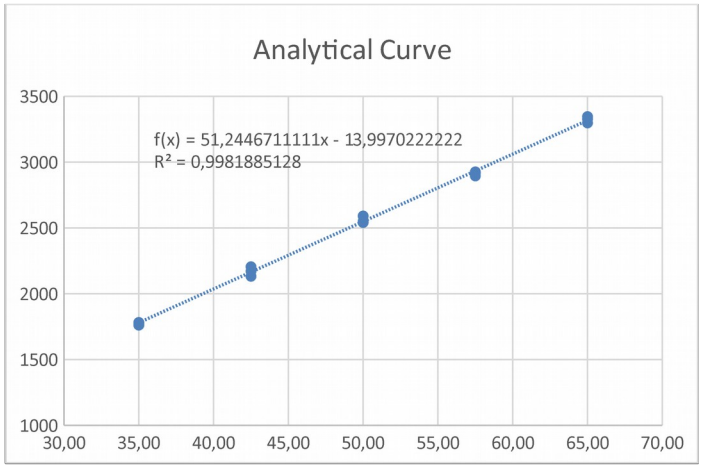
Pentravan vaginal permeation – Progesterone

ANALYTICAL CURVE`

Theoretical concentration	Real concentration (mcg/mL)	Area (HPLC)
70%	35,00	1782,318
	35,00	1761,358
	35,00	1777,510
85%	42,50	2132,986
	42,50	2205,367
	42,50	2171,479
100%	50,00	2591,330
	50,00	2550,168
	50,00	2541,088
115%	57,50	2895,224
	57,50	2926,593
	57,50	2915,816
130%	65,00	3298,204
	65,00	3346,574
	65,00	3327,533



ANALYSIS OF VARIANCE (ANOVA)

Source	*Sum of Square*	*D.F.*	*Mean of Square*	$F_{calculated}$	$F_{critical}$
Model	4,4315E+06	1	4,4315E+06	7163,51	4,67
Residual	8,0420E+03	13	6,1862E+02		
Lack of fit	2,0487E+03	3	6,8288E+02	1,14	3,71
Pure error	5,9934E+03	10	5,9934E+02		
Total	4,4394E+06	14	3,1710E+05		

D.F. = degrees of freedom

Significance of regression

If $F_{calculated\ (regression)} >> F_{critical}$: **There is a significant linear relationship between the variables**

Lack of fitness

If $F_{calculated\ (lack\ of\ fit)} < F_{critical}$: **There is no lack of fit in the linear model.**

Product:	Progesterone 5% in Pentravan
Membrane:	Porcine vaginal mucosa

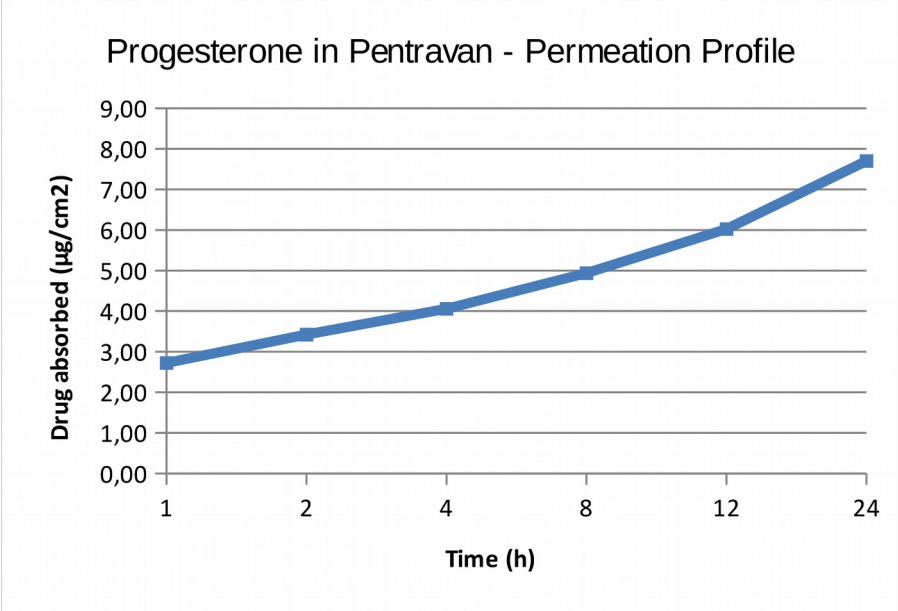
HPLC areas

Collect time (h)	Franz cell	Area
1	1	19,975
	2	26,167
	3	ND
	4	ND
	5	ND
	6	ND
	Average	**23,071**
	Standard deviation	**4,378**
2	1	ND
	2	19,363
	3	ND
	4	ND
	5	ND
	6	ND
	Average	**19,363**
	Standard deviation	**#DIV/0!**
4	1	ND
	2	16,092
	3	ND
	4	ND
	5	ND
	6	ND
	Average	**16,092**
	Standard deviation	**#DIV/0!**

Collect time (h)	Franz cell	Area
8	1	ND
	2	22,628
	3	16,454
	4	ND
	5	14,075
	6	16,181
	Average	**17,335**
	Standard deviation	**3,686**
16	1	20,462
	2	20,043
	3	21,775
	4	ND
	5	21,460
	6	20,975
	Average	**20,943**
	Standard deviation	**0,707**
24	1	30,937
	2	24,596
	3	32,190
	4	ND
	5	ND
	6	37,417
	Average	**31,285**
	Standard deviation	**5,269**

PERMEATION PROFILE					
Time (h)	Area (n=6)	µg/mL	µg (*7)		µg/cm2
1	23,07	0,72	5,06	5,06	2,72
2	19,36	0,65	4,56	6,37	3,42
4	16,09	0,59	4,11	7,55	4,06
8	17,33	0,61	4,28	9,18	4,94
12	20,94	0,68	4,77	11,21	6,02
24	31,29	0,88	6,19	14,32	7,70

Quantity of drug applied = 1881,72 µg/cm2



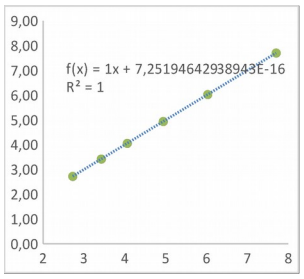
Mathematical kinetic models

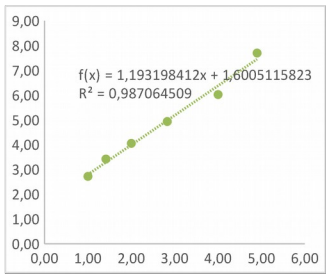
Zero order	
Time (h)	Drug (µg/cm2)
1	2,72
2	3,42
4	4,06
8	4,94
16	6,02
24	7,70

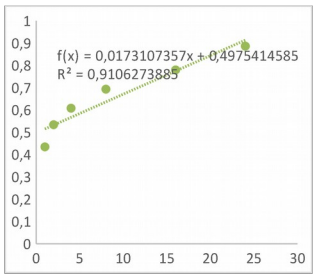
Pseudo-first order (Higuchi)	
Square-root of time	Drug (µg/cm2)
1,00	2,72
1,41	3,42
2,00	4,06
2,83	4,94
4,00	6,02
4,90	7,70

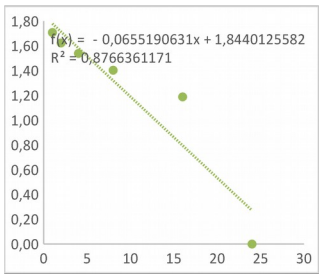
First order	
Time (h)	Drug (log µg/cm2)
1	0,4349327527
2	0,5343062011
4	0,6082018688
8	0,6934994781
16	0,7798996919
24	0,8864992224

Hixson-Crowell	
Time (h)	Square-root of non-permeated drug
1	1,71
2	1,62
4	1,54
8	1,40
16	1,19
24	0,00









Best fitted model: Higuchi
Flux: 1,19 µg/cm2/h-1
Lag time: 1,8 h
Kp 0,001 cm/h-1

Drug retained within the mucosa

Franz cell	Area	Concentration (µg/mL)	Quantity (µg)
1	15221,999	297,32	1486,58
2	15232,153	297,51	1487,57
3	ND		
4	ND		
5	ND		
6	ND		
Average		297,42	1487,08
S.D.		0,14	0,70

*mucosa diluted with 5 mL of diluent

Drug lost during application

Franz cell	Area	Concentration (µg/mL)	Quantity (µg)
1	15657,474	305,81	1529,07
2	19651,019	383,75	1918,73
3	14230,842	277,98	1389,88
4	15175,178	296,40	1482,02
5	17697,219	345,62	1728,09
6	ND		
Average		321,91	1609,56
S.D.		42,50	212,51

*mucosa diluted with 5 mL of diluent

	µg	mg
Lost in spreader/ occlusor	1609,56	1,61
Total	3110,96	3,11

Recovery		
Quantity of cream applied	70,0 mg	
Concentration of the cream	50,0 mg/g	
Quantity of drug applied	3,50 mg	
Quantity recovered	3,11 mg	
Average recovery	88,88 %	Specification: 85-115%

Permeation percentage	
Quantity of drug applied	3,50 mg
Quantity of drug absorbed (systemic effect)	0,01 mg
Quantity of drug within the mucosa (local effect)	1,49 mg
Permeation porcentage	0,4 %
Drug available for clinical effect	42,90 %