Journal of Pharma Creations (JPC)

JPC |Vol.12 | Issue 2 | Apr - Jun -2025

www.pharmacreations.com

DOI : https://doi.org/10.61096/jpc.v12.iss2.2025.104-113

ISSN: 2348-6295

Research

Development And Assessment Of Oral Disintegrating Films Containing Hydrochlorothiazide

Myadam Sunitha*, Dr. T. Mangilal[1], T. Sowmya[2], K. Tharun kumar[3]

Smt.Sarojini Ramulamma College Of Pharmacy, Seshadrinagar, Mahabubnagar, Telangana – 509 001, India

*Author for Correspondence: Myadam Sunitha
Email: teelavath@gmail.com

Published on: 09 Mar 2025

Published by:
DrSriram Publications

Abstract

The medication's efficacy and safety profile may be enhanced, dosage may be decreased, and the onset of action may be accelerated with oral disintegrating films. Compared to other conventional dose forms, it dissolves more quickly, becomes more stable, and has a longer half-life. Hydrochlorothiazide (HCT) is a antihypertensive medication used for the sublingual route in order to produce fast-dissolving films that dissolves in saliva quickly and without the need for water. HCT oral disintegrating films were designed to improve bioavailability and patient compliance. The impact on the dissolution profile is measured by HCT. The solvent casting method was used to create the HCT oral disintegrating films (ODF) using natural polymer mango peel pectin and water soluble polymer HPMC E15 of various concentration and mannitol as a plasticizer. The results showed that the medicine vanished quickly. ODF formulations are smooth and easy to swallow, and disintegration time of HF8 formulation containing mango peel pectin 4% was 12 sec while HPMC E15 (HF4) disintegrates in 22 sec. As compare to synthetic polymer, natural polymer mango peel pectin showed lesser disintegration time. HF8 releases the entire medicine within 20 minutes. Upon disintegration, no trace or fragment debris was found. Therefore, based on dissolution tests and disintegration time, the HF8 formulation was determined to be the most optimal formulation among all.

Keywords: Orally disintegrating films, Hydrochlorothiazide, Mango peel pectin, HPMC E15, Hypertension, solvent casting technique.

INTRODUCTION

Orally disintegrating tablets and Oro dissolving films are two of the fast-dissolving medication delivery technologies that have been developed as alternatives to traditional dose forms in order to help these individuals. Because oral medicine delivery has the highest compliance rate, especially among pediatric and geriatric patients, it is considered the most practical, affordable, and safest drug delivery method. Any medication delivery system's ultimate purpose is to successfully deliver the drug to the body. Among the different dosage forms, the oral

disintegrating dosage form is the most popular commercial product[1]. The film decreases the risk of choking and the fear of choking, is simple to make, easy to handle and administer, and has handy packaging. It also lessens the taste that is unpleasant. These thin polymer films are also known as melt-in-mouth dosage forms (MDF), mouth dissolving films (ODF), quick dissolving films (QDF), rapidly dissolving films (RDF), and oral dissolving films (ODF)[2]. Some formulations were developed earlier that are atorvastatin[3], zolmitriptan[4], levocetrizine dihydrocloride[5], amlodipine besylate[6], ondansetron[7], promethazine hydrochloride[8], risperidone[9].

Hydrochlorothiazide is crystalline white-off to white powder, odorless, slightly bitter in taste. It is suggested, either as monotherapy or in conjunction with other agents, for the treatment of edema linked to congestive cardiac failure, a liver disease, nephrotic disorder, chronic renal failure, acute glomerulonephritis, corticosteroid, and oestrogen therapy. Hypertension can be treated with HCT alone or in combination. In order to treat moderate to severe hypertension, the current study aimed to develop an oral disintegrating film containing the drug hydrochlorothiazide.

MATERIALS & METHODS

Chemicals

Hydrochlorothiazide obtained as a gift sample from UniChem laboratories Ltd., Mumbai. HPMC E15 was purchased from Colorcon Asia Pvt. Ltd., Hyderabad. Mango peel pectin was purchased from Shilex Chemicals Pvt. Ltd., Delhi. Mannitol and citric acid were purchased from SD Fine-Chem., Hyderabad. Sodium saccharine was purchased from HI media Lab Pvt. Ltd., Hyderabad. Mango flavour was purchased from Pentagon trading company, Hyderabad. All the chemicals and excipients used were of analytical grade.

Calibration of HCT

To a 100 millilitre volumetric flask, 100 milligrammes of carefully weighed HCT are introduced. Volume was increased to 100 ml with stock solution of 1 mg/ml of 6.8 pH phosphate buffer. The stock solution was diluted to obtain solutions with concentrations of 5, 10, 15, 20, 25, and 30 µg/ml using 6.8 pH phosphate buffer (0.5, 1, 1.5, 2, 2.5, and 3 ml stock solution are diluted with 100 ml buffer). A UV-VIS spectrophotometer (EI 1372, Electronics India, Pune, India) phosphate buffer blank 6.8 pH was used to quantify these solution's absorbance using a standard graph at wavelength 272 nm.

Fourier Transform Infrared (FT-IR) Spectroscopy

Using a FTIR spectrometer (Bruker Alpha II FTIR Spectrometer, Mumbai, India), the drug's FT-IR spectra were recorded. When using the diffuse reflectance method, mid-IR 4000-400 cm-1 was covered. The sample is first dispersed in motor-driven KBr (100 mg) and materials are subsequently triturated producing a fine powder bed within the container with a compression gauge. Five tonnes of pressure was applied for five minutes. Following the light route, the film was placed, the spectrum was recorded twice, and the characteristic peaks associated with the functional groups were determined.

Formulation Design[10]:

A natural polymer known as mango peel pectin and several HPMC E15, were used to create HCT ODFs using the solvent casting method.

Table 1: Formulation of Hydrochlorothiazide ODF

Ingredients (mg)	HF 1	H F 2	HF 3	HF 4	HF 5	HF 6	HF 7	HF 8
Hydrochlorothiazide (HCT)	25	25	25	25	25	25	25	25
HPMC E15	80	120	160	200				
Mango peel pectin					40	80	120	160
Mannitol	12	18	24	30	6	12	18	24
Citric acid	2	2	2	2	2	2	2	2
Sod. saccharine	2	2	2	2	2	2	2	2
Mango Flavor	*	*	*	*	*	*	*	*

Q.s. is represented by '*'.

Preparation of HCT ODF

We employed the solvent casting method to make hydrochlorothiazide ODF. The ODF of HCT was produced using mango peel pectine and HPMC E15. The polymer was then allowed to expand for five to six hours. The drug solution had been added to the previously described polymeric solution after HCT had been dissolved in a predetermined volume of solvent. Next was the addition of plasticisers, like mannitol. Sweetener

and flavour were also added. Mixing in a cyclo mixer about 15 to 20 minutes will homogenise the drug content. A two-hour magnetic stirrer stirs the solution to expel all air bubbles, then it is left. The solution is then cast in a square glass plate (10 cm x 10 cm x 1.7 cm, Othmro, Amazon, India) and air-dried overnight to form a film. The dried film was carefully removed from the mould, inspected for faults, and trimmed to the specific size (2x2 cm^2) for each strip. The investigation excluded film samples with cuts, air bubbles, or other problems.

Thickness measurement[11]

The film's thickness was measured five times using a micrometer screw gauge, and an average of three readings was determined.

Weight variation[12]

Using an analytical balance, the average weight was calculated for each film.

Folding endurance[13]

The value of folding endurance is determined by the number of times the film could be folded in the same way without breaking.

Drug content uniformity

By evaluating the API content in each individual strip, content consistency is ascertained. 85–115% is the maximum content homogeneity[14].

Surface pH

The film that was going to be tested was put in a Petri dish, wet with 0.5 milliliters of distilled water, and left for thirty seconds. After allowing one minute for equilibration and contacting the formulation's surface with the pH meter's electrode, the pH was recorded. For every formulation, an average of three determinations was made[15]

Assay

One film, chosen at random from the five, was weighed, then added to 100 milliliters of 6.8 pH buffer in a volumetric flask. For thirty minutes, a volumetric flask was submerged in a sonicator. The finished solution's absorbance was measured at 272 nm utilising a UV Visible spectrophotometer against a 6.8 pH buffer blank. Concentrations and formulation amount were calculated using a standard graph.

Tensile strength[16]

The greatest stress applied to the point at which the strip specimen breaks is known as its tensile strength.

***In vivo* disintegration studies**

Disintegration test equipment was used. Disintegration time indicates film disintegration and decomposition. In a stainless steel wire mesh with 25 ml of pH 6.8 simulated salivary fluids, place the desired film size (2x2 cm^2). The time it takes the film to dissolve is called disintegration time[17].

***In vitro* Dissolution test**[18]

An in-vitro dissolving analysis of the created ODF formulations was conducted using EI -1916, Electronics India, Pune, India; USP type I dissolution test instrument (basket). Drug concentration was determined using the standard graph and reported as a percentage of the drug that was released or dissolved. The release studies were conducted in six duplicates, and mean values were noted.

Release Kinetics[19]

The findings from the invitro diffusion investigation were used to investigate the order and mechanism of drug release kinetics of HCT films. The kinetic models that were plotted included the zero order, first order, and Higuchi equations; the release was calculated using the Korsmeyer-Peppas equations.

Stability Studies

The designated formulations were tagged and placed in strip packing with aluminium foil in polyethylene packets. After that, they were kept at 40°C/75% RH. Maintained for three months and assessed, in accordance with ICH Guidelines, for their outward look, medication content, and drug release at predetermined intervals[20].

RESULTS & DISCUSSION

Calibration of HCT

Prepare the stock solution by combining 50 mg of HCT with 100 ml of water. Ten millilitres of this stock solution were extracted and diluted with water to achieve a total volume of one hundred millilitres. A calibration curve was established utilising diverse concentrations (2–10 µg/ml) and the appropriate dilution of the stock solution. The absorbance was measured at 272 nm. In Figure 1, the HCT standard curve was shown. In a phosphate buffer with a pH of 6.8, HCT was calibrated; linearity was found with R^2 value of 0.9988.

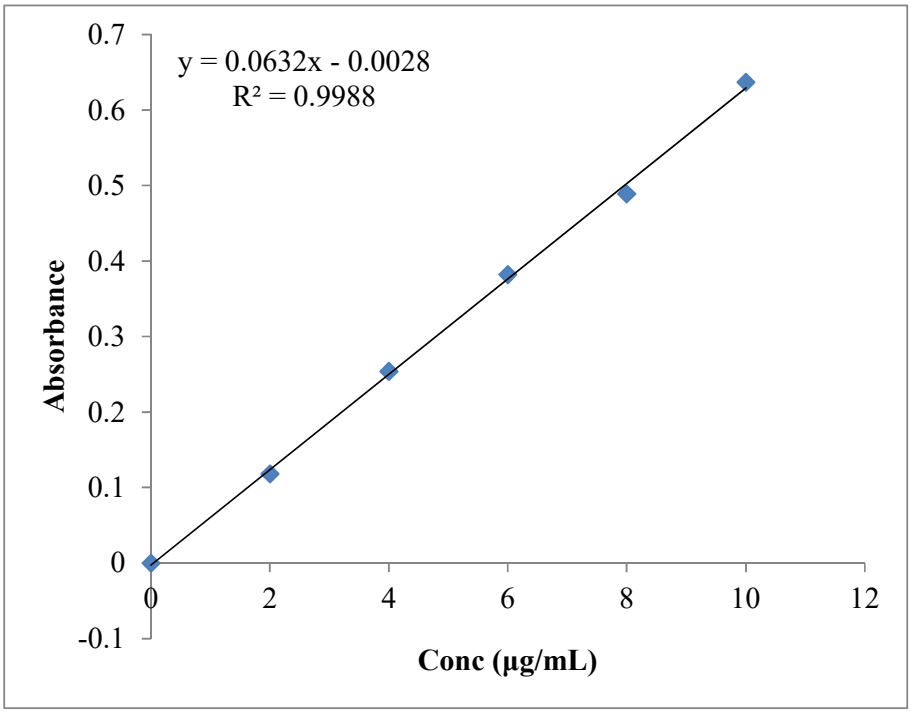

Fig 1: Standard Calibration Curve of HCT in 6.8 pH phosphate buffer

Drug – excipient Compatibility Studies

FTIR spectrometer (Bruker Alpha II FTIR Spectrometer, Mumbai, India) was used to determine the drug excipient compatibility, and the graphs from the figure were displayed. To find out if there was any interaction between the excipients and HCT, the physical mixture was put through FTIR analysis. The lack of a drug-carrier chemical interaction is confirmed by the absence of any drug-characteristic peak appearance or disappearance. Optimized sample, which were pure HCT with mango peel pectin, underwent FTIR analysis to determine the presence of the pure API in the mixture and to describe it.

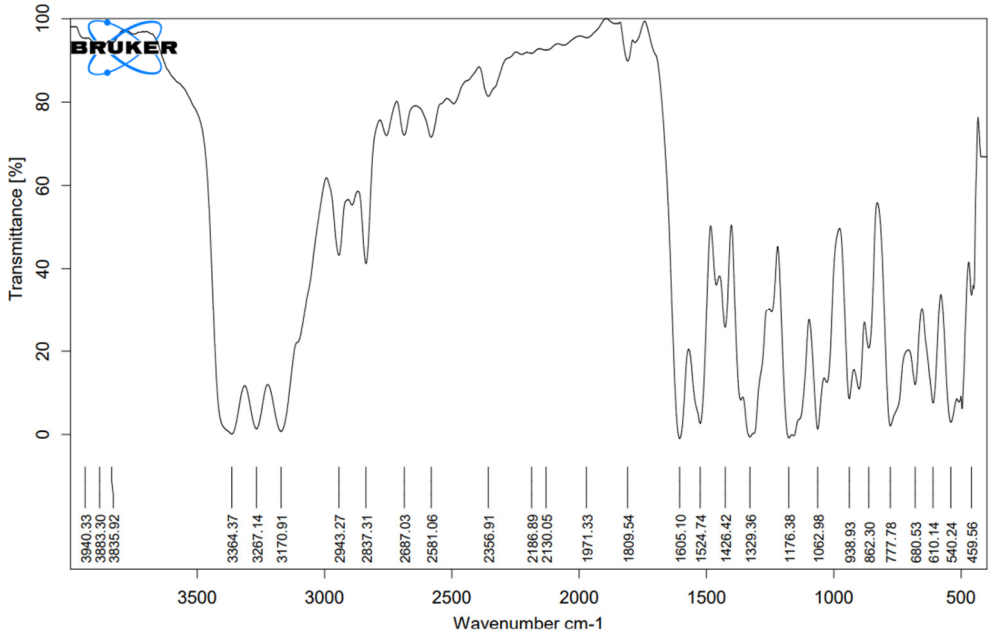

Fig 2: FTIR Spectrum of pure HCT.

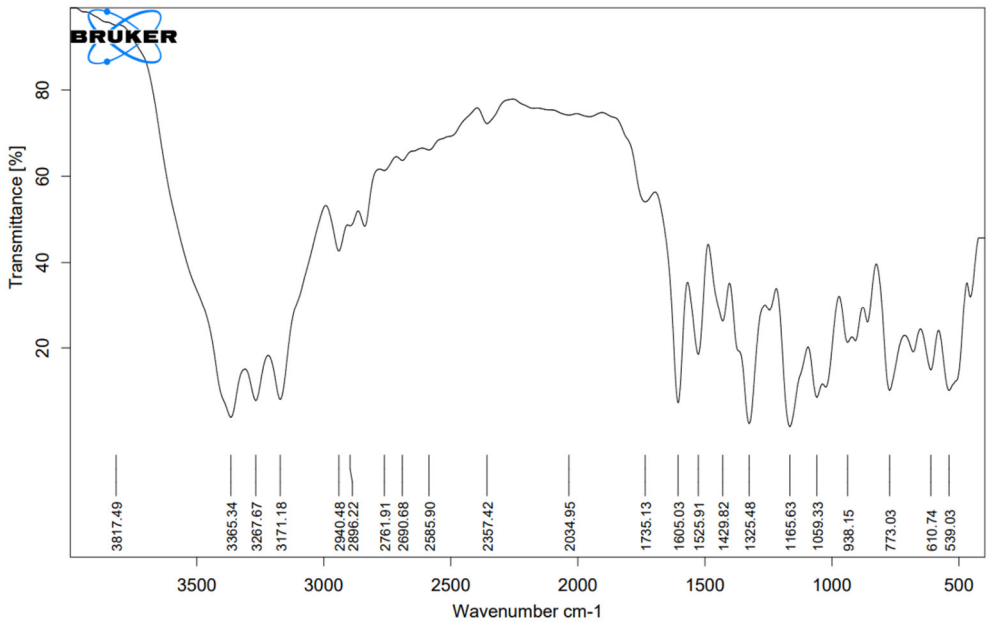

Fig 3: The optimised formulation's FTIR spectrum.

The obtained FTIR spectra are superimposed in the figure 2 and 3. The spectrum clearly shows the primary characteristic bands associated with pure HCT, and the data are in accordance with the scientific literature. For Hydrochlorothiazide, the N-H_2 absorption is observed at 3267 cm^{-1}, the SO_2 absorption at 1329 cm^{-1}, and the N-H absorption at 777 cm^{-1}. There was no interaction, based on the observed absorption peaks of the drug and excipients.

Formulation of ODF

The drug solution had been added to the previously described polymeric solution after HCT had been dissolved in a predetermined volume of solvent. Following this step, plasticizer such mannitol, sod. sachharine, and mango flavor were added. Mixing in a cyclo mixer for 15 to 20 minutes will homogenise the drug content. After putting the liquid into a prepared mold, it was allowed to air dry for 45 minutes. The film was carefully removed from the mold, examined for defects, and then cut to the right size to ensure that each strip had the right dosage (2 × 2 cm^2). The study did not include film samples with cuts, air bubbles, or other defects. ODF formulations HF1–HF4 made with HPMC E15 at doses of 80-200 mg and HF5–HF8 are made with mango peel pectin at doses between 40-160 mg.

Evaluation of ODF

The findings are displayed in the Table 2. HF1–HF8 were determined to be 95.56±0.43-119.63±0.61 µm thick. Based on the results of the aforementioned formulations, all of them demonstrated film thickness between 5 and 200 µm, which meets with the prior value's limit. It was discovered that the folding endurance value of HF1–HF8 was 101±4 -164±5. The surface pH of each film was found to be within 6-7. The disintegration time for HF1–HF8 was 12±3-29±4 sec. According to the data, the disintegration time decreased as the polymer concentration increased.

Table 2: The thickness, folding endurance, and pH of the surface and disintegration time of all formulations

F. Code	Thickness (µm)± SD	Folding endurance (folds)	Surface pH	In-vitro disintegration Time (sec)
HF 1	95.56±0.43	101±4	6.16±0.07	29±4
HF 2	97.83±0.58	111±6	6.21±0.15	26±3
HF 3	105.69±0.62	123±7	6.24±0.09	25±5
HF 4	108.24±0.45	127±5	6.32±0.14	22±4
HF 5	109.36±0.56	131±6	6.29±0.12	21±3
HF 6	112.52±0.39	134±7	6.41±0.21	19±5

HF 7	114.29±0.47	146±9	6.36±0.11	15±4
HF 8	119.63±0.61	164±5	6.25±0.07	12±3

Table 3 displays weight variation, drug content uniformity, and assay determination. For HF1- HF8 formulation weight variance fluctuates between 67.24±0.32-76.38±0.38. HF8, with a medication content percentage of 101.39±0.37, was identified as the superior formulation relative to the others. The assay findings for each formulation are ranging in between 95.26±2.17-101.46±4.27.

Table 3: Weight variation, drug content uniformity, and assay determination

F. Code	Weight variation	Drug Content Uniformity	Assay
HF 1	69.26±0.26	92.37±0.18	95.26±2.17
HF 2	71.28±0.46	94.43±0.33	97.51±4.27
HF 3	72.36±0.31	95.36±0.21	96.49±3.33
HF 4	73.14±0.28	98.41±0.18	98.62±2.51
HF 5	72.46±0.29	97.58±0.29	97.48±4.15
HF 6	73.61±0.34	99.43±0.39	96.39±5.09
HF 7	74.53±0.45	99.32±0.46	98.71±2.89
HF 8	76.38±0.38	101.39±0.37	101.46±4.27

In-vitro dissolution

For HF1 through HF8, the figure 4 displays the cumulative medication release percentage. Utilizing a Type I USP basket apparatus, the in vitro dissolution investigations were conducted in phosphate buffer with a 6.8 pH. In 20 minutes, HF4 with HPMC E15 released 93.54% of the drug; HF8 with mango peel pectin released 99.99%. As a result, it has been determined to be the best formulation.

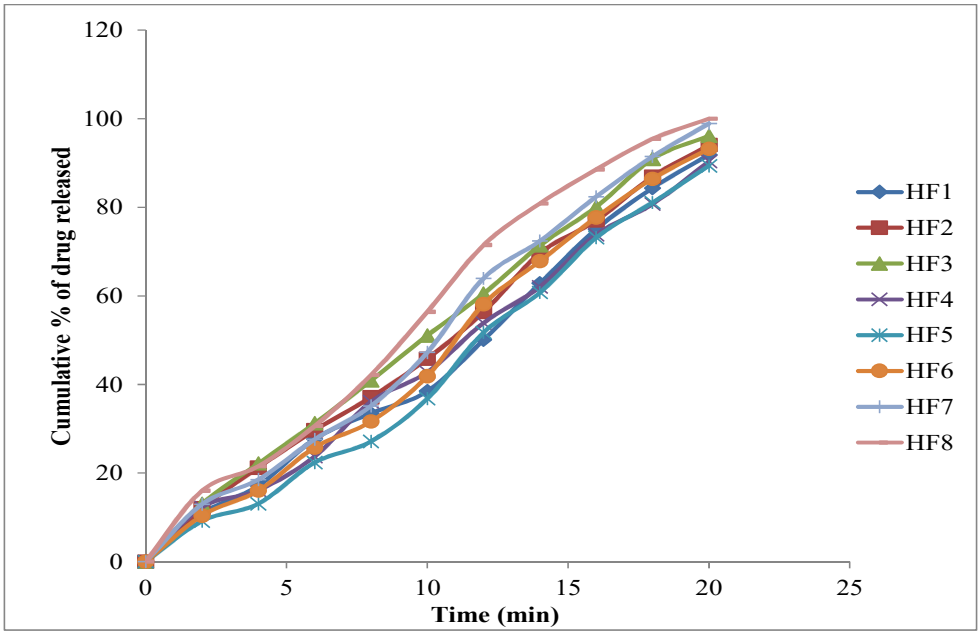

Fig 4: In vitro dissolution studies of formulations (HF1-HF8)

Application of Release Rate Kinetics to Dissolution Data:

A variety of models were used to study drug release kinetics. A number of release models, including first-order, zero-order, higuchi, and korsmeyer-peppas, were fitted to the acquired data in order to investigate the medication release rate mechanism of the dose form Kinetics.

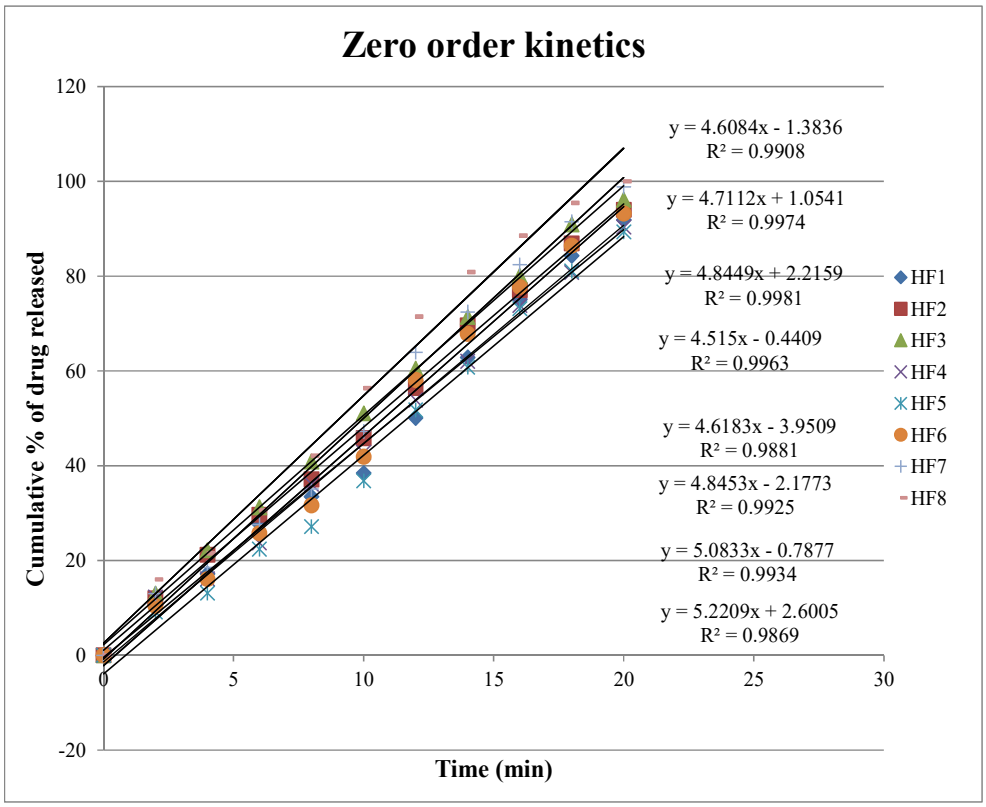

Fig 5: Zero order release kinetics graph of HCT formulations (HF1-HF8)

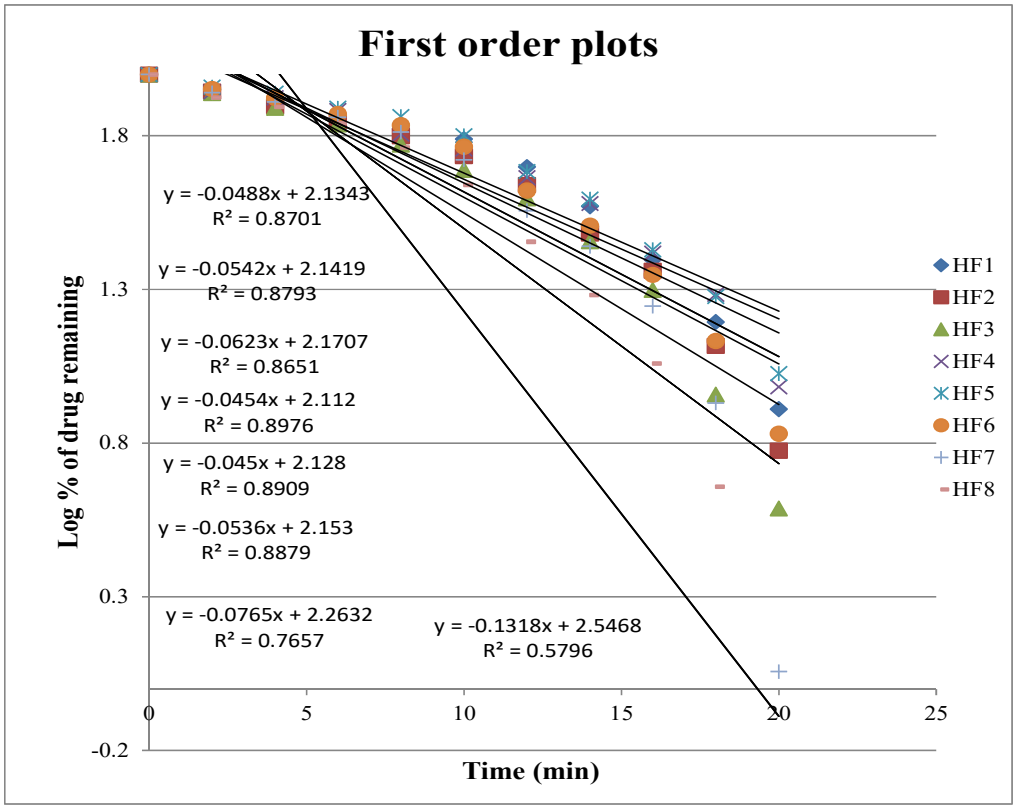

Fig 6: First order release kinetics graph of HCT formulations (HF1-HF8)

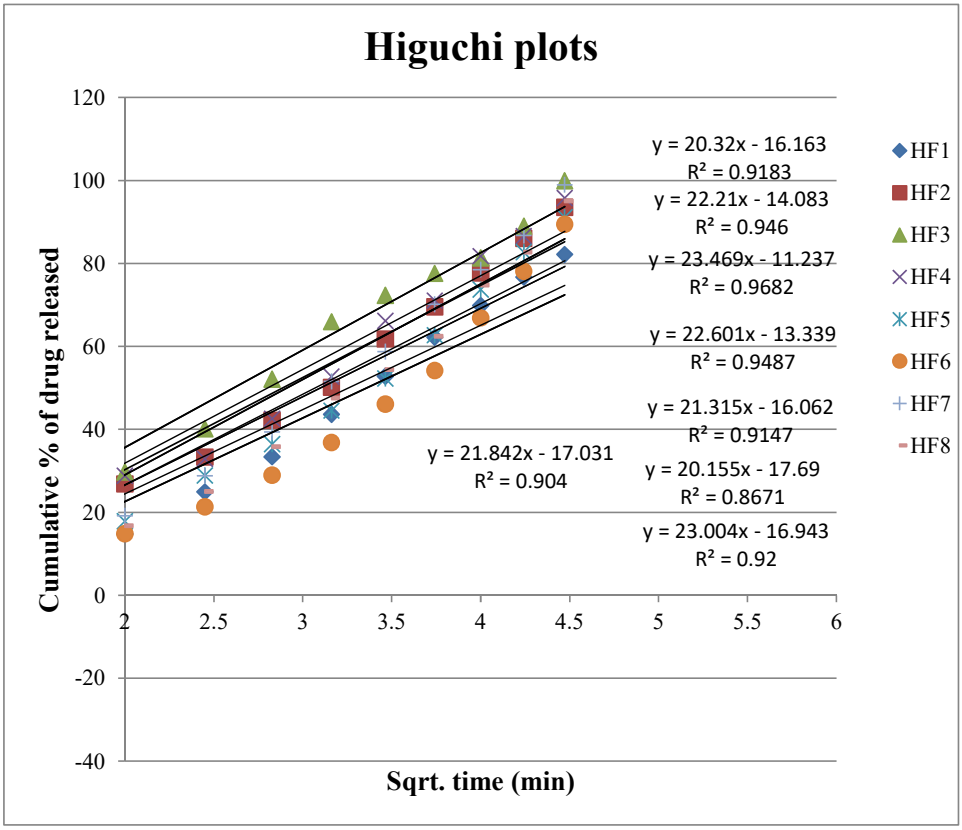

Fig 7: Higuchi release kinetics graph of HCT formulations (HF1-HF8)

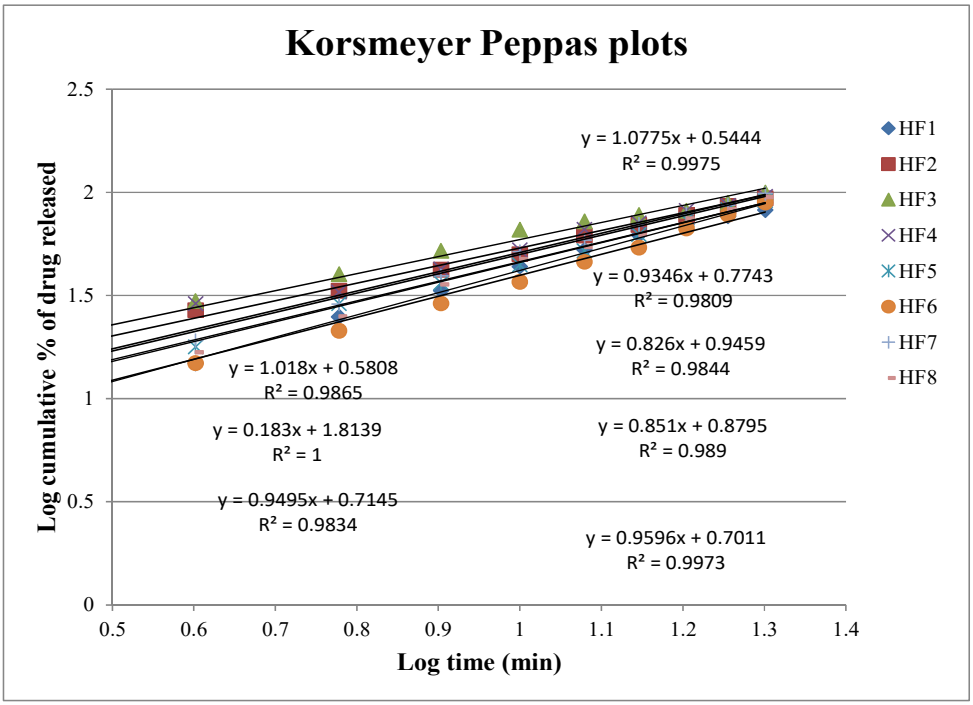

Fig 8: Korsmeyer-Peppas graph of HCT formulations (HF1-HF8)

The R^2 values of HF8 formulation obtained of zero and first order 0.9869 and 0.5796, showing that the drug

release was in accordance with Zero order. The R^2 value of Higuchi plot was 0.904 demonstrating that the diffusion of drug release was controlled. The n value of Korsmeyer-Peppas plot 0.9834 (HF8) showing that the drug release followed super case II transport being n > 0.89. This could be due to polymer relaxation and diffusion.

Stability Studies

According to ICH recommendations, stability studies were conducted to evaluate the stability of the medication formulation. The optimized HF8 formulation was packaged in aluminium with a polyethylene laminate. The samples were kept at 40°C and 75% relative humidity for three months. Changes in the formulation's color, drug content, physical appearance, and drug release properties were examined at the end of the research period. In accordance with ICH requirements, stability experiments were conducted for the optimal formulation of HF8 at room temperature and 40^0C/75%RH. The drug content percentage was examined at 0, 30, 60, and 90 days, all of which fall within the 92–108% acceptability range. It follows that the formulation is stable.

CONCLUSION

The solvent casting method was found to be successful in creating the HCT films that dissolve quickly. Orally disintegrating films (ODF) have proven to be a successful treatment for patients who are psychotic, bedridden, or travelling in places without water. HCT films were subjected to quality control testing, which included in-vitro diffusion, kinetic and stability investigations, variability in weight, thickness, folding endurance, disintegration time, and surface pH. Stability was observed for the optimized formulation HF8 at accelerated stability conditions. As a result of prepared film's enhanced dissolving rate and rapid onset of action, patient compliance improved, therapy was successful, and their popularity grew in the near future.

REFERENCES

[1] Ainley Wade and Paul J Weller, Hand book of pharmaceutical Excipients 2ndedition. The Pharmaceutical Press; pg 229-231, 383 -384.
[2] Kranthi Kumar et.al 'Formulation and evaluation of Carvedilol fast dissolving films' Int Jr Ph & A Res, jun 2015, vol 4(2), p.no 116-128.
[3] Shobana, M. (2018). Formulation and evaluation of fast dissolving oral film of sitagliptin phosphate by solvent casting method (Doctoral dissertation, Cherraan's College of Pharmacy, Coimbatore).
[4] Desu, P., & Sahu, M. INTERNATIONAL RESEARCH JOURNAL OF PHARMACY.
[5] D Jadhav, S. A. N. D. E. E. P., Kalambe, R. N., Jadhav, C. M., Tekade, B. W., & Patil, V. R. Formulation and Evaluation of Fast Dissolving Oral Film of Levocetirizine Dihydrochlorid.
[6] Shelke, P. V., Dumbare, A. S., Gadhave, M. V., Jadhav, S. L., Sonawane, A. A., & Gaikwad, D. D. (2012). Formulation and evaluation of rapidly dis integrating film of amlodipine bes ylate. Journal of drug delivery and therapeutics, 2(2).
[7] Koland, M., Sandeep, V. P., & Charyulu, N. R. (2010). Fast dissolving sublingual films of ondansetron hydrochloride: effect of additives on in vitro drug release and mucosal permeation. Journal of Young Pharmacists, 2(3), 216-222.
[8] Pathan, A., Gupta, M. K., Jain, N. K., Dubey, A., & Agrawal, A. (2016). Formulation and evaluation of fast dissolving oral film of promethazine hydrochloride using dVFferent surfactant. J. Innov. Pharm. Bio. Sci, 3(1), 74-84.
[9] Pawar, S. V., & Junagade, M. S. (2015). Formulation and evaluation of mouth dissolving film of risperidone. Int J PharmTech Res, 8(6), 218-230.
[10] Sneh Priya, Mahalaxmi Rathnanand, Udupa Nayanabhirama, Ravikiran Ongole, Sumanth K. N and Ujjwal Joshi: Preparation and Evaluation of Buccal Mucoadhesive Patch of Betamethasone Sodium Phosphate for the Treatment of Oral Submucous Fibrosis. J. Chem. Pharm. Res. 2011; 3,6:56-65.
[11] Siddiqui M D N, Garg G, Sharma P K. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents. Advances in Biological Research. 2011; 5 (6): 291-303.
[12] Aggarwal Jyoti et al. A comparative Investigation on Different Polymers Employed in the Formulation of Oral Fast Dissolving Films. International Journal Of Pharmaceutical Sciences. ISSN:0975-4725, INT.J.PH.SCI., Jan-April,2012;4(1): 1739-1741.
[13] Prasanna Kumar Desu et al. Formulation And Evaluation of Fast Dissolving Films of Zolmitriptan. International Research Journal of Pharmacy. ISSN:2230-8407, IRJP 2012,3 (5): 373-376.
[14] Sandeev D Jadhav et al. Formulation And Evaluation of Fast Dissolving Oral Film of Levocetrizine Dihydrochloride. International Journal of Pharmacy and Pharmaceutical Sciences. ISSN:0975-1491, Vol 4, Suppl 1, 2012: 337-342.
[15] Shelke PV et al. Formulation and Evaluation of Rapidly Disintegrating Film of Amlodipine Besylate. Journal Of Drug Delivery & Therapeutics. ISSN:2250-1177. 2012, 2(2): 72-75.

[16] AjayKumar Patil et al. Development and Evaluation of Fast Dissolving Film of Montelukast Sodium. World Journal of Medical Pharmaceutical and Biological Sciences. ISSN:2249-2887. 2011, 1(1): 06-12.
[17] Factor I, Naik TS, Khale A, Kanekar H. International Journal of Pharmaceutical and Evaluation of Mouth Dissolving Films : Physical and Chemical Methods. 2014;4(1):62–5
[18] Yoshifumi Murata et al. Preparation of Fast Dissolving Films for Oral Dosage from Natural Polysaccharides. ISSN:1996-1944. Materials 2010, 3:4291-4299.
[19] V. Juyal1, M. Chaudhary, P. Kumar, G. Gnanarajan, P. K. Yadav: Method development and its validation for simultaneous estimation of atorvastatin and amlodipine in combination in tablet dosage form by UV spectroscopy, using multi-component mode of analysis, J Pharma Res..; Dec 2008; 1(2); 182 - 187.
[20] ICH Q1A (R2) stability testing guidelines: stability testing of new drug substances and products. [Online]. 2003 [cited 2008 Nov10]; Available from: URL:http://www.tga.health.gov.au/docs/pdf/euguide/inch/273699r2en.pdf