International Journal of Research in Pharmacy and Life Sciences
Home Page: https://pharmaresearchlibrary.org/journals/index.php/ijrpls
CODEN (USA): IJRPL | e-ISSN: 2321–5038 | Publisher: Pharma Research Library
Int. J. Pharm. Natural Med., 2025, 13(1): 31-37
DOI: https://doi.org/10.30904/j.ijrpls.2025.4820

Formulation and Assessment of Rapidly Disintegrating Tablets of Empagliflozin by Enhancing Dissolution Rate and Bioavailability

Sai Tharun T P*[1], Dr. V. Anjaneyulu[2], Dr. Vijay Kumar Gampa[3]
[1]Department of Pharmaceutics, KGR Institute of Technology and Management, Rampally (V), Keesara(M), Medchal, Hyderabad -501302
[2]Professor&HOD, Department of Pharmaceutics, KGR Institute of technology and Management, Rampally (V), Keesara(M), Medchal, Hyderabad -501302
[3]Principal& Professor, Department of Pharmacy, KGR Institute of technology and Management, Rampally (V), Keesara(M), Medchal, Hyderabad -501302

ABSTRACT
This study developed and evaluated mouth disintegrating tablets (MDTs) of Empagliflozin to enhance patient compliance and rapid drug onset. Using UV spectrophotometry (λmax 225nm in 0.1NHCl), MDTs were prepared via direct compression with superdisintegrants SSG, Crospovidone, and Croscarmellose sodium. All formulations met pharmacopeial standards. Batch F-6 with Crospovidone showed the best performance, releasing 99% of the drug within 30 minutes. The findings confirm the effectiveness of a minimal-excipient, direct compression method for efficient Empagliflozin delivery.
Keywords: Empagliflozin, Mouth Disintegrating Tablets, Superdisintegrants, In Vitro Drug Release, Patient Compliance, UV Spectrophotometry

A R T I C L E I N F O

***Corresponding Author**
Sai Tharun T P
Department of Pharmaceutics,
KGR Institute of Technology and Management,
Rampally (V), Keesara(M), Medchal, Hyderabad -501302.

Article History:
Received 21 Mar 2025
Revised 23 April 2025
Accepted 17 May 2025
Published 07 June 2025

Citation: *Sai Tharun T P et al., Formulation and Assessment of Rapidly Disintegrating Tablets of Empagliflozin by Enhancing Dissolution Rate and Bioavailability. Int. J. Res. Pharm, L. Sci., 2025,13(1): 31-37.*

C O N T E N T S

1. Introduction

Dosage Regimen and Oral Drug Delivery

An ideal drug regimen quickly achieves and maintains therapeutic concentration throughout treatment. This is often done using conventional dosage forms administered at specific doses and intervals.

Oral Administration:

The most common and preferred method due to its simplicity, safety, cost-effectiveness, and ease of production. Most oral drugs are swallowed, though some dissolve in the mouth.

Challenges with Conventional Forms:

Tablets and capsules are widely used, but many groups such as elderly individuals, children, and patients with swallowing difficulties (e.g., due to tremors, nausea, or restricted fluid intake)—face challenges taking them.

Mouth Dissolving Tablets (MDTs):

To address these issues, MDTs were developed. They rapidly disintegrate in the mouth without water, enhancing patient convenience. They are also known as:

- Orally Disintegrating Tablets (ODTs)
- Fast dissolving or fast melting tablets
- Orodisperse

Mouth Dissolving Tablets (MDTs) are designed for rapid disintegration in the mouth without water, making them ideal for patients who have difficulty swallowing, such as children, the elderly, or those who are uncooperative or nauseated. These tablets are convenient, offer improved taste and mouthfeel, and maintain stability under various environmental conditions. They provide faster onset of action and improved bioavailability, especially for poorly

soluble drugs, and can be produced cost-effectively with existing manufacturing equipment. However, MDTs may have limitations like reduced mechanical strength and potential for unpleasant taste if not properly formulated. Common techniques for their formulation include freeze-drying, which creates highly porous and fast-dissolving tablets but is costly and fragile; tablet molding, which produces porous tablets through solvent or heat methods; spray drying, which incorporates bulking agents and superdisintegrants for rapid disintegration in under 20 seconds; and sublimation, where volatile ingredients are removed to leave a porous matrix, enabling quick tablet breakdown.

Direct compression is a straightforward and cost-effective technique for producing mouth dissolving tablets (MDTs), relying on superdisintegrants and sugar-based excipients to enhance disintegration speed and palatability. Superdisintegrants accelerate tablet breakdown, while sugar-based excipients like mannitol and sorbitol improve taste and mouthfeel. These sugars are classified into Type 1 (fast-dissolving, low moldability) and Type 2 (slow-dissolving, high moldability). The cotton candy process, or candy floss technique, creates a fast-dissolving, porous matrix using flash heat and centrifugal force, making it suitable only for heat-stable drugs. MDTs disintegrate through mechanisms such as wicking and swelling—where water penetrates and expands the tablet matrix—electrostatic repulsion between particles, deformation of compressed particles upon hydration, and gas release from effervescent agents like citric acid and bicarbonates. These mechanisms ensure rapid tablet breakdown in the mouth without water, though some require careful environmental control during manufacturing.

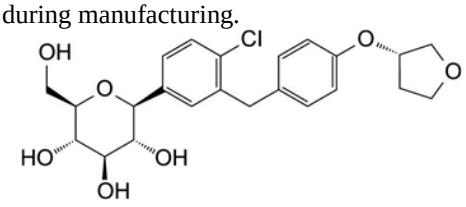

Fig.1 Empagliflozin

2. Methodology

Ingredients and Manufactures: The formulation of mouth dissolving tablets in this study utilized various pharmaceutical ingredients sourced from trusted suppliers. Empagliflozin was provided by Qualychrome Research Labs, while key excipients such as Sodium Starch Glycolate, Croscarmellose Sodium, Mannitol, Lactose, Avicel PH102, Aspartame, Magnesium Stearate, and Talc were all obtained from SD Fine Chemicals, Mumbai. Crospovidone and Peppermint flavouring were sourced from Nihal Pharma, Hyderabad. This diverse range of excipients was selected for their functional roles in tablet disintegration, taste enhancement, compressibility, and stability each contributing to the effective design of the final formulation.

Equipment and Companies

The equipment utilized in this study comprised a range of precision instruments essential for tablet formulation and evaluation. An Electronic Weighing Balance (Scale-Tec) was employed for accurate measurement of ingredients, while the Roche Friabilator from Electrolab, Mumbai, was used to assess tablet friability. Tablet compression was carried out using a CMD (Cadmach) Compression Machine. For evaluating mechanical strength, a Pfizer Hardness Tester (Mumbai) was utilized. The Labindia UV 3000+ spectrophotometer facilitated drug content analysis, and dissolution studies were performed using an Electrolab TDT-08L Dissolution Apparatus. Dimensional accuracy of the tablets was measured using Vernier Calipers (CD-6”CS). This robust set of instruments ensured reliable formulation, testing, and quality control throughout the study.

Preparation of 0.1N HCl (pH 1.2)

To prepare 0.1N hydrochloric acid, 8.5 mL of concentrated HCl was diluted to 1000 mL with distilled water.

Determination of λmax for Empagliflozin

A stock solution of Empagliflozin (1000 µg/mL) was prepared by dissolving 100 mg of drug in 10 mL methanol and diluting to 100 mL with 0.1N HCl. Serial dilutions (100 µg/mL and 10 µg/mL) were made, and the final solution was scanned between 200–400 nm. The wavelength showing maximum absorbance was recorded as the λmax.

Calibration Curve Construction

From the 100 µg/mL intermediate solution, volumes of 0.2, 0.4, 0.6, 0.8, and 1.0 mL were each diluted to 10 mL to prepare standard solutions of 2, 4, 6, 8, and 10 µg/mL. Their absorbance was measured at the determined λmax of 225 nm to plot the calibration curve.

Preparation of Oral Disintegrating Tablets

Direct compression method:

Mouth disintegrating tablets of Empagliflozin were prepared by direct compression. All ingredients were sieved (#40 mesh), mixed uniformly in stages—with the drug and excipients blended first, followed by remaining ingredients in geometric order. Magnesium stearate and talc were added last and mixed for 2 minutes. The final blend was compressed into 75 mg tablets using 6 mm flat round punches.

Evaluation of Tablets:

The pre-compression evaluation of tablets included assessment of flow and density properties.

The angle of repose, calculated using the funnel method, helped determine powder flow ability values below 30° indicated excellent flow. Bulk density and tapped density were measured to understand packing behavior; from these, **Carr’s index** and **Hausner’s ratio** were calculated to assess compressibility and flow ability. Carr’s index values below 15% and Hausner’s ratios near 1.1 suggest good powder flow, essential for efficient tablet compression and uniformity.

B) Post compression studies:

General appearance: The formulated tablets were assessed for its general appearance and observations were made for shape, colour, texture and odour.

Average weight/Weight Variation: 20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to

assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 200mg tablets and none by more than double that percentage.

Average weight = $\frac{\text{weight of 20 tablets}}{20}$

%wt variation = $\frac{\text{average wt - wt of each tablet}}{\text{Average weight}} \times 100$

Thickness: Thickness of the tablets (n=3) was determined using a Verniercalipers.

Hardness test: Hardness of the tablet was determined by using the Monsanto hardness tester (n=3) the lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

Friability test: This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the Friabilator, rotating at 25rpm for 4min.

The difference in the weight is noted and expressed as percentage.

It should be preferably between 0.5 to 1.0%.

%Friability = $[(W_1-W_2)/W_1]$ X 100

Where, W_1= weight of tablets before test,

W_2 = weight of tablets after test

Wetting time:

Five circular tissue papers were placed in a petridish of 10cm diameter. Ten millimeters of water was added to the petridish. A tablet was carefully placed on the surface of the tissue paper in the petridish at 25^0C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. These measurements were carried out in replicates of six. Wetting time was recorded using a stopwatch.

***In- Vitro* Dispersion Time:**

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of 0.1N HCL. Tablets from each formulation were randomly selected and in vitro dispersion time was performed.

Water absorption ratio(%):

A piece of tissue paper folded twice was placed in a small petridish (Internal diameter=6.5 cm) containing 6ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was w determined using the following equation.

$$\textbf{\textit{Water absorption ratio}}\ (\boldsymbol{R}) = \frac{\boldsymbol{Wa - Wb}}{\boldsymbol{Wb}} * \mathbf{100}$$

Where, Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after absorption.

Assay Procedure:

Ten tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of Empagliflozin was transferred to a 100 ml volumetric flask and 10 ml methanol is added. The drug is extracted in methanol by vigorously shaking the stoppered flask for 15 minutes. Then the volume is adjusted to the mark with 0.1N HCL and the liquid is filtered. From prepared solution take 0.1ml soluion in 10ml volumetric flask and make up to mark with 0.1 N HCL. The Empagliflozin content was determined by measuring the absorbance at 257 nm after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

6. Calculate the quantity in mg of drug in the portion taken by the formula

Assay = test absorbance/standard absorbance*standard concentration/sample concentration*purity of drug/100*100

In vitro Dissolution Study:

900 ml of 0.1N HCL was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of 37^0C±0.5^0C. A tablet was placed in the vessel and was covered; the apparatus was operated up to 30mins at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium were analyzed spectrophotometrically at λ_{max} =225nm using a UV-spectrophotometer (Lab India).

Table.9: Weight Variation Tolerance for Uncoated Tablets

Average weight of tablet(mg)	% difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

7. **Assay Procedure:**
8. Ten tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of Empagliflozin was transferred to a 100 ml volumetric flask and 10 ml methanol is added. The drug is extracted in methanol by vigorously shaking the stoppered flask for 15 minutes. Then the volume is adjusted to the mark with 0.1N HCL and the liquid is filtered. From prepared solution take 0.1ml soluion in 10ml volumetric flask and make up to mark with 0.1N HCL. The Empagliflozin content was determined by measuring the absorbance at 257 nm after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations. Calculate the quantity in mg of drug in the portion taken by the formula
9. **Assay =** test absorbance/standard absorbance*standard concentration/sample concentration*purity of drug/100*100

In vitro Dissolution Study:

900 ml of 0.1N HCL was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of 37^0C±0.5^0C. A tablet was placed in the vessel and was covered; the apparatus was operated up to 30mins at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium were analyzed spectrophotometrically at λ_{max} =225nm using a UV-spectrophotometer (Lab India).

3. Results and Discussion

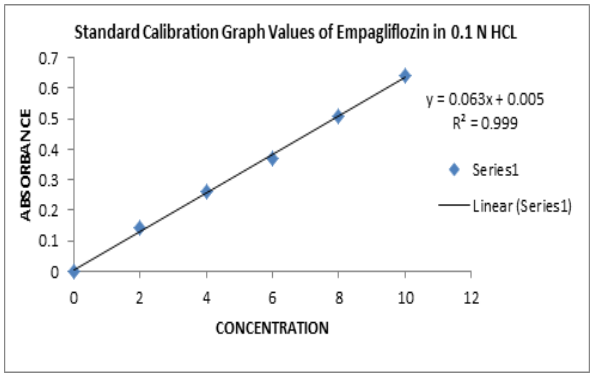

Figure.2: Standard Calibration Curve of Empagliflozin in 0.1 N HCL

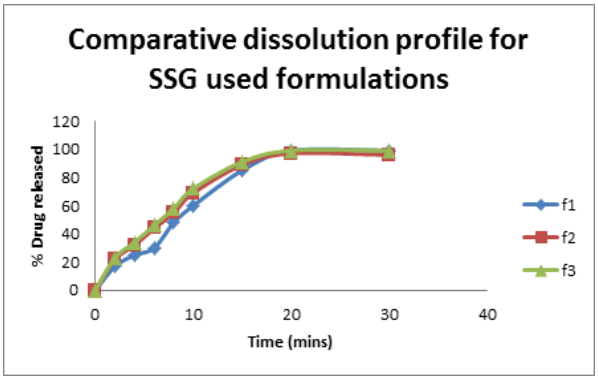

Figure 3: Comparative dissolution profiles for SSG used Formulations

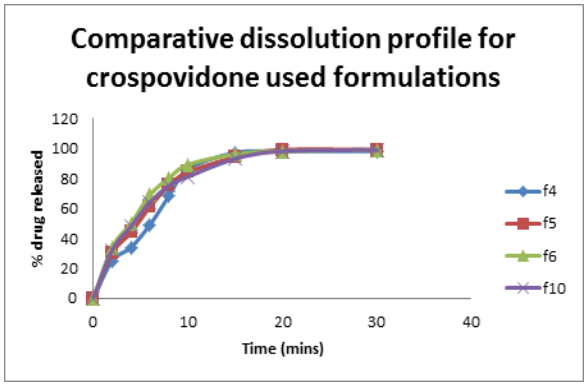

Figure.4: Comparative dissolution profiles for Crospovidone used Formulations

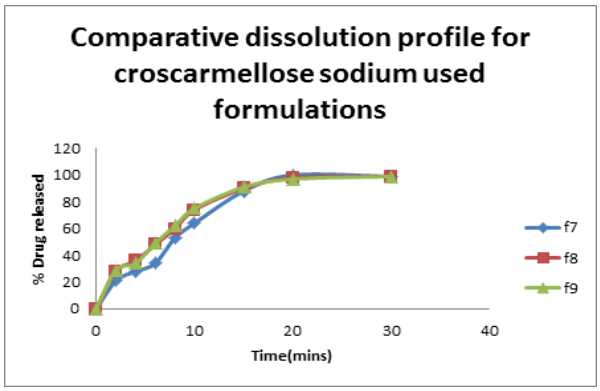

Figure 5: Comparative dissolution profiles for Croscarmellose sodium used FormulationsFig.9: SEM analysis of optimized formulation LN3

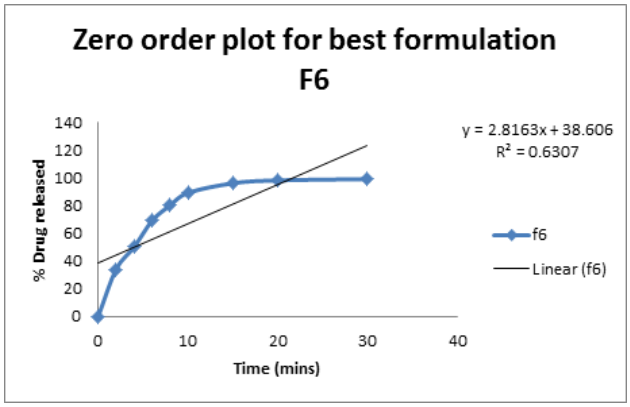

Figure 6: Zero order plot for best formulation F6

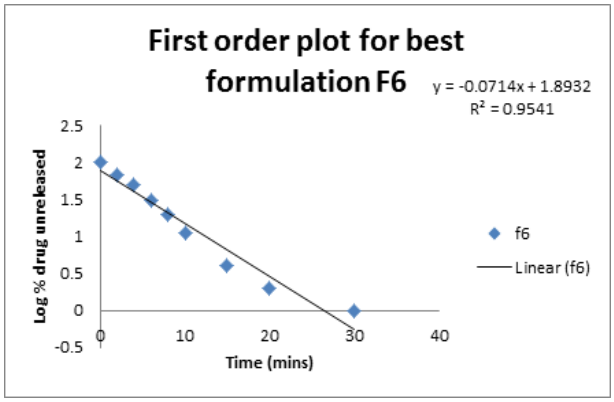

Figure 7: First order plot for best formulation F6

Table 1. Dissolution Parameters

Parameter	Details
Dissolution apparatus	USP -Type II (paddle)
Medium	0.1N HCL
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
Sample volume withdrawn	5ml
Time points	2, 4, 6, 8, 10, 15, 20 and 30mins
Analytical method	Ultraviolet Visible Spectroscopy
λmax	225 nm

Table 2. Formulation of Mouth Disintegrating Tablets of Empagliflozin

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Empagliflozin	10	10	10	10	10	10	10	10	10	10
SSG	20	40	60							
Crospovidone				20	40	60				60
CCS							20	40	60	
Mannitol	60	60	60	60	60	60	60	60	60	60
Lactose	-	-	-	-	-	-	-	-	-	52.5
MCC pH 102	92.5	72.5	52.5	92.5	72.5	52.5	92.5	72.5	52.5	-
Aspartame	5	5	5	5	5	5	5	5	5	5
Pipperment flavour	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	5	5	5	5	5	5	5	5	5	5
Megnesium stearate	5	5	5	5	5	5	5	5	5	5
Total weight (mg)	200	200	200	200	200	200	200	200	200	200

Table 3. Standard Calibration Graph Values of Empagliflozin in 0.1 N HCL

Concentration (µg/ml)	Absorbance
0	0
2	0.141
4	0.26
6	0.372
8	0.507
10	0.64

Table 4. Pre Compression Studies of Empagliflozin Oral Disintegrating Tablets

Formulation code	Bulk density (Kg/cm^3)	Tapped density (Kg/cm3)	Cars index	Hausners ratio	Angle of repose (˚)
F1	0.40	0.48	16	1.2	32.73
F2	0.39	0.48	18	1.23	34.96
F3	0.50	0.58	13	1.16	28.58
F4	0.44	0.50	12	1.1	27.92
F5	0.37	0.41	9.75	1.1	25.35
F6	0.37	0.41	9.75	1.1	33.14
F7	0.36	0.39	7.6	1.0	27.03
F8	0.41	0.45	8.8	1.0	31.85
F9	0.39	0.48	18	1.23	28.96
F10	0.41	0.45	8.8	1.0	27.85

Table 5. Post Compression Studies for Oral Disintigrating Tablets of Empagliflozin

Batch	Hardness (kg/cm2)	Friability (%)	Drug Content (%)	Thickness (mm)	Disintegration Time (sec)	Wetting Time (sec)	In vitro dispersion time	Weight variation	Water absorption ratio
F1	3.1	0.45	99.12	2.5	30	45	29	pass	61.3
F2	2.9	0.62	100.73	2.8	25	42	34	pass	69.8
F3	3.3	0.71	99.74	2.6	20	35	25	pass	73.4
F4	2.5	0.32	98.98	2.5	31	31	32	pass	86.2
F5	2.8	0.51	99.67	2.6	27	36	31	pass	84.12
F6	2.8	0.52	99.83	2.8	25	43	33	pass	93.4
F7	2.9	0.38	101.32	2.8	31	41	36	pass	64.3
F8	3.2	0.48	100.87	2.5	26	36	33	pass	74.8
F9	3.5	0.63	99.74	2.7	24	48	39	pass	76.1
F10	3.0	0.54	99.86	2.6	32	39	28	pass	82.3

Table 6. Dissolution Data of Oral Disintegrating Tablets of Empagliflozin

Time points (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	**0**	0	0	0	0
2	17	22	23	25	30	**34**	21	28	29	32
4	25	32	34	34	44	**50**	28	36	34	48
6	30	44	46	49	61	**69**	34	48	49	64
8	48	55	58	68	75	**80**	53	60	62	75
10	60	69	72	86	84	**89**	64	74	75	81
15	85	89	91	97	94	**96**	88	90	91	93
20	99	97	99	98	99	**98**	100	98	97	98
30	99	96	99	98	99	**99**	99	99	99	99

4. Conclusion

The study successfully developed a UV-Visible spectrophotometric method for Empagliflozin, identifying its λmax at 225 nm in 0.1N HCl. Mouth disintegrating tablets (MDTs) were formulated using the direct compression method with superdisintegrants like SSG, Crospovidone, and Croscarmellose sodium. All formulations met standard evaluation parameters, and in vitro drug release studies identified formulation F-6 (with Crospovidone) as the most effective, releasing 99% of the drug within 30 minutes. The study concludes that a simple, low-excipient formulation via direct compression is effective for rapidly disintegrating Empagliflozin tablets.

5. References

[1] Brahmankar D. M., Jaiswal S.B., Bio pharmaceutics& Pharmaceutics, First Edition, 1995, 335.

[2] Howard C. Ansel, Nicholas G. Popvich, Loyd V. Allen, Pharmaceutical Dosage Forms and Drug Delivery System, First Edition, 1995, 78.

[3] S. S. Biradar, S. T. Bhagavati and I. J. Kuppasad, Fast Dissolving Drug Delivery Systems: A Brief Overview,Internet J. Pharmacology, 2006, 4(2).

[4] Kuccherkar B.S., Badhan A.C., Mahajan H.S., Mouth dissolving tablets: A novel drug delivery system, Phrma Times, 2003, 35, 3-10.

[5] Kaushik D, Dureja H., Saini T. R., Mouth Dissolving Tablets: A review, Indian Drugs, 2004, 41(4), 187-193.

[6] Amin A. F., Shah T. J., Bhadani M. N., Patel M. M., Emerging trends in orally disintegrating tablets, www.pharminfo.net, 2005.

[7] Renon J. P. and Corveleyn S., Freeze-dried rapidly disintegrating tablets, US Patent No. 6,010,719, 2000.

[8] Lailla J. K., Sharma A. H., Freeze-drying and its applications, Indian Drugs, 1993, 31, 503-513.

[9] Seager H., Drug delivery products and zydis fast dissolving dosage form, J. Pharm. Phamacol., 1998, 50, 375-382.

[10] Masaki K., Intrabuccaly disintegrating preparation and production, US Patent No. 5,466,464, 1995.

[11] Lidiane M Monteiro, Viviane F Lione, Flavia A do Carmo, Lilian H do Amaral, Julianna H da Silva, Luiz E Nasciutti, Carlos R Rodrigues, Helena C Castro, Valeria P de Sousa, and Lucio M Cabral, (Sep 28-2012) Development and characterization of a new oral dapsone nanoemulsion system: permeability and in silico bioavailability studies, Int J Nanomedicine.; 7: 5175–5182., Published online 2012 Sep 28.

[12] Jan Sahai, PharmD; Gary Garber, MD; Keith Gallicano, PhD; Linda Oliveras, BSc; and D. William Cameron, MD, Effects of the Antacids in Didanosine Tablets on Dapsone (1995) Pharmacokinetics, Ann Intern Med. ;123(8): 584-587.

[13] Gunda RK, Kumar JN, Prasad AB, Madhya B, Bhargavi G, Padmaja KN, Praveen S. (May 21-2024)Development and Characterization of Fast Dissolving Tablets for Empagliflozin. Journal of Applied Pharmaceutical Sciences and Research.;7(1):27-31.

[14] Hossain MS, Jahan S, Rahman SA, Rahman M, Kumar D, Paul S, Rajbangshi JC. (Mar 1-2023)Design expert software assisted development and evaluation of empagliflozin and sitagliptin combination tablet with improved in-vivo anti-diabetic activities. Heliyon.;9(3).

[15] Krishna KV, Chandra KB.(2018) Development, characterization and evaluation of empagliflozin spherical agglomerates using spherical agglomeration technique. J Pharm Innov.; 7(3):202-7.

[16] Lakambare s, phatak a, bhadagale m, bafna v.(2023) Formulation development and optimization of empagliflozin film coated tablet using quality-by-design approach. Asian j pharm clin res.;16(1):161-7.

[17] Glund S, Mattheus M, Runge F, Rose P, Friedrich C. (Apr 1-2017)Relative bioavailability of an empagliflozin 25-mg/linagliptin 5-mg fixed-dose combination tablet. International Journal of Clinical Pharmacology and Therapeutics.; 55(4):355.

[18] Niguram P, Polaka SN, Rathod R, Kalia K, Kate AS. (Feb 1-2020)Update on compatibility assessment of empagliflozin with the selected pharmaceutical excipients employed in solid dosage forms by thermal, spectroscopic and chromatographic techniques. Drug Development and Industrial Pharmacy.;46(2):209-18.

[19] Hanif AM, Bushra R, Iffat W, Ghayas S, Perveen S, Riaz H, Alam S, Ali SI, Ismail NE.(Jul 2-2021)

Optimization of empagliflozin immediate release tablets (10 mg) using central composite rotatable design with response surface methodology. Pakistan Journal of Pharmaceutical Sciences.;34.

[20] Podichety N, Jyothi P, Pradeep K, Maddali RK.(Aug 27- 2022) Formulation and evaluation of empagliflozin drug loaded polymeric nanoparticles for the treatment of type 2 diabetes mellitus (T2DM). Current Trends in Biotechnology and Pharmacy.;16(3):308-15.