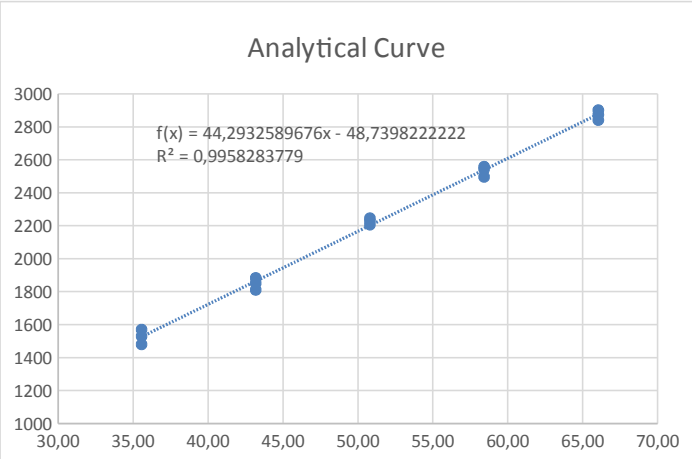
Pentravan vaginal permeation – Piroxicam

ANALYTICAL CURVE`

Theoretical concentration	Real concentration (mcg/mL)	Area (HPLC)
70%	35,56	1569,940
	35,56	1479,921
	35,56	1529,543
85%	43,18	1851,577
	43,18	1883,235
	43,18	1810,616
100%	50,80	2245,817
	50,80	2206,224
	50,80	2229,837
115%	58,42	2558,149
	58,42	2543,288
	58,42	2496,200
130%	66,04	2841,025
	66,04	2901,096
	66,04	2873,898



ANALYSIS OF VARIANCE (ANOVA)

Source	*Sum of Square*	*D.F.*	*Mean of Square*	$F_{calculated}$	$F_{critical}$
Model	3,4174E+06	1	3,4174E+06	3103,26	4,67
Residual	1,4316E+04	13	1,1012E+03		
Lack of fit	2,9040E+03	3	9,6801E+02	0,85	3,71
Pure error	1,1412E+04	10	1,1412E+03		
Total	3,4318E+06	14	2,4513E+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:	Piroxicam 2% in Pentravan
Membrane:	Porcine vaginal mucosa

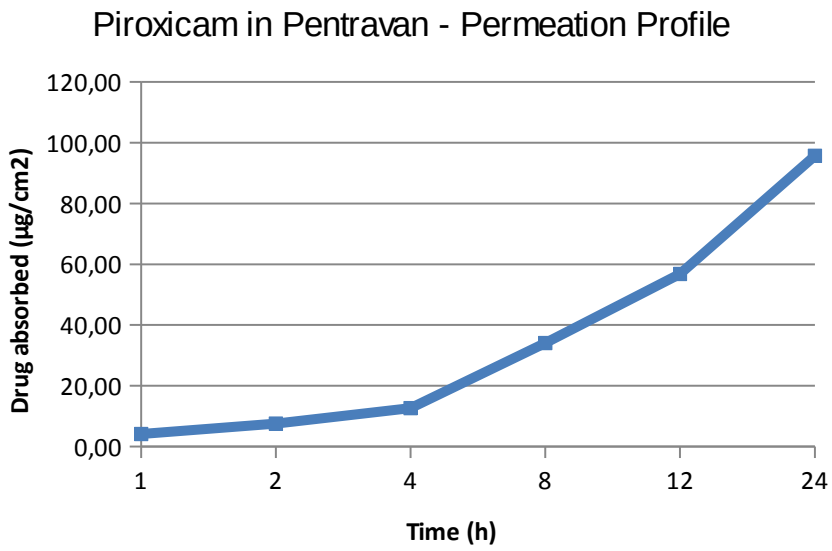
HPLC areas

Collect time (h)	Franz cell	Area
1	1	0,000
	2	0,000
	3	0,000
	4	0,000
	5	0,000
	6	0,000
	Average	**0,000**
	Standard deviation	**0,000**
2	1	14,849
	2	ND
	3	ND
	4	29,112
	5	ND
	6	24,151
	Average	**22,704**
	Standard deviation	**7,241**
4	1	51,887
	2	24,401
	3	37,904
	4	95,691
	5	24,698
	6	109,670
	Average	**57,375**
	Standard deviation	**36,789**

Collect time (h)	Franz cell	Area
8,000	1	183,248
	2	100,304
	3	142,701
	4	396,181
	5	350,233
	6	452,487
	Average	**270,859**
	Standard deviation	**147,094**
16,000	1	298,348
	2	231,989
	3	230,710
	4	491,077
	5	539,242
	6	757,219
	Average	**424,764**
	Standard deviation	**209,203**
24,000	1	630,158
	2	561,251
	3	826,907
	4	690,784
	5	739,175
	6	833,270
	Average	**713,591**
	Standard deviation	**108,173**

PERMEATION PROFILE					
Time (h)	Area (n=6)	µg/mL	µg (*7)	µg (dilution)	µg/cm2
1	0,00	1,10	7,70	7,70	4,14
2	22,70	1,61	11,29	14,04	7,55
4	57,38	2,40	16,77	23,55	12,66
8	270,86	7,22	50,51	63,28	34,02
12	424,76	10,69	74,83	105,64	56,80
24	713,59	17,21	120,48	178,02	95,71

Quantity of drug applied = 752,69 µg/cm2



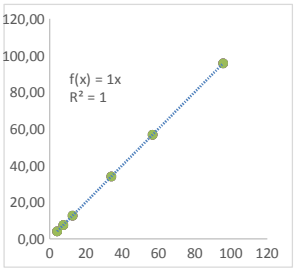
Mathematical kinetic models

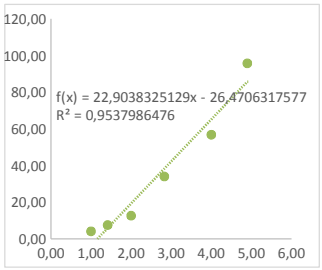
Zero order	
Time (h)	Drug (µg/cm2)
1	4,14
2	7,55
4	12,66
8	34,02
16	56,80
24	95,71

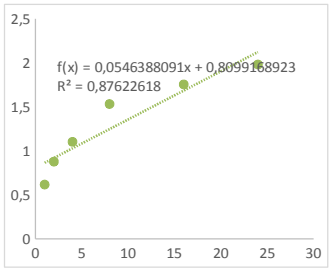
Pseudo-first order (Higuchi)	
Square-root of time	Drug (µg/cm2)
1,00	4,14
1,41	7,55
2,00	12,66
2,83	34,02
4,00	56,80
4,90	95,71

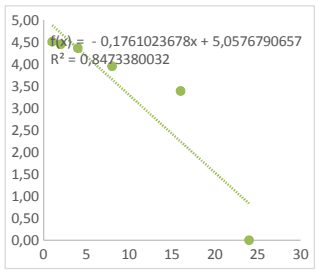
First order	
Time (h)	Drug (log µg/cm2)
1	0,6171355243
2	0,8779130177
4	1,1025470827
8	1,5317659027
16	1,7543304901
24	1,9809438346

Hixson-Crowell	
Time (h)	Square-root of non-permeated drug
1	4,51
2	4,45
4	4,36
8	3,95
16	3,39
24	0,00









Best fitted model: Zero order
Flux: **3,91 µg/cm2/h-1**
Lag time: **0,29 h** (~17 min)
Kp **0,01 cm/h-1**

Drug retained within the mucosa

Franz cell	Area	Concentration (µg/mL)	Quantity (µg)
1	5972,089	135,93	679,66
2	6154,575	140,05	700,26
3	5723,685	130,32	651,62
4	5403,329	123,09	615,45
5	5571,891	126,90	634,48
6	5511,785	125,54	627,70
Average		130,31	651,53
S.D.		6,53	32,64

*mucosa diluted with 5 mL of diluent

Drug lost during application

Franz cell	Area	Concentration (µg/mL)	Quantity (µg)
1	6036,146	137,38	686,89
2	3469,819	79,44	397,19
3	4907,017	111,89	559,43
4	2122,999	49,03	245,16
5	3422,096	78,36	391,80
6	416,610	10,51	52,53
Average		77,77	388,83
S.D.		44,88	224,39

*mucosa diluted with 5 mL of diluent

	µg	mg
Lost in spreader/ occlusor	388,83	0,39
Retained within the mucosa	651,53	0,65
Absorbed	178,02	0,18
Total	1218,38	1,22

Recovery		
Quantity of cream applied	70,0 mg	
Concentration of the cream	20,0 mg/g	
Quantity of drug applied	1,40 mg	
Quantity recovered	1,22 mg	
Average recovery	87,03 %	Specification: 85-115%

Permeation percentage	
Quantity of drug applied	1,40 mg
Quantity of drug absorbed (systemic effect)	0,18 mg
Quantity of drug within the mucosa (local effect)	0,65 mg
Permeation porcentage	12,7 %
Drug available for clinical effect	59,25 %