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FORMULATION AND IN-VITRO EVALUATION OF OLOPATADINE HYDROCHLORIDE MOUTH DISSOLVING TABLET USING NOVEL COPROCESSED SUPERDISINTEGRANT

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ABSTRACT

The purpose of present study outlines systematic approach for designing and development of Olopatadine HCl Mouth Dissolving Tablet. The objective of the present investigation is to formulate Olopatadine Hydrochloride Mouth Dissolving Tablet using novel co-processed superdisintegrant by direct compression method which gives rapid action by means of rapid release of drug as compared to conventional dosage form.Ludiflash was used as coprocessedsuperdisintegrant, another is MCC 102. Final optimized formulation was found to be promising and showed In-vitro absoration ratio of 47 sec, wetting time of 53 sec and in vitro disintegration time 36 sec facilitate faster dispersion in aqueous media and in vitro drug release was 94 % in 10 minute. Study revealed that Ludiflash gives wicking and swelling action combinely to give rapid release of drug.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms.

Mouth Dissolving Tablet disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue, that is it disperses rapidly before swallowing within 15 seconds to 3 minutes without the need of water or chewing.[1]

Drug candidate criteria for formulation:[2]

No bitter taste.

Dose lower than 20mg.

Small to moderate molecular weight.

Good stability in water and saliva.

Ability to diffuse and partition into the epithelium of the upper GIT. (logp>1, or preferably>2)

Drug: Olopatadine Hydrochloride

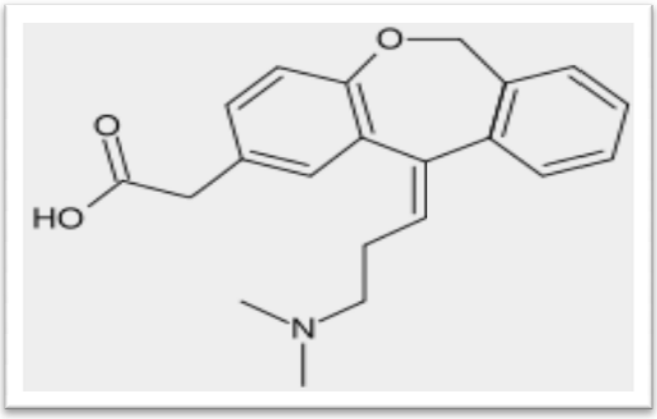

Figure no. 1: Structure of OlopatadineHCl [4,5,6,7,8]

Chemical Name: -11 Z)-3-(Dimethylamino) propylidene -6,11-dihydrodibenz (b,e oxepi-2-acetic acid, hydrochloride.

Molecular Formula: $C_{21}H_{23}N$ .HCl

Molecular Weight: 373.88

Category: Antihistaminics, Antiallergic agents.

Description: White crystalline powder.

Solubility: Sparingly soluble in water,

Freely soluble in methanol.

Storage: Store in cool and dry place protected from direct sunlight.

Melting point: 256-260^0 C.

Pk_a:9.76

Logp :3.4

Half-life: 3 hrs

Protein binding: Approximately 55% bound (mainly albumin)

Indication and Usage: Conjuctivitis, allergic(treatment), opthalmicoplopatadine is Indicated for temporary prevention of itching of the eye due to allergic conjunctivitis.

Mechanism of action: Olopatadine is a relatively selective histamine H_1-receptor antagonist that inhibits the type 1 immediate hypersensitivity reaction in vivo and in vitro. Olopatadine also inhibits the release of histamine from mast cells. Olopatadine does not affect alpha-adrenergic, dopamine, muscarinic types 1 and 2, or serotonin receptors.

MATERIALS AND METHOD

The Drug sample of OlopatadineHCl was gifted by Glenmark Pvt. Ltd, Mumbai. Excipients Ludiflash obtained from BASF Pharma and MCC102 from Bansal labLimited, Nashik, Dibasic calcium Phosphate and Magnesium stearate from Modern scientific laboratories, Nashik.

Table no.1: List of instruments

Instrument	Manufacturer
UV Visible Spectrophotometer	SHIMADZU 2450
FT-IR Spectrometer	SHIMADZU 8400S
DSC	SHIMADZU 60
Tablet Dissolution Test Apparatus	LAB INDIA-DISOTEST, 6 F 622
Friability tester	KUMAR MFG. LTD.
Tablet compression machine	GENERAL MACHINERY CO., MUMBAI.

Manufacturing of Tablets : The corresponding amount of OlopatadineHCl drug, Ludiflash, MCC 102, Magnesium stearate, Diabasic Calcium Phosphate, were accurately weighed.The powders were screened through screen #60. The screened powders were transfered to mortar and mixed for 20 minutes. Compression was carried out using 7 mm flat-faced circular punches on rotary compression machine.[1]

Table no. 2: Composition of optimized formulation (F9):

Optimized formulation	Olopatadine HCl	Ludiflash	MCC 102	Magnesium Stearate	DCP	**Total**
Quantity (mg)	10	90	21	3	6	130

Where, MCC- Microcrystalline cellulose

DCP- Dibasic Calcium Phosphate

Evaluation of tablet: [1,7,8]

Appearance: appearance (colour, size, shape)of tablet is check.

Uniformity of weight: In this test 20 tablets were weighed individually and average wt. was calculated from total wt. of all tablets. The individual wt. compared with average wt. The percentage difference in the wt. variation should be within acceptable limit (7.5%)

Hardness test: This test was determined using a Monsanto tablet hardness tester.

Friability test: Friability of tablet was tested using Roche Friabilator (limit = 1%)

Thickness: Thickness of tablet was measured using screw micrometer.

Wetting Time: Five circular tissue papers of 10 cm diameter were placed in a Petri dish with a 10-cm diameter.Ten milliliters of water containing a water-soluble dye (eosin) was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablet was noted as the wetting time.

Water absorption Ratio:A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured .

In vitro Disintegration Time: Disintegration apparatus were used.

Dissolution test: Dissolution apparatus were used for the dissolution test of tablet.

Table no.3: Evaluation test results of optimized formulation (F9)

Test	**Formulation (F9)**
Uniformity of weight (%)	130.51± 0.650
Hardness test (kg/cm^2)	2.26±0.20
Friability test (%)	0.9651±0.14
Thickness (mm)	2.91±0.01
Water absorption ratio	47±0.82
Wetting Time(sec)	53±1.35
Disintegration time (sec)	36±0.98
Dissolution test (%)	99.33±1.08

Drug polymer compatibility studies: The compatibility studies were carried out to determine any kind of chemical interaction of drug with the excipients used in the preparation of stable tablet formulation. Fourier transform infrared spectra were obtained by using an FTIR spectrophotometer (SHIMADZU 8400s)

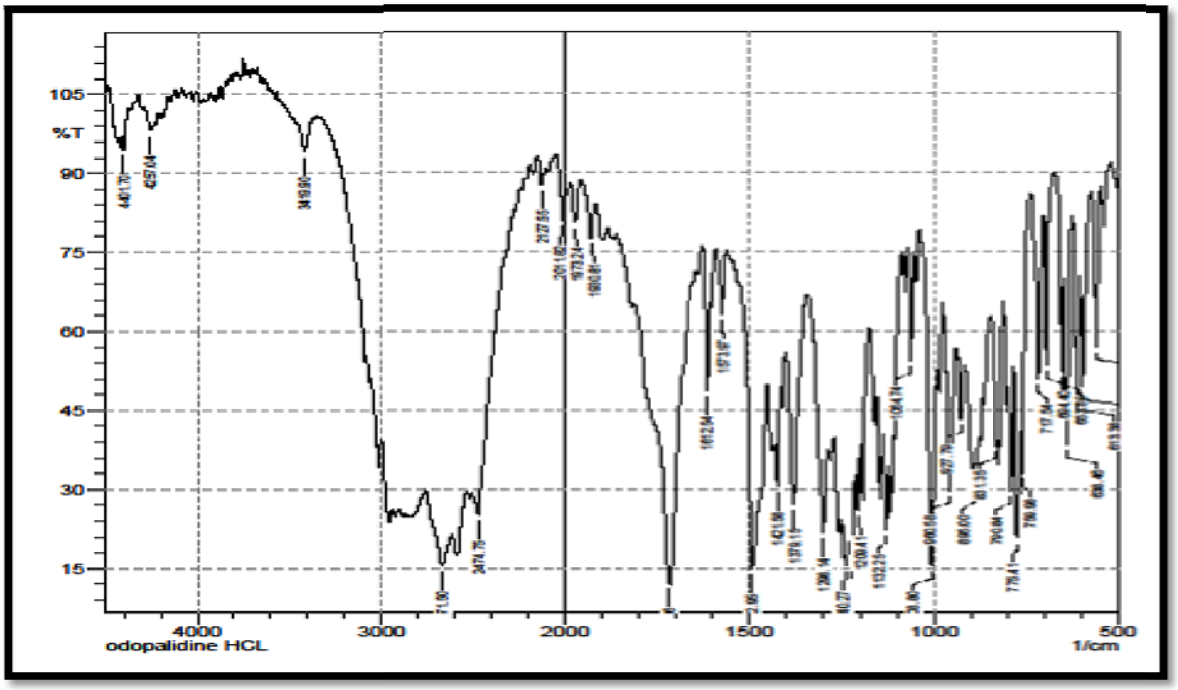

Figure no.2: FT-IR spetra of OlopatadineHCl

Table no.4: Interpretation of FTIR spectrum of OlopatadineHCl

Drug	Observed Peak (cm^{-1})	Inference
Olopatadine	1422	C-Nstretching
	3419	-OH stretching
	1491	C-C aromatic
	1717	C=O stretching
	717	Aromatic

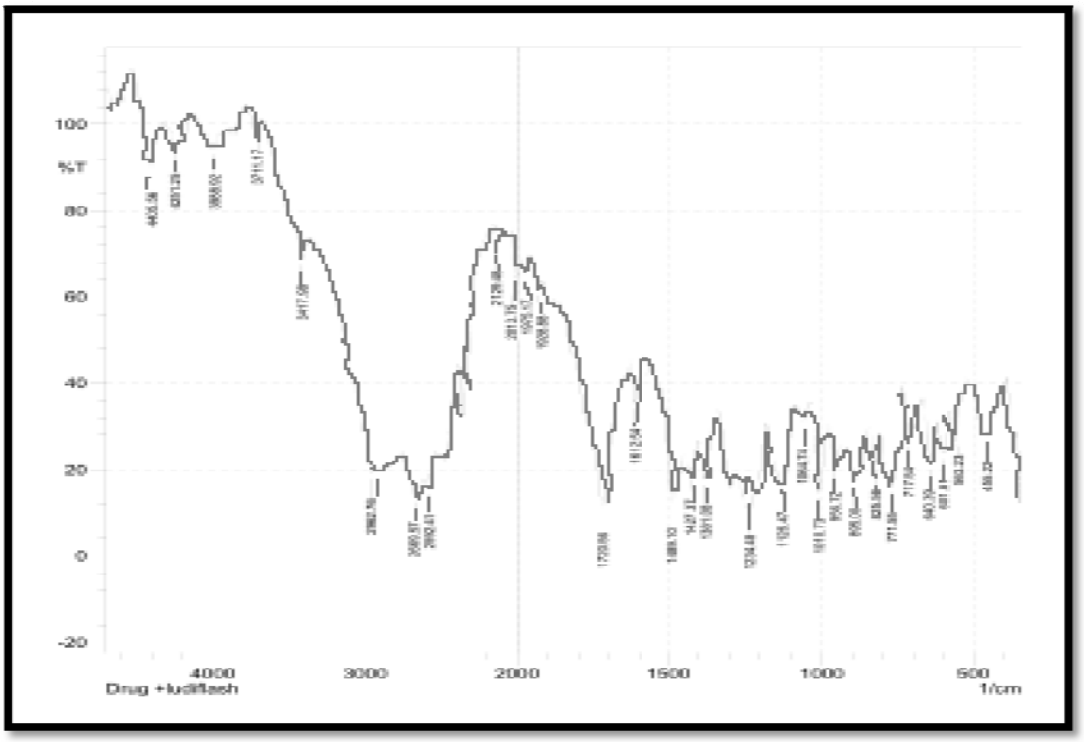

Figure no.3: FT-IR spectrum of Drug and Ludiflash

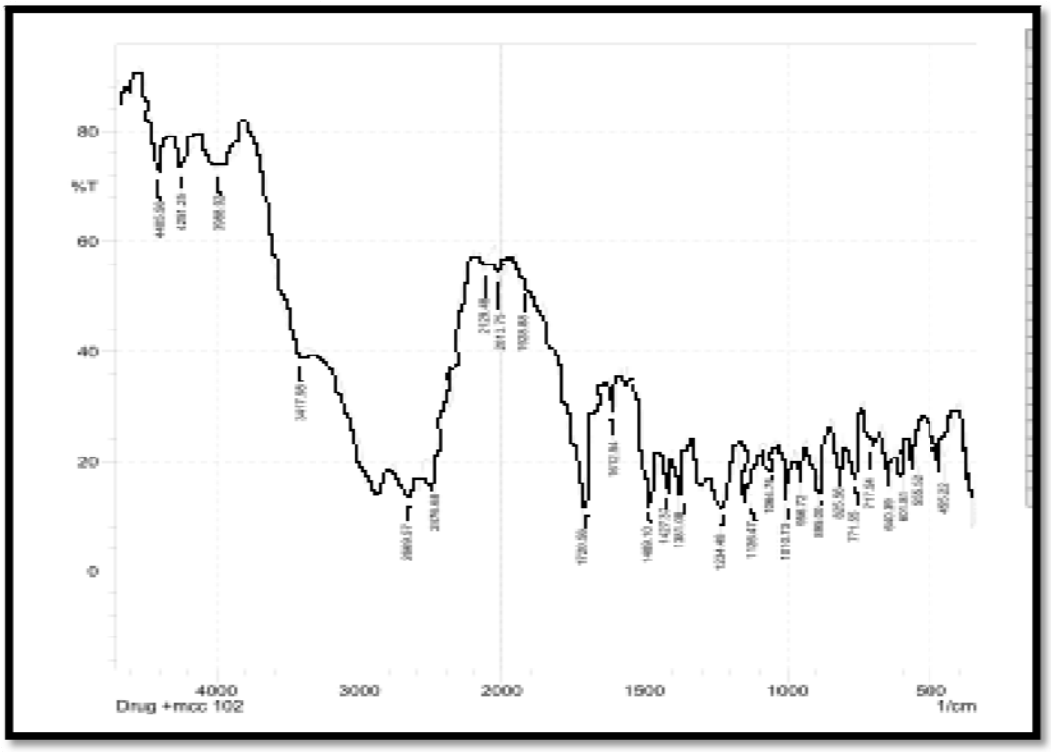

Figure no.4: FT-IR spectrum of Drug and MCC102

Table no.5: Interpretation of FTIR spectrum of OlopatadineHCl plus polymers

Functional group	C-C aromatic STR	C-N STR	O-H STR	C-O STR	aromatic
Pure drug	1491	1422	3491	1717	717
Drug + Ludiflash	1489	1426	3489	1720	717
Drug + MCC 102	1489	1427	3493	1720	717

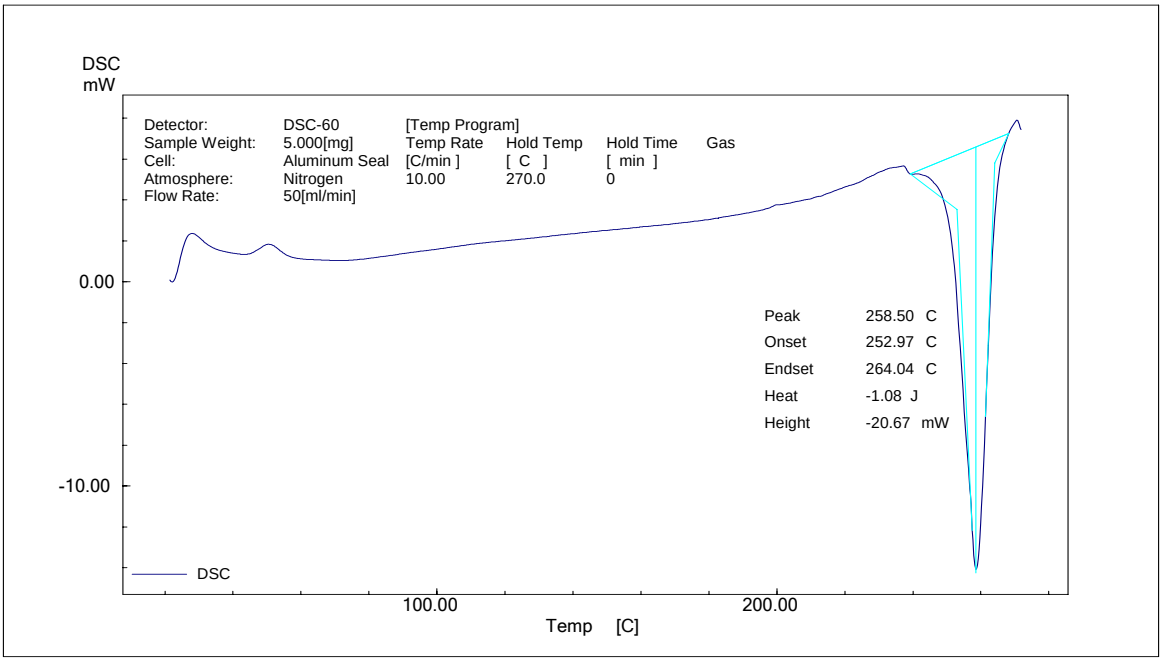

Figure no.5: DSC of OlopatadineHCl–exothermic peak at 258°C

Stability Study:

Stability testing of optimized formulation (F9):

The tablets of optimized formulation was wrapped in aluminium foil and subjected to accelerated stability studies at 40% and 75% RH for 1 month.

Table no.6: Stability data of optimized formulation (40%75%RH)

Formulation	Time	DisintergationTime (seconds)	%Drug release (disso)
F9	First day	38 ± 1	95.78±0.42
F9	After 1 Month	35± 0.98	94.70±0.42

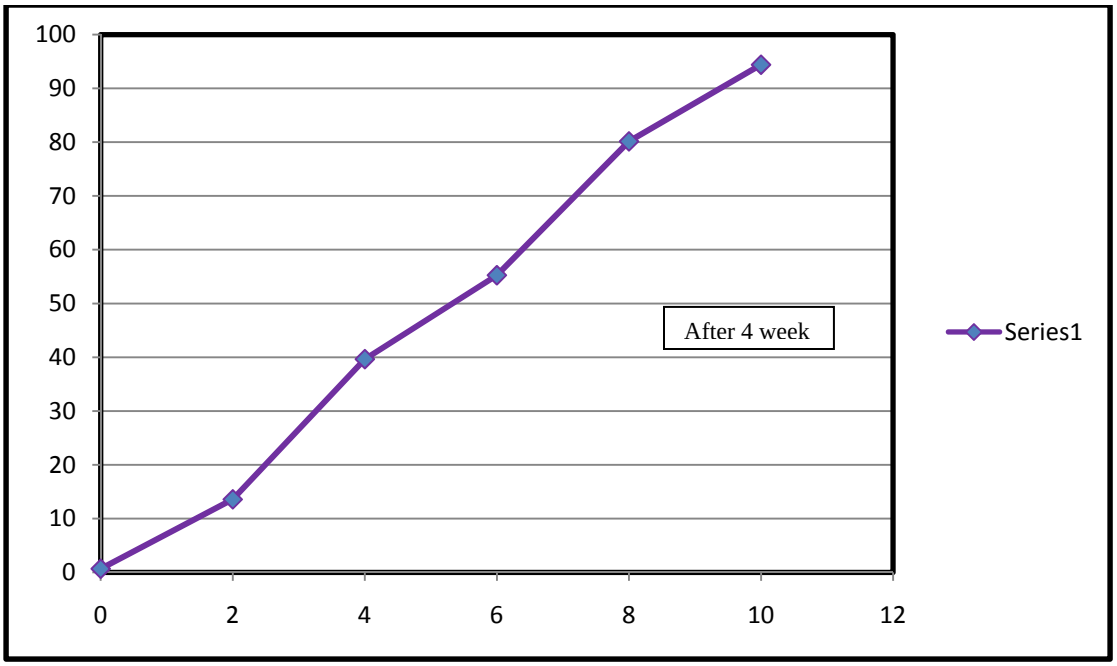

Figure no.6: Dissolution profiles of Optimized (F9) at 40^0C

RESULT AND DISCUSSION

Recent advances in novel drug delivery system aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. Approach is formulation of MDTs, because of the numerous advantages like administration without water, accuracy of dosage, easy administration, alternative to liquid dosage form, ideal for pediatric and geriatric patients and rapid onset of action. Need of the study is to formulate and *In-Vitro* evaluate Mouth Dissolving Tablet of Olopatadine Hydrochloride using novel co-processed superdiintegrant. Evaluation of Uniformity of weight, Water absorption ratio, wetting time, disintegration and dissolution study given in table no.3 The received gift samples of Drug and Polymers were found to be as per standards. FT-IR, UV. Study reports shows in figure no. 1, 2, 3 and 4 that there is drug-polymer compatibility. Optimization of the formulation by changing the concentration of polymers has been carried out. The optimized formulation is shown in table no.2. Developed a effective Mouth Dissolving Formulation of OlopatadineHCl. Stability Study of Optimized Formulation has been performed.Stability data of optimized formulation (40%75%RH) is shown in table no.6 F9 formulation was found to be promising and showed In-vitro absoration ratio of 47 sec, wetting time of 53 sec and in vitro disintegration time 36 sec which facilitate the faster dispersion in the aqueous media. And in

vitro drug release was found to be 94 % in 10 minute. The optimized formulation was found to be stable in short-term accelerated testing done for one month at 40^0C. There has been no significant difference in dissolution profile, hardness and physical appearance.

Study reveals that the rapid disintegration of tablet is found due to combined effect of wicking and swelling action of novel co-processed superdisintegrant.

CONCLUSION

From the all *In-vitro* evaluation data and stability study it is found that the Mouth Dissolving Tablet of OlopatadineHCl satisfactory complies the results.

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