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FORMULATION DEVELOPMENT AND IN VITRO EVALUATION OF LORATIDINEPOROUS TABLETS BY SUBMIMATING TECHNIQUE

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ABSTRACT

Loratadineis a try - cyclic anti- histamine, which has a selective and peripheral H1 antagonist action.It is effective in relieving nasal congestion, particularly in patients with allergic rhinitis. In present work an attempt has been made to prepare fast dissolving tablets of loratadine with increased rate of dissolution may leads to increase bioavailability. In present work fast dissolving tablet of loratadine prepared using croscamellose sodium, sodium starch glycolate and cross-povidone as superdisintegrants by direct compression method. The tablets were evaluated for various parameters like weight variation, hardness, friability, *in vitro* disintegration time, drug-polymer interaction, drug content water absorption ratio, wetting time, *in vitro* drug release, FTIR studies and short term stability studies.The tablet prepared by direct compression method passes weight variation was found in the range 201.6 to 205.6 mg which is below ±7.5%, hardness 3.5 to 5 Kg /cm2, percentage friability of 0.23 to 0.54 %, *in vitro* disintegration time of 2 to 7 min, drug content uniformity was in between 98.02 to 98.75%, FTIR study showed that there was no drug interaction with formulation additives of the tablet, short term stability studies of the formulations indicated that there are no significant change in hardness, friability, drug content and *in vitro* drug release. ($p<0.05$).

Key Words: Loratadine, direct compression method, *in vitro* drug release

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INTRODUCTION

A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit-dose powders and granules. Among the various dosage forms oral soliddosage forms have greater importance and occupy a prime role in the pharmaceutical market. Widely acceptable route of administration is said to be orally and the drugs that administered through oral route as solid dosage forms were known to be most preferred ones by the patients. 90% of the drugs which shows systemic effect were formulated as solid dosage forms. Because of these reason whenever New chemical entity (NCE) has discovered, which shows a sufficient pharmacological action, first the pharmaceutical company asks whether the drug is successfully administered by oral route or not. The oral route of administration still continues to be the most preferred route due to its manifold advantages including:Tablets and capsules represent unit dosage forms in which the accurate dose of drug

to show sufficient pharmacological action can be administered. In case of liquid oral dosage forms such as Syrups, Suspensions, Emulsions, Solutions and Elixirs the patient is asked to administer the medication of 5-30 ml. Such dosage measurements are typically error by factor ranging from 20-50 %, when the drug is self administered by patient. Solid dosage forms are less expensive to shipping and less prone for the degradation when compared to liquid dosage forms (1-4). The rationale of this investigation was to develop monolithic tablets of loratidine 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 superdisintegrants. Sublimating agents are sublimed from the tablets by drying in hot air oven at 60ºC 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.

MATERIALS AND METHODS

Formulation of Loratidine porous tablets by direct compression method (5-7)

Porous tablets of Loratidine were prepared by direct compression method employing camphor and menthol as sublimating agents. The concentrations of the above ingredients were optimized as shown in below table on the basis of trial preparation of the tablets (Table-1). All the ingredients were weighed accurately. The drug was mixed with other ingredients except magnesium stearate and the thedisintegrants which are the release rate enhancers in ascending order of their weight. The powder mix was blended for 20 min to have uniform distribution of drug in the formulation. Then, magnesium stearate was added and mixed for not more than 1 min (to ensure good lubrication.) About 200 mg of the powder mix was weighed accurately and fed into the die of single punch machinery and compressed using 8 mm flat-surface punches. The hardness of the tablets was adjusted at 4-6 kg/cm^2 using a Monsanto hardness tester.

Table-1Composition 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

Disintegration test

Disintegration time is considered to be one of the important criteria in selecting the best formulation. To achieve correlation between disintegration time in-vitro and in-vivo, several methods were proposed, developed and followed at their convenience. One

tablet was placed into each tube and the assembly was suspended into the 1000ml beaker containing water maintained at 37±2°c and operated the apparatus for 15 minutes. The assembly was removed from the liquid and the tablets were observed. If one or two tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated.

Dissolution test

Dissolution media was taken as 6.8 pH Phosphate buffer, 500ml was placed in the vessel and the USP apparatus –2 (paddle) was assembled. The medium was allowed to equilibrate to temp of 37 ± 0.5°C. Tablet was placed in the basket and placed in the vessel, the apparatus was operated for 15min at 50 rpm. At definite time intervals, 5 ml of the fluid was withdrawn; filtered and again 5ml of the fluid was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed using UV.

RESULTS AND DISCUSSION

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner'sratio and angle of repose were found to be between 12- 20, 1.11-1.26 and 30-40 respectively. Finally through the results it si found that formulations have fair to very good flow properties.From the Table-2,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-2, it is observed that based on compressibility index and it was concluded that the blend showed passable flow characteristics.

Table-2 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

The in-vitro drug release profiles of Loratidine from all the formulations F1 to F8 are shown in the Table-3 and Fig-1. 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 Loratidinei.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 disintegranti.eCrospovidone even with increase in concentration of the crospovidone.

Table-3In-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

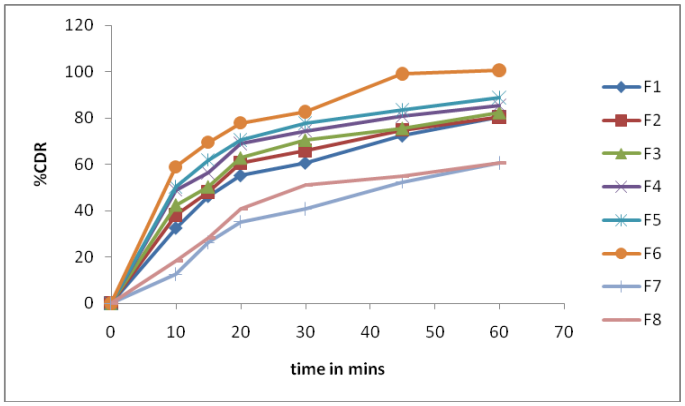

Fig-1 In-Vitro Release Profile of Loratidine from formulations F1-F8

CONCLUSION

Loratidinetablets 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.The formulation F6 containing 10% of Menthol showed disintegration time of less than 30seconds after drying. Menthol as subliming agent was found to be most effective of all other subliming agents as it had showed drastic effect on the drug release. All other parameters viz: Hardness, Thickness, Weight variation and drug content were also found to be within limits. The dissolution profiles and drug content of the tablets were found to be satisfactory even after subjecting the tablets to stability studies at 40^{o}C and 75%RH for 1 month and 3 months respectively. The formulation F6 and process can be easily scaled up and can be easily employed in large scale production because the process is simple, cost effective and precise and also yields reproducible good result that involves complex process for manufacturing the tablets.

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