# A COMPARATIVE STUDY OF MARKETED FORMULATIONS OF RAMIPRIL

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***ABSTRACT***

*The aim of present research work was to evaluate the doses form of the drug ramipril. In order to attain the aim through literature survey on hypertensive ramipril was carried on library (journal, chemical data base search), online database search (sci finder, online sites) was done. The next step is to compare the different doses forms of ramipril by using UV spectroscopy and other physical parameters. Currently various brands of ramipril were available in local market. During this alternative, the efficiency and quality of the drug was important. Hence, there is a need to reveal the quality of different brands to ensure the safety of the patient. The comparative analysis was done under five different brands of ramipril and coded as Brand-A, Brand-B, Brand-C, Brand-D and Brand-E. The different market formulations were taken as (Brand A), (Brand B), (Brand C), (Brand D), (Brand E). The physical parameters hardness, thickness, friability, weight variation, disintegration test, dissolution test were studied according to the guidelines given in the IP, BP and USP.*

***Keywords:*** *Ramipril, di-Sodium hydrogen phosphates dehydrate, 0.1 % N Hydrochloric acid, Potassium dihydrogen orthophosphate, UV Spectroscopy.*

## INTRODUCTION

### Tablet

Tablets may be defined as the solid unit dosage form of medicament or medicaments, with or without suitable excipients and prepared either by molding or by compression. According to the Indian pharmacopoeia pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents [1]. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid dose [2]. The excipients can include diluents, binders or granulating agents, glidants (flow aids) and lubricants to ensure efficient tabletting; disintegrants to promote tablet break-up in the digestive tract; sweeteners or flavours to enhance taste; and pigments to make the tablets visually attractive or aid in visual identification of an unknown tablet[3]. A polymer coating is often applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment (extending its shelf life), or to enhance the tablet's appearance [4]. They vary in shape and differ greatly in size and weight, depending on amount of medicinal substances. It is the most popular dosage form and 70 % of the total medicines are dispensed in the form of

tablet[5]. All medicaments are available in the tablet form except where it is difficult to formulate or administer [6].

**Advantages and disadvantages of the tablet dosage form**

1. They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
2. Cost is lowest of all oral dosage form.
3. Lighter and compact.
4. Easiest and cheapest to package and strip.
5. Controlled release product is possible by coating.
6. Objectionable odour and bitter taste can be masked by coating technique.
7. Suitable for large scale production.
8. Greatest chemical and microbial stability over all oral dosage form.
9. Product identification is easy and rapid, requiring, no additional steps when employing an embossed and monogrammed punch face.
10. Difficult to swallow in case of children and unconscious patients.
11. Some drugs resist compression into dense compacts, owing to amorphous nature and low density character.
12. Bitter tasting drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule is best option and offers to lowest cost [7].

**Hypertension**

Hypertension is the elevation of arterial blood pressure. Heart failure, stroke, renal failure and even death can be due to cardiovascular diseases, and the hypertension is the common cause of cardiovascular diseases. In hypertension there is often an increase in cardiac output, increased blood flow resistance by blood vessels, cardiac hypertrophy, abnormalities in renal function and often atherosclerosis and ultimately myocardial infarction due to angina [8].

**Classification of clinic blood pressure levels in adults** [9]

**Table 1.1 Classification of blood pressure levels**

| Category | Systolic (mmHg) | Diastolic (mmHg) |
|---|---|---|
| Optimal stage | <120 | <80 |
| Normal stage | 120-129 | 80-84 |
| High –normal stage | 130-139 | 85-89 |
| Mild hypertension | 140-159 | 90-99 |
| Moderate hypertension | 160-179 | 100-109 |
| Severe hypertension | >180 | >110 |
| Isolated systolic hypertension | >140 | <90 |

## PATHOPHYSIOLOGY OF HYPERTENSION

- **Heredity**: Hypertension mostly caused by the interaction of environmental factors, demographic factors and genetic factors [10].
- **Water and Sodium Retention**: If we take more concentration of sodium then it causes water retention. Some people are sodium (Na) sensitive and some demographics are associated with "salt sensitivity" *i.e* obesity, increasing age, and people with diabetes, renal disease and african american.
- **Stress and increased sympathetic nervous system (SNS) activity**: It cause vasoconstriction leads to increase heart rate.
- **Renin – Angiotensin – Aldosterone mechanism**: Renin is an enzyme released by the kidney to maintain body's sodium – potassium balance, fluid volume and BP. When blood pressure decreases, the juxta glomerular (JG) cells secrete renin. Renin acts on plasma protein, angiotensin substrate and converts into angiotensin I. With the help of angiotensin converting enzyme (ACE) angiotensin is converted into angiotensin II. Angiotensin II acts on the blood vessels walls and increases the vasoconstriction action. Due to the vasoconstriction, TPR (Total peripheral resistance) will also increase and leads to increase blood pressure. It is the first mechanism. In second mechanism, angiotensin II also stimulates adrenal cortex. This will cause the high secretion of aldosterone hormone. Aldosterone acts on kidneys and increase the reabsorption of water and sodium (Na). This causes the increase blood volume and leads to increase blood pressure (BP) [11-14].

**FLOW CHART OF PATHOPHYSIOLOGY OF HYPERTENSION**

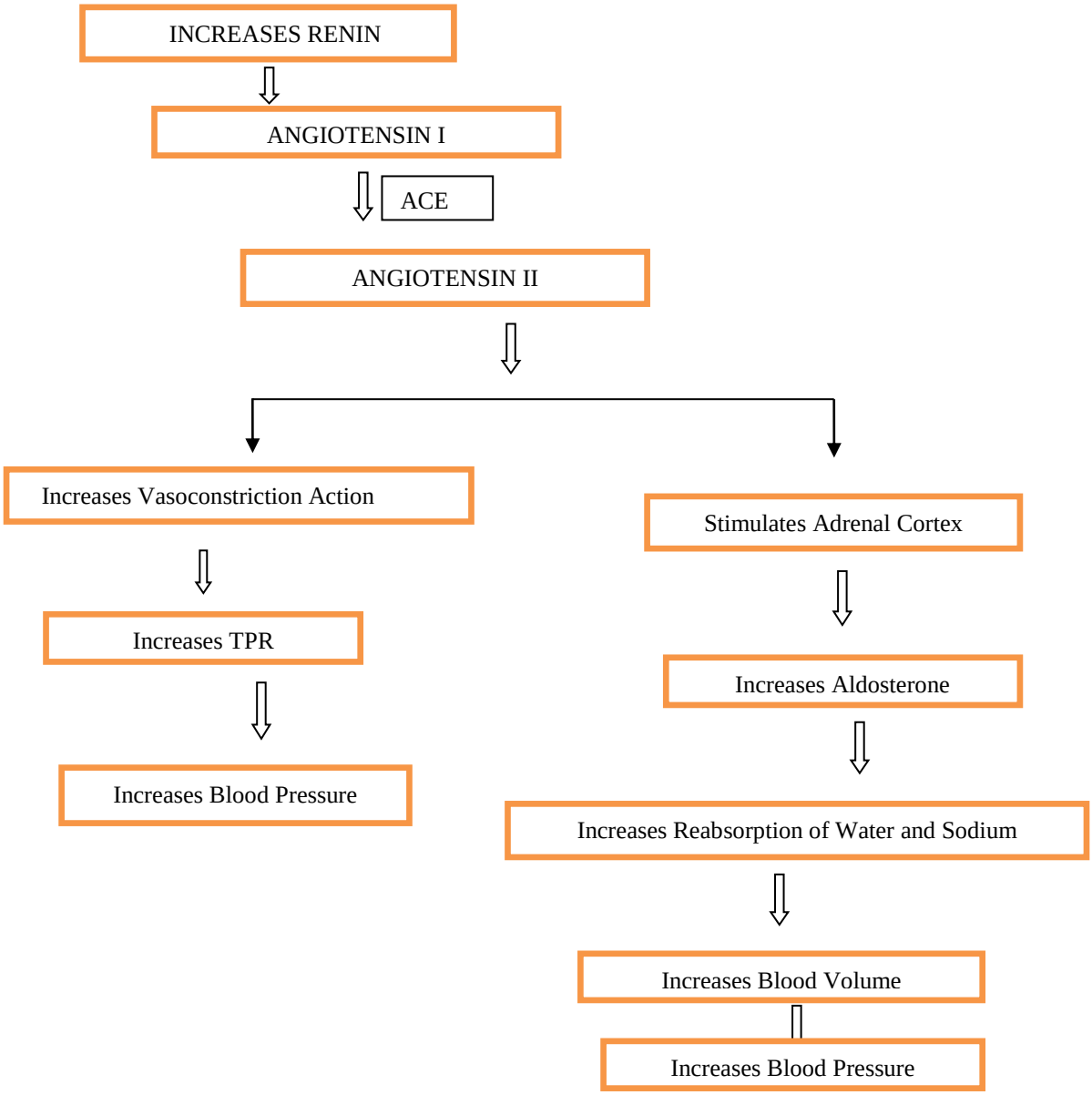


**Fig. 1.1 Pathophysiology of Hypertension**

## CAUSES OF HYPERTENSION [15]

In the majority of cases-over 90 % no specific cause for the elevated blood pressure can be identified. Almost all people with hypertension have “essential” hypertension. Some researchers believe that this type of high blood pressure may be due to hormonal factors relating to the handling of salt by the kidneys or to the elaboration of certain susbstances that cause constriction of blood vessels. These are probably genetically determined, but certain environmental factors, such as a high-salt, low-potassium diet and chronic stress, may play some role. In up to 10 % of patients, high blood pressure may be a consequence of another disorder, or a side effect of medication.This type of hypertension is referred to as secondary

hypertension. It is important to remember that these cases are relatively uncommon. However, some of the more common causes of secondary hypertension include the following:-

- Kidney disorders
- Other family member with hypertension
- Little or no exercise
- Renovascular hypertension

**Anti-hypertensive agents**

Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34 %, of ischaemic heart disease by 21 %, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. There are many classes of antihypertensives, which lower blood pressure by different means. Among the most important and most widely used drugs are thiazide diuretics, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists (ARBs), and beta blockers [16].

**Drug profile** [17-21]

**Ramipril**

Ramipril has pharmacological action as an Antihypertensive

**Trade Name:** Altace, Cardace, Zigpril, Ramistar, Odipril and Zorem

**IUPAC Name:** 2*S*-4-phenylbutan- 1-oxo -1-ethoxy- 2-yl-amino- octahydrocyclopenta-propanoyl--*b*-pyrrole, 2-carboxylic acid.

**Molecular Formula:** $C_{23}H_{32}N_2O_5$

**Molecular Mass:** 416. 52 gram/moL

**Chemical Structure:**

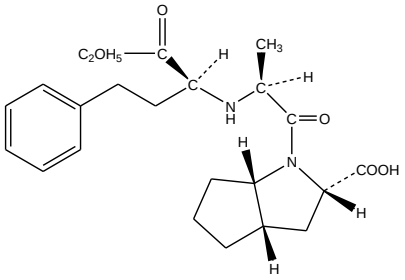


**Fig. 1.2 Structure of Ramipril**

**Description:** White, crystalline powder.

**Odor and Taste:** Odorless and bitter in taste.

**Melting Point:** 109 ˚C.

**Solubility:** Freely soluble in methanol and ethanol.

**Metabolism:** Ramipril shows hepatic biotransformation. It is a prodrug and is converted to the active metabolite Ramiprilat by liver esterase enzymes.

**Dose:** 2.5, 5 and 10 mg

**Mechanism of action**

Ramipril inhibit the actions of angiotensin converting enzyme (ACE), thereby lowering the production of angiotensin II and decreasing the breakdown of bradykinin. The decrease in angiotensin II results in relaxation of arteriole smooth muscle leading to a decrease in total peripheral resistance, reducing blood pressure as the blood is pumped through widened vessels. Its effect on bradykinin is responsible for the dry cough side effect. Ramipril, a prodrug or precursor drug is converted to the active metabolite ramiprilat by carboxylesterase1 [22, 23]. Ramiprilat is mostly excreted by the kidneys. Its half-life is variable (3-16 h), and is prolonged by heart and liver failure as well as kidney failure.

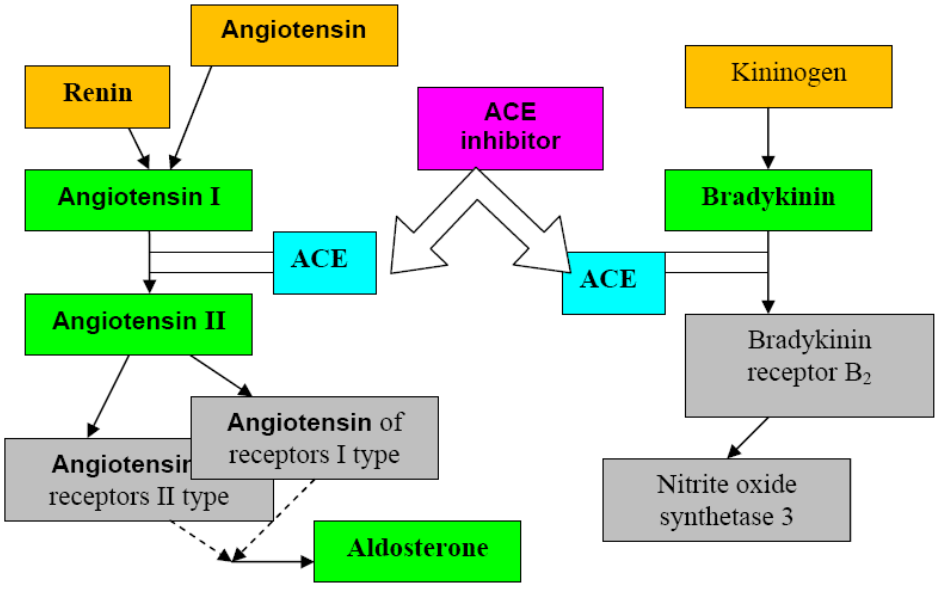


**Fig. 1.3 Mechanism of Action of Ramipril**

**Ultra-violet spectroscopy**

UV spectroscopy is type of absorption spectroscopy in which light of ultra-violet region (200-400 nm) is absorbed by the molecule. Absorption of the ultra-violet radiations results in the excitation of the electrons from the ground state to higher energy state. The energy of the ultra-violet radiation that is absorbed is equal to the energy difference between the ground state and higher energy states. Generally, the most favoured transition is from the highest occupied molecular orbital to lowest unoccupied molecular orbital. For most of the molecules, the lowest energy occupied molecular orbitals are s orbital, which correspond to sigma bonds. The p orbitals are at somewhat higher energy levels, the orbitals (nonbonding orbitals) with unshared paired of electrons lie at higher energy levels. The unoccupied or antibonding orbitals are the highest energy occupied orbitals.
In all the compounds (other than alkanes), the electrons undergo various transitions. Some of the important transitions with increasing energies are: nonbonding to $\pi^*$, nonbonding to $\sigma^*$, $\pi$ to $\pi^*$, $\sigma$ to $\pi^*$ and $\sigma$ to $\sigma^*$.

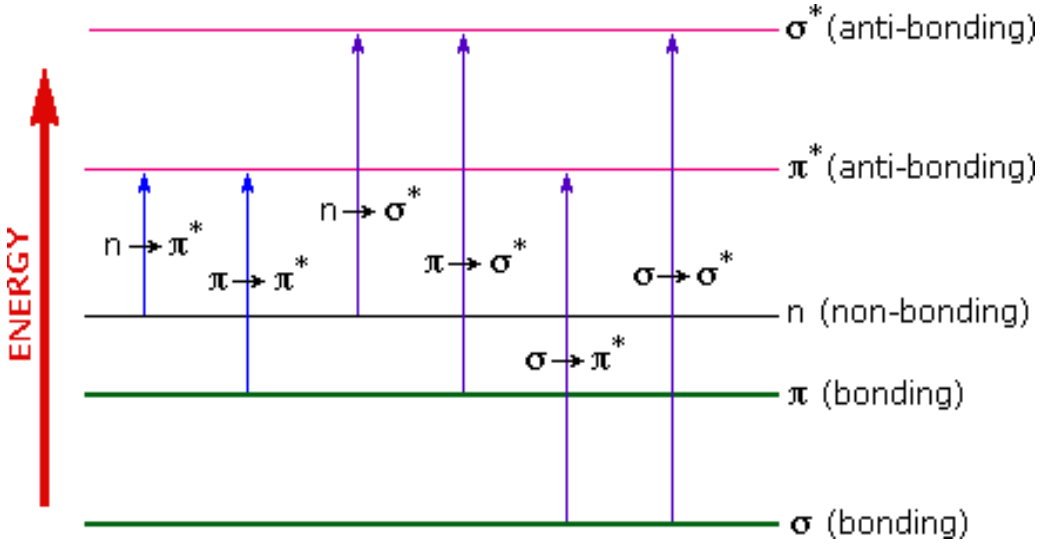


**Fig. 1.5 Types of Transitions**

**Principle of uv spectroscopy**

UV spectroscopy obeys the beer-lambert law, which states that: when a beam of monochromatic light is passed through a solution of an absorbing substance, the rate of decrease of intensity of radiation with thickness of the absorbing solution is proportional to the incident radiation as well as the concentration of the solution. The expression of beer-lambert law is-

$$A = \log(I_0/I) = \mathcal{E}cl$$

Where, A= Absorbance

$I_0$ = Intensity of Light Incident upon Sample Cell

I = Intensity of Light Leaving Sample Cell

c = Molar Concentration of Solute

l = Length of Sample Cell (cm)

Ɛ= Molar Absorptivity

From the beer-lambert law it is clear that greater the number of molecules capable of absorbing light of a given wavelength, the greater the extent of light absorption. This is the basic principle of UV spectroscopy [24].

**Instrumentation of uv spectroscopy**

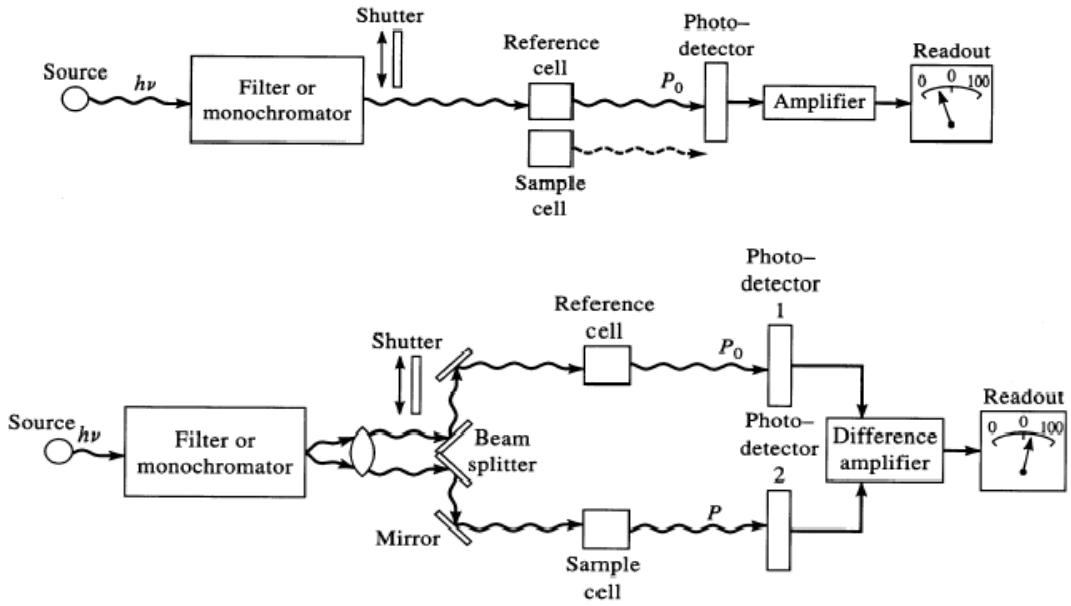


**Fig. 1.6 Instrumentation of UV Spectroscopy**

Most of the modern UV Spectrometers consist of the following parts:-

**Light Source-** Tungsten filament lamps and hydrogen-deuterium lamps are most widely used and suitable light source as they cover the whole UV region. Tungsten filament lamps are rich in red radiations; more specifically they emit the radiations of 375 nm, while the intensity of hydrogen-deuterium lamps falls below 375 nm.

**Monochromator-** Monochromators generally composed of prisms and slits. The most of the spectrophotometers are double beam spectrophotometers. The radiation emitted from the primary source is dispersed with the help of rotating prisms. The various wavelengths of the light source which are separated by the prism are then selected by the slits such the rotation of the prism results in a series of continuously increasing wavelength to pass through the slits

for recording purpose. The beam selected by the slit is monochromatic and further divided into two beams with the help of another prism.

**Sample and reference cells-** One of the two divided beams is passed through the sample solution and second beam is passé through the reference solution. Both sample and reference solution are contained in the cells. These cells are made of either silica or quartz. Glass can't be used for the cells as it also absorbs light in the UV region.

**Detector-** Generally two photocells serve the purpose of detector in UV spectroscopy. One of the photocell receives the beam from sample cell and second detector receives the beam from the reference. The intensity of the radiation from the reference cell is stronger than the beam of sample cell. This results in the generation of pulsating or alternating currents in the photocells.

**Amplifier-** The alternating current generated in the photocells is transferred to the amplifier. The amplifier is coupled to a small servometer. Generally current generated in the photocells is of very low intensity, the main purpose of amplifier is to amplify the signals many times so we can get clear and recordable signals.

**Recording devices-** Most of the time amplifier is coupled to a pen recorder which is connected to the computer. Computer stores all the data generated and produces the spectrum of the desired compound.

**Applications of uv spectroscopy**

1. Detection of functional groups.
2. Detection of extent of conjugation.
3. Identification of an unknown compound.
4. Determination of configuration of geometrical isomers.
5. Determination of the purity of a substance [25].

## MATERIAL AND METHODS

All chemicals and reagents were of high quality analytical grade. Pure Ramipril (99.98 %) was received as a gifted by Indo Swift Laboratory Baddi. Distilled water was used for all analysis. Five brands of marketed Ramipril tablets were obtained from various drug stores. The samples were properly checked for their manufacturer name, physical appearance and batch number, date of manufacturing and expiry date before purchasing. They are coded as brand A, B, C, D, and E. The labeled active ingredients was Ramipril 5 mg and packaged strip or in blister form.

**Determination of wavelength of maximum absorption**

Pure Ramipril (0.01gram) was dissolved in 50 mL of methanol in 50 mL volumetric flask to give a 200 µg/mL Ramipril stock solution ($R_o$). $R_o$ (5 mL) was further diluted to 100 mL with distilled water to give a 10 µg/mL Ramipril solution and this was scanned in the wavelength region 190 to 800 nm to determine the wavelength of maximum absorption using 5 % aqueous methanol as reagent blank.

**Preparation of reference standard**

Pure Ramipril (5 mg) was accurately weighed and dissolved in 100 mL of absolute methanol. Out of this solution, 5 mL was further diluted to 100 mL with deionised water to obtain a 12.5 µg/mL Ramipril standard solution. The absorbance of these test and reference standard solutions was taken using 5 % aqueous methanol as blank.

**Limit of detection and limit of quantification**

LOD and LOQ were determined using the expression in eqs. (1) and (2).

LOD = 3(SD/a)…… (1)

LOQ = 10(SD/a)…….. (2)

Where, SD= standard deviation of the intercept and

a = mean slope obtained from the calibration plot.

**Assay of tablet**

Accurately weighed amount of crushed tablet powder equivalent to 5 mg Ramipril, was transferred into a 100 mL volumetric flask, 50 mL of absolute methanol was added, shaken for 15 min in a vortex mixer and diluted to the 100 mL mark with the same solvent. It was then filtered using Whatman paper to obtain stock solution, $P_o$. 5 mL of $P_o$ was further diluted to 100 mL with distilled water and then assayed for content of Ramipril using the proposed method. A solution containing 12.5 µg/mL of pure Ramipril was used as standard for comparison. 20 tablets of Ramipril tablets were powdered and quantity of the powder equivalent to 5 mg of Ramipril was dissolved by shaking with 5 mL methanol followed by 30 mL of water. The solution was filtered through filter paper into a 50 mL volumetric flask and then 3 diluted to volume with water. The drug % content was expressed [26]

$$y = mx + c$$

**Weight variation**

20 tablets were selected randomly and weighed individually. The weight was calculated and individual weight was compared to the average weight. The percentage deviation of each tablet was calculated as the formula below.

$$\text{Percentage Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

The tablet passes the test according to BP 2009 if not more than two of the individual weights deviate from the average weight by ±5 % and no one deviates by ±10 %.

**Table 4.3 List of Limits of Weight Variation (BP)**

| Average Weight (mg) | Percentage Deviation (%) |
|---|---|
| 50 mg or less than | ±10 % |
| More than 50 mg or less than 250 mg | ±7.5 % |
| More than 250 mg | ±5 % |

**Hardness test**

The hardness of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling. Randomly selected 10 tablets were placed between the jaws of the hardness tester individually from each brand and the strength of the tablets was tested under hardness tester. All the tablet brands passed this non-official test according to BP 2009 (4–6 kg/cm$^2$). The pressure at which each tablet crushed was recorded.

**Thickness test**

Thickness of tablets from each brand and generic were also measured by the thickness tester. After inserting the approximate thickness of the tablets, the accurate values of those parameters were measured. Thickness of tablets was necessary not only for consumer requirements but also for packaging ±5 % variation is permissible. The pressure at which each tablet crushed was recorded according to BP 2009 specification.

**Friability test**

According to BP 2009, twenty (20) tablets from each sample were dedusted, weighed and placed in the drum of friabilator and subjected to 100 revolutions (25× 4 r/min). The tablets

were then again dedusted and weighed and percentage (%) loss was determined using the formula given below.

$$\text{Percentage Friability} = \frac{W_0 - W_1}{W_0} \times 100$$

Where $W_0$ and $W_1$ are initial and final weights respectively.

The sample passes the test if a percentage loss is not more than 1 % of the weight of the tablet tested.

**Disintegration test**

The disintegration time of randomly selected 6 tablets of each sample was determined at 37+2 °C in 0.1M HCl using disintegration apparatus, according to BP 2009 specifications. The machine was set to 30 r/min. The disintegration time was taken to be the time no granule of any tablet was left in the mesh. The disintegration time for fast releasing tablet should be within 15 minute, according to BP 2009 specifications.

**Dissolution test**

Dissolution test was conducted according to the specifications on BP 2009.

**Dissolution Study Procedure:** 500 mL of 0.1M HCl was placed into each of two dissolution vessels and the temperature was set to 37 °C. Tablets were transferred to each vessel. Basket was immersed in media. At the end of 30 min 5mL samples were withdrawn from each vessel. The withdrawn quantity of samples was replaced by the same.

The absorbance was measured at 208.5 nm by an UV spectrometer using 0.1M HCl as blank. This operation was continued for 8 h. At every 30 min intervals 5mL samples were withdrawn from the dissolution vessel and replaced with fresh dissolution medium to maintain constant volume. The absorbance of sample solution was measured at 210 nm by an UV spectrometer using 0.1M HCl as blank. The dissolution study was continued foe 8 h to get a simulated picture of the drug release in the in-vivo condition and drug dissolved at specified time periods was plotted as percent release versus time (h) curve [27].

## 5. RESULTS AND DISCUSSION

### Drug analysis of pure drug

### 5.1.1 Identification of drug

### a) Physical appearance

The drug possesses similar colour, odour, state and taste as given in official's pharmacopoeia.

**Table 5.1 Organoleptic Characters of Ramipril**

| Physical Parameters | Observations |
|---|---|
| **Colour** | White |
| **Odour** | Odourless |
| **State** | Crystalline Powder |
| **Taste** | Bitter |

### b) Determination of melting point

Melting point of Ramipril was determined by capillary fusion method. Drug was filled in the capillary tube, sealed at one end and the capillary was kept in apparatus such that sealed end was down towards the apparatus. The temperature at which drug crystals started melting and turned into liquid was recorded and the results are reported in Table 5.2.

**Table 5.2 Melting Point Analysis Data**

| Method Used | Drug | Literature Value | Experimental Value |
|---|---|---|---|
| **Capillary Fusion Method** | Ramipril | 109-112 ˚C | 107-109 ˚C |

### 5.1.2 Solubility study

The quantitative solubility study of Ramipril was carried out in various solvents. For quantitative solubility study of drug in different solvent mediums, an equilibrium solubility method was followed.

**Table 5.3 Qualitative Solubility Data of Ramipril in Different Solvents**

| Solvents | Solubility |
|---|---|
| **Distilled Water** | Poorly soluble |
| **Methanol** | Freely soluble |
| **Ethanol** | Freely soluble |

### 5.1.3 Fourier transforms infrared analysis (FTIR)

The Infra red spectroscopy of sample was carried out to identified the drug. The sample was mounted in IR compartment and taken scan at wave length 6000 $cm^{-1}$ to 400 $cm^{-1}$. For analysis, IR spectra of the pure drug have been performed & no major differences were observed in the absorption peak pattern.

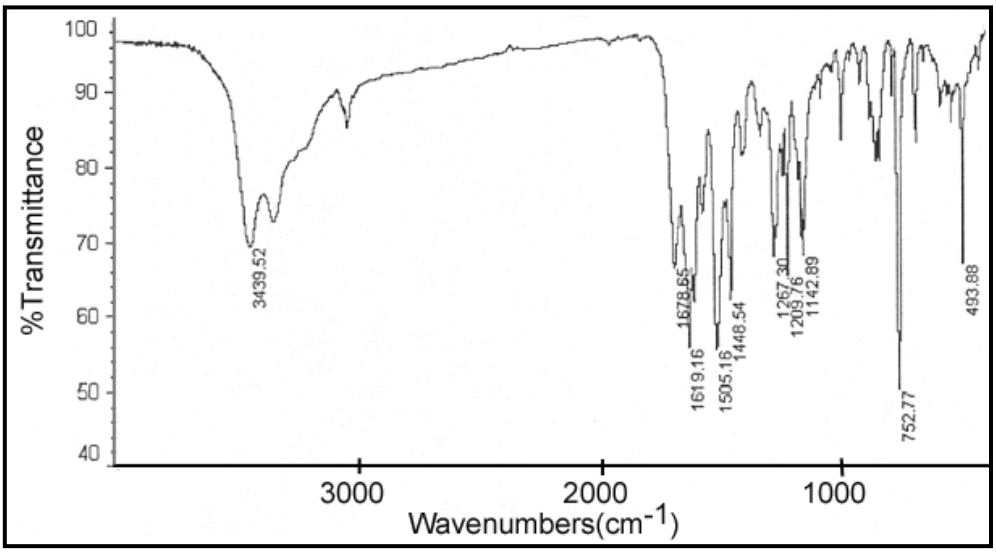


**Fig. 5.1 Reference IR Spectrum of Ramipril**

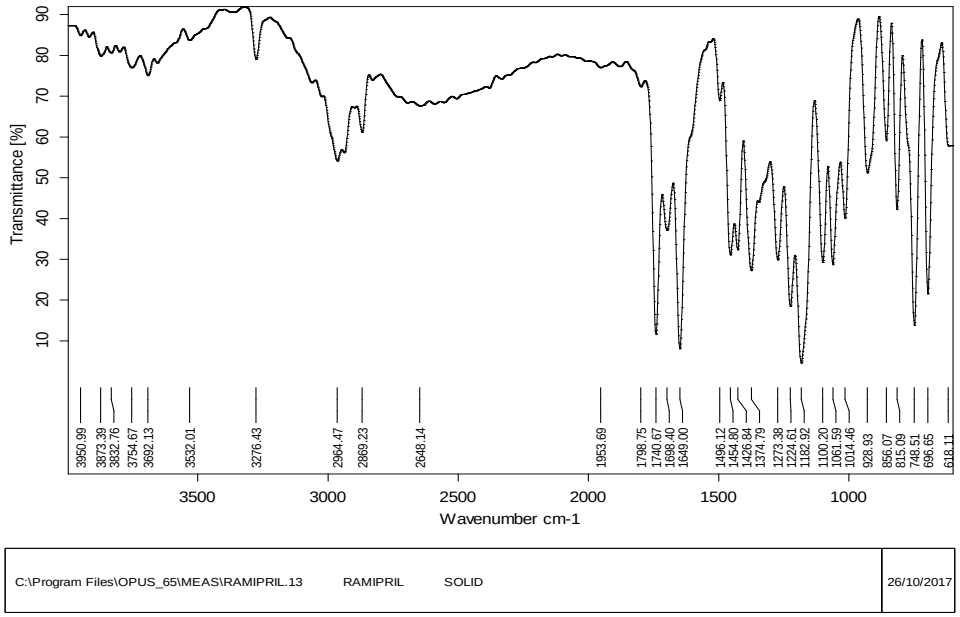


**Fig. 5.2 FTIR Spectra of Ramipril**

**Table 5.4 Interpretation of IR Spectrum of Drug**

| S. No. | Reference peak ($cm^{-1}$) | Observed peak ($cm^{-1}$) | Inference |
|---|---|---|---|
| **1.** | 3200-3400 | 3276 | N─H |
| **2.** | 2700-3000 | 2869 | O-H |
| **3.** | 1600-1700 | 1740 | C=O |
| **4.** | 1350-1550 | 1496 | C=C |

## 5.2 Physical characteristics of ramipril tablets

Five brands of ramipril (5 mg) uncoated tablets were purchased from local retail pharmacy. Five different types of brands coded as Brand A, B, C, D, and E. All the five formulations were taken all these have different physical appearance which were explained in the Table 5.5.

**Table 5.5 Physical Characteristics of Ramipril Tablets**

| Brands | Colour | Shape |
|---|---|---|
| A | Yellow oxide of iron | Circular |
| B | Red iron oxide | Biconvex faces |
| C | Red iron oxide | Circular |
| D | Yellow oxide of iron | Biconvex faces |
| E | Iron oxide red | Circular |

### 5.3 Determination of absorption maxima ($\lambda_{max}$) wavelength

**Determination of $\lambda_{max}$:** The pure Ramipril in methanol was scanned in UV-Vis spectrophotometer from 400–200 nm, to determine the $\lambda_{max}$. An absorption maximum ($\lambda_{max}$) of the drug was observed to be at 208.5nm in methanol that were in concordant with the literature value. Scan graphs are shown in Table 5.6 and Fig.5.3.

**Table 5.6 Absorption Maxima of Ramipril**

| Medium | Absorption Maxima (nm) |
|---|---|
| **Methanol** | 208.5nm |

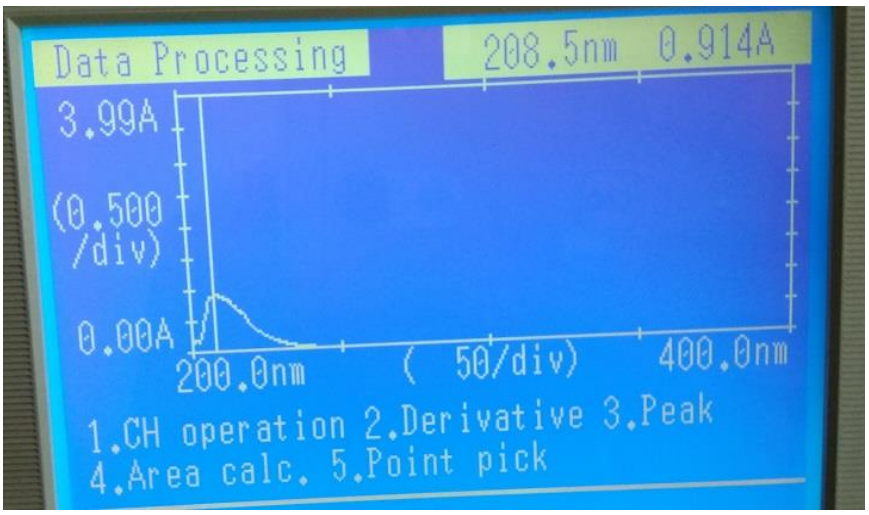


**Fig. 5.3 Absorption Maxima of Ramipril in Methanol**

### 5.3.1 Calibration curve of ramipril

The standard curve of Ramipril was done by using methanol as the medium and the maximum absorbance was found at 208.5 nm. The standard graph was constructed by making the concentrations of 5µg/mL, 10µg/mL, 15µg/mL, 20µg/mL, 25µg/mL solutions. Out of these solutions, 5 mL was further diluted to 100 mL with deionised water to obtain a 12.5 µg/mL Ramipril standard solution. The standard graph was constructed by taking the absorbance on Y–axis and concentration on X–axis. The standard calibration curve of Ramipril in methanol was shown in Fig. 5.4.

**Table 5.7 Different Absorbance of Ramipril at Same Wavelength**

| S. No. | Concentration (µg/mL) | Absorbance |
|---|---|---|
| 1. | 5 | 0.225 |
| 2. | 10 | 0.406 |
| 3. | 15 | 0.579 |
| 4. | 20 | 0.795 |
| 5. | 25 | 0.972 |

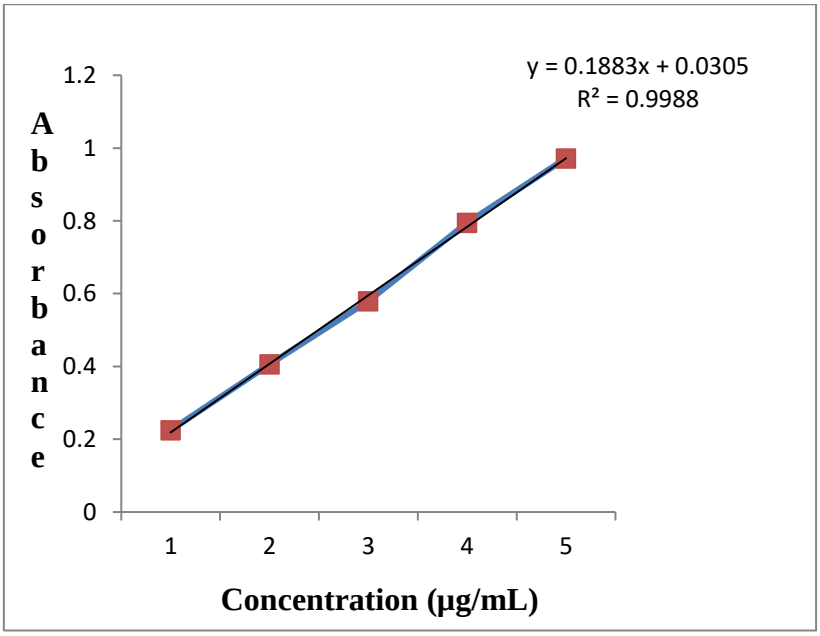


**Fig. 5.4 Calibration Curve of UV Spectrum Standard Ramipril at 208.5 nm**

The summary of validation parameters

| **Parameter** | **Results** |
|---|---|
| $\lambda_{max}$ (nm) | 208.5 |
| Beer's law linearity range | 1 – 38 µg/mL |
| Regression equation | Y= 0.188x+0.030 |
| Intercept (a) | 0.030 |
| Slope (b) | 0.188 |
| Correlation coefficient ($R^2$) | $R^2$ = 0.998 |
| Limit of Detection (LOD) | 5.213 |
| Limit of Quantitation (LOQ) | 15.79 |

### 5.4 Assay of tablets dosage form of ramipril

The weight variation test is clearly not sufficient to assure the uniform potency of tablets. So, the tablets are expressed in labeled strength. Drug content among different brands of tablets ranged from 99.3 % to 109.12 %. The drug content in Brand- A was minimum while the Brand-B had maximum drug content.

**Table 5.8 Assay of Tablets Dosage Form**

| Brands | Concentration (µg/mL) | Drug content % |
|---|---|---|
| A | 12.5 | 99.3 |
| B | 12.5 | 109.12 |
| C | 12.5 | 102.8 |
| D | 12.5 | 108.8 |
| E | 12.5 | 101.04 |

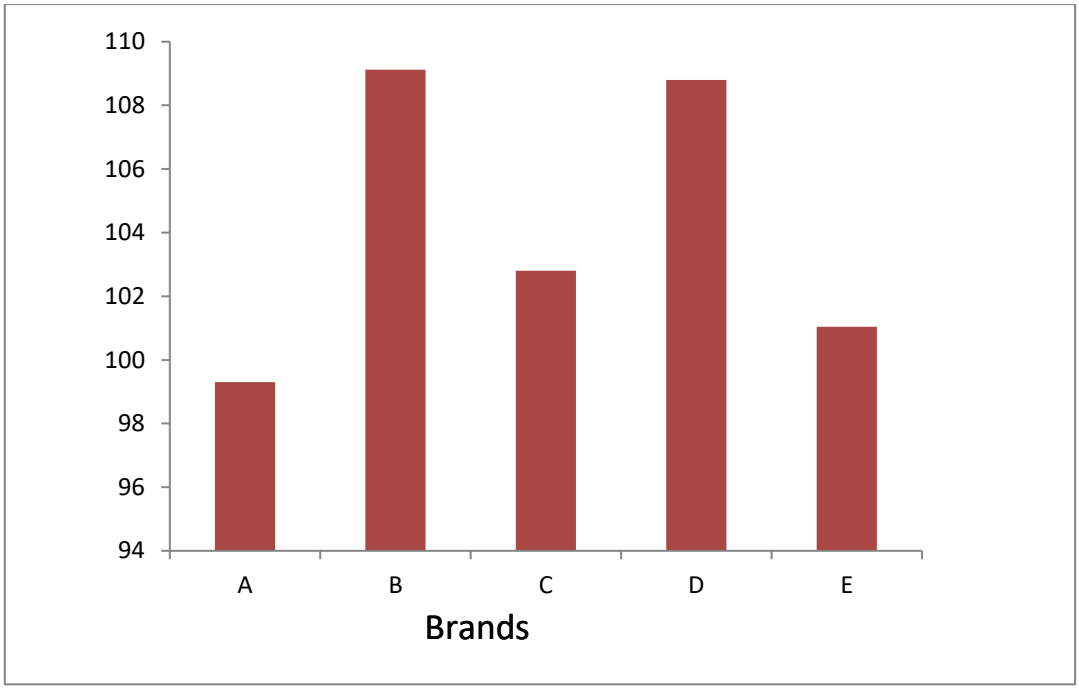


**Fig. 5.5 Percentage Assay of Ramipril**

### 5.5 Weight variation

Tablets were subject to weight variation study for uniformity of weight. All brands showed different mean weight which indicates the use of different excipients in the different brands. The weight of the tablet varied between 0.075 ± 0.017 to 0.25 ± 0.015 g for all the tablet brands. Brands B and D had same weight variation i.e. 0.25 ± 0.015g.

**Table 5.9 Weight Variation for all the Brands of Ramipril**

| Brands | Total weight of (20) tablets (g) | Average (g) | Mean±SD |
|---|---|---|---|
| A | 2.61 | 0.13 | 0.13±0.03 |
| B | 5.020 | 0.25 | 0.25±0.015 |
| C | 4.060 | 0.203 | 0.203±0.009 |
| D | 5.99 | 0.3 | 0.3±0.043 |
| E | 1.19 | 0.06 | 0.06±0.023 |

### 5.6 Hardness test

The hardness of the tablets was determined by using a hand operated hardness tester apparatus. A tablet hardness of about 4–6 kg/cm$^2$ was considered for mechanical stability. The hardness of the tablets of all the brands was ranged from 5.5 ± 0.45 to 5.75 ± 0.69 kg/cm$^2$.

**Table 5.10 Hardness Test for all the Brands of Ramipril**

| Brands | Total hardness of (6) tablets (kg/cm$^2$) | Average (kg/cm$^2$) | Mean±SD |
|---|---|---|---|
| A | 29.2 | 4.17 | 4.17 ± 0.250 |
| B | 33 | 5.5 | 5.5 ± 0.45 |
| C | 34 | 5.66 | 5.66 ± 0.605 |
| D | 34.5 | 5.75 | 5.75 ± 0.69 |
| E | 33 | 5.5 | 5.5 ± 0.45 |

### 5.7 Thickness test

After preparing the matrix tablets, all the tablets of the proposed formulations were subjected to thickness test. Thickness of tablets was necessary not only for consumer requirements but also for packaging ±5 % variation is permissible. The thickness of the tablets ranged from 5.03 ± 0.0082 to 8.05 ± 0.0082 mm. Thickness of the tablets was determined by using a digital vernier caliper (range 0–150 mm).

**Table 5.11 Thickness Test for all the Brands of Ramipril**

| Brands | Total thickness of (6) tablets (mm) | Average (mm) | Mean±SD |
|---|---|---|---|
| A | 39.3 | 6.55 | 6.55 ± 0.104 |
| B | 30.16 | 5.03 | 5.03 ± 0.008 |
| C | 48.4 | 8.06 | 8.06 ± 0.008 |
| D | 30.17 | 5.03 | 5.03 ± 0.009 |
| E | 33.5 | 5.6 | 5.6 ± 0.075 |

### 5.8 Friability test

The acceptable limits of weights loss should not be more than 1. The percentage friability of the tablets of all the five brands ranged from 0.12 % to 0.42 %. Brand-E had highest % friability while, brand D had the lowest one.

**Table 5.12 Friability Test for all the Brands of Ramipril**

| Brands | Total weight of (20) tablets | Total weight of (20) tablets after friability (gm) | % Friability |
|---|---|---|---|
| A | 2.61 | 2.60 | 0.38 |
| B | 5.020 | 5.013 | 0.14 |
| C | 4.060 | 4.051 | 0.22 |
| D | 5.99 | 5.983 | 0.12 |
| E | 1.19 | 1.185 | 0.42 |

### 5.9 Disintegration test

The disintegration time for all the five brands of Ramipril was less than 10 min. All the tablets of different brands of Ramipril passed the disintegration test were in the range of 45-seconds to 4-minutes 3-seconds. The brand-E and brand–A had maximum and minimum time taken for disintegration respectively**.**

**Table 5.13 Disintegration Time of Ramipril Tablets**

| Brands | Total time for DT (min) | Average | Disintegration time (min) Mean±SD |
|---|---|---|---|
| A | 4 | 1 | 1±0.03 |
| B | 2 | 0.4 | 0.4±0.01 |
| C | 7 | 1.4 | 1.4±0.01 |
| D | 6 | 1.2 | 1.2±0.02 |
| E | 15 | 3 | 3±0.04 |

### 5.10 Dissolution test

The cumulative percent release in 0.1M HCl for all the brands were recorded and the brand-C showed highest 95.58 % drug release for 1 h and the brand-A showed lowest 84.96 % drug release during the same time period.

**Table 5.14 Cumulative % Drug Release**

| Brands | 10 min | 20 min | 30 min | 40 min | 50 min | 60 min |
|---|---|---|---|---|---|---|
| A | 52.21 | 65.34 | 69.98 | 75.68 | 80.34 | 84.96 |
| B | 54.68 | 77.89 | 80.76 | 86.67 | 88.56 | 90.29 |
| C | 56.41 | 85.67 | 89.98 | 91.32 | 92.86 | 95.58 |
| D | 55.78 | 68.56 | 78.87 | 82.34 | 84.51 | 93.66 |
| E | 60.15 | 63.78 | 69.34 | 74.52 | 78.69 | 88.95 |

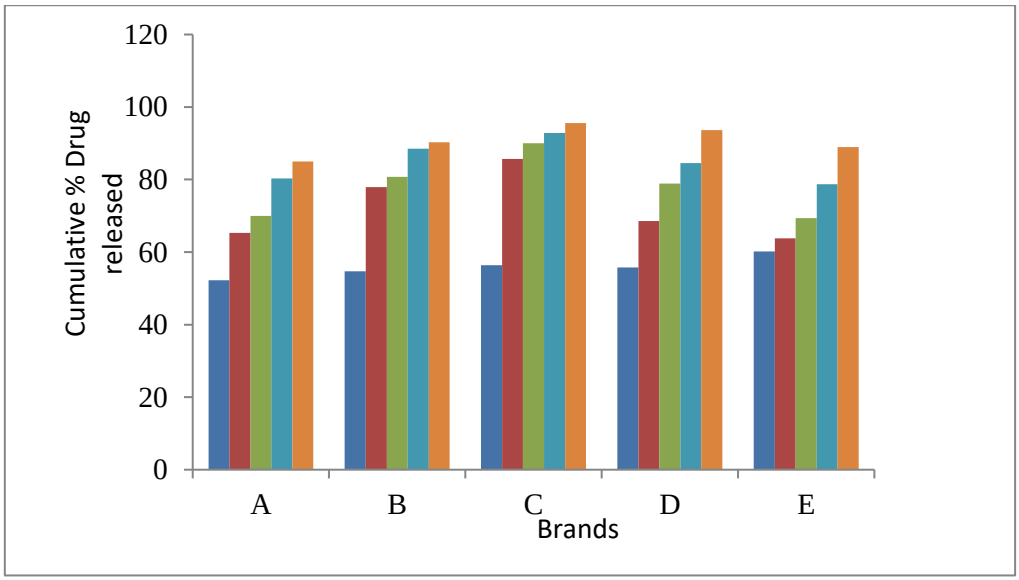


**Fig. 5.6 Cumulative % Drug Release**

## CONCLUSION

Ramipril is the additional ACE inhibitor to be introduced. ACE stands for angiotensin converting enzyme. It is a prodrug-converted in physique to Ramiprilate. It is used to treat high blood pressure (hypertension) or congestive heart failure, and to improve survival after a heart attack. The aim of present research work was to evaluate the doses form of the drug Ramipril. The next step is to compare the different doses forms of Ramipril by using UV

spectroscopy and other physical parameters. So we had carried out exhaustic literature survey till 2018 in order to meet the above mentioned objectives. Currently various brands of Ramipril were available in local market. During this alternative, the efficiency and quality of the drug was important. Hence, there is a need to reveal the quality of different brands to ensure the safety of the patient. The comparative analysis was done under five different brands of Ramipril and coded as Brand-A, Brand-B, Brand-C, Brand-D and Brand-E. The different market formulations were taken as (Brand A), (Brand B), (Brand C), (Brand D), (Brand E). The physical parameters Hardness, Thickness, Friability, Weight Variation, Disintegration test, Dissolution test were studied according to the guidelines given in the IP, BP and USP. All the marketed forms were further studied through UV spectroscopy at ASBASJSM College of Pharmacy, Bela. The standard value for Ramipril was done by using 5 % aqueous methanol as blank and the maximum absorbance was at 208.5nm. The standard and sample solutions of Ramipril was done by making concentration of 12.5µg/mL. Drug concentration and absorbance followed beer–lambert's law and the correlation coefficient value ($R^2$) is 0.998. The result of our preliminary studies weight variation, assay, thickness, hardness, friability, disintegration and dissolution of Ramipril from marketed solid dosage form were performed. Besides that, the five different brands show good results and all were within the limits.

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