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DESIGN AND IN-VITRO CHARACTERIZATION OF LORATIDINE POROUS TABLETS

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ABSTRACT

The rationale of this investigation was to develop monolithic tablets of loratadine using sublimation technique. Porous tablets of loratadine were prepared by the direct compression technique using sublimating agents like camphor, menthol and cross povidone, CCS as super disintegrants. This dissertation work was done with an aim to design an immediate release oral dosage of Loratadine and evaluation of the tablets for various parameters including in vitro drug release studies. Loratadine tablets were formulated by using microcrystalline cellulose and lactose monohydrate as fillers, camphor and menthol as subliming agents, cross povidone and CCS as super disintegrant and magnesium stearate as lubricant. The formulation F6 is formulated by using subliming agents and super disintegrants where it can ensure burst release of the drug.

Keywords: Loratadine, CCS, drug release, microcrystalline cellulose, lactose monohydrate

1. INTRODUCTION

DRUG DELIVERY SYSTEM

Dosage forms are also referred to as “Drug Delivery Systems” or “Finished Drug Products”. A drug delivery system (DDS) is defined as a formulation or a device that enables the introduction of a therapeutic substance into the body and improves its efficacy and safety by controlling the rate, time, and site of release of drugs in the body. The goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration. That is, the drug delivery system should deliver drug at a rate dedicated by the needs of the body over a specified period of treatment. Oral route of drug administration is most appealing route for delivery of drugs for various dosage forms. The tablet is one of the most preferred dosage forms, because of its ease of administration, accurate dosing and stability as compared to oral liquid dosage forms.

2. REVIEW OF LITERATURE

Bokshi *et al*., Formulated, developed, optimized and in-vitro evaluated of immediate release allylestrenol tablets. To minimize critical process parameters and since allylestrenol is heat sensitive, direct compression method was selected for the formulation of immediate release allylestrenol tablets. Tablets were prepared using cross carmellose sodium, cross povidone, pre gelatinized starch and sodium starch glycolate as disintegrants

Yeole et al., Prepared Paroxetine immediate release tablet by direct compression method. Effect of various fillers and disintegrants were also explored. Microcrystalline cellulose, Galen IQ and dicalcium phosphate were used as directly compressible fillers. In order to obtain acceptable product several trials were conducted.

Hu *et al.*, Prepared the immediate release tablet by using dry granules. The preparation was optimized by using orthogonal design which took the flow property of granules, the hardness, the disintegrating time and the dissolution rate of the tablet as indices. The optimized formulation contained 40% microcrystalline cellulose, 10% sodium carboxymethyl starch and 15% dextrin.

3. AIM AND OBJECTIVE

The rationale of this investigation was to develop monolithic

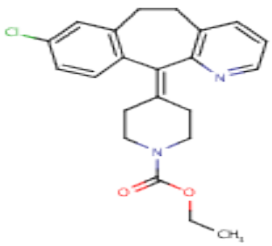
tablets of loratadine using sublimation technique. Porous tablets of loratadine were prepared by the direct compression technique using sublimating agents like camphor, menthol and cross povidone, CCS as super disintegrants. Sublimating agents are sublimed from the tablets by drying in hot air oven at 60°C for 1hr or overnight air drying. The formulations were evaluated for weight variation, hardness, drug content and *in vitro* dissolution.
Subliming agents increases the porosity of the tablets and ensures burst release of the drug.

4. DRUG PROFILE

LORATADINE

Loratadine is a derivative of azatadine and a second-generation histamine H1 receptor antagonist used in the treatment of allergic rhinitis and urticaria. Unlike most classical antihistamines (histamine H1 antagonists) it lacks central nervous system depressing effects such as drowsiness. [PubChem]

Structure:



5. MATERIALS AND METHODS

5.1 Materials

List of materials and manufacturer/suppliers

RAW MATERIALS	MANUFACTURER / SUPPLIERS
Loratidine	Provided by Chandra labs-Hyderabad
Cross caramellose sodium	Sisco research laboratories Pvt.Ltd Mumbai
Cross povidone	Sisco research laboratories Pvt.Ltd Mumbai
Lactose mono hydrate	ESSEL Fine Chem,Mumbai
Menthol	Sisco research laboratories Pvt.Ltd Mumbai
Camphor	Sisco research laboratories Pvt.Ltd Mumbai
Magnesium stearate	ESSEL Fine Chem,Mumbai
Avicel pH 102 (Microcrystalline cellulose)	ESSEL Fine Chem,Mumbai

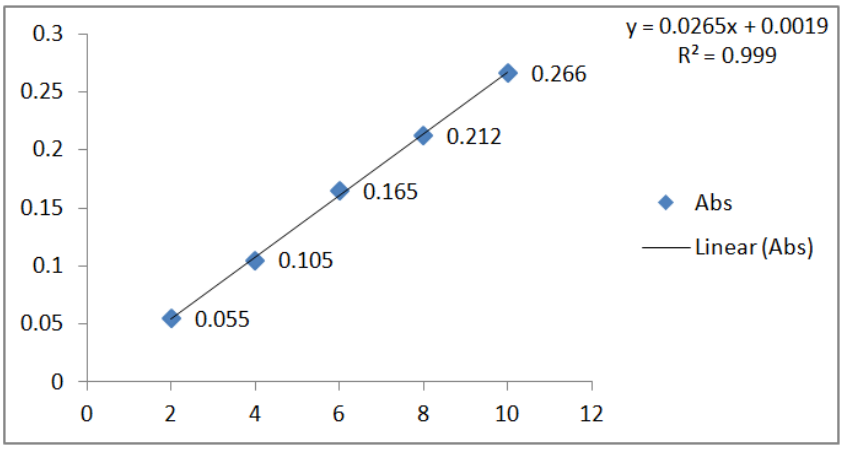
List of the equipments

EQUIPEMENTS	MODEL	MANUFACTURERS
Digital balance	AND GP-12K	Electrolab
Bulk Density Apparatus	Electrolab Model- ETD- 1020	Thermo lab
16 station Compression machine	CM D3-16	Cadmach
Tablet hardness tester	PTB-311E	PHARMATEST
Disintegration test apparatus	ED-2L	THERMO LAB
Tablet dissolution apparatus	2100C	LAB INDIA
Hot Air Oven	KLT-1244	AC MOTORS

6.METHODOLOGY

6.1 PREPARATION OF CALIBRATION CURVE FOR LORATIDINE

A. STANDARD CURVE IN 6.8 PH PHOSPHATE BUFFER



245nm ±SD, n=3

Fig 1: Standard graph of loratadine

Table 1: Composition Of Formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Loratidine	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg
Camphor	10	--	20	--	20	--	--	--
MCC	127	127	113	113	105	105	105	105
LM	42	42	42	42	42	42	42	42
Menthol	--	10	--	20	--	20	20	20
CCS	8mg	8mg	12mg	12mg	20mg	20mg	--	--
CP	--	--	--	--	--	--	12mg	20mg
Mg.stearate	3mg	3mg	3mg	3mg	3mg	3mg	3mg	3mg
Total weight	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg

MCC- Micro crystalline cellulose, CCS- Cross caramellose sodium, CP- Cross Povidone, LM- Lactose monohydrate

Table 2: Acceptance criteria for tablet weight variation

Average weight of tablet(mg)	Maximum % difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

6.2 Stability Studies

FDA and ICH specifies the guidelines for stability testing of new drug products, as a technical requirement for the registration of pharmaceuticals for human life. The ICH tripartite guidelines have established long term stability testing to be done at 25^0C/60%RH for 12 months.

Table 3: ICH Guidelines for stability study

Study	Storage Condition	Duration
Long term	25±2°C, RH 60±5%	12 months
Intermediate	30±2°C, RH 65±5%	6 months
Accelerated temperature	40±2°C, RH 75±5%	6 months

7. RESULTS

7.1 PRE-FORMULATION STUDIES

These tests were performed, and the results were illustrated in the following table:

Table 4: Description of loratadine (API)

Test	Description
Color	White to off white powder

The results were found as per specifications**.**

Table 5: T Solubilityof loratadine (API) in various solvents.

Solvents	Solubility
Water	In soluble
pH6.8 Phosphate buffer	Soluble
Methanol	Soluble
Chloroform	Soluble

7.2 PREFORMULATION STUDIES

Table 6: Pre-compression parameters for formulation batches

Formulation code	Bulk density (gm/mL)	Tapped density (gm/mL)	Compressibility index (%)	Hausner's ratio	Angle of repose
F1	0.721±0.045	0.87± 0.01	17.126±0.6	1.206±0.06	36.62⌖0.21
F2	0.710±0.043	0.873±0.04	19.714±0.7	1.251±0.04	37.46⌖0.11
F3	0.41±0.045	0.483±0.5	15.113±0.8	1.178±0.08	38.32⌖0.31
F4	0.45±0.045	0.52 ± 0.09	15.60±0.2	1.15±0.02	28.06⌖0.31
F5	0.45±0.045	0.50 ± 0.07	12.23±0.6	1.11±0.04	27.58⌖0.15
F6	0.44±0.044	0.50 ± 0.09	12.58±0.8	1.13±0.08	28.44⌖0.11
F7	0.41±0.048	0.483±0.49	15.113±0.9	1.178±0.07	38.32⌖0.33
F8	0.710±0.032	0.873±0.036	19.714±0.6	1.251±0.05	37.46⌖0.15

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner's ratio and angle of repose were found to be between 12- 20, 1.11-1.26

and 30-40 respectively. These results show that the formulations have fair to very good flow properties.

From the above Table, Preformulation studies of powder blend had shown that the blends had passable parameters like Angle of Repose, Bulk density, Tapped density, Carr's index and Hausner's ratio. From the Table, it is observed that based on compressibility index and it was concluded that the blend showed passable flow characteristics.

7.3 RESULTS OF IN-VITRO RELEASE PROFILE

Table 7: In-Vitro Release Profile of Loratidine from formulations F1-F8

Time	F1	F2	F3	F4	F5	F6	F7	F8
10 mins	32.56	38.26	42.52	48.96	50.38	58.92	12.56	18.26
15 mins	46.28	48.03	50.36	56.48	61.94	69.52	26.28	28.03
20 mins	55.23	60.58	62.85	68.92	70.56	77.89	35.23	40.58
30 mins	60.65	65.92	70.59	74.56	77.89	82.56	40.65	50.92
45 mins	72.36	74.82	75.62	80.82	83.56	98.94	52.36	54.82
60 mins	80.56	80.49	82.51	85.45	88.95	100.59	60.56	60.49

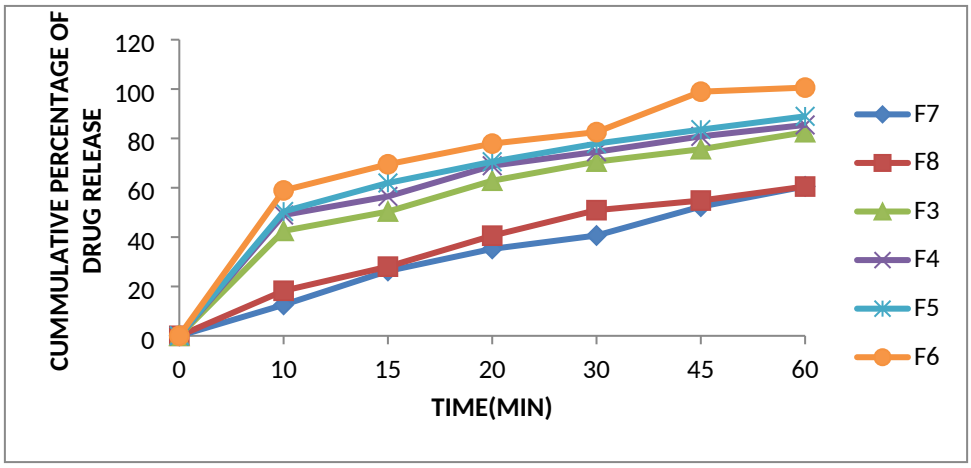


Fig 2: In-Vitro Release Profile of Loratidine from formulations F1-F6

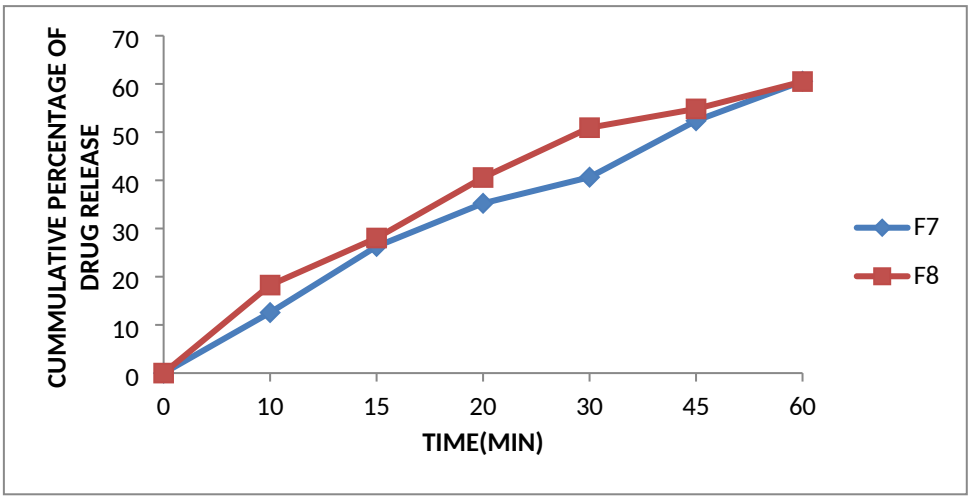


Fig 3: In-Vitro Release Profile of Loratidine from formulations F7&F8

The in-vitro drug release profiles of Loratidine from all the formulations F1 to F8 are shown in the above Tables. From the results, it is observed that the dissolution profiles of the formulated products (F1, F2, F3, F4& F5) didn't meet the proper dissolution profile of Loratidine i.e 85% of drug release in 45mins. The formulations F6 showed 98.45% of drug release within 45mins.The formulationsF7, F8 showed 60% in 60 mins after change in disintegrant i.e Crospovidone even with increase in concentration of the crospovidone.

7.4 STABILITY STUDIES

Loratidine tablets of F6 formulation were packed in HDPE (High density polyethylene) container with child resistant caps (CRC) and induction sealed. These bottles were charged for stability study at 40^{0}C &75% RH. The Loratidine porous tablets were subjected to stability studies at 40^{o}C and 75% RH for 3 months and from the above results, it was found that there is no effect on the tablets and was found to be within the limits according to ICH guidelines.

8. DISCUSSION

Immediate release tablets of Loratadine were formulated by direct compression method using Camphor and Menthol as subliming agents, Microcrystalline cellulose, Lactose monohydrate as diluents, CCS as super disintegrant, Magnesium stearate as lubricant.

The blends were analyzed for parameters such as Bulk density, Tapped density, Compressibility index and Hauser's ratio and the results were found to be within limits. After compression, all the tablets were dried at 60^{o}C for 12hrs and were evaluated for various parameters like weight variation, hardness, thickness, friability, disintegration, and in-vitro drug release. All formulations were found to have good hardness, so they were taken for further studies. The measured hardness of tablets of each batch are in the range of 3 to 3.5kg/cm^{2}. Tablets mean thickness were almost uniform in all formulations and were found to be in the range of 3.05 mm to 3.50mm. The total weight of each formulation was maintained constant, and the weight variation of the tablets was within limits of 5%. All the tablets passed the pharmacopoeia specifications for disintegration of Loratadine porous tablets within 5 minutes.

9. SUMMARY AND CONCLUSION

This dissertation work was done with an aim to design an immediate release oral dosage of Loratidine and evaluation of the tablets for various parameters including in vitro drug release studies. Loratidine tablets were formulated by using microcrystalline cellulose and lactose monohydrate as fillers, camphor and menthol as subliming agents, crospovidone and CCS as super disintegrant and magnesium stearate as lubricant. The powdered blend were compressed into tablets and were analyzed for the parameters such as average weight, disintegration time, friability, thickness, weight variation, hardness, and drug content. The formulation F6 is formulated by using subliming agents and super disintegrants where it can ensure burst release of the drug.

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