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Formulation development and evaluation of acyclovir hard candy lozenges

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Abstract

Lozenges are dosage forms made of solid materials that are meant to dissolve or disintegrate gradually in the mouth. They are flavoured and sweetened to make them taste good, and they contain one or more active substances. Although its main purpose is topical, it may also contain substances with systemic effects. Preformulation studies are typically used to evaluate the physicochemical properties of drugs and determine their compatibility with other excipients. In this study five Acyclovir hard candy lozenges were prepared and the results of the FTIR spectrophotometry indicated that the drug and excipients employed in the formulation of the hard candy lozenges were compatible, as there were no interactions between the drug and the excipients as the peaks remained the same in the FTIR graphs. The manufactured medicated lozenges were tested for drug content homogeneity, hardness, thickness, weight variation, friability, moisture content, in vitro disintegration, as well as dissolution using pharmaceutical standard procedures. The drug concentration of the prepared lozenges ranged from 98.61 to 99.62 %. Among all the formulations F5, showed maximum drug release 100.23% at 35 minutes. Accelerated stability study conducted as per ICH guidelines (zone IV) at 45°C and 75% relative humidity for the best formulation F5 over a period of 30 and 60 days and was found that prepared formulation was stable.

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INTRODUCTION

There are various forms of lozenges. They are intended to be softly dissolved in the buccal cavity to have both a localised and a systemic effect. They comprise a medical substance, sweetener, and flavouring components. are sometimes referred to as pastilles, troches, tablets, and lozenges. They can be used to treat localised mouth or throat irritation or infections, as well as to aid in the systemic absorption of medications. They can contain one or more medications in a flavoured and sweetened base. Lozenges are used for individuals who have difficulty swallowing solid

oral dose forms. They are also used for treatments that are meant to be released gradually so that the drug is present in the oral cavity at a consistent level or so that the drug is absorbed by the tissues in the throat [1][2][3].

The U.S. Food and Drug Administration (FDA) has authorised the prescription antiviral drug acyclovir for the treatment of specific herpes simplex virus (HSV) infections, including genital herpes, as well as to prevent their recurrence. Treat infections caused by the varicella-zoster virus (VZV), such as shingles (herpes zoster) and chickenpox (primary varicella infection). Acyclovir is authorised for use in a variety of dosages and forms in several groups, including those with weakened immune systems. HIV opportunistic infections (OIs) can be caused by HSV and VZV infections. An OI is defined as an infection that affects individuals with compromised immune systems—such as those living with HIV—more frequently or more severely than it does healthy individuals [4][5][6]. The formulation development and evaluation of Acyclovir Hard Candy lozenges is the goal of the current study. To assess the formulated lozenges' physiochemical characteristics, FT-IR analysis, as well as in-vitro release kinetics.

MATERIALS AND METHODS

Materials:

Acyclovir was obtained from Aurobindo Pharma and other excipients such as isomalt, sucrose, liquid glucose, dextrose, mannitol, methyl cellulose, aspartame, citric acid, propylene glycol, polyethylene glycol 200, glycerin, menthol was obtained from SD Fine Chemicals.

Methods:

Drug – Excipient compatibility study

To create a drug that is safe, easy to administer, stable, and effective, the drug and excipients must work well together. The Fourier Transform Infrared Spectrophotometer (FTIR) was used to record the sample in the range of 4000 cm-1 to 400 cm-1 using the potassium bromide pellet technique to conduct a compatibility analysis. The investigation involved an examination and analysis of the spectra.

Formulation of Acyclovir Hard Candy Lozenges:

The lozenges were made using the method of heating and congealing. The necessary amounts of sugar were dissolved in water in a beaker to create the syrupy foundation, which was then stored for heating on a hotplate. The temperature was kept between 105 and 110 °C until it thickened. The medication and all other excipients (except the plasticizer) were manually added and carefully mixed following a 30-minute heating process. A plasticizer was added to the prepared mass after it had been cooked for an additional 45 minutes. The aforementioned syrupy base was then poured into a mould that had been previously cooled and oiled, and the mould was left for ten to fifteen minutes. After being freed from the mould, the lozenges were stored to dry naturally [10].

Table 1 Formulation of Acyclovir Hard Candy Lozenges

Ingredients (mg)	F1	F2	F3	F4	F5
Acyclovir	200	200	200	200	200
Sucrose	1500	2000	-	-	-
Dextrose	1500	1000	1500	2000	-
Liquid Glucose	-	-	1500	1000	-
Isomalt	-	-	-	-	3000
Aspartame	QS	QS	QS	QS	QS
HPMC	0.25 %	0.50 %	1 %	-	2 %
Methyl Cellulose	0.50 %	0.75 %	-	1 %	-
Citric acid	60	60	60	60	60
Sodium Citrate	30	30	30	30	30
Colour	QS	QS	QS	QS	QS
Flavour	QS	QS	QS	QS	QS
Methyl Paraben	2	2	2	2	2

Evaluation parameter:

Weight variation test

Using an analytical balance, ten lozenges from each batch were measured separately in grammes. Calculations are made for the standard deviations as well as average weight. Each lozenge's weight is determined using the same method and contrasted with the average weight. In general, 10% for lozenges weighing 120 mg or less, 7.5% for lozenges weighing 120 mg to 300 mg, and 5% for lozenges weighing more than 300 mg should be the maximum weight fluctuation that occurs. [11].

$$\% \text{ Deviation} = \frac{(\text{Individual weight} - \text{Average weight})\ \text{Average}}{\text{Weight}} \times 100$$

Thickness test:

Using a vernier calliper, the thickness in millimetres (mm) was measured for each of the ten pre-weighed lozenges. Both the standard deviation and the average thickness are given. A lozenge's thickness can alter without affecting its weight.

Hardness test [11]:

A Monsanto Hardness Tester was used to determine how hard the lozenges were. Each batch's ten lozenges, each with a given weight and thickness, had their crushing strength measured in kg/cm2, and their average hardness, as well as standard deviation, were also reported.

Drug Content Uniformity

The weight of one lozenge was used to test the consistency of the content. The powder was dissolved in a 100 ml volumetric flask with 50 ml of 6.8 phosphate buffers, and the mixture was let to stand for 30 minutes. Buffer pH 6.8 was used to bring the mixture up to volume. At 272 nm, the absorbance of the diluted sample was measured. Each test's three replications were examined for mean and standard deviation [12]. The official potency range allowed for the majority of bigger dose drugs in lozenge form is not less than 90% and not more than 110% of the stated amount.

Moisture Content

One gram of the material was weighed using the gravimetric method, and it was then dehydrated for twenty-four hours [13]. The final weight was deducted from the starting weight, and the moisture content difference was computed.

$$\% \text{ Moisture content} = \frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}} \times 100$$

Mouth Dissolving Time:

Using an internal technique, the mouth dissolving time was ascertained. Using a mechanical stirrer at 50 rpm and 100 ml of pH 6.8 phosphate buffers, each lozenge was placed in a separate beaker, and the time it took for the lozenge to dissolve entirely was recorded at 37°C.

In-vitro Drug Release:

Using the modified USP type II (paddle) dissolve test apparatus, 250 ml of the phosphate buffer pH 6.8 dissolution medium was added to the beaker containing the lozenge, and it was agitated at 100 rpm. Five-millilitre aliquot samples are removed every five minutes and promptly replaced with an equivalent volume of fresh medium, such as phosphate buffer pH 6.8. A UV-visible spectrophotometer dilutes each aliquot before analysing it with a blank. The pure drug standard calibration curve is used to calculate the quantity of drug release.

Stability study

By exposing the, stability experiments were conducted in compliance with ICH recommendations. Formulations F5 in their final packing state, measured in a programmable

Table 2 Evaluation Parameter

Formulation code	Weight Variation (mg)	Hardness Kg/cm^2	Drug content (%)	Moisture content (%)	Mouth Dissolving Time(min)
F1	3.292 ± 0.032	10.5 ±0.57	98.61	0.67	10.16
F2	3.295 ± 0.112	13.6±0.64	99.52	0.73	12.26
F3	3.283 ± 0.103	15.25±0.63	99.67	0.46	18.60
F4	3.289 ± 0.132	15.45±0.43	98.61	0.18	26.77
F5	3.295 ± 0.197	15.50±0.74	99.62	1.08	32.67

environmental test chamber (CHM-10S, Remi Instruments Ltd., Mumbai, India) at 40±2°C and 75±5% relative humidity. At 30 and 60 days, aliquots were removed, and the drug content and in-vitro dissolution profile were examined for changes. Stability investigations were conducted on the chosen formulation in accordance with ICH recommendations [14].

RESULTS AND DISCUSSION

Drug – Excipients compatibility study

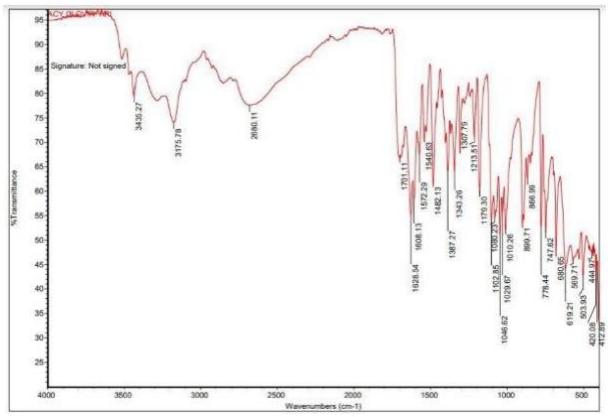

Figure 1 FTIR of Acyclovir

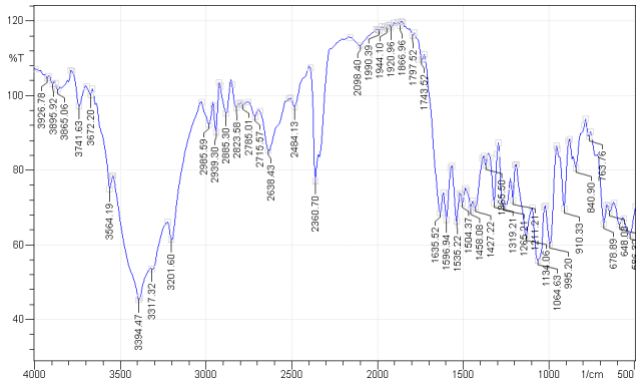

Figure 2 FTIR of Acyclovir + Sucrose

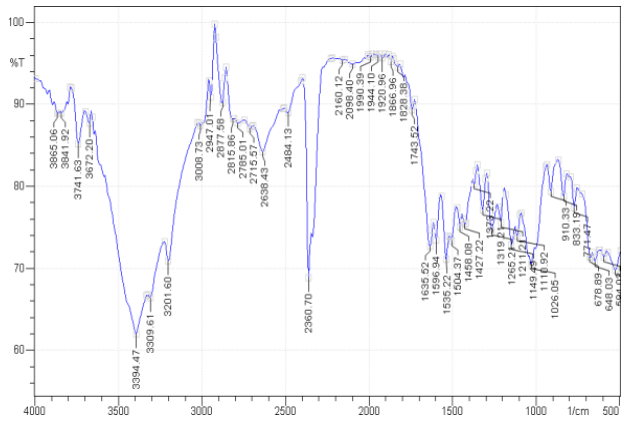

Figure 3 FTIR of Acyclovir + Dextrose

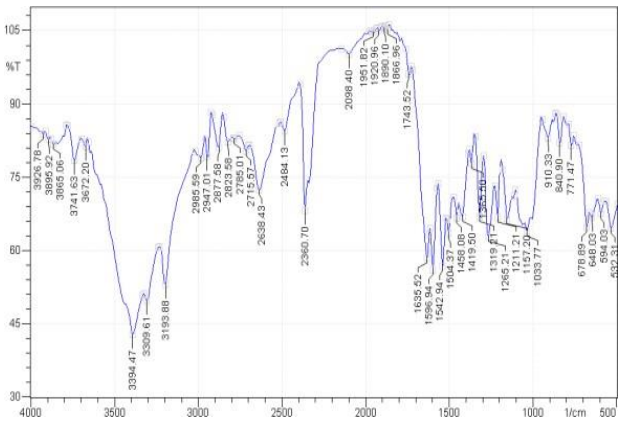

Figure 4 FTIR of Acyclovir + Isomalt

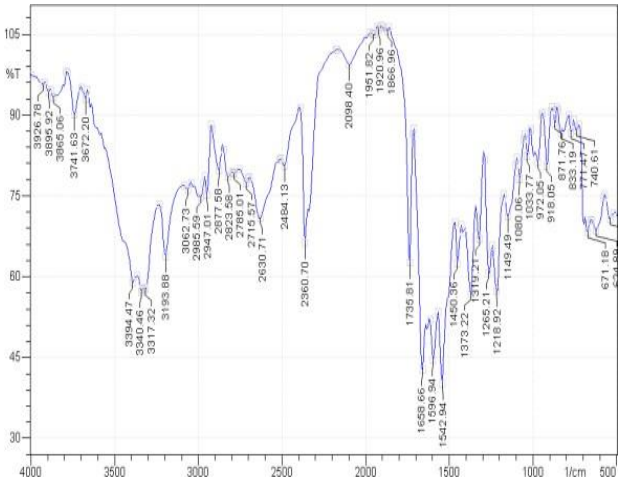

Figure 5 FTIR of Acyclovir + Aspartame

There is no disappearance of drug-specific peaks in FT-IR Spectra. This indicates that there is no interaction between drug and excipients.

In-vitro Drug Release:

Table 3 In-vitro Drug Release

Time	PERCENTAGE DRUG RELEASE (%)				
	F1	F2	F3	F4	F5
5	48.5	38.4	34.11	31.23	24.65
10	87.12	64.44	58.25	41.45	35.14
15	94.67	88.91	78.11	59.87	40.08
20	100.16	97.11	89.88	78.96	71
25	--	99.11	94.66	88.76	83.26
30	--	--	100.12	92.16	91.67
35	--	--	--	99.81	100.23

Evaluation of in-vitro drug release kinetics

Table 4 In-vitro drug release kinetics of Acyclovir Hard Candy lozenges

Formulation Code	Zero Order Profile	First Order Profile
F5	0.9902	0.917

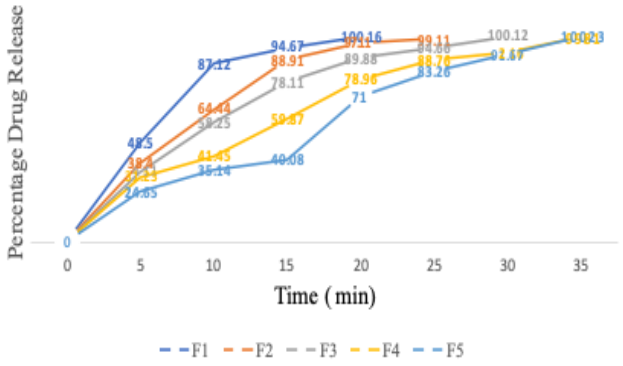

Figure 6 Cumulative percentage drug release profile for medicated Acyclovir lozenges

The in-vitro drug release study, showed that the best formulation (F5) showed the maximum drug release 100.23% at 35 minutes and zero order kinetics.

Table 5 Stability Study

Evaluation Parameter	Optimized Formulation (F5)	After Stability Study of one Month
Weight variation	3.295	3.29
Hardness	15.50 kg/cm3	15.10 kg/cm3
Moisture Content	1.08 %	1.02 %
Mouth dissolving Time	32.67 min	31.07 min
Content uniformity	99.62 %	99.02 %
Drug release	100.23 %	99.83 %

CONCLUSION

In this current study, Acyclovir Hard Candy Lozenges with a dose of 200mg were developed and evaluated. The interaction between the drug and excipients were determined by FTIR spectroscopy which indicated that there is no interaction between the drug and excipients. Lozenges were prepared by heating and coagulation technique using liquid glucose, sucrose, dextrose, isomalt, methylcellulose, HPMC, colour and flavour. Developed Acyclovir hard candy lozenges were evaluated for various physico-chemical evaluation parameters and were found to be within the standard limits. Acyclovir hard candy lozenges with Isomalt (F5) was optimized. In-vitro drug release study indicated that formulation (F5) showed maximum drug release100.23% at 35 minutes. This study suggested that Acyclovir Hard Candy Lozenges can be considered as the potential delivery system for the treatment of Herpes simplex virus.

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Conflict of Interest: The Author declares that there is no conflict of interest.

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