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DEVELOPMENT AND VALIDATION OF STABILITY INDICATING HPTLC METHOD FOR THE ESTIMATION OF MOMETASONE FUROATE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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Abstract: The selected drug Mometasone furoate is a corticosteroid with anti-inflammatory. An extensive literature surveys reveals that various analytical method were reported for the estimation of Mometasone furoate in pharmaceutical dosage form. So, it was thought to develop simple, precise, accurate and specific stability indicating HPTLC of Mometasone furoate in pharmaceutical dosage. Simple Spectrophotometric method was developed using chloroform: ethyl acetate: glacial acetic acid (9:1: 0.5v/v)as a solvent. Absorbances were measured at 248nm for Mometasone furoate. The calibration plot showed good linearity relationship with correlation coefficient of 0.9995 for Mometasone furoate in concentration range of 100-600 µg/ml. Accuracy (% recovery) was found to be 99.69% - 100.63% for Mometasone furoate and in accordance with ICH guidelines**.**

Index Terms – Stability Indicating HPTLC, Mometasone Furoate, Methanol, chloroform, ethyl acetate, glacial acetic acid

I. INTRODUCTION

corticosteroid (glucocorticoid) having an anti-inflammatory activity. The exact mechanism of MF on allergic rhinitis has not been recognized. Corticosteroids showed a wide range of effects on various cell types such as mast cells, eosinoplills, neutrophills, macrophages, and lymphocytes[1,2]. The chemical name of MF is (11β, 16α)-9, 21-dichloro-11hydroxy-16-methyl-3,20-dioxopregna-1,4-dien17-yl 2-furoate. It is white or off-white crystalline powder, soluble in acetone, dichloromethane, and slightly soluble in ethanol. Practically insoluble in water[3,4,5]. It is official in Indian and British pharmacopoeia.

Literature survey indicate that many analytical methods are reported for determination of MF using HPLC, HPTLC, RP-HPLC, in different solvents but no spectroscopic method was available for estimation of MF in bulk and pharmaceutical dosage form (cream) using dichloromethane as solvent.

MATERIALS AND METHODS:

Reagents and chemicals:

MF with 99.56% purity as at work standard was obtained as gift sample from Envee drug Private Limited, nadiad, Gujrat,India. methanol, Ethanol, acetone and octanol was purchased from Loba chemie Pvt. Ltd, Mum. Distilled water and all other chemicals used were analytical grade, cream formulation was purchased from local pharmacy. A double-beam Shimadzu-1700 UV- Visible spectrophotometer, with spectral bandwidth of 2nm, along with of ±0.5nm wavelength accuracy for all the weighing throughout the research work, weighing balance Shimadzu AUX220 was used.

Stock Solution (Standard) of Mometasone Furoate: Stock solution (1000µg/ml) of MF was prepared in Methanol

Spectral characteristics of Mometasone Furoate:

Solution of Mometasone Furoate (100µg/ml) was prepared by relevant dilution of standard solution and scanned at 200nm to 400nm.

Preparation of Calibration curve:
Appropriate dilutions of the stock solution of MF was done with dichloromethane to yield calibration standard solutions with concentrations 1,2,3,4,5&6 µl. All the solutions scanned in rang of 248nm for determining the absorption maxima. The λ_{max} of MF was recorded 248.0nm. Beer's lambert's range for MF was selected and standard curve of the drug was plotted[8,9].

Method for the determination Mometasone Furoate in cream:
Accurately weighed 1g of sample equivalent to 1mg of MF was dissolved in volumetric flask (100ml) with Methanol. 4ml of above solution taken and diluted up to 10ml in volumetric flask, the solution was filtered using Whatman filter paper[10]. The resultant solution was of 4µg/ml.

Method Validation[3]:
The method was validated with respect to LOD, Accuracy, linearity, LOQ and Precision as per the ICH Q2 (R1) guidelines.

Linearity:
The standard curve was obtained with six different concentrations of reference standard solution in range of 100-600µg/ml for the HPTLC method. All the values were performed in triplicate. The linearity was evaluated by linear regression analysis, which be situated to calculate the coefficient of correlation and slope[11].

Precision:
Precision was checked by taking five replicates of 300µg/ml for repeatability. For inter-day and intra-day (300µg/ml) where analysed for three times for consecutive three days and three thrice a day respectively. For Intermediate Precision: (Ruggedness) six repeats of 300µg/ml were analysed by different analysts. The data were analysed at 248nm. The percentage Relative Standard Deviation (% R.S.D.) of the analytical response were calculated[12,13,14].

Accuracy:
Accuracy was performed at three levels (80%, 100% and 120%) by taking 200µg/ml as 100%. To determine accuracy standard solution was added[16,17].

Limit of detection (LOD) and Limit of quantification (LOQ)[18]:
The LOD and LOQ were calculated using following formulae;

LOD = 3 × (standard deviation of y-intercept/slope of the calibration curve)

LOQ = 10 × (standard deviation of y-intercept/slope of the calibration curve)

Where,
SD = standard deviation of response and
S = average of the slope of the calibration curve

Forced degradation study of Mometasone furoate

Procedure for Stress degradation study in acidic medium for API
Accurately weighed 10mg of Mometasone furoate, transferred it into 10 ml volumetricflask and made up the volume with methanol. 1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 0.1 N HCl was added to the flaskand kept for 3 hrs. The flask solution was neutralized with 0.1 N NaOH and made up to the mark. 1 µl of the resulting solution (100ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study in acidic medium for Cream sample:
Accurately weighed quantity of cream equivalent to 10mg of Mometasone furoate, transferred it into 10 ml volumetric flask and made up the volume with methanol. Sonicated for about 15mins with occasional shaking and the solution was filtered using filter paper the resulting solution obtain 1000 ng/band.1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 0.1 N HCl was added tothe flask and kept for 3hrs. The flask solution was neutralized with 0.1 N NaOH and made up to the mark. 1 µl of the resulting solution (100 ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study in Basic medium for API
Accurately weighed 10mg of Mometasone furoate, transferred it into 10 ml volumetricflask and made up the volume with methanol. 1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 0.1 N NaOH was added to the flaskand kept for 3 hrs. The flask solution was neutralized with 0.1 N HCL and made up to the mark. 1 µl of the resulting solution (100ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study in Basic medium for Cream sample:
Accurately weighed quantity of cream equivalent to 10mg of Mometasone furoate, transferred it into 10 ml volumetric flask and made up the volume with methanol. Sonicated for about 15mins with occasional shaking and the solution was filtered using filter paper the resulting solution obtain 1000 ng/band.1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 0.1 N NaOHwas added tothe flask and kept for 3hrs. The flask solution was neutralized with 0.1 N HCL and made up to the mark. 1 µl of the resulting solution (100 ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study oxidative condition for API

Accurately weighed 10mg of Mometasone furoate, transferred it into 10 ml volumetricflask and made up the volume with methanol. 1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 3% H_2O_2 was added to the flaskand kept for 3 hrs. The flask solution made up to the mark. 1 µl of the resulting solution (100ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study in oxidative condition for Cream sample:

Accurately weighed quantity of cream equivalent to 10mg of Mometasone furoate, transferred it into 10 ml volumetric flask and made up the volume with methanol. Sonicated for about 15mins with occasional shaking and the solution was filtered using filter paper the resulting solution obtain 1000 ng/band.1 ml of aliquot from this stock solution was transferred to 10 ml volumetric flask and 2 ml of 3% H_2O_2 was added tothe flask and kept for 3hrs. The flask solution was made up to the mark. 1 µl of the resulting solution (100 ng/band) was applied on the plate and chromatogram was recorded at 248 nm. The amount of drug and acid degraded products were calculated.

Procedure for Stress degradation study in photolytic medium for API

Accurately weighed 10mg of Mometasone furoate, was irradiated with sun light for 3 hrs. A solution was prepared by dissolve drug sample in the dilute. From this stock solution of 1000 µg/ml, working standard solution of 100µg/ml was prepared. 1µl of the resulting solution was applied on the plate and chromatogram was recorded at 248nm.

Procedure for Stress degradation study in photolytic medium for Cream sample:

Accurately weighed 10mg of Mometasone furoate cream, was irradiated with sun light for 3 hrs. A solution was prepared by dissolve drug sample in the dilute. The solution sonicated about 15min and then filtered using filter paper From this stock solution of 1000 µg/ml, working standard solution of 100µg/ml was prepared. 1µl of the resulting solution was applied on the plate and chromatogram was recorded at 248nm.

Procedure for Stress degradation study in thermal medium for API

Accurately weighed 10mg of Mometasone furoate, was placed in hot air oven 75 C for 3 hrs. A solution was prepared by dissolve drug sample in the dilute. From this stock solution of 1000 µg/ml, working standard solution of 100µg/ml was prepared. 1µl of the resulting solution was applied on the plate and chromatogram was recorded at 248nm.

Procedure for Stress degradation study in thermal medium for Cream sample:

Accurately weighed 10mg of Mometasone furoate cream, was placed in hot air oven 75 c for 3 hrs. A solution was prepared by dissolve drug sample in the dilute. The solution sonicated about 15min and then filtered using filter paper. From this stock solution of 1000 µg/ml, working standard solution of 100µg/ml was prepared. 1µl of the resulting solution was applied on the plate and chromatogram was recorded at 248nm.

RESULTS DISUCUSSION

SOLUBILITY

Table 1 Table Type Styles

Sr.No	Solvent	MF
1	Dichloromethane	soluble
2	Methanol	Very soluble
3	Water	insoluble
4	Ethanol	Slightly soluble
5	acetone	soluble

Linearity:

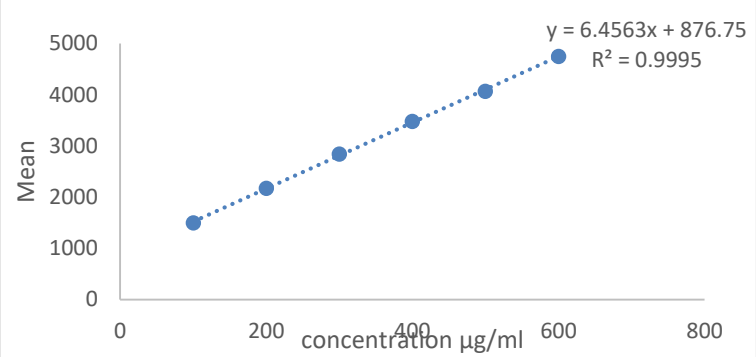
Linearity for different concentration of drug was performed and r^2 value was noticed to be **0.999** for Mometasone Furoate.

Table 2: Linearity data of Mometasone Furoate

Conce (µg/ml)	Absorbance (n=5)	SD	%RSD
100	1498.34	26.31	1.75
200	2174.48	43.47	1.99
300	2841.24	11.09	0.39
400	3499.52	58.95	1.68
500	4088.28	45.06	1.10
600	4774.58	44.27	0.92

Table 3: Regression Analysis Data for calibration Curves

Parameter	Mometasone furoate
Linearity	100-600µg/ml
Linearity Equation	y=6.4583x+876.276
Slope	6.4583x
Intercept	876.276
Correlation Coefficient	0.9995



Precision:

Repeatability:

Precision was performed and % RSD was observed as 0.89.

Table 4: Repeatability data for Mometasone Furoate

Sr. No.	Conce (µg/ml)	Absorbance of MF
1	300	2789.2
2	300	2765.1
3	300	2793.8
4	300	2744.9
5	300	2798.2
6	300	2808.6
	MEAN	2783.3
	SD	23.71
	%RSD	0.85

Inter-Day:

The % RSD was instituted to be >2% for inter-day

Table 5: Inter-Day Precision Data for Mometasone Furoate

Sr. No.	Conc. (µg/ml)	Mean	SD	%RSD
1	100	1531.83	16.28	1.06
2	300	2795.3	55.11	1.97
3	500	4121.5	19.868	0.48

Intra-Day:

Table 6: Intra-Day Precision Data for Mometasone Furoate

Sr. No.	Conc. (µg/ml)	Mean	SD	%RSD
1	100	1534.56	10.05	0.65
2	300	2833.86	21.94	0.77
3	500	4133.0	44.89	0.94

The method precision gave results obtained within 2% RSD suggesting manner is precise

Accuracy:

Accuracy was performed and %recovery was originated to be 99.14% to 100.31% for Mometasone Furoate.

Table 7: Results of recovery studies for marketed cream

Level of spiking	Conc. of sample (µg/ml)	Std. added (µg/ml)	Total conc of MF (µg/ml)	Mean Conc. Found (µg/ml) (n=3)	SD	%RSD	% Recovery
0%	200	0	200	200.05	1.18	0.59	100.02
80%	200	160	360	359.98	1.57	0.43	99.99
100%	200	200	400	399.66	1.67	0.40	99.83
120%	200	240	440	440.40	0.93	0.21	100.20

Limit of Detection and Quantitation:

Table 8: LOD & LOQ date for Mometasone Furoate

Parameter	Concentration(µg/ml)
LOD	11.038
LOQ	33.45

Specificity: The purity of mometasone furoate was assessed by comparing respective at start and end position . good match was obtained between standerd and sample of mometasone furoate.

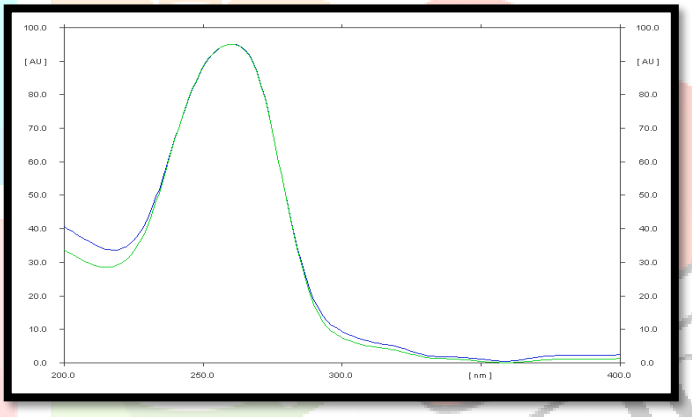


Table 12: Summary of Validation Parameters for Mometasone Furoate

Sr.No.	PARAMETER	MOMETASONE FUROATE
1	LEARITY	
	Linearity Equation	y = 6.4583x+ 876.28
	Slope	6.4583x
	Intercept	876.28
	Correlation Coefficient (r2)	0.9995
2	RANGE (µg/ml)	100-600
3	ACCURACY (Percent recovery)	100.20-99.83
4	PRECISION (Percent RSD)	
	Repeatability	0.85
	Intra-day	1.97 - 0.48
	inter-day	0.65- 0.94
5	LOD (µg/ml)	11.038
6	LOQ (µg/ml)	33.45
7	SPECIFICITY	Specific

Forced Degradation Study:

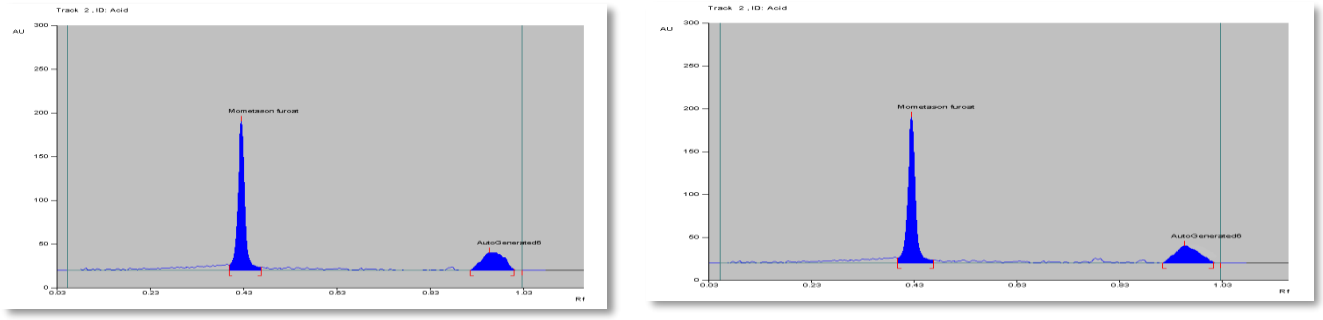


Fig: 1 Densitogram of APT &Cream sample of Mometasone furoate and its degradation products in the acidic degradation study

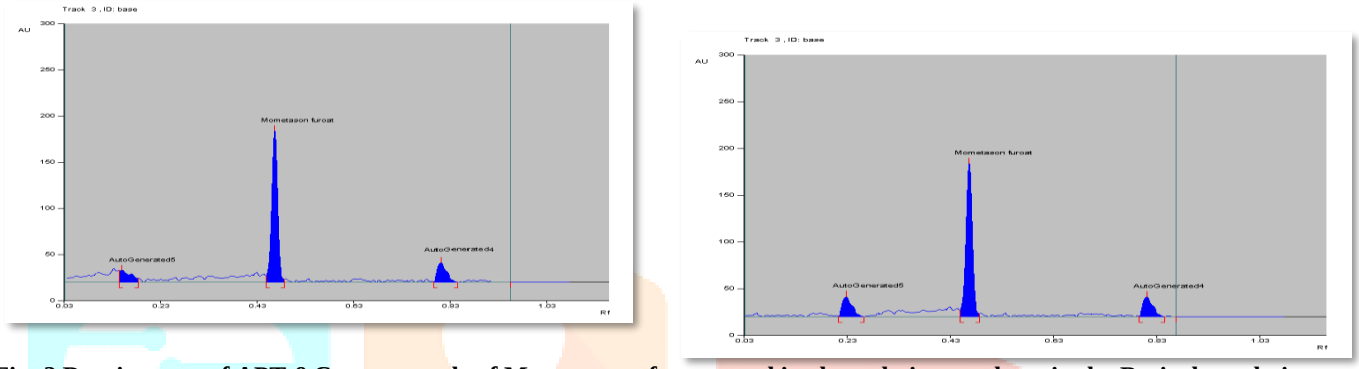


Fig: 2 Densitogram of APT &Cream sample of Mometasone furoate and its degradation products in the Basic degradation study

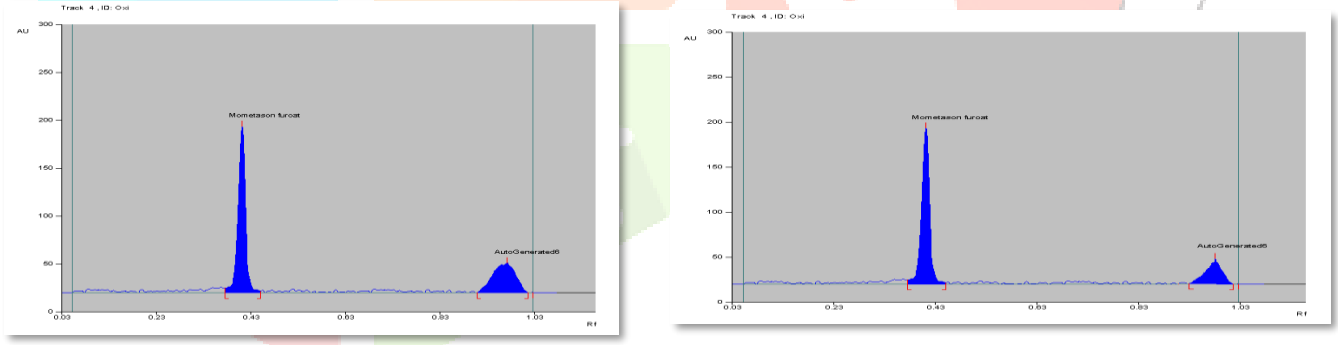


Fig: 3 Densitogram of APT &Cream sample of Mometasone furoate and its degradation products in the oxidative degradation study

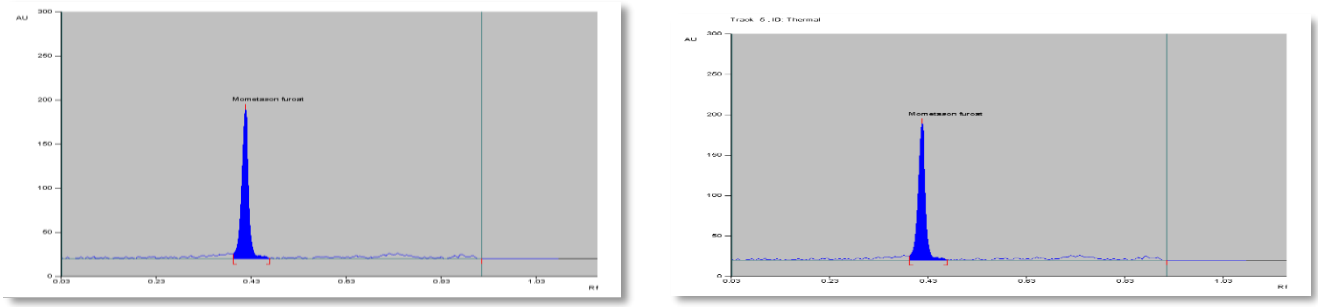


Fig: 4 Densitogram of APT &Cream sample of Mometasone furoate degradation in the thermal degradation study

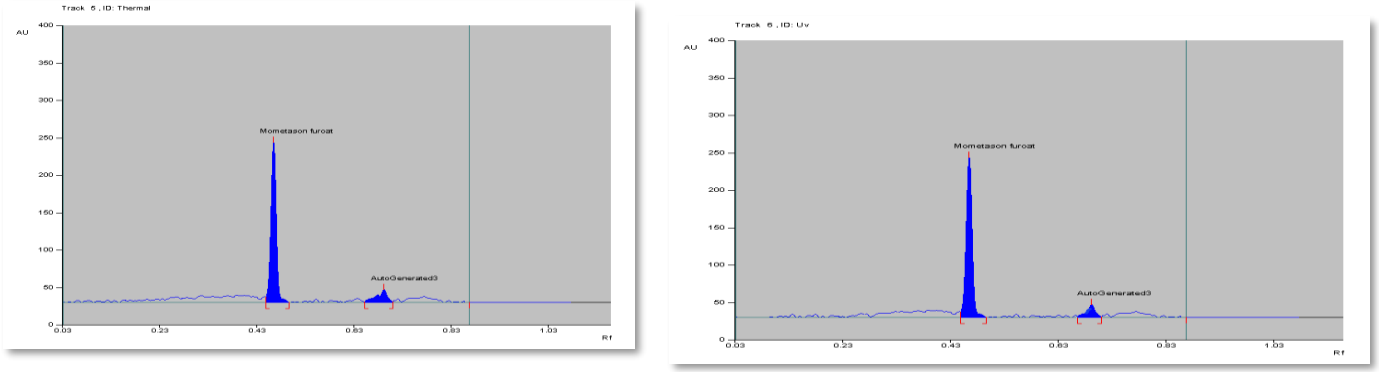


Fig: 5 Densitogram of APT &Cream sample of Mometasone furoate and its degradation products in thephotolytic degradation study

Summary of Force Degradation Study

Sr.no	Degradation Condition	Number of Degradation product	% Degradation based on area for API:	% Degradation based on area for Cream sample:
1	Acid	1	18.99	19.60
2	Base	2	11.58, 29.40	11.44, 25.46
3	Oxidative	1	27.28	26.57
4	Thermal	-	-	-
5	Photolytic	1	10.41	11.23

CONCLUSION:

Thus, it can be determined that techniques in present research work were simple, sensitive and reproducible when checked for validation parameters like accuracy, precision and ruggedness for monotonous purpose of Mometasone Furoate in bulk along with pharmaceuticals (cream).

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