Comparative Assessment of the Physical And Structural Similarity Of Topical Drug Products Containing Lidocaine And Prilocaine

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PURPOSE & OBJECTIVE

The objective of the study was to identify quality attributes that may be critical to the performance of two topical creams, each containing both lidocaine and prilocaine (2.5%; 2.5%) as well as a topical gel containing both lidocaine and prilocaine (2.5%; 2.5%). The generic lidocaine; prilocaine topical cream (2.5%; 2.5%) had demonstrated bioequivalence (BE) to the reference listed drug (RLD) cream and served as a positive control for bioequivalence (BE), compared to the RLD cream. The topical gel containing both lidocaine and prilocaine (2.5%; 2.5%) served as a negative control for BE compared to the RLD cream. The physical and structural characterizations for each of the three drug products included an assessment of pH, density, water activity, work of adhesion (WOA), phase distribution (of the drug), drying profile and rheological characteristics.

METHOD(S)

The pH of the products was evaluated using a Mettler Toledo pH meter with an InLab® microprobe. The density was determined using a Accupyc™ II 1340 pycnometer from Micromeritics. Water activity was measured using a Aqualab series 3E water activity meter. The WOA was determined using a TA-3 texture analyzer. Phase distribution studies were conducted using a filtration centrifuge (Accuspin™ Micro 17) and drug was quantified in each phase using high performance liquid chromatography. The drying profile was determined using thermo gravimetric analysis, isothermally at 32°C. Rheological properties were characterized using a TA HR2 rheometer. All studies were conducted in triplicate and data are reported as mean ± S.D.

RESULT(S)

Table 1: Quality Attributes of Lidocaine-2.5%,Prilocaine-2.5% Cream and Gel Products

Quality Attribute	Number of Samples	Lidocaine2.5%, Prilocaine2.5% RLD Cream		Lidocaine-2.5%, Prilocaine-2.5% Generic Cream		Lidocaine-2.5%, Prilocaine-2.5% Gel
pH	3	9.22 ± 0.08		8.92 ± 0.03		7.76 ± 0.05
Density (g/cc)	3	1.0142 ± 0.0002		1.0148 ± 0.0002		1.0374 ± 0.0001
WOA (g.sec)	3	59.427 ± 0.338		65.893 ± 0.614		3.186 ± 0.207
Particle Size of API (µm)	-	Lidocaine and Prilocaine are completely dissolved in the formulation				
Globule Size, d50 (µm)	100 globules	3.30		3.00		---
Drug in Aqueous Phase (µg/g)	3	Lidocaine	1.64 ± 0.06	Lidocaine	1.74 ± 0.12	---
		Prilocaine	1.99 ± 0.06	Prilocaine	2.11 ± 0.15	
Drug in Oil Phase (µg/g)	3	Lidocaine	23.45 ± 0.36	Lidocaine	23.21 ± 0.18	---
		Prilocaine	23.47 ± 0.18	Prilocaine	23.12 ± 0.22	
Water Activity	3	1.003 ± 0.002		1.004 ± 0.007		1.002 ± 0.005
Drying,T50 (min)	3	3.37 ± 0.15		3.82 ± 0.73		7.9 ± 0.46
Rheology Yield Stress(Pa)	3	36.7 ± 1.2		35.7 ± 0.6		15.7 ± 2.3

Figure 1: Drying Profile of Lidocaine-2.5%,Prilocaine-2.5% Cream and Gel Products

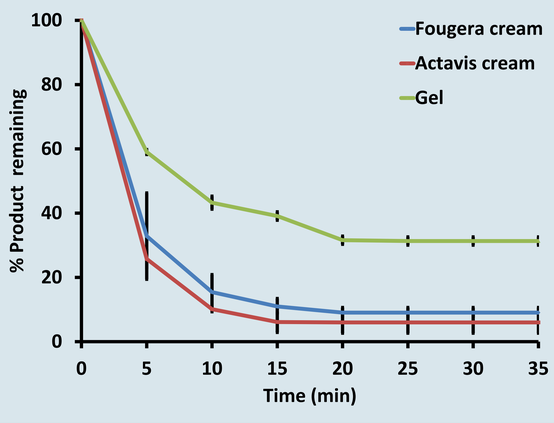
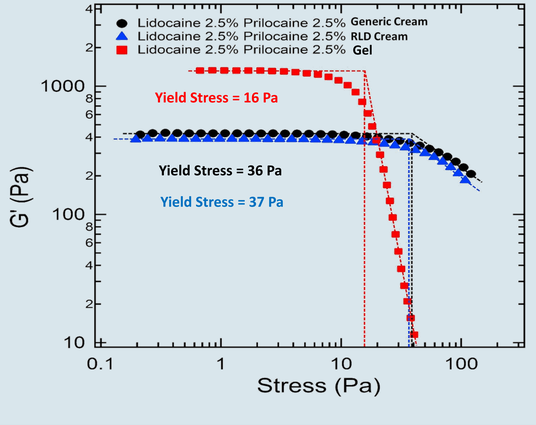


Figure 2: Yield Stress of Lidocaine-2.5%,Prilocaine-2.5% Cream and Gel Products



CONCLUSION(S)

The generic lidocaine prilocaine topical cream appeared to be similar to the RLD lidocaine prilocaine topical cream with respect to the quality attributes evaluated in this study, and both the topical creams were distinctly different from the lidocaine prilocaine topical gel (negative control). The following quality attributes of the formulation: pH, WOA, drying profile and rheological characteristics appear to be critical attributes that can differentiate between the topical creams and gel drug products. Studies are currently underway to identify additional quality attributes that may be critical to the evaluation of cream formulations containing the eutectic mixture of lidocaine and prilocaine.

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