

TABLE 37

Excess MgO Concentration (wt %) and pH				
	Est-15	Est-16	Est-17	Est-18
Excess MgO Concentration	0%	6.9%	16.9%	23.3%
pH	7.48	8.95	9.66	10.28

[0356] The cumulative amount of estradiol across human cadaver skin was calculated using the measured estradiol concentrations in the receiver solutions.

TABLE 38

Cumulative Amount of Estradiol ( $\mu\text{g}/\text{cm}^2$ )				
Time	Est-15	Est-16	Est-17	Est-18
4.75 hours	0.08	0.09	0.05	0.02
15.75 hours	0.21	0.31	0.19	0.13
19.75 hours	0.26	0.41	0.26	0.19
23.75 hours	0.32	0.53	0.36	0.27

[0357] The cumulative amount of estradiol that permeated across the human cadaver skin at 24 hours for Est-16 (0.53

$\mu\text{g}/\text{cm}^2$ ) with a calculated excess MgO concentration of 6.9% was slightly higher than that from the formulation without MgO (Est-15,  $0.32 \mu\text{g}/\text{cm}^2$ ). Thus, the formulation of Est-16 provided up to 2-fold more estradiol flux than in the absence of MgO (Est-15). This result indicated that MgO enhances the permeation of estradiol.

[0358] The cumulative amount of estradiol across human cadaver skin at 24 hours decreased from 0.53 to  $0.27 \mu\text{g}/\text{cm}^2$  when the excess MgO concentration in the dried patch was increased from 6.9% to 23.3%. This behavior may be because the high concentration of MgO made the adhesive matrix more hydrophobic and the amount of MgO that could be dissolved by the small amount of water on the top of the skin was reduced.

## Example 12

[0359] An in vitro skin permeation study was conducted using four phenylpropanolamine hydrochloride transdermal systems, designated PPA-17, PPA-18, PPA-19, and PPA-20, the compositions of which are set forth in Table 39. The matrix patches were prepared and evaluated using the same procedures as set forth in Example 3. The theoretical percent weight for each ingredient after drying (calculated assuming all the volatile ingredients were completely removed during drying) is listed in Table 40.

TABLE 39

Component Weight and Weight Percent Based on Total Solution Weight				
	PPA-17 g (wt %)	PPA-18 g (wt %)	PPA-19 g (wt %)	PPA-20 g (wt %)
PPA-HCl	0.5 (6.9)	0.5 (6.0)	0.5 (5.9)	0.5 (5.7)
MgO	0	0.11 (1.3)	0.26 (3.1)	0.50 (5.7)
DI water	1.0 (13.9)	2.0 (24.0)	2.0 (23.6)	2.0 (22.9)
Methyl alcohol	0.5 (6.9)	0.5 (6.0)	0.5 (5.9)	0.5 (5.7)
PG	0.2 (2.8)	0.2 (2.4)	0.2 (2.4)	0.2 (2.3)
HPMC	0.02 (0.3)	0.02 (0.2)	0.02 (0.2)	0.02 (0.2)
PIB adhesive (30% solid)	4 (55.4)	4 (48.0)	4 (47.2)	4 (45.9)
Heptane	1.0 (13.9)	1.0 (12.0)	1.0 (11.8)	1.0 (11.5)

[0360]

TABLE 40

Component Weight and Weight Percent Based on Dried Film Weight				
	PPA-17 g (wt %)	PPA-18 g (wt %)	PPA-19 g (wt %)	PPA-20 g (wt %)
PPA-HCl	0.5 (26.0)	0.5 (24.6)	0.5 (22.9)	0.5 (20.7)
MgO	0	0.11 (5.4)	0.26 (11.9)	0.50 (20.7)
PG	0.2 (10.4)	0.2 (9.9)	0.2 (9.2)	0.2 (8.3)
HPMC	0.02 (1.0)	0.02 (1.0)	0.02 (0.9)	0.02 (0.8)
PIB adhesive	1.2 (62.5)	1.2 (59.1)	1.2 (55.0)	1.2 (49.6)