International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.2, pp 1047-1050, April-June 2010

Development of Discriminatory Method for Dissolution of Carvedilol Marketed Formulations

T.E.G.K Murthy, G. Sowjanya*

Department of Pharmaceutics,Bapatla College of pharmacy, Bapatla. A. P, India

***Corres author: sowjanya.gummalla@gmail.com**
Phone No. 9652245335

ABSTRACT: Carvedilol (BCS Class II drug) is a nonselective β-adrenergic blocking agent with α_1-blocking activity and it is mainly used in the management of hypertension. Two commercial brands of carvedilol drug, of strength 12.5mg were used for the Invitro dissolution studies. In the present study four dissolution media [pH 1.2 (0.1 N Hcl), pH 4.5 Acetate buffer, pH 6.8 phosphate buffer, and Distilled water] with different agitation speeds (50, 75 and 100 rpm) were employed. An agitation speed of 100 rpm showed more drug release profile than 50 and 75 rpm. The dissolution rate was found to be influenced by the dissolution medium and paddle speed. The dissolution studies conducted with water in presence of paddle set at 50 rpm is more suitable for discrimination of marketed formulations of Carvedilol.
Key words: Carvedilol, Dissolution of Carvedilol, Method for Dissolution of Carvedilol

INTRODUCTION

Hypertension is a chronic medical condition in which the blood pressure is elevated. Carvedilol (BCS Class II drug) is a nonselective β-adrenergic blocking agent with α_1-blocking activity and it is mainly used in the management of hypertension. Not only it is useful in the management of Hypertension but also used in the treatment of other cardiovascular diseases like angina pectoris, cardiac arrhythmias, Heart Failure and Left Ventricular Dysfunction following Myocardial Infarction etc (1).

Carvedilol, is chemically *(±)-1-(Carbazol-4-yloxy)-3-[[2-(o-methoxyphenoxy) ethyl] amino]-2-propanol.* It is a white to off-white powder with a molecular weight of 406.5. It is freely soluble in dimethylsulfoxide, soluble in methylene chloride and methanol, sparingly soluble in 95% ethanol and isopropanol, slightly soluble in ethyl ether and practically insoluble in water (2). Discriminative dissolution studies are necessary to investigate the influence of composition, method of manufacturing and to compare with the approved formulations. The drug Carvedilol is having low aqueous solubility and hence manufacturers of Carvedilol tablets may adopt different techniques to enhance its dissolution rate. These studies were undertaken to identify the suitable dissolution conditions which can differentiate the existing marketed formulations of Carvedilol.

EXPERIMENTAL

Materials and methods

Two solid dosage formulations of Carvedilol were studied: Cardivas (Batch No. GK81400) and Carloc (Batch No.D71411).They were purchased from the local pharmacy and coded as Brand A and Brand B. Carvedilol standard was obtained from Sun pharmaceutical industries ltd, India. All the chemicals and reagents used were of analytical grade. Four dissolution media were prepared as per USP procedure.

Quality control tests on marketed Carvedilol tablets

The commercially available two different brands of Carvedilol were subjected to different official quality control tests like weight variation, friability, drug content, disintegration time, content uniformity and dissolution studies. To determine the discriminative condition the formulations were further subjected to dissolution studies in different dissolution mediums and various revolution conditions. The detailed dissolution procedures are presented below,

Dissolution media

The four dissolution media employed were 0.1N Hcl, pH 4.5 Acetate Buffer, pH 6.8 Phosphate Buffer and Distilled water. The preparation of 0.1N Hcl, pH 4.5 Acetate Buffer, and pH 6.8 Phosphate Buffer was from USPXXIII, 1995 (3). These media were selected based on the FDA guidance for industry.

Dissolution test apparatus

In Vitro dissolution studies were performed on dissolution tester USP TDT-08L (Electro lab, Mumbai) employing paddle method. The volume of dissolution medium used was 900ml and various dissolution media employed were 0.1N Hcl, pH 4.5 Acetate Buffer, pH 6.8 Phosphate Buffer and Distilled water. The temperature was maintained at 37^0c and rotations per minute were maintained at 50 rpm, 75 rpm and 100 rpm. Then at each interval of time (5, 10, 15, 20, 25, 30 minutes), 5ml of samples were collected and replaced with same amount of the solution. Samples withdrawn were filtered through Whatmann filter paper (no.41), and analyzed at 285nm, using UV-Visible double beam spectrophotometer.

Interpretation of dissolution data

The similarity factor is calculated from the dissolution data generated in different dissolution mediums and at various revolutions. The similarity factor is calculated by following equation (4),

$$f_2 = 50\log\left\{\left[1+\left(\frac{1}{n}\right)\sum_{t=1}^{n}\left(R_t - T_t\right)^2\right]^{-0.5} \times 100\right\}$$

Where n is the number of dissolution sampling times, and R_t and T_t are the individual or mean percent dissolved at each time point for the reference and test dissolution profiles respectively.

TABLE-1 INVITRO DISSOLUTION PARAMETERS OF CARVEDILOL FROM MARKETED TABLETS

S. No	Dissolution Medium	RPM	DE (%)		K_{min}^{-1}		$t_{50(min)}$		$t_{90(min)}$		Similarity Factor (f_2)
			A	B	A	B	A	B	A	B	
1.	0.1N Hcl	50	63.07	67.48	0.290	0.323	2.4	2.1	7.9	7.1	65.15
		75	78.14	69.9	0.315	0.369	2.2	1.9	7.3	6.2	88.55
		100	73.48	73.5	0.666	0.642	1.0	1.1	3.5	3.6	99.89
2.	pH 4.5	50	66.87	73.29	0.074	0.107	9.3	6.4	30.9	21.3	48.3
		75	70.19	78.11	0.124	0.170	5.6	4.1	18.5	13.5	53.8
		100	70.44	74.9	0.178	0.223	3.9	3.1	12.9	10.3	66.4
3.	pH 6.8	50	48.97	37.77	0.042	0.019	16.4	34.8	54.5	115	36.94
		75	50.07	39.03	0.065	0.020	10.7	33.5	35.0	111	30.85
		100	50.35	44.58	0.085	0.022	8.1	31	27	103	29.52
4.	Water	50	42.94	20.08	0.034	0.008	20.1	86.4	66.8	287	27.36
		75	45.01	21.27	0.043	0.0085	16.1	82	53.6	272	25.99
		100	46.19	22.37	0.044	0.009	15.6	77	51.8	257	25.93

FIGURE-1 COMPARATIVE DISSOLUTION PROFILES OF CARVEDILOL TABLETS IN FOUR MEDIA AT 50 RPM.

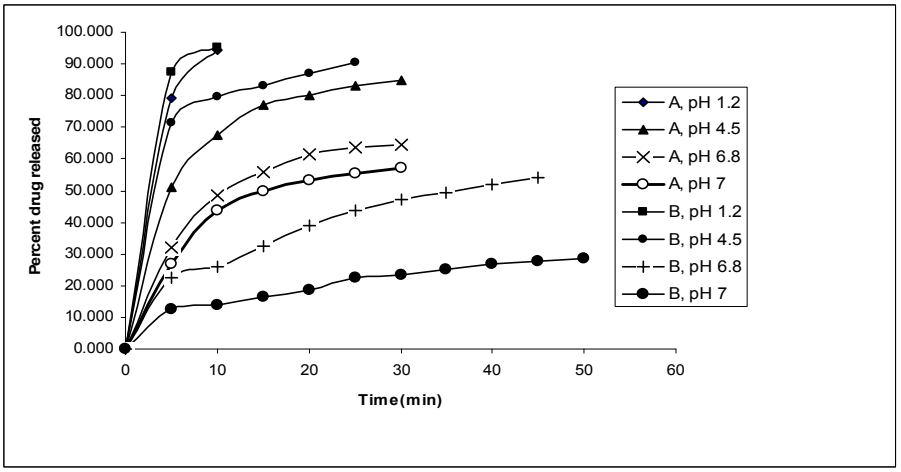


FIGURE-2 COMPARATIVE DISSOLUTION PROFILES OF CARVEDILOL TABLETS IN FOUR MEDIA AT 75 RPM.

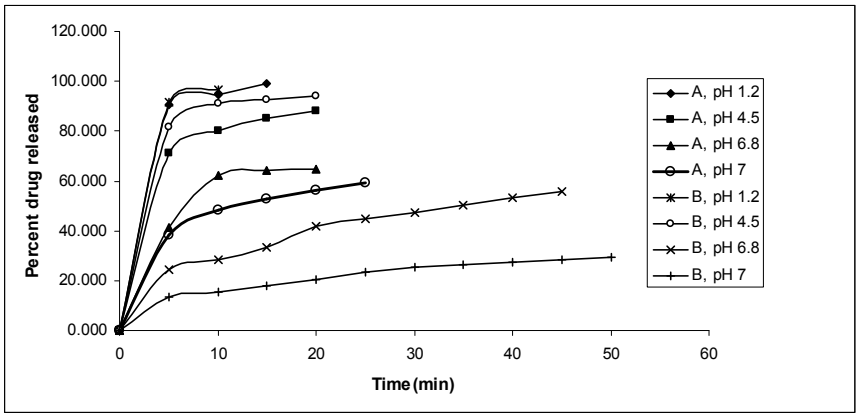
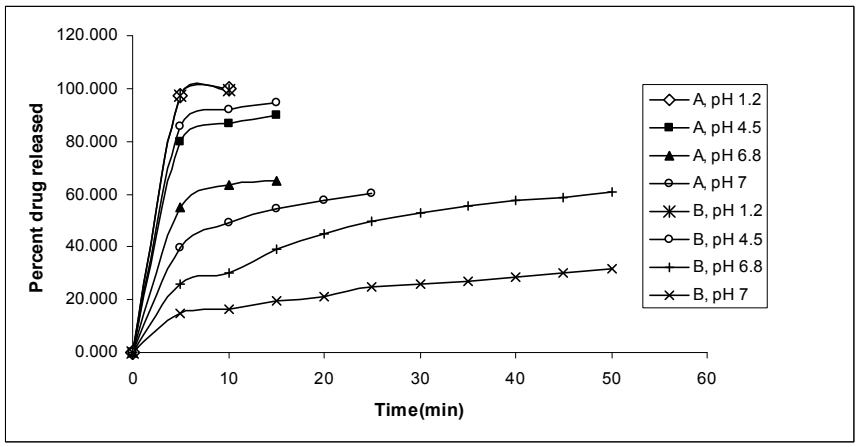


FIGURE-3 COMPARATIVE DISSOLUTION PROFILES OF CARVEDILOL TABLETS IN FOUR MEDIA AT 100 RPM



RESULTS AND DISCUSSION

The coating status, color, shape and various QC parameters of all the commercial products were recorded. All the tablets compiled various compendia requirements. Weight variation was found to be less than 5%, friability values are less than 1%. All the tablets were disintegrating within 15 minutes and the amount of drug dissolved in 0.1N Hcl was found to be more than 95% during 30minutes dissolution study. To identify differences from different brands attributed by either Excipients or the method of manufacturing, the selected formulation dissolution profile are evaluated.

In Vitro dissolution studies for two commercial brands of Carvedilol tablets i.e., Cardivas and Carloc were conducted using four different dissolution media (0.1N Hcl, pH 4.5 Acetate Buffer, pH 6.8 Phosphate Buffer and Distilled Water) at three different agitation speeds (50,75,100 RPM). A comparison of the dissolution profiles of the two commercial brands of Carvedilol drug in the four different media at three different agitation speeds was showed in Figures 1 to 3.The dissolution rate followed first order kinetics as the graphs drawn in between amount of drug dissolved verses time were found to be linear. Invitro dissolution parameters i.e., T_{50} (time for dissolution of 50% of drug), T_{90} (time for dissolution of 90% of drug), DE (dissolution efficiency), K min^{1}, and similarity factor (f_2) were calculated and shown in table 1. The similarity of the dissolution profiles was determined using the similarity factor, f2 .Two dissolution profiles are considered to be similar when the f2 value is greater than 50 and dissimilar when less than 50 (5). The f_2 values were found to be greater than 50 in 0.1N Hcl at 50, 75, 100 rpm and in pH 4.5 Acetate buffer at 75,100 rpm. While in other cases it was found to be less than 50. Among the various dissolution media the drug release was faster at 100 rpm, 0.1N Hcl and it is suitable to maintain sink conditions.

CONCLUSION

From this experimental work it is concluded that the dissolution rate of Carvedilol from tablet dosage forms is dependent on dissolution medium and rpm conditions of the paddle employed in dissolution. It was also concluded that the usage of water as dissolution media and operating the apparatus with paddle setted 50rpm is more suitable for discrimination of Carvedilol tablets. The influence of Excipients, techniques on improvement of dissolution efficiency can be studied by conducting dissolution studies in the identified discriminatory condition.

REFERENCES

1. http://en.wikipedia.org/wiki/Hypertension
2. http://www.rxlist.com/coreg-drug.htm
3. USP 27/NF 22, Asian edition: General test procedures. Rockville MD: U.S. Pharmacopoeial convention; 2000.
4. http://www.dissolutiontech.com/DTresour/200805Articles/DT200805_A05.pdf
5. http://www.dissolutiontech.com/DTresour/200611Articles/DT200611_A02.pdf

*****