

SUPPLEMENTARY MATERIALS

Box S1 Manipulation procedure for obtaining an extemporaneous LPV/r suspension.

Part I - Preparation of kit components in the hospital pharmacy

The pharmacist should prepare the following components of the kit in the compounding laboratory of the hospital pharmacy. For the preparation of the syringe (**A**), it is necessary to operate under the hood (chemical hood UNI EN 14175 or vertical laminar flow hood) using the correct personal protective equipment (PPE).

A. 50-ml Luer-lock syringe containing the dose of the medicinal product to be given:

1. Crush the tablets finely in a mortar.
2. Weigh the exact amount of dose to be dosed.
3. Load the dosed powder in the syringe from the bottom after removing the plunger.
4. Insert the plunger and take it to the end of the ride without compacting the powder.
5. Plug the syringe with a stopper.
6. Label the syringe in the agreement of the Good Compounding Practice.

B. 50-mL Luer-lock syringe containing 20 mL of the suspension vehicle having the following composition:

- sodium carboxymethyl cellulose, 0.2 g
- trisodium citrate dihydrate, 0.26 g
- citric acid, 0.2 g
- water, to 20 mL.

Part II - Preparation of the extemporaneous oral antiretroviral suspension at the bedside

The nurse/medical doctor receive a kit, including:

- A.** 50-ml Luer-lock syringe containing the drug dose patient needs.
- B.** 50-ml Luer-lock syringe containing suspending solution.
- C.** Sterile Female-Female Luer Lock Connector.

The nurse/medical doctor should prepare the extemporaneous suspension immediately before the administration as follow:

1. Connect the syringe **A** to syringe **B** by using the female-female Luer-lock connector **C**.
2. Transfer the content of syringe **B** in syringe **A**.
3. Repeat point 2 at least 50 times to mix the suspension or until all the powder is entirely and finely suspended (no aggregates are visually noted).
4. Administer the entire suspension volume to the patient.
5. Check the syringe for suspension residuals. Eventually, wash the syringe with a glucose solution to be given to the patient.

Figure S1 Chromatograms of placebo and drug-loaded vehicles.

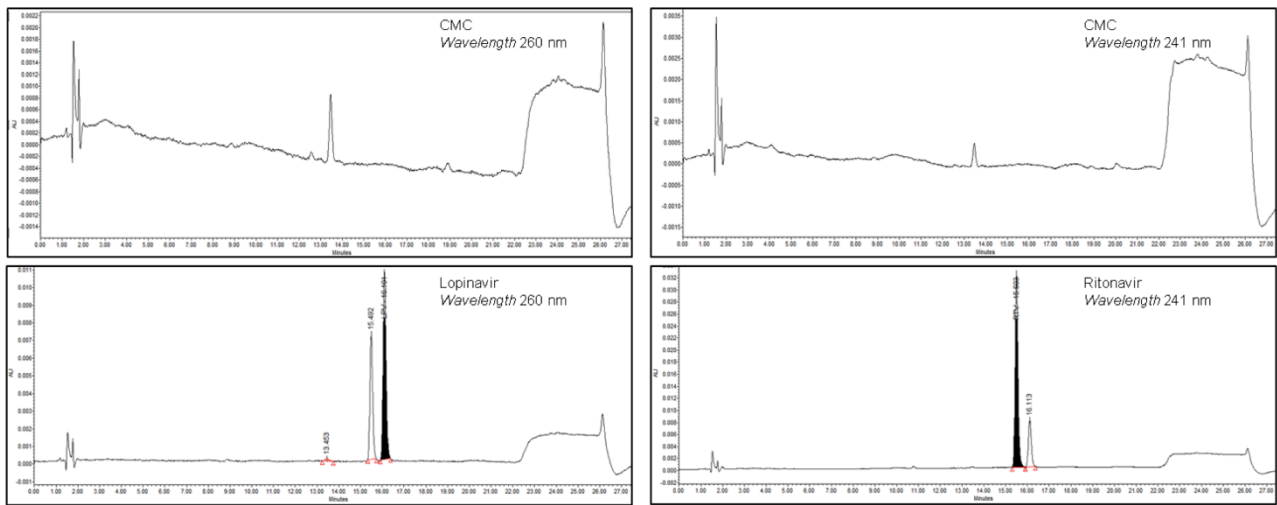


Figure S2 Chromatograms of lopinavir/ritonavir suspension at room temperature after 1 and 15 days.

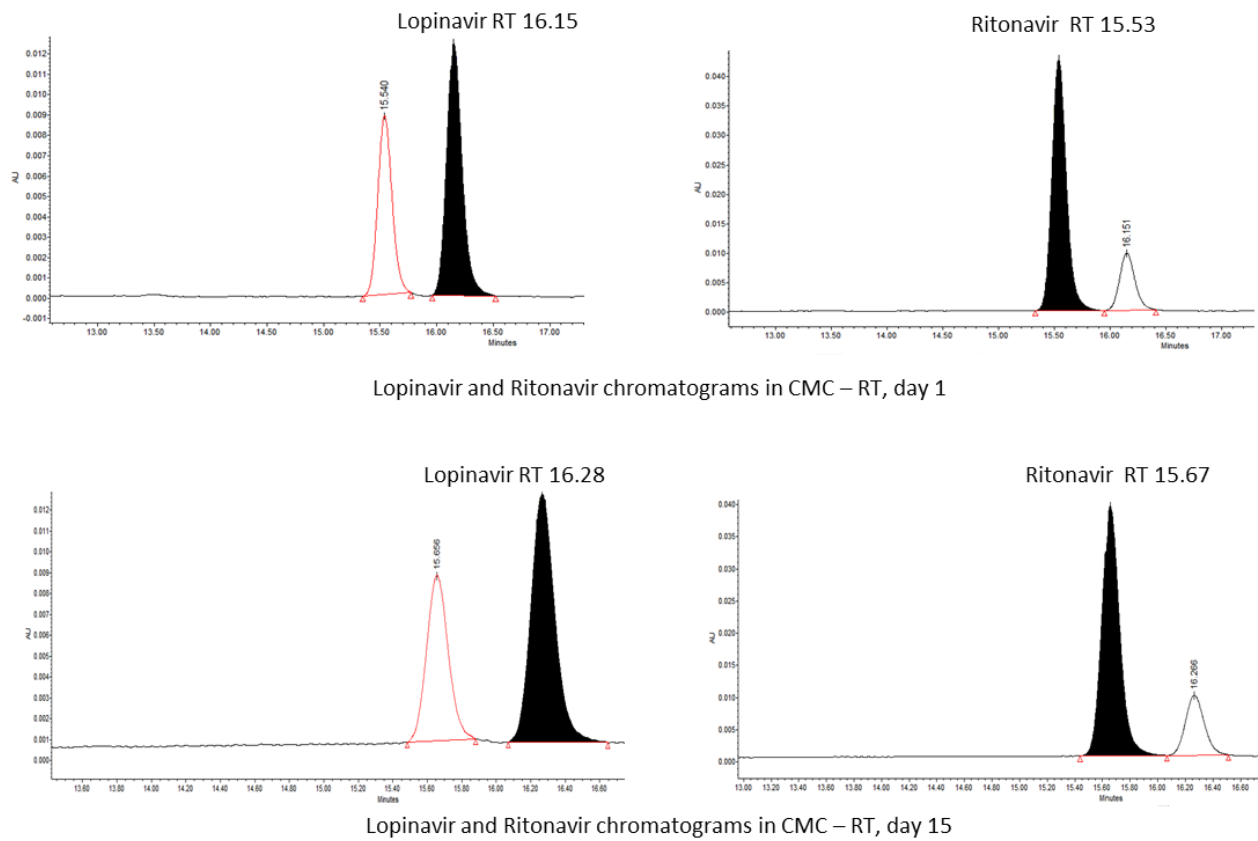


Table S1 Summary of Area weighted cumulative distributions of LPV/r suspension at different times after preparation and after manual handshaking (HS).

% of the total particle area	Particle size (μm)				
	0	30 min	90 min	180 min	180 min + HS
5	< 0.54	< 0.55	< 0.59	< 0.64	< 0.57
10	< 0.58	< 0.60	< 0.64	< 0.79	< 0.64
15	< 0.61	< 0.64	< 0.71	< 0.88	< 0.67
20	< 0.64	< 0.67	< 0.79	< 0.98	< 0.71
25	< 0.67	< 0.71	< 0.83	< 1.04	< 0.79
30	< 0.71	< 0.75	< 0.93	< 1.12	< 0.83
35	< 0.75	< 0.82	< 0.98	< 1.22	< 0.88
40	< 0.80	< 0.85	< 1.04	< 1.29	< 0.93
45	< 0.83	< 0.89	< 1.09	< 1.39	< 0.96
50	< 0.88	< 0.93	< 1.15	< 1.51	< 1.00
55	< 0.93	< 0.98	< 1.27	< 1.68	< 1.04
60	< 0.95	< 1.04	< 1.36	< 1.88	< 1.09
65	< 0.98	< 1.09	< 1.60	< 2.21	< 1.15
70	< 1.04	< 1.15	< 1.88	< 2.69	< 1.22
75	< 1.09	< 1.22	< 2.46	< 3.22	< 1.29
80	< 1.15	< 1.30	< 3.20	< 3.78	< 1.43
85	< 1.29	< 1.51	< 3.78	< 4.45	< 1.80
90	< 1.68	< 2.33	< 4.45	< 5.52	< 3.22
95	< 3.05	< 4.18	< 5.51	< 7.23	< 4.69
99	< 4.79	< 4.96	< 6.71	< 8.97	< 5.52
Median	0.88	0.93	1.15	1.51	1.00
Span	1.25	1.86	3.31	3.13	2.58

Table S2 Raw data of analytical analyses of filtered suspension containing lopinavir and ritonavir.

Storage condition	Drug	Time	Retention time	Peak area
At room temperature	Lopinavir	0	16.11	96100
			16.10	104381
			16.08	92974
		1	16.15	132810
			16.15	119491
			16.15	127986
		4	16.25	114300
			16.23	104271
			16.24	115522
	15	16.26	115580	
		16.27	92950	
		16.28	127399	
	Ritonavir	0	15.50	292019
			15.49	314154
			15.47	281628
		1	15.53	431365
			15.54	386080
			15.54	406412
		4	15.59	343562
			15.58	314912
			15.59	346637
15		15.65	353380	
		15.66	294156	
		15.67	376310	
At 4°C	Lopinavir	0	16.11	96100
			16.10	104381
			16.08	92974
		1	16.17	93851
			16.17	88714
			16.16	83902
		4	16.25	110524
			16.24	107702
			16.25	105979
		15	16.27	67995
			16.27	69525
			16.28	63369

	Ritonavir	0	15.50	96100
			15.49	104381
			15.47	92974
		1	15.55	284736
			15.56	268107
			15.55	255910
		4	15.60	322363
			15.60	327809
			15.60	319944
		15	15.66	214967
			15.66	210706
			15.67	203725