, combine xanthan gum and glycerin to create a slurry then add to water to form part A and heat to 75ºC. In a separate beaker add ingredients from part B and heat to 75ºC while stirring. Once both parts are at 75ºC, add Part B into Part A and mix for 10 minutes at 75ºC using a propeller blade. Cool to 60ºC using the propeller blades. Change the blade to side sweep at 60ºC and cool further to 40ºC to add part C.

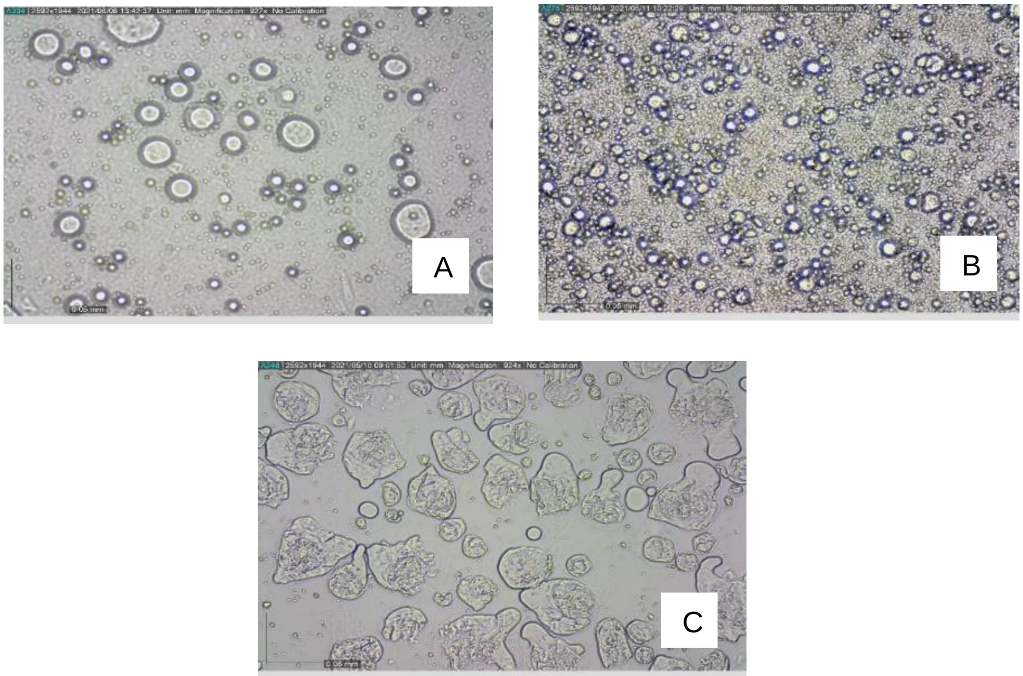
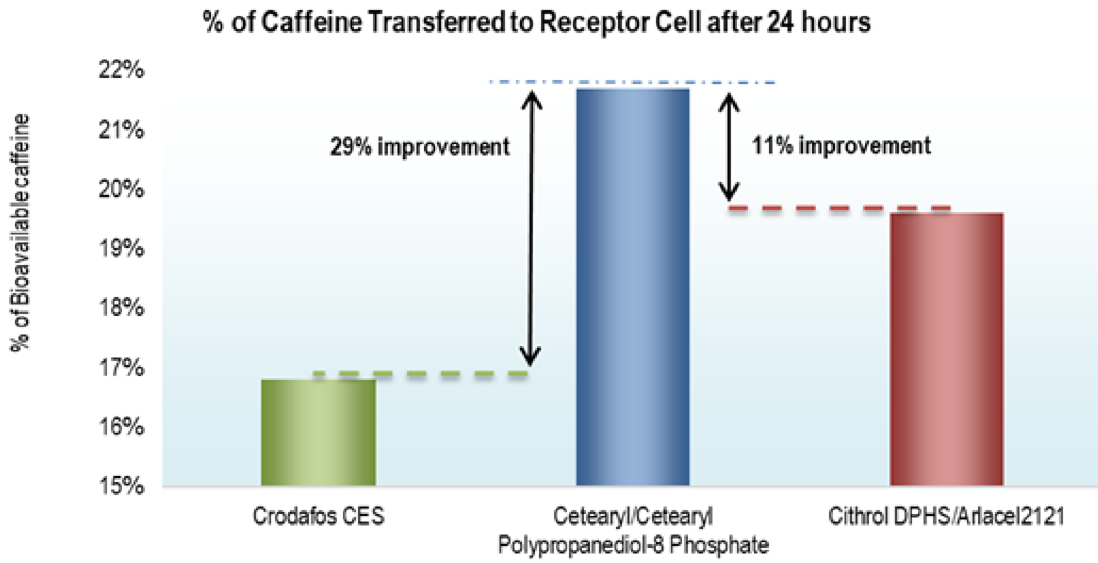


Figure 2: Microscope photos showing the structure of each formulation containing (A) Crodafos CES, (B) Cetearyl/Cetearyl Polypropanediol-8 Phosphate, and (C) Cithrol DPHS and Arlacel 2121 at a magnification of 927x.

The structure of the three formulations were characterized via microscopy. The formulation containing Crodafos CES, Figure 2A, was not found to have particles inside the oil droplets and thus did not constitute a W/O/W emulsion. The formulation containing Cetearyl/Cetearyl Polypropanediol-8 Phosphate, Figure 2B, was found to have uniform droplets with particles seen inside the oil droplets. The formulation containing the combination of Cithrol DPHS and Arlacel 2121, Figure 2C, showed formation W/O/W emulsion however, the droplets were irregular and showing signs of instability.

The efficacy of the three formulations to entrap and transport caffeine thru a STRAT-M membrane was evaluated using Franz Cell diffusion studies. These studies showed that the formulation containing Cetearyl/Cetearyl Polypropanedil-8 Phosphate was able to transfer more caffeine to the receptor compartment. Outperforming Crodafos CES by 26% at the 4h interval, 16% at the 7h interval, and 29% at the final 24h point. Cetearyl/Cetearyl Polypropanediol-8 Phosphate even showed superior performance when compared to the multiple emulsifier formulation, exceeding the performance of the Arlacel 2121/Cithrol DPHS formulation by nearly 5% at the 4h interval, 5% at the 7h interval and 11% at the 24h point, Graph 2.

Time Interval	Cetearyl/Cetearyl Polypropanediol-8 Phosphate	Crodafos CES	Arlacel 2121/ Cithrol DPHS
4 h	3.54%	2.80%	3.38%
7 h	6.70%	5.78%	6.38%
24 h	21.70%	16.80%	19.60%



Graph 2: Percent of bioavailable caffeine in the receptor cell after 24h.

It has been shown that using Cetearyl/Cetearyl Polypropanediol-8 Phosphate as the sole emulsifier in a topical formulation results in a multiple emulsion in one step. This multiple emulsion made with Cetearyl/Cetearyl Polypropanediol-8 Phosphate showed an increased ability to transfer caffeine to the receptor cell when compared to an O/W emulsion and to a traditional W/O/W emulsion using multiple emulsifiers. The ability to transport water-soluble actives, such as caffeine, more effectively can improve the efficacy of the formulation.

Conclusion

New high performing and sustainable ingredients such as Cetearyl/Cetearyl Polypropanediol-8 Phosphate are necessary to drive Purposeful Beauty. This novel emulsifier provides various functional benefits including formation of W/O/W emulsions in one step, improved transport of water-soluble actives, SPF boosting in inorganic sunscreens, and a wide pH tolerance. In addition to its performance benefits, Cetearyl/Cetearyl Polypropanediol-8 Phosphate boasts numerous sustainability credentials, being PEG-free, vegan suitable, 100% bio-based carbon and 100% derived natural according to ISO 16128. The emulsifier Cetearyl/Cetearyl Polypropanediol-8 Phosphate with its superior performance and strong sustainability profile is an example of smart science being used to improve lives.

Conflict of Interest Statement

The authors of this paper are all employees of Croda International Plc or Croda Inc a wholly owned subsidiary of Croda International Plc.

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