

Cleoderm™

Beyond Use Date Study

Updated June 2025

Acne is caused by a variety of factors, some common ones include sebum overproduction (often the result of excessive androgen hormones), abnormal shedding of follicular epithelium, colonization with *c. acnes*, and inflammation.¹ Patients may suffer from multiple overlapping issues and may present with different types of lesions such as open or closed comedones (accumulation of sebum/keratin), or inflammatory lesions (rupture of follicle resulting in inflammation). Given the overlapping and various pathogeneses, customized or combination treatment via compounding may be indicated to suitably treat some patients. Given this need, Fagron evaluated several common active ingredients for use for acne or acne induced hyperpigmentation in our Cleoderm™ vehicle.

Why Cleoderm™?

Cleoderm™ is used cosmetically as a topical vehicle for conditions including aging skin, rosacea, and acne. Cleoderm™ contains hyaluronic acid sodium salt, often used topically in cosmetic preparations for skin hydration. It also contains plant-based anti-inflammatory ingredients from Cleome Gynandra extract, such as rutin and hydroxycinnamic acid thought to have anti-inflammatory and antioxidant activity. Peptide anti-inflammatory palmitoyl tripeptide-8 as well as bisabolol are also key ingredients studied for their anti-inflammatory properties.²

In a recent study, the tolerability of Cleoderm™ was evaluated in a study of 54 healthy volunteers. Not only did this study note that Cleoderm™ demonstrated no irritating, sensitizing, or comedogenic properties, it also noted that 60% of study subjects exhibited a decrease in the number of acne lesions after product use.³

Method ^{4,5}

Samples were prepared by wetting each active pharmaceutical ingredient with a levigating agent. Formulation excipients and quantities are specified in Table 1. Formulations were mixed for 4 minutes at a medium mixing speed using the FagronLab EMP, then passed through a three-roll ointment mill three times. The resultant mixture was packaged in Topi-Click (polypropylene) containers for long term storage at room temperature.

Potency was evaluated for each active pharmaceutical ingredient using stability indicating methods. Antimicrobial effectiveness testing (AET) per USP <51> was performed for all samples at timepoints 0 and at the final stable timepoint for each formulation.

Table 1. Formula Composition

Formula	Ethoxy Diglycol	BHT	Sodium Metabisulfite	Propylene Glycol	Citric Acid 50% Solution
Adapalene 0.1% - 0.3%	5%	-	-	-	-
Dapsone 5%	5%	-	-	-	-
Dapsone 10%	10%	-	-	-	-
Hydroquinone 2%	5%	0.03%	0.2%	-	As needed to pH 4.5-5
Hydroquinone 10%	5%	0.03%	1%	-	As needed to pH 4.5-5
Adapalene 0.1% - 0.3% Benzoyl Peroxide 1% - 5%	2.5%	-	-	-	-
Azelaic Acid 15% - 20% Niacinamide 4%	-	-	-	25%	-
Niacinamide 4% Tretinoin 0.025%	5%	0.1%	-	-	-
Benzoyl Peroxide 2.5 – 10%	-	-	-	-	-
Niacinamide 1%	5%	-	-	-	-
Niacinamide 5%	10%	-	-	-	-
Spironolactone 1 – 5%	10%	-	-	-	-
Metronidazole 0.75 – 5%	10%	-	-	-	-
Tranexamic Acid 1 – 5%	-	-	-	-	-
Estriol 0.1 – 1%	10%	-	-	-	-
Progesterone 0.5 -2 %	5%	-	-	-	-

Results ^{4,5}

Table 2. Single API Formulations

API	Elapsed Time (Days)	% Recovery (Room Temperature, 15-30 °C)			
		Low Concentration (SD)	pH	High Concentration (SD)	pH
Adapalene 0.1% - 0.3%	0	100.00 (0.3)	5.00	100.00 (0.34)	5.04
	7	96.21 (0.21)	5.02	99.95 (0.24)	5.08
	14	95.39 (0.14)	5.04	100.69 (0.25)	5.07
	30	95.33 (0.15)	5.02	100.72 (0.12)	5.02
	60	95.41 (0.35)	5.03	100.60 (0.31)	5.07
	90	96.36 (0.84)	5.00	100.48 (0.43)	5.01
	120	95.65 (0.17)	5.01	101.06 (0.18)	5.03
	150	92.23 (1.8)	5.01	76.57 (0.14)*	5.02
	180	92.29 (0.35)	5.02	-	-

Dapsone 5% - 10 %	0	100.00 (0.06)	4.95	100.00 (0.087)	5.05
	7	99.78 (0.22)	5.01	98.84 (0.15)	5.11
	14	99.59 (0.12)	5.15	97.45 (0.26)	5.17
	30	100.32 (0.15)	5.17	99.08 (0.13)	5.14
	60	99.06 (0.20)	5.12	97.68 (0.13)	5.12
	90	98.89 (0.39)	5.14	98.08 (0.40)	5.10
	120	99.62 (0.44)	5.07	96.46 (0.17)	5.03
	150	99.26 (0.22)	4.90	98.31 (0.11)	5.00
	180	99.56 (0.38)	4.99	98.10 (0.24)	5.10
Hydroquinone 2% - 10%	0	100.00 (0.28)	4.79	100.00 (0.99)	4.57
	7	99.07 (0.61)	4.62	100.44 (0.62)	4.49
	14	98.57 (0.31)	4.71	99.98 (0.40)	4.69
	30	98.76 (0.54)	4.44	100.16 (0.84)	4.08
	60	96.19 (0.21)	4.20	100.51 (0.60)	3.67
	90	96.31 (0.50)	3.92	100.12 (0.18)	3.52
	120	113.99 (0.34)**	3.39	99.94 (0.41)	3.39
	150	-	-	99.64 (0.42)	3.36
	180	-	-	98.95 (0.19)	3.35
Benzoyl Peroxide 2.5% - 10%	0	100.00 (1.0)	4.82	100.00 (0.19)	4.72
	7	98.92 (0.20)	4.64	100.22 (0.26)	4.67
	14	99.33 (0.17)	4.63	99.90 (0.43)	4.70
	30	99.50 (0.28)	4.65	100.00 (0.30)	4.69
	60	98.48 (0.37)	4.68	99.36 (0.28)	4.52
	90	98.30 (0.94)	4.67	99.88 (0.35)	4.48
	120	98.06 (0.74)	4.63	99.03 (0.30)	4.51
	150	98.15 (0.30)	4.66	98.72 (0.19)	4.50
	180	97.52 (0.46)	4.65	99.23 (0.37)	4.51
Niacinamide 1% - 5%	0	100.00 (0.37)	5.38	100.00 (0.21)	5.39
	7	98.99 (0.27)	5.22	100.42 (0.53)	5.50
	14	98.95 (0.48)	5.24	99.90 (0.39)	5.51
	30	99.57 (0.43)	5.26	99.91 (0.42)	5.52
	60	99.55 (0.34)	5.22	99.72 (0.12)	5.42
	90	99.76 (0.46)	5.23	99.76 (0.32)	5.50
	120	99.26 (0.52)	5.25	100.54 (0.21)	5.51
	150	99.94 (0.45)	5.22	100.05 (0.67)	5.53
	180	99.72 (1.05)	5.25	100.84 (0.57)	5.50

Spironolactone 1% - 5%	0	100.00 (0.28)	5.12	100.00 (0.36)	5.08
	7	99.79 (0.29)	5.15	99.60 (0.32)	5.04
	14	96.52 (0.26)	5.12	98.63 (0.09)	5.09
	30	96.39 (0.13)	5.13	98.02 (0.10)	5.07
	60	96.21 (0.31)	5.06	97.34 (0.36)	5.09
	90	96.74 (0.10)	5.07	97.39 (0.12)	5.05
	120	92.19 (0.35)	5.09	95.39 (0.30)	5.03
	150	92.46 (0.12)	5.07	95.13 (0.36)	5.05
	180	93.10 (0.06)	5.09	94.96 (0.21)	5.06
Metronidazole 0.75% - 5%	0	100.00 (0.82)	5.13	100.00 (0.41)	5.14
	7	98.07 (0.75)	5.16	97.08 (1.26)	5.15
	14	98.57 (0.31)	5.21	97.89 (0.49)	5.23
	30	98.25 (1.08)	5.18	97.88 (1.24)	5.20
	60	98.00 (0.19)	5.12	98.49 (0.92)	5.11
	90	98.06 (0.56)	5.08	98.18 (0.37)	5.11
	120	98.00 (0.34)	5.09	97.51 (0.14)	5.11
	150	97.80 (0.64)	5.10	95.80 (0.56)	5.13
	180	97.62 (0.45)	5.12	96.72 (0.76)	5.12
Tranexamic Acid 1% - 5%	0	100.00 (0.87)	5.91	100.00 (0.85)	6.38
	7	99.68 (0.77)	5.83	100.31 (0.68)	6.52
	14	99.20 (0.38)	5.79	100.45 (0.64)	6.45
	30	98.61 (0.76)	5.69	101.11 (0.79)	6.43
	60	98.78 (0.64)	5.59	100.75 (0.28)	6.43
	90	99.14 (1.38)	5.51	100.83 (1.31)	6.41
	120	98.92 (0.97)	5.53	100.82 (0.88)	6.46
	150	98.90 (0.65)	5.49	101.05 (0.53)	6.44
	180	99.69 (2.25)	5.55	100.87 (0.40)	6.41
Estriol 0.1% - 1%	0	100.00 (0.70)	5.15	100.00 (0.53)	5.13
	7	100.63 (0.21)	5.09	102.13 (1.09)	5.05
	14	101.53 (0.06)	5.15	100.84 (0.44)	5.20
	30	102.74 (0.59)	5.07	100.72 (1.18)	5.11
	60	102.94 (1.33)	5.13	101.67 (0.94)	5.17
	90	103.31 (1.88)	5.14	102.43 (1.73)	5.15
	120	104.32 (0.27)	5.17	101.48 (0.40)	5.09
	150	104.30 (0.53)	5.06	101.24 (0.49)	5.06
	180	103.23 (0.20)	5.09	101.95 (0.43)	5.05

Progesterone 0.5% - 2%	0	100.00 (0.26)	5.18	100.00 (0.32)	4.98
	7	100.05 (0.27)	5.16	98.91 (0.30)	4.97
	14	99.58 (0.49)	5.18	97.58 (0.19)	4.97
	30	99.64 (0.31)	5.23	98.31 (0.37)	4.55
	60	99.48 (0.13)	5.21	98.71 (0.11)	4.94
	90	99.22 (0.34)	5.13	97.87 (0.64)	4.95
	120	98.73 (0.76)	5.14	97.41 (0.31)	4.91
	150	98.82 (0.38)	5.12	97.24 (0.32)	4.93
	180	99.18 (0.20)	4.96	98.09 (0.06)	5.06

SD= Standard Deviation

*The adapalene 0.3% sample in Cleoderm™ presented a content lower than the minimum acceptable limit for the specification, at 150 days, making it impossible to continue the study.

**The hydroquinone 2.0% sample in Cleoderm™ presented a content higher than the maximum acceptable limit for the specification, at 120 days, making it impossible to continue the study.

Table 3. Adapalene and Benzoyl Peroxide

Elapsed Time (days)	% Recovery (SD)		pH	% Recovery (SD)		pH
	Adapalene 0.1%	Benzoyl Peroxide 1.0%		Adapalene 0.3%	Benzoyl Peroxide 5.0%	
t=0	99.43 (0.16)	102.47 (0.36)	4.98	99.59 (0.35)	102.82 (0.20)	4.67
t=7	100.22 (0.56)	101.70 (0.39)	4.90	99.80 (0.36)	102.52 (0.33)	4.53
t=14	100.87 (0.35)	100.11 (0.24)	4.83	99.66 (0.23)	101.77 (0.34)	4.48
t=30	100.64 (0.33)	100.14 (0.14)	4.86	99.52 (0.82)	100.42 (0.53)	4.47
t=60	99.65 (0.31)	99.16 (0.41)	4.62	99.62 (0.33)	100.91 (0.14)	4.42
t=90	99.04 (0.34)	98.42 (0.19)	4.40	99.41 (0.26)	99.59 (0.25)	4.63
t=120	99.30 (0.37)	99.07 (0.22)	4.51	99.32 (0.22)	100.46 (0.33)	4.31
t=150	99.59 (0.42)	99.34 (0.19)	4.43	99.52 (0.28)	100.72 (0.33)	4.25
t=180	99.95 (0.60)	100.13 (0.18)	4.51	99.95 (0.33)	99.72 (0.32)	4.51

SD= Standard Deviation

Table 4. Azelaic Acid and Niacinamide

Elapsed Time (days)	% Recovery (SD)		pH	% Recovery (SD)		pH
	Azelaic Acid 15.0%	Niacinamide 4.0%		Azelaic Acid 20.0%	Niacinamide 4.0%	
t=0	104.20 (1.81)	107.93 (1.99)	4.50	102.04 (0.51)	107.22 (0.47)	4.49
t=7	100.15 (1.34)	104.10 (0.27)	4.53	100.81 (0.91)	107.00 (0.58)	4.52
t=14	100.01 (1.01)	102.52 (0.30)	4.49	100.27 (1.51)	104.83 (0.50)	4.50
t=30	100.20 (0.16)	103.26 (0.30)	4.32	98.38 (0.14)	102.59 (2.00)	4.46
t=60	99.44 (0.37)	100.98 (1.17)	4.37	97.16 (0.22)	106.68 (2.46)	4.42

t=90	100.83 (0.53)	102.56 (0.33)	4.49	98.55 (0.59)	105.25 (0.30)	4.48
t=120	102.84 (0.19)	103.33 (0.21)	4.46	101.02 (0.57)	103.18 (0.78)	4.50
t=150	100.04 (0.79)	104.66 (0.61)	4.51	101.81 (0.28)	107.42 (0.65)	4.48
t=180	98.09 (1.00)	106.64 (0.96)	4.50	105.64 (1.44)	107.76 (1.19)	4.49

SD= Standard Deviation

Table 5. Niacinamide and Tretinoin

Elapsed Time (days)	% Recovery (SD)		pH
	Niacinamide 4.0%	Tretinoin 0.025%	
t=0	99.37 (0.61)	107.84 (0.87)	5.60
t=7	97.49 (0.21)	107.06 (0.22)	5.53
t=14	99.63 (0.33)	106.12 (0.15)	5.50
t=30	105.74 (0.17)	99.92 (0.33)	5.48
t=60	105.93 (0.52)	99.51 (0.35)	5.48
t=90	101.56 (0.46)	99.99 (0.43)	5.47
t=120	99.89 (0.25)	99.45 (0.30)	5.50
t=150	98.58 (0.24)	99.68 (0.28)	5.52
t=180	98.06 (0.42)	98.11 (0.10)	5.47

SD= Standard Deviation

Discussion

All samples met requirements for AET per USP <51> at timepoints 0 and the final tested timepoint (varied depending on final stability of the formulation).

- Adapalene 0.1-0.3% was stable for 120 days (Adapalene 0.1% was stable for 180 days)
- Dapsone 5-10% was stable for 180 days
- Hydroquinone 2-10% was stable for 90 days (Hydroquinone 10% was stable for 180 days)
- Adapalene 0.1-3% and Benzoyl Peroxide 1-5% combinations were stable for 180 days
- Azelaic Acid 15-20% and Niacinamide 4% combinations were stable for 180 days
- Niacinamide 4% and Tretinoin 0.025% was stable for 180 days
- Benzoyl Peroxide 2.5-10% was stable for 180 days
- Niacinamide 1-5% was stable for 180 days
- Spironolactone 1-5% was stable for 180 days
- Metronidazole 0.75-5% was stable for 180 days
- Tranexamic Acid 1-5% was stable for 180 days
- Estriol 0.1-1% was stable for 180 days
- Progesterone 0.5-2% was stable for 180 days

References

1. Oge, L, Broussard A, Marshall M. Acne Vulgaris: Diagnosis and Treatment. Am Fam Physician. 2019; 100(8): 475-484.
2. Polonini H, Zander C, Radke J. Cleoderm Clarifying Cream: a novel, topical vehicle using plant-based excipients and actives targeting acne and oily skin. Journal of Cosmetics Dermatological Sciences and Applications. 2021; 11(4): [10.4236/jcdsa.2021.114031](https://doi.org/10.4236/jcdsa.2021.114031)
3. Polonini H, Ameneiro-Alvarez A, Zander C. Safety assessment of a novel topical vehicle for personalized treatments in acne. Journal of Cosmetics, Dermatological Sciences and Applications. 2022; 12(4): doi 10.4236/jcdsa.2022.124016
4. Marianni B, Mansourian M, Koulouridas S, Podapsonelonini H. Compatibility of Active Pharmaceutical Ingredients in Cleoderm: A Comprehensive Study for Enhanced Topical Dermatological Treatments. IJPC. 2024; 28(5): 415-424.
5. Marianni B, Silva C, Polonini H. Compatibility of active pharmaceutical ingredients combinations compounded in Cleoderm, a cream base for personalized dermatological treatments. IJPC. 2-25; 29(2). 150-162.

Looking for more information? Check out the complete publication in the September/October 2024 edition of IJPC or reach out to the FACTS team at facts.support@fagronacademy.us