IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND ITS EVALUATION OF MOUTH DISSOLVING TABLET OF ANTI ALLERGIC DRUG CLEMASTINE

Vaibhav R. Garg, Dr. Manjeet Singh, Dr. Rajesh Z. Mujariya

Student, Executive Director, Principal

Department of Pharmaceutics,

Institute of Pharmaceutical Science and Research (IPSR), Balaghat

Abstract: Mouth dissolving tablet or dispersible tablets is a widely acceptable dosage forms which dissolves rapidly in the saliva without water. It enhanced efficacy and bioavailability thus reducing the dose and dosing frequency to minimize the side effects. The purpose of this research was to develop mouth dissolving tablets of Clemastine. Clemastine is also known as Meclastin, is a first-generation antihistaminic drug. It can be used in allergic symptoms including sneezing, runny nose and red, itchy, tearing eyes. In the present study attempt has been made to formulate Clemastine mouth dissolving tablet by directcompression method and optimize mouth dissolving Clemastine tablets containing superdisintegrants viz crosspovidone, Crosscarmellose and Indion 414 in the different ratios (1:1, 1:2 & 1:3) along with directly compressible mannitol (Pearlitol SD200) to enhance mouth feel and to compare the optimized formulation of each superdisintegrant. Compatibility study were done in FT-IR shows that there is no significant interactions occur between clemastine and excipients. The blend of excipients developed were evaluated (pre formulation) was examined for angle of repose, bulk density, tapped density, % compressibility and hausner's ratio. The angle of repose of the developed excipients blend was found to be < 27°, Carr's index in the range of 11-15% and Hausner's ratio in the range of 1.12-1.15. Mouth dissolving tablets of Clemastine fumarate were prepared using the above co-processed superdisintegrants and evaluated. The systematic formulation approach helped in understanding the effect of formulation processing variables. The prepared batches of tablets were evaluated for various parameters like various taste, thickness, hardness, friability, drug content uniformity, wetting time, In vitro disintegration time, and In-vitro dissolution time. All the parameters were found to be within limits. Based on in vitro disintegration time (approximately 30 s), promising formulation F8 was tested for in vitro drug release pattern in pH 6.8 Phosphate buffer and short-term stability (at 40^0C/75% RH for 3 months).The developed formulation of Clemastine batch F8 (9 % Indion 414) showed good palatability and dispersed within 30 seconds as compared to crosscarmellose sodium and crosspovidone. Based on the in vitro drug release characteristics from clemastine mouth dissolving tablet it was concluded that the Indion 414 has a great potential in the formulation of Mouth dissolving tablets of Clemastine.

KEYWORDS: Mouth Dissolving Tablets; Clemastine; Indion 414; Crosscarmellose sodium; Crosspovidone; Superdisintegrants.

1. INTRODUCTION

Drug Delivery Systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance[1].

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of administration, accurate dosage, self-medication, pain avoidance, versatility, leading to high levels of patient compliance. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is 'Dysphagia' or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of conditions like:

1. Parkinsonism
2. Motion sickness
3. Unconsciousness
4. Elderly patients
5. Children
6. Mentally disabled persons
7. Unavailability of water

Improved patient compliance has achieved enormous demand. Consequently demand for their technologies is also increasing many folds. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects. It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in Novel Drug Delivery Systems (NDDS) aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Pharmaceutical technologists have put in their best efforts to develop a Fast Dissolving Drug Delivery System, i.e Mouth Dissolving Tablet[1].

1.2 MOUTH DISSOLVING TABLET (MDT)

It is a tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 s to 3 min. Most of the MDTs include certain super disintegrants and taste masking agents.

1.3 IDEAL PROPERTIES OF MDT

A) A Mouth Dissolving Tablet should
[i] Not require water or other liquid to swallow.
[ii] Easily dissolve or disintegrate in saliva within a few seconds.
[iii] Have a pleasing taste.
[iv] Leave negligible or no residue in the mouth when administered.
B. Be portable and easy to transport.
C. Be able to be manufactured in a simple conventional manner within low cost.
D. Be less sensitive to environmental conditions like temperature, humidity etc.

1.4 ADVANTAGES OF MDT

A) No need of water to swallow the tablet.
B) Can be easily administered to pediatric, elderly and mentally disabled patients.
C) Accurate dosing as compared to liquids.
D) Dissolution and absorption of drug is fast, offering rapid onset of action.
E) Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach.
F) Advantageous over liquid medication in terms of administration as well as transportation.
G) First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
H) Free of risk of suffocation due to physical obstruction when swallowed thus offering improved safety.

I) Suitable for sustained/controlled release actives.

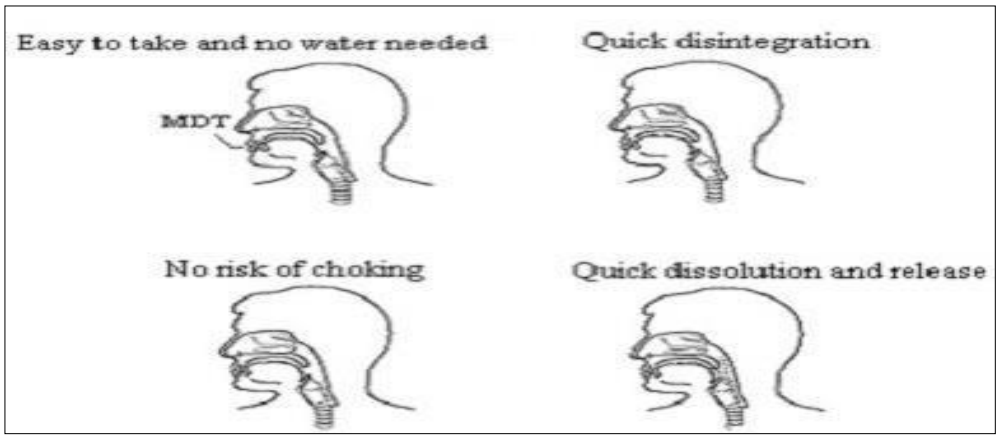

Fig. 1: Advantages of MDT

2. MATERIAL AND METHOD[3]:-

The drug Clemastine was a gift sample from Loba chemicals, Mumbai and the Crosscarmellose sodium, Crosspovidone, Indion 414, Mannitol (Pearlitol) SD 200, Microcrystalline cellulose, Magnesium Stearate, Talcum powder, Povidone, Aspartame, were purchased from Sudarshan chemicals Raipur C.G. Other solvents and materials used in this study were of analytical grade.

3. PREPARATION OF MOUTH DISSOLVING TABLETs BY DIRECT COMPRESSION METHOD[3]:-

The mouth dissolving tablet prepared by superdisintegrant addition method.The tablets were formulated employing direct compression method using 8 mm biconcave punches. It is the process by which tablets are compressed directly from mixtures of the drug andexcipients without preliminary treatment such as granulation. Drug (10 mg), super disintegrants in different ratios and excipients were blended using mortar and pestle. The drug and the disintegrants were sieved through mesh # 120 before blending. The mixture was evaluated for angle of repose, bulk density and compressibility. The mixture was mixed with 1% magnesium stearate as lubricant and mint as flavoring agent. The powder blends were then compressed by using Fluidpack multistation rotary tablet machine using 8 mm punch. The hardness was adjusted to 2-5 kg/cm2.

Table No. 1: Formulation of Mouth Disssolving Tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
CLEMASTINE[13]	10	10	10	10	10	10	10	10	10
Microcrystalline Cellulose[14]	39	39	39	39	39	39	39	39	39
Crosscarmellose Sodium[16]	9	13.5	18	-	-	-	-	-	-
Crosspovidone[17]	-	-	-	9	13.5	18	-	-	-
Indion 414[18]	-	-	-	-	-	-	9	13.5	18
Povidone[19]	1	1	1	1	1	1	1	1	1
Mannitol (Pearlitol SD200)[15]	89	84.5	80	89	84.5	80	89	84.5	80
Aspartame[20]	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Talcum powder[21]	1%	1%	1%	1%	1%	1%	1%	1%	1%
Magnesium Stearate[22]	1%	1%	1%	1%	1%	1%	1%	1%	1%

4. PROCEDURE FOR EVALUATION OF TABLET[23]:-

The tablets were compressed using 8 mm diameter, round, biconcave punches on a Fluidpack multistation rotary tablet machine. The tablet weight was kept 150 mg and hardness between 2 –5 kg/cm2. Other parameters like size, thickness, shape, hardness, friability, weight variation, wetting time were carried out.

4.1. Taste and Colour

The tablets of prepared formulations were observed for taste and colour.

Method:-

Taste was observed by taste panels. Colour comparisons require that a sample be compared against some colour standard.

4.2. Thickness and Shape

Shape and thickness was measured using sliding Caliper scale.

Method:-

Five or Ten tablets from each formulation were selected and their crown thickness was measured with a sliding Caliper scale. Shapes of the tablets were observed.

4.3. Hardness

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacturing, packing and shipping.

Method:-

The Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet and zero reading is taken. The upper plunger is then forced against a spring by turning threaded bolt until the tablets break. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of break is recorded and zero force reading is deducted from it.

4.4 Friability

Tablets were tested for friability using Roche Friabilator. This is important to know the mechanical strength of the tablet while handling.

Method:-

Twenty tablets were weighed initially and transferred to the Friabilator. The instrument was set to 25 rpm for 100 rotations. The resulting tablets were reweighed and percentage loss was calculated using the formula.

Friability= (Initial weight – Final Weight) / Initial Weight ×100

Conventional compressed tablet that lose less than 0.5 to 1.0% was acceptable.

4.5. Weight Variation

Weight variation was measured to ensure that tablet contain proper amount of drug.

Method:-

Weighed 20 tablets individually, calculated the average weight and compared the individual tablet weights to the average. The tablets meet the test if not more than two tablets are outside the percentage limit and none of the tablet differs by more than two times the percentage limit. The weight variation tolerance for uncoated tablets differs depending on average weight of the tablets.

4.6. Wetting time

This is carried out to measure the time, which is required for the complete wetting of tablet formulations.

Method:-

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

4.7. IN-VITRO DISINTEGRATION TEST[5]

Wire Basket Type Disintegration Apparatus:-

The disintegration taster consists of 6 glass tubes that was 3 inch long and 10-mesh screen at the bottom, one tablet was placed in each tube and basket was placed in 1 litre beaker of simulated gastric fluid at 370C ± 20C. The basket assembly containing the tablet up and down through distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.

4.8. IN-VITRO DISSOLUTION STUDY[5]:

The development of dissolution methods for mouth dissolving tablet is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent mouth dissolving tablet. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for mouth dissolving tablet much in the same way as their ordinary tablet counter parts.

The USP 2 Paddle apparatus is used for this purpose which is the most suitable and common choice for orally-disintegrating tablets, with a paddle speed of 50 rpm commonly used. Typically the dissolution of mouth dissolving tablet is very fast when using USP monograph conditions; hence slower paddle speeds may be utilized to obtain a profile. The USP 1 Basket apparatus may have certain applications but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

5. RESULT

5.1. CHARACTERIZATION OF PURE DRUG (CLEMASTINE):-

Table No. 2: Characterization of Pure Drug (Clemastine).

Sr. No	Characterization	Specification	Result
1.	Description	Almost white, crystalline powders, odorless	Almost white powder
2.	Solubility	Soluble in DMSO (25 mg/ml), ethanol (25mg/ml), chloroform, methanol and water (partly miscible)	Complies
3.	Identification by FT-IR	To match with working standard	Matches with the working standard
4.	Melting range	172.9^0C	Complies
5.	Sulphated ash	Not more than 0.1%	Complies

6.	Loss on drying	Not more than 0.5%	Complies
7.	Heavy Metals	20 ppm max	Complies
8.	Assay	98.0-100.5%	Complies

5.2. IDENTIFICATION OF PURE DRUG (CLEMASTINE):-

Pure drug has been identified by using technique like IR and Solubility Test.

INFRA-RED SPECTROPHOTOMETRY Apparatus

An infra-red spectrophotometer for recording the spectra in the infra-red region consists of an optical system capable of providing the monochromatic light in the region of 4000 to 625 cm-1 (about 2.5 to 16 mm) and the means of measuring the quotient of the intensity of the transmitted light and the incident light.

Preparation of sample:-

A sample of the Clemastine is being examined may be prepared by the following ways.

Discs – Triturate about 1 mg of the Clemastine with approximately 300 mg of dry, finely powdered potassium bromide IR. These quantities are usually suitable for a disc 13 mm in diameter. Grind the mixture thoroughly, spread it uniformly in a suitable die and compress under vacuum at a pressure of about 800 Mpa. Mount the resultant disc in a suitable holder in the spectrophotometer. Several factors, such as inadequate or excessive grinding, moisture or other impurities in the halide carrier, may give rise to unsatisfactory discs.

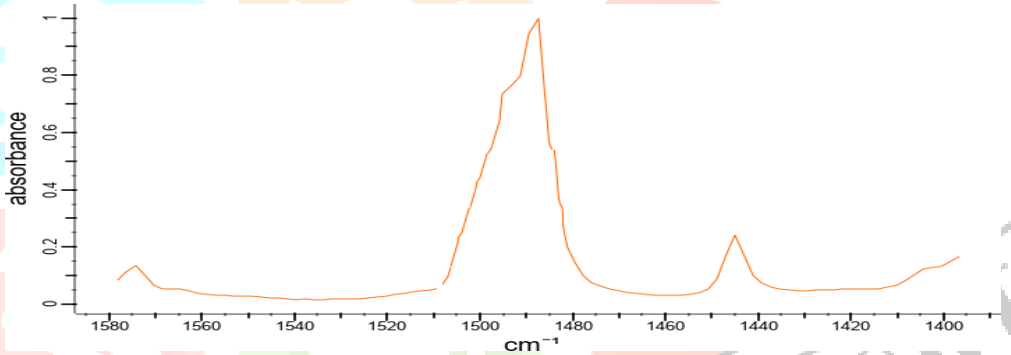

Fig No. 2: IR Spectra of Clemastine Powder

5.3 SOLUBILITY TEST:-

Solubility Test is performed as per mention in the I.P. and following results were obtained –

Table No. 3: Solubility Test of Pure Drug (Clemastine).

Sr. No.	Solvents	Solubility
1.	Ethanol	Freely Soluble
2.	Chloroform	Freely Soluble
3.	Methanol	Freely Soluble
4.	DMSO	Freely Soluble
5.	Water	Partly soluble

6. PREFORMULATION STUDY[4]

Pre-formulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rational development of dosage forms.

Table No. 4: Preformulation study of pure drug Clemastine.

Sr. No.	Characterization	Specification	Result
1.	Description	Almost white, crystalline powders, odorless	Almost white powder
2.	Solubility	Freely soluble in ethanol (95%), in chloroform and in DMSO; partly soluble in water	Complies
3.	Melting range	172.9 °C	Complies
4.	Identification by FT-IR	To match with working standard	Matches with the working standard
5.	Loss on drying	Not more than 0.5%	Complies
6.	Assay	98.0-100.5%	Complies

7. COMPATIBILITY STUDY

7.1. Objective

To analyze the compatibility between Clemastine and excipients proposed to incorporate into the formulation.

Procedure:-

Clemastine is mixed with excipients in different ratio. These mixtures were kept in a 6ml glass white colour vials and packed properly. These vials are exposed to

[i] Room temperature

[ii] 30°c / 65% relative humidity and

[iii] 40°c / 75%RH.

16 gm of blend is prepared which is filled in 3 vials.

7.2.1. Objective:-

To analyze the compatibility between Clemastine and excipients proposed to incorporate into the formulation.

Table No. 5: Compatibility study sheet of pure drug Clemastine at Room Temperature

Sr. No.	Drug + Excipients	Proportion	Initial Observation of color	Final observation		conclusion
				2nd week	4th week	
1.	Drug	NA	White	White	White	Compatible
2.	Drug + MCC (PH-102)	1:10	White	White	White	Compatible
3.	Drug + Cross carmellose sodium	1:10	White	White	White	Compatible
4.	Drug + Cross povidone	1:10	Creamy - White	Creamy - White	Creamy - White	Compatible
5.	Drug + Indion 414	1:10	White	White	White	Compatible
6.	Drug + Povidone	1:10	White	White	White	Compatible
7.	Drug + Pearlitol SD200	1:10	White	White	White	Compatible

7.2.2. Objective:-

To analyze the compatibility between Clemastine and excipients proposed to incorporate into the formulation.

Table No. 6: Compatibility study sheet of pure drug Clemastine at 30˚ C / 65 % RH

Sr. No.	Drug + Excipients	Proportion	Initial Observation of color	Final observation		Conclusion
				2nd week	4th week	
1.	Drug	NA	White	White	White	Compatible
2.	Drug + MCC (PH-102)	1:10	White	White	White	Compatible
3.	Drug + Cross carmellose sodium	1:10	White	White	White	Compatible
4.	Drug + Cross povidone	1:10	Creamy–White	Creamy - White	Creamy - White	Compatible
5.	Drug + Indion 414	1:10	White	White	White	Compatible
6.	Drug + Povidone	1:10	White	White	White	Compatible
7.	Drug + Pearlitol SD200	1:10	White	White	White	Compatible

7.2.3. Objective:-

To analyze the compatibility between Clemastine and excipients proposed to incorporate into the formulation.

Table No. 7: Compatibility study sheet of pure drug Clemastine at 40˚C ±2˚C / 75% ± 6% RH

Sr. No.	Drug + Excipients	Proportion	Initial Observation of color	Final observation		Conclusion
				2nd week	4th week	
1.	Drug	NA	White	White	White	Compatible
2.	Drug + MCC (PH-102)	1:10	White	White	White	Compatible
3.	Drug+ Cross carmellose sodium	1:10	White	White	White	Compatible
4.	Drug+ Cross povidone	1:10	Creamy - White	Creamy - White	Creamy - White	Compatible
5.	Drug + Indion 414	1:10	White	White	White	Compatible
6.	Drug + Povidone	1:10	White	White	White	Compatible
7.	Drug + Pearlitol SD200	1:10	White	White	White	Compatible

8. Evaluation

8.1. Evaluation of Powder parameters (Pre-Formulation):-

Table No. 8: Pre-formulation Studies of Various batches

Batch	Angle of Repose (θ)/ ± SD	Bulk Density (g/cc)/ ±SD	Tapped Density (g/cc)/ ±SD	(%) Compressibility /±SD	Hausner's Ratio/ ±SD
F1	33.31^0 ± 0.003	0.45 ± 0.007	0.54± 0.003	14.25± 1.601	1.15 ± 0.802
F2	32.45^0 ± 0.201	0.43 ± 0.017	0.50± 0.017	12.64± 1.032	1.13 ± 0.010
F3	33.52^0 ± 0.045	0.54 ± 0.024	0.66± 0.038	15.14± 1.926	1.15 ± 0.802
F4	31.12^0 ± 0.675	0.46 ± 0.003	0.54 ± 0.003	12.42± 0.954	1.13 ± 0.010
F5	38.43^0 ± 1.852	0.44 ± 0.014	0.48 ± 0.024	5.22± 1.590	1.05 ± 0.017
F6	33.63^0 ± 0.219	0.45 ± 0.007	0.50 ± 0.017	5.27± 1.573	1.05 ± 0.017
F7	32.07^0 ± 0.378	0.46 ± 0.003	0.56 ± 0.003	6.38± 1.180	1.13 ± 0.010
F8	31.05^0 ± 0.738	0.52 ± 0.007	0.54 ± 0.003	4.44± 1.866	1.03 ± 0.024
F9	32.72^0 ± 0.106	0.54 ± 0.014	0.60 ± 0.017	11.68 ± 0.692	1.12 ± 0.007

8.2. Evaluation of Mouth Dissolving Tablet (Post-Formulation):-

Table No. 9: Physical Evaluation of Formulated Tablet batches

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)/± SD	2.63 ±0.00	2.66 ±0.01	2.65 ±0.01	2.64 ±0.01	2.66 ±0.01	2.63 ±0.00	2.53 ±0.02	2.54 ±0.02	2.56 ±0.01
Hardness (kg/cm^2)/±SD	3.8 ±0.17	3.4 ±0.19	2.7 ±0.07	3.6 ±0.10	3.3 ±0.00	3.6 ±0.10	3.4 ±0.19	3.1 ±0.07	2.7 ±0.21
Friability (%w/w)/± SD	0.23 ±0.11	0.75 ±0.06	1.18 ±0.21	0.55 ±0.00	0.43 ±0.04	1.09 ±0.18	0.14 ±0.14	0.34 ±0.07	0.35 ±0.07
Wetting time (sec)/ ± SD	20 ±0.51	16 ±1.21	15.9 ±0.50	17 ±0.86	18 ±0.19	20 ±0.55	18 ±0.50	14 ±1.92	29 ±3.73
Disintegration time (sec)/± SD	27 ±0.86	23 ±0.54	24 ±0.19	29 ±1.57	26 ±0.51	27 ±0.86	25 ±0.15	18 ±1.96	21 ±1.25
Drug content (%w/v)/± SD	87.55 ±0.20	87.82 ±0.10	88.18 ±0.01	87.49 ±0.22	87.82 ±0.10	78.42 ±3.43	87.98 ±0.05	95.13 ±0.93	92.78 ±1.64
Dissolution (%w/v)/± SD	67.91±5.83	81.34 ±1.02	69.2 ±5.38	89.45 ±1.84	85.55 ±0.46	87.95 ±1.31	89.99 ±2.03	95.49 ±3.98	91.68 ±2.63

Table No. 10: Standard Calibration Curve

Conc. (mcg/ml)	Absorbance	± S.D.
0	0.0000	0.00
15	0.223	± 0.036
30	0.287	± 0.012
45	0.343	± 0.01
60	0.401	± 0.034
75	0.438	± 0.049
90	0.524	± 0.084

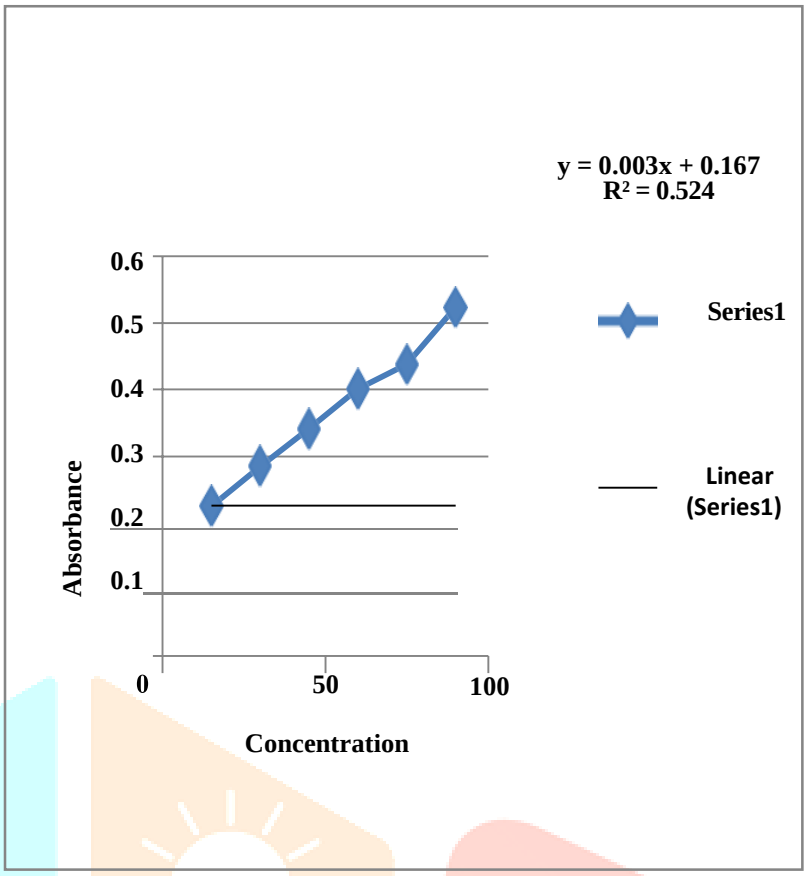

Fig. No. 10: Standard Calibration Curve of Clemastine

Table No. 11: Comparative Study of % Drug Release from Mouth Dissolving Tablet of Batch F1, F2 and F3

Time in Min	% drug release		
	F1	F2	F3
30 sec	9.45	14.74	11.09
60 sec	20.42	29.77	21.88
90 sec	31.72	48.41	33.41
2	43.19	61.50	44.99
3	53.34	77.81	56.81
4	67.72	81.33	69.1

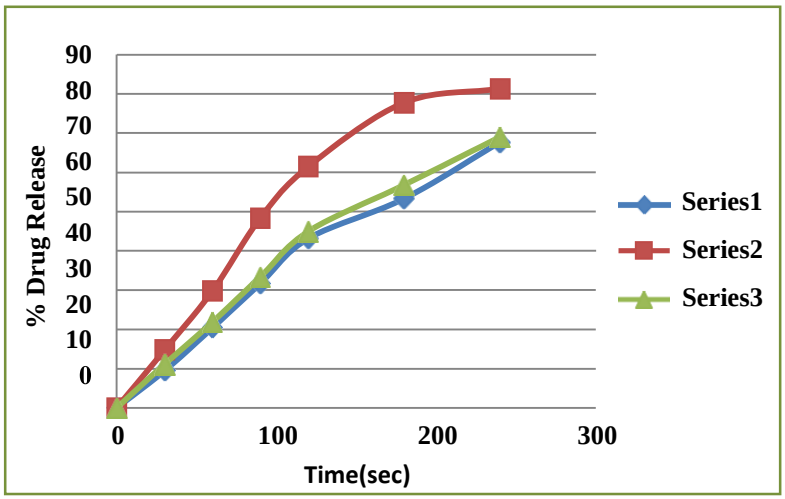

Fig. No. 4: Comparative study of % Drug release (Batch F1, F2 and F3)

Table No. 12: Comparative study of % Drug release from Mouth Dissolving Tablet of Batch F4, F5 and F6

Time in Min	% drug release		
	F4	F5	F6
30 sec	13.73	14.97	13.6
60 sec	27.76	29.96	27.48
90 sec	41.56	45.8	41.74
2	57.27	61.72	36.97
3	73.13	78.2	72.7
4	89.44	85.4	87.94

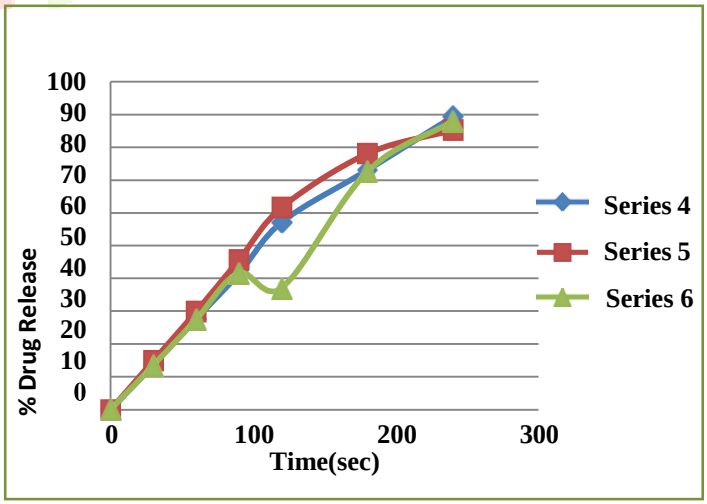

Fig No. 5: Comparative Study of % Drug Release (Batch F4, F5 and F6)

Table No. 13: Comparative study of % Drug release from Mouth dissolving tablet of Batch F7, F8 and F9

Time in Min	% drug release		
	F7	F8	F9
30 sec	14.58	14.73	14.17
60 sec	29.55	29.33	28.68
90 sec	45.0	45.08	43.13
2	61.61	61.28	59.17
3	77.36	78.16	75.15
4	89.98	95.48	91.68

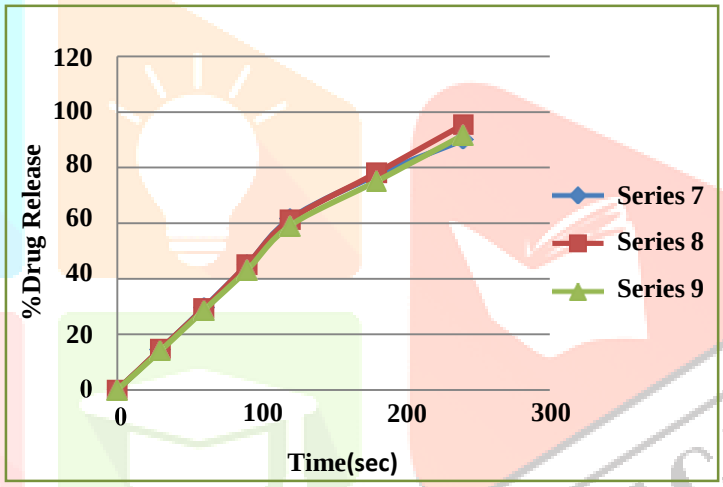

Fig No. 6: Comparative Study of % Drug release (Batch F7, F8 and F9)

9. Mechanism of Release from Matrix Tablets:-

From the data obtained after applying all suitable mathematical models we can conclude that the optimized formulations selected are proposed to explain the mechanism of release of drug from formulation

Table No. 14: Drug Release Kinetic Study of Optimized Batch

MODELS		F8 (Clemastine)
Korsemeyerpeppas	n	0.988
Zero order	R	0.977
First order	R	0.847
Higuchi model	R	0.997
Best fit model		Higuchi

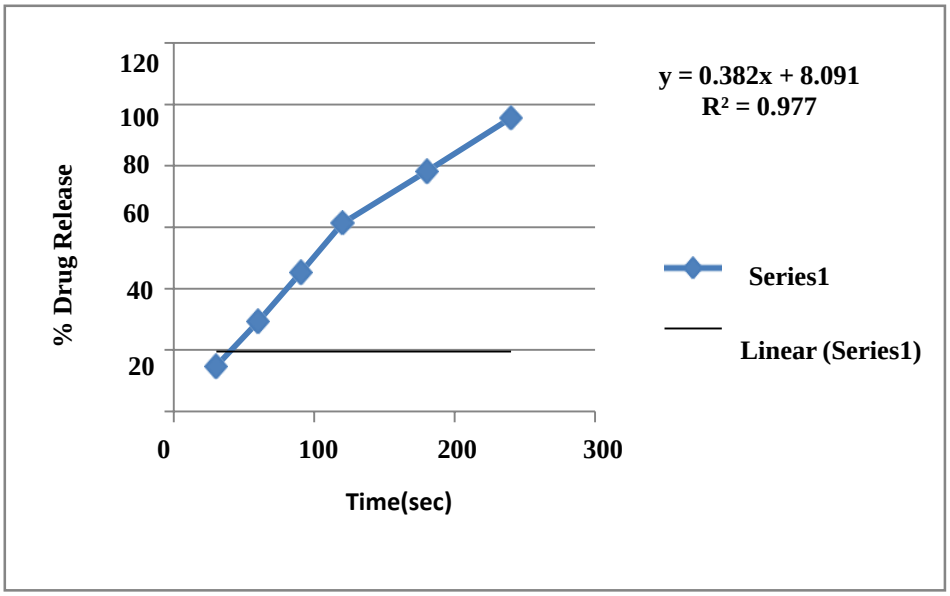

Fig No. 7: Curve Fitting Data of the Release Rate Profile of Zero Order.

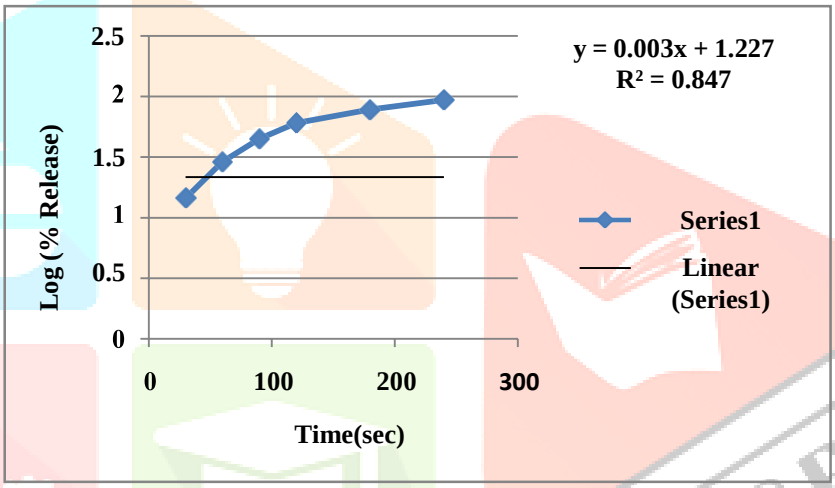

Fig No.8: Curve Fitting Data of the Release Rate Profile of First Order.

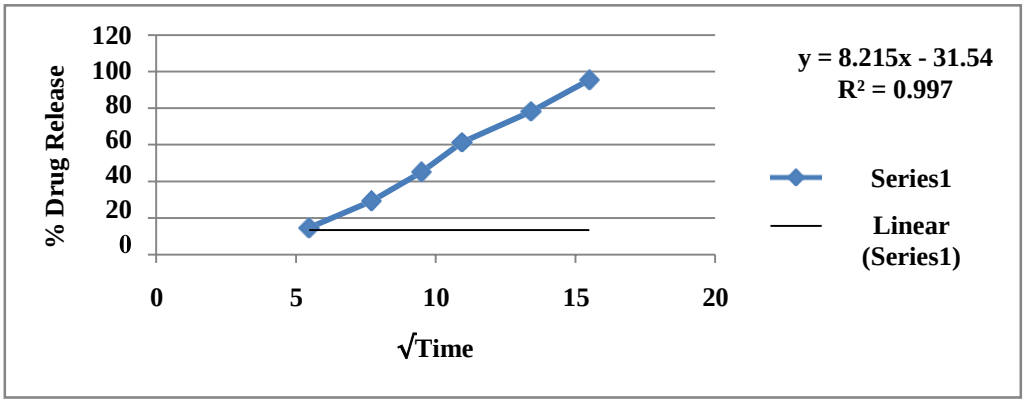

Fig No. 9: Curve fitting data of the release rate profile of Higuchi Model

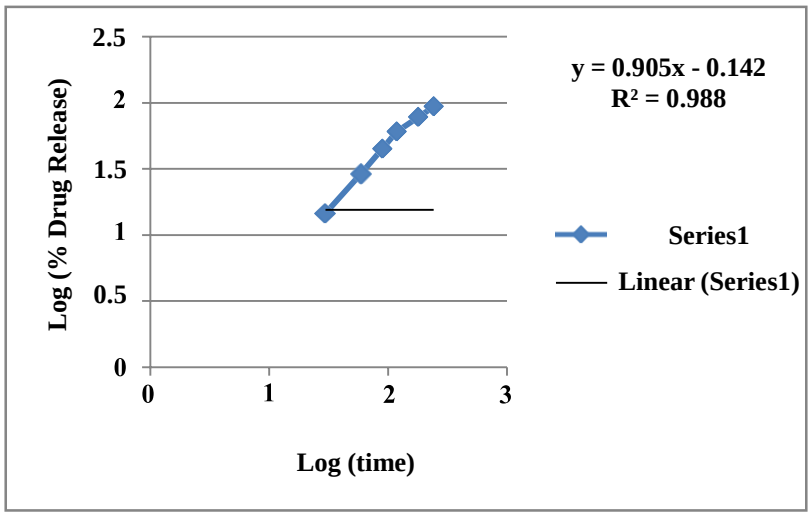

Fig No.10: Curve Fitting Data of the Release Rate Profile of Korsemeyer- peppas

10. DISCUSSION

- The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. These superdisintegrats accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking tablets and therefore disintegration. The disintegration is reported to have an effect on dissolution characteristics as well.
- Clemastine drug is available from Loba Chemical and Characterization of Drug and various parameters comply with reference standard.
- In the identification of Clemastine, FT-IR studies was the prominent peaks of Clemastine (Fig No.2) was observed.
- In Standard calibration curve of Clemastine, it was found to be soluble in Ethanol. Standard solution about 10 mg of reference Clemastine was accurately weighed and dissolved in 100 ml of ethanol. Aliquot portions 2-12 ml of standard Clemastine solution was transferred to 100 ml volumetric flask and 5 ml of ethanol was added to each. The solutions were mixed; each was completed to 100 ml with ethanol and finally kept aside for 25 minutes. The absorbances were measured at 360nm against appropriate blanks prepared similarly.
- Mouth dissolving clemastine tablets were prepared using different superdisintegrants. Nine batches of tablets were prepared by varying the concentrations of superdisintegrants. Tablets were prepared by direct compression method. Tablets were obtained of uniform weight due to uniform die fill with acceptable weight variation as per pharmacopoeial specifications. Tablet was formulated by using different super disintegrants such as Crosscarmellose, Crosspovidone and Indion 414 in the ratio of 6%, 9% and 12% as represented by F1 to F9 respectively.
- Various physical evaluations of tablets were taken to formulate the Mouth dissolving tablet so as to disintegrate with in the mouth of the patient. These formulations were evaluated for the pre compression and post compression parameters (Table No. 8,9).
- Tapped density of the formulations was in between 0.48-0.66 gm/ml, where as the bulk density was in the range of 0.43-0.54 gm/ml. The compressibility values varied from 4.44%-15.14%. The angle of repose values of the formulations varied from 31.05˚ to 38.36˚. From these values, it was evident that these blends had good flow properties (Table No.8).
- Physical parameters confirmed to the requirements such as taste, and color. Weight variation was found within the specification of I.P 2007. Average weight of all the 9 formulation was found in the range of 142-150 mg.
- Thickness of the all the formulations was found to be in the range of 2.53- 2.66 mm.
- Hardness of the F3, F6 and F9 formulation was found to be 2.7 Kg/cm2, 3.6 Kg/cm2 and 2.7 Kg/cm2 respectively and was comparatively less than other formulation such as F2, F5, F8 having 3.4 Kg/cm2, 3.3 Kg/cm2 and 3.1 Kg/cm2 respectively where as F1, F4 and F7 formulation had hardness of 3.8 Kg/cm2, 3.6 Kg/cm2 and 3.4 Kg/cm2 respectively (Table No.9).

- Friability of the F2, F5 and F8 was found to be 0.75, 0.43 and 0.34 % respectively where as F1, F4 and F7 had friability of 0.23, 0.55 and 0.14 % respectively and F3, F6 and F9 had 1.18, 1.09 and 0.35 % respectively (Table No.9).
- Wetting time of the formulation F1, F4 and F7 was found to be 20 sec, 17 sec, 18 sec respectively where as F2, F5 and F8 was 16 sec, 18 sec and 14 sec respectively and F3, F6 and F9 had 15.9 sec, 20 sec and 29 sec respectively (Table No.9).
- Drug content of the F1, F4 and F7 was found to be 87.55 %, 87.49 % and 87.98 % w/v respectively where as F2, F5 and F8 was , 87.82 %, 87.82 % and 95.13 % w/v respectively and F3, F6 and F9 had 88.18 %, 78.42 % and 92.78 % w/v respectively (Table No.9).
- Disintegration time of different bacthes of formulation are found to be less than 30 seconds. Among the 9 formulations F2, F5 and F8 showed 23 sec, 26 sec and 18 sec respectively by basket method. Thus the formulation F2, F5 and F8 containing 9 % super disintegrant such as crosscarmellose sodium, crosspovidone and Indion 414 showed the faster disintegration compared to 6 % and 12% superdisintegrants (Table No.9).
- In vitro dissolution study of Different Formulation with 9 % crosscarmellose sodium, crosspovidone and Indion 414 showed maximum dissolution rates with 81.34 %, 85.5 % and 95.49 % respectively of the drug released in 4 minutes. Formulation with 9 % Indion 414 released 95.49 % of the drug in 4 minutes as compared to formulation containing 9 % crosscarmellose sodium and crosspovidone. Formulation with 9 % Indion 414 was superior compared to other superdisintegrants (Table No.9).
- In the drug release kinetic studies of optimized formulation with 9% Indion 414 were treated by zero order, first order, Higuchi model and korsemeyer peppas equation(Table No.14).
- The release exponent R value of standardized formulation for Clemastine of F8 were found to be 0.988, 0.977, 0.847 and 0.997 respectively. (Fig no. 7,8,9,10)
- The best fitted model for the optimized formulation of F8 batch was found to be higuchi model. Higuchi model show the maximum release of drug having R value 0.996. (Table No.14).

11. CONCLUSION

- In present study Clemastine Mouth disolving tablet prepared using different types and concentration of superdisintegrants by direct compression method which was confirmed by various characterization and evaluation studies.
- Indion 414 as superdisintegrant gives better result as compared to crosscarmellose sodium and crosspovidone.
- Tablets disintegrate within 30 sec in mouth having better mouth feel.

12. SUMMARY

- Mouth dissolving tablets are those that dissolve or disintegrate quickly in the oral cavity, resulting in solution or suspension. In the present study Mouth dissolving tablet of Clemastine was prepared by direct compression method using crosspovidone, Crosscarmellose andIndion 414 as superdisintegrants.
- FT-IR study shows that there is no significant interactions occur between drug and excipients.
- The tablets prepared were evaluated for various parameters like various density parameters, thickness, hardness, friability, disintegration time, wetting time and In-vitro dissolution time. All the parameters were found to be within limits.
- The developed formulation of Clemastine batch F8 (9 % Indion 414) showed good palatability and dispersed within 30 seconds as compared to crosscarmellose sodium and crosspovidone.

13. REFERENCES

1. Tejvir Kaur, Bhawandeep Gill, Sandeep Kumar, G.D. Gupta, "Mouth Dissolving Tablets: A Novel Approach To Drug Delivery", *International Journal of Current Pharmaceutical Research*, Vol 3, Issue 1, 2011, 1-7.
2. Abdul Sayeed, Mohd.Hamed Mohiuddin, "Mouth dissolving tablets: An Overview", *International Journal of Research in Pharmaceutical and Biomedical Sciences*, Vol. 2 (3) Jul – Sep 2011, 959-970.
3. Kamal Saroha, Pooja Mathur*, Surender Verma, Navneet Syan and Ajay Kumar, "Mouth dissolving tablets: An overview on future compaction in oral formulation technologies", *Pelagia Research Library, Der Pharmacia Sinica*, 2010, 1 (1): 179-187.
4. Ajoy bera and ashish mukherjee, "a detailed study of mouth dissolving drug delivery system", *acta chim. Pharm. Indica: 3(1), 2013, 65-93.*
5. Dali shukla, subhashis chakraborty, sanjay singh, brahmeshwar mishra, "mouth dissolving tablets ii: an overview of evaluation techniques", *scientia pharmaceutica*. 2009; 77; 327–341.
6. Velmurugan S and Sundar Vinushitha, "Oral Disintegrating Tablets: An Overview", *International Journal of Chemical and Pharmaceutical Sciences*, 2010, Dec., Vol.1 (2), 1-12.
7. Himanshu Deshmkh, Chandrashekhara S.*, Nagesh C., Amol Murade, Shridhar Usgaunkar, "Superdisintegrants: A Recent Investigation and Current Approach", *Asian J. Pharm. Tech*. 2012;Vol. 2: Issue 1, Pg 19-25.
8. N. Damodharan*, M. Mothilal, G. Vasundhara, "Formulation and Optimization of Fast Dissolving", *International Journal of PharmTech Research Cinnarizine Tablets*, April-June 2010, Vol.2, No.2, pp 1095-1100.
9. SHIRSAND SB, SARASIJA SURESH, P. V. SWAMY, "Formulation Design of Novel Fast Disintegrating Tablets of Prochlorperazine Maleate", *International Journal of PharmTech Research*, Jan-Mar 2010, Vol.2, No.1, pp 125-129.
10. Patel NJ, Dr. C.S.R. Lakshmi, Hitesh P. Patel, Sagar Akul, "FORMULATION AND EVALUATION OF ORAL DISPERSIBLE TABLETS OF CINNARIZINE USING SUBLIMATION TECHNIQUE", International Journal of Pharmaceutical Sciences Review and Research, Volume 6, Issue 2, January – February 2011; PP 178- 182.
11. Nagendrakumar D*, Raju S.A .S.B.Shirsand and M.S.Para, "DESIGN OF FAST DISSOLVING GRANISETRON HCL TABLETSUSING NOVEL CO –PROCESSED SUPRDISINTEGRANTS", *International Journal of Pharmaceutical Sciences Review and Research*, Volume 1, Issue 1, March – April 2010; PP 58-62.
12. Mahore JG*, Wadher KJ, Umekar MJ, "Formulation and in vitro Evaluation of Taste Masked Orodispersible Tablet of Metoclopramide Hydrochloride", *International Journal of PharmTech Research*, July-Sept 2010, Vol.2, No.3, pp 1827-1835.
13. https://en.wikipedia.org/wiki/Clemastine.
14. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 348.
15. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 1177.
16. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 2215.
17. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 558.
18. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 2215.

19. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 1617.

20. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 135.

21. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 2033.

22. Raymond C., (1986), *Handbook of pharmaceutical excipients*, A joint publication of the American pharmaceutical Association and Royal pharmaceutical society of Great Britian, 4th Ed., pharmaceutical press USA, 1986, PP. 1122.

23. Lachmann L., Liebermann HA., Kiang JL., (1987), The theory and practice of Industrial Pharmacy, 3rd Ed., Varghese Publishing House, Bombay, pp-296-301.