Online Available at www.thepharmaresearch.info

THE PHARMA RESEARCH, A JOURNAL

The Pharma Research (T. Ph. Res.), (2010), 4; 61-73.
Published on- 15 Dec 2010



*Original Article*

ISSN 0975-8216

# FORMULATION AND EVALUATION OF MODIFIED RELEASE CAPSULES OF LANSOPRASOLE

**Margaret Chandira, Ankit Sharma ,D. Bhowmik, B. Jayakar***

**Affiliated to:**

*Department of Pharmaceutical science, Vinayaka missions college of Pharmacy, Vinayakamission University, Salem,Tamilnadu*

For Email Click Here

## ABSTRACT

Immediate release dosage form of Lansoprazole results rapid dissolution and rapid rise in plasma drug concentration within a short period after administration. Subsequently due to metabolism and elimination the plasma drug concentration falls below the therapeutic level. Thus require a modified release dosage form. The object of the study is to investigate controlled release property of Hypromellose pthalate by avoiding gastric release of Lansoprazole. Three coating material used in formulation Mannitol (First layer), Povidone (Second Layer) and HPMCP (Final Layer). different concentration of enteric coating, sub coating material used, and optimized the formula on basis of drug release in acid media (pH 1.2) and buffer media (pH 6.8). Drug release from capsules in acid media found 0.8 to 1.2 % and in buffer media upto 94.9 % drug released in 60 min. no impurity found in related substances test.In capsule formulation positive and encouraging results in accordance to the aim were obtained.

**Keywords:** Lansoprazole, HPMCP, Povidone, Mannitol.

## INTRODUCTION

Solid dosage formulation and design usually involves a serious of compromises, since producing the desired properties frequently involves competing objectives. The correct selection and balance of excipients materials and processes in a solid dosage formulation, to achieve the desired response is not in practice easy to achieve. Furthermore it is essential to develop tablet formulations and processing methods which may be validated. Pellets are of a great interest to the pharmaceutical industry for a variety of reasons. Palletized products not only offer flexibility in dosage form design and development, but are also utilized to improve the safety and efficiency of bioactive agents. Pellets range in size, between 0.5 to 1.5 mm,

though other sizes could be prepared, depending on the processing technique. Pharmaceutical pellets are agglomerates of fine powder particles, nearly spherical or cylindrical in shape with a narrow particle size distribution. In Order to Develop an Oral modified release Capsules of Lansoprazole, Study Focuses on controlled release property of Hypermellose pthalate by avoiding gastric release of Lansoprazole. Most PPIs absorption takes place in proximal small intestine. But PPIs are acid sensitive so a stable form should be formulated which would bypass the stomach and release the drug in small intestine.

Immediate release dosage form of Lansoprazole results rapid dissolution and rapid rise in plasma drug concentration within a short period after administration. Subsequently due to metabolism and elimination the plasma drug concentration falls below the therapeutic level. Thus require a modified release dosage form which provides intestinal release of the drug by avoiding gastric release. Looking into aforementioned characteristics, attempts have been made to develop Pellets of certain drug molecule like Lansoprazole. Selected drug candidate show most of the desirable properties for the preparation of enteric coated Pellets.

## MATERIAL AND METHODS

Lansoprazole procured by Dr.Reddys lab,hydrabad, Mannitol BP, Lactose BP, Povidone BP K 30 procured by Loba chemie,cochin, Sodium hydroxy methyl Benzoate, Sodium hydroxy Propyl Benzoate, HPMCP BP (40 cps), Cetyl alcohol BP procured by S.D.Chemicals,Mumbai.

**Capsules Description:**

Cream colored hard gelatin capsules having LANZAP printed on both body and cap filled with white to off white spherical pellets

Standard weight – 460 mg

Label Claim – 30 mg

## STANDARD FORMULA FOR PRELIMINARY TRIAL

**Table No.1: Standard formula**

| DRUG MIXING | | | | | | |
|---|---|---|---|---|---|---|
| **Ingredients** | **Batch to batch Quantity in Percentage (%)** | | | | | |
| | **F-1** | **F-2** | **F-3** | **F-4** | **F-5** | **F-6** |
| Lansoprazole | 8.5 | 8.5 | 8.5 | 8.5 | 8.5 | 8.5 |
| Mannitol BP** | 42.608 | 41.578 | 40.535 | 40.408 | 39.128 | 38.408 |
| Light Magnesium carbonate BP | 6.098 | 6.098 | 6.098 | 6.098 | 6.098 | 6.098 |
| Lactose BP | 4.634 | 4.634 | 4.634 | 4.634 | 4.634 | 4.634 |
| Carmellose Calcium BP | 3.049 | 3.049 | 3.049 | 3.049 | 3.049 | 3.049 |
| Sucrose BP ** 25#/30# | 11.585 | 11.585 | 11.585 | 11.585 | 11.585 | 11.585 |
| Mannitol BP | **3.5** | **4.0** | **4.5** | **5.0** | **5.28** | **5.5** |
| Sucrose BP (syrup grade) | 6.098 | 6.098 | 6.098 | 6.098 | 6.098 | 6.098 |
| Povidone BP K 30 | 0.365 | 0.365 | 0.365 | 0.365 | 0.365 | 0.365 |
| Sodium hydroxy methyl Benzoate | 0.0067 | 0.0067 | 0.0067 | 0.0067 | 0.0067 | 0.0067 |
| Sodium hydroxy Propyl Benzoate | 0.00061 | 0.00061 | 0.00061 | 0.00061 | 0.00061 | 0.00061 |
| Purified water @ | 86.60 | 86.60 | 8.660 | 86.60 | 86.60 | 86.60 |
| **SUB COATING** | | | | | | |
| Povidone BP (K30) | **3.40** | **3.63** | **3.84** | **4.0** | **4.2** | **4.5** |
| Isopropyl alcohol BP @ | 45.757 | 45.757 | 45.757 | 45.757 | 45.757 | 45.757 |
| **ENTERIC COATING** | | | | | | |
| HPMCP BP (40 cps) | **8.5** | **8.8** | **9.06** | **9.2** | **9.4** | **9.6** |
| Cetyl alcohol BP | 1.006 | 1.006 | 1.006 | 1.006 | 1.006 | 1.006 |
| TiO2 BP | 0.649 | 0.649 | 0.649 | 0.649 | 0.649 | 0.649 |
| Acetone BP @ | 74.486 | 74.486 | 74.486 | 74.486 | 74.486 | 74.486 |
| Isopropyl alcohol BP @ | 49.657 | 49.657 | 49.657 | 49.657 | 49.657 | 49.657 |

@ Quantity non contributory in final quantity

## CRITICAL PROCESS PARAMETER

**Table No 2: Blending, Micronization & their Critical Parameter**

| S.No. | Stages | Name of Parameters | Operation parameter |
|---|---|---|---|
| 1 | Micronization | Main air Pressure | 6.5 kg/cm$^2$ |
| | | Cyclic air pressure | 5.1-5.3 kg/cm$^2$ |
| 2 | Blending (Drug Mixing) | RPM | 12 |
| | | Time | 60 min |

**Table No.3: Process Parameter during Sub Coating**

| S.No. | Name of Parameters | Operation parameter |
|---|---|---|
| 1 | Inlet temp ($^O$C) | 60.0-68.0 |
| 2 | Exhaust Temp ($^O$C) | 51.0-52.0 |
| 3 | Pump RPM | 20-25 |
| 4 | Atomization air pressure (Kg/cm$^2$) | 3.0 |
| 5 | Pan RPM | 13 |
| 6 | Gun Distance From Bed (cm) | 25 |
| 7 | Spray rate (gm/min/gun) | 150 |
| 8 | Drying Time (Min) | 45 |

**Table No.4: Process Parameter during Enteric Coating**

| S.No. | Name of Parameters | Operation parameter |
|---|---|---|
| 1 | Inlet temp ($^{o}$C) | 60-66 |
| 2 | Exhaust Temp ($^{o}$C) | 50-51 |
| 3 | Pump RPM | 35 |
| 4 | Atomization air pressure (Kg/cm$^{2}$) | 3.5 |
| 5 | Disc RPM | 10-13 |
| 6 | Gun Distance From Bed (cm) | 25 |
| 7 | Spray rate (gm/min/gun) | 110 |
| 8 | Drying Time (Min) | 45 |

**Table No.5: Process Parameter during Capsule Filling**

| S.No. | Name of Parameters | Operation parameter |
|---|---|---|
| 1 | Speed of the machine | 96 SPM |

**TEST AND SPECIFICATIONS**

**Table No.6: Test Specification of Process during various stages**

| S.No. | Stages | Tests | Specifications |
|---|---|---|---|
| 1 | Drug mixing | Content uniformity | 100 ± 15 % RSD NMT 6.0 % |
| | | Moisture content before drug coating | For information |
| 2. | Drug Coating | Moisture content after drug coating | Desired Moisture content NMT 2.0 % w/w after drying for 12 hrs at inlet temp not exceeding 40$^{o}$C |
| | | Assay | 90-110 % w/w |
| 3. | Sub Coating | Weight build up | NLT 4.0 % from the actual weight of dug coated pellets |
| | | Content uniformity | 85 %- 115 % RSD NMT 6.0 % |
| | | Assay | NLT 7.86 % and NMT 9.13 % |
| 4 | Enteric coating | Drug Release Profile at acid stage | NMT 2.0 % at acid stage |
| | | Drug Release Profile at Buffer stage | NLT 85 % at buffer stage |
| | | Solvent Content | For IPA NMT 5000 ppm<br>For acetone NMT 5000 ppm |
| | | Related Substances | Unknown Impurity NMT 0.3 %<br>Lansoprazole Sulphones NMT 0.5 %<br>Total Impurities NMT 0.1 % |
| | | Individual weight variation | Standard weight ± 6.0 % |
| 5 | Capsule filling | Drug Release Profile in acid Stage | NMT 10 % of the labeled amount of lansoprazole is dissolved in 60 min |
| | | Drug Release Profile Buffer stage | NLT 80 % (Q) of the labeled amount of lansoprazole dissolved in 60 min |
| | | Assay | (90 % -110 %) |
| | | Related Substances | NMT 2.0 % |
| | | LOD | NMT 5.0 % w/w |
| 6 | Stability Study | Drug Release in acid stage | NMT 10 % of the labeled amount of lansoprazole is dissolved in 60 min |
| | | Drug Release in buffer stage | NLT 80 % (Q) of the labeled amount of lansoprazole dissolved in 60 min |
| | | Assay | NLT 27.0 mg and NMT 33.0 mg |
| | | Related Substances | NMT 2.0 % |

**Table No 7: Process Parameter during Drug coating**

| S.No. | Name of Parameters | Operation parameter |
|---|---|---|
| 1 | Pump RPM | 12-65 |
| 2 | Atomization air pressure ($Kg/cm^2$) | 2.1-2.2 |
| 3 | Pan RPM | 36 |
| 4 | Gun Distance From Bed (cm) | 30-32 |
| 5 | Spray rate (gm/min/gun) | 130 |
| 6 | Spray on time min (min ) | 2-3 |
| 7 | Spray Off Time (min) | 5 |

## FORMULATION OF MODIFIED RELEASE CAPSULES

### Micronization of active ingredient

Micronization of Lansoprazole carried out for getting desired particle size. Fluid energy mill (Malvern) is used by maintaining its cyclic pressure 5-6 $kg/cm^2$ and Main air pressure 6-7 $kg/cm^2$ results depicted in table no.8

### Drug Mixing

Blend the Micronized Drug with Light magnesium carbonate, mannitol, Lactose, carmellose calcium. Blending operation carried out in Double cone Blender for 60 min at 12 rpm. In the preliminary formulation trial, content uniformity of batches F-1 to F-6 found well within the limits. Average content uniformity obtained 95 to 99 % w/w. Maximum uniformity of content of Lansoprazole achieved in Batch F-3. Individual. Results depicted in table no.9

### Drug Coated Pellets

### Syrup Preparation:

Sucrose Syrup prepared in steam kettle with Binder Povidone and Sodium methyl paraben & Sodium Propyl Paraben. Syrup preparation successfully done by maintaining Variables – top stirrer rpm, Paddle stirrer rpm and temperature of Kettle.

### Coating:

Centrifugal coating pan used for drug coating. During coating an additional mannitol layer also applied. Ratio of Mannitol is changing in each batch to optimize the effect of outer layer Mannitol in release rate of drug. Peristaltic pump rpm, inlet temp and outlet temperatures of air were critical variable observed during coating. Ratio of Mannitol variedin Batch to optimize the effect of outer layer Mannitol in release rate of drug. Assay of content of Lansoprazole found 99.3 % w/w which is most optimum among all the batches.

### Drying:

Drying of drug coated pellets is done in Tray dryer. Drying Temperature and Drying Times were important variables of Drying. Moisture content observed after 12 hrs of drying observed in batch F-3 as 0.91 % w/w which is least among all batches.resuts depicted in table no.10

**Sub coated Pellets**

**Sub Coating solution Preparation:**

Solution Prepared in stirrer. Povidone is sub coated material used with isopropyl alcohol as vehicle. Ratio of Povidone is changing in each batch to optimize the sub coating layer and monitor the influence of Drug release.

**Sub Coating:**

Centrifugal coater is used for Sub coating. Peristaltic pump rpm, Powder charging rpm and Disc rpm are critical variable observed during coating. Sub coated pellets having some weight build up than drug coated pellets. Ration of Povidone varied in all batches to optimize Sub coating layer. Weight build up observed from 4.1 to 4.6 % w/w.

**Enteric coated Pellets**

**Enteric Coating solution Preparation:**

Solution prepared in stirrer. Hypromellose pthalate with acetone, cetyl alcohol, and isopropyl alcohol used as vehicle. Titanium dioxide also used as opacifier in solution. Ratio of HPMCP is changing in each batch to optimize the enteric coating layer thickness and also to optimize the drug release.

**Enteric Coating:**

Centrifugal coater is used for Sub coating. Peristaltic pump rpm, Powder charging rpm and Disc rpm are critical variable observed during coating. Centrifugal coater is used for enteric coating. Peristaltic pump rpm, Powder charging rpm and Disc rpm are critical variable observed during coating. Enteric coated pellets evaluated for Content uniformity and Drug release profile in acid and buffer media. Average content uniformity observed 93 to 99 % w/w while best results obtained with batch F-2. Average drug release in acid media found 0.6 to 1.05 % while Drug release in buffer media observed as 84.4 to 96.8 % .Related substances and solvent content test also been carried out. Individual results depicted in tables. As Quantity of HPMCP increasing in formulation, release of drug is decreasing. Formulation batch F-3 given desired result. Drug released in buffer media from enteric coated Pellets was 96.8 % which is maximum among all other batches.

**Capsule filling:**

Enteric coated pellets filled in gelatin capsules by capsule filling machine. Individual weight variation of filled weight is critical parameter observed. Enteric coated pellets filled in hard gelatin capsules. Capsules evaluated for Individual fill content of capsules, Individual weight variation of capsules Found well within limits. Drug release from capsules in acid media found 0.8 to 1.2 % and in buffer media upto 94.9 % drug released in 60 min. Related substance test carried out for testing impurity after Capsules filling.

**Table No.8: Micronization of Lansoprazole**

| Result | Particle size (µm) | | | |
|---|---|---|---|---|
| Volume under % | 10 % | 50 % | 90 % | 100 % |
| Size (µm) | 0.48 | 2.66 | 7.41 | 17.62 |

**Table No. 9: Content uniformity of Lansoprazole in Drug mix (Blend)**

Limits: Content of Lansoprazole 100 ± 15 %

| Sample No. | Batch to Batch Content Uniformity (in %) | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| 1 | 98.5 | 101.2 | 104.5 | 99.2 | 91.2 | 95.6 |
| 2 | 95.8 | 90.6 | 99 | 98.2 | 90.5 | 94.8 |
| 3 | 95.6 | 99.8 | 97 | 99.6 | 99.5 | 96.8 |
| 4 | 92.5 | 87.3 | 101.2 | 91.2 | 98.2 | 98.9 |
| 5 | 96.0 | 100.7 | 98.9 | 98.6 | 91.5 | 99.1 |
| 6 | 92.1 | 90.5 | 96.5 | 97.5 | 99.2 | 99.5 |
| 7 | 89.6 | 103.3 | 98.8 | 101.3 | 96.2 | 98.6 |
| 8 | 100.1 | 95.2 | 99.5 | 101.5 | 99.1 | 99.1 |
| 9 | 94.9 | 95.3 | 96.3 | 100.5 | 99 | 92.8 |
| 10 | 90.6 | 91.4 | 100.7 | 103.1 | 91.8 | 99.1 |
| Avg. | 95.0 | 95.7 | 99.3 | 99.1 | 95.7 | 97.46 |

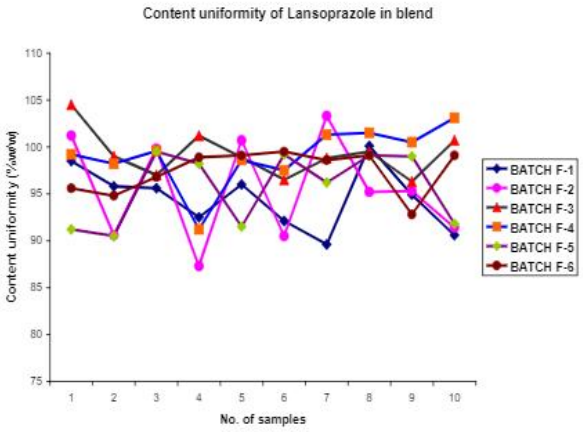



Figure No.1: Content Uniformity in Drug Mixing stage

**Table No.10: Drying of Drug coated pellets**

Limit: Moisture content: NMT 2.0 % w/w after 12 Hr

| Parameter | Batch F -1 | | | Batch F -2 | | | Batch F-3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Drying time (hrs) | | | Drying time (hrs) | | | Drying time (hrs) | | |
| | 5 | 10 | 12 | 5 | 10 | 12 | 5 | 10 | 12 |
| Moisture content | 3.35 | 3.38 | 1.93 | 3.36 | 3.37 | 1.92 | 2.27 | 1.75 | 0.91 |
| **Parameter** | **Batch F -4** | | | **Batch F -5** | | | **Batch F-6** | | |
| | Drying time (hrs) | | | Drying time (hrs) | | | Drying time(hrs) | | |
| | 5 | 10 | 12 | 5 | 10 | 12 | 5 | 10 | 12 |
| Moisture content | 3.12 | 3.45 | 1.50 | 3.32 | 3.15 | 1.14 | 3.10 | 1.90 | 0.98 |

Figure No.2: Moisture Content of Drug coated Pellets during and after Drying

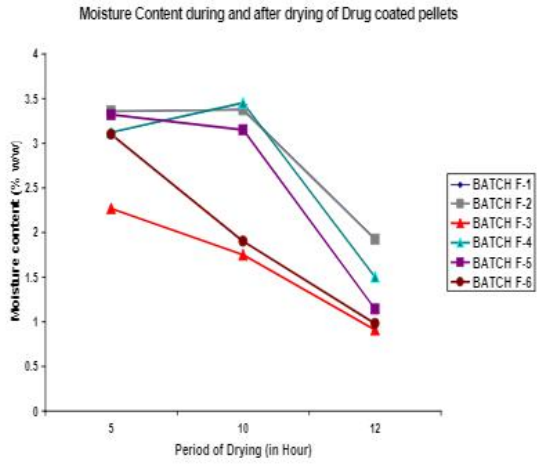


**Table No.11: Assay of Drug Coated pellets**
Limit: Content of Lansoprazole 90 to 110 % w/w

| Sample No. | No. of Batches | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| 1 | 96.8 | 97.5 | 102.5 | 97.2 | 98.3 | 99.3 |

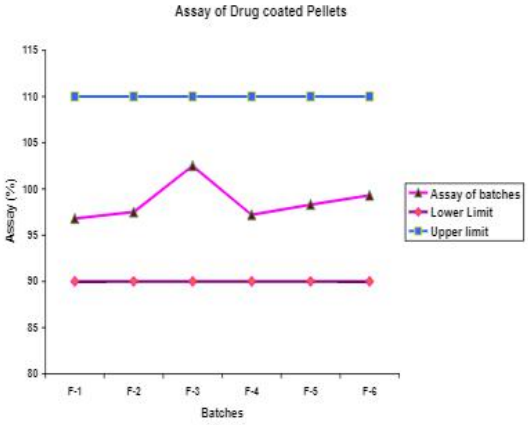



Figure No.3: Assay of Lansoprazole in Drug Coated Pellets

**Table No. 12: Weight Build up after sub coating**
Limit: NLT 4.0 % from the actual weight of dug coated pellets

| Batch No. | No. Of Batches | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| Actual build up | 4.69 % | 4.50 % | 4.50 % | 4.12 % | 4.51 % | 4.35 % |

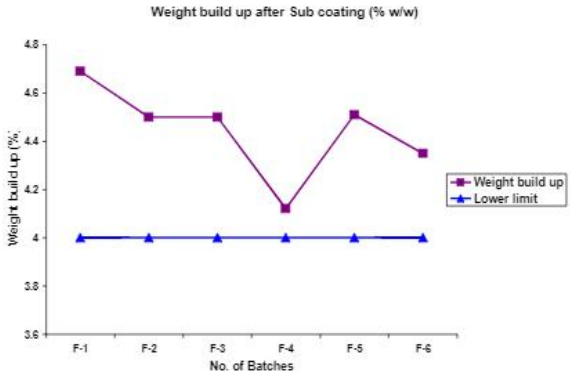



Figure No.4: Weight Build up of Sub Coating

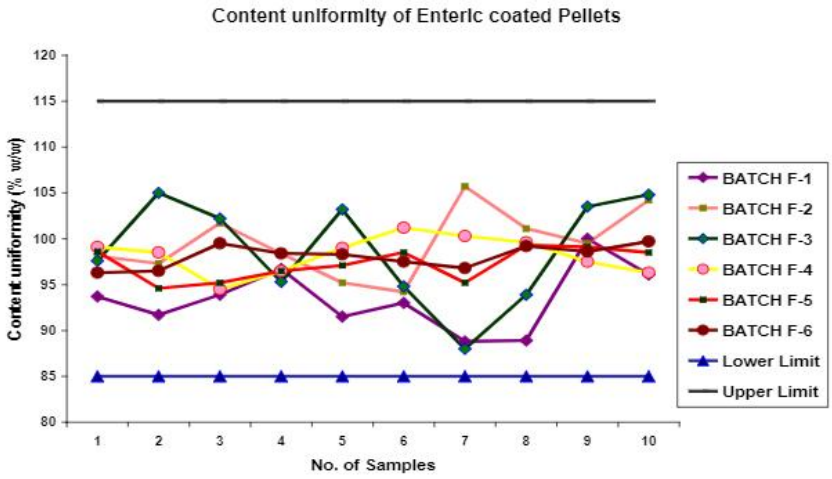



Figure No.5: Content Uniformity of Lansoprazole in Enteric coated Pellets

**Table No. 13: Assay of Lansoprazole in Enteric coated pellets**
Limits: Content of Drug NLT 7.86 % and NMT 9.13 % w/w

| Parameter | No. of Batches | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| Assay | 8.181 % | 8.548 % | 8.066 % | 8.452 % | 8.440 % | 8.510 % |

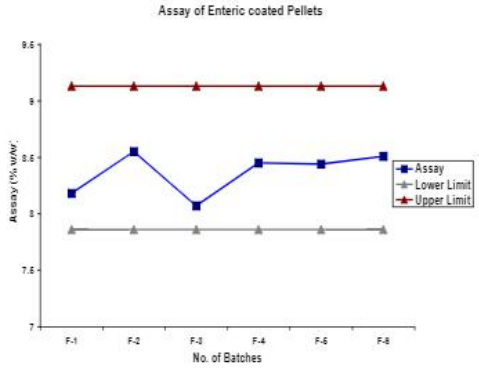



Figure No.6: Assay of Lansoprazole in Enteric coated Pellets

**Table No. 14: Drug release in acid media from enteric coated Pellets**
Limits: NMT 2.0 % content of drug release in acid media within 60 min

| No. of samples | Content of Lansoprazole released in acid Media (in 60 min) | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| 1 | 0.5 | 0.6 | 0.5 | 0.7 | 0.2 | 0.1 |
| 2 | 1.1 | 0.9 | 0.4 | 0.7 | 0.4 | 0.4 |
| 3 | 1.6 | 1.5 | 0.2 | 0.6 | 0.0 | 0.6 |
| 4 | 1.1 | 1.1 | 1.2 | 1.0 | 0.5 | 0.2 |
| 5 | 0.9 | 0.5 | 1.1 | 0.3 | 1.1 | 0.9 |
| 6 | 1.1 | 0.4 | 0.3 | 0.9 | 0.2 | 1.6 |
| Min | 0.5 | 0.4 | 0.2 | 0.3 | 0.0 | 0.1 |
| Max | 1.6 | 1.5 | 1.2 | 1.0 | 1.1 | 1.6 |
| Avg | 1.05 | 0.83 | 0.61 | 0.7 | 0.4 | 0.6 |

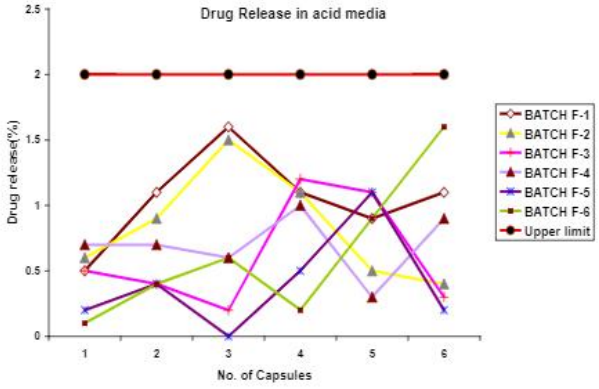



Figure No.7: Drug release profile in acid media from enteric coated Pellets

**Table No. 15: Drug release profile in Buffer media from enteric coated Pellets**

Limits: NLT 85 % content of drug release in Buffer Medium within 60 min

| Batches | Content of Lansoprazole (%) Released in Buffer Media | | | | | | |
|---|---|---|---|---|---|---|---|
| | Sampling Time (Min) | | | | | | |
| | 5 | 10 | 15 | 20 | 30 | 45 | 60 |
| F-1 | 8.7 | 17.6 | 22.4 | 34.6 | 56.8 | 71.6 | 84.4 |
| F-2 | 12.6 | 19.5 | 28.2 | 37.5 | 61.8 | 76.9 | 90.1 |
| F-3 | 17.3 | 21.5 | 38.5 | 52.9 | 68.42 | 88.2 | 96.8 |
| F-4 | 16.5 | 23.4 | 36.9 | 48.4 | 58.2 | 82.4 | 91.2 |
| F-5 | 15.9 | 25.6 | 36.3 | 44.7 | 61.6 | 82.5 | 89.5 |
| F-6 | 13.7 | 21.8 | 37.1 | 48.6 | 57.9 | 77.8 | 88.4 |

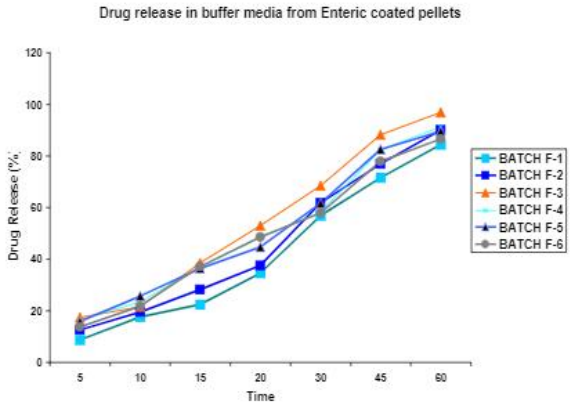



Figure No.8: Drug Release of Enteric coated Pellets in Buffer Media (pH 6.8)

**Table No.16: Solvent content of Enteric Coated pellets**

Limit: For IPA NMT 5000 ppm For acetone NMT 5000 ppm

| Solvents | No. of Batches | | | | | |
|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 |
| IPA (ppm) | 7.34 | 356.372 | 370.770 | 381.120 | 379.254 | 381.152 |
| Acetone (ppm) | 1.10 | 432.995 | 547.119 | 475.120 | 489.125 | 510.124 |

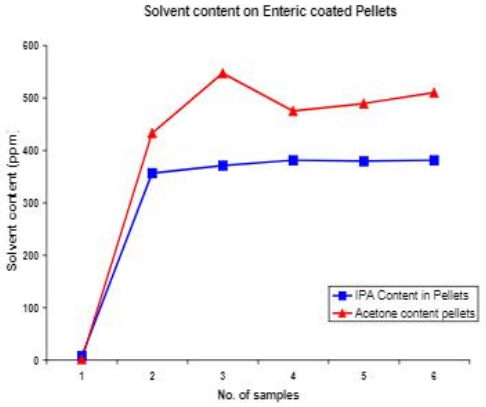



Figure No.9: Solvent Content of Enteric coated Pellets

**Figure No.10: Drug release in acid media from Capsules**

Limits: NMT 10 % of the labeled amount of lansoprazole is dissolved in 60 min

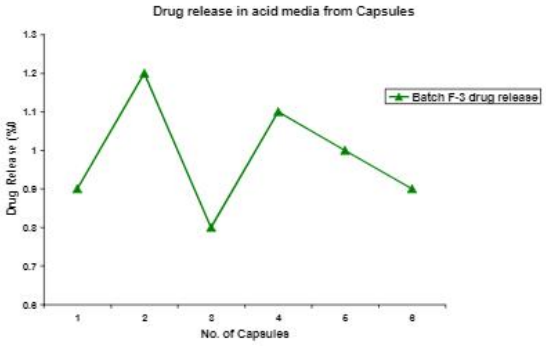
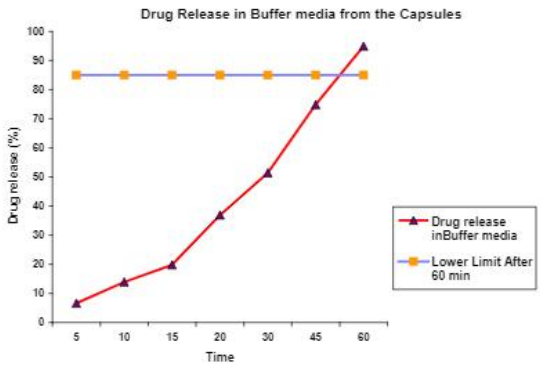



**Figure No.11: Drug release in Buffer media from Capsules**

**Limit:** NLT 80 % (Q) of the labeled amount of lansoprazole dissolved in 60 min



## SUMMARY AND CONCLUSION

Formulation of modified release capsules carried out with six preliminary trials. In the preliminary formulation trial, content uniformity of batches F-1 to F-6 found well within the limits. Average content uniformity obtained 95 to 99 % w/w. Drug mix (Blend) processed in centrifugal coating pan for drug coating during coating ratio of Mannitol varied in each batch to optimize the effect of outer layer Mannitol in release rate of drug. Assay of content of Lansoprazole found 96.8 to 102.5 % w/w. Drug coated pellets dried in tray drier, moisture content observed after 12 hrs of drying observed in batch F-3 as 0.91 % w/w which is least among all batches.Sub coated pellets again coated with HPMCP, enteric coated pellets evaluated for Content uniformity and Drug release profile in acid and buffer media. Average content uniformity observed 93 to 99 % w/w while best results obtained with batch F-2.while Batch F-3 contain 98.8 %. Average drug release in acid media found 0.6 to 1.05 % while Drug release in buffer media observed as 84.4 to 96.8 % .Batch F-3 Average release of active in acid media was 0.6 % which is comparatively lowest among all formulation. Most optimization factor was Release of drug in buffer media and Batch F-3 released 96.8 % of active in 60 min of multipoint dissolution study and Batch f-3 fulfill the criteria of objective. So on basis of in process and quality control data Batch F-3 optimized and forwarded for next processing stages.

Enteric coated pellets filled in gelatin capsules by capsule filling machine. Capsules evaluated for Individual fill content of capsules, individual weight variation of capsules found well within limits. Drug release from capsules in acid media found 0.8 to 1.2 % and in buffer media upto 94.9 % drug released in 60 min. no impurity found in related substances test.In capsule formulation positive and encouraging results in accordance to the aim were obtained. Percentage of mannitol 3.5 % to 5.5 %, povidone 3.4 to 4.5 % and Enteric coating layer HPMCP 8.5 % to 9.6 % used. as percentage of coating layer increasing, drug release from enteric coated pellets in acid media (pH 1.2) is decreasing from 1.05 % to 0.4 % after 60 min of dissolution study, while in buffer media (pH 6.8) drug release is increasing Batch F-1(84.4), Batch F-2 (90.1 %), Batch F-3 (96.8 %) while release rate is decreasing Batch F-4 (91.2%), Batch F-5 (89.5%), Batch F-6 (88.4%). After filling enteric coated pellets in hard gelatin capsules drug release in acid media found 0.8 % and in buffer media it was 94.9 %.

## REFERENCE

1. Lecomte F, Siepmann J, Walther M, MacRae J R. “Polymer blends used for the coating of multiparticulates: Comparison of aqueous and organic coating techniques” Pharmaceutical Research (2004) pp 21.
2. Kleinebudde P, Knop K. “Direct pelletization of pharmaceutical pellets in fluidbed processes” (2007) Elsevier pp 780-811.

3. Ghebre-Sellassie, Knoch A. "Pelletization techniques" Encyclopedia of Pharmaceutical Technology (2002) Third ed. Informa Helathcare.
4. Bauer K H, Lehmann K, Osterwald H P, Rothgang G. "Equipment for sugar coating and film coating processes Coated pharmaceutical dosage forms" (1998) Medpharm Scientiphic Publishers.
5. Jones D M "Solution suspension layering. Pelletization techniques" (2005) TTC Workshop. Binzen, Germany.
6. Kleinebudde P, Knop K. "Direct pelletization of pharmaceutical pellets in fluidbed processes." (2007) Elsevier pp 780-811.
7. Ghebre-Sellassie, Knoch A. "Pelletization techniques" Encyclopedia of Pharmaceutical Technology. (2002) Third ed. Informa Helathcare.
8. Korakianiti S E, Rekkas D M, Dallas P P, Choulis H N "Optimization of the Pelletization Process in a Fluid-Bed Rotor Granulator Using Experimental Design." AAPS Pharmscience (2000) pp1-5.
9. Paterakis P G, Korakianiti E S, Dallas P P, Rekkas D M "Evaluation and simultaneous optimization of some pellets characteristics using a 33 factorial design and the desirability function." International Journal of Pharmaceutics (2002) 248: pp 51-60.
10. Holm P, Bonde M, Wigmore T "Pelletization by granulation in a rotary processor RP-2. Part 1. Effects of process and product variables on granule growth." Pharmaceutical Technology Europe (1996) 8: 22 – 36.
11. Rashid H A, Heinamaki J Z, Antikainen O, Zilruusi J "Effects of process variables on the size, shape and surface characteristics of microcrystalline cellulose beads prepared in a centrifugal granulator." Drug Development and Industrial Pharmacy (1999) 25: 605.
12. Korakianti E S STP Pharma Sci (2002) 12: 191
13. Liew V C, Wan C S L, Heng P W S "Role of base plate rotational speed in controlling spheroid size distribution and minimizing oversize particle formation during spheroid production by rotary processing." Drug Development and Industrial Pharmacy (2000) 26: 953 – 963.
14. Kleinebudde P, Knop K. "Direct pelletization of pharmaceutical pellets in fluid bed processes." Elsevier (2007) pp 780-811.
15. Vertommen. "Internal and external structure of pellets made in a rotary processor." International Journal of Pharmaceutics (1996) 146: 21 – 29.
16. Olsen, K. Fluid bed equipment Pharmaceutical Pelletization Technology. Marcel and Dekker, New York, (1989) First ed. pp 39-69.
17. Jacob M. Granulation equipment Granulation. Elsevier, (2007) pp 417-476.
18. Felton L A. "Film Coating of Oral Solid Dosage Form" Encyclopedia of

Pharmaceutical Technology. Third ed. Informa Helathcare, (2007) pp 1729 – 1747.

19. Kleinebudde P, Knop K. "Direct pelletization of pharmaceutical pellets in fluid bed processes." Elsevier, (2007); pp 780-811.
20. Gu L, Liew C V, Heng, "Wet spheronization by rotary processing – A multistage single-pot process for producing spherodis". Drug Development and Industrial Pharmacy (2004) 30: 111-123
21. Kleinebudde P, Knop K. "Direct pelletization of pharmaceutical pellets in fluidbed processes" Elsevier, (2007) pp 780-811.
22. Kleinebudde P, Knop K. "Direct pelletization of pharmaceutical pellets in fluidbed processes" (2007) Elsevier, pp 780-811.
23. Parikh D M. "Batch size increase in fluid-bed granulation" Pharmaceutical Process Scale-up. (2006) CRC Press, New York, pp 267-324.
24. Ghebre-Sellassie "Mechanism of pellet formation and growth" Pharmaceutical Pelletization Technology First ed Marcel Dekker, New York, (1989) pp 123 – 144.
25. Dybdahl H P. "Advanced granulation theory at particle level - free learning summary" (2005).
26. Bauer K H, Lehmann K, Osterwald H P, Rothgang G. "Equipment for sugar coating and film coating processes Coated pharmaceutical dosage forms" Medpharm Scientiphic Publishers, Stuttgart (1998).
27. Felton L A. "Film Coating of Oral Solid Dosage Form" Encyclopedia of Pharmaceutical Technology Third ed. Informa Helathcare, (2007) pp 1729 – 1747.
28. Lehman K. "Chemistry and application properties of polymetacrylate coating systems" Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms. Marcel Dekker, (1997) pp 101-176.
29. Frohoff-Huelsmann A M, Schmitz A, Lippold C B. "Aqueous ethyl cellulose dispersions containing plasticizers of different water solubility and hydroxypropyl methylcellulose as coating material for diffusion pellets- Drug release rates from coated pellets" International Journal of Pharmaceutics (1999) 177: 69-82.