	Citric Acid	D-Mannitol	DSS	Kollicoat-IR	Lutrol F127	NaOAc	NONE	Plur PE10500	SDC	SDS
Complexing Agent										
Gelucire 44/14	-	-	-	-	-	-	-	-	-	-
Gelucire 50/13	-	-	-	-	-	-	-	-	-	-
Klucell EF	+	-	-	-	-	-	-	+	-	+
Lutrol F127	-	-	+	-	-	-	-	+	+	-
Luviskol VA64	+	-	-	-	-	+	-	-	-	+
PEOX50	-	-	-	-	-	-	-	-	+	-
PEOX500	+	-	-	-	+	-	-	-	-	+
Plasdone K-12	+	-	-	-	-	-	-	+	-	+
Plur PE10500	+	-	+	-	+	-	-	+	+	-
Plur PE6800	+	-	-	-	-	-	-	-	-	-
Pluronic F108	-	-	-	-	+	-	-	-	-	-
PMAMVE	-	-	+	-	+	-	-	-	+	+
PVP 40	-	-	-	-	-	-	-	-	-	-
PVP K90	+	-	+	-	-	-	-	-	-	+
PVP10	+	-	-	-	-	-	-	-	-	-
Soluplus	+	-	-	-	-	+	-	+	+	+
Tetronic 1107	+	-	+	-	-	-	+	-	-	-
TPGS	+	-	+	-	-	-	-	-	+	-
+ Redispersable complex Abiraterone acetate formulation in water										
- non-redispersable complex Abiraterone acetate formulation in water										

Figure 1

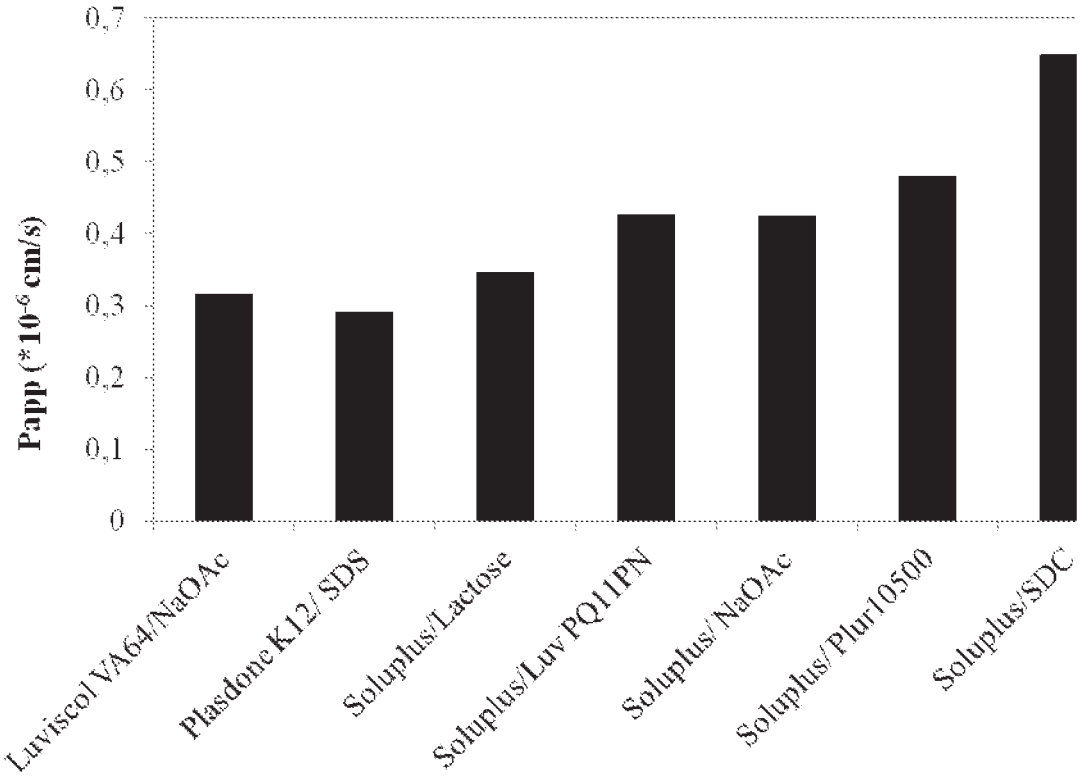


Figure 2

SDC ratio to Abiraterone acetate	Soluplus ratio to Abiraterone acetate		
	2X	3X	4X
	Redispersibility and stability		
0.2X	not dispersable	dispersable, unstable	dispersable, unstable
0.6X	not dispersable	dispersable, stable	dispersable, stable
1X	dispersable, unstable	dispersable, stable	dispersable, stable
	PAMPA permeability (10^{-6} cm/s)		
0.2X	0.504	0.584	0.784
0.6X	0.665	0.699	0.677
1X	0.629	0.604	-

Figure 3

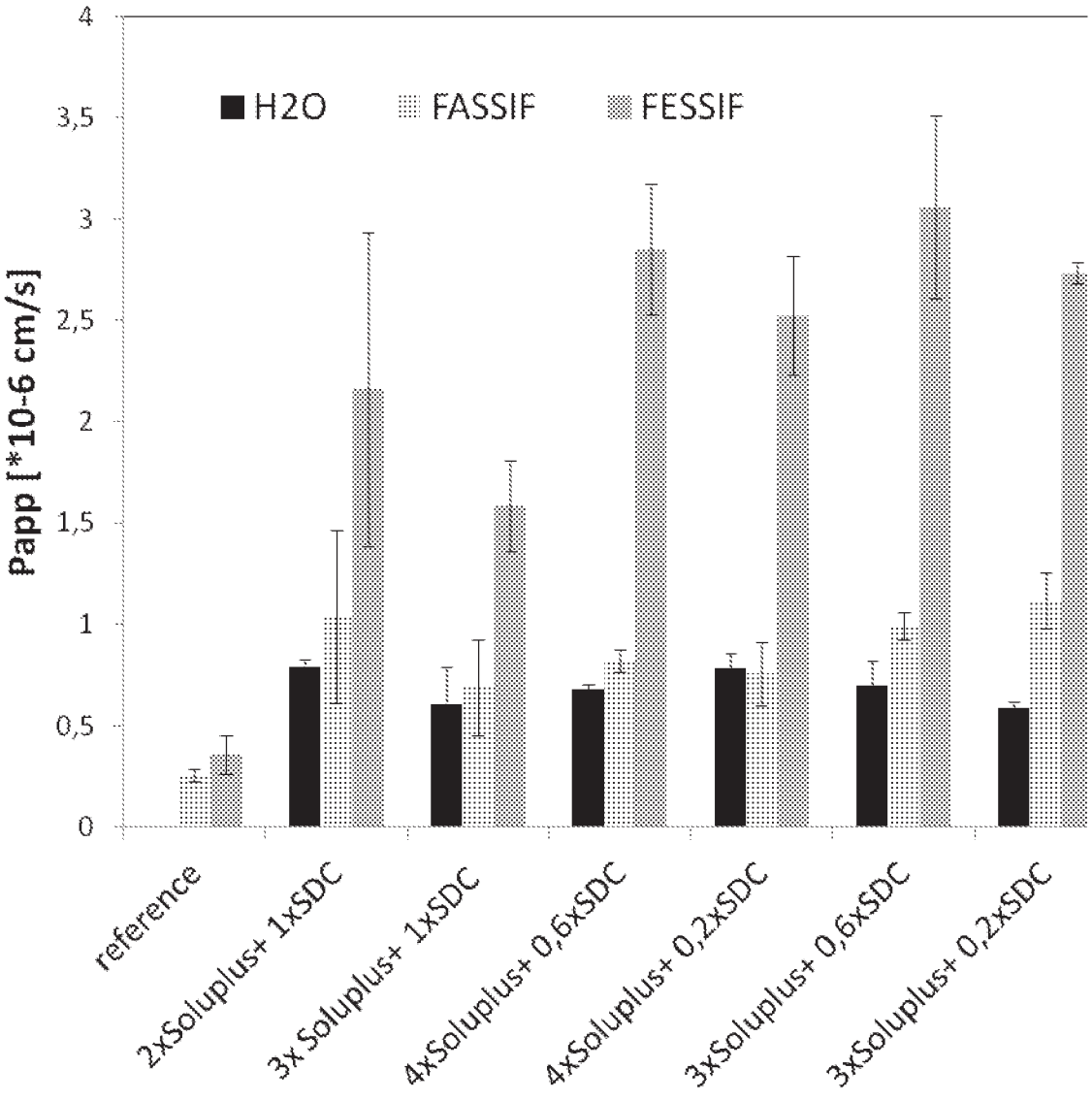

H2O
FASSIF
FESSIF
Papp [*10-6 cm/s]
4
3,5
3
2,5
2
1,5
1
0,5
0
reference
2xSoluplus+ 1xSDC
3x Soluplus+ 1xSDC
4xSoluplus+ 0,6xSDC
4xSoluplus+ 0,2xSDC
3xSoluplus+ 0,6xSDC
3xSoluplus+ 0,2xSDC

Figure 4

	Solvent	Concentration of Components	
Solution 1/a	Tetrahydrofuran	Abiraterone acetate 10 mg/mL	Soluplus® 40 mg/mL
Solution 1/b	Tetrahydrofuran	Abiraterone acetate 20 mg/mL	Soluplus® 80 mg/mL
Solution 1/c	Tetrahydrofuran	Abiraterone acetate 40 mg/mL	Soluplus® 160 mg/mL
Solution 2/a	purified water	Sodium deoxycholate 1.500 mg/mL	-
Solution 2/b	purified water	Sodium deoxycholate 1.340 mg/mL	-
Solution 2/c	purified water	Sodium deoxycholate 1.260 mg/mL	-

Figure 5

Solution 1	**Solution 2**	**Solvent 1: Solvent 2 ratio**	**Appearance of redispersed formulation**
Solution 1/a	Solution 2/a	1 : 4	milky solution
Solution 1/b	Solution 2/b	1 : 9	milky solution
Solution 1/c	Solution 2/c	1 : 19	milky solution

Figure 6

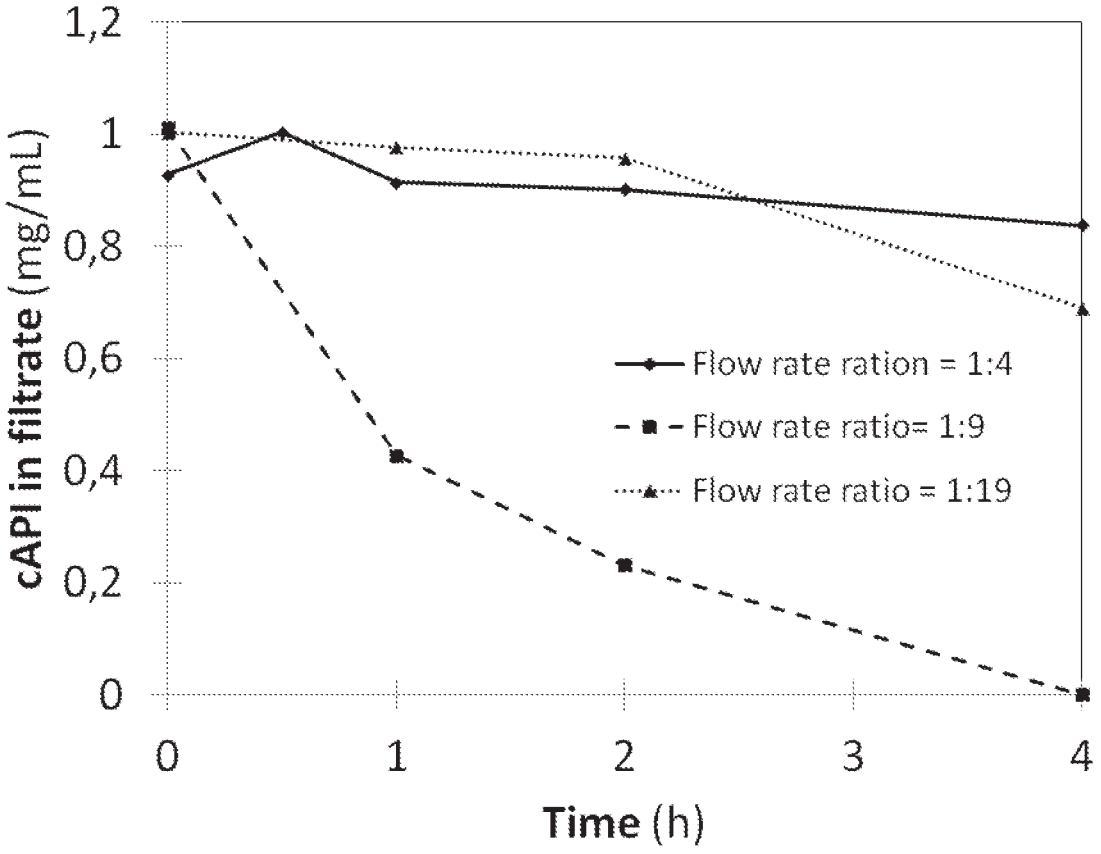

1,2
1
0,8
0,6
0,4
0,2
0
cAPI in filtrate (mg/mL)
0
1
2
3
4
Time (h)
Flow rate ration = 1:4
Flow rate ratio= 1:9
Flow rate ratio = 1:19

Figure 7

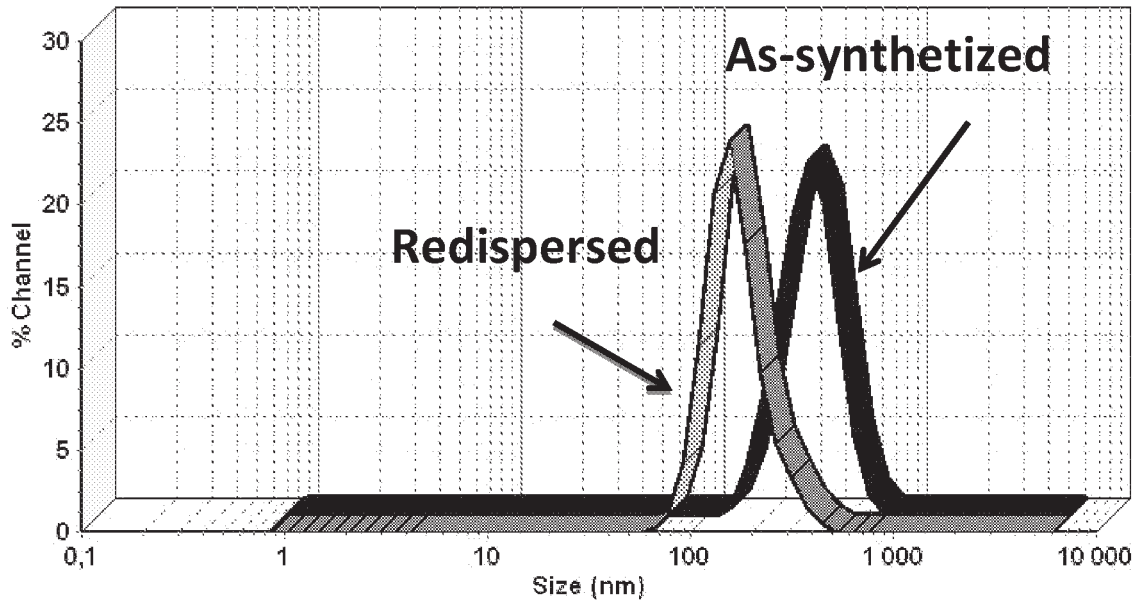


Figure 8

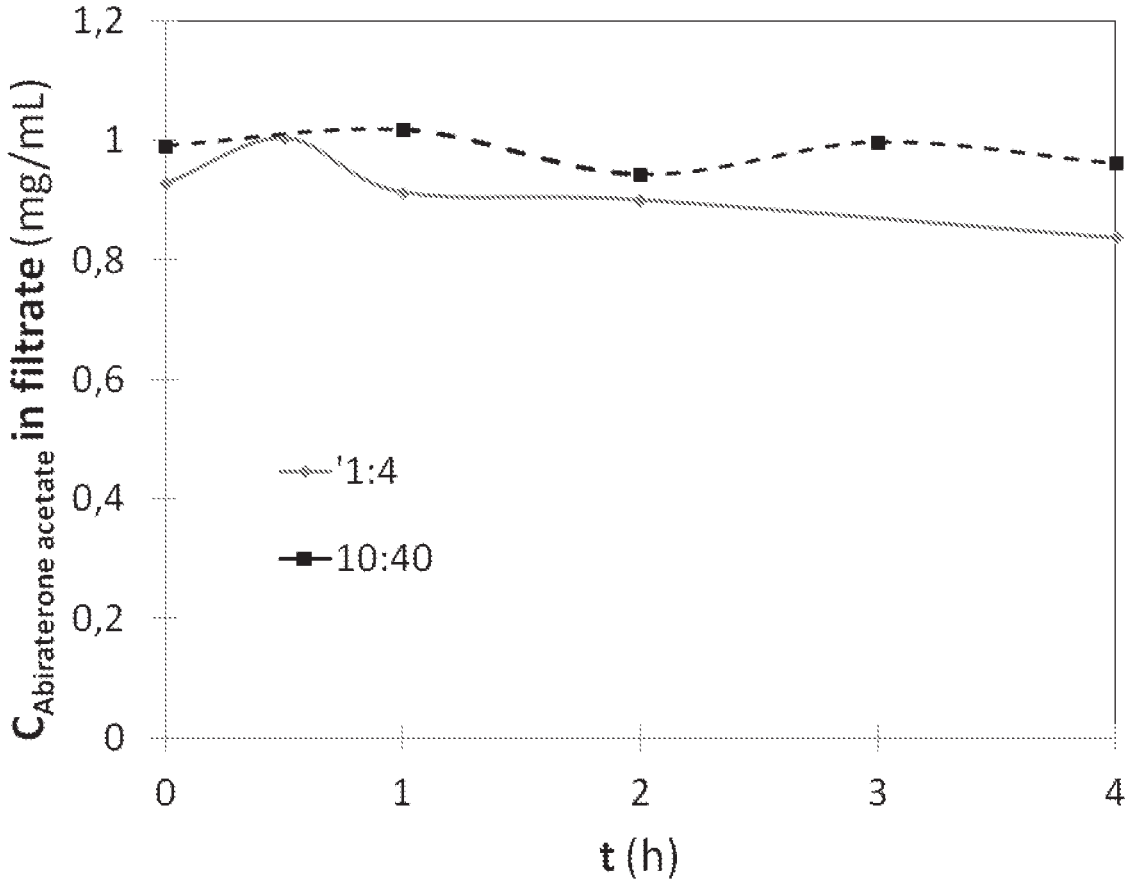


Figure 9

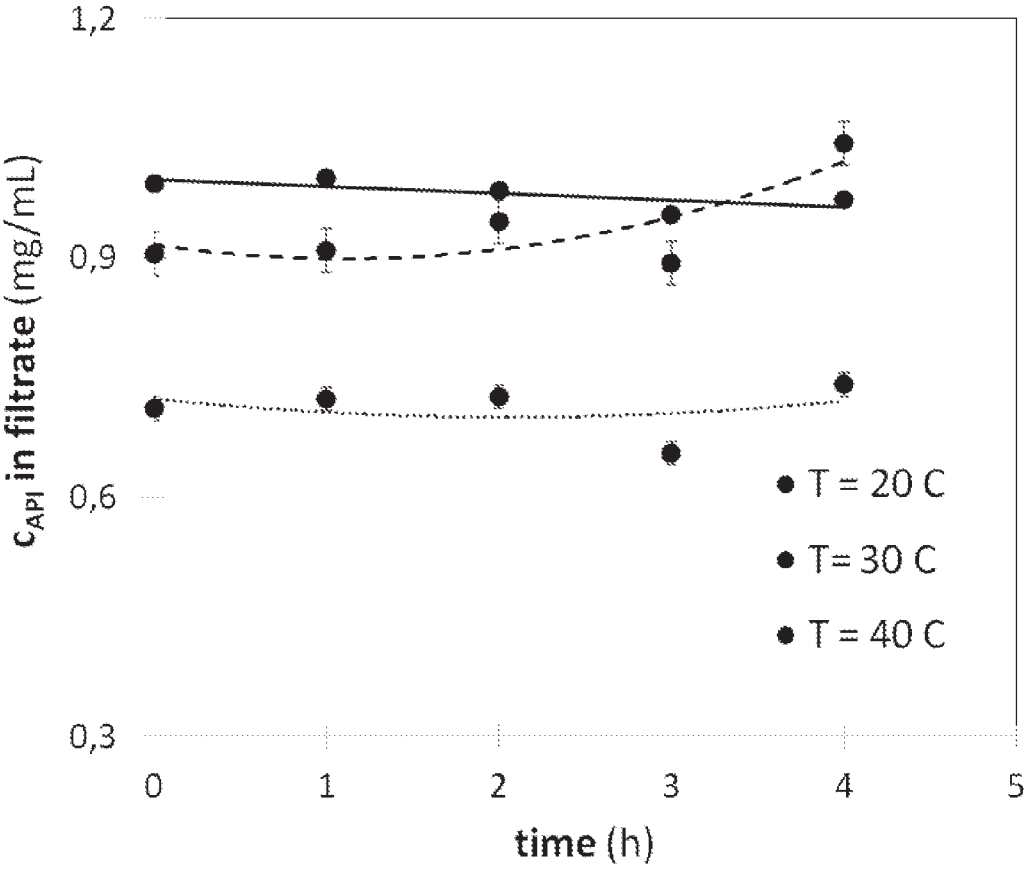


Figure 10

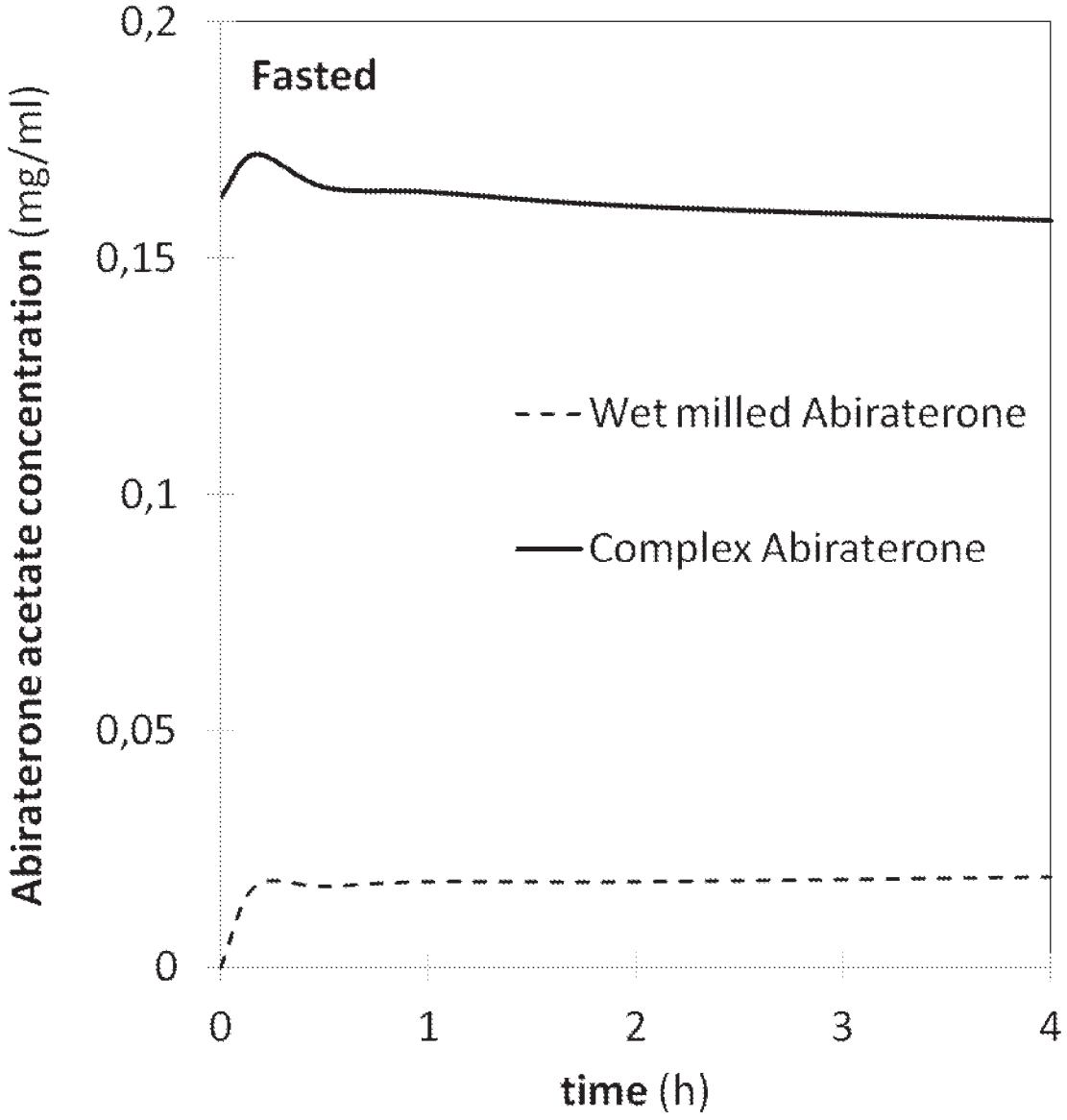

Fasted
Abiraterone acetate concentration (mg/ml)
0,2
0,15
0,1
0,05
0
Wet milled Abiraterone
Complex Abiraterone
0
1
2
3
4
time (h)

Figure 11

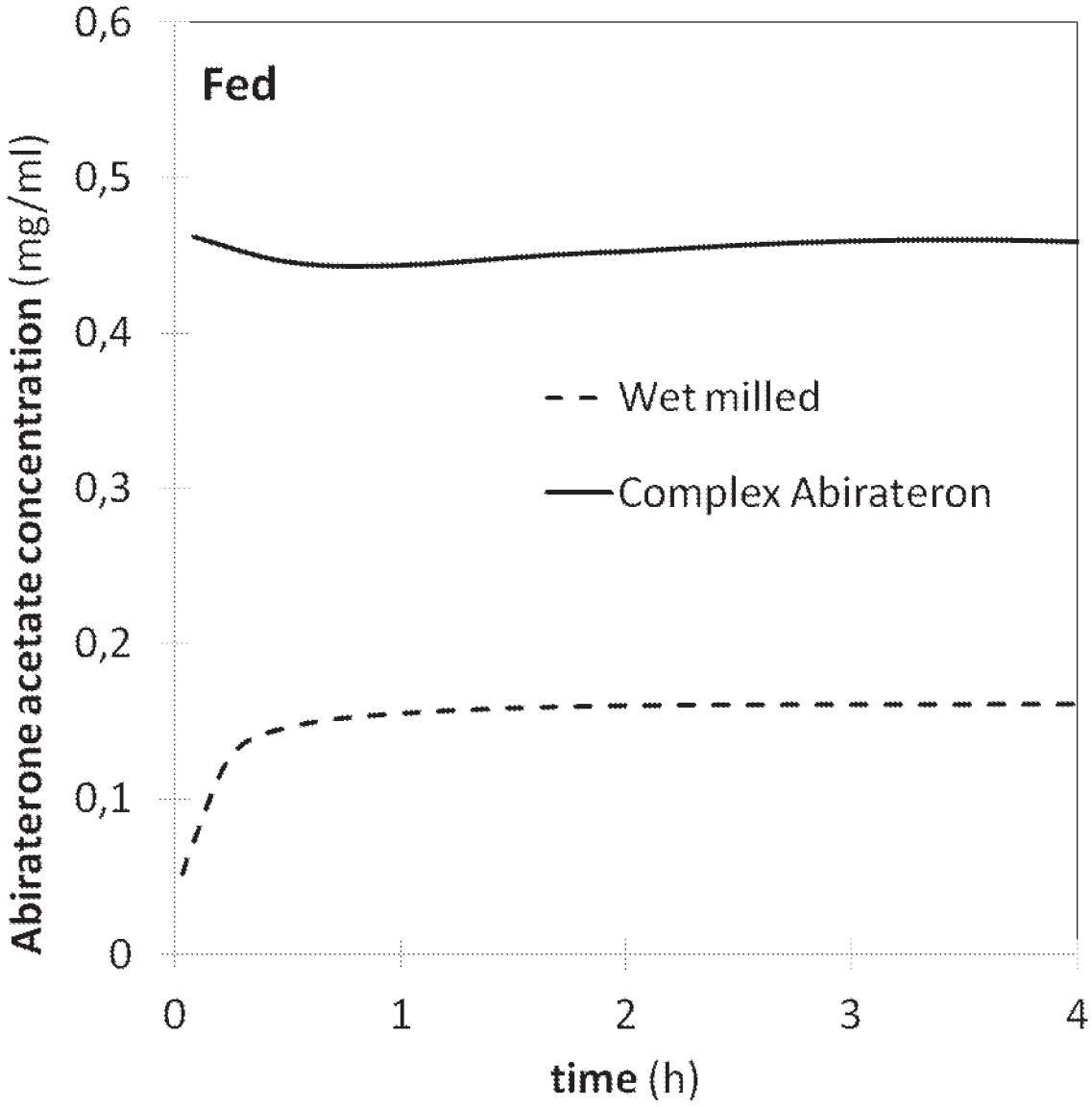

Fed
Abirateron acetate concentration (mg/ml)
0,6
0,5
0,4
0,3
0,2
0,1
0
Wet milled
Complex Abirateron
0
1
2
3
4
time (h)

Figure 12

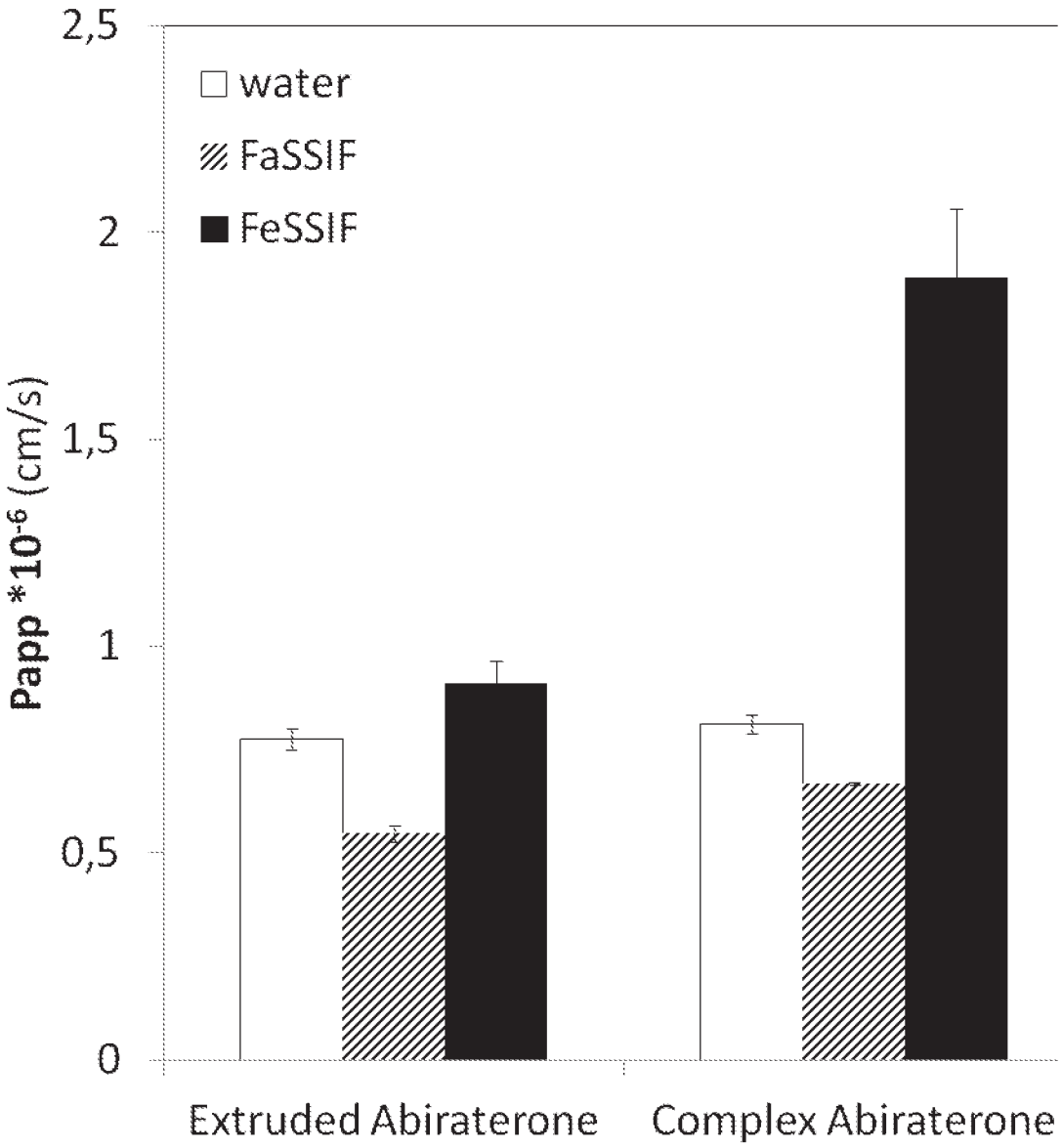

2,5
2
1,5
1
0,5
0
Papp *10-6 (cm/s)
water
FaSSIF
FeSSIF
Extruded Abiraterone
Complex Abiraterone

Figure 13

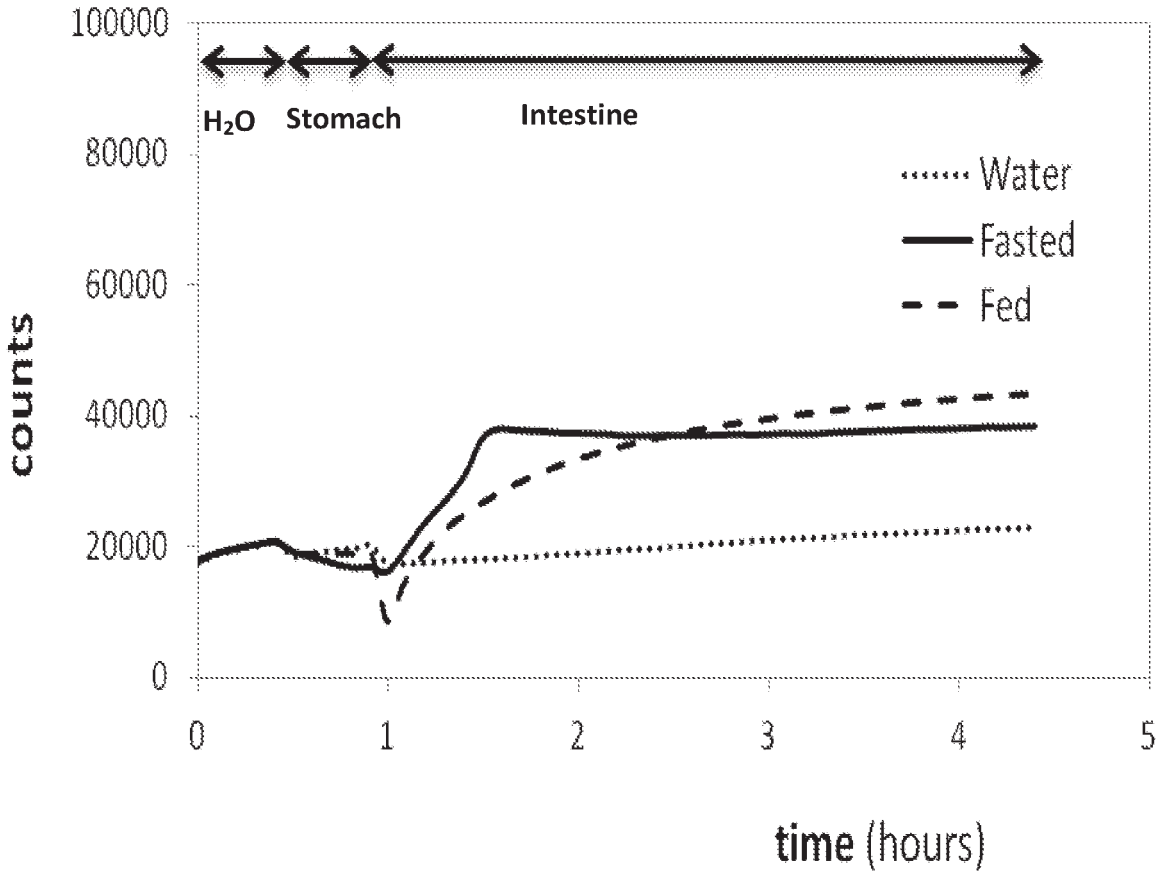

100000
80000
60000
40000
20000
0
counts
H2O
Stomach
Intestine
Water
Fasted
Fed
0
1
2
3
4
5
time (hours)

Figure 14

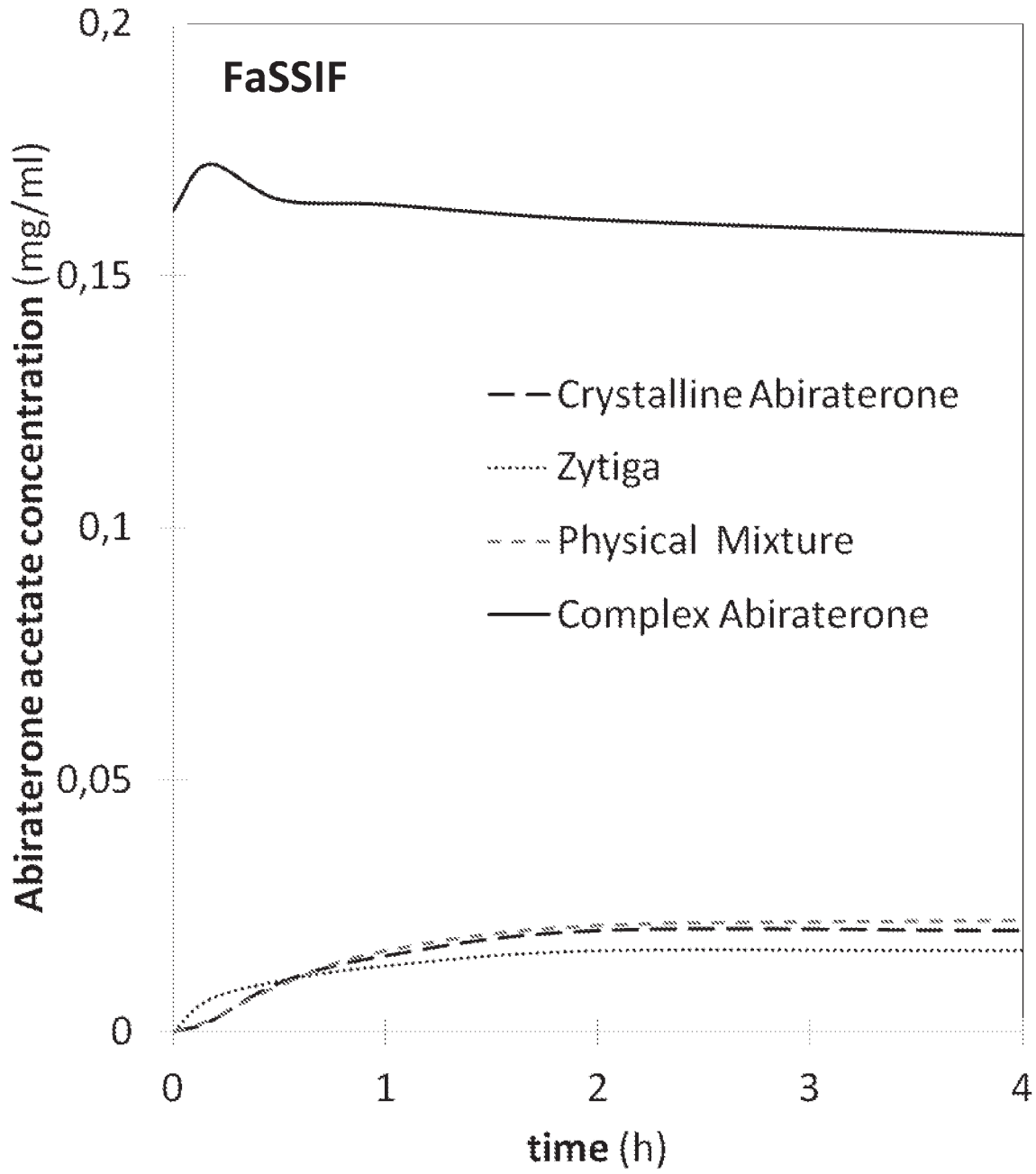

FaSSIF
Abiraterone acetate concentration (mg/ml)
0,2
0,15
0,1
0,05
0
0
1
2
3
4
time (h)
Crystalline Abiraterone
Zytiga
Physical Mixture
Complex Abiraterone

Figure 15

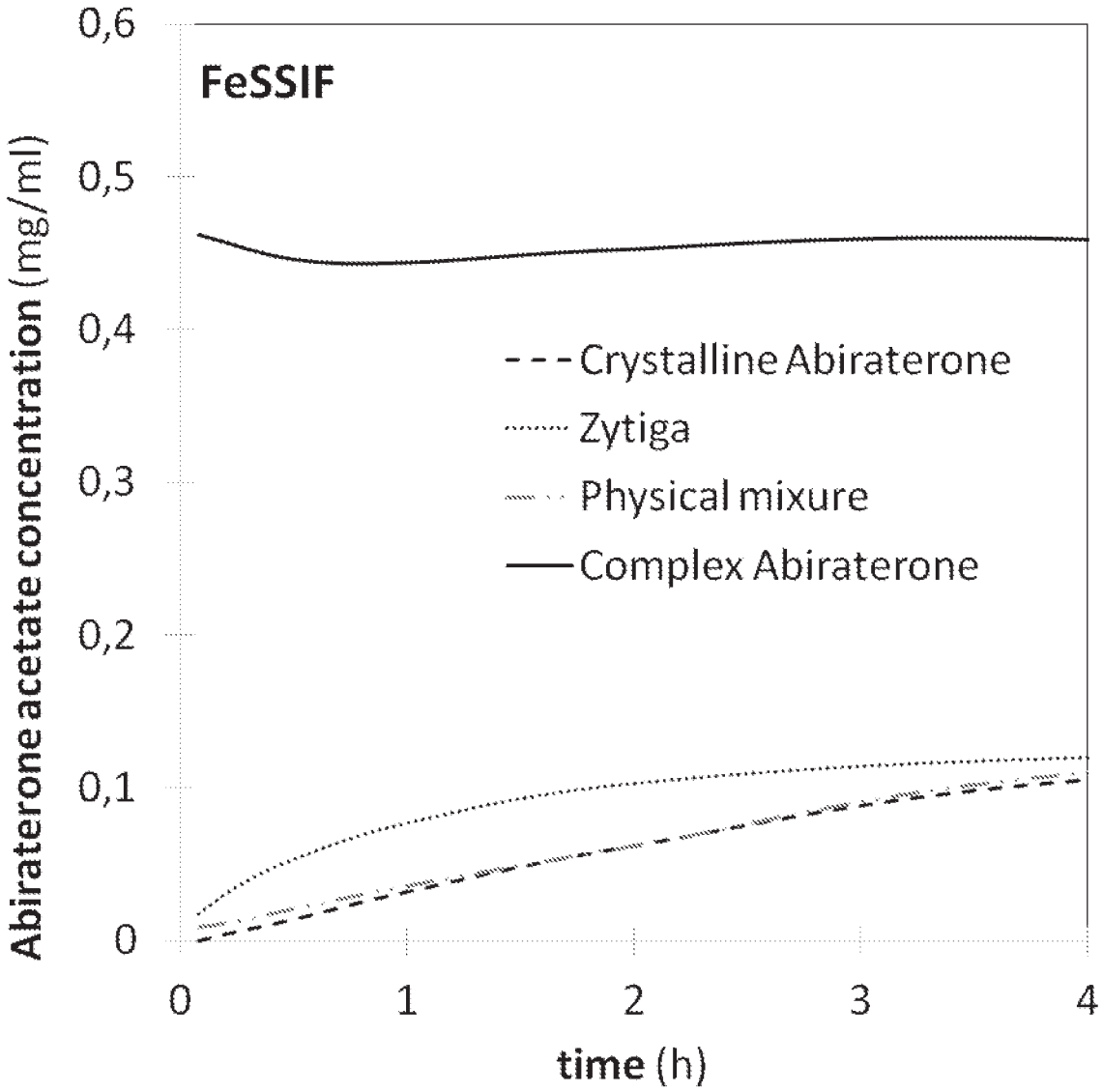

FeSSIF
Abiraterone acetate concentration (mg/ml)
0,6
0,5
0,4
0,3
0,2
0,1
0
0
1
2
3
4
time (h)
Crystalline Abiraterone
Zytiga
Physical mixure
Complex Abiraterone

Figure 16

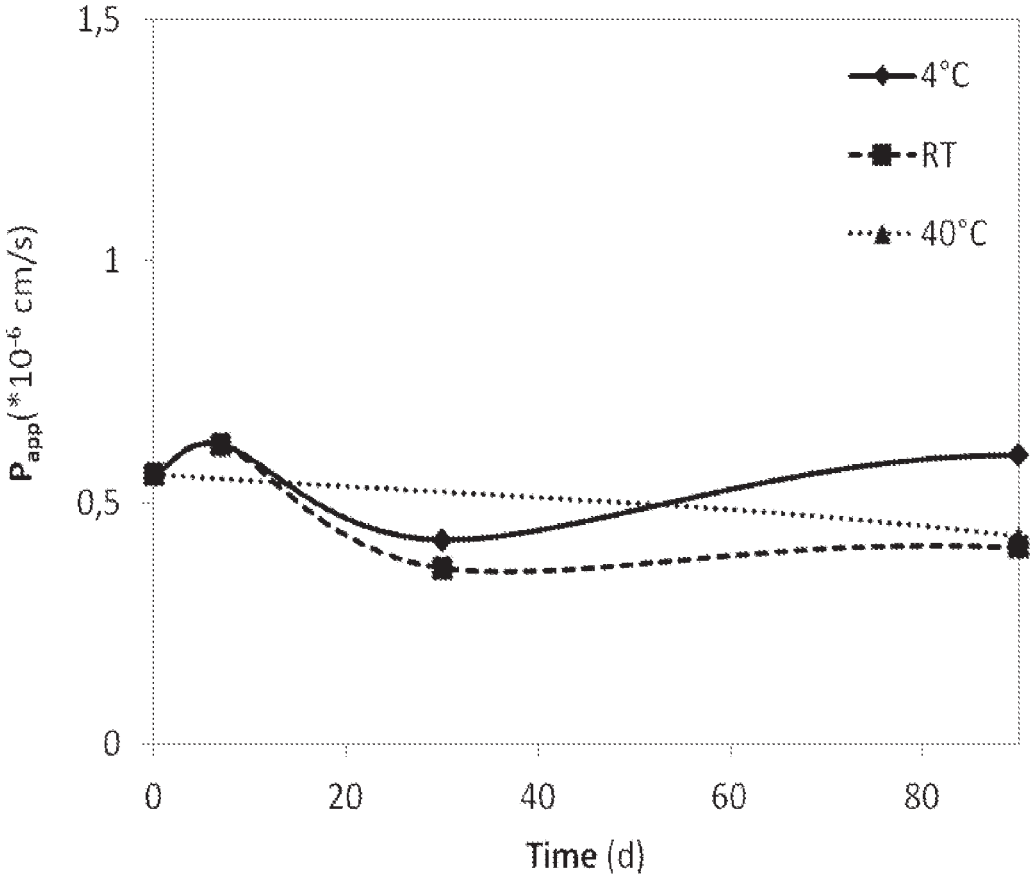


Figure 17

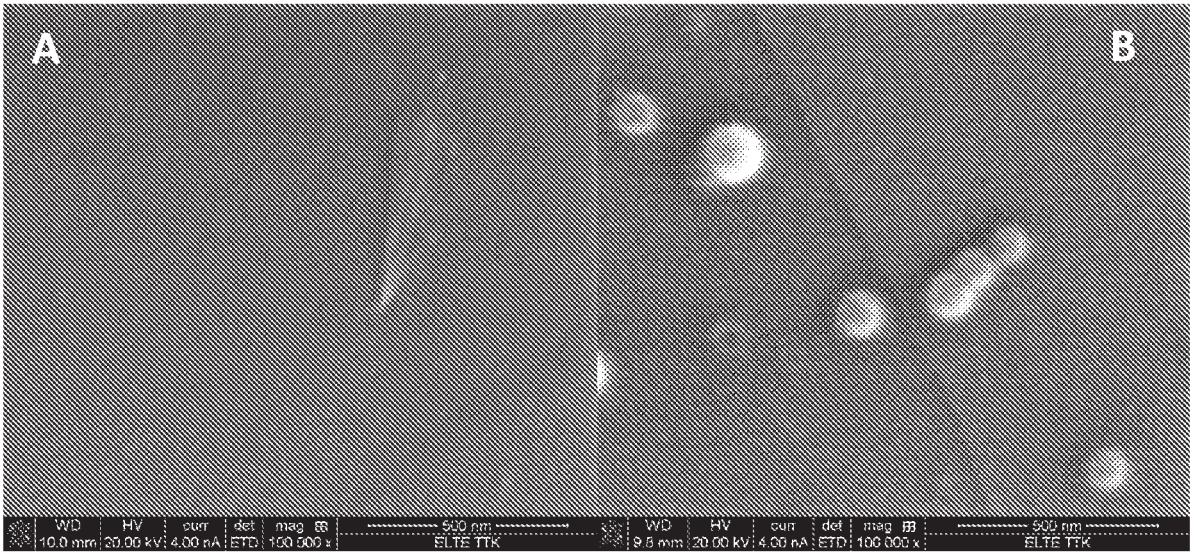


Figure 18

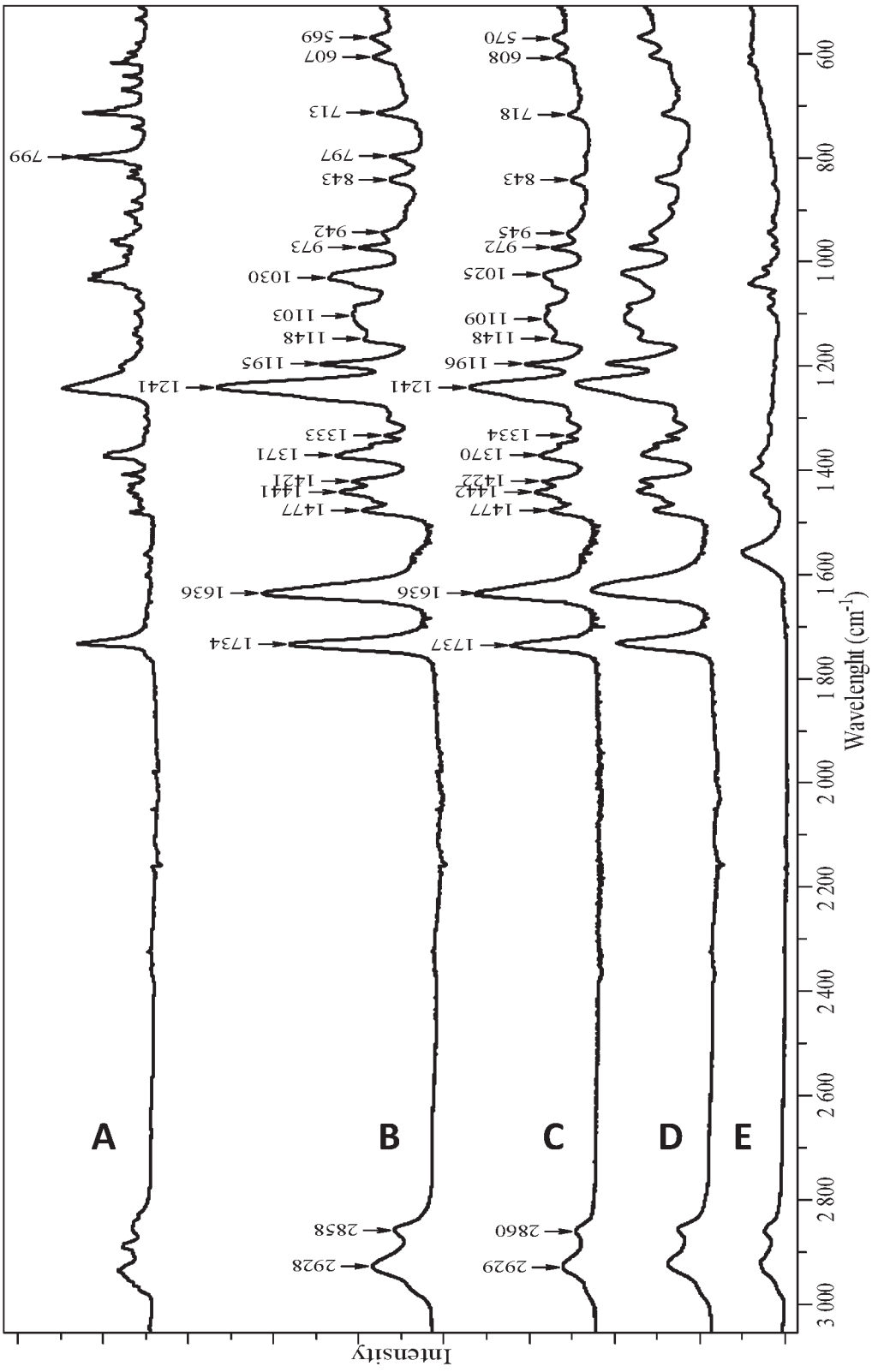

A
B
C
D
E
799
1241
1195
1148
1103
1030
973
942
843
797
713
607
569
1636
1734
1477
1441
1421
1371
1333
2858
2928
1737
1636
1477
1442
1422
1370
1334
1241
1196
1148
1109
1025
972
945
843
718
608
570
2860
2929
Intensity
3 000
2 800
2 600
2 400
2 200
2 000
1 800
1 600
1 400
1 200
1 000
800
600
Wavelenght (cm-1)

Figure 19

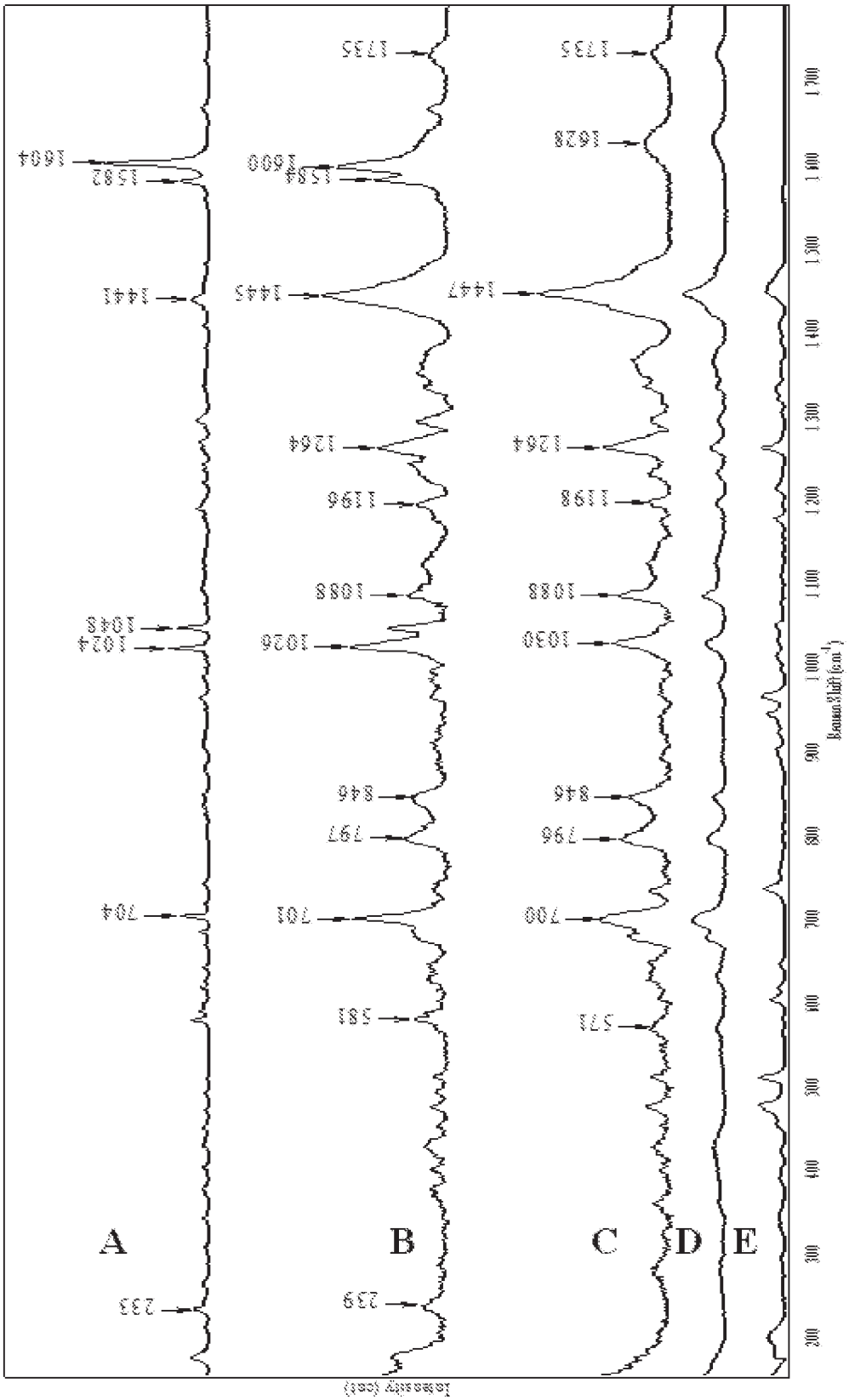

A
B
C
D
E
233
704
1024
1048
1441
1582
1604
239
581
701
797
846
1026
1088
1196
1264
1445
1584
1600
1735
571
700
796
846
1030
1088
1198
1264
1447
1628
1735
Intensity (cnt)
Raman Shift (cm-1)

Figure 20

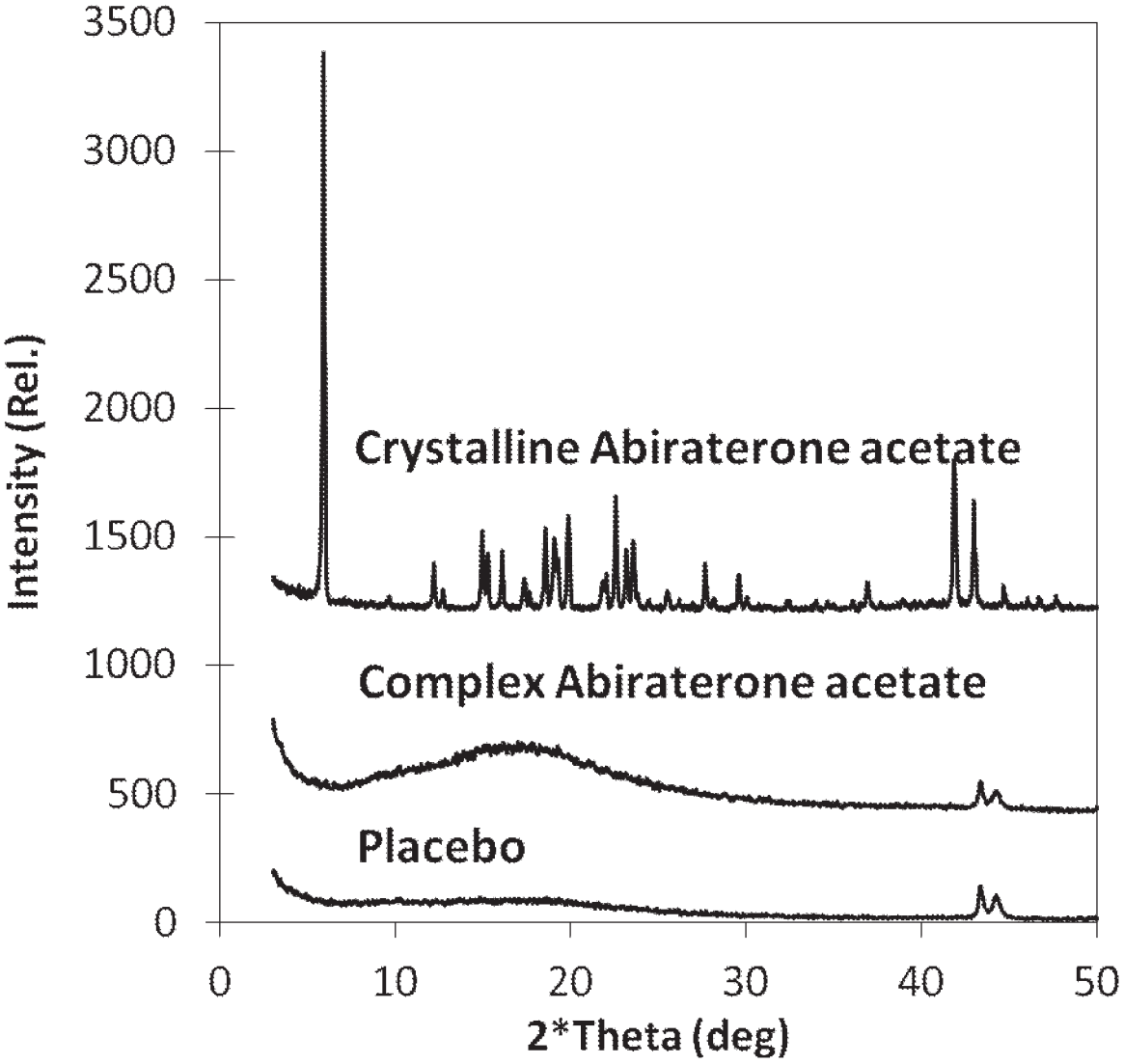


Figure 21

	pH
Right after the production	
Reconstitution with 50 mL purified water	7.35
After 2 months storage	
Reconstitution with 50 mL purified water	7.40

Figure 22

Bottle ID	Water content (%)	Average	SD
U0161	1.85		
U0161	1.74	1.84	0.10
U0161	1.93		

Measured at RH=75%

Figure 23

Bottle ID: U0920	$c_{Solution}$ (mg/mL)	Abiraterone acetate content (mg)
$V_{Ph.Eur\ water}$= 50 mL	1.0404	52.02
Rinsing with $V_{Ph.Eur\ water}$= 10 mL	0.0747	0.75
Rinsing with $V_{Methanol}$= 10 mL	0.0390	0.39
	Total	**53.16**

Figure 24

Composition of complex Abiraterone acetate granulation		
Granulated complex Abiraterone	active ingredient	31.32 w/w%
Lactose-monohydrate (Flowlac 100)	filler	31.32 w/w %
Microcrystalline-cellulose (Vivapur 101)	filler	15.66 w/w %
Croscarmellose sodium	disintegrant	14.99 w/w %
Sodium-deoxycholate	absorption supporting agent	6.71 w/w %

Figure 25

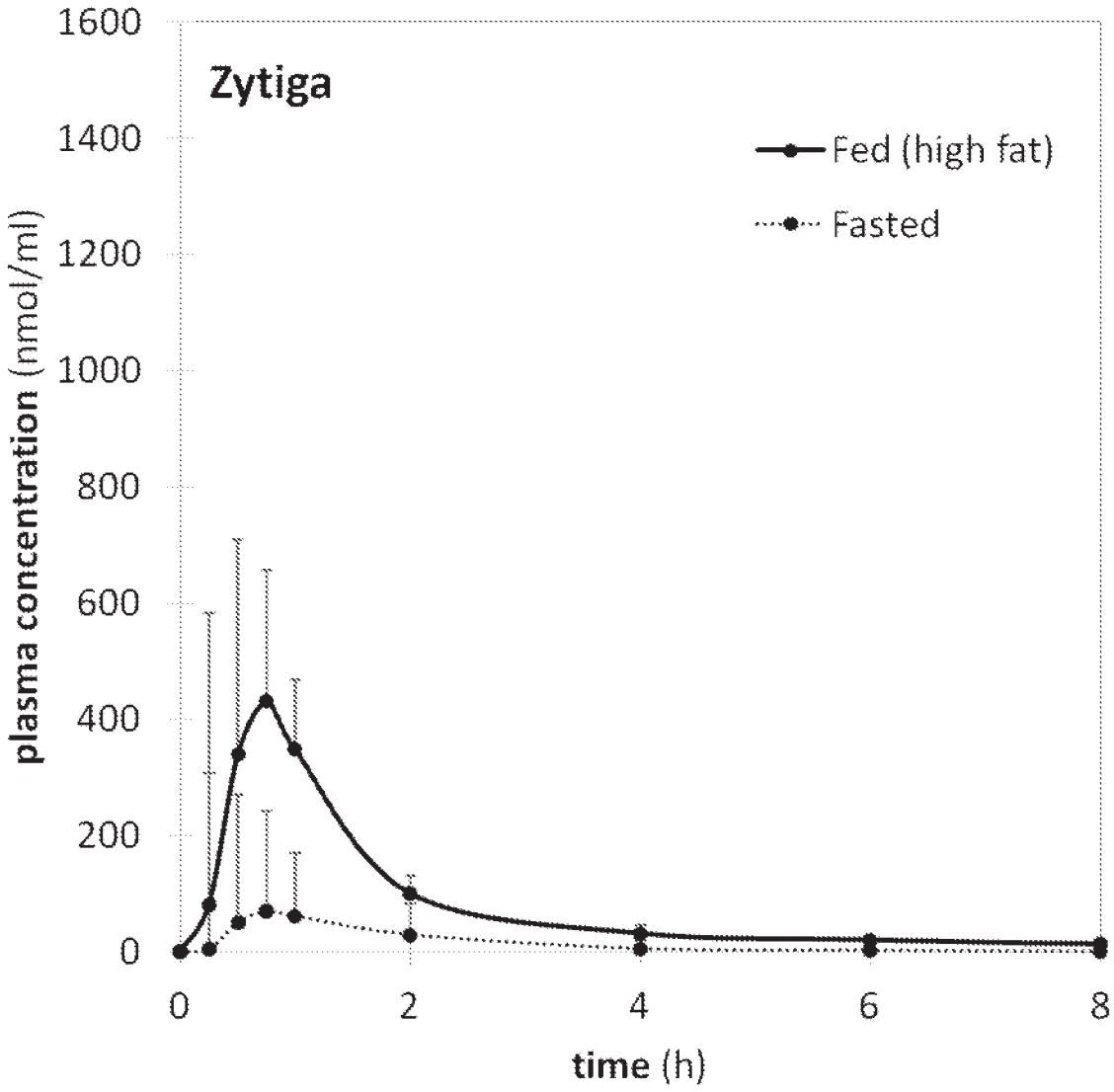

Zytiga
Fed (high fat)
Fasted
plasma concentration (nmol/ml)
1600
1400
1200
1000
800
600
400
200
0
0
2
4
6
8
time (h)

Figure 26

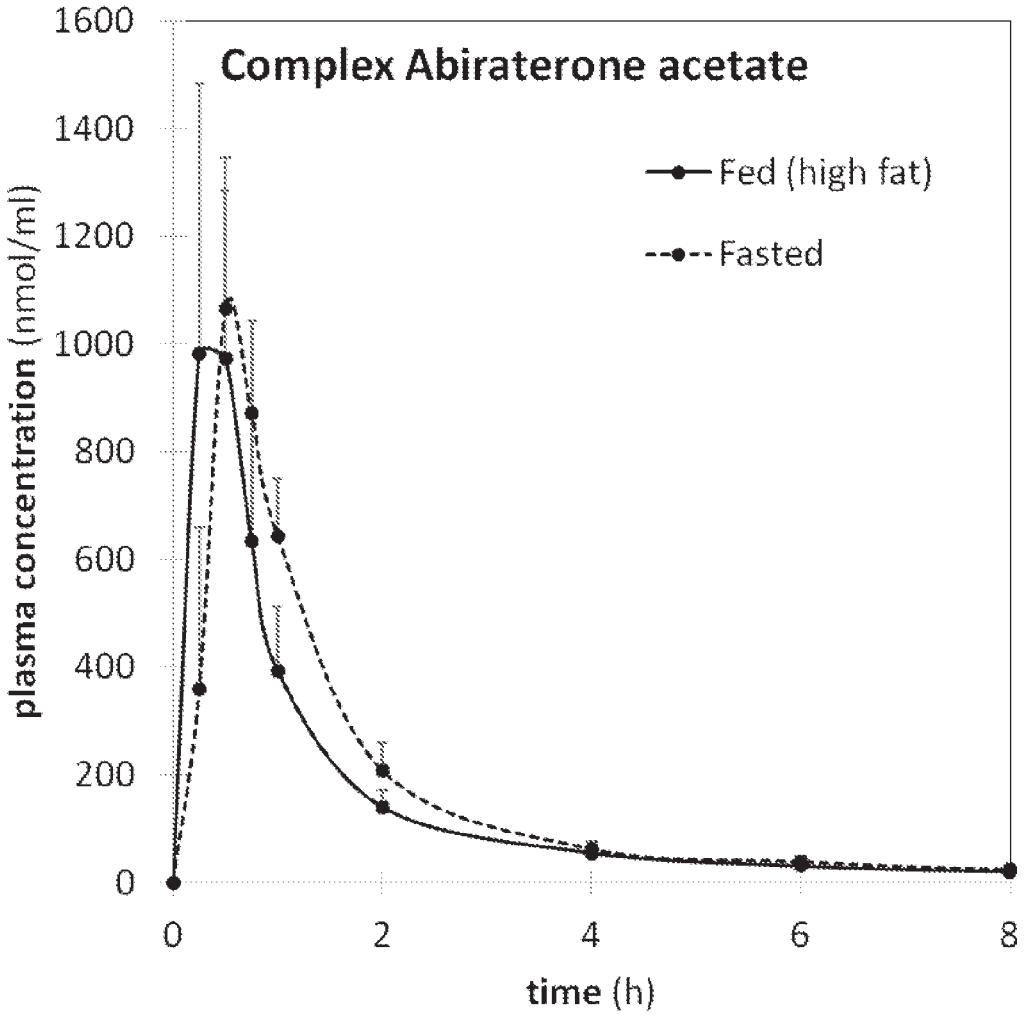


Figure 27

Test article	Feeding condition	t_{max} (h)	C_{max} (nmol/ml)	AUC_{last} (h*nmol/ml)
Complex Abiraterone	Fasted	0.50 ± 0	1064 ± 219	1575 ± 339
Complex Abiraterone	High fat meal	0.38 ± 0.13	1086 ± 433	1345 ± 435
Zytiga	Fasted	1.06 ± 0.54	76 ± 38	138 ± 75
Zytiga	High fat meal	0.81 ± 13	443 ± 215	773 ± 300

Figure 28

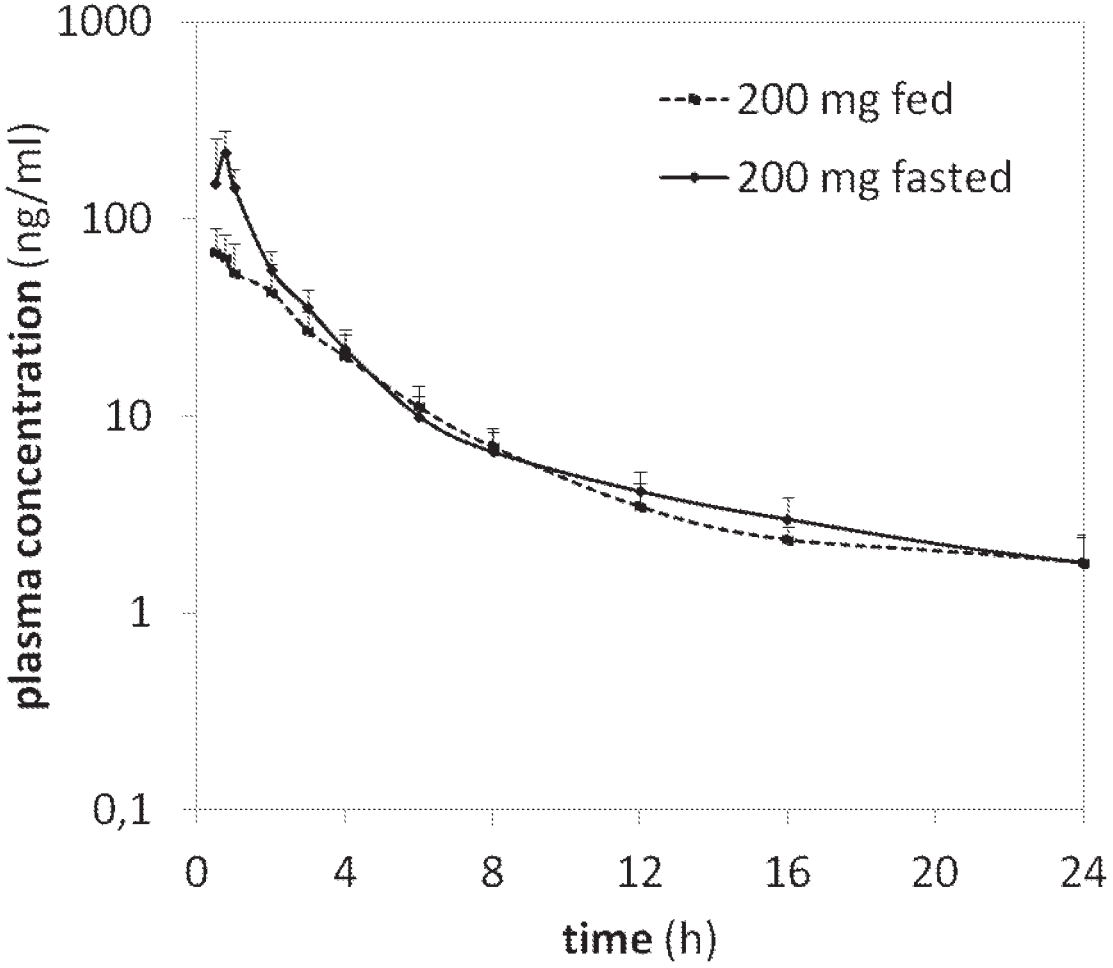


Figure 29

	ZYTIGA FASTED*	COMPLEX ABIRATERONE, FASTED	COMPLEX ABIRATERONE, FED
Dose (mg)	1000	200	200
AUC_{last} (ng*h/ml) (% of 1000 mg Zytiga)	503 (100)	399 (80)	295 (59)
C_{max} (ng/ml)	93.5	206	72
Variability (AUC_{last} CV%)	0.5	0.3	0.2
Variability (max/min AUC_{last})	9	2.3	2.2
Food effect (fed/fasted AUC_{last})	5	0.74	
$t_{1/2}$ (h)	16	15	13

Figure 30