Original Research Article **Pharmaceutics**

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

INVITRO DISSOLUTION STUDIES OF LANSOPRAZOLE EC PELLETS 12% W/W – A COMPARATIVE DISSOLUTION PROFILE WITH REFERENCE SAMPLE

VENKATESWARA REDDY BOYA[1*] AND DR. K. S. SEKHARA RAO[2]

**[1]Research Scholar of Koneru Lakshmaiah,Education Foundation, (Department of Management), Vaddeswaram, Guntur Dist., Andhra Pradesh, India.*
[2]Associate Professor & RPAC Chairman, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur Dist., AP, India.

ABSTRACT

The purpose of this study was carried out to prove better *invitro* results of Lansoprazole EC Pellets 12% w/w in comparison with market reference sample (Cipla Pharmaceuticals Ltd.). This study was conducted on antiulcer drug for the treatment of ulcers, as many people are getting affected from ulcers worldwide. One of the popular drug Lansoprazole is a Proton Pump Inhibitor (PPI) which helps to reduce acid secretion from parietal cells. Lansoprazole and LANZOL-30 samples were tested for comparative dissolution studies in multimedia of 0.1N Hydrochloric acid, pH 4.5 Acetate buffer, pH 6.8 Phosphate buffer for 12 units each by using method reference from USP-41. The Comparative Dissolution Profile (CDP) of Lansoprazole EC Pellets 12% w/w sample was found good when compared with reference sample of LANZOL-30. The f2 values were found more than 50 (89 in 0.1 N HCl, 75 in pH 4.5 Acetate buffer & 73 in pH 6.8 Phosphate buffer) in all the three media with reference to dissolution guidelines of Medicines Control Council (MCC), South Africa. Thus, the CDP was considered acceptable and better *invitro* results have been achieved for the formulation Lansoprazole EC Pellets 12% w/w.

KEYWORDS: ***Ulcer, Lansoprazole, Proton Pump Inhibitor, USP, MCC, CDP***

VENKATESWARA REDDY BOYA*

Research Scholar of Koneru Lakshmaiah, Education Foundation, (Department of Management), Vaddeswaram, Guntur Dist., Aandhra Pradesh, India.

Received on: 18-06-2018
Revised and Accepted on: 10-08-2018
DOI: http://dx.doi.org/10.22376/ijpbs.2018.9.4.p39-44

INTRODUCTION

Lansoprazole is a Proton Pump Inhibitor (PPI) used in treating gastric ulcers and Gastro Esophageal Reflux Disease (GERD) and also maintaining all grades of Erosive Esophagitis (EE). lansoprazole is highly acid labile and presents many formulation challenges and to protect it from acidic environment of the stomach, an enteric coated pellets formulation is tried in the present study. The enteric polymers are becoming very popular.[1-2] Lansoprazole is acid labile drug which undergo changes when comes in contact with acidic media, this degradation leads to lower bio availability and low potency of Lansoprazole. As per the studies, Lansoprazole has been reported as an anti-proliferative effect in cancer cells. Lansoprazole inhibited cyst development via inhibition of cell proliferation.[3] Proton pump inhibitors are a class of medication widely used in practice, both as prescription and self administered over the counter (OTC), due to a high incidence of chronic gastritis and gastric ulcer, as well as Helicobacter pylori infection. They have a good therapeutic index and a low incidence of side effects. Though, a few anaphylactic reactions for omeprazole and derivates have been described case reports or small series.[4] A drug called Lansoprazole is Proton-pump inhibitor (PPI), whose core action is a definite and long-lasting decrease of stomach acid creation by blocking the hydrogen/potassium adenosine triphosphatase enzyme system (gastric proton pump) of the parietal cells in stomach.[5] Pellets can be manufactured by the compaction and drug-layering being which are most commonly used processing methods today. Pellets may have diverse applications in pharmaceutical industries. It just requires an innovative bend to use it to derive maximum cost-effectiveness. The proper formulation, processing conditions and processing equipment is very important in pellets manufacturing. To enable a controlled release rate of different drugs, coating can be done on pellets. The delivery of the drug at a specific site within the gastrointestinal tract or to sustain the action of drugs over a prolonged period of time, controlled release oral solid dosage forms are usually intended. The larger surface area of pellets enables itfor immediate release products for better dispersal. It is used to avoid powder dusting in the chemical industries. Pellets confirm improved flow properties and flexibility in formulation development and manufacturing. The coating material may be colored with a dye material so that the beads of different coating thickness will be darker in color and distinct from those having less coats. The pellets or granules are blended in the desired proportions of different thickness of coatings to give the desired effect. The abovementioned objective of the title can be established through comparative dissolution study of Lansoprazole formulation F3 with a market reference sample (LANZOL-30) for *invitro* studies in multimedia as per the guidelines of MCC.

MATERIALS AND METHODS

Table 1
Ingredients used in the formulation with manufacturing formula

S. No.	Ingredients	Quantity (in g)	Rationale	Vendor
Drug Coating				
1.	Sugar Spheres ASTM (20#24)	223.0	Core	Credo Life Sciences Pvt. Ltd.
2.	Lansoprazole	70.0	API	Nifty Labs Pvt. Ltd.
3.	Hypromellose (HPMC-E5)	15.0	Film forming Polymer	C. Jivanlal & Company
4.	Sodium Lauryl Sulphate (SLS)	2.5	Surfactant	Godrej Industrial Ltd.
5.	Hydroxy Propyl Cellulose (HPC)	3.0	Disintegrate	Huzhou Zhan Wang Pharmaceutical
6.	Sodium Hydroxide (NaOH)	0.35	Alkalizer	Merck
7.	Purified Talc	1.0	Anti-tacking agent	Neelkanth Mine chem.
8.	Purified Water#	500	Solvent	Credo Life Sciences Pvt. Ltd.
Sub Coating				
9.	Drug Coated Pellets	314.85	NA	NA
10.	Hypromellose (HPMC E5)	50.0	Film forming Polymer	Taianruitai cellulose Co. Ltd, china
11.	Purified Talc	1.0	Anti-tacking agent	Neelkanth Mine chem.
12.	Purified water#	900	Solvent	Credo Life Sciences Pvt. Ltd.
Enteric Coating				
13.	Sub Coated Pellets	365.85	NA	NA
14.	Methacrylic Acid Copolymer Dispersion (L-30D)*	365 (109.5 g of Solid content)	Enteric Polymer	Dhara life sciences Pvt, Ltd, Gujarat.
15.	Purified Talc	9.0	Anti-tacking agent	Neelkanth Mine Chem
16.	Titanium Dioxide	2.5	Opacifier	Huntsman P and A, Italy
17.	Triethyl Citrate	0.8	Plasticizer	Sigma-Aldrich
18.	Sodium Hydroxide	12.35	Alkalizer	Merck
19.	Purified Water#	340	Solvent	Credo Life Sciences Pvt. Ltd.

 # Does not contribute to the final weight.
****1000 g of L-30D dispersion is equivalent to 300 g of solid content (30%).***

Table 2
Process parameters for the formulation

S. No.	Stage	Equipment	Process Parameters			
			Inlet Temperature	Product Temperature	Atomization air Pressure	Spray Pump Speed
1.	Drug Coating	Fluid Bed Equipment (GPCG 1.1 Wurster Coater)	53-57°C	38-42°C	0.8-1.5 bar	2-4 RPM
2.	Sub Coating		53-57°C	38-42°C	0.8-1.5 bar	2-4 RPM
3.	Enteric Coating		53-57°C	38-42°C	0.8-1.5 bar	2-4 RPM

Manufacturing Procedure of Pellets

Drug Coating Solution preparation & Drug Coating

Taken Purified water 500.0g into a cleaned SS container andadded Lansoprazole 70.0 g, Hypromellose (HPMC-E5) 15.0g, Sodium carbonate 15.0g, Sodium Lauryl Sulphate 2.5g, Hydroxy propyl cellulose 3.0g and Sodium Hydroxide 0.350g one after another and under stirring and continue the stirring to get the uniform dispersion. Charged the sugar spheres (20#24) into FBE (GPCG 1.1) bowl and set the process parameters as per the Table 2 and started the coating.

Drying

Dried the Drug Coated Pellets in the FBE (GPCG 1.1) for 30 minutes and maintained the Drying Parameters like product Temperature between 40±5°C and atomization air pressure between 1.0-2.0 bar throughout the drying Process.

Barrier Coating Solution Preparation & Barrier Coating

Taken Purified water 900.0 g into a cleaned SS container and added Hypromellose (HPMC E5) 40.0 g and Purified Talc 1.0g one after another and mix well to get the uniform solution. Set the process parameters as per the Table 2 and started the barrier coating solution on drug coated pellets.

Drying

Dried the Barrier Coated Pellets in the FBE (GPCG 1.1) for 30 minutes and maintained the Drying Parameters like product Temperature between 40±5°C and atomization air pressure between 1.0-2.0 bar throughout the drying Process.

Enteric Coating solution preparation & Enteric Coating

Taken Purified water 330.0 g into a cleaned SS container and to this added L-30 D 450.0 g, Purified Talc 13.0g, Titanium Dioxide 5.5g, Triethyl Citrate 15.2g, Sodium Hydroxide 0.95g one after other under stirring and continue the stirring until uniform dispersion was obtained. Set the process parameters as per the Table 2 and started the Enteric coating solution on Barrier coated pellets.

Drying

After Enteric Coating dried the Pellets in FBE (GPCG 1.1) for 30 minutes and maintained the Drying Parameters like product Temperature between 40±5°C and atomization air pressure between 1.0-2.0 bar throughout the drying Process.

Sifting of Enteric Coated Pellets

After completion of Drying, sifted the pellets through 16#20 sieve and collected the Good Pellets in a duly labeled sample cover and recorded the weight of the good pellets and retains and Passing of #16/20.The Materials which were used in the experiments were gifted by M/s Credo Life Sciences Private Limited, Hyderabad.

METHODS[6]

Table 3
Instruments used for testing

S. No.	Equipment Name	Make	Model
1	Analytical balance	Mettler Toledo	ML204T
2	pH Meter	Mettler Toledo	Five Easy Plus FP20
3	UV/VIS Spectro photo meter	PerkinElmer	Lambda 365
4	Dissolution Test Apparatus	Lab India	DS-8000
5	Dissolution Test Apparatus	Electro Lab	EDT-14LX

Dissolution (By UV)

The dissolution test has been performed in 900 mL of 0.1 N Hydrochloric Acid (HCl), pH 4.5 Acetate buffer and pH 6.8 phosphate buffer media with USP type II (Paddle), 50 rpm, temperature 37°C ± 0.5°C and checked the absorbance at 306 nm for all the media and calculated for f2 value. The acceptable value for f2 should not be less than 50.

RESULTS AND DISCUSSIONS

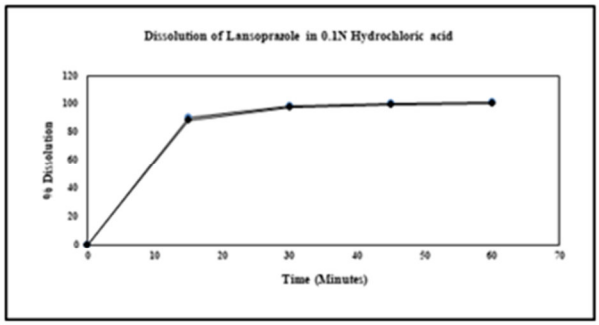
Table 4
Comparative Dissolution Profile of Reference Sample and Formulation F3

Reference Sample (Rt) Details		Test Sample (Tt) Details	
Product name	LANZOL-30	Product name	Lansoprazole EC Pellets 12% w/w
Strength	30 mg	Strength	12%
Batch No.	GL7220	Batch No.	RD/LS/001 (F3)
Mfg. Date	Apr. 2017	Mfg. Date	Apr. 2018
Exp. Date	Mar. 2019	Exp. Date	Mar. 2020
Manufactured by	Cipla Pharmaceuticals Ltd.	Manufactured by	Credo Life Sciences Pvt. Ltd.

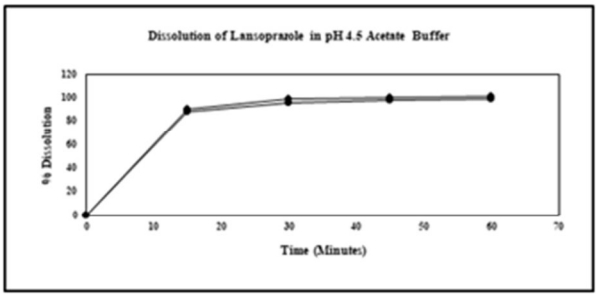
Time Points	Dissolution of Reference sample in 0.1N HCl													
(minutes)	B-1	B-2	B-3	B-4	B-5	B-6	B-7	B-8	B-9	B-10	B-11	B-12	Mean	SD
15	90	91	90	90	89	89	89	90	90	90	89	91	90	0.72
30	97	98	97	99	98	97	100	99	100	98	97	97	98	1.16
45	101	101	101	101	99	99	99	102	98	99	100	99	100	1.24
60	102	102	102	102	101	100	100	103	99	101	101	100	101	1.16
Time Points	**Dissolution of Reference sample in pH 4.5 Acetate buffer**													
(minutes)	**B-1**	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**	**B-9**	**B-10**	**B-11**	**B-12**	**Mean**	**SD**
15	91	92	91	90	89	90	90	91	91	91	90	92	91	0.89
30	98	99	98	100	99	98	101	100	101	99	98	98	99	1.16
45	102	102	102	102	100	100	100	103	99	100	101	100	101	1.24
60	103	103	103	103	101	101	101	104	100	101	102	101	102	1.24
Time Points	**Dissolution of Reference sample in pH 6.8 Phosphate buffer**													
(minutes)	**B-1**	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**	**B-9**	**B-10**	**B-11**	**B-12**	**Mean**	**SD**
15	97	98	98	100	98	98	100	99	100	99	97	98	99	1.09
30	101	102	101	102	100	99	100	102	98	100	101	99	100	1.31
45	102	103	102	103	101	101	101	103	99	101	102	100	102	1.24
60	103	101	101	101	100	100	100	104	101	100	100	100	101	1.31
Time Points	**Dissolution of F3 sample in 0.1N HCl**													
(minutes)	**B-1**	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**	**B-9**	**B-10**	**B-11**	**B-12**	**Mean**	**SD**
15	89	90	88	88	87	88	88	89	88	89	88	89	88	0.79
30	96	96	96	98	97	96	98	98	98	97	95	96	97	1.06
45	99	100	99	100	98	98	98	100	97	98	99	97	99	1.08
60	100	101	101	101	99	99	99	101	98	99	100	99	100	1.06
Time Points	**Dissolution of F3 sample in pH 4.5 Acetate buffer**													
(minutes)	**B-1**	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**	**B-9**	**B-10**	**B-11**	**B-12**	**Mean**	**SD**
15	88	89	87	87	86	87	87	88	88	88	87	89	88	0.90
30	95	95	95	97	96	95	97	97	98	96	95	95	96	1.08
45	98	99	99	99	97	97	97	99	96	97	98	97	98	1.06
60	99	100	100	100	98	98	98	100	97	98	99	98	99	1.06
Time Points	**Dissolution of F3 sample in pH 6.8 Phosphate buffer**													
(minutes)	**B-1**	**B-2**	**B-3**	**B-4**	**B-5**	**B-6**	**B-7**	**B-8**	**B-9**	**B-10**	**B-11**	**B-12**	**Mean**	**SD**
15	94	94	94	96	95	94	96	96	97	95	94	94	95	1.08
30	98	98	98	98	96	96	96	98	95	96	97	96	97	1.11
45	99	99	99	99	97	97	97	99	96	97	98	97	98	1.11
60	100	100	100	100	98	98	98	101	97	98	99	98	99	1.24

Table 5
f2 Calculation for Comparative Dissolution Profile

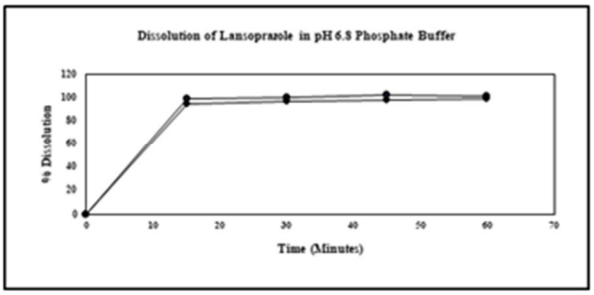
Dissolution Details		0.1N HCl, 900 mL, Paddle, 50 RPM		
Time (mins)	Reference (Rt) % Dissolution (Recovery)	Test (Tt) % Dissolution (Recovery)	(Rt-Tt)	(Rt-Tt)2
0	0	0	0	0
15	90	88	2	4
30	98	97	1	1
45	100	99	1	1
60	101	100	1	1
			n	4
			f2	89



Dissolution Details		pH 4.5 Acetate buffer, 900mL, Paddle, 50 RPM		
Time (mins)	Reference (Rt) % Dissolution	Test (Tt) % Dissolution	(Rt-Tt)	(Rt-Tt)2
0	0	0	0	0
15	91	88	3	9
30	99	96	3	9
45	101	98	3	9
60	102	99	3	9
			n	4
			f2	75



Dissolution Details		pH 6.8 Phosphate buffer, 900mL, Paddle, 50 RPM		
Time (mins)	Reference (Rt) % Dissolution	Test (Tt) % Dissolution	(Rt-Tt)	(Rt-Tt)2
0	0	0	0	0
15	99	95	4	16
30	100	97	3	9
45	102	98	4	16
60	101	99	2	4
			n	4
			f2	73



DISCUSSIONS

We have compared F3 formulation of Lansoprazole EC Pellets 12% w/w with a reputed manufacturer (Cipla Pharmaceuticals Ltd.) sample LANZOL-30 for Comparative Dissolution Profile (CDP) as per the guidelines of Medicines Control Council (MCC), South Africa (SA) [7] and USP-40.[6] The acceptance criteria for f2 value must not be less than 50 as per USP-40 [6] and MCC, SA.[7] The f2 value achieved is 89 in 900 mL of 0.1 N Hydrochloric Acid (HCl) with USP type II (Paddle), 50 rpm, temperature 37°C ± 0.5°C and absorbance at 306 nm. The f2 value achieved is 75 in 900 mL of pH 4.5 Acetate buffer with USP type II (Paddle), 50 rpm, temperature 37°C ± 0.5°C and absorbance at 306 nm. The f2 value achieved is 73 in 900 mL of pH 6.8 Phosphate buffer with USP type II (Paddle), 50 rpm, temperature 37°C ± 0.5°C and absorbance at 306 nm. The Equipment's and Instruments used in analysis were Pre-Qualified and Pre-calibrated. The Comparative Dissolution Profile of F3 formulation of Lansoprazole EC Pellets 12% w/w and LANZOL-30 were reviewed and found the results were well within the acceptance criteria of f2 value.

ACKNOWLEDGEMENTS

I am deeply grateful to my Managing Director (A. Siva Rama Prasad), Directors (A. Vamsi Krishna, K. Madhava Rao & E. Vineeth Rao) and Plant Head (N. Ramgopal Prasad) of M/s Credo Life Sciences Private Limited for their generous support. Firstly, I would like to thank Dr. K. S. Sekhara Rao, Associate Professor & RPAC Chairman, Koneru Lakshmaiah Education Foundation, (K.L. University) Vaddeswaram, Guntur Dist., AP, India for his guidance and support. I would also like to thank Dr. K. Ch. Sri Kavya, Associate Dean, Academic Research, Koneru Lakshmaiah Education Foundation, (K.L. University) Vaddeswaram, Guntur Dist., AP, India for her kind support. I extend my very special gratitude to my wife, daughter & late son Master Praveen Kumar Reddy Boya, who entered eternity on 12th November 2011. He was the one who gave me immense inspiration and energy to continue my academics. And finally, last but by no means least, I'm very much thankful, also to my colleagues of Credo Life Sciences Private Limited, Hyderabad.

CONCLUSION

Based on the results and discussion of f2 values, it was decided that the Comparative Dissolution Profile of Lansoprazole EC Pellets 12% w/w sample was as good as the reference sample of LANZOL-30. The f2 values were found more than 50 in all the three media (0.1 N Hydrochloric Acid, pH 4.5 Acetate buffer & pH 6.8 Phosphate buffer) with reference to dissolution guidelines of Medicines Control Council (MCC), South

Africa.Hence the CDP was considered acceptable and better invitro results have been achieved for Lansoprazole EC Pellets 12% w/w.

AUTHOR CONTRIBUTION STATEMENT

It is my individual idea and the study was carried out on my own by taking guidance from my guide cum co-author Dr. K. S. Sekhara Rao, Koneru Lakshmaiah Education Foundation (KL University) Vaddeswaram, Guntur Dist., AP, India.

CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES

1. Venkateswarlu P. Formulation and in vitro evaluation of lansoprazole delayed release capsules. Int J Innov Pharm Res. 2013; 4: 328-6. Available from: file:///C:/Users/Dell/Downloads/328-336.pdf.
2. Singh SK, Borkhataria CH, Seth NR, Patel RP, Singh S, Parmar GR. Formulation and in vitro evaluation of lansoprazole micropellets. Int. J. Pharm Tech Res. 2009;1(4):1530-40. Available from: http://sphinxsai.com/PTVOL4/index_pharm_10_vol4.htm
3. Nantavishit J, Chatsudthipong V, Soodvilai S. Lansoprazole reduces renal cyst in polycystic kidney disease via inhibition of cell proliferation and fluid secretion. Biochem Pharmacol. 2018;154:175–82. DOI: http://dx.doi.org/10.1016/j.bcp.2018.05.005
4. Zamfirescu M. Proton pump inhibitors immediate hypersensitivity – a lansoprazole anaphylaxis case discussion. Alergologia. 2018;1(1):24–9. DOI http://dx.doi.org/10.26416/aler.2.1.2018.1471.
5. Sakai H, Fujii T, Takeguchi N. Proton-Potassium (H+/K+) ATPases: Properties and Roles in Health and Diseases. The Alkali Metal Ions: Their Role for Life. Springer International Publishing; 2016. p. 459–83. DOI:http://dx.doi.org/10.1007/978-3-319-21756-7_13
6. United States Pharmacopeia, USP-41-NF36. Official Monograph/Lansoprazole. 2018: v3; p. 2350.
7. Medicines Control Council. July 2015. Available from: http://www.mccza.com/documents/0ca3cfe72.07_Dissolution_Jun15_v5.pdf.