

Comparison of Dissolution Apparatus for Testing of Transdermal Systems

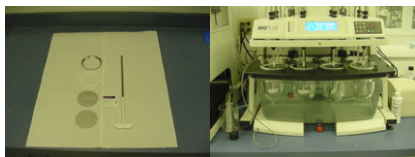
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PURPOSE

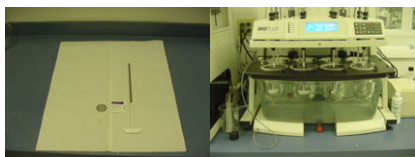
To study the effect of different dissolution apparatus on the Release Rate (Dissolution) of transdermal systems. The U. S. Pharmacopoeia sets out the guidelines for the testing of Transdermal Systems in Monograph <724> Drug Release. Vivelle-Dot™, an Estradiol Transdermal System manufactured by Noven Pharmaceuticals, Inc., and marketed by Novogyne, a woman’s health product company jointly owned by Noven and Novartis, was examined. Two sizes, 10.0 cm² and 2.5 cm², were assayed for release rate.

Three apparatus were compared:

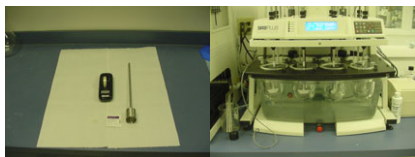
1. A modified Apparatus 5, (Paddle over Screen), consisting of the transdermal unit sandwiched between two screens held together with an outside stainless steel ring and an inside Teflon ring. The release surface is parallel with the bottom of the paddle blade.
2. USP Apparatus 5, (Paddle over Disk), consisting of a stainless steel disk designed for holding the transdermal system at the bottom of the vessel with the release surface also parallel with the bottom of the paddle blade.
3. A modified apparatus 6, (Cylinder), consisting of a cylinder stirring element with the transdermal unit attached to the outside of the cylinder with two-sided tape.



Modified Apparatus 5



USP Apparatus 5



Modified Apparatus 6

METHOD

The experiment was performed using the three apparatus described previously, (N = 6). Deionized water was used as the receiving phase and aliquots were manually withdrawn from the vessels at 2, 4 and 6 hours. The temperature of the dissolution media was 32.0 ± 0.5 °C.

The amount of Estradiol in the aliquots was measured by HPLC and % Label claim was calculated. The HPLC conditions were:

Column: Supelcosil LC-18-DB (3.3 cm x 0.46 cm, 3_μm)
Mobile Phase: 40/60 Acetonitrile/Water
Flow Rate: 2.0 mL/min.
Injection Volume: 25_μL
Detection: UV at 210 nm wavelength

RESULTS AND DISCUSSION

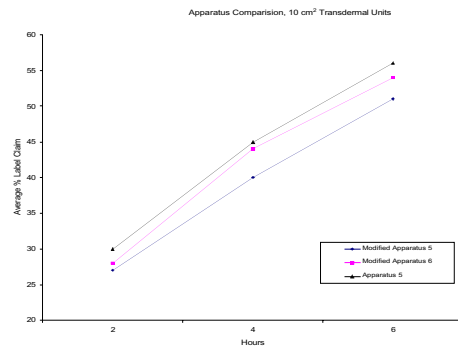
Estradiol release rates are summarized in the following tables:

10.0 cm ² Vivelle-Dot™ % Label Claim			
	2 Hours	4 Hours	6 Hours
Modified Apparatus 5	27 %	40 %	51 %
Apparatus 5	30 %	45 %	56 %
Modified Apparatus 6	28 %	44 %	54 %

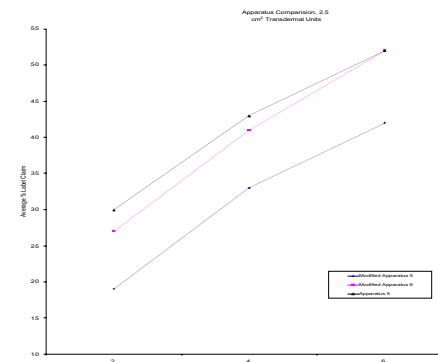
Table 1.

2.5 cm ² Vivelle-Dot™ % Label Claim			
	2 Hours	4 Hours	6 Hours
Modified Apparatus 5	19 %	33 %	42 %
Apparatus 5	30 %	43 %	52 %
Modified Apparatus 6	27 %	41 %	52 %

Table 2.



Graph 1.



Graph 2.

The % label claim discrepancies between the 10.0 cm² and 2.5 cm² transdermal units employing the Modified Apparatus 5 were examined more closely. The release rates of units from both sizes were assayed again without the top screen. The units were taped down with the two-sided tape used with Modified Apparatus 6. The Estradiol release rates are summarized in the table below.

10.0 cm ² and 2.5 cm ² % Label Claim Without Top Screen			
	2 Hours	4 Hours	6 Hours
10.0 cm ²	30	45	56
2.5 cm ²	28	43	53

Table 3.

CONCLUSION

Release rate was affected by the choice of dissolution apparatus, especially significant was Modified Apparatus 5 and the smaller 2.5 cm² unit. The Paddle over Screen (Apparatus Modified Apparatus 5) showed the lowest release rate, while Apparatus 5 (Paddle over Disk) the highest release rate. Modified Apparatus 6 released Estradiol slightly less than Apparatus 5 but was greater than the Modified Apparatus 5 technique.

The difference in release rates between the 10.0 and 2.5 cm² units using the Modified Apparatus 5 technique can be attributed to the use of the top screen. The top screen inhibited the release rate slightly in the 10.0 cm² unit and significantly in the 2.5 cm² units.

The choice of dissolution apparatus should be considered during the development of dissolution methods since it can affect the results and the length of the test, i.e., another useful method development strategy.