

Waiver for Bio-equivalence study on Escitalopram Oxalate Tablets 10 mg:

The Bio-equivalence study was carried out on Escitalopram Oxalate Tablets 20 mg. Based on acceptable Bio-equivalence study for Escitalopram Oxalate Tablets 20 mg, a bio-waiver is requested for Escitalopram Oxalate Tablets 10 mg as per following considerations: [Ref.: CPMP Note for Guidance on Investigation of Bioavailability and Bioequivalence].

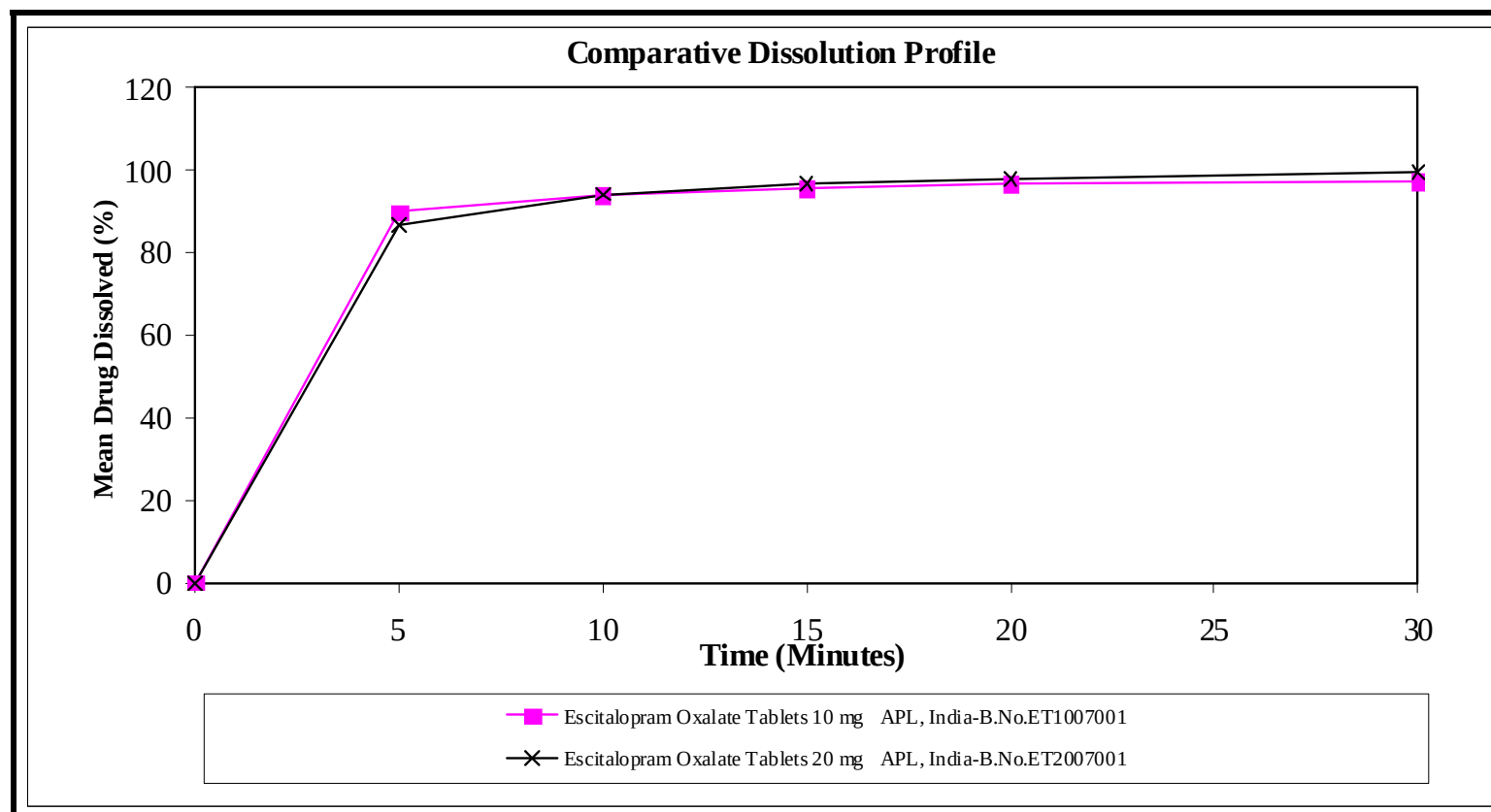
1. Escitalopram Oxalate Tablets 10 mg & 20 mg Tablets are manufactured by the same manufacturer i.e. Aurobindo Pharma Limited (Unit III) and using the same manufacturing process.
2. The Escitalopram exhibits linear and dose-proportional pharmacokinetics throughout its therapeutic dose range following single or multiple doses [Rao (2007)]. The single- and multiple-dose pharmacokinetics of escitalopram is linear and dose-proportional in a dose range of 10 to 30 mg/day [Cipriani et al (2007)].
3. The qualitative composition of Escitalopram Oxalate Tablets 10 mg is the same as that of Escitalopram Oxalate Tablets 20 mg.
4. Escitalopram Oxalate Tablets 10 mg are dose proportional (i.e Step-down formula) with Escitalopram Oxalate Tablets 20 mg. Thus, the ratio of amount of active substance and the excipients is the same for all the strengths.
5. The dissolution profile of Escitalopram Oxalate Tablets 10 mg is similar to Escitalopram Oxalate Tablets 20 mg. The dissolution profile of Escitalopram Oxalate Tablets 10 mg (Batch No. ET1007001) was compared to Escitalopram Oxalate Tablets 20 mg, (Batch No. ET2007001) i.e. Test Batch used in Bio-equivalence Study) in different media viz. 0.1N HCl, pH-4.5 Acetate buffer and pH 6.8 phosphate buffer and was found similar. The results are presented overleaf:

Comparative dissolution profile of Escitalopram Oxalate Tablets in 0.1N HCl

Unit No	Dissolution Profile (% drug released in 900 ml 0.1N HCl/50 rpm/paddle)									
	Escitalopram 10mg Tablets					Escitalopram 20mg Tablets				
	Aurobindo Pharma Ltd. Batch No. ET1007001					Aurobindo Pharma Ltd. Batch No. ET2007001*				
Min →	5	10	15	20	30	5	10	15	20	30
1	95	96	97	97	97	80	91	94	97	99
2	91	94	95	96	97	75	86	90	92	95
3	92	96	97	98	98	89	97	101	102	103
4	93	97	98	99	94	91	98	101	102	103
5	77	83	86	90	96	94	100	101	102	103
6	87	91	94	95	97	80	91	95	97	99
7	90	95	96	97	97	84	91	94	95	98
8	87	93	95	96	97	81	88	91	93	96
9	88	93	95	96	102	95	99	101	101	102
10	91	96	98	100	99	90	96	98	98	99
11	95	98	98	99	98	90	95	97	98	99
12	93	97	98	98	98	93	99	100	101	101
Average	89.9	94.1	95.6	96.8	97.5	86.9	94.3	96.8	98.0	99.6
%RSD	4.95	4.29	3.50	2.69	1.93	4.95	4.90	4.14	3.70	2.71

* Batch used in bio-equivalence study

Comparative dissolution profile of Escitalopram Oxalate Tablets in 0.1N HCl



The dissolution profile of Escitalopram Oxalate Tablets 10 mg is similar to Escitalopram Oxalate Tablets 20 mg in 0.1N HCl.

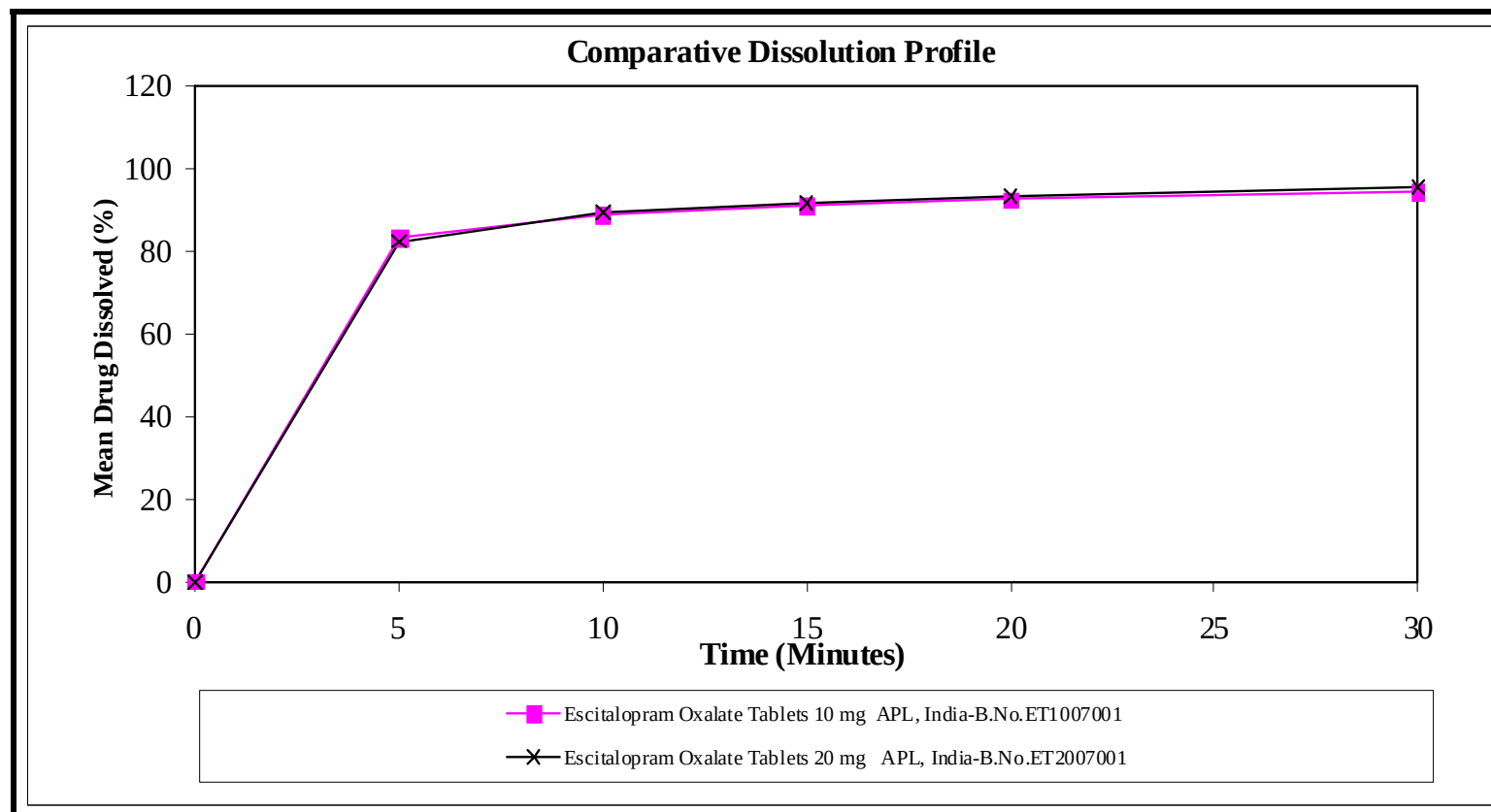
(**Note:** No F_2 calculation is necessary since more than 85 % of the drug is released within 15 minutes).

Comparative dissolution profile of Escitalopram Oxalate Tablets in pH 4.5 Acetate buffer

Unit No	Dissolution Profile (% drug released in 900 ml pH 4.5 Acetate buffer/50 rpm/paddle)									
	Escitalopram Oxalate Tablets 10 mg					Escitalopram Oxalate Tablets 20 mg				
	Aurobindo Pharma Ltd. Batch No. ET1007001					Aurobindo Pharma Ltd. Batch No. ET2007001*				
Min →	5	10	15	20	30	5	10	15	20	30
1	80	90	92	93	94	76	85	87	89	91
2	85	90	92	93	94	76	85	88	90	92
3	82	88	90	92	93	80	87	89	92	95
4	78	85	88	89	92	86	92	94	95	97
5	80	86	89	90	94	94	99	100	101	101
6	84	88	91	92	93	88	96	97	98	99
7	85	89	91	92	95	76	84	88	91	94
8	86	91	93	94	95	80	85	88	91	93
9	89	92	93	94	96	89	94	96	98	100
10	82	88	91	94	94	76	83	85	88	91
11	87	91	92	93	97	81	88	90	92	94
12	80	89	91	94	97	87	95	97	98	99
Average	83.2	88.9	91.1	92.5	94.5	82.5	89.4	91.6	93.5	95.7
%RSD	4.95	2.32	1.65	1.76	1.66	4.95	6.15	5.42	4.63	3.83

* Batch used in bio-equivalence study

Comparative dissolution profile of Escitalopram Oxalate Tablets in pH 4.5 Acetate buffer



The dissolution profile of Escitalopram Oxalate Tablets 10 mg is similar to Escitalopram Oxalate Tablets 20 mg in pH 4.5 acetate buffer.

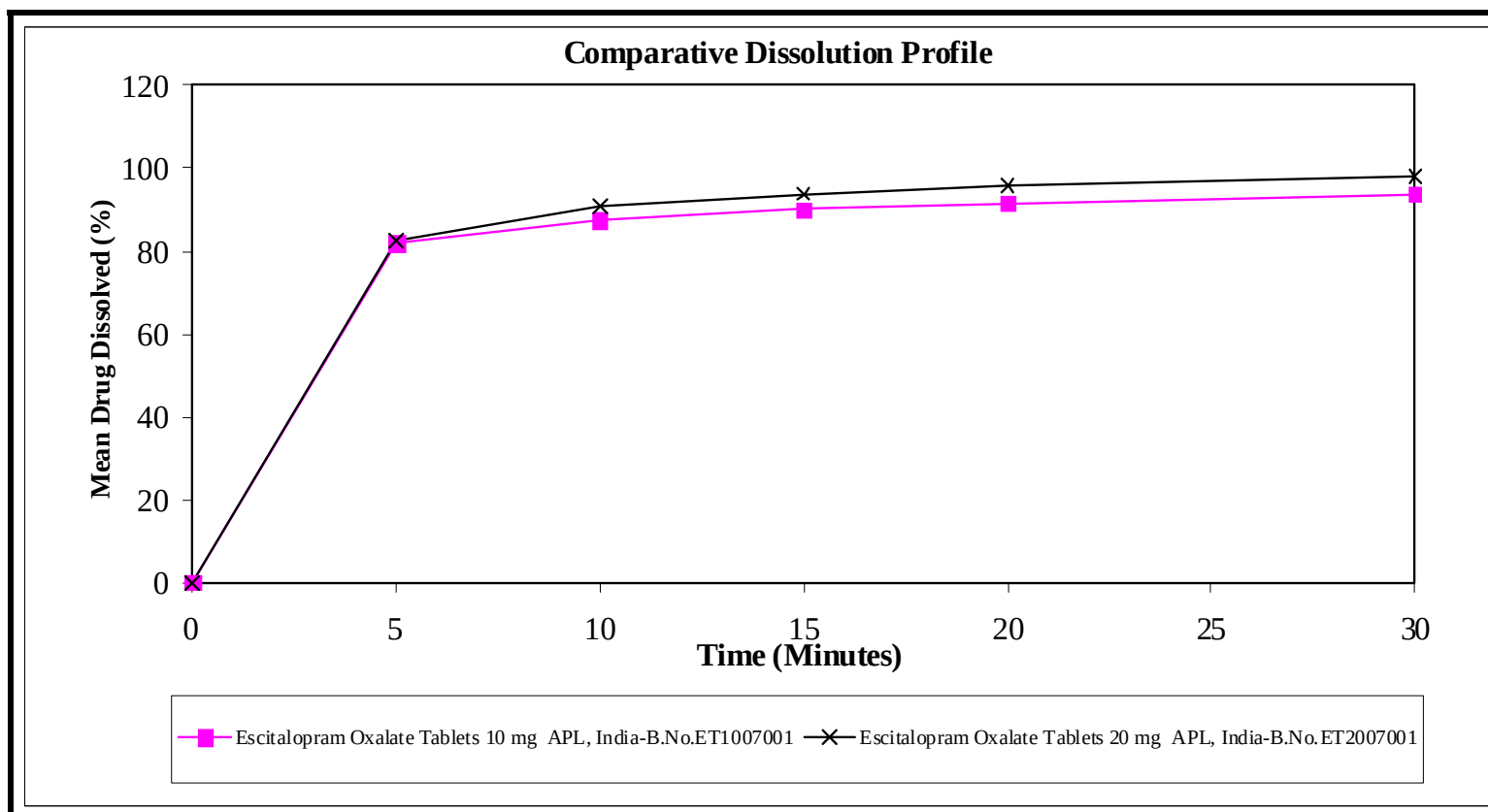
(**Note:** No F_2 calculation is necessary since more than 85 % of the drug is released with in 15 minutes).

Comparative dissolution profile of Escitalopram Oxalate Tablets in pH 6.8 Phosphate buffer

Unit No	Dissolution Profile (% drug released in 900 ml pH 6.8 phosphate buffer/50 rpm/paddle)									
	Escitalopram Oxalate Tablets 10 mg					Escitalopram Oxalate Tablets 20 mg				
	Aurobindo Pharma Ltd. Batch No. ET1007001					Aurobindo Pharma Ltd. Batch No. ET2007001*				
Min →	5	10	15	20	30	5	10	15	20	30
1	79	88	92	93	95	81	89	92	94	97
2	82	88	91	91	95	86	94	96	98	99
3	85	89	91	93	95	82	88	91	93	96
4	87	92	94	95	89	79	89	93	96	98
5	76	80	84	86	93	86	95	97	99	100
6	80	85	88	90	93	81	92	95	98	99
7	80	86	88	91	89	82	88	91	93	95
8	76	81	84	86	96	79	89	93	95	98
9	88	92	94	95	94	86	94	97	98	100
10	85	90	92	93	95	81	92	95	97	99
11	82	88	91	92	96	86	94	96	98	99
12	84	90	92	94	96	82	88	91	93	95
Average	82.0	87.4	90.1	91.6	93.8	82.6	91.0	93.9	95.8	98.0
%RSD	4.95	4.40	3.77	3.31	2.64	4.95	2.97	2.70	2.45	1.91

* Batch used in bio-equivalence study

Comparative dissolution profile of Escitalopram Oxalate Tablets in pH 6.8 Phosphate buffer



The dissolution profile of Escitalopram Oxalate Tablets 10 mg is similar to Escitalopram Oxalate Tablets 20 mg in pH 6.8 phosphate buffer.

(**Note:** No F_2 calculation is necessary since more than 85 % of the drug is released within 15 minutes).