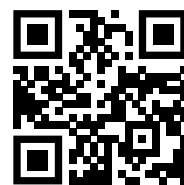




Stability Assessment of Compounded Bracketed Estradiol 0.01- 0.2%, Estriol 0.04- 0.8%, Progesterone 1-20%, Testosterone 0.025 - 0.5% and DHEA 0.2- 4% in Medisca VersaPro™ Cream Base

The physical, chemical, and microbiological stability of two different concentrations of combined Estradiol (0.01% and 0.2% w/w), Estriol (0.04% and 0.8% w/w), Progesterone (1% and 20% w/w), Testosterone (0.025% and 0.5% w/w) and DHEA (0.2% and 4% w/w) compounded in VersaPro Cream Base were evaluated over time. The formulations were packaged in tightly-closed, light resistant, plastic containers and stored at controlled room temperature (25°C) for the duration of the study. Physicochemical characteristics were analyzed at predetermined time points (0, 30, 60, 90, 120, 150 and 180 days) and each formula tested had the organoleptic properties inspected, the pH measured, and the API concentrations assayed using a validated, stability-indicating HPLC-UV method. The antimicrobial preservative effectiveness was also tested using a validated method according to USP <51>. The results showed that the concentration of the bracketed Estradiol, Estriol, Progesterone, Testosterone and DHEA formulations remained within USP specification (90 to 110 %) for at least 180 days at the tested conditions (*Table 1*). No significant changes in organoleptic properties or pH were observed. Antimicrobial preservative effectiveness also met USP <51> requirements for both concentrations (*Table 2*). In conclusion, Estradiol 0.01%, Estriol 0.04%, Progesterone 1%, Testosterone 0.025%, DHEA 0.2% in VersaPro Cream Base and Estradiol 0.2%, Estriol 0.8%,

Progesterone 20%, Testosterone 0.5%, DHEA 4% in VersaPro Cream Base were found to be physically, chemically and microbiologically stable for up to 180 days at the tested conditions. Therefore, an extended beyond-use date of 180 days may be assigned to this bracketed range of active concentrations if the same vehicle and conditions are respected.



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Table 1. Stability of Estradiol, Estriol, Progesterone, Testosterone and DHEA Combinations in VersaPro Cream Base at 25°C for 180 days.

| Time Points | E2 0.01% | E3 0.04% | P 1% | T 0.025% | DHEA 0.2% | E2 0.2% | E3 0.8% | P 20% | T 0.5% | DHEA 4% |
|------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|------------------|
| Assay (%)^a | | | | | | | | | | |
| Initial | 100 ± 0.00 | 100 ± 0.00 | 100 ± 0.00 | 100 ± 0.00 | 100 ± 0.55 | 100 ± 0.25 | 100 ± 0.19 | 100 ± 0.10 | 100 ± 0.01 | 100 ± 0.13 |
| 30 days | 99.25 | 99.53 | 99.07 | 99.78 | 100.14 | 101.03 | 101.43 | 100.04 | 100.98 | 101.11 |
| 60 days | 95.25 | 96.09 | 95.33 | 95.44 | 96.6 | 98.94 | 99.78 | 98.17 | 99.64 | 99.74 |
| 90 days | 96.32 ± 0.00 | 97.32 ± 0.00 | 94.75 ± 0.00 | 96.94 ± 0.01 | 97.51 ± 0.12 | 100.75 ± 0.05 | 101.00 ± 0.06 | 99.25 ± 0.02 | 100.66 ± 0.49 | 100.45 ± 1.22 |
| 120 days | 97.81 ± 0.00 | 98.52 ± 0.01 | 96.54 ± 0.00 | 99.56 ± 0.01 | 99.32 ± 0.10 | 102.19 ± 0.07 | 102.49 ± 0.01 | 100.83 ± 0.03 | 102.79 ± 0.80 | 102.24 ± 2.42 |
| 150 days | 97.11 ± 0.00 | 97.86 ± 0.01 | 96.25 ± 0.00 | 99.06 ± 0.04 | 99.23 ± 0.16 | 101.89 ± 0.28 | 102.17 ± 0.10 | 100.34 ± 0.05 | 102.41 ± 1.38 | 101.98 ± 3.19 |
| 180 days | 96.09 ± 0.00 | 96.69 ± 0.00 | 96.35 ± 0.00 | 97.54 ± 0.08 | 97.46 ± 0.04 | 99.99 ± 0.02 | 101.23 ± 0.00 | 99.89 ± 0.04 | 101.39 ± 1.29 | 100.93 ± 3.32 |
| pH | | | | | | | | | | |
| Initial | 5.14 | | | 5.16 | | | | | | |
| 30 days | 5.26 | | | 5.27 | | | | | | |
| 60 days | 5.07 | | | 5.03 | | | | | | |
| 90 days | 4.91 | | | 4.86 | | | | | | |
| 120 days | 4.93 | | | 4.90 | | | | | | |
| 150 days | 4.89 | | | 4.87 | | | | | | |
| 180 days | 4.86 | | | 4.76 | | | | | | |

^a Reported as Mean ± SD of duplicate determinations, except 30 and 60 days. E2 = Estradiol, E3 = Estriol, P = Progesterone, T = Testosterone, DHEA = Dehydroepiandrosterone

Table 2. Antimicrobial Preservative Effectiveness of Estradiol, Estriol, Progesterone, Testosterone and DHEA Combinations in VersaPro Cream Base.

| Identification | Method | Test Performed | Specification ^a | Result ^b |
|--|----------|-------------------------------------|----------------------------|---------------------|
| Estradiol 0.01%, Estriol 0.04%, Progesterone 1%, Testosterone 0.025%, DHEA 0.2% in VersaPro Cream Base | USP <51> | Antimicrobial Effectiveness Testing | Category 2 | Pass |
| Estradiol 0.2%, Estriol 0.8%, Progesterone 20%, Testosterone 0.5%, DHEA 4% in VersaPro Cream Base | USP <51> | Antimicrobial Effectiveness Testing | Category 2 | Pass |

^a Category 2 includes topically used products made with aqueous bases or vehicles, such as emulsions.

^b Product must meet the following for (i) Bacteria: NLT 2.0 log reduction from initial count at 14 days; no increase from 14 days count to 28 days. (ii) Yeast and mold: No increase from the initial calculated count at 14 and 28 days.

Medisca Formula

[F 008 949](#) Dehydroepiandrosterone 0.2%-4%, Estradiol 0.01%-0.2%, Estriol 0.04%-0.8%, Progesterone 1%-20%, Testosterone 0.025%-0.5% Topical Cream (Emulsion, 500g)

For More Information

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