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DESIGN AND EVALUATION OF OMEPRAZOLE MULTI UNIT PELLET SYSTEM

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Abstract:

The work was aimed to persude the Oral drug delivery system becomes challenging when the drug product needs to be delivered in modified release pattern in elderly patients, especially since it is difficult to swallow for them. Multiparticulates are the choice of dosage form when fast disintegration is desirable without loss of original release profile. The effect of sugar spheres containing enteric coated pellets of Omeprazole. Multiple unit dosage forms of Omeprazole were formulated by Wurster process. The sugar spheres were coated with the drug, HPMC E5, Eudragit L30D55 and then with PEG6000. The Optimized formulations showed plastic deformation and maintain their integrity with no considerable change in their surface properties. In vitro release profile of formulation F9 containing sugar spheres coated with, Eudragit L30D55 and PEG 6000 as cushioning agent showed release up to 97% at the end of 45 Mins in buffer. The results prove that there is no potent incompatibility between the drug and the polymer. The F9 formulation was best suited for multiple unit pellets systems of Omeprazole.

Key words: Omeprazole, HPMC E5, Extrusion-Spheronization, Solution/Suspension layering, MUPS

1. INTRODUCTION

1.1 Ulcer

A peptic ulcer is a sore in the lining of stomach or duodenum. The duodenum is the first part of small intestine. Peptic ulcers are found in the stomach are called as gastric ulcers, in the duodenum are called duodenal ulcers.

1.2 Causes of peptic ulcer [2, 3, 4:]

Peptic ulcers are caused by acid and pepsin (an enzyme) produced in the stomach. Patients who develop ulcers often produce greater amounts of acid than people without ulcers. Also, the ulcer patient may not have strong enough natural defenses in the stomach or intestinal wall to resist the effect of acid and pepsin. Doctors do not yet know all the reasons for too much acid production, but many believe the key to healing an ulcer is to control the amount of acid produce

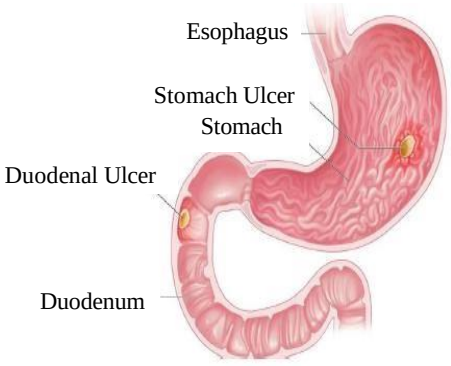

Figure.1: Peptic ulcer occur in the

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1.3.1 Duodenal Ulcer Symptoms:

Pain that awakens patients from sleep. Burning sensation in the upper abdomen. Pain in the back, lower abdomen or chest area may occasionally occur. Pain that occurs when the stomach is empty (about two hours after a meal or during the night).

1.3.2 Gastric Ulcer symptoms:

Gastric ulcer pain may be less severe than duodenal ulcer pain and is noticeably higher in the abdomen. Eating may increase pain rather than relieve pain. Pain is described as aching, nagging, cramping or dull. Other symptoms may include nausea, vomiting and weight loss. Some ulcers may produce no symptoms at all. However, occasional painless bleeding, anemia (low blood count), or the passage of black tarry stool may be the first sign of peptic ulcer disease.

2. Introduction of Novel Drug Delivery System [8, 9]:

Incorporating an existing medicine into a novel drug delivery system (NDDS) can significantly improve its performance in terms of efficacy, safety and improved patient compliance. In the form of a NDDS, an existing drug molecule can get new life, thereby increasing its market value and competitiveness. Multipaticulate dosage forms are pharmaceutical formulations in which the active substance is present as a number of small independent subunits with diameter of 0.05-0.2 mm. To deliver the recommended total dose, these subunits are filled into a capsule or compressed into a tablet. They provide many advantages over single-unit systems because of their small size. Multi unit pellets system are less dependent on gastric emptying, resulting in less inter and intrasubject variability in gastrointestinal transit time. They are also better distributed and less likely to cause local irritation. Recently much emphasis is being laid on the development of Multipaticulate dosage forms in preference to single unit systems because of their potential benefits such as increased bioavailability, reduced risk of systemic toxicity, reduced risk of local irritation and predictable gastric emptying.

2.1 Advantages of pellets [10, 11]:

They can be divided in to desired dosage strength without process or formulation changes.When pellets containing the active ingredient are in the form of suspension, capsules, or disintegrating tablets, they offer significant therapeutic advantages over single unit dosage forms. They can also be blended to deliver incompatible bio-active agents.They can also be used to provide different release profile at the same or different sites in the gastro intestinal tract.Pellets offer high degree of flexibility in the design and development of oral dosage form like suspension, sachet, tablet and capsule.

2.2 Disadvantages Of Pellets [10,11]:

- Dosing by volume rather than number and splitting into single dose units as required.
- Involves capsule filling which can increase the costs or tabletting which destroy film coatings on the pellets.
- The size of pellets varies from formulation to formulation but usually lies between 1 to2mm.

2.3 Desirable properties of pellets [10, 11]:

Uncoated pellets:

1. Uniform spherical shape.
2. Uniform size.
3. Good flow properties.
4. Reproducible packing.
5. High strength.
6. Low friability, Low dust.
7. Smooth surface.
8. Ease of coating.

Once coated:

1. Maintain all of the above properties.
2. Have desired drug release characteristics

2.4 Growth Mechanism Of Pellets [12,13]:

In order to select and optimize any pelletization/granulation process, it is important to understand the fundamental mechanisms of granule formation and growth. Different theories have been postulated related to the mechanism of formation and growth of pellets. The mechanism of pellet formation and growth, the following steps were proposed: Nucleation, coalescence, layering and abrasion transfer.

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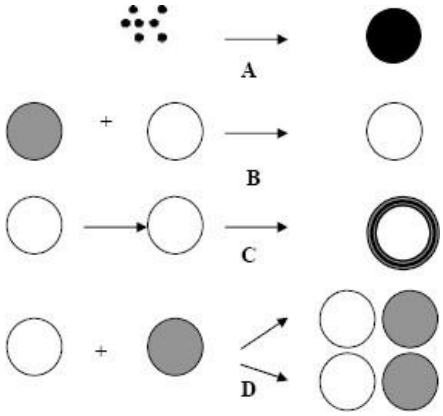

Figure: 2 Pellet growth mechanisms. (A) Nucleation, (B) Coalescence, (C) Layering and (D) Abrasion transfer.

3. PELLETIZATION TECHNIQUES

Compaction and drug layering are the most widely used pelletization techniques in pharmaceutical industry. Of the compaction techniques, extrusion and spheronization is the most popular method. Recently, however, melt pelletization has been used frequently in making compaction pellets using a different type of equipment, e.g. a high-shear mixer. Other pelletization methods, such as Globulation, balling and compression are also used in the development of pharmaceutical pellets although in a limited scale.

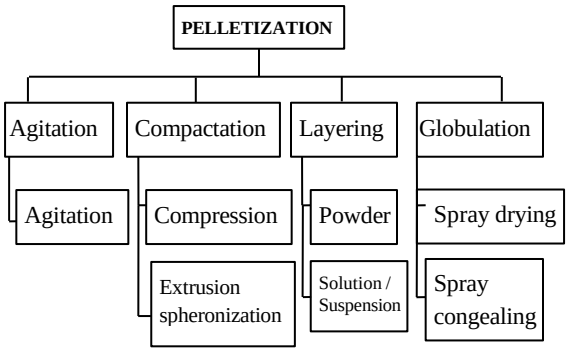

Figure: 3 Different pelletization techniques

4. LITERATURE REVIEW

M. Marvola et al., (1998), developed a multiple unit site specific drug formulation allowing targeting of drug release in the colon by enteric polymer as binders and coating materials. Ibuprofen and furosemide were the model drugs. Methacrylate copolymer, hydroxypropyl methylcellose acetate succinate and cellulose acetate phthalate were used as enteric polymer. The main conclusion was that drug release can be targeted on the distal part of the small intestine and the colon by preparing film-coated matrix pellets in which enteric polymers dissolving at PH have been used both as binders in the pellets and as coating material.

US Patent by Lundberg et al, 2000, explained new pharmaceutical dosage form comprising a core material that contains a proton pump inhibiter, one or more alkaline reacting compounds and optionally pharmaceutical excipients having a water soluble separating layer and an enteric coating layer.

Bai et al,(2005), invented a pulsatile drug delivery system comprising of plurality of particle that are divided in to several individual delivery units, each having its own distinct composition. Drug delivery was controlled by the rupture of the membrane. The timing of release was controlled by the thickness of coating and the amount of water soluble polymer to achieve the pulsed release. The individual particles had the same composition of internal core, but the thickness of the external coating layer varied.

J. Siepmann. Et al., (2007), studied the use of polymer blends as coating material for controlled drug delivery system and their advantages. But these systems are more complex than coatings based on only one polymer. The blended polymers can be incompatible and care has to be taken using these types of formulations.

5. AIM OF THE STUDY

The aim of the present study was to formulate anti ulcer drug Omeprazole multiple unit pellets system (MUPS) and study the *invitro* release pattern. Anti ulcer drugs under the category of proton pump inhibitor are acid labileDrugs. These drugs will degrade in acidic environment and will lead to therapeutic inefficacy. It is necessary to bypass the acidic pH of the stomach (single unit or multiple units) by using different enteric polymers. Omeprazole is an acid labile drug and it will degrade in acidic environment. Therefore to bypass the acidic pH of the stomach Omeprazole is formulated as enteric coated pellets. The present work was carried out for preparation of Omeprazole enteric coated pellets to prevent drug release in stomach

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5.1 AIM AND OBJECTIVE

The objective of the work is to develop a stable, pharmaceutically equivalent, robust. Omeprazole, which is an orally administered anti ulcer drug.□
Pellets are of great interest to the pharmaceutical industry for variety of reasons. Pelletized products not only offer flexibility in dosage form design and development, but are also utilized to improve safety and efficacy of bio active agents.
To formulate and evaluate multiple unit particulate system of anti ulcer drug .To study the release profile of the dosage form and to compare their drug release profiles with the innovator .To study the stability of dosage form.

6. MATERIALS AND METHODS

Table .1: List of Chemicals Used

Sl no	NAME OF MATERIAL	MANUFACTURING COMPANY
1	Omeprazole	Enal Drugs Ltd. Hyderabad
2	Sugar spheres	Sanmour pharma pvt.ltd, Mumbai
3	NaoH Pellets	Himedia laboratories, pvt. Ltd. Mumbai
4	Light magnesium Oxide	S.D fine chemicles,pvt.itd Mumbai
5	Magnesium stearate	Loba chemie, pvt. Ltd. Mumbai
6	Hydroxy propyl methyl cellulose E 5	Himedia laboratories, pvt. Ltd. Mumbai
7	Tri ethyl Amine	S.D fine chemicles,pvt.itd Mumbai
8	Talc	Loba chemie, pvt. Ltd. Mumbai
9	Polyethylene Glycol	Himedia laboratories, pvt. Ltd. Mumbai
10	DM water	DM water plant sri ram eng co.
11	Titanium Dioxide	S.D fine chemicals, pvt.ltd. Mumbai
12	Iso Propyl alcohol	Himedia laboratories, pvt. Ltd. Mumbai
13	Eudragit L-30 D	Sanmour pharma pvt.ltd. Mumbai
14	Triethyl citrate	Loba chemie, pvt. Ltd. Mumbai
15	Polysorbate 80	Himedia laboratories, pvt. Ltd. Mumbai

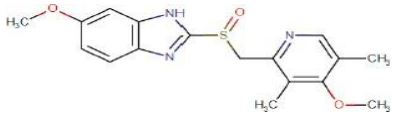
6.1 LIST OF EQUIPMENTS:

Table .2: Instruments Used for Formulation Development

EQUIPMENT	MANUFACTURER
Electronic single pan balance	Shimadzu
Mechanical sifter & sieve	Retsec
Tapped density tester USP	Electro lab
Blender	Rimek
Mechanical stirrer	Remi motors
Fluidized bed dryer	Retch
PH meter	Elico India
Dissolution test apparatus USP	Lab India
UV	Lab India
FTIR	Germany

6.2 DRUG PROFILE: OMEPRAZOLE

Generic name: Omeprazole
Class: Proton Pump Inhibitor
Structure:



Chemical Name: 5-methoxy-2-[[(4-methoxy 3, 5 dimethylpyridin2yl) methyl] Sulfinyl]-1H-benzimidazole.
Molecular formula: C17H19N3O3S.
Molecular weight: 345.416g/mol.
Description: Omeprazole is a white to off-white crystalline powder.
Solubility: Freely soluble in ethanol and methanol, slightly soluble in acetone and is propane and very slightly soluble in water.
Standards: Omeprazole contains not less than 99.0 per cent and not more than 101.0 per cent of Omeprazole.
Heavy metals: Not more than 20ppm.
Sulphate Ash: Not more than 0.2 %,
Loss on drying: Not more than 0.2%.
Solubility: Omeprazole is freely soluble in diethyl form amide; soluble in methanol; sparingly soluble in ethanol; Slightly soluble in ethyl acetate, dichloromethane and acetonitrile; very slightly

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soluble in ether; and practically insoluble in hexane and water.
Melting point: 178-182 co
Half life: 1.5 (± 1.0) hours

Pharmacology of Omeprazole

Omeprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit ant cholinergic or histamine H2- receptor antagonist properties, but rather suppress gastric acid secretion by specific inhibition of the (H+,K+)-ATP as enzyme system at the secretary surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, Omeprazole has been characterized as a gastric acid pump inhibitor which blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus.

6.3 EXCIPIENT PROFILE

6.3.1 EUDRAGIT L30 D

Non Proprietary Names: Methacrylic Acid - Ethyl Acrylate Copolymer (1:1) Dispersion 30 Per Cent"**Ph. Eur :** Methacrylic Acid Copolymer Dispersion **USP/NF :** Methacrylic Acid Copolymer LD" JPE **Chemical Name :** Poly (methacylic acid-co-ethyl acrylate) 1:1 **Molecular Weight :** 250,000. **Structural formula :**EUDRAGIT® L 30 D-55 is the aqueous dispersion of an anionic copolymer based on methacrylic acid and ethyl acrylate. The rastio of the carboxyyl groups to the ester groups is approx 1:1. **Category :** Film former; tablet binder; tablet diluent. **Description :** Milky-white liquid of low viscosity with a faint characteristic odour. **PH :** 2.1 - 3.0.

7. PREFORMULATION STUDIES

To formulate an ideal formulation, the pre-formulation studies are usually the quantitative assessment of chemical stability of drug as well as stability in presence of other recipients for a formulation. Reformulation may be described as a phase of the research and development process where the formulation scientist characterizes the physical, chemical and mechanical properties of new drug substances, in order to develop stable, safe and Effective dosage forms. Ideally the reformulation phase begins early in the discovery process such the appropriate physical, chemical data is available to aid the selection of new chemical entities that enter the development process during this evaluation possible interaction with various inert ingredients intended for use in final dosage form are also considered in the present study.

The following reformulation studies were performed:

1. Solubility analysis
2. Bulk density
3. Tapped density
4. Melting point
5. Loss on drying
6. Identification of drug- recipients compatibility

8. COMPATIBILITY STUDY:

Drug- excipient compatibility studies:

IR spectra of drug, drug and polymers and excipients were obtained by using Bruker optic GMBH FTIR spectrometer.

Method:

FTIR spectra of pure drug, and its physical mixture were obtained by using KBr pellets methods. About 2% (w/w) of samples was mixed with potassium bromide (KBr) disc. Each disc was scanned at a resolution of 4 cm-1 over a wave number region of 400–4000 cm-1 by a FTIR spectrometer.

9. FORMULATION OF OMEPRAZOLEMUPS

Different batches of MUPS (F1 to F9) were formulated using the ingredient given in the

Table .3: Formula for Omeprazole pellets:

Batch no.		F1	F2	F3	F4	F5	F6	F7	F8	F9
Sl. no.	Ingredients	mg/unit	mg/unit	mg/unit	mg/unit	mg/unit	mg/unit	mg/unit	mg/unit	mg/unit
A	DRUG LAYERING									
1	Sugar Spheres	135.5	140.5	145.5	150.5	155.5	160.5	165.5	170.5	175.5
2	Omeprazole	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00
3	Light Mg O_2	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
4	HPMC E5	20	20	25	25	30	30	35	40	40
5	Tri ethyl Amine	10	10	10	10	10	10	10	10	10
6	Polyethylene Glycol 6000	6	6	6	6	6	6	6	6	6
7	NAOH	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

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Batch no.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
8	D M water	qs	qs	qs	qs	qs	qs	qs	qs	qs
	Total	225	230	240	245	255	260	270	280	285
B	**SUB COATING OF OMEPRAZOLE PELLETS**									
9	Omeprazole layered pellets	225	230	240	245	255	260	270	280	285
10	HPMC E 5	20	20	25	25	30	30	35	40	40
12	Talc, USP	10	10	10	10	10	10	10	10	10
13	Titanium Dioxide	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
14	Magnesium Stearate	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
15	D M water	qs	qs	qs	qs	qs	qs	qs	qs	qs
	Total	264	269	284	289	304	309	324	339	344
C	**ENTERIC COATING OF OMEPRAZOLE PELLETES**									
16	Eudragit L-30 D	70.00	65.00	60.00	55.00	50.00	45.00	40.00	35.00	30.00
17	Triethyl citrate, NF	9.25	9.25	9.25	9.25	9.25	9.25	9.25	9.25	9.25
18	Talc, USP	12	12	12	12	12	12	12	12	12
19	Polysorbate 80, NF	3.75	3.75	3.75	3.75	3.75	3.75	3.75	3.75	3.75
20	Titanium Dioxide	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
21	Purified water	qs	qs	qs	qs	qs	qs	qs	qs	qs
	Total	359	359	369	369	378.75	379	389	399	399

10. Preparation of drug loading solution:

Took weighed 1/3rd of the total quantity of dematerialized water in stainless steel vessel and heat the water up to80-85ºC. Take purified water in SS container to that add Sodium hydroxide and Omeprazole under continuous stirring. Take Purified water in another SS container to that add light magnesium oxide, magnesium stearate, talc under continuous stirring. Add HPMC E5 to the Purified water under continuous stirring. Add solutions obtained in step and stir for 15 min.

In process check:

Table .4: FBC Parameters

Inlet temp	48ºC – 50ºC
Bed temp	42ºC - 48ºC
Atomizing air pressure	2.0– 5.0Kg/cm^2
Spray Rate	15 ml/min

Drug loading Process

Equipment Used: - Fluid Bed Processor with Wurster facility (bottom spray).

Figure: 4 fluid bed granulator with a top spray system

2. STAGE-II:

Sub Coating Preparation method:

Took weighed 1/3rd of quantity of dematerialized water in stainless steel (SS) vessel and heat the water up to80-85^{0}C. Carry out the setup and operation of Homogenizer. Take the purified water in a tank and start stirring by adding HPMC E5 after that add Magnesium stearate, Talc, Titanium Dioxide and IPA and stir until the clear solution is obtained. Filter the above solution through 100# nylon cloth into another SS vessel Cooled the solution up to room temperature under stirring

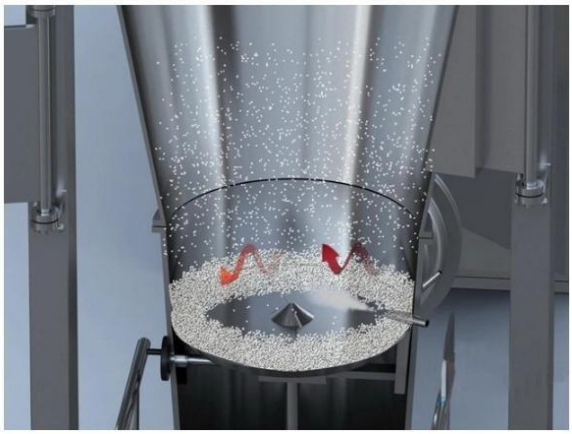

Figure: 5 SUB COATING (FBC)

STAGE-III: Enteric coating

Preparation of coating solution:

Purified water was taken in a stainless steel vessel. Carry out the operation of mechanical stirrer &

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colloidal mill. Dissolve Separately NaoH and Triethyl citrate in water with continuous stirring. Dissolve Separately Polysorbate 80 in purified water. Pour the Drug Coat L30D in SS Tank & gradually add the solution obtained Continue stirring for another 15-20mins. Finally pass the above solution step no 7 though #100 nylon cloth into separate SS container.

Figure: 6 Enteric coating (FBC)

HAUSNER'S RATIO:

It is measurement of frictional resistance of the drug. The ideal range should be 1.2 –1.5.
It is the determined by the ratio of tapped density and bulk density.

$$\text{Hausner's ratio} = v_i / v_t$$

Where vt = Tapped volume
vi = untapped volume

Limits:

Table .5: limits of Hausner's ratio value

S.No	Hausner's ratio	Flow
1	1-1.2	Free flowing
2	1.2-1.6	Cohesive powder

11. ANGLE OF REPOSE

Angle that can be obtained between the free surface of a powder heap and horizontal plane. The angle of repose was measured by allowing the pellets to fall over a graph sheet placed on horizontal surface through a funnel kept at a certain convenient height. The height of the heap was measured and then circumference of the base of heap was drawn on a graph sheet with the help of a pencil. The radius of the circle obtained was measured. The angle of repose is given as,

Table 6: limits of angle repose value

Angle of Repose (Degrees)	Type of Flow
<20	Excellent
20-30	Good
30-34	Passable
>40	Very Poor

12. RESULTS AND DISCUSSION

12.1 CALIBRATION CURVE OF OMEPRAZOLE:

Calibration curve of Omeprazole was determined by plotting absorbance/concentration (mcg/ml) at 302nm, the results obtained. The linear regression analysis was done on absorbance data points. A straight line generated to facilitate the calculation of amount of drug, the equation is as follows: Y = mx +

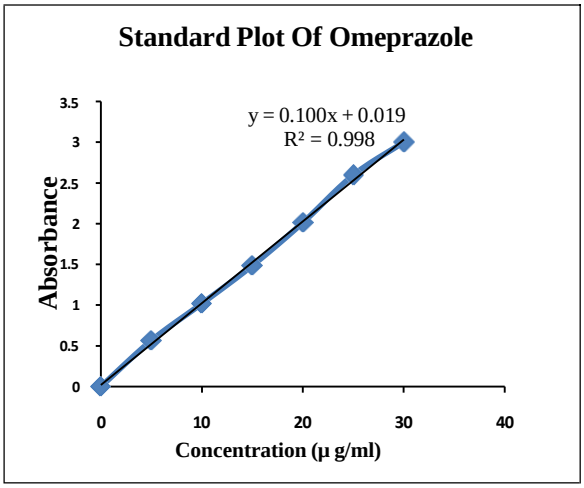

Figure.7 : Standard plot of Omeprazole

The above graph showed the standard curve of the Omeprazole and from it correlation coefficient value was calculated as 0.998. The above graph showed the linearity in curve and therefore it revealed that it follows the beers law.

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13. ASSAY STUDIES

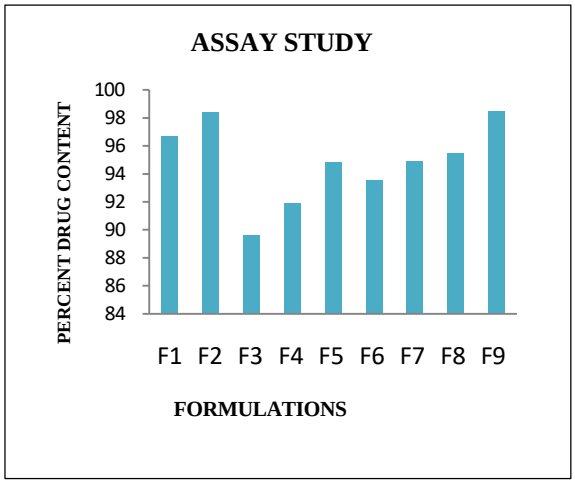

Figure. 8 : percent assay of various formulations

Above graph showed the percent drug content in each formulations and it was observed that the all formulations content the drug within the limit (not less than 89% and not more than 109%)

GASTRIC ACID RESISTANCE TEST:

Results for the acid resistant test

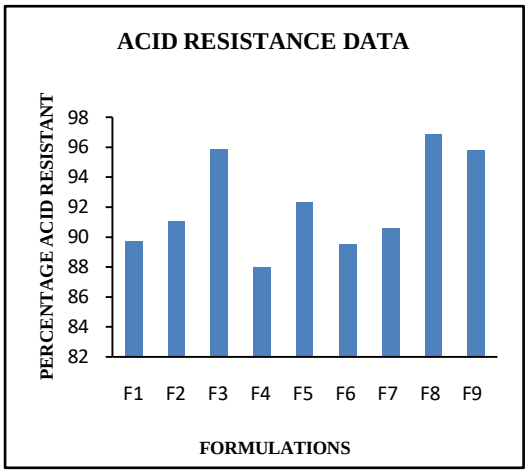

Figure.9 : Acid resistance dissolution data

The above graph showed the percent acid resistant of all formulations and it was observed that the all formulations have better acid resistant.

14. INVITRO DISSOLUTION STUDIES:

Results for invitro dissolution studies were given the table and graph for formulations F1 to F3, F4 to F6 and F7 to F9 in 0.1N HCL were showed respectively and graph for formulation F1 to F3, F4 to F6 and F7 to F9 in phosphate buffer pH6.8 were showed.

Table No.7: Cumulative percentage of Omeprazole release in 0.1N HCL and phosphate Buffer pH 6.8

Cumulative Percent drug release in 0.1 N HCL									
TIME (MIN)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
15	0.67	0.65	0.61	0.70	0.73	0.59	0.56	0.52	0.49
30	0.72	0.69	0.65	0.72	0.66	0.62	0.60	0.58	0.57
45	0.85	0.83	0.90	0.80	0.77	0.74	0.71	0.68	0.64
60	0.91	0.87	0.85	0.83	0.96	0.81	0.79	0.76	0.71
75	1.13	1.08	1.06	1.03	1.20	1.01	0.98	0.95	0.88
90	1.36	1.30	1.27	1.24	1.44	1.21	1.18	1.14	1.06
45	0.85	0.83	0.90	0.80	0.77	0.74	0.71	0.68	0.64
60	0.91	0.87	0.85	0.83	0.96	0.81	0.79	0.76	0.71
75	1.13	1.08	1.06	1.03	1.20	1.01	0.98	0.95	0.88
90	1.36	1.30	1.27	1.24	1.44	1.21	1.18	1.14	1.06
105	1.59	1.52	1.48	1.45	1.48	1.41	1.38	1.33	1.24
120	1.82	1.74	1.70	1.66	1.92	1.62	1.58	1.52	1.42
90	1.36	1.30	1.27	1.24	1.44	1.21	1.18	1.14	1.06
105	1.59	1.52	1.48	1.45	1.48	1.41	1.38	1.33	1.24
120	1.82	1.74	1.70	1.66	1.92	1.62	1.58	1.52	1.42
Cumulative Percent drug release in phosphate buffer pH 6.8									
125	55.13	58.01	60.22	62.11	70.15	65.22	67.33	69.45	71.25
140	67.04	62.11	65.09	67.41	69.05	72.18	75.13	77.03	79.10
155	65.34	75.65	67.45	71.07	73.19	76.24	79.06	82.18	85.09
170	67.57	72.56	75.34	79.13	82.67	86.56	90.20	94.15	97.87

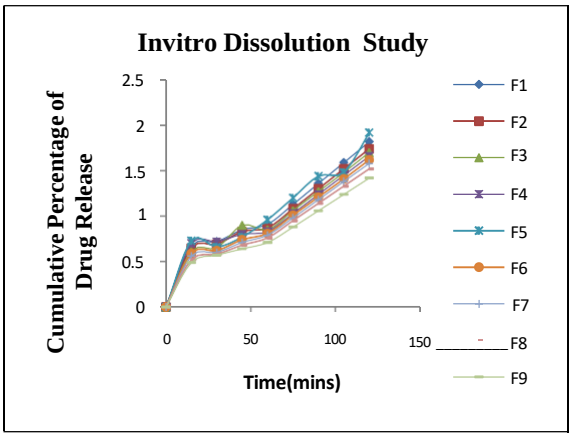

Figure.10: Cumulative Percentage of Release of Omeprazole in 0.1N HCL

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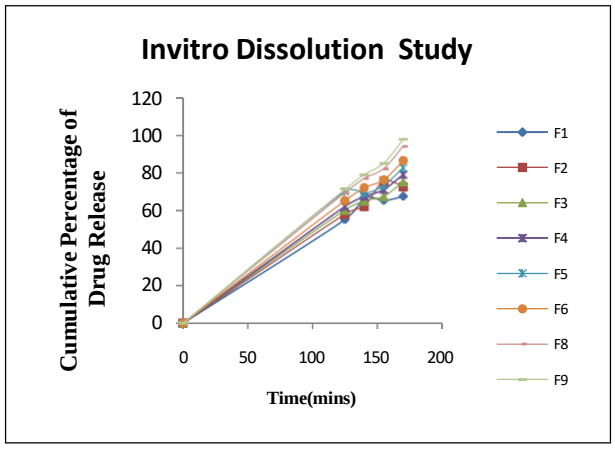

Figure.11: Cumulative Percentage of drug Release of Omeprazole in phosphate buffer pH6.8

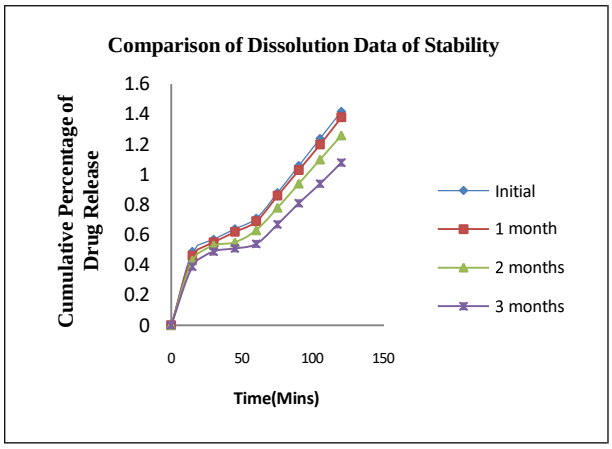

Figure.12: Comparison of Dissolution Data of Stability IN 0.1 N HCL

15. Accelerated stability study

Stability profile of Formulation F9

Table No. 8: Dissolution data of stability

1) IN 0.1 N HCL					
S.No.	Time(min)	Cumulative % drug release			
		Initial	1 month	2 months	3 months
1	0	0	0	0	0
2	15	0.49	0.46	0.43	0.39
3	30	0.57	0.55	0.53	0.49
4	45	0.64	0.62	0.55	0.51
5	60	0.71	0.69	0.63	0.54
6	75	0.88	0.86	0.78	0.67
7	90	1.06	1.03	0.94	0.81
8	105	1.24	1.20	1.10	0.94
9	120	1.42	1.38	1.26	1.08
2) IN PHOSPHATE BUFFER 6.8					
10	125	68.25	68.25	68.25	68.25
11	140	77.10	77.10	77.10	77.10
12	155	84.09	83.96	83.70	83.65
13	170	97.76	97.73	97.65	97.55

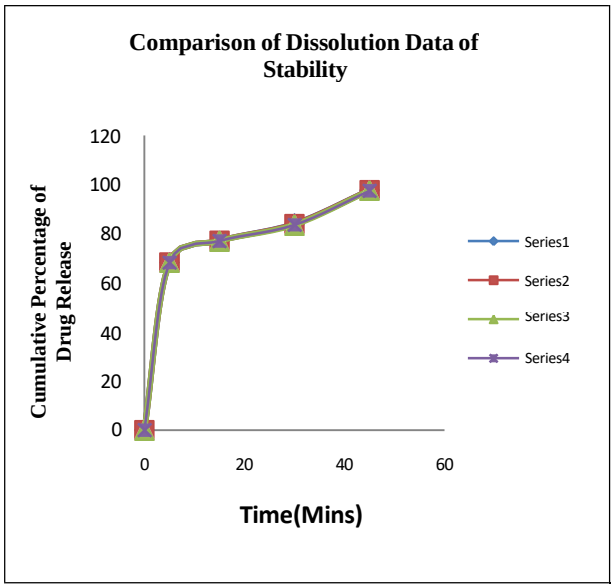

Figure.13: Comparison of Dissolution Data of Stability IN 6.8 pH Phosphate Buffer

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RELEASE KINETICS

Table: 9 Zero order and higuchi model release kinetic data of Omeprazole MUPs

Cumulative(%) release	Time (t)	Root (t)	log(%) release	log (t)	log (%) remain	Release rate (cumulative % release / t)	1/cum% release	Peppas log q/100	Hixson crowell model	Modified cube root equation
0.0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.5	15	3.87	-0.31	1.18	2.00	0.03	2.04	-2.31	0.79	0.62
0.6	30	5.48	-0.24	1.48	2.00	0.02	1.75	-2.24	0.83	0.69
0.6	45	6.71	-0.19	1.65	2.00	0.01	1.56	-2.19	0.86	0.74
0.7	60	7.75	-0.15	1.78	2.00	0.01	1.41	-2.15	0.89	0.80
0.9	75	8.66	-0.06	1.88	2.00	0.01	1.14	-2.06	0.96	0.92
1.1	90	9.49	0.03	1.95	2.00	0.01	0.94	-1.97	1.02	1.04
1.2	105	10.25	0.09	2.02	1.99	0.01	0.81	-1.91	1.07	1.15
1.4	120	10.95	0.15	2.08	1.99	0.01	0.70	-1.85	1.12	1.26
71.3	125	11.18	1.85	2.10	1.46	0.57	0.01	-0.15	4.15	17.19
79.1	140	11.83	1.90	2.15	1.32	0.57	0.01	-0.10	4.29	18.43
85.1	155	13.04	1.93	2.23	1.17	0.50	0.01	-0.07	4.40	19.35
97.87	170	14.66	1.99	2.33	0.33	0.46	0.01	-0.01	4.61	21.24

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RELEASE KINETICS

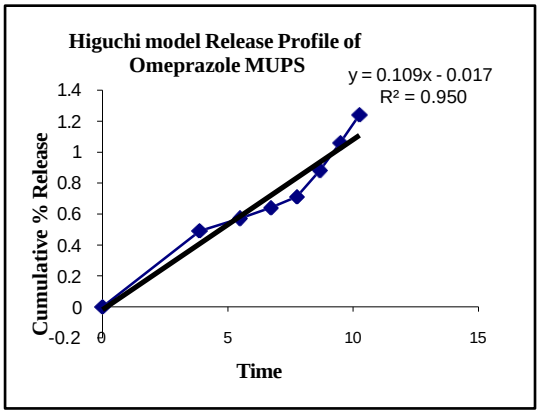

Figure 14: Zero Order Release Profile of Omeprazole MUPS

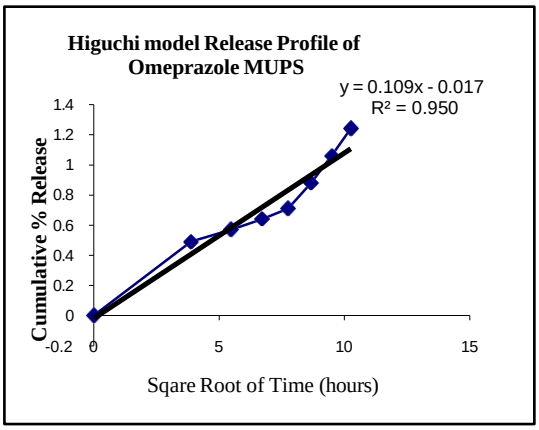

Figure 15: Higuchi Model Release Profile Of Omeprazole

16. SUMMARY AND CONCLUSION

The study was undertaken with an aim to design and evaluation of Omeprazole multi unites pellet system. The active pharmaceutical ingredient, Omeprazole was selected by using Eudragit L-30D, HPMC E5 as retarding agents and formulated as Enteric Coated Pellets comparable to the innovators product. In the present work, reformulation studies were conducted to know the drug recipients compatibility by using FTIR spectroscopy. Based on the

Results, suitable recipients were selected for formulation development. FTIR spectra revealed that there was no significant interaction between drug and polymer. Pellets were prepared by using Suspension layered method. Finished products were evaluated for friability test, assay, and *In-vitro* release studies performed for 2hrs in acidic media at 0.1N HCL, after those 45 mines in 6.8 pH Phosphate buffer. From the evaluation it was concluded that percent friability and percent assay for all formulations from F1 to F9 were found within the limit. *Inviter* Dissolution study showed that Formulation F9 having the better resistance in 0.1 N HCL and good release in phosphate buffer pH 6.8. From the above results and discussion it might be concluded that the formulation F9 of enteric coated pellets of Omeprazole was found to be stable in acidic medium and shows better drug release in basic medium. Therefore it was an ideal and optimized formulation of enteric coated pellets. Then the optimized formulation F9 was compared with marketed product by an *invitro* study, it shows that the formulation F9 was good as compared with marketed one. The stability study was carried out for formulation F9 at 1, 2, 3 month for *invitro* dissolution study and from this it was observed that there were no changes and clearly showing that the optimized formulation F9 was stable.

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Oral Suspension (ready to use, **Dry Suspension)** Particle size (<500 µm)	**Sanchet** Particle size <500 µm	**Mulparticulate Tablet** Particle size <500µm - <800 µm	**Capsule** Particle size <500 µm

Figure: 16 Flexibility of pellets in development of dosage form

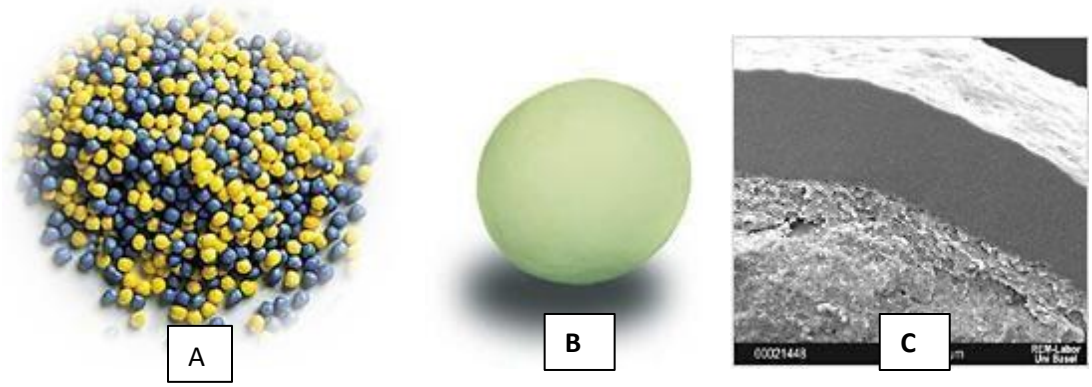

Figure: 17. (a) Pellets, (b) Perfect pellet, (c) Coated pellet

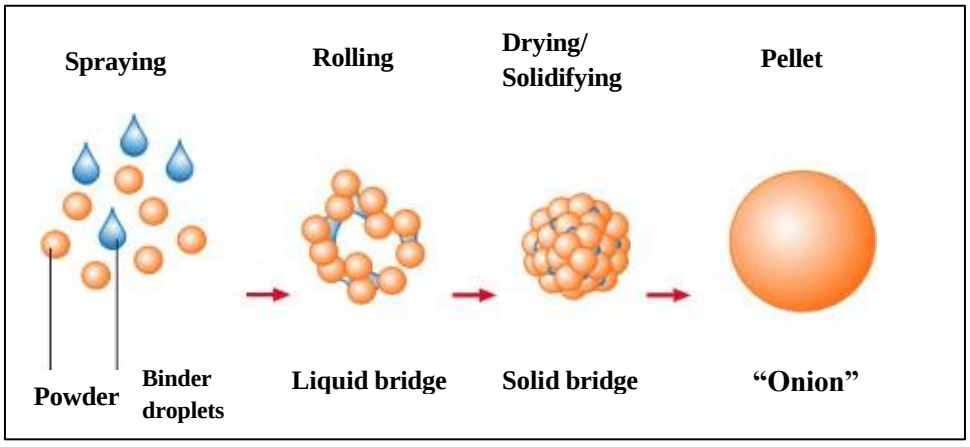

Figure 18: Process principles of direct pelletizing

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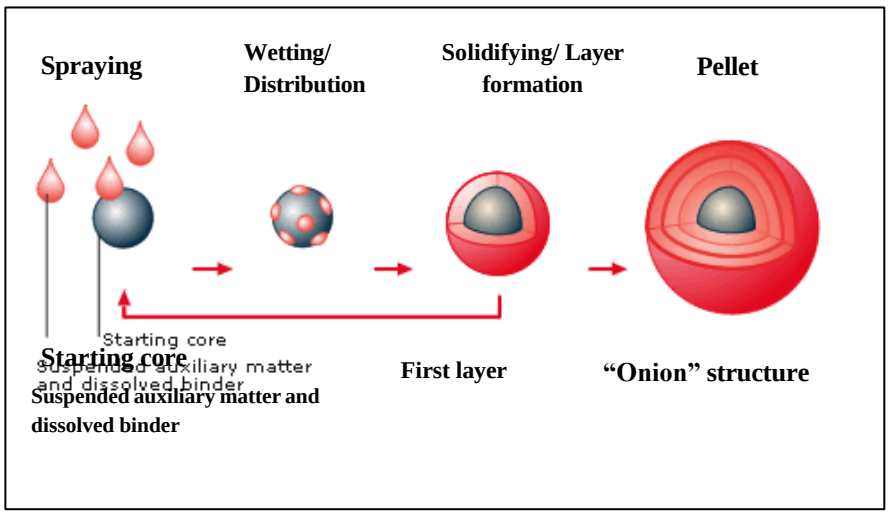

Figure.19: Principle of the suspension and solution layering process

Figure.20: fully assembled fluid bed coater