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Formulation Development and Evaluation of Chewable Tablets Containing Non- Sedating Antihistamine

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Abstract

The present study focused on developing and assessing chewable tablets designed for various patient age groups, including children, the elderly, and adults. These tablets, which contain an antihistamine aimed at treating allergic rhinitis, were formulated using specific super disintegrants and specialized excipients. The research will investigate the bioavailability of these chewable tablets containing the commonly used anti-allergic medication loratadine.

KEYWORDS: Loratadine, chewable tablet, MCC, Sodium CMC, Flavoring agent.

Introduction:

A chewable tablet of loratadine is another formulation of the medication designed for ease of use, particularly for children or those who have difficulty swallowing standard tablets. Like the oral dispersible tablet, loratadine in this form is used to treat allergy symptoms such as sneezing, runny nose, and itchy or watery eyes.

MATERIALS AND METHOD:

Chewable tablets containing Loratadine 5 mg were prepared by selecting the excipients used in pre-formulation studies. The aqueous wet granulation process was used to create the chewable Loratadine tablet, while mannitol, lactose monohydrate, and microcrystalline cellulose were used as diluents. Ethyl Cellulose is a polymer used to hide flavours. Binders include Povidone and maize starch. In addition, we've employed aspartame and raspberry tastes as sweeteners. As a flavour enhancer, citric acid is employed. Pharma grade colours like FD&C Red No. 40, FD&C Yellow No. 6, and D&C Yellow No. 10 are utilised as colours. Colloidal silicon dioxide, magnesium stearate, and sodium starch glycolate act as disintegrants, glidants, and lubricants, respectively

Preparation of Granules

Sifting: Sift through a 40# mesh using loratadine (micronized), ethyl cellulose, lactose monohydrate, and mannitol.

Dry mixing: Place the aforementioned ingredients in a Rapid Mixer Granulator (RMG) and mix slowly for 15 minutes.

Prepare the binder by dissolving Povidone K 30, and D&C Yellow in clean water. To fully dissolve, thoroughly stir.

Making starch paste requires separately dissolving D&C Yellow and maize starch in a little amount of filtered water. Both ingredients should be added to the necessary amount of heated water while being continuously stirred in order to dissolve thoroughly. Granulation: Slowly add the starch paste or binder solution to the dry mix ingredients and finely granulate.

Dry the moist bulk in a fluidized bed dryer at 60 degrees Celsius.

Sifting and Milling: Using 20# mesh, sift the dry grains. Granules that are oversize are totally passed through a 20# mesh screen after passing through a multi-mill equipped with a 2.0 mm screen.

Lubrication: Place the granules that have been through the sifting process in a blender and add the citric acid, raspberry flavour, aspartame, and colloidal silicon dioxide. 20 minutes of gentle blending. Then, add the 60# mesh-sifted magnesium stearate, and mix for 5 minutes at a slow speed.

Compression: Use 12 mm flat standard punches with a plain surface on both sides to compress the mix. With the use of an eight station tablet compression machine, the weight, hardness, and thickness were controlled to produce homogeneous tablets.

Ingredients						
	Trial 001	Trial 002	Trial 003	Trial 004	Trial 005	Trial 006
Loratadine (Micronised)	5	5	5	5	5	5
Micro crystalline Cellulose (Avicel-pH 101)	180	180	----	----	----	-----
Lactose Monohydrate	200	206	335.75	340.75	310.75	161
Mannitol (Pearlitol 25C)	132.75	132.75	150	150	150	350
Ethyl Cellulose (Ethocel Std 10FP)	----	----	25	20	----	---
Micro crystalline cellulose and Guar gum (Avicel-CE 15)	----	----	----	----	50	----
Povidone K-30	10	10	----	----	----	----
Maize Starch	----	----	18	18	18	18
Purified Water	q s	q s	q s	q s	q s	q s
D & C Yellow No 10	1.25	1.25	1.25	----	1.25	---
D & C Red No 40	----	----	----	----	----	1
FD &C Yellow No 6	----	----	----	1.25	----	--
Citric Acid	2	2	2	2	2	2
Raspberry flavour	2.50	2.50	2.50	2.50	2.50	2.5
Aspartame	6	6	6	6	6	5
Sodium starch glycolate	6	----	----	----	----	----
Colloidal silicon dioxide	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	3	3	3	3	3	4
Tablet weight (mg)	**550**	**550**	**550**	**550**	**550**	**550**

EVALUATION OF CHEWABLE TABLETS (Gandhi PP et al., 2010)

All the batches of tablets were evaluated for various physical parameters like thickness, weight variation, friability, hardness, drug content and dissolution as per pharmacopoeial standards.

Thickness (United State Pharmacopoeia-30, 2007)

For consistency in tablet size, the thickness of the tablet is crucial. Due to variations in the granulation's density, the pressure applied to the tablets, the speed of the compression machine, and other factors, tablet thickness can alter without affecting weight. Vernier callipers were used to measure and record the thickness of ten randomly chosen tablets.

SWeight variation (United State Pharmacopoeia-30, 2007)

The weight of each of the 20 pills was measured using a digital weighing scale. The weight of each pill was determined individually and compared to the average. The tablet passes the USP test if no more than two tablets deviate from the % limit, Average weight = Weight of 20 tablets

Table: Weight variation

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

Crushing strength (United State Pharmacopoeia-30, 2007)

Tablets need to be strong enough to endure mechanical manipulation during production, packing, and delivery. They also need to be resistant to friability. The strength of a tablet's crushing is often measured by hardness. Different properties of disintegration and dissolution are brought by by changes in hardness. Using a Schleuniger hardness tester, the tablet's crushing strength was ascertained.

Friability test

The Roche Friabilator was used to assess the friability of tablets (Electrolab, Mumbai). The tablets were dropped from a height of six inches in each rotation while being exposed to the combined effects of abrasions and shock in a Friabilator at a speed of 25 rpm. A friabilator was filled with a pre-weighed sample of tablets and rotated 100 times. A delicate muslin cloth was used to dust the tablets, and they were reweighed. The following formula determines the friability:

F= (1-Wo/W) X 100

Where, Wo is the weight of the tablets before the test and W is the weight of the tablet after the test.

%Friability = (Loss in weight / Initial weight) x 100

Content uniformity test (United State Pharmacopoeia-30, 2007)

Each formulation's ten pills were pulverised separately. A volumetric flask was used to dissolve the powdered sample, which contained 100 mg of the medication, before being combined and filtered. The filtrate was appropriately diluted with medium, required amounts of phosphate buffer pH 7.4, and drug concentration was measured against a blank using a UV spectrophotometer at 278 nm. It was determined what proportion of the medication was in the pills.

IN VITRO DISSOLUTION STUDIES

The tablet samples were subjected to in-vitro dissolution studies using USP

At 37°C and 50 rpm, a Type-II(Paddle) dissolving equipment (LABINDIA DISSO2000) is used. The dissolve media was 900 mL of 0.1 N HCl, as per the USFDA's official guidance. Five millilitre samples (5 ml) were taken at 15, 30, 45, and 60 minutes and replaced with an equivalent volume of new dissolving media. A 200 ml volumetric flask containing 20 ml of methanol and 40 mg of

loratadine was then sonicated for about 10 minutes to create the standard stock solution of loratadine. Next, 140 ml of diluent was added, dissolved using a sonicator, and diluted with diluent to the appropriate level. To obtain a standard stock solution, 100 ml of dissolving medium and about 5.0 ml of standard stock solution were combined.

STABILITY STUDIES

Further accelerated stability experiments including selected Loratadine chewable tablets lasting up to three months at 400C and 75% RH were performed. The goal of stability testing is to establish a retest period for the drug substance or a shelf life for the drug product as well as recommended storage conditions. Stability testing provides evidence on how the quality of a drug substance or drug product changes over time under the influence of various environmental factors, such as temperature, humidity, and light (ICH guideline 1996).

RESULTS AND DISCUSSION:

Weight variance was within a 5% range, in accordance with pharmacopoeial requirements. It was discovered that tablets ranged in thickness from 3.7 to 4.3 mm. It was discovered that the hardness for several formulations ranged from 10 to 12 kP, suggesting adequate mechanical strength. The table below lists the physical characteristics of Loratadine chewable tablets. All of the formulations had friability < 0.5%, which indicates that the tablet has strong mechanical resilience

Trial	Weight variation range (mg)	Friability (%)	Hardness range (Newton)	Diameter(mm)	Thickness (mm)
001	545-555	0.282	70-80	12±0.03	3.9±0.04
002	545-560	0.265	45-55	12±0.04	4.3±0.03
003	543-557	0.296	75-87	12±0.03	3.9±0.02
004	548-560	0.315	80-88	12±0.03	3.8±0.02
005	543-557	0.248	85-97	12±0.04	3.9±0.02
006	548-556	0.180	90-105	12±0.04	3.7±0.02

Drug content uniformity

By measuring the absorbance at 278 nm, the drug concentration in different formulations was spectrophotometrically determined. The medication concentration ranged from 98.20% to 102.00% in all formulations. Table 5.10 displays the findings of the drug content of all batches.

Content uniformity of the tablets

Sl. No.	Trials	Drug content (%) (Mean ± SD)
1	Trial -01	100.84 ± 1.08
2	Trial-02	99.06 ± 0.96
3	Trial-03	99.80 ± 1.21
4	Trial-04	98.20 ± 1.05
5	Trial-05	102.00 ±1.08
6	Trial-06	101.00 ±1.02

IN VITRO DISSOLUTION STUDIES

While creating a novel formulation, formulation variables and manufacturing challenges must be taken into account. Results of dissolving experiments on formulation T-1 revealed that 96.9% of the medication was released after 15 minutes and 111.5% was released after 60 minutes. According to the findings of the dissolving experiments conducted on the formulations T-02 and T-03, Loratadine was released in amounts of 87.0%, 24.8%, and 63.8% at the end of 15 and 60 minutes, respectively. Results of dissolving experiments on formulations T-04, T-05, and T-06 revealed that 26.4%, 29.4%, and 25.4 of Loratadine were released after 15 minutes and 88.8%, 99.3%, and 95.2% of the drug were released after 60 minutes, respectively. On Figure 5.7, the dissolution studies were displayed.

The most effective trial was Trial 5, which included a formulation without the use of ethyl cellulose and had a 100% drug content at the end of 60 minutes. So, it was ultimately determined that Trial 5 is the optimal formulation that conforms with all desirable qualities of chewable tablets. The formulation Trial 5 of the Loratadine chewable tablet revealed a stable recipe with improved patient compliance and medication release

Time (mints)	Mean % drug release (Mean ± SD)					
	Trial-01	Trial-02	Trial-03	Trial-04	Trial-05	Trial-06
15	96.9 ± 4.16	87.0 ±5.57	24.8±2.57	26.4±5.17	29.4±2.61	25.4±2.51
30	105.1±3.78	97.5 ±3.41	38.0±3.34	49.4±8.64	55.4±2.77	51.6±2.78
45	109.2±1.96	103.4±4.55	53.8±3.98	70.5±12.26	80.4±2.81	76.5±2.71
60	111.5±1.67	105.8±1.90	63.8±7.52	88.8±9.59	99.3±3.37	95.2±3.46

STABILITY STUDIES

The ICH-recommended storage conditions are 40°C 2°C and 75 5%RH for the duration of the storage term for the optimal batch (Trial no. 5) of Loratadine chewable tablets. During a 6-month withdrawal period, the chewable pills were examined for chemical characterisation, including the dissolving profile.

PRODUCT: Loratadine chewable tablets 5mg
PACK: HDPE Container with 40 tablets (100cc with 1g silica bag)
Batch No: Trial no 5
Description: Yellow coloured, flat circular uncoated tablets

Stability studies of Loratadine chewable tablets 5mg (Trial 5)

Test parameter	Limit	initial	1 month 40° C/ 75%RH	2 month 40° C/ 75%RH	3 month 40° C/ 75%RH	6 month 40° C/ 75%RH	3 month 25° C/ 60%RH	6 month 25° C/ 60%RH
Description	As above	As above	As above	As above	As above	As above	As above	As above
Loss on drying(%w/w)	NMT 4.0% (w/w)	1.80	2.00	2.20	2.30	2.80	2.00	2.40
Assay	95-105%	102.0%	101.2%	100.8%	100.2%	99.5%	100.8%	100.1%
Dissolution	Time(min)							
Condition: 900ml, 0.1N HCl, 50 rpm, USP Type-II	15	29.4±2.61	25.4±2.90	23.22±2.40	22.23±2.70	20.16±2.40	22.40±2.50	23.42±2.40
	30	55.4±2.77	53.2±2.10	51.01±2.50	50.02±2.30	48.01±2.46	51.02±2.32	50.42±2.46
	45	80.4±2.81	78.10±2.62	77.10±2.20	75.12±2.67	73.20±2.40	76.20±2.46	75.02±2.66
	60	99.3±3.37	98.6±2.40	97.61±2.46	96.42±2.20	95.66±2.30	97.20±2.40	98.06±2.21

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