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Formulation and Evaluation of Chewable Tablets of Loratadine by Direct Compression Method

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Abstract
Since last few years, there has been an enhanced demand for more patient compliance dosage forms. For this an attempt has been made in the present work to design and evaluate chewable tablets. Chewable tablets have the advantages of both conventional tablet and liquid dosage formulation, especially in geriatric and pediatric. Oral route of administration has received more attention in the pharmaceutical field. Chewable dosage forms have been demonstrated to improve therapeutic efficacy and better bioavailability. Loratadine is a peripherally selective piperidine histamine receptor blocker, which competitively antagonizes histamine at the H1 receptor site. Histamine is amine autocoids which causes many signs and symptoms of allergy. It stimulates the cells to release chemicals that produce effects associated with allergy and commonly acts on α-adrenergic receptor or 5-HT receptor. Loratadine acts as a selective antagonist of peripheral histamine H1-receptor that serves to eliminate effects mediated by histamine (an endogenous chemical mediator released during allergic reactions) or block one type of histamine receptor (H1 receptor). Loratadine is a second-generation H1 histamine antagonist drug used to treat allergies. Loratadine is used for the symptomatic relief of allergy such as hay fever (allergic rhinitis), urticaria and seasonal allergies including sneezing, itchy and runny nose, and tearing and redness of the eyes.

Keywords: Loratadine, chewable tablet, histamine receptor, urticaria etc.

1. Introduction
It is a peripherally selective piperidine histamine receptor blocker, which competitively antagonizes histamine at the H1 receptor site. They lack anti-cholinergic side effect and having non-sedating property because they do not cross the blood brain barrier [1]. Loratadine is a second-generation H1histamine antagonist drug used to treat allergies [2]. Structurally, it is closely related to tri-cyclic antidepressants and distantly related to the atypical antipsychotic. It is white to off white solid. It is under the therapeutic category of tricyclic antihistamine [3]. The empirical formula of loratadine is $C_{22}H_{23}ClN_2O_2$. The IUPAC name of the drug is Ethyl 4-(8-chloro-5, 6-dihydro-11-H benzo [5, 6] cyclohepta (1, 2-b) pyridin-11-ylidine) 1-piperidinecarboxylate. The molecular weight is 382.883 g/mol. The melting point is 132 – 137 °C. The BCS class of the drug is class II. The structural formula of the drug is given below:

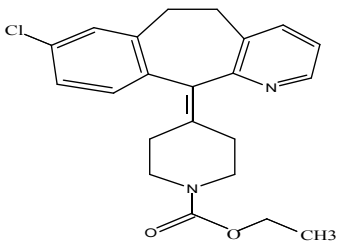

Fig 1: Structural representation of Loratadine Hydrochloride

The half life of the drug is 8 hours. It is highly bound drug to plasma proteins (90 – 99%) and does not cross the blood brain barrier. Loratadine is metabolized by rapid isoenzyme of the Cytochrome P450 system. CYP3A4 and CYP2D6 enzymes are mainly responsible for the metabolism of drug and have rapid first pass metabolism. Approximately 40% of the dose is excreted in urine and 42% in the faeces over a period of 10 day and mainly in the form of conjugated metabolites. Approx. 27% of the dose is eliminated in the urine during the first 24 hours. About less than 1% of the active substances excreted unchanged in active form as loratadine.

2. Materials and methods

Loratadine hydrochloride was provided by the Sky Lab, Rohtak as a gift sample. Lactose, Microcrystalline cellulose, Povidone K 30, Maize Starch, Colloidal Silicon dioxide, Magnesium Stearate, Talcum, Aspartame, Isopropyl Alcohol also provided by the Sky Lab, Rohtak as a gift sample. We are very thankful to Sky Lab, Rohtak.

3. Experimental methods

3.1 Formulation of chewable tablet by direct compression method [4, 5, 6]

Table 1: Formulation of trial batches using different concentration of excipients by Direct Compression method

Batch No.	D 01	D 02	D 03	D 04	D 05	D 06
Ingredients	**mg/tab**	**mg/tab**	**mg/tab**	**mg/tab**	**mg/tab**	**mg/tab**
Loratadine	10	10	10	10	10	10
Lactose	155	100	70	90	85	85
Micro Crystalline Cellulose	-	50	60	50	50	50
Povidone K-30	20	10	20	15	15	10
Maize starch	120	153	154	150	150	150
Aspartame	20	12	25	20	15	25
Colloidal Silicon dioxide	6	7	-	6	5	5
Magnesium stearate	10	8	8	9	10	7
Talc	9	-	3	-	10	8
Isopropyl Alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total	350	350	350	350	350	350

3.2 Preparation of chewable tablet by Direct Compression

Loratadine tablet each weighing 350 mg containing 10 mg of Loratadine was formulated as follows:

- Loratadine, Lactose, Microcrystalline cellulose, Povidone-K30, Maize Starch, Aspartame, Colloidal silicon dioxide were weighed accurately and sifted through sieve no.40.
- Magnesium Stearate was weighed and sifted through sieve no.60 and mixed in the above mixture.
- The mixture was blended in quanta blender for 30 minutes (min.).
- Finally, remaining Magnesium Stearate and Talc was weighed and sifted through sieve no.60, then mixed with the above granular blend and blended for 5 min. in blender.
- The tablets were compressed into tablets using 16 station compression machine equipped with round and standard concave tooling of 8 mm with target weight of each tablet 350 mg.
- Six trial batches of Chewable tablets of Loratadine were formulated using Direct Compression method as shown in table 1.

4. Evaluation of chewable tablet [7, 8, 9]

4.1 Pre-compression studies

Table 2: Bulk density, Tapped density, Angle of Repose, Hausner's ratio, Carr's index value of Different batches blend of Loratadine

Batch No.	Bulk Density	Tapped density	Angle of Repose	Hausner's ratio	Carr's index
D 01	0.474	0.648	37.4 (Passable)	1.37 (Poor)	26.8 (Poor)
D 02	0.488	0.634	35.8 (Passable)	1.29 (Passable)	23.8 (Passable)
D 03	0.471	0.665	37.2 (Passable)	1.41 (Poor)	29.2 (Poor)
D 04	0.496	0.635	35.5 (Passable)	1.28 (Passable)	21.8 (Passable)
D 05	0.493	0.625	30.5 (good)	1.26 (Passable)	21.1 (Passable)
D 06	0.522	0.629	29.7 (good)	1.20 (fair)	17.0 (fair)

From aforementioned results it was found that batches D 05, D 06 exhibited acceptable flow properties with respect to angle of repose, Carr's index, Hausner's ratio.

4.2 Post-compression evaluation

Table 3: Evaluation parameters of tablets from different batches

Batch No.	Average weight (mg)	Thickness (mm)	Friability (%)	Hardness (kp)	Drug content
D 01	344	3.7	0.18	3.1	98.6
D 02	343	3.5	0.17	2.41	100.6
D 03	345	3.37	0.13	3.0	97.3
D 04	344.5	3.62	0.15	2.2	99.2
D 05	343	3.5	0.05	1.5	97.7
D 06	343.7	3.6	0.07	2.0	99.8

From aforementioned results of post compression parameters of formulated batches were found to be satisfactory.

4.3 *In-vitro* drug release studies

In vitro drug release rates of loratadine from chewable tablets were determined using USP type 2 apparatus (paddle). Trial formulation batches were prepared using direct compression and its release profile was compared to select the manufacturing process for further studies. Release profile of formulations (D 01 to D 06) is given in table 7.12. The cumulative % drug release was shown in Fig. 7.10.

Table 4: *In-vitro* Release profile of direct compression trial batches (D 01 to D 06)

Time (min.)	% Cumulative drug release (Dissolution medium 0.1 N HCl)					
	D 01	D 02	D 03	D 04	D 05	D 06
0	0	0	0	0	0	0
5	4.58	5.54	4.71	8.70	14.34	17.30
10	17.78	19.93	19.63	26.96	33.21	37.16
20	39.27	42.61	42.59	50.37	58.14	64.65
30	57.75	62.04	61.26	68.03	76.93	82.10
45	75.53	78.44	77.35	82.11	96.66	99.15

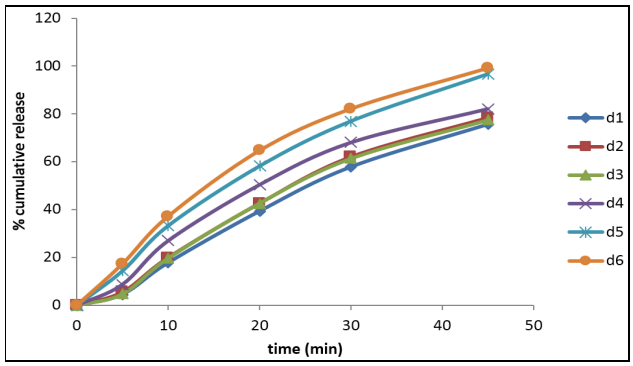

Fig 2: % cumulative drug release rate of direct compression method (D 01 to D 06)

5. Comparison of Finally Selected Formulation with Marketed Formulation (Claritin)

The release profile of final optimized batch from direct compression method (D 06) was compared to commercially marketed product. Release profile of both batches was given in table 5 and % cumulative drug release was shown in fig. 3.

Table 5: *In-vitro* drug release of final batch & commercial marketed product (Claritin)

Time (min.)	% cumulative drug release (Dissolution medium 0.1 N HCl)	
	D 06	Claritin tablet
0	0	0
5	17.30	18.5
10	37.16	32.25
20	64.65	65.14
30	82.10	79.94
45	99.15	98.66

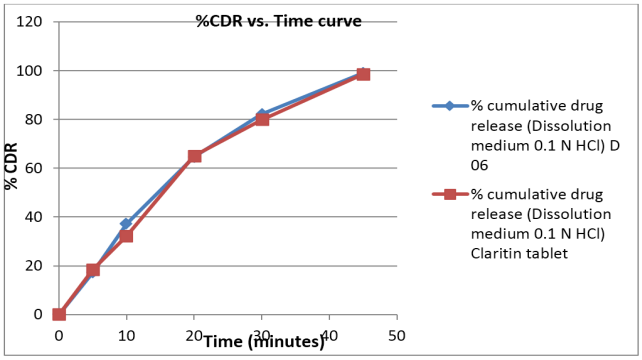

Fig 3: Comparison of % cumulative drug release rate of marketed formulation with final formulation (D 06)

6. Summary

The present research work involved the formulation and evaluation of a chewable tablet of loratadine by direct compression. Six formulations were developed keeping different concentration of excipients. Magnesium stearate was used as lubricant, Superdisintegrants Povidone (Polyvinylpyrrolidine) was used in varying concentrations and aspartame as a sweetening agent. Lubricated blends were characterized for physical properties like bulk density, tapped density, angle of repose, Carr's index, Hausner's ratio; all blends showed satisfactory properties. All lubricated blends were compressed into tablets using round shaped punches. Tablets were evaluated for Weight variation, thickness, hardness, percentage (%) friability, drug content and *in-vitro* release studies. One of the selected best formulations (D 06) was compared with that of the marketed conventional tablet formulation of Loratadine (Claritin) for its *in vitro* drug release performance.

7. Conclusion

Chewable tablets of loratadine can be formulated by employing Povidone as superdisintegrant, aspartame as a sweetening agent and magnesium stearate as lubricant. FTIR spectra data showed that Loratadine and excipients used found to be compatible. In the solution state stability study it was found that the Loratadine drug solution was stable up to 24 hours. The physical compatibility study at 40 °C/75% RH showed that Loratadine and excipients used were found to be physically stable. Melting point of loratadine was found to be 134 °C. Formulation was prepared by direct compression. FTIR spectra of pure drug loratadine was compared with selected formulation (D 06) and found to be satisfactory. Comparison of formulation (D 06) with the marketed tablet formulation of loratadine (Claritin) showed better drug release profile.

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