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Comparative Evaluation of Two Different Marketed Brands of Enalapril maleate

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ABSTRACT

Efficacy of pharmaceuticals dosage form generally depends on their formulation properties and manufacturing methods, hence it is likely that the quality of dosage form may vary. Renin acts on angiotensinogen to form angiotensin I, which is converted to angiotensin II by angiotensin-converting enzyme (ACE). Angiotensin II, a potent vasoconstrictor increases blood pressure by increasing vasopressin production and aldosterone secretion. Enalaprilat, the active metabolite of enalapril, inhibits ACE, hence decreases levels of angiotensin II resulting in less vasoconstriction and decreased blood pressure. The study was exclusively experimental that used IP and other standard books to check in vitro quality of enalapril maleate tablet using different analytical techniques and procedure. Test for weight variation, hardness, friability, disintegration time, and dissolution were conducted. The dissolution test was performed at pH 6.8 for both the brands of the tablet. Further all the tablets passed weight variation, hardness, friability and disintegration test as per the pharmacopoeial standard. Hence we can conclude that both the brands of tablets are equal and both the brands contain equal quantity of active pharmaceutical ingredient (API). Both the brands having higher and lower costs exert similar action.

Keywords: Enalapril maleate, *In Vitro*, Dissolution test, Enalapril

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INTRODUCTION

Post marketing surveillance works as a confidential tool to analyze the quality, therapeutic effectiveness and safety of commercially available medicines. Particulars acquired from such surveillance may help to accelerate the improvement of existing regulations as well as future product development. In this current research study we evaluated physical parameters of commercially available enalapril maleate tablets.

The oral route of drug administration is the most important method of administrating drugs for systemic effects. Nevertheless, it is probable that at least 80% of all drugs to produce systemic effects are administered by oral route. When a new drug is discovered, one of the first question a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effects by the oral route. Drugs that are administrated orally solid dosage forms represent the preferred class of product of the two oral solid dosage forms commonly employed, the tablets and the capsules, the tablet has a number of advantages[1].

Tablets are divided into two general classes, whether they are made by compression or moulding. Compressed and moulded tablets are prepared for large scale and small scale production respectively[2]. The choice of tablet manufacturing method depends on the dose and the drug's physical properties, compressibility and flow of the blend[3]. Direct compression is a process by which tablets are compressed directly from mixtures of the drug and excipients, without any preliminary treatment. An active pharmaceutical ingredient (API), a diluent and a lubricant constitute a formula for direct compression[4]. The emergence of direct compression was made plausible after the trade availability of directly compressible tablet vehicle that have both fluidity and compressibility. Numerous common manufacturing issues are ascribed to incorrect powder flow, which include non-uniformity in blending, under or over dosage and incorrect filling. The simpleness of the direct compression is clear that requires a new and critical approach to the selection of raw materials, flow properties of powder blends and effect of formulation variables on compressibility. Additional advantage of direct compression method includes wealth and processing without moisture and heat[1,5]. Despite

the fact that it is not well documented in the published writings, it would seem crystal clear that fever chemical stability problems would be experienced in tablet prepared by direct compression as compared to those made by wet granulation process. The primary cause of instability in tablet is moisture. Moisture plays a significant role not in drug stability but in the compressibility characteristics of granulation. One other aspect of stability that warrants increasing attention is the effect of tablet aging on dissolution rates.

Tablets prepared by granulation show variation in dissolution profile which is not commonly observed in tablets made by direct compression. The active drug particles are liberated after disintegration of tablet prepared by direct compression, resulting in comparatively faster dissolution[6]. This is extremely important because the official compendium now requires dissolution specification in most solid dosage forms. Highly potent drugs with low flow ability are not generally prepared by direct compression due to the limitation of this method[7].

Enalapril maleate is the maleate salt form of enalapril, a derivative combination of L-alanine and L-proline. Enalapril maleate is an angiotension converting enzyme inhibitor which lowers blood pressure by reducing peripheral vascular resistance without comparatively increasing cardiac output, heart rate or cardiac contractility. Entire grades of essential hypertension particularly in patients with diabetes and other chronic kidney disease such as glomerulosclerosis can be treated with enalapril. It is also indicated in the treatment of heart failure. Hence, an attempt was made for preparation of a new formulation of enalapril maleate tablet by direct compression with an aim of reducing the lag time and providing faster onset of action to reduce the blood pressure immediately[8].

MATERIALS AND METHODS

Direct compression method is used for tablet preparation. Various pharmaceutical parameters given in USP were studied for enalapril maleate tablet formulation available in the local market as well as for new formulation. These parameters include appearance, weight variation, hardness, friability, content uniformity, disintegration and dissolution tests[9].

Materials

Pure enalapril maleate powder (Sum pharma, Gurgaon, Haryana), monobasic sodium phosphate (Merck), phosphoric acid (Merck), acetonitrile (Merck). Different brand of enalapril maleate were purchased from the market.

Methods

Determination of weight variation

Twenty tablets from both of the brands of enalapril maleate were weighed individually with the mentioned analytical balance and average weight and the percent deviation was determined for each brand[10].

Hardness test

The hardness of three tablets from each batch was measured individually. An anvil driven by electric motor presses the tablet at a horizontal position and constant load until the tablet breaks. The hardness was measured in terms of kg/cm2[11].

Friability test

This test was done for 20 tablets, starting by weighing them and then operating the friabilator at 25 rpm for 4 minutes, re-weighing the tablets to determine the loss in their weight[12].

Disintegration test

The disintegration time was determined in Phosphate buffer (pH 6.8) at 37˚C. Disintegration apparatus with a basket rack assembly containing six open-ended tubes and 10-mesh screen on the bottom was used. A tablet was placed in each tube of the basket and the time for complete disintegration of the six tablets was recorded[13].

Drug Content

Initially weigh the tablet and then powder it. Now the powdered tablets are transferred into a 100 ml volumetric flask and add 0.1 HCl up to mark. Now filter the solution and discard first few ml of filtrate. Take 10 ml of filtrate should be taken into a 50 ml volumetric flask and add 0.1 N HCl up to the mark and analyzed spectrophotometrically. The concentration of the content of the drug (µg/ml) was calculated by using the standard calibration curve of the respective drug [14].

Drug content is calculated by using the formula

Concentration of the in (µg/ml) × 100 × 50 × 1000

Dissolution studies of Enalapril maleate tablets

The dissolution test was used to compare between Enalapril maleate tablets. The USP paddle method was used for all the in vitro dissolution studies. In this method, Phosphate buffers (pH 6.8) were used as dissolution media. The rate of stirring was 50 ± 2 rpm. The tablets were placed in 900 mL of Phosphate buffer (pH 6.8) at 37 ± 0.1°C. At appropriate intervals (5, 10, 15, 30, and 60 min), 5 mL of the samples were taken and filtered. The dissolution medium was then replaced by 5 mL of fresh dissolution fluid to maintain a constant volume. The samples were then analyzed by UV-spectrophotometer (USP 31, 2010).

RESULTS AND DISCUSSION

Different brands of Enalapril maleate tablet were evaluated that are listed in local index of registered pharmaceutical products. All formulation tablets with 5 mg potency were selected and then evaluated with same standard procedure. Various pharmaceutical parameters namely weight variation, hardness test, friability test, disintegration test and dissolution test were performed according to USP (2008). Results are given in table 1.

Table 1: Evaluation of different quality control parameters of Enalapril maleate tablets

Sample (Tablet Brands)	Weight variation test limit (%)	Hardness (kg/cm^2)	Friability (%)	Disintegration Time (min/sec)	Enalapril maleate Content (%)
A	1.91±0.04	7.55±0.05	0.35±0.02	4.46±0.08	98.3±0.41
B	1.30±0.05	6.45±0.34	0.68±0.35	4.27±0.15	96±0.65

Weight variation

During the study, at first the weight variation is the key to controlling crushing strength and friability of tablet was assessed. The test stated that both the sample of Enalapril maleate coded A and B have passed the weight variation uniformity test as specified in the Indian Pharmacopoeia (not exceed 5% deviation) (table 1).

Hardness

After weight variation hardness is the second most important physical feature for assessing tablet. In this current research evaluation study, it was found that A and B brands of enalapril maleate successfully passed the tablet crushing strength or hardness test. Both these commercial brands have acceptable crushing strength of range between 4kg/cm^2 to 10 kg/cm^2 (table 1).

Friability

In the friability test, both tablet brands showed impressive friability values. The friability values for both Enalapril maleate brands were ranged from 0.3 to 0.7%. In both formulations the percent (%) friability was less than 1% which ensures that all the tablets of both brands of formulation were mechanically stable (table 1).

Disintegration

The disintegration time of both the tablet brands of enalapril maleate A and B was found to be satisfactory as compared to uncoated USP tablet having disintegration time standards as low as 5 minutes (table 1).

Drug Content

The drug content of both the brands of enalapril maleate showed little differences (table 1).

Dissolution

Dissolution was another studied important quantity control parameters directly related to the absorption and bioavailability of drug. The study revealed that at different time intervals drug release rate was better (figure 2) (table 2).

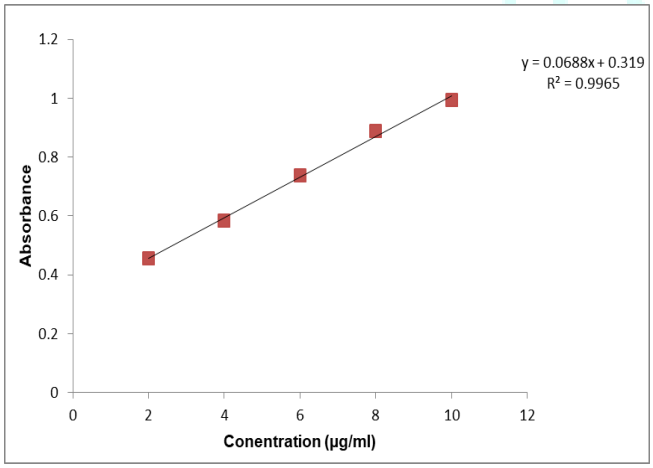

Figure 1: Calibration curve of Enalapril maleate in phosphate buffer 6.8

Table 2: Calibration curve data of Enalapril maleate tablets in phosphate buffer 6.8.

TIME (min)	Concentration (µg/ml)	Absorbance
5	2	0.457±006
10	4	0.584±007
15	6	0.737±0.10
30	8	0.888±0.14
60	10	0.993±002

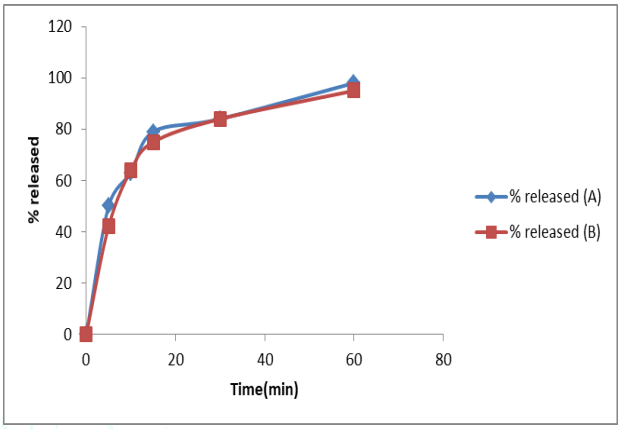

Figure 2: Drug % release of both the brands (A and B)

Table 3: Observation of drug % released of both brands

Time (min)	% drug released (A)	% drug released (B)
0	0	0
5	50.78±0.65	42.76±0.97
10	63.54±0.39	64.45±0.67
15	79.67±0.78	75.76±0.65
30	84.82±0.69	84.45±0.43
60	98.21±0.42	95.34±0.66

CONCLUSION

Enalapril maleate is a well-established and commonly used antihypertensive medicine. Therapeutic response of any formulation depends on its quality parameters. Study results confirm that weight variation and friability test of both enalapril maleate tablet brands conform to the specification. Variation was found in hardness, disintegration time and dissolution profile during the test procedure. Furthermore, it confirms that an ideal tablet should have sufficient hardness to maintain its mechanical stability but not too much as harder tablet can delay disintegration time or alter dissolution profile. Finally as quality control parameters are related to each other, from initial step to pharmacological action of the drug, a high quality tablet should meet all the standard quality parameters to exert its desired therapeutic response.

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