JOURNAL OF SCIENTIFIC RESEARCH IN ALLIED SCIENCES
ISSN NO. 2455-5800
DOI No. 10.26838/JUSRES.2021.7.5.511
Contents available at www.jusres.com

FORMULATION & EVALUATION OF DESLORATADINE FAST DISINTEGRATING TABLET

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ARTICLE INFO

Article History
Received: Sept 2021
Accepted: Oct 2021
Keywords:
fast dissolving tablets, Desloratadine, drug delivery systems, drug-resin

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ABSTRACT

ORIGINAL RESEARCH ARTICLE

Fast dissolving drug delivery have gained significant appeal and acceptability as innovative drug administration methods, owing to their ease of use and patient compliance. Patients' low acceptability and compliance continue to drive the demand for non-invasive delivery solutions. In the GI tract, uterus, major blood arteries, and airway smooth muscle, desloratadine compete with unbound histamine for binding to H1-receptors. The goal of this study was to create and formulate Desloratadine fast-dissolving tablets. Fifteen sets of formulation were made with an exactly weighed amount of drug-resin complex combined with various proportions of super disintegrant (1.5 percent, 3 percent, 4.5 percent, 6 percent, 7.5 percent) (Sodium starch glycolate, Crospovidone, Croscarmellose Sodium). The formulation was tested for thickness, hardness, wetting time, friability, and other factors. In addition, the compositions were tested for in vitro disintegration and dissolution times. In vitro dissolving tests revealed that all formulations released more than 90% of the medication after 10 minutes. 7.5 percent Crospovidone (F-10) showed the greatest increase in dissolving rate among all formulations. Within 10 minutes, 97.12 0.37 percent of the product was released. The best formulation was discovered to be F-10, which had a shorter disintegration time and higher drug release.

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INTRODUCTION:

Despite tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low-cost therapy, self-medication, non-invasive method, and ease of administration leading to a high level of patient compliance. Recently, fast disintegrating drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance. In some cases, such as motion sickness, sudden episodes of allergic attacks or coughing, and unavailability of water, swallowing conventional tablets may be difficult. "Oro Dispersible Tablet" is defined as an uncovered tablet for a buccal cavity, where it disperses before ingestion". Fast disintegrating tablets (FDT) are also known as fast-dissolving, mouth dissolving, rapid-dissolve, quick disintegrating.

The need for non-invasive delivery systems persists due to patients' poor acceptance and compliance with existing

delivery regimes, the limited market size for drug companies and drug uses, coupled with the high cost of disease management.

There are some under mentioned mechanisms by which the tablet is broken down into smaller particles and then subsequently result in a solution or suspension of the drug

The mechanisms are-

The high swell ability of disintegration
Chemical reaction
Capillary action.

Desloratadine competes with free histamine for binding at H_1-receptor in the GI tract, uterus, large blood vessels, and bronchial smooth muscles.

This blocks the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine. The present study is aimed to formulate and evaluate fast disintegrating tablets of desloratadine.

MATERIAL AND METHOD:

UV Calibration curve of desloratadine:

Add 50ml of 0.2M potassium dihydrogen orthophosphate in a 200ml of volumetric flask. Add 3.6ml of 0.2M Sodium hydroxide is added and makeup to the volume with distilled water.

An accurately weighed quantity (100mg) of pure Desloratadine is dissolved in a sufficient amount of methanol and made up to 100ml with methanol to produce 1mg/ml solution. From this 10ml of the solution is pipetted out and made up to 100ml with the 0.1N Hydrochloric acid buffer solution. From this 2-20ml are pipetted out and diluted to 100ml with the 0.1N Hydrochloric acid buffer solution. The solution is scanned within the range of 200-400 nm in a UV-Spectrophotometer. The absorbance of the solutions is measured at the λmax. The calibration graph is drawn by taking a concentration in X-axis and respective absorbance in Y-axis to get a straight line as per Beers law.

Preparation of drug-resin complex (DRC):-

The drug and resin are passed through a #40 mesh screen before mixing. The drug desloratadine is dispersed in purified water (100ml) under stirring by using a magnetic stirrer at 100 rpm at room temperature (25-27˚C). The pH of the drug dispersion is adjusted to pH 6.5 ±0.5 with 2% W/V citric acid solution. The resin is then added to the pH-adjusted drug dispersion and stirred for 3 hours. The drug resinate dispersion is filtered through Whatman filter paper No;41 and dried at 60˚C. The dried mass is passed through the #24 mesh.

Selection of ion–exchange resin (IER):-

The DRC is prepared with two different resins viz INDION-204 and INDION- 234. In each case, 100mg of Desloratadine in deionized water is stirred with resin containing various drug-resin ratios (1:1, 1:2, 1:3, 1:4, 1:5) by using a magnetic stirrer and stirred for 3 hours at 100 rpm at room temperature. Then the dispersion is filtered through Whatman filter paper No; 41. The amount of drug-loaded is determined indirectly by estimating the amount remaining to be loaded in solution spectrophotometrically at 242 nm in UV-Spectrophotometer. The resin to which the drug is bound to the maximum percentage is selected for further studies. The following formula is used to calculate the percentage of drugs bound to the resin.

$$\%\text{Drug Bound to Resin} = \frac{(\text{Total amount of drug}) - (\text{unbound drug})}{(\text{Total amount of drug})} \times 100$$

EVALUATION OF DRUG RESIN COMPLEX

Fourier Transform-Infra Red (FT-IR) Studies:

Desloratadine, indion-234 and DRC are subjected to Fourier Transform Infra Red Spectroscopy studies (Shimadzu, Japan). Samples are prepared using KBr disc method and spectra are recorded over the range 400-4000 per cm. Spectra are analyzed for drug-resin interaction and functional groups involved in the complexation process.

Differential Scanning Colorimetric (DSC)studies:

A Differential Scanning Calorimeter (DSC Q200 V24.4 Build 116) is used. The equipment is calibrated using indium and zinc. Samples are heated at 10°C per minute in aluminum pans under a Nitrogen atmosphere. The onset of the melting points and enthalpies of fusion are calculated. The cell had a nitrogen purge flowing approximately at 30 cube cm per minute. The cell and sample are held isothermally at 79°C for 30 minutes to purge the headspace and sample with nitrogen before heating. The cell and sample are then heated to 400°C while monitoring heat flow.

Formulation of fast dissolving tablet of Desloratadine

An accurately weighed quantity of drug-resin complex is mixed with different ratios of (1.5%, 3%, 4.5%, 6%, 7.5%) super disintegrant (Sodium starch glycolate, Crospovidone, Croscarmellose Sodium). The drug-resin complex along with super disintegrant is mixed with Microcrystalline cellulose, Mannitol, Saccharin sodium, and Peppermint flavor in geometrical dilution. Then Magnesium stearate and Talc are added, mixed, and compressed into tablets using a single punch tablet punching machine to produce flat-faced tablets weighing 200mg each with 8mm diameter. The compositions of the different formulations are given in Table-5.

The flow characteristics are measured by the angle of repose. The angle of repose is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

$$\tan \theta = h/r \quad \theta = \tan^{-1}(h/r)$$

Where,

h=Height of the pile.

r=Radius of the base of the pile.

θ=Angle of repose.

The angle of repose is determined by the fixed funnel method. The powder mass is allowed to flow through the funnel kept on a stand at a fixed height. The powders are carefully poured through the funnel on the piece of paper placed on the horizontal surface until the apex of the conical pile just reached the tip of the funnel. The height of the pile and radius of the conical pile is noted and the angle of repose is calculated by the above-said formula.

Post Compression Evaluation

Thickness and Diameter

Tablet thickness and diameter is important characteristic of the tablets. In reproducing appearance and also in counting by using filling equipment. The thickness and diameter of the fast-dissolving tablets are determined by using a vernier caliper.

Hardness

The hardness of the tablet is indicative of its tensile strength and is measured in terms of the load/pressure required to crush it when placed on its edge. The hardness is a function of the physical properties of granules like their hardness and deformation under load, binders, and above all the compression force. The hardness influences disintegration and dissolution times and is such a factor that may affect bioavailability. The hardness of the tablet is determined by using the Monsanto hardness tester.

Weight Variation Test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation. The tablets meets the USP test , If no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limits. USP specification for the uniformity of weight

Uniformity of content

Ten tablets are selected randomly and powdered. The average weight is calculated.

The average weight of the tablet powder is dissolved in 100ml of 0.1N Hydrochloric acid, stirred for 60 minutes by using a magnetic stirrer at 100rpm maintained at room temperature. The dispersion is filtered and collected by the filtrate. One ml of filtrate is diluted to 100ml with 0.1N Hydrochloric acid. The absorbance of this solution is measured at 242 nm using 0.1N Hydrochloric acid as blank and the content of desloratadine is estimated.

Wetting Time:

Ten milliliters of distilled water containing Methylene blue, water-soluble dye is placed in a Petri dish of 10 cm diameter. Tablets are carefully placed in the center of the Petri dish and the time required for water to reach the upper surface of the tablet is noted as the wetting time. Three tablets are selected and the average wetting time is calculated.

In-Vitro Disintegration Time

The disintegration time is defined as the time necessary for the Fast disintegrating tablet to completely disintegrate until no solid residue remains or only a trace amount of soft residue remains on the screen. Disintegration time is measured in 900 ml artificial saliva (pH 5.8), according to the USP 24 methods without disc at 37 ±0.5°C. The disintegration time of 3 individual tablets are recorded and the average is reported. As per the European Pharmacopoeia (EP), the orodispersible tablets should disintegrate within 3 minutes.

In-Vitro Dissolution Test:

The release rate of desloratadine from the fast dissolving tablet is determined using dissolution testing apparatus type -1(paddle method). The dissolution test is performed using 900ml of 0.1N HCL, at 37 ±0.5°Cand 50 rpm.A sample (5ml) of the solution is withdrawn from the dissolution apparatus at 5,10,15,20,25,30 min. The samples are replaced with a fresh dissolution medium of same quantity. The absorbance of these solutions is measured at 242 nm in UV-Spectrophotometer.

RESULT AND DISCUSSION:

UV Calibration Curve:

The drug showed no adulteration and showed a purity of desloratadine. Also, the R^2 value was found to be 0.9994 best fit of a linear line.

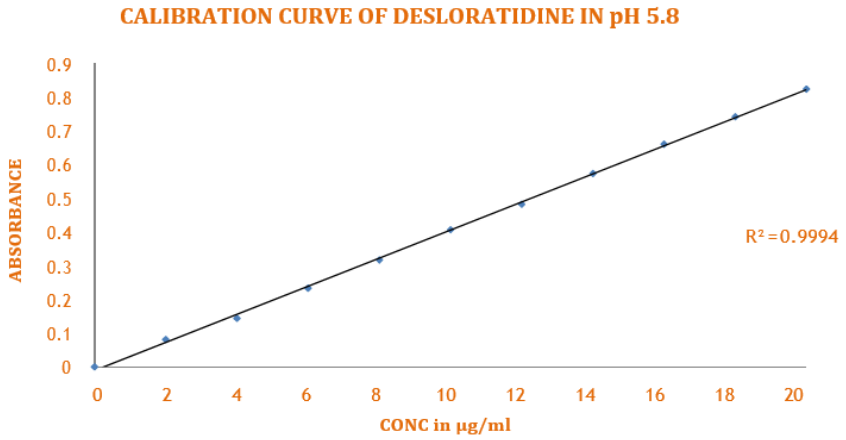

Figure 1: UV Absorption calibration curve of Desloratadine at various concentration levels

FTIR Spectrometry:

For the nitration between the active pharmaceutical ingredients and excipients, FTIR studies were performed for pure drug, excipient only, and a mixture of drug excipients to avoid the chances of interaction if any.

From the study, it was observed that there is no interaction found between the drug and excipients as all the peaks of FITR observed in the drug alone were also present in the mixture.

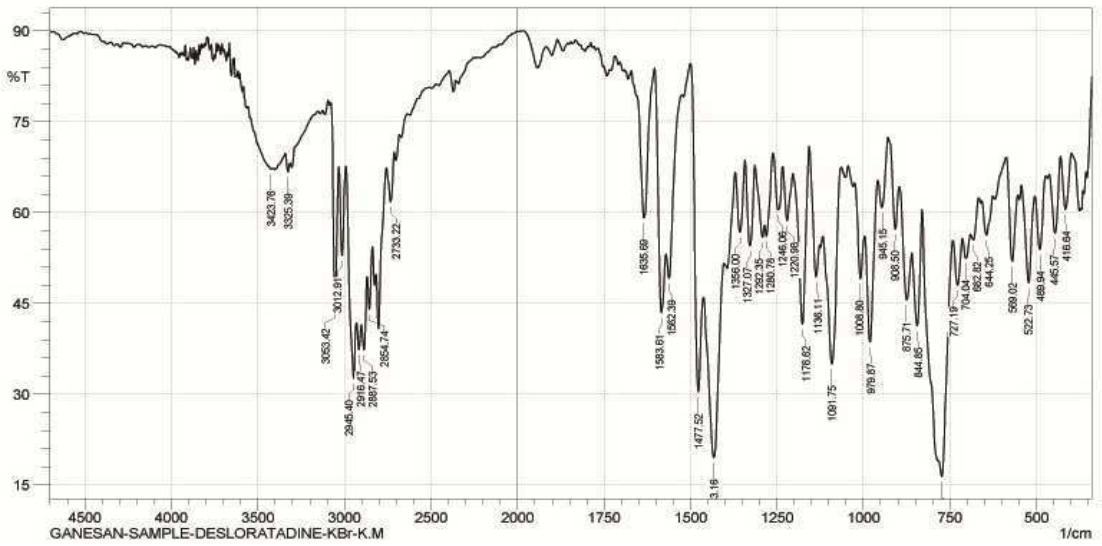

Fig 2: FTIR spectrogram of Desloratadine

Fig 3: FTIR spectrogram of Indion 234

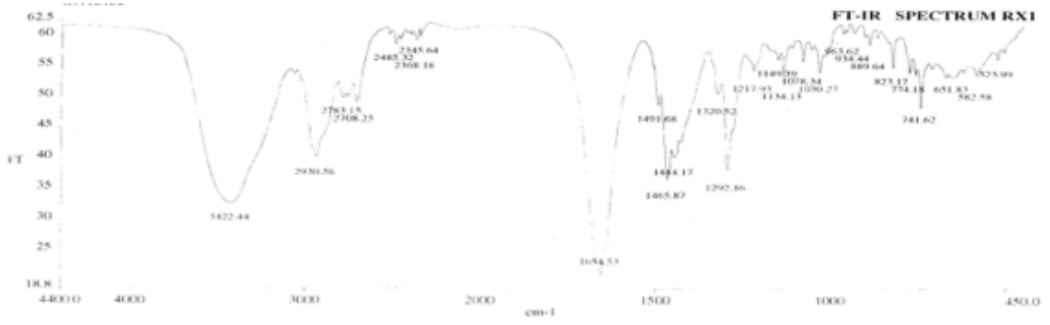

Fig 4: FTIR spectrogram of DRC (Drug-Resin Complex)

DSC Thermogram:

Also, the DSC thermogram was performed for pure drug Desloratadine and found to have a sharp peak at 155.67ºC. Also, the DSC of resin showed a blunt peak at 96.99ºC. Both the peaks were present in the final DSC of DRC. The DSC thermogram is shown in Fig 5-7.

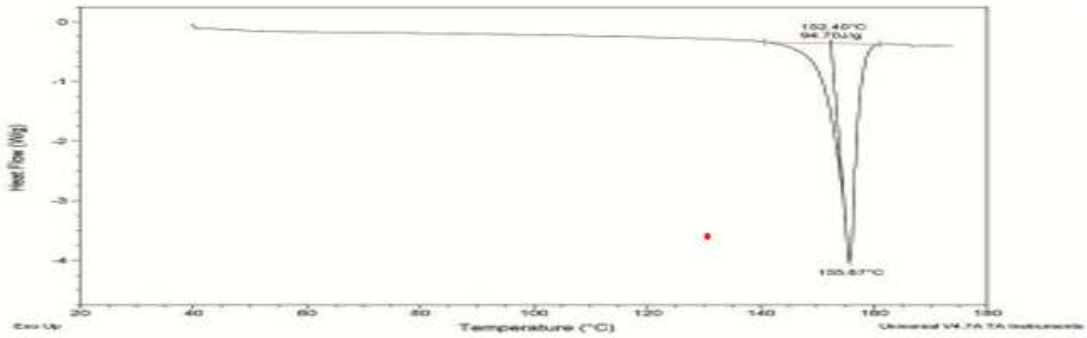

Fig 5: DSC Thermogram of Delsoratadine

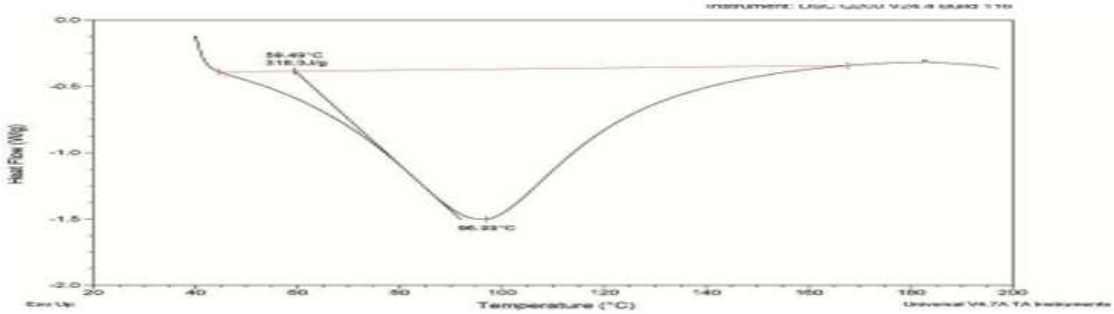

Fig 6: DSC Thermogram of Resin

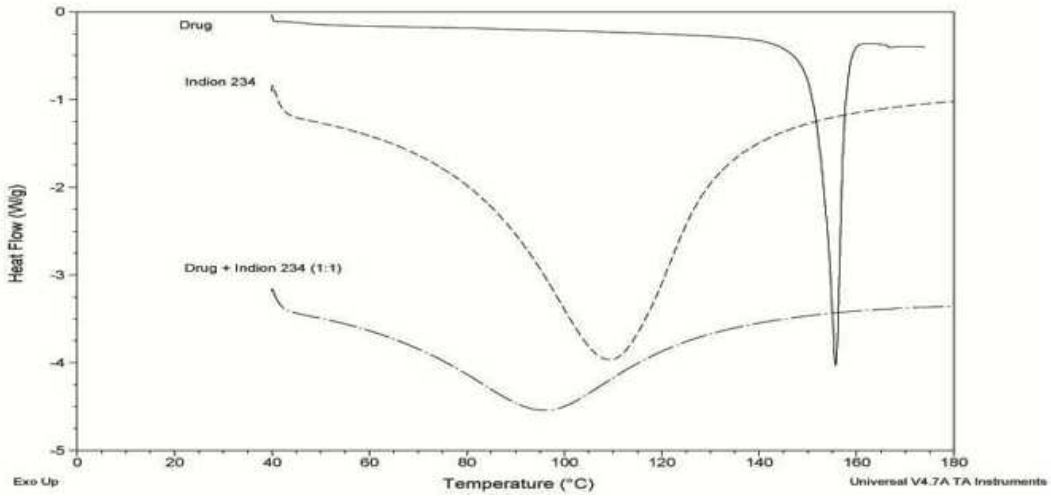

Fig 7: DSC Thermogram of DRC

Formulations of fast dissolving tablets:

Table 1: Formulation ratio of fast dissolving tablets of Delsoratadine

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
DRC (Eq.to 5mg of desloratadine) (mg)	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45	34.45

Sodium Starchglycolat (mg)	3	6	9	12	15	–	–	–	–	–	–	–	–	–	–
Crospovidone (mg)	–	–	–	–	–	3	6	9	12	15	–	–	–	–	–
Croscarmellose sodium(mg)	–	–	–	–	–	–	–	–	–	–	3	6	9	12	15
Mannitol (mg)	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
Microcrystalline cellulose(mg)	99.55	96.55	93.55	90.55	87.55	99.55	96.55	93.55	90.55	87.55	99.55	96.55	93.55	90.55	87.55
Sodium saccharin (mg)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Peppermint flavor (mg)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium stearate (mg)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Talc (mg)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total Weight (mg)	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200

15 batches of the formulations were prepared according to the proposed ratio of the ingredients. The angle of repose was calculated for the mixture of the formulations and found to have as follows. (Table 2)

Table No. 2: Results of Angle of Repose of all 15 formulations

Formulation	**Angle of Repose (˚)**
F1	31.79
F2	30.27
F3	30.80
F4	29.91
F5	29.49
F6	29.74
F7	29.92
F8	29.07
F9	29.51
F10	29.55
F11	29.25
F12	29.49
F13	28.35
F14	28.84
F15	28.72

Evaluation of the formulations:

All the formulations were evaluated for Thickness, Hardness Uniformity, and wetting time.

Table No. 3: Results of evaluation of the formulations

Formulation code	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Weight variation range(mg)	Wetting time (sec)
F1	3	8	3	202.08-234.84	47
F2	3	8	3	200.84- 233.4	56
F3	3	8	3	191.9-223	40
F4	3	8	3	204.12-237.2	35
F5	3	8	3	179.24-208.3	27
F6	3	8	3	182.04-211.56	26
F7	3	8	3	182.93-212.59	14
F8	3	8	3	178.78-207.76	8
F9	3	8	3	179.92-209.08	8
F10	3	8	3	185.72-215.82	5
F11	3	8	3	178.52-207.46	17
F12	3	8	3	183.12-212.8	16
F13	3	8	3	184.13-213.97	17
F14	3	8	3	184.51-214.43	14
F15	3	8	3	182.97-212.63	11

All the prepared tablet formulations were found to be good without capping and chipping. The flow properties of all formulations show within the acceptable range. All the formulations were found to have the same thickness and hardness properties. There is very little weight variation was observed among all the formulations.

Disintegration Time and dissolution rate:

Table No 3: Results of disintegration time and dissolution rate of all the formulations

Formulation code	Disintegration time (sec)	Max % of drug release at 10 min (Avg ± S.D)
F1	48	95.82 ± 0.67
F2	47	95.75 ± 1.095
F3	44	96.42± 0.538
F4	30	91.83 ± 0.66
F5	20	92.19 ± 0.844
F6	23	96.68 ± 0.658
F7	16	94.54 ± 0.586
F8	10	93.48 ± 0.588
F9	8	96.55 ± 0.528
F10	6	97.12 ± 0.374
F11	15	90.95 ± 0.374
F12	13	91.55 ± 0.769
F13	14	93.43 ± 0.597
F14	11	95.09 ± 0.757
F15	10	93.71 ± 0.527

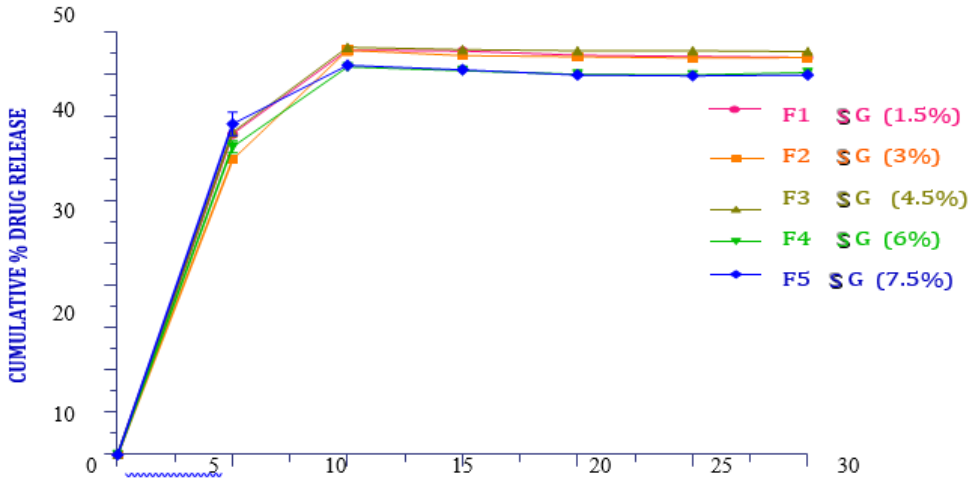

Fig 8: Comparison of In vitro Release Profile of Desloratadine Containing Different Percentage of Crospovidone

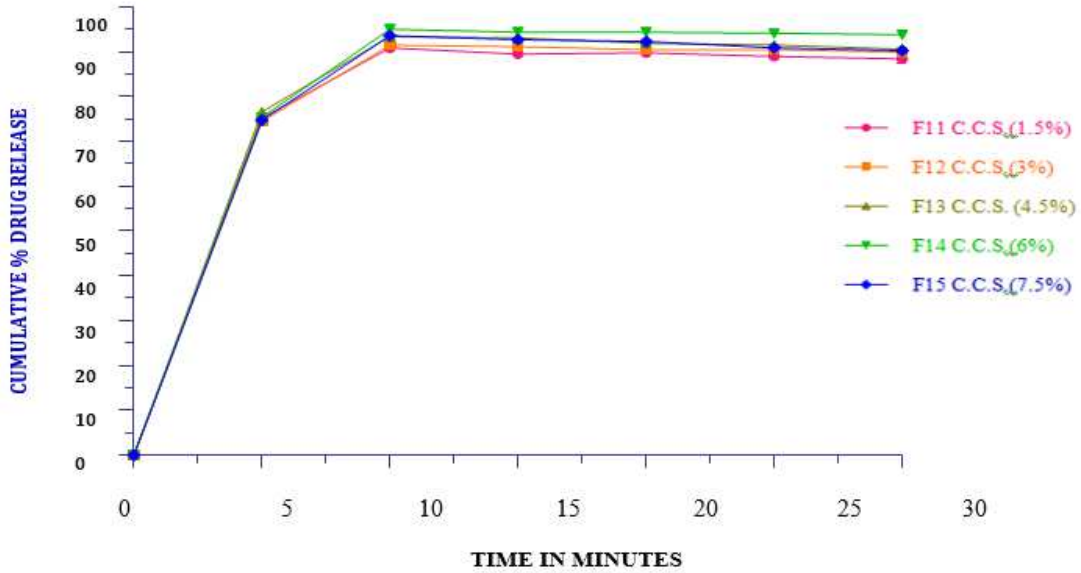

Fig 9: Comparison of invitro release profile of desloratadine containing different percentage of croscarmellose sodium

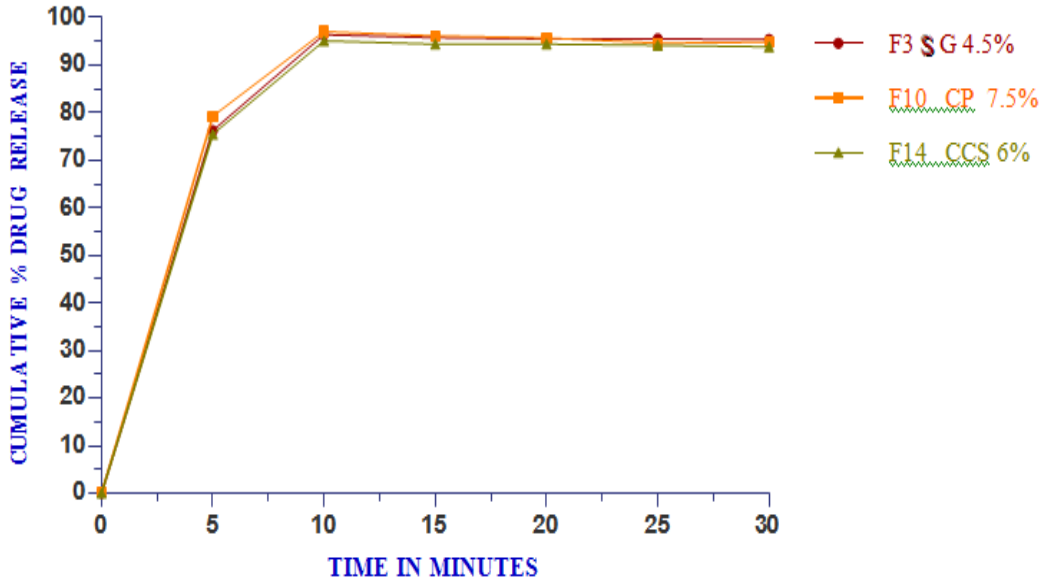

Fig 12: Comparison of in-vitro release profile of desloratadine containing different super disintegrants

Disintegration time is measured in 900 ml of artificial Saliva (PH 5.8) at 37± 0.5°C. The disintegration time of 3 tablets is recorded and the average is reported. The dissolution test is determined by USP dissolution testing apparatus type-2 (paddle method). It is performed using 900ml of 0.1N Hydrochloric acid at 37± 0.5°C and 50 rpm. A 5ml sample solution is withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25, and 30 minutes. The samples are replaced with a fresh dissolution medium of the same quantity. The absorbance of the solution is measured at 242 nm in a UV-Spectrophotometer.

The indion-234 resin was selected for the preparation of DRC (1:5). The maximum drug loading was found to be 88.19±0.68%. The disintegration time of the tablets decreased with an increase in the concentration of super disintegrants. The faster disintegration effect of crospovidone tablets may be attributed to its rapid capillary activity and pronounced hydrating with little tendency to gel formation. The fast dissolving tablet formulations were subjected to precompression and post-compression parameters and the results were found to be within the acceptable limits. *In vitro* dissolution studies of, all formulations showed more than 90% drug release within 10 minutes. The maximum increase in the dissolution rate was observed with 7.5% Crospovidone (F-10) amongst all formulations. 97.12 ± 0.37% release was occurring within 10 minutes. F-10 was found to be the best formulation as this showed less disintegration time and more drug release.

CONCLUSION:

Fast dissolving tablets of desloratadine can be successfully prepared by direct compression method using selected super disintegrants to improve disintegration/dissolution of the drug in the oral cavity and hence better patient compliance and effective therapy.

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