DRUG DISCOVERY

Development and characterization of felodipine fast dissolving tablets

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ABSTRACT

Objective: The current study's objective is to develop and characterise fast-dissolving tablets (FDT) for felodipine. Felodipine an excellent calcium channel blocker. It is primarily used to effectively control angina pectoris and hypertension. It has a limited bioavailability after oral administration due to its extremely low solubility in GI fluid. Thus, it is imperative to develop Felodipine appropriate dosage forms in order to ensure consistent bioavailability. Hence, it is necessary to develop appropriate dose forms, such as a mouth-dissolving or disintegrating tablet, in order to obtain improved patient compliance. *Methods:* Using various quantities of Ac-di-sol & Explotab as Super-disintegrants, FDT formulations of felodipine were prepared 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 modelling was applied to the in-vitro dissolution profiles. *Conclusion:* The best formulation (F_5), which is likewise identical to the marketed product (PLENDIL-5) (f2= 87.35, f1= 1.97), contained 6 mg of Ac-di-sol and 6 mg of Explotab. Formulation (F_5) follow first order, whereas release mechanism found to be fickian type (n= 0.449).

Keywords: Felodipine, super-disintegrants, Explotab, Ac-di-sol, Fickian.

1. INTRODUCTION

The pharmaceutical market gives Fast Dissolving Tablets (FDT) a unique place. FDT was regularly replaced with melt-in-the-mouth pills and oral dissolving tablets (Gunda et al., 2018). Rapid disintegrating tablets can be readily available for disintegration, they breakdown 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 result. FDTs can be prepared using a variety of procedures, some of which are cotton candy process, granulation techniques, named technologies (Durasolv, Orosolv), spray drying, trituration, moulding, lyophilization/freeze drying and mass extrusion (Gunda et al., 2016).

Felodipine belongs to the class of CCB (Blocker of Calcium Channel), antihypertensive and anti-anginal agent. One of the main issues with this

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medication is that it dissolves very poorly in GI fluid, which leads to poor bioavailability when taken orally. So, it is necessary to develop a fast-dissolving tablet for the chosen medicine in order to enhance dissolution and prevent the first pass effect there by improving patient compliance (Tapas et al., 2009; Kumar et al., 2012; Rao et al., 2016).

An attempt was made to maximize the drug delivery from formulation with the help of combination super disintegrants at various concentrations (Ac-di-sol, Explotab) by formulating the Fast-dissolving tablets for Felodipine. Tablets by Direct Compression Techniques have a Unique Nature in the Form of Less Time Consumption, Rapid Production and Economy in the Operational Management among the Many Methods of Manufacturing Techniques Available (Gunda et al., 2016; Gunda et al., 2021).

2. MATERIALS AND METHODS

Materials

Felodipine was a gift sample procured from Meditech Pharma Pvt Ltd, India. Avicel, Explotab, Ac-di-sol were procured from National Scientifics, Guntur. Other excipients were procured from High Chemie Ltd, vadodara.

Preparation of Felodipine Fast Dissolving Tablets

The direct compression approach was used in the production of felodipine FDT as per the Formulae (Table 1). All of the components were sifted using 40 meshes (#40) to produce a uniform fine blend. Lubricants were screened through #60, combined with the mixture above and mixed well. These blends were subjected to compression to produce FDT using a tablet minipress (8 stations) and circular punches that measure 8 mm in diameter. IPQC tests were performed on the acquired tablets. For storage and subsequent processing, finished tablets were transferred to airtight, light-resistant containers (Gunda et al., 2017).

Evaluation of Felodipine fast dissolving tablets

Hardness

It was carried out with the help of Monsanto Tablet Hardness Tester (Gunda et al., 2020).

Friability/Durability

Twenty tablets were weighed and noted as W_0 cumulatively (Initial weight). The pills were then deducted 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).

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

Assay

20 tablets were chosen and ground in an impartial manner. The powder corresponding to 100 mg of felodipine was weighed, added to a 100 mL volumetric flask with 60 mL of methanol and then sonicated for 10 minutes to completely solubilize the medication. The methanolic solution was then diluted with water to make up the required volume. Prepare a further 2 mL aliquot from that for dilution in 100 mL of 0.1 N HCl. Using a UV-visible spectrophotometer, the resulting solution was analyzed for its absorbance at 362 nm.

Thickness

It was measured with the help of verinier calipers (Gunda and Manchineni, 2020).

Wetting time

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

In-vitro Dissolution Study

Felodipine FDT was analyzed for drug release study utilising a Lab-India dissolution test apparatus and 900 ml of pH 6.8 buffers in accordance with the recommended method as outlined in the monograph. Using a UV-visible spectrophotometer, samples' absorbance was measured at 362 nm and the data was subjected to kinetic modeling (Higuchi, 1963; Peppas, 1985).

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 #. Time of disintegration was noted (Gunda et al., 2016).

3. RESULTS AND DISCUSSION

9 different formulations of felodipine fast-dissolving tablets were prepared utilising the direct compression method using varying ratios of super disintegrants in accordance with the formulae (Table 1). Pharmaceutical product performance tests were conducted on the developed formulations. Table 2 displayed the information.

Table 1 Formulae for the Preparation of Felodipine Fast dissolving 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
Felodipine	5	5	5	5	5	5	5	5	5
Avicel pH 102	37.5	38.5	39.5	38.5	39.5	40.5	39.5	40.5	41.5
Lactose	37.5	38.5	39.5	38.5	39.5	40.5	39.5	40.5	41.5
Ac-Di-Sol	8	8	8	6	6	6	4	4	4
Explotab	8	6	4	8	6	4	8	6	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

Table 2 Post-Compression Parameters

S. No	Formulation Code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Average Weight (mg)	Drug Content (%)	Wetting Time (sec)	Disintegration Time (sec)
1	F_1	3.8±0.125	3.675±0.48	0.55±0.07	99.32±0.45	99.775±0.8	37.5±2.3	50.75±1.8
2	F_2	3.75±0.225	3.65±0.04	0.45±0.065	99.85±0.95	99.525±2.05	42.5±2.2	58.35±2.2
3	F_3	3.85±0.205	3.54±0.05	0.45±0.06	98.2±0.55	99.39±1.12	45±2.01	62.95±2.1
4	F_4	4.05±0.33	3.705±0.495	0.5±0.06	100.04±1.1	100.5±1.35	51.65±1.9	61.15±1.5
5	F_5	4±0.34	3.68±0.055	0.4±0.055	100.11±0.54	100.25±2.6	56.65±1.8	68.75±2.3
6	F_6	4.1±0.32	3.57±0.065	0.4±0.005	99.18±0.89	100.115±1.67	59.15±1.7	73.35±1.9
7	F_7	4±0.18	3.79±0.49	0.6±0.065	100.85±0.76	99.5±1.03	53.75±1.6	64.75±1.01
8	F_8	3.95±0.19	3.765±0.05	0.5±0.06	100.81±0.15	99.25±2.28	58.75±2.0	72.35±1.9
9	F_9	4.05±0.17	3.655±0.06	0.5±0.055	100.27±0.44	99.115±1.34	61.25±2.0	76.95±1.3

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 37±2.3 to 61.25±2 sec. All the formulations showed DT time in the range of 50.75±1.8 to 76.95±1.3 sec and the same was represented (Figure 1, 2). Dissolution profiles of Felodipine fast dissolving tablets were well fit to kinetic modeling, results presented (Table 3) and the same was shown (Figure 3, 4, 5, 6).

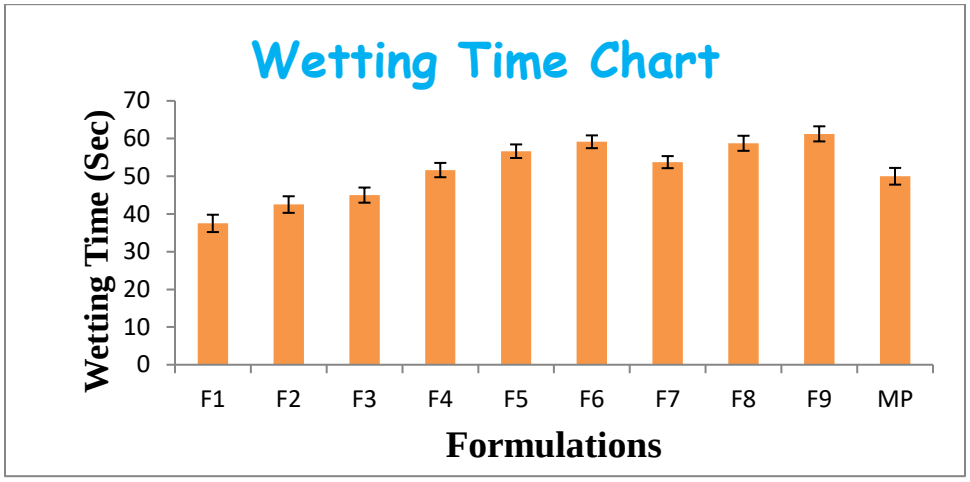

Figure 1 Wetting Time Chart

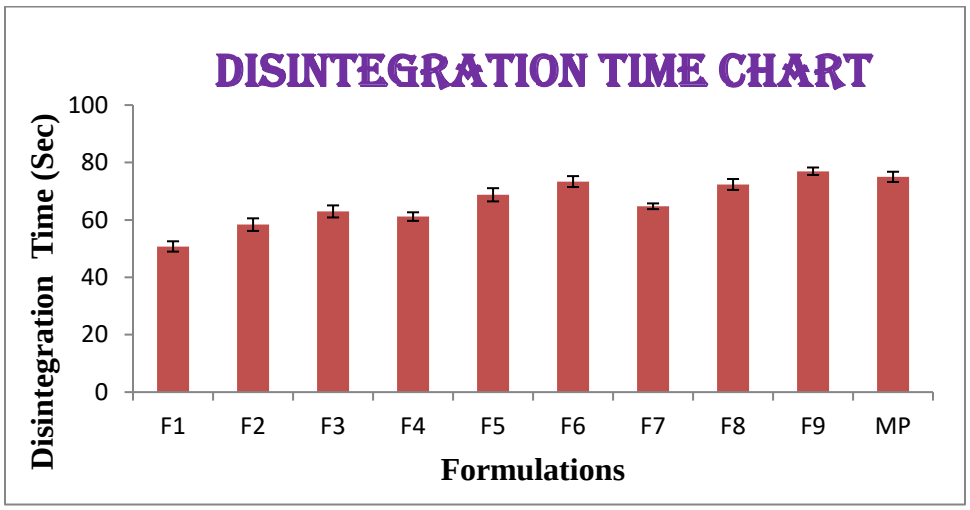

Figure 2 Disintegration Time Chart

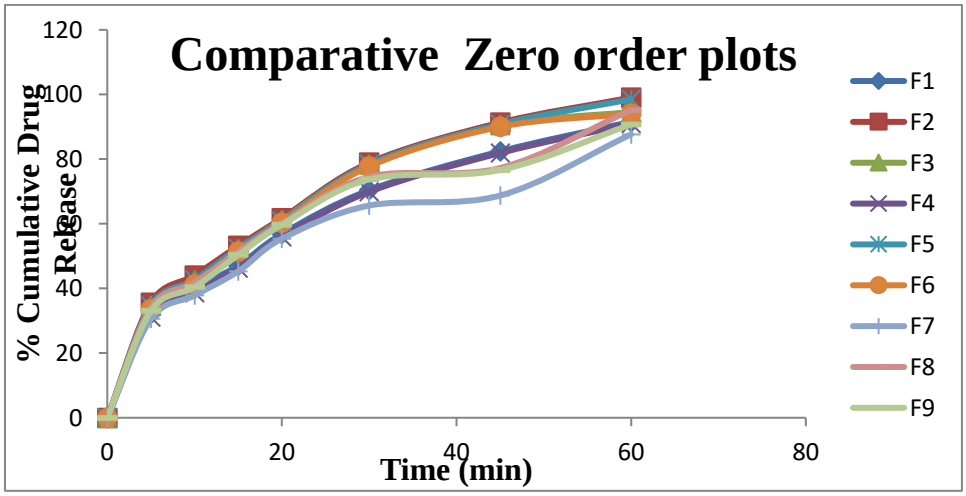

Figure 3 Comparative Zero order plots

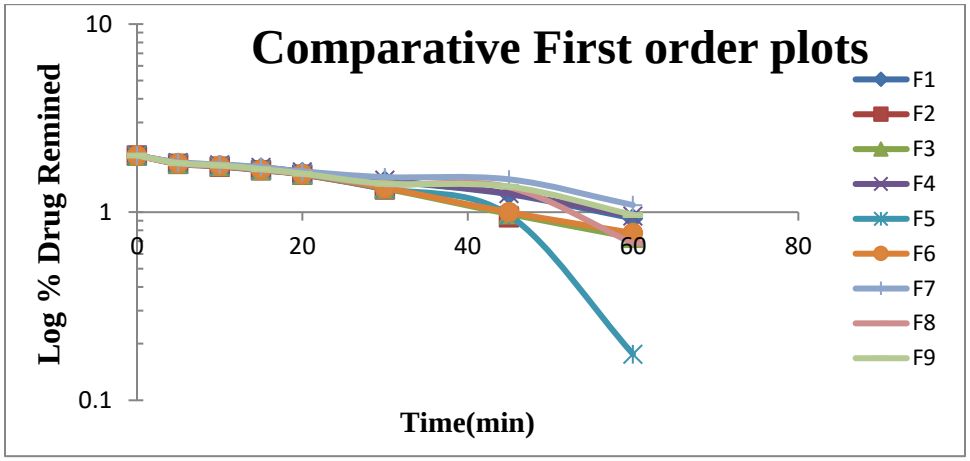

Figure 4 Comparative First order plots

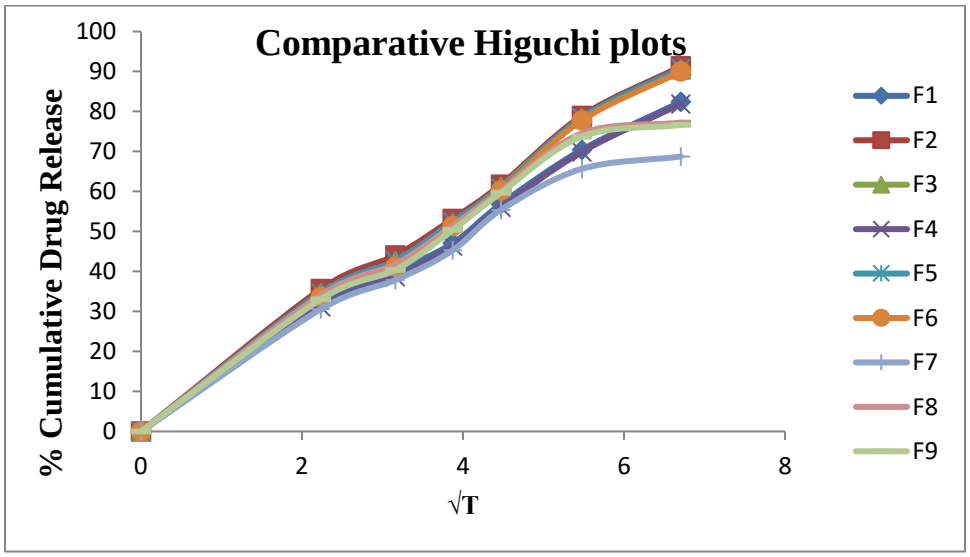

Figure 5 Comparative Higuchi plots

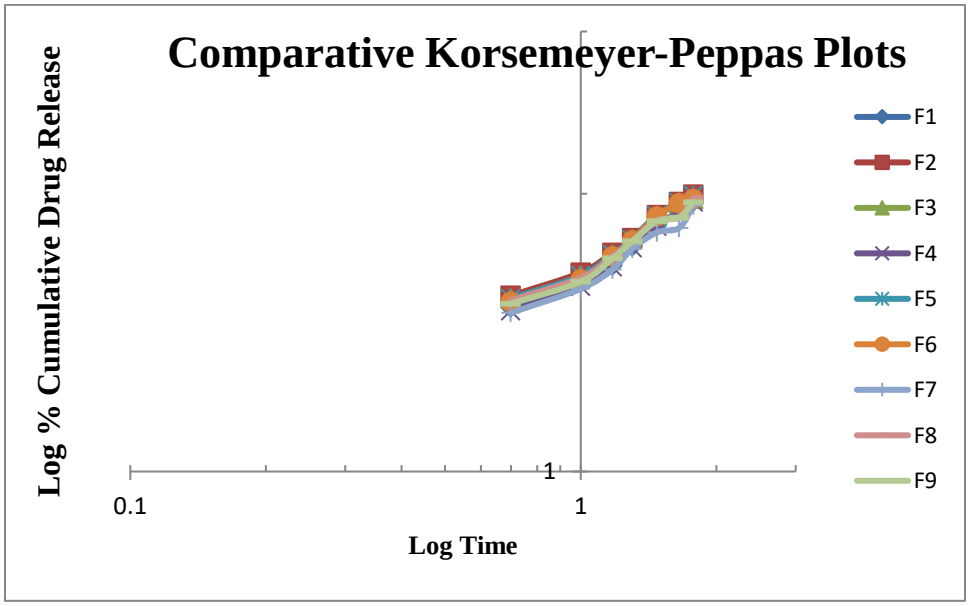

Figure 6 Comparative Korsmeyer-Peppas plots

F_5 is regarded as the best formulation among all batches (based on Desirability). F5, which contained 6 mg of Explotab and Acdi-sol 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.

Table 3 Statistical Parameters

S. NO	Formulation Code	Statistical Parameters											
		Zero order			First order			Higuchi			Korsmeyer-peppas		
		a	B	r	A	b	r	a	b	r	a	b	r
1	F_1	21.714	1.333	0.933	1.954	0.016	0.994	2.634	11.857	0.997	1.176	0.443	0.995
2	F_2	24.439	1.450	0.927	1.984	0.023	0.994	3.414	12.959	0.995	1.226	0.438	0.994
3	F_3	24.278	1.403	0.919	1.984	0.022	0.995	3.624	12.617	0.992	1.215	0.440	0.992
4	F_4	20.960	1.336	0.937	1.958	0.016	0.995	2.000	11.846	0.997	1.153	0.456	0.995
5	F_5	23.686	1.453	0.930	1.986	0.022	0.995	2.779	12.948	0.996	1.206	0.449	0.994
6	F_6	23.525	1.406	0.922	1.986	0.021	0.995	2.990	12.605	0.993	1.194	0.451	0.991
7	F_7	21.156	1.200	0.921	1.916	0.011	0.951	3.702	10.738	0.991	1.179	0.419	0.990
8	F_8	23.928	1.314	0.916	1.915	0.014	0.963	4.530	11.828	0.991	1.230	0.416	0.991
9	F_9	23.744	1.269	0.910	1.919	0.014	0.965	4.716	11.492	0.990	1.218	0.417	0.990

Table 4 Dissolution/ Kinetic Parameters

S.NO	Formulation Code		Kinetic Parameters			
		$t_{10\%}$ (Min)	$t_{1/2}$ (Min)	$t_{90\%}$ (Min)	Wetting Time (Sec)	Disintegration Time (Sec)
1	F_1	2.871	18.888	62.763	37.5±2.3	50.75±1.8
2	F_2	2.030	13.357	44.384	42.5±2.2	58.35±2.2
3	F_3	2.095	13.780	45.791	45±2.01	62.95±2.1
4	F_4	2.904	19.108	63.495	51.65±1.9	61.15±1.5
5	F_5	2.070	13.616	45.246	56.65±1.8	68.75±2.3
6	F_6	2.133	14.032	46.627	59.15±1.7	73.35±1.9
7	F_7	4.207	27.677	91.969	53.75±1.6	64.75±1.01
8	F_8	3.226	21.225	70.531	58.75±2.0	72.35±1.9
9	F_9	3.273	21.530	71.544	61.25±2.0	76.95±1.3

The *in-vitro* dissolution profile of F_5 was compared with Marketed product (PLENDIL-5) tablets, shows similarity f2= 87.35; f1= 1.97 and the same was presented (Figure 7).

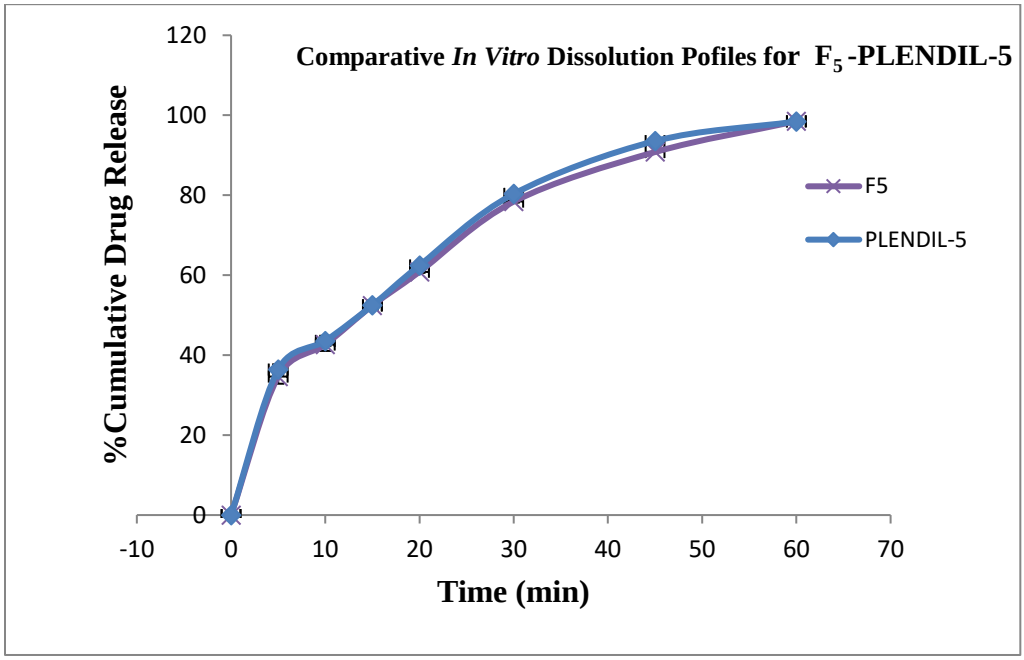

Figure 7 Comparative *In-vitro* Dissolution Profiles for F_5, Plendil-5

4. CONCLUSION

The current study focuses on the impact of using super-disintegrants for the development of felodipine FDT, such as explotab and ac-di-sol. F_5 follows first order type of kinetics, higuchi type model whereas the mechanism of drug release follows fickian diffusion. The best formulation F_5 may be used for the effective management of Hypertension and Angina Pectoris.

Informed consent

Not applicable.

Ethical approval

Not applicable.

Conflicts of interests

The authors declare that there are no conflicts of interests.

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Data and materials availability

All data associated with this study are present in the paper.

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