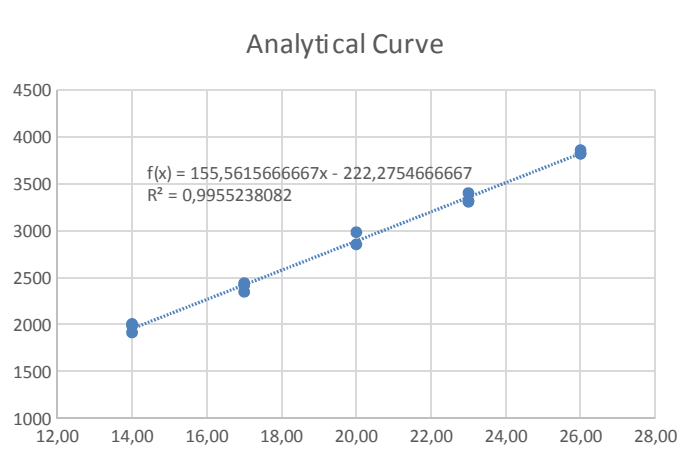
Pentravan vaginal permeation – Testosterone

ANALYTICAL CURVE`

Theoretical concentration	Real concentration (mcg/mL)	Area (HPLC)
70%	14,00	2006,401
	14,00	1914,394
	14,00	1987,692
85%	17,00	2348,12
	17,00	2440,759
	17,00	2419,354
100%	20,00	2853,951
	20,00	2854,445
	20,00	2982,909
115%	23,00	3400,471
	23,00	3307,723
	23,00	3318,684
130%	26,00	3819,058
	26,00	3822,081
	26,00	3858,296



ANALYSIS OF VARIANCE (ANOVA)

Source	*Sum of Square*	*D.F.*	*Mean of Square*	$F_{calculated}$	$F_{critical}$
Model	6,5337E+06	1	6,5337E+06	2891,19	4,67
Residual	2,9378E+04	13	2,2599E+03		
Lack of fit	2,8091E+03	3	9,3636E+02	0,35	3,71
Pure error	2,6569E+04	10	2,6569E+03		
Total	6,5632E+06	14	4,6880E+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:	Testosterone 0.3% in Pentravan
Membrane:	Porcine vaginal mucosa

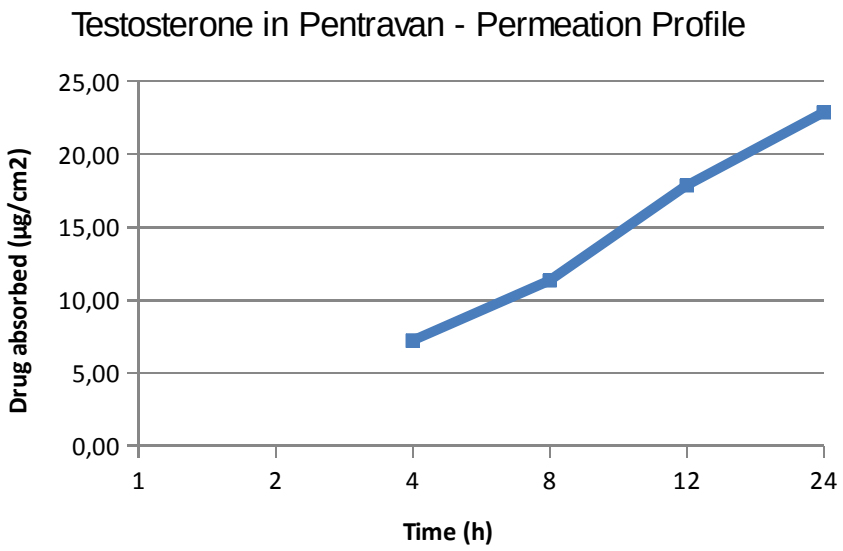
HPLC areas

Collect time (h)	Franz cell	Area
1	1	ND
	2	ND
	3	ND
	4	ND
	5	ND
	6	ND
	Average	**#DIV/0!**
	Standard deviation	**#DIV/0!**
2	1	ND
	2	ND
	3	ND
	4	ND
	5	ND
	6	ND
	Average	**#DIV/0!**
	Standard deviation	**#DIV/0!**
4	1	89,445
	2	82,248
	3	44,104
	4	ND
	5	88,782
	6	ND
	Average	**76,145**
	Standard deviation	**21,606**

Collect time (h)	Franz cell	Area
8	1	161,818
	2	184,103
	3	98,373
	4	119,906
	5	177,429
	6	97,255
	Average	**139,814**
	Standard deviation	**39,460**
16	1	366,706
	2	301,872
	3	201,722
	4	233,009
	5	374,312
	6	201,310
	Average	**279,822**
	Standard deviation	**79,270**
24	1	338,839
	2	372,035
	3	296,605
	4	271,363
	5	246,871
	6	321,315
	Average	**307,838**
	Standard deviation	**45,689**

PERMEATION PROFILE					
Time (h)	Area (n=6)	µg/mL	µg (*7)	µg (dilution)	µg/cm2
1					
2					
4	76,14	1,92	13,43	13,43	7,22
8	139,81	2,33	16,29	21,09	11,34
12	279,82	3,23	22,59	33,21	17,85
24	307,84	3,41	23,85	42,54	22,87

Quantity of drug applied = 112,90 µg/cm2



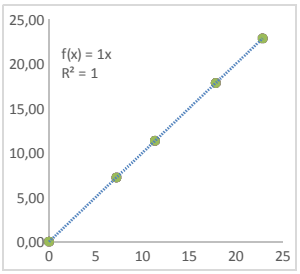
Mathematical kinetic models

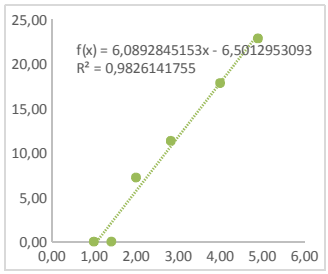
Zero order	
Time (h)	Drug (µg/cm2)
1	0,00
2	0,00
4	7,22
8	11,34
16	17,85
24	22,87

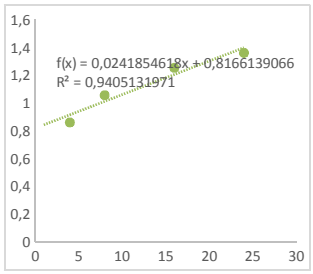
Pseudo-first order (Higuchi)	
Square-root of time	Drug (µg/cm2)
1,00	0,00
1,41	0,00
2,00	7,22
2,83	11,34
4,00	17,85
4,90	22,87

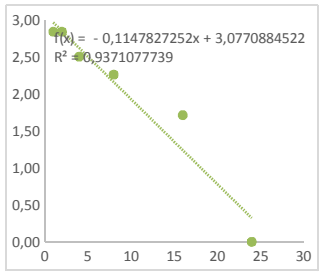
First order	
Time (h)	Drug (log µg/cm2)
1	Erro:502
2	Erro:502
4	0,858522
8	1,0545582709
16	1,2517443393
24	1,359275029

Hixson-Crowell	
Time (h)	Square-root of non-permeated drug
1	2,84
2	2,84
4	2,50
8	2,26
16	1,71
24	0,00









Best fitted model: Higuchi
Flux: **6,09 µg/cm2/h-1**
Lag time: **1,14 h** (~17 min)
Kp **0,05 cm/h-1**

Drug retained within the mucosa

Franz cell	Area	Concentration (µg/mL)
1	1849,935	13,32
2	1092,084	8,45
3	1332,021	9,99
4	ND	
5	1060,032	8,24
6	ND	
Average		10,00
S.D.		2,35

*mucosa diluted with 5 mL of diluent

Drug lost during application

Franz cell	Area	Concentration (µg/mL)
1	ND	
2	ND	
3	2280,134	16,09
4	3309,374	22,70
5	2605,068	18,18
6	ND	
Average		18,99
S.D.		3,38

*mucosa diluted with 5 mL of diluent

	µg	mg
Lost in spreader/ occlusor	94,94	0,09
Retained within the mucosa	50,01	0,05
Absorbed	42,54	0,04
Total	187,49	0,19

Recovery		
Quantity of cream applied	70,0 mg	
Concentration of the cream	3,0 mg/g	
Quantity of drug applied	0,21 mg	
Quantity recovered	0,19 mg	
Average recovery	89,28 %	Specification: 85-115%

Permeation percentage	
Quantity of drug applied	0,21 mg
Quantity of drug absorbed (systemic effect)	0,04 mg
Quantity of drug within the mucosa (local effect)	0,05 mg
Permeation porcentage	20,3 %
Drug available for clinical effect	44,07 %