RESEARCH ARTICLE

Development and Characterization of Fast Dissolving Tablets for Empagliflozin

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Abstract

Objective: The current study's objective is to develop and evaluate fast-dissolving tablets (FDT) for Empagliflozin. Empagliflozin, new class of oral hypoglycemic agent. It is indicated as an adjunct to exercise and diet to improve glycemic control in adult patients of type-2 diabetes. It acts by inhibiting sodium glucose co-transporter (SGLT-2). Since oral absorption of empagliflozin from tablet is comparatively poor, hence an effort was made to enhance its absorption by formulating it as the fast dissolving tablet.

Methods: Using various quantities of Kollidon-CL & Ac-Di-Sol as Superdisintegrants, FDT formulations of Empagliflozin were preared utilising the Direct Compression technique. Nine trials were developed and assessed for Pharmaceutical Product Performance.

Results: Findings indicate that all formulations meet the acceptance criteria, and kinetic modeling was applied to the *in-vitro* dissolution profiles.

Conclusion: The best formulation (F_1) containing 6 mg of Kollidon-CL and 6 mg of Ac-Di-Sol showed promising results for quicker disintegration and may produce patient compliance by rapid onset of action and preventing first pas effect too. Formulation (F_1) follows first order, whereas the release mechanism was found to be non-fickian type (n = 0.762).

Keywords: Empagliflozin, Superdisintegrants, Ac-Di-Sol, Kollidon-CL, Non-Fickian.

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Introduction

The pharmaceutical market gives fast-dissolving tablets (FDT) a unique place. FDT was regularly replaced with oral disintegrating tablets, melt-in-the-mouth pills and oral/mouth dissolving tablets.[1]

Rapid disintegrating tablets can be readily available for disintegration. They break down in the mouth within 60 seconds. Based on the manufacturing process, they show changes in typical organoleptic features, including masking sweetness or taste and better palatability. Additionally, they show changes in quality control metrics like breaking index, drug release from formulation, stability, and clinical results. FDTs can be prepared using a variety of procedures, some of which are the cotton candy process, granulation techniques, named technologies (Durasolv, Orosolv), spray drying, trituration, molding, lyophilization/freeze drying, and mass extrusion.[2]

Empagliflozin is a sodium-glucose co-transporter (SGLT-2) inhibitor that is a new class of oral hypoglycemic agent. Such inhibition of SGLT-2, it prevents the reabsorption of glucose from the glomerular filtration of a kidney. Since oral absorption of empagliflozin from a tablet is comparatively poor (takes almost 3 hours to get absorbed), hence an effort was made to enhance its absorption by formulating it as the fast dissolving tablet. The objective of the present work is to develop fast dissolving empagliflozin tablets and to study the effect of functionality differences of super disintegrants (Kollidon-CL, Ac-Di-Sol) on the tablet properties.[3-5]

Tablets by direct compression techniques have a unique nature in the form of less time consumption, rapid production, and economy in operational management among the many methods of manufacturing techniques available.[2,6]

Materials and Methods

Materials

Empagliflozin was a gift sample procured from Meditech Pharma Pvt Ltd, India. Avicel, Ac-Di-Sol, and Kollidon-CL were procured from National Scientifics, Guntur. Other excipients were procured from High Chemie Ltd, Vadodara.

Preparation of Empagliflozin fast dissolving Tablets

The direct compression approach was used in the production of empagliflozin FDT as per the formulae presented in Table 1. About 10 mg of empagliflozin with β-CD in the different ratios was taken. β-cyclodextrin was taken in a mortar-pestle. Subsequently, the drug was incorporated slowly into it and trituration was further continued for one hour and passed through sieve no. # 60. All the ingredients were mixed step by step with the drug: β-cyclodextrin inclusion complex and triturated continuously for 15 minutes. Subsequently, talc and magnesium stearate were mixed and passed through sieve no. #60. The powder was compressed using 8 8-station

Table 1: Formulae for the Preparation of Empagliflozin Oral Disintegrating Tablets

Name of Ingredients	*Quantity of Ingredients per each tablet (mg)*								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Empagliflozin Mixture	20	20	20	20	20	20	20	20	20
Avicel pH 102	32	32.5	33	32.5	33	33.5	33	33.5	34
Pearlitol	32	32.5	33	32.5	33	33.5	33	33.5	34
Kollidon-CL	6	6	6	5	5	5	4	4	4
Ac-Di-Sol	6	5	4	6	5	4	6	5	4
Talc	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total Weight	100	100	100	100	100	100	100	100	100

rotary tablet punching machine (RIMEK minipress) using 8 mm circular punches and the same hardness was used for the required number of tablets. In-Process Quality Control (IPQC) tests were performed on the acquired tablets. For storage and subsequent processing, finished tablets were transferred to airtight, light-resistant containers.[7]

Evaluation of Empagliflozin Fast-dissolving tablets

Hardness

It was carried out with the help of Monsanto tablet hardness tester.[8]

Friability/Durability

Twenty tablets were weighed and noted as W_0 cumulatively (Initial weight). The pills were then dedusted with a Roche Friabilator for 4 minutes at a speed of 25 rpm and weighed again recorded as (W). The following equation was used to obtain the percentage of friability (%Friability ≤1).

Friability (%) = $(W_0 - W) / W_0 \times 100$

Assay

About 20 tablets were chosen and ground in an impartial manner. The powder corresponding to 100 mg of empagliflozin was weighed, added to a 100 mL volumetric flask with 60 mL of phosphate buffer solution (PBS) pH 6.8, and then sonicated for 10 minutes to completely solubilize the medication. The resulting solution was then diluted with PBS pH 6.8 to make up the required volume. Prepare a further 2 mL aliquot from that for dilution in 100 mL of PBS pH 6.8. Using a UV-visible spectrophotometer, the resulting solution was analyzed for its absorbance at 222 nm.

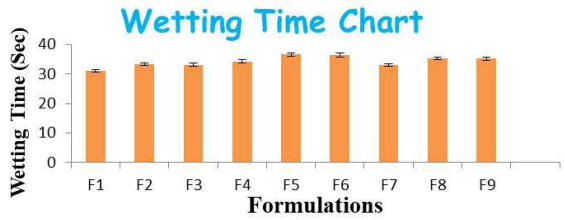

Figure 1: Wetting Time Chart

Thickness

It was measured with the help of verinier calipers.[9]

Wetting time

Tablets were placed on a petri dish containing paper that had been soaked in 5 mL of distilled water to measure the wetting time of the tablets. The tablet's wetting time was measured in seconds.

In-vitro Dissolution Study

Empagliflozin ODT was analyzed for drug release study utilizing a Lab-India USP type-II tablet dissolution test apparatus and 900 mL of PBS pH 6.8 buffer in accordance with the official method. Using a UV-visible spectrophotometer, samples' absorbance was measured at 222 nm and the data was subjected to kinetic modeling.[10,11]

Disintegration test

According to the guidelines of the modified disintegration test for tablets, this test was conducted. Only 2 mL of medium were allowed to fall below the sieve in a cylindrical cylinder with 10 #. The time of disintegration was noted.[12]

Results and Discussion

About 9 different formulations of Empagliflozin fast-dissolving tablets were prepared utilizing the direct compression method using varying ratios of super disintegrants in accordance with the formulae shown in Table 1. Pharmaceutical product performance tests were conducted on the developed formulations. Table 2 displays the information.

All tablets were discovered to be less brittle and to have acceptable mechanical strength. The produced tablets' uniformity of weight and drug content were both within acceptable ranges. All the formulations showed wetting time in the range of 30.98 ± 0.46 to 35.41 ± 0.42 sec and the same was represented as Figure 1. All the formulations showed Disintegration time in the range of 31.34 ± 0.42 to 41.13 ± 0.2 sec and the same was represented as Figure 2.

Dissolution profiles of empagliflozin fast dissolving tablets were well fit to kinetic modeling, results presented

Table 2: Post-Compression Parameters

Formulation Code	*Hardness (kg/cm²)*	*Thickness (mm)*	*Friability (%)*	*Average Weight (mg)*	*Drug Content (%)*	*Wetting Time (sec)*	*Disintegration Time (sec)*
F_1	3.75 ± 0.057	3.77 ± 0.053	0.293 ± 0.01	99.31 ± 0.46	99.22 ± 0.703	30.98 ± 0.46	31.34 ± 0.418
F_2	3.75 ± 0.105	3.76 ± 0.0525	0.338 ± 0.015	99.86 ± 0.94	98.45 ± 0.7245	33.17 ± 0.531	32.81 ± 0.441
F_3	3.7 ± 0.104	3.76 ± 0.055	0.349 ± 0.013	98.19 ± 0.56	96.9 ± 0.575	33.38 ± 0.454	34.08 ± 0.394
F_4	3.7 ± 0.057	3.73 ± 0.041	0.302 ± 0.007	100.01 ± 1.09	98.32 ± 0.788	34.28 ± 0.563	32.39 ± 0.181
F_5	3.7 ± 0.105	3.72 ± 0.04	0.347 ± 0.012	100.10 ± 0.53	97.56 ± 0.81	36.46 ± 0.634	33.86 ± 0.203
F_6	3.65 ± 0.104	3.73 ± 0.043	0.358 ± 0.01	99.19 ± 0.90	96.01 ± 0.66	36.68 ± 0.557	35.13 ± 0.155
F_7	3.65 ± 0.079	3.73 ± 0.041	0.354 ± 0.01	100.85 ± 0.75	97.86 ± 0.678	32.99 ± 0.424	38.39 ± 0.2
F_8	3.65 ± 0.126	3.72 ± 0.042	0.399 ± 0.015	100.81 ± 0.19	97.09 ± 0.699	35.18 ± 0.495	39.86 ± 0.223
F_9	3.6 ± 0.126	3.72 ± 0.044	0.409 ± 0.013	100.26 ± 0.45	95.54 ± 0.549	35.41 ± 0.418	41.13 ± 0.175

Table 3: Statistical Parameters

S. No.	*Formulation Code*	*Kinetic parameters*											
		Zero Order			*First order*			*Higuchi*			*Korsmeyer-peppas*		
		a	*b*	*r*	*a*	*b*	*r*	*a*	*b*	*r*	*a*	*b*	*r*
1	F_1	4.985	3.195	0.995	2.234	0.053	0.879	9.150	17.936	0.972	0.852	0.762	0.989
2	F_2	3.916	3.124	0.996	2.187	0.045	0.890	9.475	17.411	0.966	0.825	0.768	0.983
3	F_3	3.313	2.988	0.996	2.120	0.035	0.928	9.321	16.607	0.963	0.792	0.776	0.986
4	F_4	4.709	3.102	0.996	2.140	0.040	0.934	8.978	17.404	0.972	0.832	0.766	0.990
5	F_5	3.640	3.030	0.996	2.127	0.037	0.929	9.303	16.878	0.965	0.805	0.772	0.984
6	F_6	3.037	2.895	0.996	2.093	0.031	0.946	9.149	16.074	0.962	0.769	0.781	0.986
7	F_7	4.855	2.943	0.994	2.079	0.031	0.970	8.298	16.561	0.973	0.821	0.760	0.989
8	F_8	3.786	2.872	0.995	2.076	0.029	0.965	8.623	16.036	0.967	0.792	0.767	0.984
9	F_9	3.183	2.737	0.995	2.060	0.025	0.968	8.469	15.231	0.964	0.755	0.776	0.986

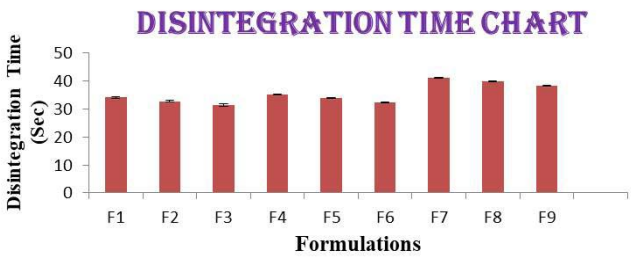

Figure 2: Disintegration Time Chart

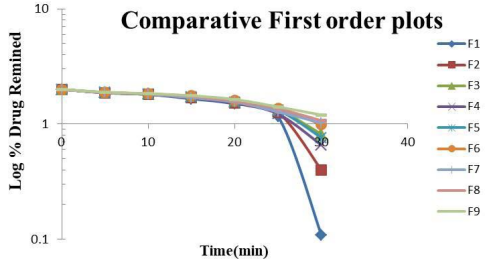

Figure 4: Comparative First order plots

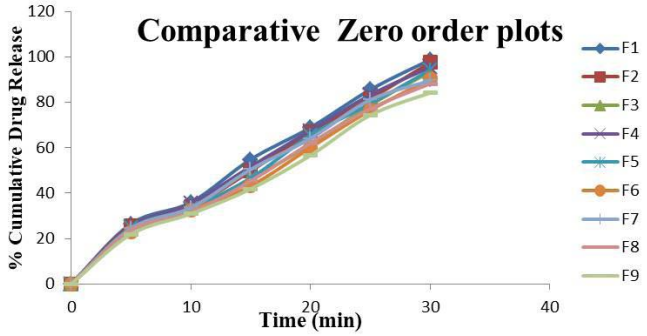

Figure 3: Comparative Zero order plots

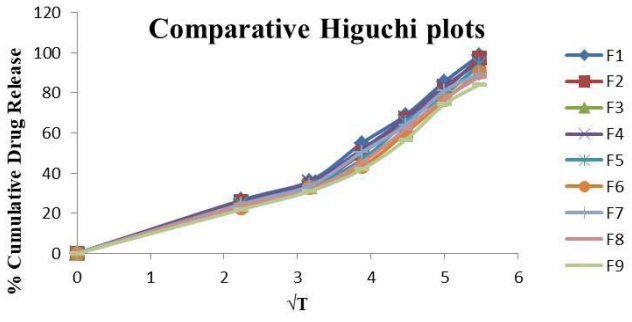

Figure 5: Comparative Higuchi plots

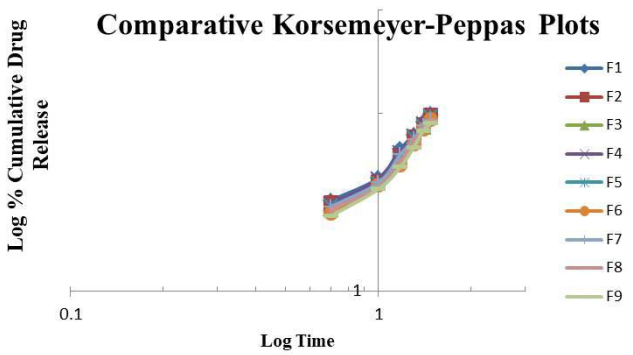

Figure 6: Comparative Korsmeyer-Peppas plots

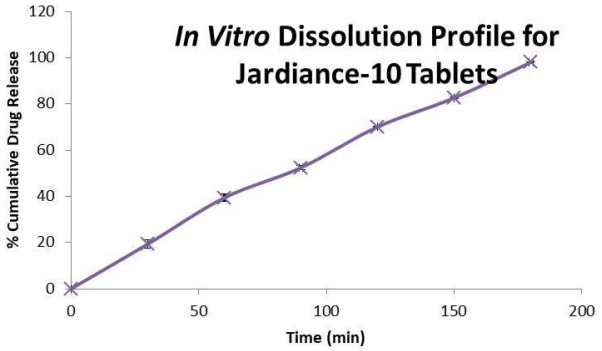

Figure 7: *In-vitro* Dissolution Profiles for Jardiance-10

Table 4: Kinetic Parameters

S. No.	Formulation Code	Kinetic Parameters (min)				
		$t_{10\%}$	$t_{25\%}$	$t_{50\%}$	$t_{75\%}$	$t_{90\%}$
1	F_1	0.865	2.362	5.692	11.384	18.914
2	F_2	1.014	2.768	6.671	13.341	22.166
3	F_3	1.307	3.569	8.600	17.200	28.577
4	F_4	1.139	3.110	7.493	14.987	24.900
5	F_5	1.249	3.411	8.220	16.440	27.316
6	F_6	1.495	4.082	9.836	19.672	32.686
7	F_7	1.456	3.976	9.581	19.162	31.837
8	F_8	1.566	4.276	10.304	20.607	34.239
9	F_9	1.794	4.898	11.804	23.607	39.223

in Table 3 and the same was shown in Figures 3-6.

F_1 is regarded as the best formulation among all batches (based on Desirability). F_1, which contained 6 mg of Ac-Di-Sol and Kollidon-CL in equal amounts, produced promising dissolution characteristics that aid in achieving the goal of the study through faster disintegration and rapid dissolution. Table 4 provides a summary of the data for the derived kinetic parameters.

The *in-vitro* dissolution profile of marketed product **(**Jardiance-10**)** tablets was presented as Figure 7.

Conclusion

The current study focuses on the impact of using superdisinterants for the development of Empagliflozin FDT, such as Ac-Di-Sol and Kollidon-CL. F_1 follows zero-order type of kinetics, Higuchi type model, whereas the mechanism of drug release follows non-fickian diffusion. The best formulation F_1 may be used for the effective management of Type-II Diabetes mellitus, also contributes to reduced hyperglycemia and assists in weight loss and reduction of blood pressure.

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