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Formulation and evaluation of a dapsone and fexofenadine HCl immediate release combination tablet

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***Abstract*---**The purpose of the study was to formulate a conventional (immediate release) tablet using a combination of Dapsone and Fexofenadine HCl. Dapsone is a sulfone with anti-inflammatory, immunosuppressive, antibiotic, and antibacterial properties. Fexofenadine HCl is a non-sedating antihistamine approved for the treatment of allergies, whereas Dapsone is used to prevent bacteria from growing and causing red, itching welts. Fexofenadine HCl is an antihistamine that is used to treat allergic symptoms by blocking a natural substance called histamine. Direct compression methods were used to formulate the tablets, which contained super disintegrating polymers such as Ac-di-sol (Croscarmellose sodium). Four tablet formulations were compounded using the direct compression method, with polymer varying ratios. According to the evaluation results, formulations met the specifications when compared to official pharmacopoeias and standards. Different parameters, such as

hardness, friability, weight variation, and dissolution studies, were used to evaluate tablets. This formulation of tablet combination of Dapsone and Fexofenadine HCl releases the drug within 60 minutes. Thus, the trial was a success in terms of achieving our goal of developing a tablet with few excipients and a simple manufacturing method.

***Keywords*---**dapsone, fexofenadine HCl, urticaria, immediate release, super disintegrant.

Introduction

This research work is concerned with design and characterization of oral immediate release tablet of Dapsone and Fexofenadine HCl in combination in order to provide immediate relief from pain,swelling,itching and to inhibit the growth of bactaria. Immediate release drug delivery systems are designed to provide immediate drug levels in short period of time. Immediate release drug delivery is desirable for drugs having long biological half life,high bioavailability,lower clearance and lower elimination half life. But main criterion for immediate release dosage form is poor solubility of the drug and the need of immediate action of drug to treat unwanted defect condition or any allergic condition[1]. Drug delivery systems (DDS) distribute therapeutic medications throughout the body as needed to produce the intended therapeutic impact safely. Typically, such systems are created to enhance active compounds' water solubility and chemical stability, and ii) in-vitro ,iii) decrease side effects while increasing pharmaceutical activity.[2] Therapeutic effectiveness and short and long-term biological effects are influenced by drug delivery routes and the physicochemical features of those routes. Each delivery technique has advantages, disadvantages and each requires a unique delivery vehicle design.

Oral delivery has emerged as the most appealing route, owing to its ability to produce solid formulations with a long shelf life, convenience of administration, and enhanced immunological response.[3] Immediate release tablets are designed to dissolve and release their dose form without the need of special coatings or other rate-controlling procedures. Immediate release tablets crumble quickly and dissolve quickly to release the medication. Disintegration, solubility and different physiological variables all affect medication bioavailability in the mouth.[4,5] The word "instant relief" comes to . mind, when any pharmacological formulation in which galenic modifications do not significantly or purposely slow the rate of drug release from the formulation or drug absorption In this scenario, immediate release may be achieved by using a suitable pharmaceutically acceptable diluent or carrier that does not significantly slow down the rate of drug release and/or absorption. As a result, the phrase excludes formulations that have been adjusted to give "modified," "controlled," "sustained," "prolonged," "extended," or "delayed" drug release.[5-6]Urticaria, sometimes known as "hives," is a common skin condition that affects between 15 and 25% of the population at some point in their lives. Adults are more often than children, and women are more likely than males, with peak frequency in the third to fifth decades of life.

The emergence of pruritic "wheals," which are well-circumscribed patches of non-pitting edema with blanched centres and elevated borders that affect only the superficial sections of the dermis and are visible in association with surrounding erythema of the skin, characterises this disorder.[8,9] Angioedema affects around 40% of urticaria suffers swelling that occurs beneath the skin.[10-12] Fewer studies show that second-generation antihistamines are effective in the treatment of acute urticaria, a biologic condition that normally disappears in a few of weeks. We can find controlled research that show that any antihistamine is superior in the treatment of acute Urticaria. Second-generation H1 antihistamines are preferred for therapy.[13] Because of their substantial drowsiness and adverse effects, as well as their short duration of action, first-generation H1 antihistamines are less favoured.[13]For the treatment of urticaria, second-line antihistamines and an antibiotic are compounded in single-unit dose form. Dapsone is an antibiotic that is used to regulate and minimise bacterial development, while antihistaminics are used to treat allergic diseases and diminish wheals and sores on the body.

Materials and Methods

Dapsone was provided as a complimentary sample by Research-lab Fine Chem Industries (Mumbai, India). Sreekara Organics supplied the Fexofenadine HCl (Telangana). Ashland Inc. Netherland provided the E4M polymer as a free sample. Fine Chem Ltd supplied Ac-Di-Sol and microcrystalline cellulose (Avicel pH 102). (Mumbai, India). Fine Chem Ltd provided the magnesium stearate, talc, and sodium saccharine (Mumbai, India). All of the reagents used in this experiment were of analytical quality.

Methods[14]

Identification of pure drug

Identification of pure drug was carried out by Fourier Transform Infra-red Spectrophotometry (Shimadzu 8400) scanned in the range of 200-400nm.

Drug-excipient compatibility study

Studies of drug-excipient compatibility are important to ascertain drug and excipients are compatible with each other. DSC graph and IR spectra are used to study drug-excipient compatibility.

FTIR study

FTIR (Shimadzu 8400s)spectrophotometer were used in the range of 400-4000 cm^{-1} using potassium bromide discs (Mixing ratio1:1) The samples were hermetically sealed in aluminium pans and heated at a constant rate of 10°C/ min over a temperature range of 40 to 300°C.

Drug-excipient compatibility study
DSC study

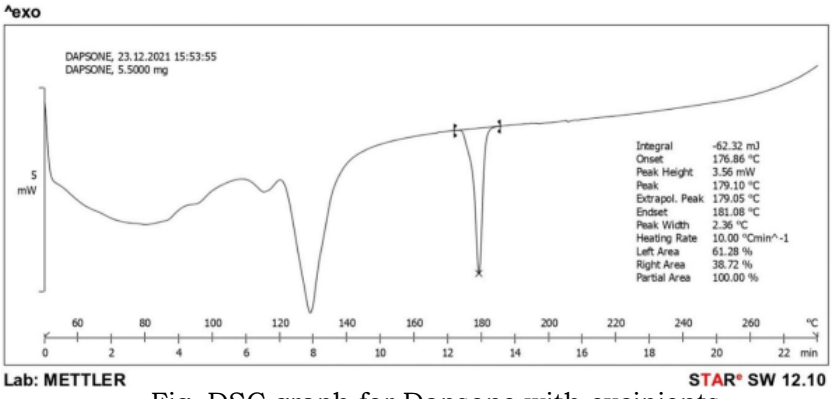

Fig. DSC graph for Dapsone with excipients

The DSC thermogram for Dapsone in combination with various excipients shows the peak onset temperature (Tonset) [176.86°C] and peak transition temperature (Tpeak) [179.10°C]. The thermogram of Dapsone showed a sharp endothermic peak at ~180°C and a peak onset ~176°C. In this thermogram, the melting endotherm of Dapsone (T onset and T peak) was well preserved, with light broadening shifting towards the lower temperature range.

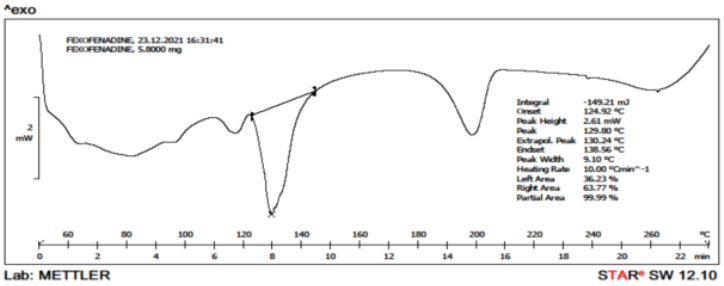

Fig- DSC graph for Fexofenadine HCl with excipients

Similarly, Fexofenadine HCl in combination with various excipients shows an onset temperature (Tonset) [124.92°C] and a peak transition temperature (Tpeak) [129.80°C]. The thermogram of Fexofenadine HCl showed a sharp endothermic peak at ~269°C and a peak onset ~258°C. In this thermogram, the melting endotherm of Fexofenadine HCl (T onset and T peak) was well preserved, with light broadening shifting towards the lower temperature range. These shifts in peak in both graphs to a lower temperature range might be due to the drug being mixed with excipients and do not necessarily indicate probable incompatibility.

FTIR spectroscopy

The FTIR spectrums of pure Dapsone as well Fexofenadine HCl and physical mixtures of drugs and polymers were studied separately as per the excipients used in the formulation. It was observed that there were no major shifts in the main peaks of either drug. This indicates that there were no compatibility problems with the drug with the polymers and excipients used in the formulation. Dapsone had peaks at 3063.06 (=C-H stretching), 3333.10 (N-H stretching), 1589.40 (C=C stretching), 1280.78 (C-N stretching), and 1134.18 (S=O stretching), while Fexofenadine HCl showed characteristic peak values at 3037 (C-H stretching); 1705 (-COOH stretching) ; 3294 (O-H stretching) and 1334 (C-N stretching). These peak values were in accordance with previously reported spectra of Fexofenadine HCl

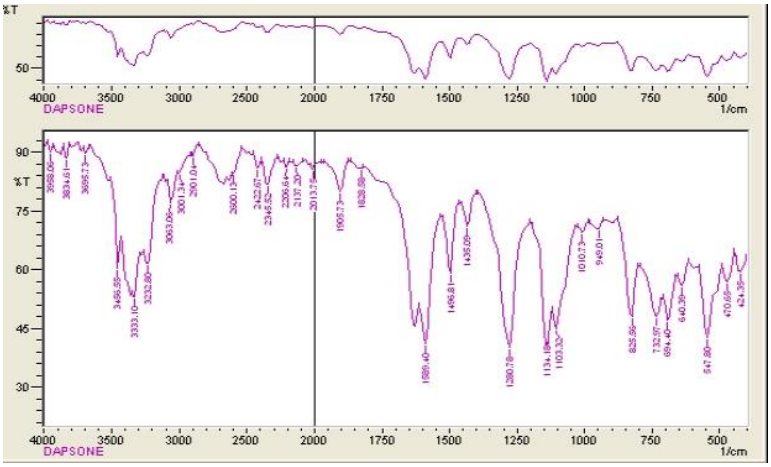

Fig. FTIR of Dapsone

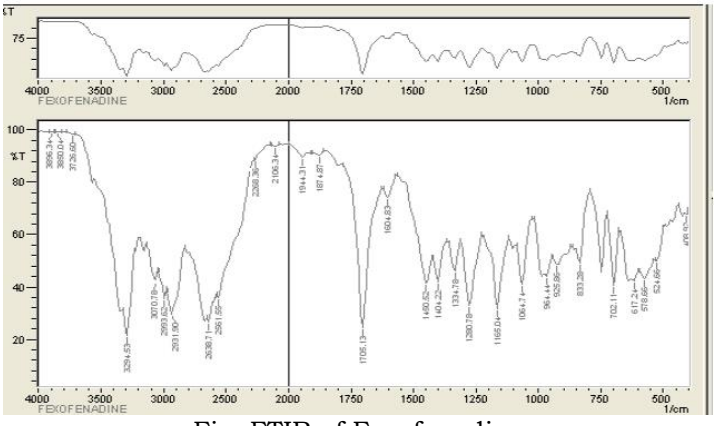

Fig FTIR of Fexofenadine

UV spectroscopy

The linearity of the responses of both drugs was verified at 2–10 µg/ml concentrations. The calibration curve was obtained by plotting the absorbance

versus the concentration data and was treated by linear regression analysis. The equation of the linearity curve for Dapsone obtained was y = 0.1238x + 0.0066. The linearity curve was found to be linear for mentioned concentrations (the correlation coefficient (r^2) of determination was 0.9996) (Fig.5). Similarly, the equation of the linearity curve for Fexofenadine HCl obtained was y = 0.036x+ 0.0555. The linearity curve was found to be linear for mentioned concentrations. (the correlation coefficient (r^2) of determination was 0.9991)

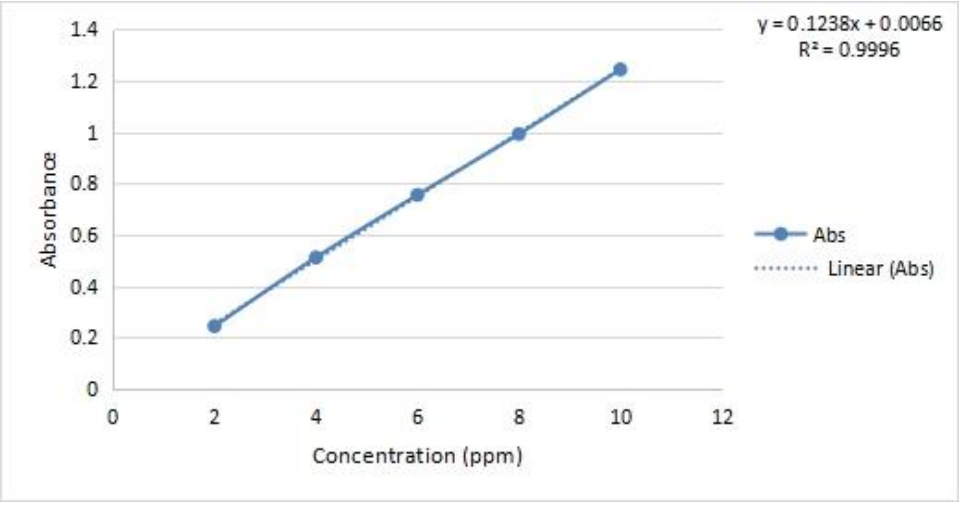

Fig. Calibration curve of Dapsone

Fig. Calibration curve of Fexofenadine HCl

Precompression studies

Angle of repose[15,16]- The highest angle achievable between the surface of a pile of powder and the horizontal plane is known as angle of repose. The angle of repose may be used to calculate the frictional force in a loose powder. It is a measure of the powder's flow characteristics.Angle of repose is the maximum angle that may be achieved between the surface of a pile of powder and the horizontal plane. The

frictional force in a loose powder may be calculated using the angle of repose. It is a measurement of the powder's ability to flow through the funnel's sides. Angle of repose and powder flow characteristic are related.

$$\text{Angle of repose} = \theta = \tan^{-1}(H/R)$$

Where, H = Height of pile in centimeter
R = Radius of pile in centimeter
When the angle of repose is less than 25°, the flow was said to be excellent, and if the angle of repose is more than 40°, the flow is considered to be poor.

Bulk density (ρ_b)[17]- Using an electronic digital balance, weigh a 20g sample and pour carefully from the side wall into a 100 ml capacity "Class A" graduated measuring glass cylinder. Slowly level the surface of the sample in the cylinder and examine the occupied volume.

$$\rho_b = \frac{M}{Vb}$$

where, ρ_b = Bulk density
M = Mass of power blend
Vb = Bulk volume of powder blend

Tapped density- By dividing the mass of a powder by the tapped volume in cm^3, the tapped density was calculated. A sample of around 50 cm^3 of powder is carefully put into a 100 ml graduated cylinder after passing through a standard sieve no. 20. The cylinder was dropped 100 times from a height of 1 inch at 2-second intervals onto a hard wood surface. The final tapped volume in cm^3 of the sample contained in the cylinder was then divided by the weight of the sample in grammes to obtain the tapped density of each formulation. It was determined using the following equation:

$$\rho_t = \frac{M}{Vt}$$

where, ρ_t = Tapped Density
M = Mass of powder blend
Vt = Tapped volume of powder blend

Hausner's ratio:-It is the ratio of the tapped density to the bulk density. It is calculated as follows-

$$\text{Hausner's ratio} = \frac{Tapped\ density\ (\rho t)}{Bulk\ density\ (\rho b)}$$

A good flow has been indicated by a Hausner's ratio greater than 1.25, and a poor flow may have a value of 1.5.

Carr's index:-It is also called as Carr's Index or Carr's Compressibility Index, an indication of the compressibility of a powder. It is calculated as follows-

Carr's Index= $\frac{\rho t - \rho b}{\rho t} \times 100$

Where, ρt = Tapped Density
ρ_b = Bulk Density

Preparation of tablet by direct compression method

Tablets were prepared by using tablet compression machine. Accurately weighed amount of powder mixture for different batches was fed manually into die. The weighed amount of powder mixture was and into the die and release to compressed at a predetermined compression pressure of 5-6 N at optimum speed of rotation, using standard concave punches. (Brand Name-Rimek, Mini Press-II, Karnavati Engineering Ltd., Ahmadabad, Gujarat).

Table 1
Composition of Sustained release tablet of batches DF1-DF4

Name of ingredients	DF1	DF2	DF3	DF4
Dapsone (mg)	50	50	50	50
Fexofenadine HCl(mg)	120	120	120	120
Ac-di-sol(mg)	X	XX	XXX	XXXX
Avicel pH102 ((mg)MCC	XXX	XX	XXX	XXXX
Talc (mg)	8	8	8	8
Magnesium stearate(mg)	2	2	2	2
Sodium saccharine(mg)	2	2	2	2

(MCC indicates microcrystalline cellulose)

Evaluation of tablets
Thickness

The thickness of the tablet was measured by using Vernier calliper by picking the tablets randomly. Randomly selected tablets from all batches were tested for thickness and were found to be 0.50±0.005cm. Standard deviation values were determined and were found to be within the range.

Hardness[18]

Using a Monsanto hardness tester, the force required to crush the tablet is calculated. Three tablets from a batch are tested for hardness. Hardness is measured in Kg/cm^2. The compressed tablets from all batches F1-F4 were found to be within the limit as per standard record, which lies in between 5.3 ±0.057 to 5.5 ±0.115 kg/cm^2 (n=3).

Weight variation test

The weight variation test is also called as uniformity of weight; it is the official quality control test. It is performed to ensure that each tablet dosage form has the accurate amount of drug. As per the U.S.P., randomly select 20 tablets and then accurately weigh selected 20 tablets individually and calculate the average weight. The tablets from batches F1-F4 were evaluated for % weight variation, which showed a % weight variation of between 0.18-4% from the average weight of the tablet complying as per standard (for >324mg±5.0% deviation).

Friability test [19]

Friability Test: The Roche Friabilator was used to determine the tablets' friability. Five tablets were carefully weighed and placed in the tumbling chamber, where they were tumbled at 25 rpm for 4 minutes. The % weight loss was calculated using the formula below after the tablets were weighed again.

$$\%\text{friability} = \frac{Initial\,weight - Final\,weight}{Initial\,weight} \times 100$$

Drug content[20]

The formulated tablets batches DF1-DF4 were tested for assay by UV spectroscopy. Absorbance of NTG in methanol is recorded at 225nm and 290nm (λmax) over concentration range 5µg-50 µg. % assay was found to be in between 96.23 to 101.69, which is complying as per the standard record limit (95%-105%).

Dissolution study

A dissolution study for formulated batches was performed separately for the immediate and sustained release layers as per USP by using USP-II apparatus (paddle type) dissolution test apparatus (Electrolab TDT08L, Mumbai, India). The dissolution medium for the immediate release tablet layer and for the sustained release layer were 900ml of 0.1N hydrochloric acid and 900ml of 0.01N hydrochloric acid, respectively. The medium was allowed to equilibrate to a temperature of 37±0.5°C. A sample (1 ml) of the solution was withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25, 30, 45, 60 min time intervals and the samples were replaced with fresh dissolution medium. A tablet from each batch was placed in the vessel and covered; the apparatus was operated for up to 1 hour at 100 rpm for the immediate release layer and 12 hours for the sustained release layer. The sample was withdrawn at specified time intervals and replaced with a fresh 1ml of medium. The aliquots were filtered through Whatmann filter paper No. 42. The absorbance of the sample solution was measured using UV spectroscopy against the corresponding media as a blank for the immediate release layer and the sustained release layer at 290 nm and 225 nm, respectively.

Table 2
Pre compression evaluation parameters- Angle of Repose (ɵ)

Batch	Sample weight (gm)	Height of pile (h) in cm	Radius (r) in cm			Angle of Repose (θ)			Mean θ	S.D (+-)	Angle of repose
			r1	r2	r3	θ1	θ2	θ3			
DF1	5.004	1.5	2.8	2.7	2.6	27.92	28.81	29.68	28.80	±0.8	Excellent
DF2	5.002	1.5	2.8	2.7	2.8	27.92	28.81	27.92	28.21	±0.5	Excellent
DF3	5.001	1.6	2.8	2.8	2.6	29.68	29.68	31.38	30.24	±0.9	Excellent
DF4	5.002	1.5	2.6	2.7	2.6	29.68	28.81	29.68	29.39	±0.5	Excellent

±S.D. n=3

Table 3
Pre compression evaluation parameters- Bulk density

Batch	Mass of powder M (gm)	Bulk volume of powder V_0			Bulk density Db			Mean Db	S.D. ±
		V_{01}	V_{02}	V_{03}	Db1	Db2	Db3		
DF1	25.004	61	59	60	0.41	0.42	0.41	0.41	±0.005
DF2	25.002	61	59	60	0.41	0.42	0.41	0.41	±0.005
DF3	25.001	59	61	60	0.42	0.41	0.41	0.41	±0.005
DF4	25.002	59	61	60	0.42	0.41	0.41	0.41	±0.005

±S.D. n=3

Table 4
Pre compression evaluation parameters- Tapped Density

Batch	Mass of powder M (gm)	Bulk Volume	Tapped volume of powder V_t			Tapped density Dt			Mean Dt	S.D. ±
			V_{t1}	V_{t2}	V_{t3}	Dt1	Dt2	Dt3		
D	25.00	61	59	60	59	0.42	0.41	0.42	0.43	±0.005

F 1	3								
D F 2	25.00 1	62	60	61	59	0.42	0.41	0.42	0.42	±0.005
D F 3	25.00 2	62	60	61	59	0.42	0.41	0.42	0.42	±0.005
D F 4	25.00 4	62	60	61	59	0.41	0.41	0.42	0.42	±0.005

Table 6
Pre compression evaluation parameters- Carr's Index

Batch	Tapped Density (Dt)	Bulk Density (Db)	Carr's Index 100 x (Dt)-(Db)/ (Dt)	Flow Character
DF1	0.42	0.41	2.38	Excellent
DF2	0.42	0.40	4.76	Excellent
DF3	0.42	0.41	2.38	Excellent
DF4	0.42	0.41	2.38	Excellent

Table 7
Pre compression evaluation parameters- Hausner's ratio

Batch	Tapped Density (Dt)	Bulk Density (Db)	Hausner Ratio	Flow Character
DF1	0.42	0.41	1.02	Excellent
DF2	0.42	0.40	1.05	Excellent
DF3	0.42	0.41	1.02	Excellent
DF4	0.42	0.41	1.02	Excellent

Table 8
Post-compression evaluation parameters

Formulation Code	Average weight (gm)	Thickness (cm)	Hardness (Kg/cm^2)	Friability (%)	Assay (%)	
					Dapsone	Fexofenadine HCl
F1	0.301	0.49±0.011	5.5	0.48	99.00	98.55
F2	0.296	0.49±0.005	5.4	0.48	98.21	98.00
F3	0.305	0.51±0.000	5.4	0.36	99.62	96.72
F4	0.299	0.49±0.00	5.5	0.32	99.36	96.30

±S.D. n=3

In vitro Dissolution studies

Table 9
Data of In-vitro drug release studies of immediate release matrix tablet of Dapsone (%)

Time (min)	D1	D2	D3	D4
5	11.20297	20.2315	20.646	21.2058
10	20.28646	28.895	28.7803	32.26288
15	29.08516	39.552	32.093	48.20146
20	32.41277	39.552	43.899	57.52977
25	44.2393	53.062	67.062	62.34132
30	57.29994	68.0722	78.7995	74.20282
45	77.53543	80.1135	88.907	87.44833
60	89.05718	98.425	96.551	97.64602

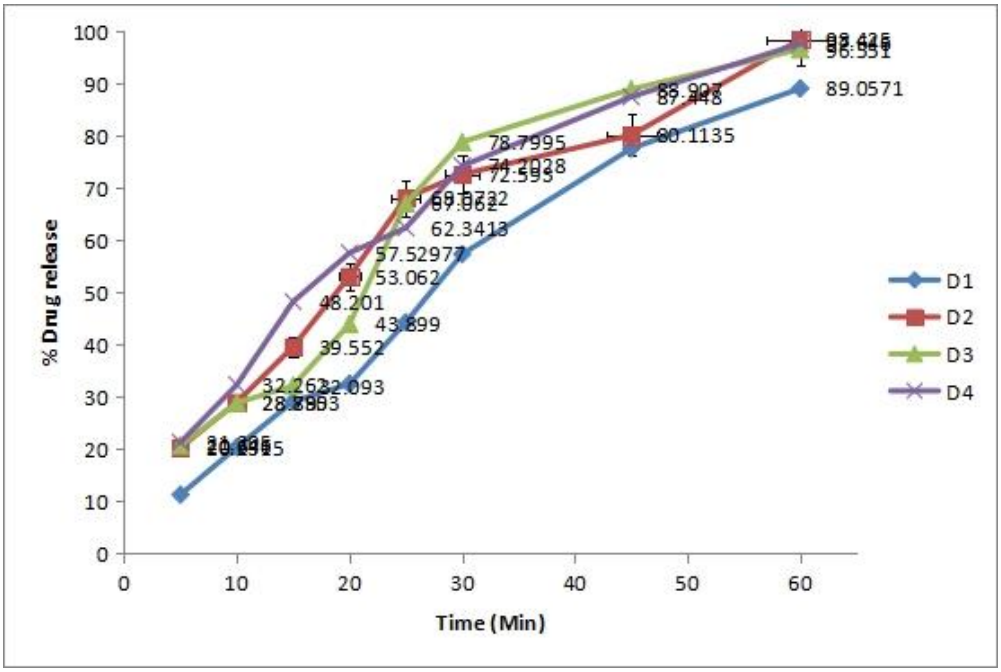

Fig. : In-vitro drug release profile of immediate release matrix tablet of Dapsone

Table 10
Data of In-vitro drug release studies of sustained release matrix tablet of Fexofenadine HCl (%)

Time (min)	F1	F2	F3	F4
5	9.3728	10.4725	4.08	6.8986
10	19.0807	26.658	17.053	24.527
15	35.9707	35.558	32.104	36.692
20	44.819	44.939	56.7096	46.846
25	57.225	67.7234	70.6615	61.8642
30	78.6855	73.8402	82.6375	78.3934
45	90.8505	83.6168	89.2869	88.2388
60	96.9501	97.8299	96.6237	97.3281

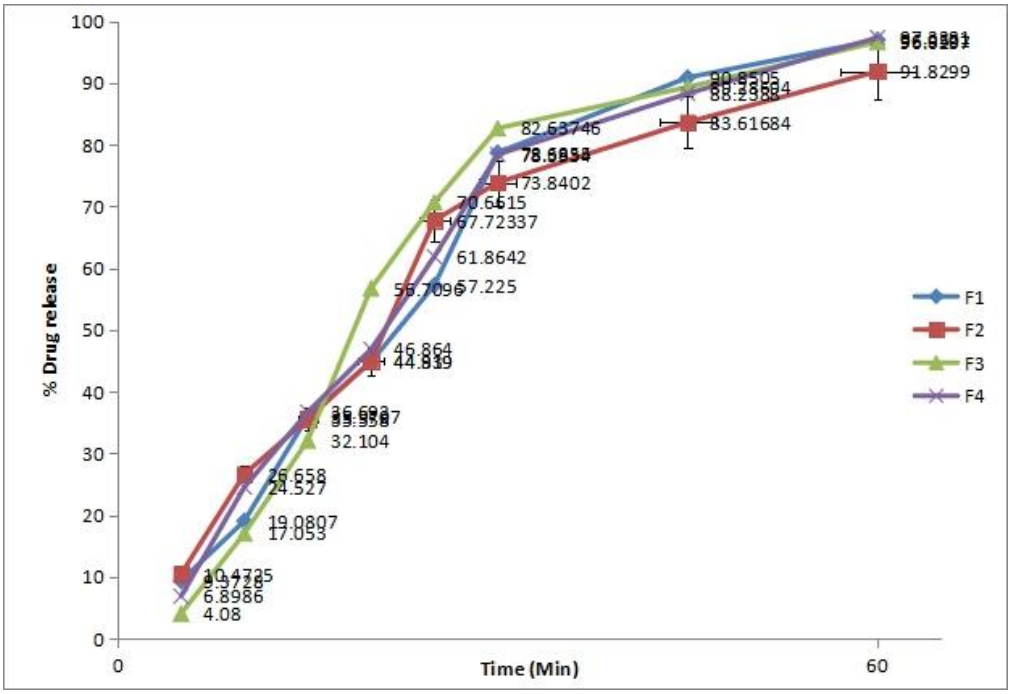

Fig. In-vitro drug release profile of Sustained release matrix tablet of Fexofenadine HCl

Conclusion

The purpose of this study was to develop,assess and evaluate the tablet and the objectives were met.Based on the findings of the completed tests of differential scanning calorimetry and IR studies it was stated that there is no substantial drug excipient interaction . As a result,we may determine that drug and other excipients are compatible . The dissolution time of tablet was less than one minute for release of certain amount of drug from all the tablet formulations. The drug release in optimized formulation of batch 2 was found to be 98.425 % for Dapsone and 98.7299 Fexofenadine HCl % in 60 mins. The optimized

formulation also showed satisfactory hardness, friability, drug content, weight variation, dissolution. The objective of the present work of formulation and evaluation of immediate release tablet for treatment of urticaria has been achieved.

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References

1. Patel HP, Patel JK, Patel RR; Formulation Development & Optimization of Multiple Unit Particles System (mups) Containing Ramipril and Hydrochlorothiazide. International Journal of Pharmaceutical Sciences, 2010; 2(1): 448- 456
2. Park K. Controlled drug delivery systems:past forward and future back. J Control Release 2014;190:3-8.
3. Homayun B, Lin X, Choi HJ. Challenges and Recent Progress in Oral Drug Delivery Systems for Biopharmaceuticals. *Pharmaceutics*. 2019;11(3):129. Published 2019 Mar 19. doi:10.3390/pharmaceutics11030129.
4. Jadhav SB, Mali AD, Rajeghadage SH and Bathe ARS: Formulation and evaluation of immediate release tablets of Imipramine hydrochloride. International Journal of Biomedical and Advance Research 2014; 5(11): 559-65.
5. Patel N, Natarajan R and Rajendran NN: Formulation and evaluation of immediate release bilayer tablets of Telmisartan and Hydrochlorothiazide. International Journal of Pharmaceutical Sciences and Nanotechnology 2011; 4(3): 1477-82.
6. Jon Gabrielsson, Nils-Olof Lindberg and Torbjorn Lundstedt , Multivariate Methods in Pharmaceutical Applications, J.Chemom 2002; 16:141-160
7. Dedhiya et al, "Lercanidipine immediate release compositions" United States Patent Application 2006 0134212
8. Eriksson et al, "New oral immediate release dosage form" United States Patent Application 20060034 911
9. Poonawalla T, Kelly B. Urticaria : a review. *Am J Clin Dermatol.* (2009) 10:9–21. doi: 10.2165/0128071-200910010-00002
10. PubMed Abstract | CrossRef Full Text | Google Scholar
11. Kanani A, Betschel SD, Warrington R. Urticaria and angioedema. *Allergy Asthma Clin Immunol.* (2018) 14 (Suppl. 2):59. doi: 10.1186/s13223-018-0288-z
12. Powell RJ, Leech SC, Till S, Huber PA, Nasser SM, Clark AT, British Society for Allergy and Clinical Immunology. BSACI guideline for the management of chronic urticaria and angioedema. Clin Exp Allergy. 2015;45(3):547–65
13. Lee, E.E., Maibach, H.I. Treatment of Urticaria. *Am J Clin Dermatol* 2, 27–32 (2001). https://doi.org/10.2165/00128071-200102010-00005.
14. Mahdy AM, Webster NR. Pharmacology. Elsevier Ltd; 2011. Histamine and antihistamines; pp. 324–9.

15. Cartensen JT, Rhodes CT (2005) Preformulation. In: Cartensen JT, Rhodes CT (eds.). Drug Stability principles and practices (3rd edn)., Marcel Dekker Inc., New York, USA.
16. Maurya SD, Tilak VK, Dhakar RC, Verma KK, Soni U, Gupta, Preparation and evaluation of floating tablet of famotidine through solid dispersion, International Journal of Current Research and Review, 2011; (2)1: 21-30.
17. Thoke SB, Sharma Y., Rawat S, Nangude, SFormulation development & evaluation of effervescent tablet of Alendronate sodium with vitamin D3, Journal of Drug Delivery & Therapeutics; 2013; 3(5):65-74.
18. Tomar M, Singh AK, Sinha AR. Physical parameter of microcrystalline cellulose and the most acceptability in pharmaceutical industries: J of inno in p'ceutical and bio Sci., 2015; 570-578.
19. RaoNGR, Kumar M, Reddy MS, Kistayya C, Reddy BM. Development and evaluation of fast dissolving tablets of fosinopril by a sublimation method. Int J Pharm Sci Drug Res 2012;4:230-5.
20. Chavan PM and Ughade S: Preparation, characterization and evaluation of tablet for colonic delivery. Int J Pharm Sci & Res 2018; 9(5):2027-33. doi: 10.13040/IJPSR.0975-8232.9(5).2027-33.
21. Michaels A.S, ChandrasekaranS.K, Shaw J.E. Drug permeation through human skin: Theory and invitro experimental measurement. AIChE J. 2004;21(5) 16 Williams AC, Barry BW.Penetration enhancers.Adv drug deliv rev.2004;56(5):603-618.