(RESEARCH ARTICLE)

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Comparative *in-vitro* evaluation of two brands of carvedilol uncoated tablets

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Abstract

Comparative study is just a comparison study, according to formal properties, function, purpose and effectiveness. The main purpose of comparative study is, to compare a particular drug of different brands with the help of their stability, efficacy and evaluation parameters. Here we compare the carvedilol drugs different two marketed. It acts as anti-hypertensive agent so, it mainly preferred for arterial fibrillation, inhibits tachycardia, prevention of stroke, heart failure, it also works by blocking a natural substance like epinephrine, which results to cause lowers the heart rate, blood pressure and strain on the heart. In comparative studies we determined their efficacy and effectivity on the basis of various *in-vitro* tests like weight variation, friability, hardness, dissolution and disintegration. It can be concluded that standard quality control parameters always should be maintained not only for carvedilol or its combination but also for all kinds of medicine for getting better drug products. The parameters in this comparative study between these two brands showed somewhat variation because every brand have their own method or processing or manufacturing and formulation properties. Mainly these parameters can show the different efficacy and effectivity and made them unique from each other.

Keywords: Carvedilol uncoated tablets (3.125mg); *In-vitro* evaluation; Two available marketed brands.

1. Introduction

Carvedilol uncoated tablets [1, 2, 3, 4, 5] are generally single layer tablets prepared by a single compression of granules or multi-layer tablets consisting of parallel layers prepared by compression of granules of different compositions. Carvedilol is a lipophilic vasodilating non-cardio selective beta-blocker. It shows sympathomimetic activity. It is metabolized in the liver and rapidly absorbed by oral administration. It blocks norepinephrine binding to alpha-1 adrenergic receptors. This shows reduction in arterial blood pressure, decreasing beta-adrenoreceptor vasoconstrictor tone. It is racemic mixture of (±)-1-(carbazol-4-yloxy)-2-propanol. Carvedilol maintains normal ratio of high-density lipoproteins to low-density lipoproteins. For enhancing aqueous solubility of drugs solid dispersion technique is highly effective. By adding Crospovidone, low concentration of Ac-di-sol, etc. to increase disintegration rate of the tablets. Carvedilol helps to reduces renin release through beta-blockade. Carvedilol is freely soluble in dimethyl sulfoxide, soluble in methanol and methylene chloride, sparingly soluble in 95% ethanol and isopropanol and partially insoluble in gastric fluid, water and intestinal fluid.

There are many uses of carvedilol such as it is mainly used in hypertension. It shows antioxidant effect. It is also used in the treatment of atherosclerotic disease. It shows reduction of vascular smooth muscle migration. It prevents formation of oxidized low density lipoproteins and vascular smooth muscle inhibition. Carvedilol is used in the treatment of heart failure. Also, it is used to treat Diabetes Mellitus. Carvedilol is used in ischemic heart disease. It is used in patient with

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cirrhosis. Carvedilol is used in patient with ST-segment elevation myocardial infraction treated with primary percutaneous coronary intervention.

Advantages of carvedilol are non-toxic, anti-hypertensive, gives proper therapeutic response, achieved proper therapeutic range in minimal dose, etc. Carvedilol shows multiple side effects such as dizziness, lightheadedness, drowsiness, reduce blood flow, chest pain, dry eyes, etc. Carvedilol is contraindicated in hypersensitivity, chronic obstructive pulmonary disease with bronchial obstruction, patient with severe hepatic dysfunction, severe hypotension, second- or third-degree AV block, patient with metabolic acidosis, etc.

IUPAC Name of Carvedilol: 1-(9H-carbazol-4-yloxy)-3-[2-(2-methoxyphenoxy) ethyl amino] propan-2-ol.

Molecular Formula of Carvedilol: $C_{24}H_{26}N_2O_4$

Molecular Weight of Carvedilol: 406.5 g/mol.

Structure of Carvedilol:
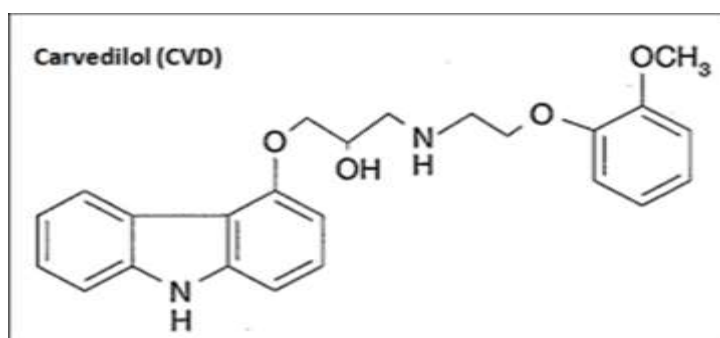
2. Material and methods

Comparative *in-vitro* quality control parameters between the commercially available tablet brands of uncoated Carvedilol in market were studied through the evaluation of weight variation, hardness, friability, disintegration time and dissolution profile. The evaluation was done by performing various test procedures related to the measurement of the quality of tablets.

2.1. Sample Collection

To carry out the study, the Carvedilol 3.125 mg uncoated tablets of two different top-level brands were purchased from the drug store. Both the tablet brands of Carvedilol were labelled to contain 3.125 mg of Carvedilol per tablet. After the purchase of the tablets, both the brands were coded as A and B.

2.2. Chemicals

Potassium-di-hydrogen phosphate, Sodium hydroxide and Distilled water. All chemicals are used for analytical grade.

2.3. Equipments

Monsanto Hardness Tester, Roche Friability Apparatus, U.S.P. II Dissolution Apparatus, Disintegration Apparatus, Analytical Balance, Vernier Caliper.

2.4. Methods

For the comparative evaluation, following quality control tests were performed for the tablet brands A and B by referring Indian Pharmacopoeia 2018 to check the *in-vitro* quality of Carvedilol uncoated tablets.

2.5. Procedure

2.5.1. Dimensional Parameters

The thickness and diameter of tablets were determined by using the digital Vernier Caliper [8].

2.5.2. Friability Test

It was performed using Roche Friabilator. 10 tablets were weighed and placed in apparatus. The apparatus was rotated at a speed of 25 rpm. The apparatus was made to rotate for 4 min. The tablets were then weighed and the weights were compared with the initial weights. The percentage friability was calculated using the formulas given in following equation. Calculate the % Friability by following given formula [6, 7, 8]

$$\%Friability = \frac{W_1 - W_2}{W_1} \times 100$$

Where,
W1= initial weight of tablets before rotation
W2= final weight of tablets after rotation

2.5.3. Hardness Test

The significance of performing hardness test of tablets is to determine the crushing strength of tablets. Hardness of a tablet is defined as the force required to break the tablet. Monsanto Hardness tester, Pfizer hardness tester, Strong Cobb hardness tester, Erweka hardness tester are the different hardness tester apparatus for calculating hardness of the tablet. Place the tablet in between the fixed jaw and moving jaw of the apparatus. By means of screw job, the pressure is applied on the tablets and moving jaw is moved. The point at which the tablet gets broken down, the reading is measured by means of scale. Take 5 readings for accurate and precise result and calculate the mean of 5 readings. Unit of hardness is Kg/cm2 [8, 9, 10]

2.5.4. Weight Variation Test

The weight variation is done by comparing the individual weight of the tablet to the average weight of the tablets. For weight variation test 20 tablets are needed. The average weight of 20 tablets were weighed and then it was compared with individual tablet weight. The weight variation is expressed in % [8, 11]

$$\%Weight\ variation = \frac{W_1 - W_2}{W_1} \times 100$$

Where, W1 = individual weight of tablet, W2= average weight of tablets

Table 1 Weight Variation Limits

| IP/BP	Limit[tablet]
80 mg or Less	±10
80-250 mg	±7.5
250 mg or More	±5

2.6. Disintegration

It was performed using USP disintegration device. Six tablets were placed in Disintegration test apparatus. It was maintained at 37± 0.2C℃ containing distilled water. The time taken for a tablet to disintegrate was noted down. Time should be recorded after the complete breakdown of the tablet [8, 11].

2.7. Dissolution

Dissolution is an evaluation parameter in which we determine the time required to dissolve tablet in a particular solvent in *in-vitro* manner. For dissolution purpose here U.S.P II Dissolution apparatus used with gastric buffer pH 1.3 dissolution medium in which drug is completely soluble. During the process discard the few ml samples from medium in specific time interval, such as 5, 10, 15, 20 min etc. Those discarded medium absorbance check under UV at specific wavelength 242 nm and determine the percent release of drug in a graphical manner. [9, 13, 14, 15]

Table 2 Dissolution parameter

Sr. No.	Parameters	Specifications
1.	Apparatus	U.S.P. II Dissolution Apparatus (Paddle type)
2.	Dissolution medium	Gastric Buffer pH 1.3, USP II, 50 rpm, 900 ml
3.	Volume of medium	900 ml
4.	Temperature	37± 0.5^{0}C
5.	Discarded volume	10 ml
6.	Speed of paddle rotation	50 RPM
7.	Time interval of sampling	5 minutes
8.	Absorbance detection wavelength	242 nm
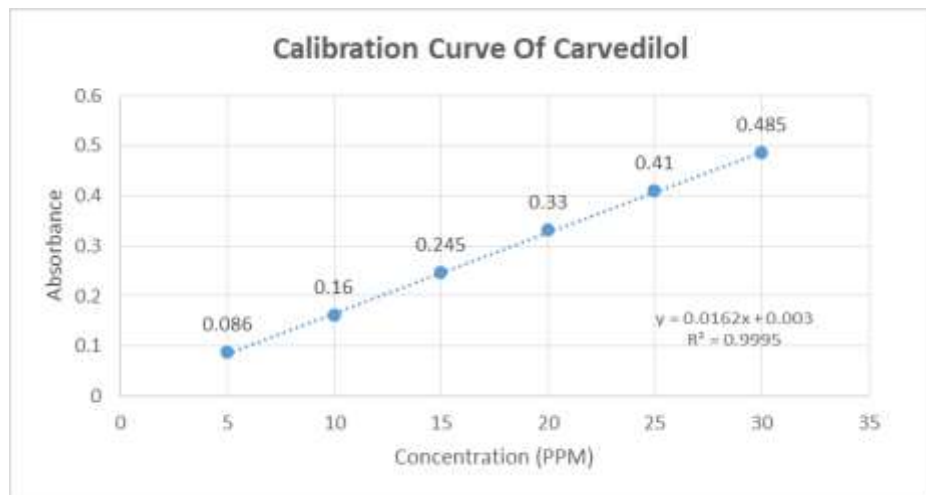
Figure 1 Calibration curve of carvedilol
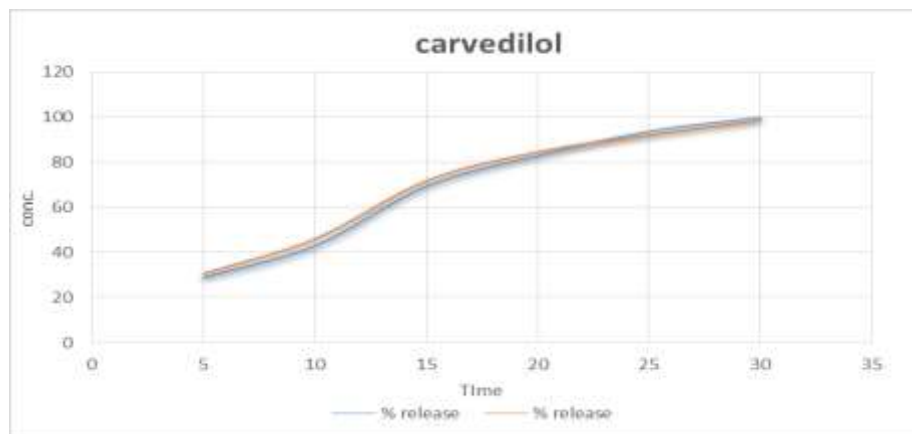
Figure 2 Percent (%) release of carvedilol

3. Result and Calculations

Table 3 Weight of Tablets [Milligram (mg)]

Sr. No.	Brand A	Brand B
1	114	121
2	113	122
3	114	123
4	114	123
5	114	121
6	116	122
7	113	121
8	114	122
9	114	122
10	114	123
11	115	122
12	113	122
13	114	123
14	116	121
15	114	122
16	113	122
17	114	123
18	114	122
19	113	122
20	114	121
Total	2280 mg	2440 mg

Average weight of tablets: Brand A=114 mg, Brand B= 122 mg.

Weight Variation of Brand A:

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

Table 4 Percent weight variation of brand A

Sr. No.	Weight of tablet (mg)	% weight variation
1	114	0
2	113	-0.877
3	114	0
4	114	0
5	114	0
6	116	1.75
7	113	-0.877
8	114	0
9	114	0
10	114	0
11	115	0.877

12	113	-0.877
13	114	0
14	116	1.75
15	114	0
16	113	-0.877
17	114	0
18	114	0
19	113	-0.877
20	114	0

Weight Variation of Brand B:

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

Table 5 Percent weight variation of brand B

Sr. No.	Weight of tablet (mg)	% weight variation (%)
1	121	-0.8197
2	122	0
3	123	0.8197
4	123	0.8197
5	121	-0.8197
6	122	0
7	121	-0.8197
8	122	0
9	122	0
10	123	0.8197
11	122	0
12	122	0
13	123	0.8197
14	121	-0.8197
15	122	0
16	122	0
17	123	0.8197
18	122	0
19	122	0
20	121	-0.8197

3.1. Friability Test

Brand A: Initial wt. (W_1): 2.28 gm, Final wt. (W_2): 2.275 gm

$$\%Friability = \frac{W_1 - W_2}{W_1} \times 100$$

$$\%Friability = \frac{2.280 \ - 2.275}{W_1 \ 2.280} \times 100$$

% Friability= = 0.219 %

Brand B: Initial wt. (W1): 2.440 gm, Final wt. (W2): 2.434 gm

$$\%Friability = \frac{W_1 \ - W_2}{W_1} \times 100$$
$$\%Friability = \frac{2.440 \ - 2.434}{2.440} \times 100$$

% Friability= = 0.25 %

3.2. Hardness Test

Table 6 Hardness test parameter for brand A

Sr. No.	Hardness (kg/cm^2)
1	5.2
2	5
3	4.9
4	4.8
5	5.1
Average Hardness	25/5= 5 kg/cm^2

Table 7 Hardness test parameter for brand B

Sr. No.	Hardness (kg/cm^2)
1	5.4
2	4.9
3	5.1
4	5
5	4.9
Average Hardness	25.3/5= 5.06 kg/cm^2

Table 8 Comparative results of both brands

Parameter	Brand A	Brand B
Colour	White	Sunset Yellow
Weight Variation	± 7.5	± 7.5
Friability	0.219 %	0.25 %
Hardness	5 kg/cm^2	5.06 kg/cm^2
Disintegration Time	14 min	15 min
% Release	99.97 %	98.8 %

4. Conclusion

Carvedilol is well known anti-hypertensive drug also commonly used for heart patients. Any formulation quality and efficiency depend on their evaluation parameter and their specification. Evaluated carvedilol brands shows result under specification which based on standard values. Weight variation and friability both shows result as per specification or standard value which given in Indian Pharmacopeia. But little variation seen in hardness, disintegration time, dissolution time during the test procedure. These parameters are passed all parameters as per pharmacopeia.

Compliance with ethical standards

Acknowledgments

We thank our lab technician and other helpers who made this study possible.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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