Scientia Pharmaceutica

Supplementary Material: Application of Lactose Co-Processed Excipients as an Alternative for Bridging Pharmaceutical Unit Operations: Manufacturing an Omeprazole Tablet Prototype via Direct Compression

Table S1. Quality Target Product Profile (QTPP) for omeprazole film-coated tablets

QTPP Element	Target	Justification
Dosage form	Tablet	Pharmaceutical equivalence requirement: same dosage form
Dosage design	Delayed release tablets	Pharmaceutical equivalence requirement: same dosage design
Route of administration	Oral	Pharmaceutical equivalence requirement: same route of administration
Dosage strength	20mg	Pharmaceutical equivalence requirement: same strength
Stability	At least 24-month shelf-life at room temperature	Equivalent to or better than RLD shelf-life
Drug product quality attributes	Physical Attributes	Pharmaceutical equivalence requirement: Must meet the same compendial quality standards
	Identification	
	Assay	
	Content Uniformity	
	Degradation Product	
	Dissolution	

1. Materials and Methods

1.1. Tablet production

Table S2. Proposed Formula quali-quantitative omeprazole delayed-release tablets (F1, F2)

Component	Justification	Tablet Composition	
		mg	%
OMZ	API	20.0	10.0
Microcelac® 100	Diluent	170.0	85.0
Explotab®	Disintegrant	8.0	4.0
Pruv®	Lubricant	2.0	1.0
Total		200.0	100.0

F1

Component	Justification	Tablet Composition	
		mg	%
OMZ	API	20.0	10.0
Tabletosse® 70	Diluent	170.0	85.0
Explotab®	Disintegrant	8.0	4.0
Pruv®	Lubricant	2.0	1.0
Total		200.0	100.0

F2

Table S3. Proposed Formula quali-quantitative omeprazole delayed-release tablets (F3, F4)

Component	Justification	Tablet Composition	
		mg	%
OMZ	API	20.0	10,0
Microcelac® 100	Diluent	170.0	85,0
Explotab®	Disintegrant	8.0	4,0
Pruv®	Lubricant	2.0	1,0
Total		200.0	100.0

F3

Component	Justification	Tablet Composition	
		mg	%
OMZ	API	20.0	10.0
Avicel PH102	Diluent	42.5	21.3
DuraLac®	Diluent	127.5	63.8
Explotab®	Disintegrant	8.0	4.0
Pruv®	Lubricant	2.0	1.0
Total		200.0	100.0

F4

Table S4. Preparation parameters of applied coating suspensions

Parameter	Opadry® II	Aquarius™ Control ENA
% weight coating in purified water	8	20
Agitation (rpm)	410	390
Homogenization time (min)	45	60
Final Sieve mesh (μm)	250	800

Table S5. Summary of applied in-process coating parameters

Parameter	Opadry® II	Aquarius™ Control ENA
Spray Rate (g/min)	3.5	1.5
Atomizing pressure (bar)	0.8	1.0
Preheat outlet temperature (°C)	42	40
Inlet temperature (°C)	70	63
Outlet temperature (°C)	40	42
Drum speed (rpm)	30	30
Weight gain (%)	2	10

1.2. *Hardness, friability, disintegration and thickness*

Friability was measured taking a sample of whole tablets corresponding as near as possible to 6.5 g. Tablets were carefully dedusted prior to testing and accurately weighted before placing g them in the drum. Drum rotated 100 times using a speed of 25 rpm. Tablets were dedust again and before accurately weigh.

For the disintegration test, one dosage unit was placed in each of the six tubes of the basket-rack assembly. The apparatus was operated using either water maintained at a temperature of 37 ± 2°C. The tablets were visually examined until all six disintegrate completely. This time was recorded with the use of a stopwatch.

Tablet diameter and band thickness were measured using a digital caliper with a precision of 0.01 mm. Each tablet was individually placed between the caliper jaws, and measurements were taken at the widest point for diameter and at the band region for thickness. 10 measurements were performed and the average value with its correspondent standard deviation was recorded.

Tablet hardness was determined using a PharmaTest PTB hardness tester. Each tablet was placed between two platens of the instrument, with diametral loading applied across the diameter of the tablet. One platen remained stationary while the other moved to apply increasing force until the tablet fractured. The force required to cause fracture was recorded in Newtons (N). Measurements were conducted on a minimum of 10 tablets, and the average hardness value was calculated.

2. Results and Discussion

Prilosec OTC Inactive Ingredients: Glyceryl monostearate, hydroxypropyl cellulose, hypromellose, iron oxide, magnesium stearate, methacrylic acid copolymer, microcrystalline cellulose, paraffin, polyethylene glycol 6000, polysorbate 80, polyvinylpyrrolidone, sodium stearyl fumarate, starch, sucrose, talc, titanium dioxide, triethyl citrate.

Table S6. Extended results of specific surface area for the omeprazole formulation prototypes.

	Pore Volume cm^3/g			Pore Size (nm)		
	Single point adsorption total pore volume of pores	BJH Adsorption cumulative volume of pores	BJH Desorption cumulative volume of pores	Adsorption average pore width (4V/A by BET)	BJH Adsorption average pore diameter (4V/A)	BJH Desorption average pore diameter (4V/A)
F1	0.001436	0.001700	0.001687	8.561300	13.3243	13.4038
F2	0.001187	0.001302	0.001294	5.658800	12.0757	12.0671
F3	0.001241	0.001372	0.001370	8.044487	11.4631	11.2676
F4	0.001674	0.001869	0.001865	9.567583	13.4582	12.2317

Table S7. Descriptive statistics of each analyzed variable

	N	Minimum	Maximum	Mean	Std. Deviation
PSDX10	12	4.15	6.39	5.6108	0.80136
PSDX50	12	91.54	145.25	111.0908	20.98678
PSDX90	12	245.68	301.39	275.515	18.59371
PSDX100	12	334.17	425.06	398.4425	35.19701
Cohesion kPa	12	0.04	0.38	0.2242	0.11041
UYSkPa	12	0.17	1.46	0.8492	0.42077
MPSkPa	12	4.81	5.79	5.1842	0.3331
FF	12	3.95	29.35	8.8808	7.49872
AIF	12	31.22	37.24	34.1875	1.9242
BDgml	12	0.59	0.68	0.64	0.03075
SSikPa@2.00kPa	12	1.44	1.81	1.5842	0.11958
SSikPa@1.75kPa	12	1.3	1.6	1.4175	0.11128
SSikPa@1.50kPa	12	1.12	1.44	1.2533	0.11665
SSikPa@1.25kPa	12	0.96	1.28	1.085	0.1143
SSikPa@1.00kPa	12	0.78	1.06	0.8942	0.10149
SSikPa@3.00kPa	12	1.77	2.27	1.9708	0.16839
Surface Area m2g	12	0.5853	0.7683	0.645258	0.0527567
Single point adsorption total pore volume of pores	12	0.001182	0.00171	0.0013845	0.00020096
BJH Adsorption cumulative volume of pores	12	0.001299	0.002083	0.00156067	0.00028267
BJH Desorption cumulative volume of pores	12	0.001287	0.002073	0.00155383	0.0002828
Adsorption average pore width 4VA by BET	12	0.79288	9.91806	7.9580558	2.35457233
BJH Adsorption average pore diameter 4VA	12	11.2095	15.5604	12.580342	1.2498424
BJH Desorption average pore diameter 4VA	12	11.1157	15.7667	12.242575	1.2595064

Table S8. Proximity Matrix, the Euclidean distance for each case is given. The smaller the value, the closer and more similar the cases are to each other

Formulation	Case	1	2	3	4	5	6	7	8	9	10	11	12
	1	0.000											
F1	2	3.289	0.000										
	3	24.085	26.181	0.000									
	4	41.063	41.129	77.419	0.000								
F2	5	31.162	29.826	63.498	3.622	0.000							
	6	36.523	38.037	75.362	22.608	14.858	0.000						
	7	31.173	42.074	70.594	23.616	19.997	27.930	0.000					
F3	8	15.018	17.801	52.228	26.471	16.447	21.459	10.906	0.000				
	9	24.530	35.863	65.804	42.949	33.666	29.541	10.207	8.275	0.000			
	10	44.036	63.402	51.729	81.900	73.106	74.489	41.836	47.681	30.122	0.000		
F4	11	62.718	88.663	79.169	98.696	92.780	90.243	46.779	63.365	36.583	5.390	0.000	
	12	60.420	85.653	77.105	109.252	101.901	94.045	56.714	67.410	41.467	8.955	5.177	0.000