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Research Article

A Study on Chewable Tablets for the Anti-Allergic Drug

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Abstract:
Abstract: According to this theory, the interface between the layers should fuse together during compaction and be strongly held together following tablet ejection by adhesion forces. This is not always the case, and since the individual layers' compressibility and compact ability shouldn't be the reason for delamination, it is necessary to find other physical mechanisms that might explain the issues with delamination. Stability experiments were conducted on the improved dosage form formulations to identify physical and chemical changes that occurred during storage. On storage, the improved formulation's physicochemical property did not change considerably. the few alterations in in vitro release that were seen both before and after preservation. According to the outcome, the formulation was stable under the necessary storage conditions.
Keywords: Tablets, Loratadine, Chewable Tablets, physical mechanisms, drug, Anti-Allergic.

1. Introduction

Tablets that must be broken and eaten in between the teeth before intake are known as chewable tablets. These pills are provided to individuals who detest swallowing and to youngsters who have trouble swallowing.

The production of a successful tablet formulation requires the careful selection of components in order to provide a durable solid dosage form. Achieving satisfactory manufacturing performance may depend on selecting the right excipient to carry out a particular function in a tablet formulation, such as disintegration or lubrication. To cover up disagreeable flavours and simplify paediatric dosage, sweeteners—both natural and synthetic—are one kind of functional excipient frequently utilised in chewable tablet formulations.

Chewable formulations should ideally disintegrate smoothly, taste well, and leave no harsh or unappealing aftertaste. They break down in the mouth when chewed, releasing their components as a result. As a result, there isn't as much of a delay before stomach absorption as there is with tablet disintegration (Biradar SS et al., 2006). [1-2]

Loratadine, a piperdine derivative, is used to treat allergic skin disorders, specifically atopic dermatitis and urticaria, allergic rhinitis, acute coryza, and ocular allergies, at doses of 10 mg once daily in adults and 5 mg in children between the ages of 2 and 12 years. Loratadine lacks CNS depressant effects (Kay GG and Harris AG, 1999). [3]

Youngsters have trouble swallowing the regular Loratadine pills. Thus, chewable pills are best for avoiding this issue. In order to increase cooperation among youngsters, it was decided to create Loratadine into a chewable tablet. Moreover, chewable pills provide a faster release of the active components, leading to a faster absorption of those chemicals and a quicker beginning of action (Jagdale S et al., 2010). [4]

When an active component is intended to operate locally rather than systemically, chewable tablets are frequently used (European Patent Application, 1990).

A pleasant chewable tablet is one that can be consumed with little to no water (Gary ML and Patrick M, 2008). [5]

Wet granulation or direct compression is typically used in the production of chewable tablets. To take advantage of the increased absorption properties of these forms, medically and/or physiologically active chemicals are increasingly being included in micronized and submicron forms in tablet formulations (Chavkin et al., 1998 and Kashid et al., 2009). [6]

In order to eliminate too much gas from the stomach and intestines, they are also utilised in the administration of antacids and carminatives (Kanig JL and Rudnic EM). Since it is not hygroscopic, mannitol is frequently used as an excipient in chewable tablets that contain medications that are sensitive to moisture (Bankar UV and Sharma MM, 1992). [7]

The organoleptic features of odour, taste, look, and mouth feel create problems with chewable tablet formulations, especially those containing pharmaceutically active substances. To achieve the required organoleptic qualities, both the formula components and the production procedure are important (Mithal BM, 1997 and Singhavi I& Bhatia N, 2006). [8]

Advantages of chewable tablets (Drug Dosage Form II a & b)

1. Provide quick and complete disintegration of the tablet and thus obtain a rapid drug effect after swallowing and dissolution.
2. Easy administration, especially for children and elderly people.
3. Could be administered when water is not available.

The major goal of the current study is to establish a stable formula with greater patient compliance and drug release by formulating and evaluating Loratadine chewable tablet dosage forms with various excipients and their influence on formulations. Wet granulation was the production technique employed.

4. Make sure the tablet dissolves completely quickly so that you may get a quick medication impact after eating.
5. Simple administration, particularly for young children and the elderly.
6. May be used if water is not readily accessible.

The major goal of the current study is to establish a stable formula with greater patient compliance and drug release by formulating and evaluating Loratadine chewable tablet dosage forms with various excipients and their influence on formulations. The manufacturing process used was wet granulation process.

Review of Literature:

Hema Chaudhary et al. (2013) demonstrated that the objective was to develop and optimise Granisetron hydrochloride (GH) fast dissolving oro-dispersible films using a two-factor, three-level Box-Behnken design. The two independent variables, X1 (polymer) and X2 (plasticizer), were chosen based on preliminary studies conducted prior to the implementation of the experimental design. The construction of contour plots for the prediction of responses of the dependent variables, such as drug release (Y1), disintegration time (Y2), and Y3 (tensile strength), was examined using a second-order polynomial equation. The compositions of the optimum formulation were found using the Response surface plots, and the statistical validity of the polynomials was verified. The improved formulation was then assessed using the Franz-type diffusion cell. In anticipating the values of dependent variables for preparation

and optimization, the designs define the function of the generated polynomial equation and contour plots.

According to Gabriel Marceln-Jiménez et al. (2012), the objectives of the current investigation were: (1) to provide a specialised technique for UPLC-MS/MS-based SIL plasma level quantification; (2)to compare oral SIL bioavailability in Mexican men with pharmacokinetic data in other populations; (3) to fulfil local regulatory requests; and (4) to describe the relative tolerability of a new 50-mg chewable tablet. This was a randomized, single-dose, 3-period, 6-sequence crossover study in healthy male volunteers. In each period, subjects received single oral doses of 100 mg of sildenafil (1 commercial [reference*], 1 generic [test 1 †], or 2 chewable generic tablets [test 2 ffi]), with a 4-day washout period between each dose. Serial blood samples were collected for up to 24 hours. SIL was measured in heparinized plasma by using a validated UPLC-MS/MS method. Pharmacokinetic parameters included Cmax, AUC0- 24, and AUC0-□. Bioequivalence was established if 90% CIs for mean test: reference ratios of log-transformed Cmax and AUC fell within the range of 0.80 to 1.25.

Tolerability was assessed on the basis of a clinical interview with the subject and monitoring of vital signs. Demographic data showed a homogeneous population. Validation of analytical method proved to be linear within the range of 1 to 1000 ng/mL, with selectivity, accuracy, and precision. 90% CIs for test 1: reference ratios were 86.52 to 113.56, 94.75 to 108.84, and 94.97 to 108.82 for the logarithm parameters Cmax, AUC0-24, and AUC0-□, respectively. The 90% CIs for the test 2:reference ratios were 82.14 to 107.24, 98.26 to 112.56, and 99.19 to 113.34 for Cmax, AUC0-24, and AUC0-□. Regarding relative tolerability, slight cephalea was the most common adverse effect. The developed analytical method was validated in compliance with local requirements and was useful for sildenafil measurement. This single-dose study under fasting conditions suggests that both test products met the Mexican regulatory criteria for assuming bioequivalence in these healthy, male Mexican volunteers. The clinical data suggest that the chewable tablets were well tolerated by volunteers.

In this study, the manufacture and trophic characteristics of perilla chewable tablet were examined, according to Jinhong Wu et al., 2012. The following steps were used to create the perilla chewable tablet: combining the basic ingredients with the excipients, creating wet granules, drying, tableting, and coating. The following was chosen as the best formula: 0.5% perilla essence, 0.5% perilla essence powder, 0.1% sucralose, 2% erythritol, 2% vitamin C, 0.5% magnesium stearate, 8% perilla powder, 2.5% perilla extract powder, 20% isomaltooligosaccharide, 20% microcrystalline cellulose, 44.4% lactose. Nutrient analysis findings revealed that the perilla chewable tablet was full of important vitamins and minerals that are beneficial to human health. [9]

By examining hard fats as the matrix basis and sweetening chemicals as corrigents, Hiroyuki Suzuki et al. (2004) demonstrated that the goal of this study was to create acetaminophen chewable tablets with suppressed bitterness and better oral sensation. Hard fats included Witocan H and 42/44, Witocan H-15, W-35, S-55, E-75, and E-85. In light of better oral sensation, Witocan H and 42/44 were chosen. Tablets containing a Witocan H/Witocan 42/44 combination had varying melting properties and rates of drug release depending on their ratios, but those with a Witocan H/Witocan 42/44 ratio of 92.5% (w/w) and above demonstrated effective drug release. As sweetening agents, sucrose, xylitol, saccharin, saccharin sodium, aspartame, and sucralose were employed, either alone or in combination with cocoa powder or Benecoat BMI-40. While both the Witocan H and Witocan 42/44 (92.5:7.5, w/w) combination tablets containing 1% (w/w) aspartame and 5% (w/w) Benecoat BMI-40 effectively controlled bitterness and sweetness, the former tablet demonstrated superior drug release. In light of its suppressed bitterness, low sweetness, enhanced oral

sensation, and effective drug release, the Witocan H tablet with Sc1-B5 is recommended as the finest acetaminophen chewable tablet. [10]

According to Hiroyuki Suzuki et al. (2003), several formulations with a few matrix bases and corrigents were investigated for the creation of oral chewable tablets that reduced the harsh taste of acetaminophen, which is frequently used as an antipyretic for young children. As matrix bases, corn starch/lactose, cacao butter, and hard fat (Witepsol H-15) were utilised; as bitter taste correctors, sucrose, cocoa powder, and commercial bittermasking powder combination (Benecoat BMI-40) manufactured from lecithin. By contrasting test samples with standards solutions that included quinine at varying doses, the degree of the bitter taste was assessed using volunteers. The bitter taste of the medicine was most effectively suppressed by Witepsol H-15 for the tablets consisting of drug and matrix base, and the bitter intensity generally increased with Witepsol H-15 quantity. When the corrigents were evaluated for their ability to suppress the acetaminophen solution's bitter taste, Benecoat BMI-40 stood out as having the most inhibitory effect. Also, the bitterness levels of chewable tablets manufactured from one matrix base and one corrigent and from one matrix base and two other kinds of corrigents were studied. In order to make them bearable to chew and swallow, the tablets consisting of Witepsol H-15/Benecoat BMI-40/sucrose, Witepsol H-15/cocoa powder/sucrose, and Witepsol H-15/sucrose worked best at masking the bitter taste. The medicine released well from the dose forms that were most effective at concealing bitter taste, showing that masking had no impact on bioavailability. [11]

Objectives:

1. Preformulation research DSC analyses are used to investigate potential chemical interactions between the medicine and the excipient.
2. Wet granulation process for creating chewable Loratadine tablets with various excipients.
3. Assessment of the blend: Hausner's ratio, bulk density, tapped density, compressibility index, and loss on drying
4. Assessment of chewable tablets: Weight fluctuation; hardness; friability; thickness; homogeneity of drug content
5. Making use of USP dissolving apparatus 2, evaluating in vitro release characteristics (paddle).
6. The improved formulation will undergo accelerated and intermediate stability tests in accordance with ICH Guidelines.

Evaluation of Chewable Tablets (Gandhi PP et al., 2010) [12]

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, which is stated in Table 4.11, and if no tablet differs by more than twice.

$$\text{Average weight} = \frac{\text{Weight of 20 tablets}}{20}$$

Table 1: 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).

Result 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.

Table 2: Evaluation of Loratadine chewable tablets

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. [13-14]

Table 3: 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.

The most effective trial was Trial 5, which included a formulation without the use of ethyl cellulose and had 100% drug content at the end of 60 minutes. So, it was ultimately determined that Trial 5 is the optimal formulation that conforms to 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.

Table 4: Percentage cumulative drug release of all formulations

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

: Percentage cumulative drug release of all formulations

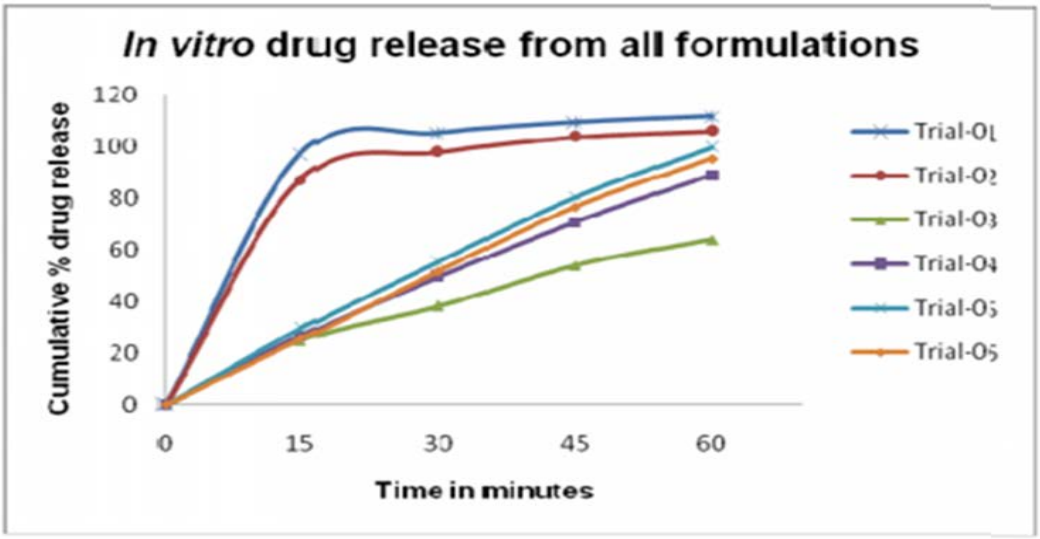

Figure 1: Percentage cumulative drug release of all formulations

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 [15-17]

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

Table 5: 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

Figure 2: Chewable tablets of Loratadine

Conclusion:

Uncoated pills that dissolve quickly in the mouth before being ingested are known as orally disintegrating tablets or orodispersible tablets. Within three minutes, they are gone. These pills combine the benefits of both liquid and traditional tablet forms, making it simple to consume the medication when it is administered in a liquid dose form. Chewable pills must be broken and thoroughly consumed while being eaten in between the teeth. Chewable formulations should ideally disintegrate smoothly, taste well, and leave no harsh or unappealing aftertaste. Bi-layer tablets may be the best alternative to prevent physical separation from causing chemical incompatibilities across APIs and to allow for the creation of various drug release patterns. A bi-layer tablet, with one layer for rapid release as a loading dose and a second layer for maintenance dosage, is appropriate for the sequential release of two medications in combination as well as for sustained release of a tablet (Alderborn G, et al, 1982) [18]

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