Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: www.ijrpns.com

https://doi.org/10.36673/IJRPNS.2021.v10.i03.A25

DEVELOPMENT AND CHARACTERIZATION OF FAST DISSOLVING TABLET OF ENALAPRIL MALEATE

Karunakar Prasad Dwivedi*[1] and Amresh Gupta[1]

[1*]Goel Institute of Pharmacy and Sciences, Lucknow affiliated to Dr. APJ Abdul Kalam Technical University, Lucknow, Uttar Pradesh, India.

ABSTRACT

For the better treatment of a disease, buccal delivery is mostly priffered route from the ancient decade. This is the novel concept in buccal drug delivery is fast dissolving tablets (FDTs) are mostly accepted in the current situation. Mouth dissolving tablets are solid dosage forms which, when placed in the mouth, disintegrate, dissolve and release active agent within a few minutes without the need for water. It has more significance to geriatric, Pediatric, bedridden patients because they have a problem in swallowing and the patient with dysphasia. It is more useful for the traveler and busy patients who don't have easy access to water. Mouth dissolving tablets are prepared by various technologies with the aid of superdisintegrants. Mouth dissolving tablets are more trustworthy than predictable dosage forms like capsules, tablets because of better patient compliance. The advancement in this field allows the development of an economic and better way of disease management with avoidance of several problems related to the other delivery systems.

KEYWORDS

Fast dissolving tablets (FDTs), Mouth dissolving tablets, Superdisintegrants and Enalapril maleate.

Author for Correspondence:

Karunakar Prasad Dwivedi,
Goel Institute of Pharmacy and Sciences,
Lucknow affiliated to Dr. APJ Abdul Kalam Technical University,
Lucknow, Uttar Pradesh, India.

Email: dwivedi.karunakar7@gmail.com

INTRODUCTION

A quick dissolving drug conveyance framework, by and large, is a tablet which deteriorates or breaks down in the buccal depression without the need for water or biting. Most fast dissolving delivery system films must contain substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed via the patient's saliva along with the soluble and insoluble excipients. Enhanced patient compliance is a main benefit of the fast-dissolving drug delivery systems. Other

benefits of fast-dissolving tablet systems include easy of swallowing, no water needed for administration, and accuracy of dosage. These additional, superior benefits allow patients to take their medication anytime and anyplace under all conditions. These tablets are any very porous or integrally soft-molded matrices or tablets compacted at very low compression forces in order to maximize tablet porosity and minimize oral dissolution or disintegration time. Quick-Dis™ however, comprises a tough, solid, soft, flexible film and does not need special packaging. It is thin and can be approved in a patient's pocket, wallet[1].

Buccal cavity is that area of mouth defined by the lips, cheeks, hard palate, soft palate and floor of mouth. It is consists of two regions.

Outer buccal vestibule, which is bounded via cheeks, lips, teeth and gingival (gums).

Buccal cavity proper, that extends from teeth and gums back to the fauces (which lead to pharynx) with the roof with the hard and soft palate. The tongue projects from the surface of the cavity[2].

The drug administered via the buccal mucosa achievement access to the systemic circulation done a network of arteries and capillaries. The main artery supplying the blood to the buccal cavity is the external carotid artery. The intravenous backflow goes over branches of capillaries and veins and finally taken up by the jugular vein. Salivary glands are current in the surface of the mouth underneath the tongue. They are also identified as sublingual glands. They are produce mucin in turn produces saliva. The fluid which is produced in the glands becomes mix by the food, so the food gets easily chewed. The absorption is transmission of the drug from its site of administration into systemic circulation, therefore it can be said that absorption is directly proportional layer thickness. The absorption of the drug follows in this way Sublingual >Buccal > Gums>Palatal. Due to high permeability and rich blood supply, the sublingual route can yield fast onset of action thus the drug with short delivery period can be carried and dose regimen is normal.

MATERIAL AND METHODS

Materials

Pre-formulation studies

Prior to the development of the doses form , it is essential that certain fundamental physical and chemical properties of potential drug molecules and other derived properties of powder are determined .this information commands many of the subsequent event and approaches in formulation and development. This first learning phase is known as Pre-formulation. The meaning of the word is quite literal in that it defines the step to be under taken before formulation proper it is normal for Pre-formulation to be performed on potential active drugs[3].

Identification

Organoleptic properties

Organoleptic properties of drug such as description, color, odor, and taste were observed.

Description

State: White crystalline powder

Colour: White

Odour: Odourless

Taste: Bitter

Determination of Solubility of Drug

The approximately solubilities of the articles of the pharmacopeia are given here primarily as information; they are not meant to be applied as test for identifying materials. However, they may indirectly help in the preliminary evaluation of the integrity of our article. They have been indicated by descriptive terms in the accompanying table and reference t a temperature of 15º to 30ºC.

Solubility of Enalapril maleate was checked in various solvents like methanol, ethanol, distilled water, dimethyl formide. 100mg of drug was accurately weighed and transferred into a Stoppard tube containing 0.1ml of solvent. If completely dissolved, the drug is to be very soluble. If insoluble, added 0.9ml of solvent to it and is said to be freely soluble on complete dissolution. Otherwise, added 2ml of solvent to same. The drug, if completely dissolved in the solvent. Then is said to be freely soluble. If insoluble, further 7ml of same solvent was added and observed to be

sparingly soluble on complete dissolution. On further addition of 10ml of solvent it is said to be slightly soluble, if completely dissolved. If it is completely dissolved in the above solution, accurately weighed 1 mg of drug and added 10ml of solvent. If the solvent dissolution the drug, it is said to be very slightly soluble[4,5]. The solubility was determined by dissolving drug in different solvents like methanol, ethanol, distilled water dimethyl formide. The result of solubility analysis is given in the Table No.2. Enalapril maleate was soluble in methanol, soluble in ethanol, soluble in distilled water, soluble in dimethyl formide.

Determination of Melting Point by Capillary Melting Method

Point of Enalapril maleate was determined by capillary method using the melting point apparatus.

Procedure

- First powder the crystalline substance.
- Take a capillary tube and seal one end by heating it.
- Fill the capillary tube with the substance. To fill the tube, make a heap of the powdered substance on the porous plate. Push one end of the capillary tube into the heap. Some of the substance will enter the capillary tube.
- Now tap the sealed end of the capillary tube on the porous plate gently. Fill the capillary tube upto 2-3mm.
- Attach the capillary tube to a thermometer using a thread.
- Take liquid paraffin in a beaker and place it over a piece of wire gauze placed over a tripod stand.
- Clamp the thermometer carrying the test tube to an iron stand and immerse them in the bath of liquid paraffin. The surface tension of the bath liquid is sufficient to hold the capillary tube in position.
- Heat the beaker slowly while constantly stirring the contents using a stirrer to maintain a uniform temperature throughout.
- When the temperature is within 15^{o} of the melting point of the pure substance, the flame is reduced. Then the temperature rises slowly.
- Note the temperature (t_1) when the substance starts melting.
- Again note the temperature (t_2) when the substance has completely melted.
- The average of the two readings gives the correct melting point of the substance[3]

Melting Point of Enalapril maleate was determined by capillary method using the melting point apparatus. Standard melting point of Enalapril maleate is 143^{o}C to144^{o}C.

Determination of P^{H}

Electrometric method for determination of P^{H}

Numerous indicator electrodes are available for the determination of pH and without doubt, the glass electrode the most widely used. The glass electrode consists of a thin glass bulb of special glass blown at the end of a glass tube and the bulb is filled with dilute acid, e.g. decinormal hydrochloric acid. A silver- silver chloride electrode (a silver wire electrolytic ally coated with silver chloride) makes the necessary electrical connection with the acid. Whose pH remains Constance (pH_k). Several type of glass are used to make the pH-sensitive glass bulb and those made of Lithia glass are suitable over most of the range Ph 0 to 14. When the glass bulb is immersed in a solution of unknown pH (pH^{x}) potential E_H is set up across the glass according to the equation:

To measure the pH of a solution, the bulb of the glass electrode and a suitable reference electrode is immersed in a sample of the solution and the two electrodes connected to a P^{H} meter. The reference electrode is essential for the second electrical contact with the solution and must, of course, have a constant potential irrespective of P^{H} of the solution.

Procedure

- Before use, remove electrode from storage solution, rinse, and blot, dry with a soft tissue paper.
- Calibrate the instrument with standard buffer solution.

- Once the instrument is calibrated remove the electrode from standard solution; rinse, blot and dry.
- Dip the electrode in the sample whose pH has to be measured.
- Stir the sample to ensure homogeneity and to minimize CO_2 entrainment.
- Note down the reading (pH) from the pH meter[6,7].

Micromeritics

Angle of Repose

The flow property was determined by measuring the Angle of Repose. In order to determine the flow property, the Angle of Repose was determined. It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal.

Angle of repose= $\tan^{-1}$ (h/r)

Where, h = height r = radius

Procedure

- 5gms of the sample was taken.
- The sample was passed through the funnel slowly to form a heap.
- The height of the powder heap formed was measured.
- The circumference formed was drawn with a pencil on the graph paper. The radius was measured and the angle of repose was determined. This was repeated three times for a sample.

The angle of repose of the Enalapril maleate was found 38.35. The flow property of Enalapril maleate is fair.

Bulk density

Bulk density is ratio of given mass of powder and its bulk volume. Bulk density was determined by measuring the volume of known mass of powder sample that has been passed through the screen in to graduated cylinder or through volume measuring apparatus in to cup.

Bulk density = M / V0

Where M= mass of the powder; V0=bulk volume of the powder.

Apparatus

Bulk density apparatus.

Procedure

- Insert the main lead in the main plug.
- Switch the instrument by switching on the main switch.
- Place the sample under test in measuring cylinder of capacity 50ml supplied with the instrument.
- Insert the two measuring cylinder in the plate form on the central shaft.
- Select the time for which the test is to be carried out by rotating timer knob.
- Once you select the time the central shaft start moving up and down 60 strokes per minute.
- Calculated bulk density.

The bulk density of the Enalapril maleate was found 0.38gm/ml.

Tapped density

A known quantity of powder was transferred to a graduated cylinder and volume V0 was noted. The cylinder fixed to a density determination apparatus, tapped for 100 times then reading was observed. The density is achieved by mechanically tapped by a measuring cylinder containing the powder sample. After observing the initial volume the cylinder is mechanically tapped and volume reading were taken until little further volume changes is observed.

Tapped density= m / Vr

Where m = mass of the powder, Vr = final tapping volume of the powder**.**

The tapped density of Enalapril maleate was found 0.56gm/ml.

Compressibility index and Hausner's ratio

The basic procedure is to measure the unsettled apparent volume,(VO), and the final tapped volume, (Vf), of the powder after tapping the material until no further volume changes occur. The compressibility index and the Hausner's ratio are calculated as follows:

Compressibility index = 100 × Vo-Vf/Vo

Hausner's ratio = Vo/Vf

Where, Vo = apparent volume, Vf= final tapped volume.

Alternatively, the compressibility index and Hausner's ratio may be calculated using measured values of bulk density and tapped density as follows:

Compressibility index = 100× tapped density / bulk density

Hausner's ratio =tapped density/ bulk density

For the compressibility index and the Hausner's ratio, the generally accepted scale of flow ability is described in the following table[7,8,9].

Compressibility of the Enalapril maleate after 100 tapping was found 30.77%.

The Hausner's ratio of Enalapril maleate was found 1.40

Partition coefficient

The oil water partition coefficient is a measure of a molecules lipophilic character that is its preference for the hydrophilic or lipophilic phase. If a solute is added to a mixture of two immiscible liquids, it will distribute between the two phase and reach an equilibrium at a constant temperature. The distribution of the solute (unaggregated and undissociated) between the two immiscible layers can be described thus;

$K = C_U/C_{L\backslash}$

Where,

K is the distribution constant or partition constant.

C_U is the concentration of the drug in the upper phase and.

C_L is the concentration of the drug in the lower phase.

Procedure

One the most common ways of the measuring partition coefficient is used the shake flask method. It relies on the equilibrium distribution of a drug between an oil and aqueous phase prior to the aqueous phase should be saturated with the oil phase and vice- versa. The experiment should carried out at constant temperature. The drug (10mg) should be add to the aqueous phase (50ml) and the oil phase (50ml) which, in the case of octanol, as it is less dense than water, will sit on the top of the water. The system is mixed and then left to reach equilibrium (usually at list 24 hr). The two phases are separated and the concentration of the drug is measured in each phase (by UV spectroscopy) and a partition coefficients calculated[3].

The standard partition coefficient is 2.45. The observed value was 2.45 and was within the range as per official standard.

Drug-Excipient compatibility study

IR spectroscopy

The IR spectra were recorded using IR spectrophotometer. The samples were prepared by mixing the drug and the excipients in 1:1 ratio and the mixtures were stored in closed containers for one week. IR spectrum of the samples was taken using KBr pellet method. The physical mixtures of Enalapril maleate and excipients were scanned in the wavelength region between 4000 and 400cm-[1] and compared to check compatibility of drug with excipients[4,10-12].

UV Spectroscopy

ʎmax for pure Enalapril maleate in water

Apparatus

VU spectroscopy (semadzu)

The 1µg/ml sample was prepared and scanned between 200-400nm. The drug showed maximum absorption at 208nm. So the $ʎ_{max}$ of Enalapril maleate was found to be 208nm[71].

Preparation of standard curve for Enalapril maleate

10mg of Enalapril maleate pure drug was accurately weighed and transferred into a 10ml volumetric flask, dissolved in little quantities of distilled water, then made up to 10ml with water (1000µg/ml). From this solution, 1ml of solution was withdrawn into a 10ml volumetric flask & made up to 10ml with distilled water to get a concentration of 100µg/ml. From this, again pipette out 1ml of solution and diluted to 10ml with distilled water to get a concentration of 10µg/ml. Absorbance of this was measured at 208nm using UV/VIS spectrophotometer against blank (distilled water)[13,14].

Standard curve in phosphate buffer pH 6.8

Preparation of phosphate buffer pH 6.8

Dissolve 28.80g of disodium hydrogen phosphate and 11.45g of potassium dihydrogen phosphate in sufficient water to produced 1000ml[3].

λ_{max} for pure Enalapril maleate in phosphate buffer 6.8 pH

The 10µg/ml sample was prepared and scanned between 200-400nm. The drug showed maximum absorption at 212nm. So the λ_{max} of Enalapril maleate was found to be 212nm.

Preparation of standard curve

10mg of Enalapril maleate pure drug was accurately weighed and transferred into a 10ml volumetric flask, dissolved in little quantities of phosphate buffer 6.8,then made up to 10ml with phosphate buffer 6.8 (1000µg/ml). From this solution, 1ml of solution was withdrawn into a 10ml volumetric flask and made up to 10ml with 6.8phosphate buffer to get a concentration of 100µg/ml. From this, again pipette out 1ml of solution and diluted to 10ml with 6.8 phosphate buffer to get a concentration of 10µg/ml. Absorbance of this was measured at 212nm using UV/VIS spectrophotometer against blank (6.8phosphate buffer).

Assay of drug (UV Spectroscopy method)

An assay is an analytical procedure in laboratory medicine, pharmacology, environmental biology and molecular biology for qualitatively assessing or quantitatively measuring the presence, amount, or functional activity of a target entity (the analyte). The analyte can be a drug, a biochemical substance, or a cell in an organism or organic sample. The measured entity is normally called the analyte, the measure and or the target of the assay.

Preparation of standard solution

1000mg of Enalapril maleate pure drug was accurately weighed and transferred into a 100ml volumetric flask, dissolved in little quantities of distilled water, then made up to 100ml with water (10mg/ml). Absorbance of this was measured at 208 nm using UV/VIS spectrophotometer against blank (distilled water).

Preparation of sample solution

10mg of Enalapril maleate pure drug was accurately weighed and transferred into a 100ml volumetric flask, dissolved in little quantities of distilled water, then made up to 100ml with distilled water. From this solution, 10ml of solution was withdrawn into a 100ml volumetric flask and made up to 100ml with distilled water to get a concentration of 0.01mg/ml. Absorbance of this was measured at 208 nm using UV/VIS spectrophotometer against blank (distilled water).

% Assay = (Sample absorbance /Standard absorbance) × (Standard concentration /Test concentration) ×100

Thin layer chromatography

Thin-layer chromatography (TLC) is a chromatography used to separate non-volatile mixtures. TLC can be used for monitoring the progress of a reaction, identification compounds present in a given mixture, and determination of purity of a substance. The process is similar to paper chromatography with the advantage of faster runs, better separations, and the choice between different stationary phases. Different compounds in the sample mixture travel at different rates due to the differences in their attraction to the stationary phase, and due to differences in solubility in the solvent. By changing the solvent, or perhaps using a mixture, the separation of components can be adjusted.

Procedure

- Preparation TLC plate with silica gel.
- Reference solution**.** About 10.0mg Pharmacopoeial standard sample of Enalapril maleate dissolved in methanol and dilute with the same solvent to 10.0ml.
- Mobile phase: chloroform - methanol (9:1).
- Samples that are applied: 5µl applied the test solution and investigation solutions.
- Over a path of 10 cm from the starting line.
- Detection: Examination in ultraviolet light at 254nm[15].

R_f = Distance traveled by solute

Distance travelled by solvent

Loss on drying

Loss on drying is the loss of weight expressed as percentage w/w resulting from water and volatile matter of any kind that can be driven off under specified condition. The carried out on a well-mixed sample of the substance. If the substance is in the form of large crystals, reduced the size by rapid crushing a powder.

Procedure

- Handling the container you always need tongs or gloves
- Weigh a prepared porcelain dish with lid record weight (W_1).
- Place approx. 1.0g of sample into the porcelain dish with lid, record the weight (W_2) to± 1 mg.
- Place the porcelain into the drying oven with lid in tilted position at 105 ± 2°C for exactly two hours.
- After the 2-hour time period, take the porcelain dish out of the oven, being careful not to create turbulence. Replace lid to closed position.
- Place the porcelain dish in the desiccators and allow cooling for at least 30 minutes.
- Reweigh the container with closed lid (W_3) to ± 1mg.

Calculation

The % loss on drying is calculated by the following equation:

$$\% \text{ loss of drying} = \frac{W_2 - W_3}{W_2 - W_1} \times 100$$

Where,

W_1 = weight of porcelain with lid

W_2 = weight of porcelain with lid and sample before drying

W_3 = weight of porcelain with lid and sample after drying

Formulation Development

By Direct compression method

The critical parameters to formulate a fast dissolving tablet are choice of superdisintegrant and optimization of concentration of superdisintegrant. The main criteria for fast dissolving tablets into disintegrate or dissolve rapidly in buccal cavity in 15-60 seconds, without need of water and should have pleasant mouth feel. The superdisintegrant (croscarmellose, and Sodium Starch Glycolate) were used to formulate the tablets. All the ingredients as shown in Table No.1 were co-ground in a pestle and motor and then lactose and magnesium stearate were added and mixed for 10 minutes. All the ingredients were passed through # 60-mesh separately. The mixed blend of drug-excipient was compressed using a single punch tablet machine[16,17].

By Sublimation method

The fast dissolving tablets of Enalapril maleate were prepared using camphor as subliming agent. Sodium starch glycolate, crosscarmellose as superdisintegrant. Lactose is used as diluents in quantity sufficient; SLS is used as surfactants and magnesium state as lubricant. Sucrose is used as sweetener. All the ingredients were passed through mesh screen No.60 and weighed in geometrical order. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using single tablet punching machine. Sublimation was performed from tablets by keeping in hot air oven at 60ºC for 1 hour. Six formulations were prepared. The composition of formulations is shown in Table No.18[18].

Evaluation of the Fast Dissolving tablets (FDT)

Quality control tests for FDTs of all formulations were performed, and the average values were calculated. All the tablets were evaluated for different parameters as weight variation, hardness, friability, drug content, wetting time, water absorption ratio, disintegration time and *in vitro* dissolution study.

Tablet thickness

The thickness of three tablets from each batch was determined using a Vernier caliper. The thickness was measured in centimeters.

Weight Variation

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance (Shimadzu). The individual weighed is then

compared with average weight for the weight variations.

Hardness

The strength of tablet is expressed as tensile strength (kg/cm2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester). Three tablets from each formulation batch were tested randomly and the average readings were noted.

Friability

Friability of the tablets was determined using Roche Friabilator. This device consists of a plastic chamber that is set to revolve around 25rpm for 4 min dropping the tablets at a distance of 6 inches with each revolution. Pre weighed sample of 20 tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F%) is given by the formula,

% Friability = (Initial weight - Loss in weight) / Initial weight*100

Friability below 1% was considered as acceptable.

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 10mg of Enalapril maleate was dissolved in 100 ml of phosphate buffer solution, pH 6.8., filtered, diluted suitably and analyzed for drug content at 212nm using UV-Visible spectrophotometer (Shimadzu 1700, Tokyo, Japan).

Wetting time and water absorption ratio

A piece of tissue paper folded twice was placed in a small petri dish (internal diameter = 6.5cm) containing 6ml of phosphate buffer solution, pH 6.8. A tablet was placed on the paper and time required for complete wetting was measured using a stop watch. The wetted tablet was then weighed. Water absorption ratio (R) was determined using following equation,

$$R = \frac{Wa - Wb \times 100}{Wa}$$

Wa = Weight of tablet after water absorption,

Wb = Weight of tablet before water absorption

Wetting time

***In vitro* disintegration time**

10ml of phosphate buffer solution, pH 6.8 was placed in a petridish of 10cm diameter. The tablet was then carefully positioned in the center of the petridish and the time required for the tablet to completely disintegrate into fine particles was noted.

***In- vitro* disintegration time**

In-vitro disintegration times for Fast dissolving tablets of Enalapril maleate were determined using USP disintegration test apparatus with 900ml of phosphate buffer solution, pH 6.8 as medium maintained at a temperature of 37} 2°C. The time in seconds taken for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured.

***In-vitro* Dissolution Study**

The release rates of Enalapril maleate from fast dissolving tablets were determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer 6.8, at 37±0.5°C and 50rpm. A sample (5ml) of the solution was withdrawn from the dissolution apparatus at regular intervals of 1 mins for 30 mins. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a Whitman filter. Absorbance of these solutions was measured at 212nm using UV Spectrophotometer. Cumulative percentage of drug release was then calculated.

Stability studies

In order to determine the change in *In-vitro* release profile on storage, stability studies of optimized batch i.e., F9 was carried out at 40°C in a humidity chamber having 75% RH.

Samples were withdrawn at regular intervals of 30 days during the study of 60 days. Formulation is evaluated for change in *In-vitro* drug release pattern, hardness, wetting time, weight variation, percent drug content and dispersion time[19,20].

Stability study

Stability study is for developed formulation were carried out ICH guideline by storing the selected

formulation at 40ºC/75% related humidity F9 was selected on the basis of their high % drugs release and also result of in vitro disintegrating time, wetting time, in-vitro dissolution study. The tablets were analyzed for the colure, hardiness, content uniformity, % drugs release, *in-vitro* disintegrating time up to for one month. From the obtained data of tablets evaluation parameter indicated that stable formulation can be development by sublimation method.

RESULTS AND DISCUSSION

Pre-formulation study

In Pre-formulation studies various characteristic of drug such as identification analytical method, Micromeritics, solubilities study, loss on drying and partition coefficients were evaluated. The results for this studies are shown in Table No.42.

Formulation and evaluation

Enalapril maleate fast dissolving tablet were prepared by direct compression method and sublimation method was carried out by using superdisintegrant (crosscarmellose and starch glycolate) camphor use as subliming agent and other excipient as mention in formulation chart (Table No.17, Table No.18). Total No. of nine formulation were prepared by direct compression method and sublimation method.

The Pre-formulation studies such as bulk density, tapped density, angle of repose, compressibility index, Hausner's ratio. All the Pre-formulation studies were found the prescribed limits and indicated fair flow properties. The FTIR also revealed there is no interaction between the pure drugs and Excipients use for the formulation. Calibration curve of was prepared in distilled water at ʎmax 208nm. Regression value (R2) was found to be 0.994, y=1.069x in the range of 0.1-0.6µg/ml. and Calibration curve of was prepared in Phosphate buffer pH 6.8 at ʎmax 212nm. Regression value (R2) was found to be 0.999, y=0.491x in the range of 0.1-0.6µg/ml. Assay of Enalapril maleate is determined by UV Spectroscopy method. The % assay or purity of standard value is 98.5% to 101.5%. The observed value was 98.35% within the range of official standard. Not any impurity was detected. Purity of Enalapril maleate was carried out by TLC. The standard Rf value of Enalapril maleate is 0.55. The observed value was 0.53 within the range as per official standard. None of the inactive ingredient was detected. The moisture uptake was determined by Loss on drying (LOD) method at 105ºC. The Standard value of loss of drying is not more than 1%. The observed value was 1% within range per official standard. It was observed that drug form in lower mean particle size had high moisture uptake tendency by approx. (0.3-0.7% w/w). The data obtained from physicochemical parameter such as hardness, friability, weight variation, drugs content, wetting time, disintegration time, in-vitro dissolution are shown in (Table No.19 to Table No.38). Out of all formulation in direct compression method, F9 direct compression was found satisfactory. The angle of repose was ranged between 38.85º±1.54 the compressibility index value were found to be in the range of 80.34% the Hausner's ratio were found to be in the range of 1.22±0.02. The bulk density and tapped were found to be in range of 0.43±0.0058 and 0.52±0.0058.

All evaluation parameter of F9 was here, The hardness was found 3.09±0.10. Thickness of varied from 4.44±0.044mm. The loss of total weight of tablets due friability was 0.19±0.18. The drug content was 99.69±0.63%. The wetting time was 35.11±0.22 sec. disintegration time was found 69.60±0.63 sec. the water absorption ratio was 209.65±0.89. Dissolution test was carried out 50rpm using phosphate buffer (PH6.8) 87.10%. In direct compression method F9 was show satisfactory results.

Out of all formulation in sublimation method, F9 sublimation method was found satisfactory. The angle of repose was ranged between 32.28ºC±1.26. the compressibility index value were found to be in the range of 15±0.1% the Hausner's ratio were found to be in the range of 1.18±0.03. The bulk density and tapped were found to be in range of 0.53±0.007 and 0.63±0.05.

All evaluation parameter of F9 was here, the hardness was found 2.4±0.21. Thickness of varied

from 4.67±0.19 mm. the loss of total weight of tablets due friability was 0.59±0.07. The drug content was 99.85±1.79%. The wetting time was 37±2.51 sec. disintegration time was found 56±1.21 sec. the water absorption ratio was 98±1.08. Dissolution test was carried out 50rpm using phosphate buffer P^H 6.8 88.31%. In sublimation method F9 was show satisfactory results.

Stability study was carried out for the best formulation of F9 formulation (sublimation method)at 40^oC and 75% RH for one month, 15 days interval the formulation was examined for physical appearance, hardness, friability, thickness, drugs contents, disintegration time, dissolution study, wetting time revealing excellent of the formulated formulation.

Table No.1: The solubility of drugs

S.No	Descriptive term	Part of solvent required for part of solute
1	Very soluble	Less than1
2	Freely soluble	From 1 to 10
3	Soluble	From 10to 30
4	Sparingly soluble	From 30 to 100
5	Slightly soluble	From 100 to 1000
6	Very slightly soluble	From 1000 to 10,000
7	Practically insoluble	10,000 or more

Table No.2: Solubility profile of Enalapril maleate

S.No	Solvent	solubility
1	Methanol	Soluble
2	Ethanol	Soluble
3	Distilled water	Soluble
4	Dimethyl formide	Soluble

Table No.3: Melting point of Enalapril maleate

S.No	Note the temperature when the substance		melting point of the given substance $(t_1+t_2)/2(^oc)$	Mean ± SD
	starting melting $t_1(^oc)$	completely melted $t_2(^oc)$		
1	130	140	145	144.6±0.988
2	140	145	142.5	
3	140	150	145	

Table No.4: Determination of pH of Enalapril maleate

S.No	pH	Mean ± SD
1	2.54	2.53±0.09
2	2.44	

Table No.5: Angle of repose of Enalapril maleate

S.No	Height	radius	angle of repose(ɵ)	Mean ± SD
1	2.8	3.25	40.69	38.35±0.895
2	2.6	3.2	39.00	
3	2.7	3.15	40.36	

Table No.6: Bulk density of Enalapril maleate

S.No	mass of powder (gm)	volume of powder (ml)	bulk density(gm/ml)	Mean ± SD
1	5	12	0.41	0.38±0.03
2	5	14	0.35	
3	5	13	0.38	

Table No.7: Tapped density of Enalapril maleate

S.No	Mass of powder (gm)	final tapped volume (ml)	tapped density(gm/ml)	Mean ± SD
1	5	8	0.62	0.56±0.06
2	5	9	0.55	
3	5	10	0.5	

Table No.8: % compressibility index

S.No	tapped density (gm/ml)	bulk density (gm/ml)	Compressibility index (%)	Mean ± SD
1	0.625	0.416	33.44	30.77±6.64
2	0.555	0.351	35.67	
3	0.5	0.384	23.2	

Table No.9: Hausner's ratio

S.No	tapped density (gm/ml)	bulk density (gm/ml)	Hausner's ratio	Mean ± SD
1	0.625	0.416	1.33	1.40±0.153
2	0.555	0.351	1.58	
3	0.5	0.384	1.30	

Table No.10: Flow properties and corresponding Angle of repose, Compressibility index and Hausner's ratio

S.No	Flow properties	Angle of repose(θ)	Compressibility Index (%) or Carr's index	Hausner's ratio
1	Excellent	25-30	<10	1.00-1.11
2	Good	31-35	11-15	1.12-1.18
3	Fair	36-40	16-20	1.19-1.25
4	Passable	41-45	21-25	1.26-1.34
5	Poor	46-55	26-31	1.35-1.45
6	Very poor	56-65	32-37	1.46-1.59
7	Very very poor	>66	>38	>1.6

Table No.11: Partition coefficient determination

S.No	Absorbance of upper layer (oil)	Absorbance of lower layer(water)	Conc. of C_U (µg/ml	Conc. Of C_L(µg/ml)	partition coefficient	Mean ± SD
1	0.395	0.161	3.72	1.51	2.46	2.45±0.011
2	0.399	0.162	3.76	1.52	2.44	
3	0.400	0.163	3.77	1.53	2.46	

Table No.12: Standard calibration curve in water

S.No	Concentration	Absorbance
1	0	0
2	0.1	0.126
3	0.2	0.235
4	0.3	0.329
5	0.4	0.429
6	0.5	0.528
7	0.6	0.621

Table No.13: Standard calibration curve in phosphate buffer 6.8 pH

S.No	Concentration(µg/ml)	Absorbance
1	0.0	0.0
2	0.1	0.050
3	0.2	0.102
4	0.3	0.150
5	0.4	0.199
6	0.5	0.244
7	0.6	0.292

Table No.14: % Assay of Enalapril maleate

S.No	Standard abs	Test abs	Standard conc	Test conc	Specification	Results
1	304	0.299	10mg/ml	0.01mg/ml	98.0%-101.5%	98.3%

Table No.15: Thin layer chromatography of Enalapril maleate

S.No	Mobile phase	Solute distance(cm)	Solvent distance (cm)	R_f		Detection in ultraviolet light at 254 nm
				Specification	Results	
1	Chloroform: methanol (9:1)	3.3	7.0	0.55	0.53	Violet

Table No.16: Loss on drying of Enalapril maleate

S.No	W_1 (gm)	W_2 (gm)	W_3 (gm)	% Loss of Drying	
				Specification	Results
1	69.87	70.87	70.86	Not more than 1.0%	1%

Pre-compression study of powder blend

Table No.17: Pre-compression parameter of powder blend (direct compression method)

Formulation code	Bulk density (gm/ml) ± SD	Tapped density (gm/ml) ± SD	Angle of repose (◦) ±SD	Carr index (%) ±SD	Hausner's ratio ± SD
F1	0.39±0.0059	0.45±0.0022	27.88±1.29	12.9±1.12	1.15±0.02
F2	0.40±0.0060	0.47±0.0018	30.00±1.66	14.93±1.34	1.18±0.03
F3	0.37±0.0038	0.40±0.0032	27.75±1.03	6.41±1.21	1.07±0.04
F4	0.39±0.0037	0.44±0.0023	33.57±0.38	12.23±1.41	1.14±0.04
F5	0.41±0.0028	0.49±0.0039	35.34±0.45	16.31±1.61	1.19±0.02
F6	0.50±0.0083	0.60±0.0041	28.60±3.88	16.7±1.53	1.20±0.03
F7	0.43±0.0055	0.51±0.0044	25.74±1.80	16.94±1.58	1.20±0.04
F8	0.43±0.0024	0.51±0.0036	27.95±2.26	15.00±2.23	1.18±0.04
F9	0.43±0.0058	0.52±0.0058	32.85±1.45	18.34±2.02	1.22±0.02

Table No.18: Pre-compression parameter of powder blend (sublimation method)

Formulation code	Bulk density (gm/ml) ± SD	Tapped density (gm/ml) ± SD	Angle of repose (◦) ±SD	Carr index (%) ± SD	Hausner's ratio ± SD
F1	0.49±0.007	0.65±0.01	31.25±1.56	17±1	1.30±0.03
F2	0.52±0.007	0.62±0.01	32.02±1020	16±1.51	1.19±0.04
F3	0.53±0.007	0.61±0.02	33.1±1.70	13±1.20	1.15±0.03
F4	0.53±0.007	0.64±0.01	32.20±0.88	17±2..51	1.20±0.03
F5	0.50±0.007	0.63±0.01	32.43±1.48	20±1.58	1.26±0.03
F6	0.54±0.007	0.65±0.02	32.72±1.22	16±1.55	1.20±0.04
F7	0.52±0.007	0.63±0.38	34.87±1.32	17±1.39	1.21±0.04
F8	0.51±0.007	0.62±0.02	33.04±1.34	17±2.20	1.21±0.04
F9	0.53±0.007	0.63±0.05	32.28±1.26	15±2.01	1.18±0.03

Table No.19: Formulation of Enalapril maleate fast dissolving tablet (Direct compression method)

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	ENM	5	5	5	5	5	5	5	5	5
2	Crosscarmellose	10	15	20	25	28	30	35	38	40
3	SSG	40	38	35	30	28	26	25	22	20
4	Mg. stearate	100	100	100	100	100	100	100	100	100
5	Lactose	50	50	50	50	50	50	50	50	50
6	Sucrose	120	120	120	120	120	120	120	120	120
7	SLS	30	30	30	30	30	30	30	30	30
8	Starch (20% conc)	q.s	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table No.20: Formulation of Enalapril maleate fast dissolving tablet (Sublimation method)

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	ENM	5	5	5	5	5	5	5	5	5
2	Camphor	10	15	20	25	30	35	40	45	50
3	Crosscarmellose	10	15	20	25	28	30	35	38	40
4	SSG	40	38	35	30	28	26	25	22	20
5	Mg stearate	100	100	100	100	100	100	100	100	100
6	Lactose	50	50	50	50	50	50	50	50	50
7	Sucrose	120	120	120	120	120	120	120	120	120
8	SLS	30	30	30	30	30	3	30	30	30
9	Starch (20% conc)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

EVALUATION PARAMETER BY DIRECT COMPRESSION METHOD

Table No.21: Evaluation of fast dissolving tablet of Enalapril maleate (Direct compression method)

Evaluation parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)±SD	4.71± 0.040	4.5 ±0.039	4.56± 0.05	4.87± 0.045	5.01± 0.049	4.83± 0.042	4.87± 0.042	4.53± 0.050	4.44± 0.044
Hardness (kg/cm^2) ±SD	3.83± 0.12	3.71 ±0.31	3.56± 0.25	3.56± 013	3.49± 0.23	3.42± 0.37	3.41± 0.34	3.20± 0.06	3.09± 0.10
%Friability ±SD	0.52± 0.18	0.60 ±0.14	0.62± 0.19	0.58± 0.11	0.59± 0.16	0.59± 0.14	0.64± 0.10	0.68± 0.10	0.19± 0.18
Disintragration time (sec) ± SD	98.16± 0.61	96.11± 0.42	90.51± 0.23	88.20± 0.23	87.86± 0.82	86.52± 0.41	78.52± 0.84	71.69± 0.76	69.60± 0.63
Wetting (sec)±SD	40.22± 0.25	38.90± 0.11	37.45± 0.20	36.65± 0.24	36.75± 0.35	36.25± 0.53	35.90± 0.47	35.78± 0.58	35.11± 0.22
Water absorption a ratio	141.68± 0.56	149.27± 0.78	156.34± 0.81	150.65± 0.45	148.36± 0.78	155.28± 0.91	180.91± 0.78	193.69± 0.54	209.65± 0.89
Content uniformity(%)±SD	99.27 ± 0.63	96.99± 0.55	99.81± 0.35	98.85± 0.20	97.81± 0.44	98.92± 0.87	69.97± 0.38	98.64± 0.29	99.69± 0.63

Table No.22: Drugs release profile of direct compression method (F1)

S.No	Time (min)	ABS	Conc(µ/ml)	Conc(mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.122	0.272912424	0.000818737	0.736863544	15.73725	1.168415
3	2	0.168	0.362525458	0.001087576	0.978818737	20.57635	1.291736
4	3	0.244	0.490835031	0.001472505	1.325254582	26.50506	1.423331
5	4	0.290	0.584521385	0.001753564	1.578207739	32.56417	1.499184
6	5	0.330	0.653767821	0.001961303	1.765173116	36.30347	1.547821
7	10	0.429	0.883910387	0.002651731	2.386558045	46.73117	1.678810
8	15	0.490	0.99185336	0.00297556	2.678004073	54.56009	1.728845
9	20	0.509	1.044806517	0.00313442	2.820977597	57.41957	1.751436
10	25	0.587	1.215885947	0.003647658	3.282892057	64.65787	1.817286
11	30	0.623	1.250509165	0.003751527	3.376374745	67.52751	1.829487

Table No.23: Drugs release profile of direct compression method (F2)

S.No	Time (min)	ABS	Conc(µ/ml)	Conc(mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.174	0.354378819	0.001063136	0.956822811	19.13646	1.281862
3	2	0.214	0.435845214	0.001307536	1.176782077	23.53564	1.371726
4	3	0.241	0.490835031	0.001472505	1.325254582	26.50509	1.423329
5	4	0.312	0.635437882	0.001906314	1.715682281	34.31365	1.535467
6	5	0.375	0.763747454	0.002291242	2.062118126	41.24236	1.615344
7	10	0.434	0.883910387	0.002651731	2.386558045	47.73116	1.678802
8	15	0.456	0.928716904	0.002786151	2.507535642	50.15071	1.700277
9	20	0.521	1.061099796	0.003183299	2.86496945	57.29939	1.75815
10	25	0.571	1.16293279	0.003488798	3.139918534	62.79837	1.797948
11	30	0.624	1.270875764	0.003812627	3.431364562	68.62729	1.836497

Table No.24: Drugs release profile of direct compression method (F3)

S.No	Time (mints)	ABS	Conc(µ/ml)	Conc(mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.157	0.309572301	0.000928717	0.825845218	16.7169	1.223156
3	2	0.236	0.470468432	0.001411405	1.280264769	25.4053	1.404924
4	3	0.329	0.6598778	0.001979633	1.781670061	35.6334	1.551857
5	4	0.369	0.741344196	0.002224033	2.001629328	40.03259	1.602414
6	5	0.438	0.877800407	0.002633401	2.370061150	47.40122	1.67579
7	10	0.489	0.99185336	0.00297556	2.678004073	53.56008	1.728841
8	15	0.539	1.081466395	0.003244399	2.919959267	58.39919	1.766407
9	20	0.580	1.16904277	0.003507128	3.156415479	63.12831	1.800224
10	25	0.640	1.287169043	0.003861507	3.475356415	69.50713	1.842029
11	30	0.680	1.374745418	0.004124236	3.711812627	74.23625	1.870616

Table No.25: Drugs release profile of direct compression method (F4)

S.No	Time (mints)	ABS	Conc(µ/ml)	Conc(mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.213	0.433808554	0.001301426	1.171283096	23.42566	1.369692
3	2	0.341	0.694501018	0.002083503	1.875152749	37.50305	1.574067
4	3	0.387	0.788187373	0.002364562	2.128105906	42.56212	1.629023
5	4	0.432	0.879837067	0.002639511	2.375560081	47.5112	1.676796
6	5	0.489	0.99592668	0.00298778	2.689002037	53.78004	1.730621
7	10	0.521	1.061099796	0.003183299	2.86496945	57.29939	1.75815
8	15	0.558	1.136456212	0.003409369	3.068431772	61.36864	1.787946
9	20	0.612	1.246435845	0.003739308	3.365376782	67.30754	1.828064
10	25	0.672	1.368635438	0.004105906	3.695315682	73.90631	1.868682
11	30	0.687	1.399185336	0.004197556	3.777800407	75.55601	1.878269

Table No.26: Drugs release profile of direct compression method (F5)

S.No	Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.158	0.323828921	0.000971487	0.874338086	17.48676	1.242709
3	2	0.246	0.49898167	0.001496945	1.347250509	26.94501	1.430478
4	3	0.347	0.706720978	0.002120163	1.90814664	38.16293	1.581642
5	4	0.412	0.83910387	0.002517312	2.265580448	45.31161	1.656209
6	5	0.435	0.885947047	0.002657841	2.392057026	47.84114	1.679802
7	10	0.498	1.014256619	0.00304277	2.738492872	54.76986	1.738542
8	15	0.531	1.081466395	0.003244399	2.919959267	58.39919	1.766407
9	20	0.597	1.215885947	0.003647658	3.282892057	65.65784	1.817287
10	25	0.656	1.33604888	0.004008147	3.607331976	72.14664	1.858216
11	30	0.698	1.421588595	0.004264766	3.838289206	76.76578	1.885168

Table No.27: Drugs release profile of direct compression method (F6)

S.No	Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
1	0	0	0	0	0	0	-
2	1	0.182	0.370672098	0.001112016	1.000814664	20.01629	1.301384
3	2	0.259	0.527494908	0.001582485	1.424236253	28.48473	1.454612
4	3	0.341	0.694501018	0.002083503	1.875152749	37.50305	1.574067
5	4	0.397	0.808553971	0.002425662	2.183095723	43.66191	1.640103
6	5	0.412	0.83910387	0.002517312	2.265580448	45.31161	1.656209
7	10	0.498	1.014256619	0.00304277	2.738492872	54.76986	1.738542
8	15	0.531	1.081466395	0.003244399	2.919959267	58.39919	1.766407
9	20	0.579	1.179226069	0.003537678	3.183910387	63.67821	1.803991
10	25	0.678	1.380855397	0.004142566	3.728309572	74.56619	1.872542
11	30	0.702	1.429735234	0.004289206	3.860285132	77.2057	1.887649

Table No.28: Drugs release profile of direct compression method (F7)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log % DR
0	0	0	0	0	0	-
1	0.213	0.433808554	0.001301426	1.171283096	23.42566	1.369692
2	0.314	0.639511202	0.001918534	1.726680244	34.5336	1.538242
3	0.358	0.729124236	0.002187373	1.968635438	39.37271	1.595195
4	0.412	0.83910387	0.002517312	2.265580448	45.31161	1.656209
5	0.476	0.969450102	0.00290835	2.617515275	52.35031	1.718919
6	0.534	1.087576375	0.003262729	2.936456212	58.72912	1.768854
7	0.598	1.217922607	0.003653768	3.288391039	65.76782	1.818013
8	0.634	1.291242363	0.003873727	3.486354379	69.72709	1.843402
9	0.679	1.382892057	0.004148676	3.733808554	74.67617	1.873182
10	0.712	1.450101833	0.004350305	3.915274949	78.3055	1.893792

Table No.29: Drugs release profile of direct compression method (F8)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.123	0.250509165	0.000751527	0.676374745	13.52749	1.131217
2	0.256	0.521384929	0.001564155	1.407739308	28.15479	1.449552
3	0.385	0.784114053	0.002352342	2.117107943	42.34216	1.626773
4	0.432	0.879837067	0.002639511	2.375560081	47.5112	1.676796
5	0.521	1.061099796	0.003183299	2.86496945	57.29939	1.75815
6	0.587	1.195519348	0.003586558	3.22790224	64.55804	1.80995
7	0.621	1.264765784	0.003794297	3.414867617	68.29735	1.834404
8	0.634	1.291242363	0.003873727	3.486354379	69.72709	1.843402
9	0.712	1.450101833	0.004350305	3.915274949	78.3055	1.893792
10	0.785	1.598778004	0.004796334	4.316700611	86.33401	1.936182

Table No.30: Drugs release profile of direct compression method (F9)

TIME (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.256	0.521384929	0.001564155	1.407739308	28.15479	1.449552
2	0.345	0.702647658	0.002107943	1.897148676	37.94297	1.579131
3	0.423	0.861507128	0.002584521	2.326069246	46.52138	1.667653
4	0.497	1.012219959	0.00303666	2.73299389	54.65988	1.737669
5	0.531	1.081466395	0.003244399	2.919959267	58.39919	1.766407
6	0.562	1.144602851	0.003433809	3.090427699	61.80855	1.791049
7	0.591	1.203665988	0.003610998	3.249898167	64.99796	1.8129
8	0.692	1.409368635	0.004228106	3.805295316	76.10591	1.881418
9	0.762	1.551934827	0.004655804	4.190224033	83.80448	1.923267
10	0.792	1.613034623	0.004839104	4.355193483	87.10387	1.940037

Evaluation parameter by sublimation method

Table No.31: Evaluation of fast dissolving tablet of Enalapril maleate (Sublimation method)

Evaluation parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)±SD	4.69 ±0.12	4.82± 0.15	4.74± 0.10	4.59± 0.17	4.69± 0.15	4.72± 0.21	4.78±0. 15	4.60± 0.14	4.67± 0.19
Hardness (kg/cm^2)±SD	2±0.11	2.1± 0.11	2.3± 0.10	2.2± 0.12	2.8± 0.18	2.1± 0.10	2.1±0.2 1	2.1± 0.10	2.4± 0.21
%friability ±SD	0.54± 0.11	0.74± 0.13	0.57± 0.11	0.68± 0.09	0.65± 0.07	0.58± 0.06	0.75± 0.11	0.69± 0.13	0.59± 0.07
Disintragration time (sec) ± SD	90± 2.51	97±2.0	86± 2.40	75±1.0	79± 2.8	85± 1.75	64± 1.35	68± 2.15	56± 1.21
Wetting (sec)±SD	39± 2.0	38± 2.40	40± 1.89	43±2.25	41± 1.0	42± 2.25	40± 1.35	42± 1.35	37± 2.51
Water absorption ratio	85±1	85± 1.25	80± 1.05	±1.21	72± 1.20	90± 1.88	92± 1.15	96± 1.73	98± 1.08
Content uniformity (%)±SD	98.18± 0.72	91.30± 0.87	93.56± 0.27	97.50±0 .77	98.96 ±0.27	99.18±0 .76	98.65±1 .23	99.30± 0.90	99.85± 1.79

Table No.32: Drugs release profile of sublimation method (F1)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ML * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.123	0.250509165	0.000751527	0.676374745	13.52749	1.131217
2	0.234	0.476578411	0.001429735	1.286761711	25.73523	1.410528
3	0.287	0.584521385	0.001753564	1.578207739	31.56415	1.499194
4	0.342	0.696537678	0.002089613	1.880651731	37.61303	1.575338
5	0.423	0.861507128	0.002584521	2.326069246	46.52138	1.667653
6	0.493	1.00407332	0.00301222	2.710997963	54.21996	1.734159
7	0.534	1.087576375	0.003262729	2.936456212	58.72912	1.768854
8	0.573	1.16700611	0.003501018	3.150916497	63.01833	1.799467
9	0.592	1.205702648	0.003617108	3.255397149	65.10794	1.813634
10	0.621	1.264765784	0.003794297	3.414867617	68.29735	1.834404

Table No.33: Drugs release profile of sublimation method (F2)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.183	0.37270878	0.001118126	1.006313646	20.12627	1.303763
2	0.243	0.49490835	0.001484725	1.336252546	26.72505	1.426919
3	0.312	0.635437882	0.001906314	1.715682281	34.31365	1.535467
4	0.342	0.696537678	0.002089613	1.880651731	37.61303	1.575338
5	0.395	0.804480652	0.002413442	2.17209776	43.44196	1.637909
6	0.412	0.83910387	0.002517312	2.265580448	45.31161	1.656209
7	0.482	0.981670061	0.00294501	2.650509165	53.01018	1.724359
8	0.523	1.065173116	0.003195519	2.875967413	57.51935	1.759814
9	0.592	1.205702648	0.003617108	3.255397149	65.10794	1.813634
10	0.632	1.287169043	0.003861507	3.475356415	69.50713	1.842029

Table No.34: Drugs release profile of sublimation method (F3)

Time (mints)	ABS	Conc (µ/ml)	Conc mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.152	0.309572301	0.000928717	0.835845214	16.7169	1.223156
2	0.234	0.476578411	0.001429735	1.286761711	25.73523	1.410528
3	0.289	0.588594705	0.001765784	1.589205703	31.78411	1.50221
4	0.332	0.676171079	0.002028513	1.825661914	36.51324	1.56245
5	0.393	0.800407332	0.002401222	2.161099796	43.222	1.635705
6	0.412	0.83910387	0.002517312	2.265580448	45.31161	1.656209
7	0.495	1.00814664	0.00302444	2.721995927	54.43992	1.735917
8	0.552	1.124236253	0.003372709	3.035437882	60.70876	1.783251
9	0.642	1.307535642	0.003922607	3.530346232	70.60692	1.848847
10	0.686	1.397148676	0.004191446	3.772301426	75.44603	1.877636

Table No.35: Drugs release profile of sublimation method (F4)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.182	0.370672098	0.001112016	1.000814664	20.01629	1.301384
2	0.234	0.476578411	0.001429735	1.286761711	25.73523	1.410528
3	0.382	0.778004073	0.002334012	2.100610998	42.01222	1.623376
4	0.432	0.879837067	0.002639511	2.375560081	47.5112	1.676796
5	0.493	1.00407332	0.00301222	2.710997963	54.21996	1.734159
6	0.532	1.083503055	0.003250509	2.925458248	58.50916	1.767224
7	0.562	1.144602851	0.003433809	3.090427699	61.80855	1.791049
8	0.634	1.291242363	0.003873727	3.486354379	69.72709	1.843402
9	0.671	1.366598778	0.004099796	3.689816701	73.79633	1.868035
10	0.693	1.411405295	0.004234216	3.810794297	76.21589	1.882046

Table No.36: Drugs release profile of sublimation method (F5)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.192	0.391038697	0.001173116	1.055804481	21.11609	1.324613
2	0.251	0.511201629	0.001533605	1.380244399	27.60489	1.440986
3	0.324	0.6598778	0.001979633	1.781670061	35.6334	1.551857
4	0.432	0.879837067	0.002639511	2.375560081	47.5112	1.676796
5	0.486	0.989816701	0.00296945	2.672505092	53.4501	1.727949
6	0.534	1.087576375	0.003262729	2.936456212	58.72912	1.768854
7	0.596	1.213849287	0.003641548	3.277393075	65.54786	1.816559
8	0.634	1.291242363	0.003873727	3.486354379	69.72709	1.843402
9	0.662	1.348268839	0.004044807	3.640325866	72.80652	1.86217
10	0.701	1.427698574	0.004283096	3.854786151	77.09572	1.88703

Table No.37: Drugs release profile of sublimation method (F6)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.152	0.309572301	0.000928717	0.835845214	16.7169	1.223156
2	0.241	0.490835031	0.001472505	1.325254582	26.50509	1.423329
3	0.289	0.588594705	0.001765784	1.589205703	31.78411	1.50221
4	0.352	0.716904277	0.002150713	1.935641548	38.71283	1.587855
5	0.431	0.877800407	0.002633401	2.3700611	47.40122	1.67579
10	0.498	1.014256619	0.00304277	2.738492872	54.76986	1.738542
15	0.534	1.087576375	0.003262729	2.936456212	58.72912	1.768854
20	0.597	1.215885947	0.003647658	3.282892057	65.65784	1.817287
25	0.656	1.33604888	0.004008147	3.607331976	72.14664	1.858216
30	0.712	1.450101833	0.004350305	3.915274949	78.3055	1.893792

Table No.38: Drugs release profile of sublimation method (F7)

Time (mints)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.152	0.309572301	0.000928717	0.835845214	16.7169	1.223156
2	0.234	0.476578411	0.001429735	1.286761711	25.73523	1.410528
3	0.351	0.714867617	0.002144603	1.930142566	38.60285	1.586619
4	0.385	0.784114053	0.002352342	2.117107943	42.34216	1.626773
5	0.431	0.877800407	0.002633401	2.3700611	47.40122	1.67579
6	0.487	0.99185336	0.00297556	2.678004073	53.56008	1.728841
7	0.581	1.183299389	0.003549898	3.19490835	63.89817	1.805488
8	0.631	1.285132383	0.003855397	3.469857434	69.39715	1.841342
9	0.681	1.386965377	0.004160896	3.744806517	74.89613	1.874459
10	0.721	1.468431772	0.004405295	3.964765784	79.29532	1.899248

Table No.39: Drugs release profile of sublimation method (F8)

Time (mins)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.213	0.433808554	0.001301426	1.171283096	23.42566	1.369692
2	0.342	0.696537678	0.002089613	1.880651731	37.61303	1.575338
3	0.423	0.861507128	0.002584521	2.326069246	46.52138	1.667653
4	0.496	1.010183299	0.00303055	2.727494908	54.5499	1.736794
5	0.534	1.087576375	0.003262729	2.936456212	58.72912	1.768854
6	0.586	1.193482688	0.003580448	3.222403259	64.44807	1.80921
7	0.634	1.291242363	0.003873727	3.486354379	69.72709	1.843402
8	0.695	1.415478615	0.004246436	3.821792261	76.43585	1.883297
9	0.752	1.531568228	0.004594705	4.135234216	82.70468	1.91753
10	0.795	1.619144603	0.004857434	4.371690428	87.43381	1.941679

Table No.40: Drugs release profile of sublimation method (F9)

Time (mins)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.256	0.521384929	0.001564155	1.407739308	28.15479	1.449552
2	0.346	0.704684318	0.002114053	1.902647658	38.05295	1.580388
3	0.431	0.877800407	0.002633401	2.3700611	47.40122	1.67579
4	0.498	1.014256619	0.00304277	2.738492872	54.76986	1.738542
5	0.523	1.065173116	0.003195519	2.875967413	57.51935	1.759814
6	0.598	1.217922607	0.003653768	3.288391039	65.76782	1.818013
7	0.645	1.313645621	0.003940937	3.546843177	70.93686	1.850872
8	0.689	1.403258656	0.004209776	3.788798371	75.77597	1.879531
9	0.734	1.49490835	0.004484725	4.036252546	80.72505	1.907008
10	0.803	1.635437882	0.004906314	4.415682281	88.31365	1.946028

Table No.41: Accelerated stability study of optimized formulation F9 at 40ºC/75%RH for one month

S.No	Period	Hardness (kg/cm^2)	Disintegration time (sec)	Wetting time (sec)	Drug content (%)	%drugs release
1	0 Day	2.4±0.21	56±1.21	37±2.51	99.85±1.79	88.31
2	15 day	2.6±0.50	57±1.52	38±2.53	98.40±1.42	87.13
3	30 day	2.8±0.71	55±1.34	35±2.30	97±1.21	86.20

Table No.42: Results Pre-formulation study

S.No	Pre-formulation Study	Results
Organoleptic properties		
1	Description	White crystalline powder
2	Colour	White
3	Odour	Odourless
4	Taste	Bitter
Identification		
5	UV absorption maxima	208, 212
6	TLC	R_f =0.56
7	Melting point	143-144ºC

8	Infra-red spectra	No change spectra
9	**Assay of Drugs**	98.5 to101.5%
Calibration Curve		
10	In water	ʎmax y =1.069x
11	In phosphate buffer P^H 6.8	ʎmax y =0.491x
Micromeriticas		
12	Bulk density	0.38±0.03gm/ml
13	Tapped density	0.56±0.06gm/ml
14	Carr' s index	13.77±6.64 (flow property- poor)
15	Angle of repose	38.35±0.895 (flow property -fair)
16	**Loss of Drying**	1%
17	**P^H**	2.53±0.09
18	**Solubility**	Methanol, ethanol, distilled water, dimethyl formide
19	**Partition Cofficients**	2.45±0.011(lipophilic in nature)
20	**Drug- Excipients Intrection**	No interaction

Table No.43: Drugs release profile of direct compression method (F9)

Time (mins)	ABS	Conc (µ/ml)	Conc (mg/ml)	AMT IN 900ml * D.F.	%DR	Log %DR
0	0	0	0	0	0	-
1	0.247	0.521384929	0.001564155	1.407739308	29.25472	1.449553
2	0.315	0.702647658	0.002107943	1.897148676	38.84296	1.579137
3	0.439	0.861507128	0.002584521	2.326069246	47.42137	1.667654
4	0.473	1.012219959	0.003036665	2.73299389	53.55987	1.737668
5	0.512	1.081466395	0.003244399	2.919959267	57.40917	1.766410
6	0.547	1.144602851	0.003433809	3.090427699	60.79854	1.791063
7	0.583	1.203665988	0.003610998	3.249898167	63.79795	1.81298
8	0.666	1.409368635	0.004228106	3.805295316	71.16594	1.88141
9	0.743	1.551934827	0.004655804	4.190224033	82.79447	1.92326
10	0.759	1.613034623	0.004839104	4.355193483	87.17388	1.94003

Table No.44: Drugs release profile of sublimation method (F9)

TIME (mins)	ABS	CONC(µ/ml)	CONC(mg/ml)	AMT IN 900ml * D.F.	%DR	LOG%DR
0	0	0	0	0	0	-
1	0.257	0.521384929	0.001564155	1.407739308	28.15479	1.449552
2	0.348	0.704684318	0.002114053	1.902647658	38.05295	1.580388
3	0.437	0.877800407	0.002633401	2.3700611	47.40122	1.67579
4	0.501	1.014256619	0.00304277	2.738492872	54.76986	1.738542
5	0.519	1.065173116	0.003195519	2.875967413	57.51935	1.759814
6	0.587	1.217922607	0.003653768	3.288391039	65.76782	1.818013
7	0.653	1.313645621	0.003940937	3.546843177	70.93686	1.850872
8	0.687	1.403258656	0.004209776	3.788798371	75.77598	1.879531
9	0.721	1.49490835	0.004484725	4.036252546	80.72513	1.907008
10	0.799	1.635437882	0.004906314	4.415682281	87.31363	1.946028

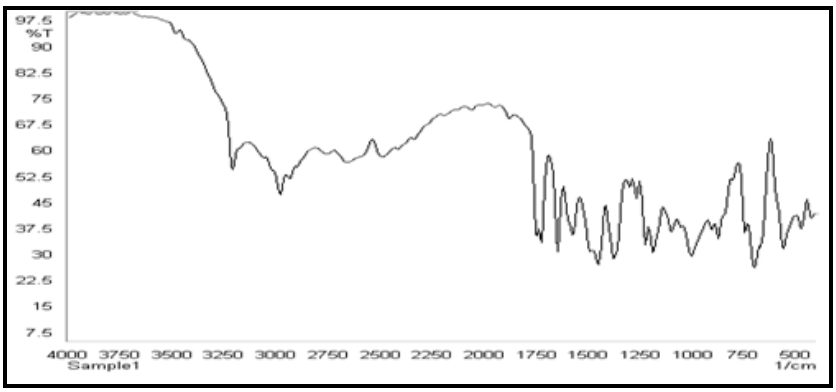


Figure No.1: FTIR of pure Enalapril maleate

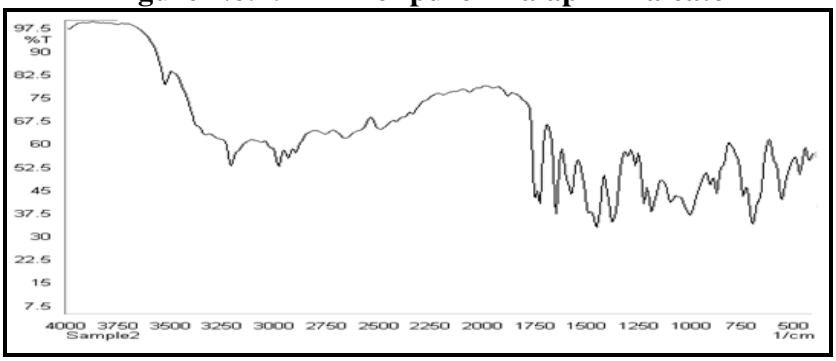


Figure No.2: FTIR of drugs + excipients

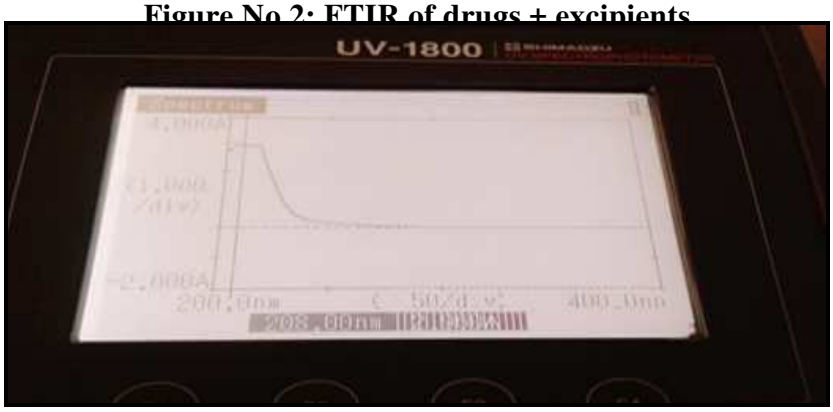


Figure No.3: Standard curve Enalapril maleate in water

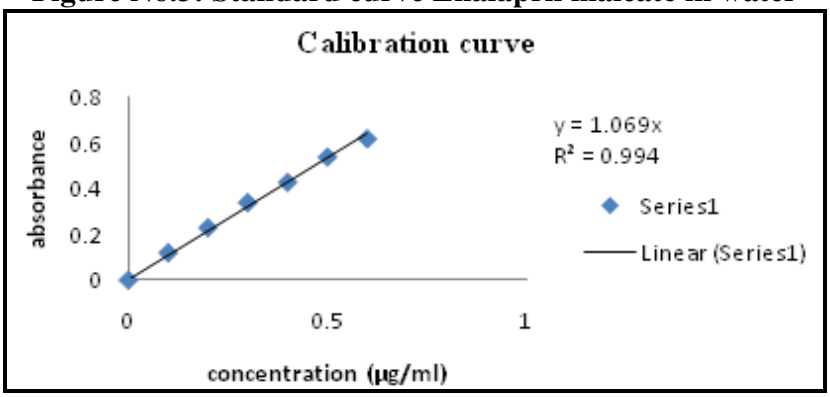


Figure No.4: Calibration graph of Enalapril maleate in water

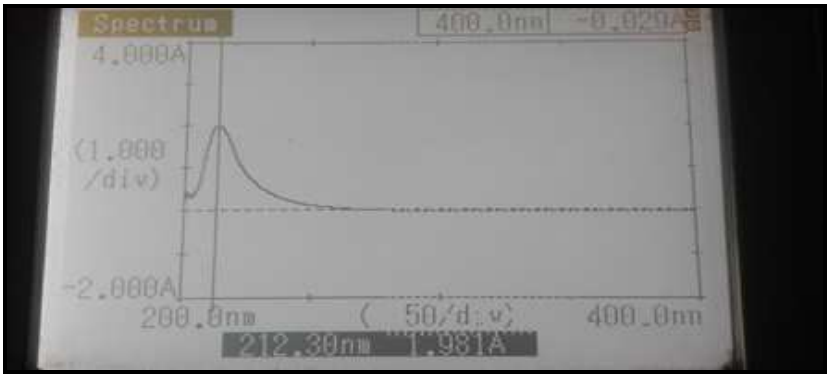


Figure No.5: Spectra of Enalapril maleate in phosphate buffer 6.8 PH

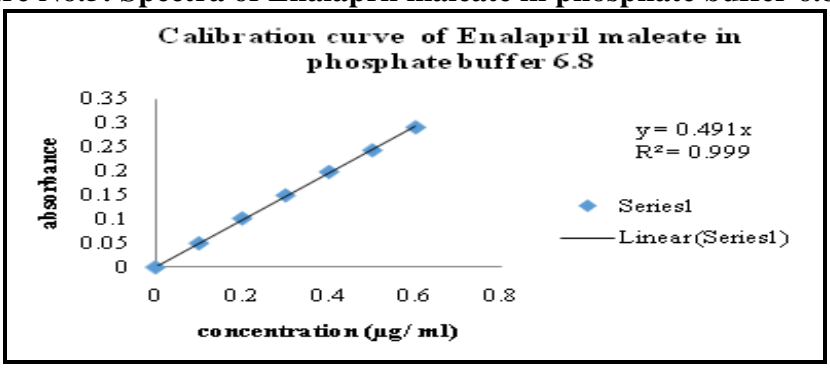
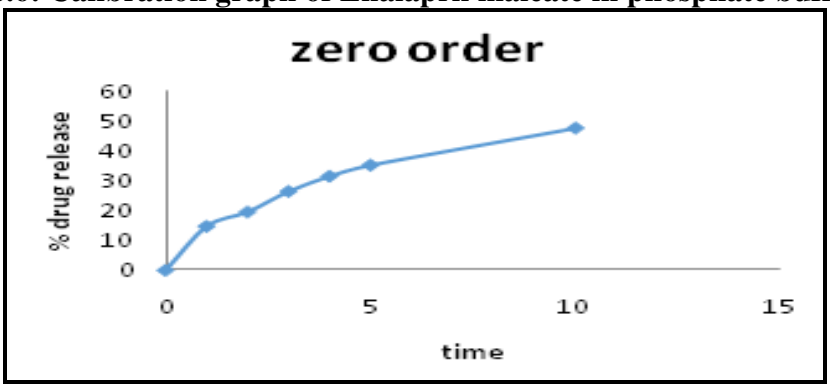


Figure No.6: Calibration graph of Enalapril maleate in phosphate buffer 6.8 PH



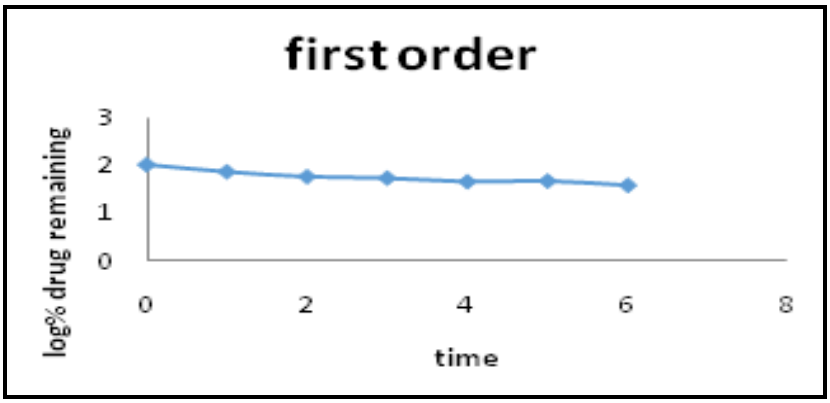


Figure No.7: Zero order and first order dissolution profile of direct compression method (F1)

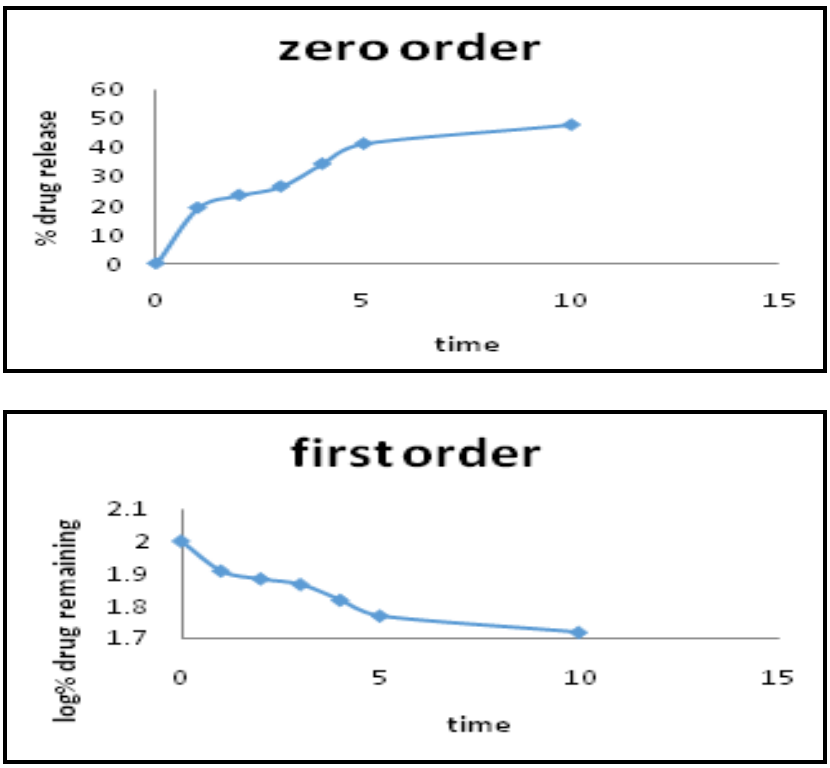


Figure No.8: Zero order and first order dissolution profile of direct compression method (F2)

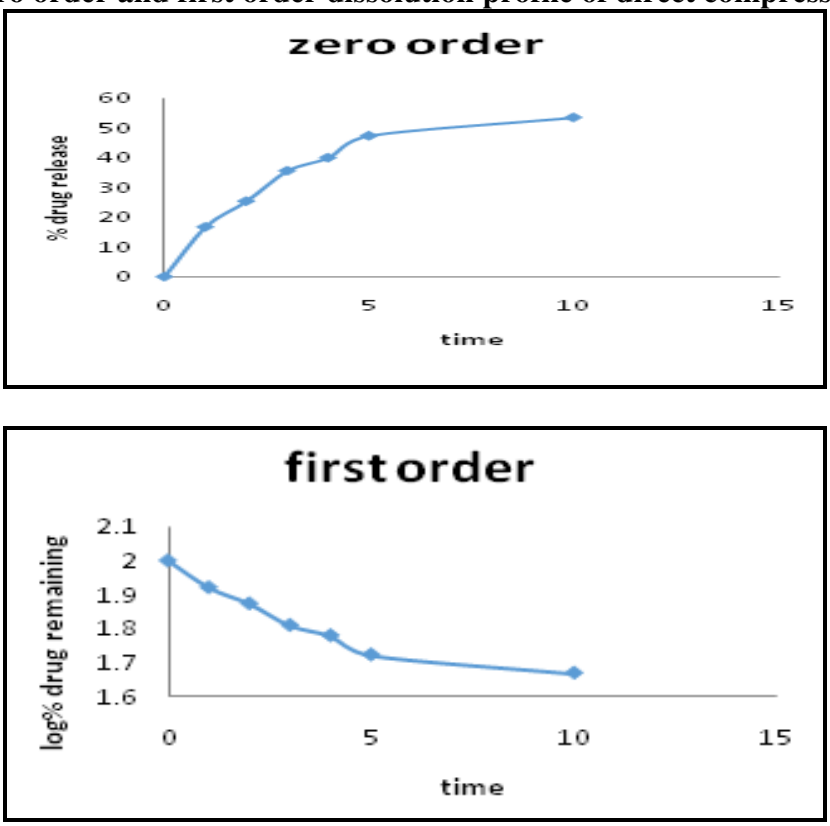
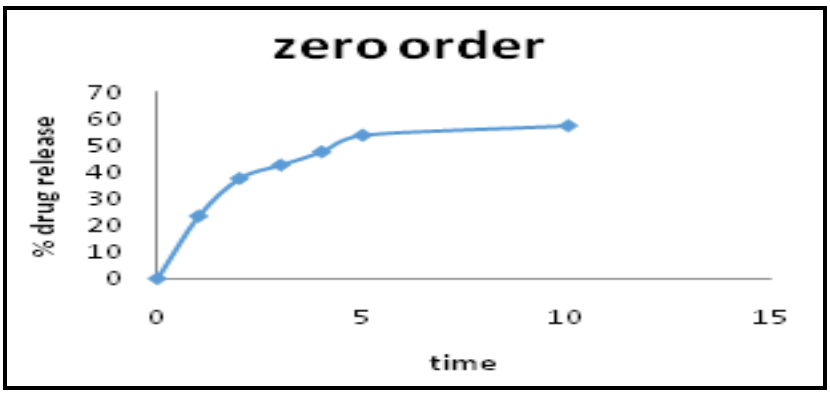


Figure No.9: Zero order and first order dissolution profile of direct compression method (F3



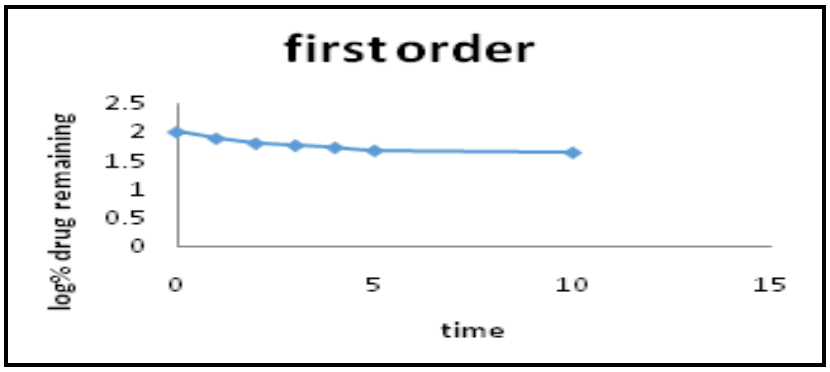
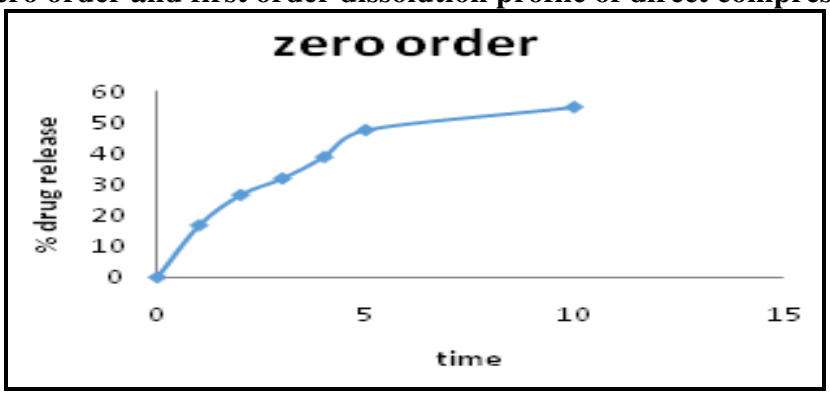


Figure No.10: Zero order and first order dissolution profile of direct compression method (F4



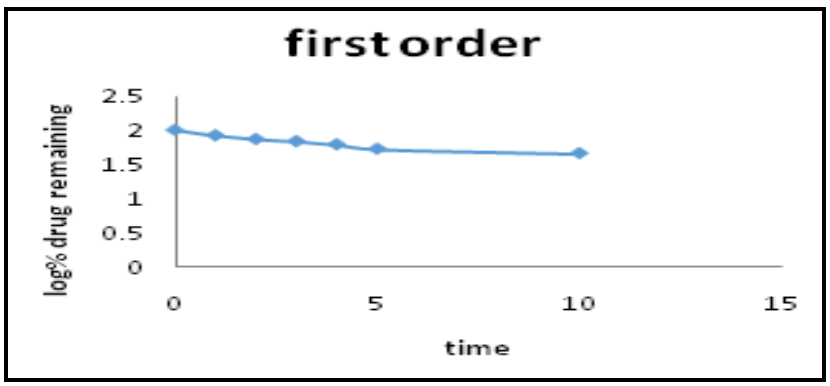


Figure No.11: Zero order and first order dissolution profile of direct compression method (F5)

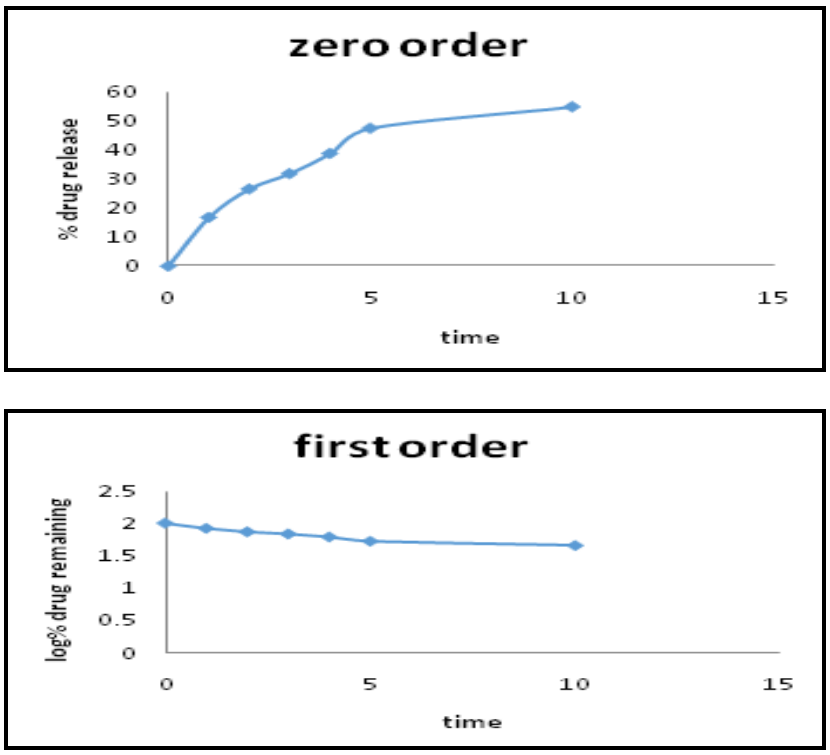


Figure No.12: Zero order and first order dissolution profile of direct compression method (F6)

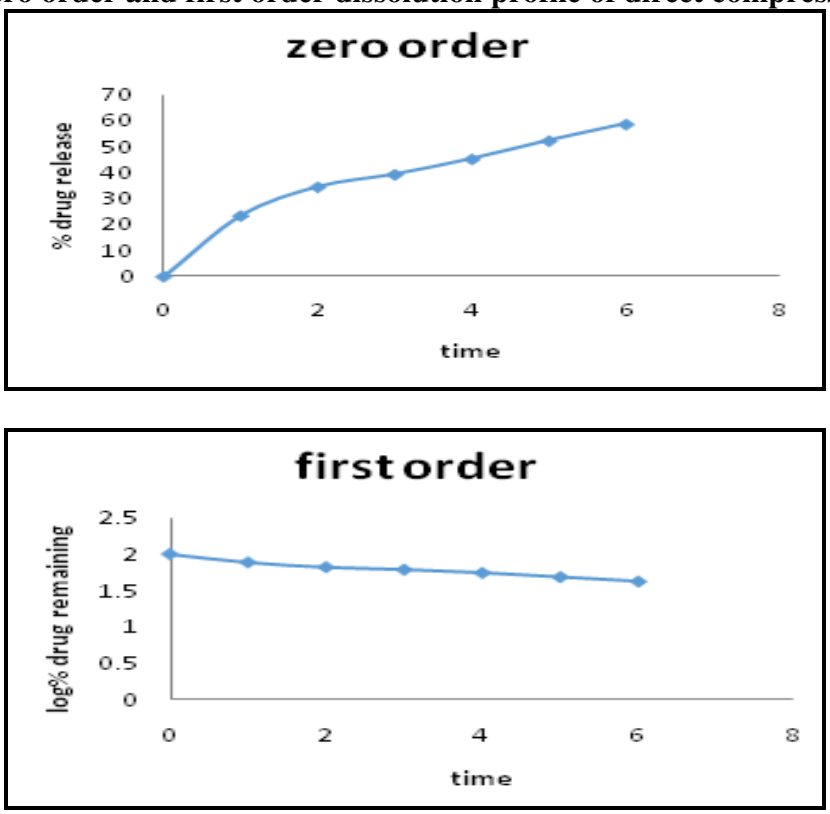
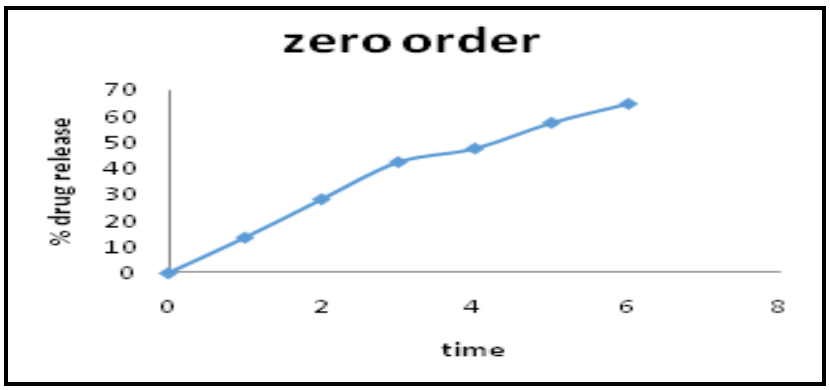


Figure No.13: Zero order and first order dissolution profile of direct compression method (F7)



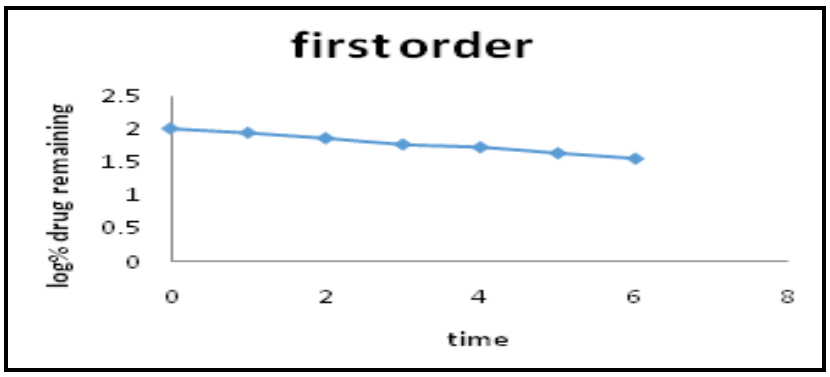
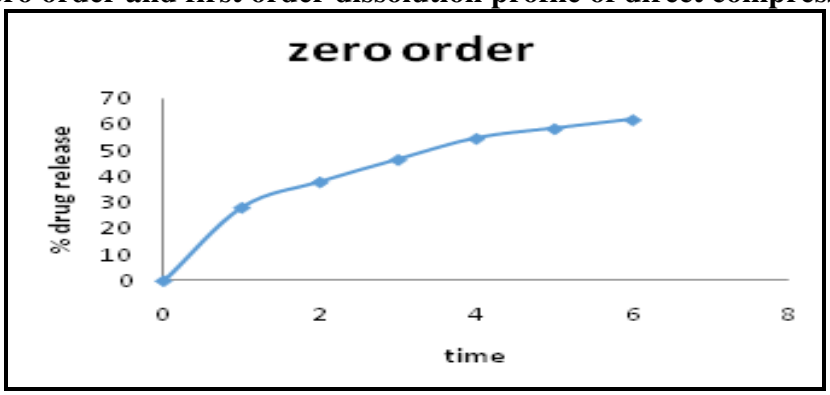


Figure No.14: Zero order and first order dissolution profile of direct compression method (F8)



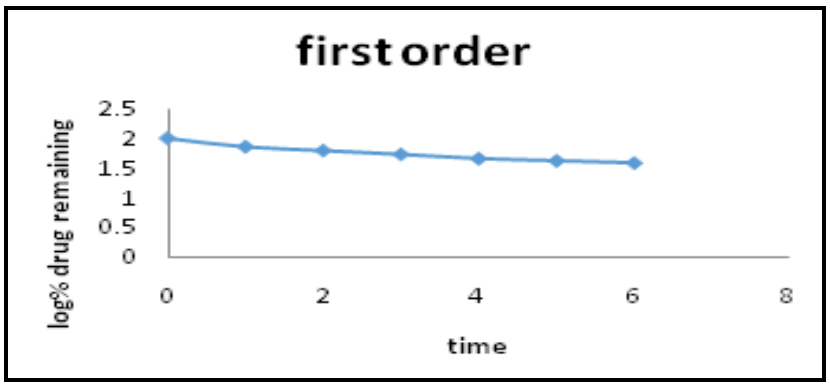


Figure No.15: Zero order and first order dissolution profile of direct compression method (F9)

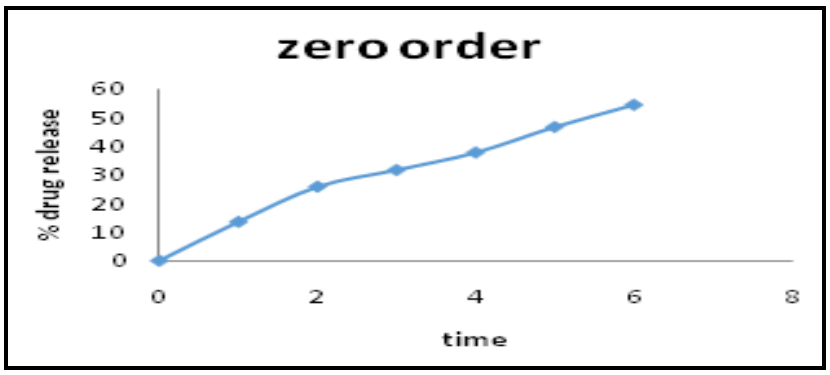
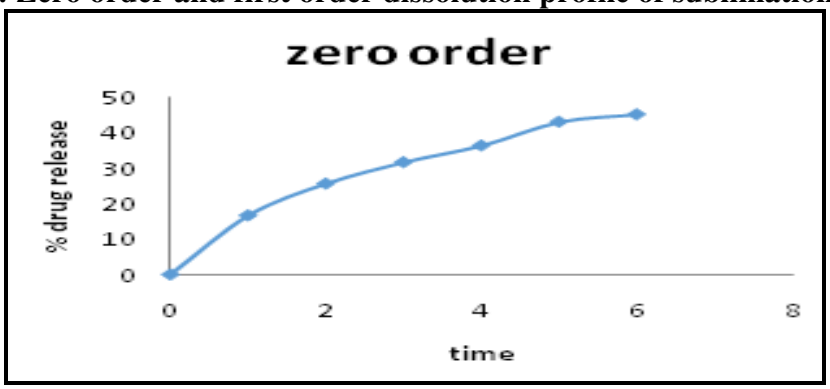


Figure No.16: Zero order and first order dissolution profile of sublimation method (F1)



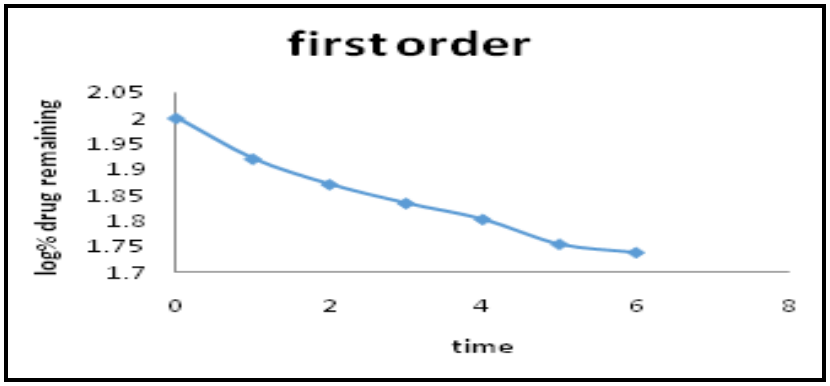


Figure No.17: Zero order and first order dissolution profile of sublimation method (F2)

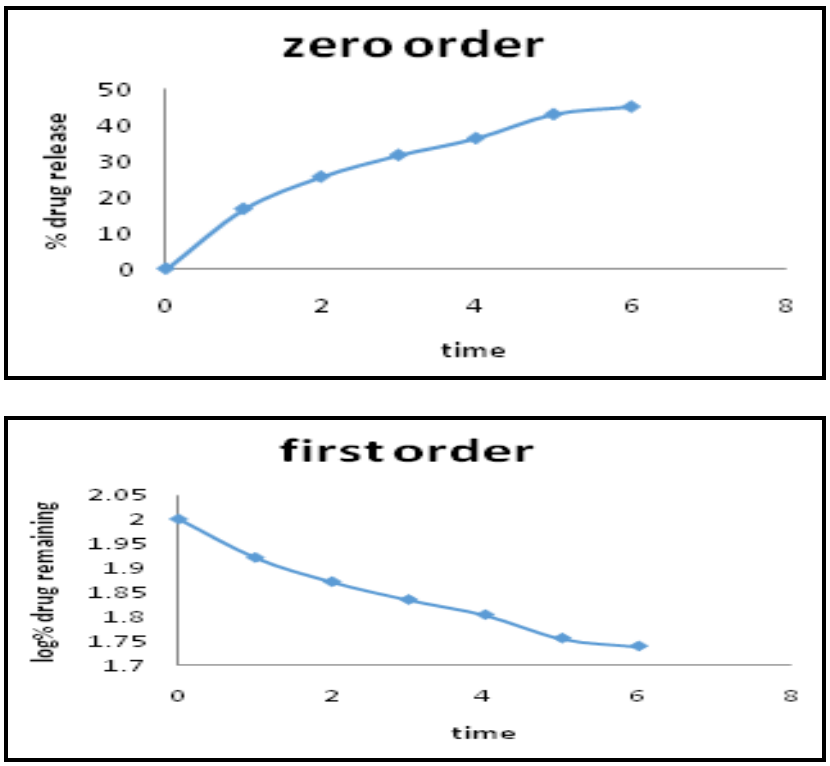


Figure No.18: Zero order and first order dissolution profile of sublimation method (F3)

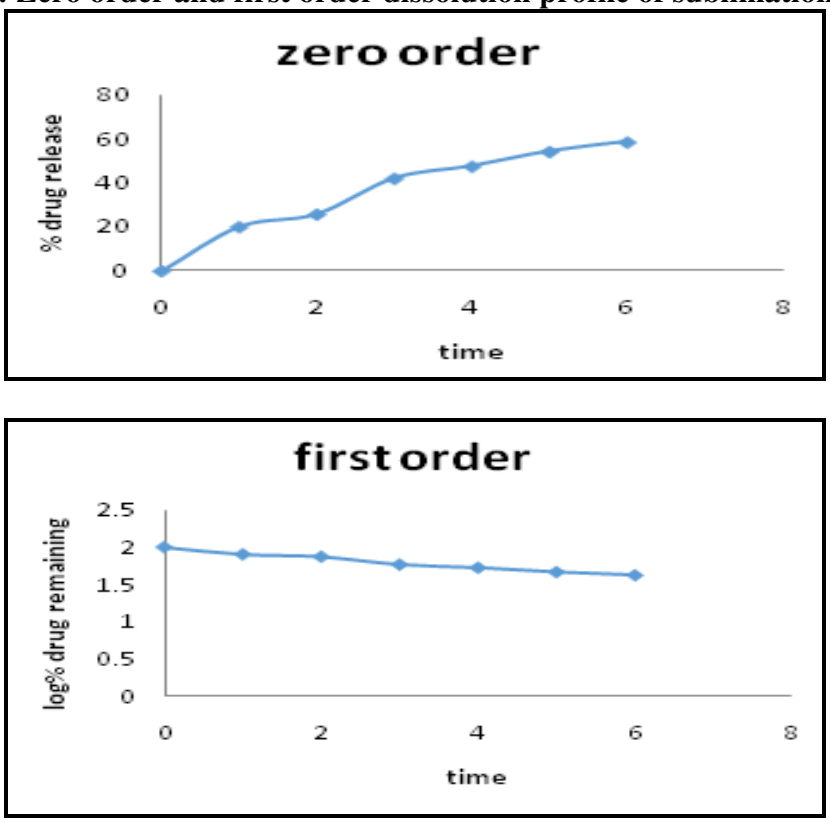
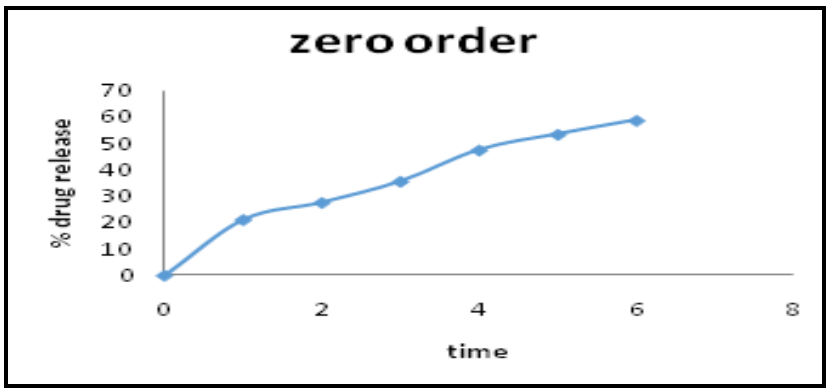


Figure No.19: Zero order and first order dissolution profile of sublimation method (F4)



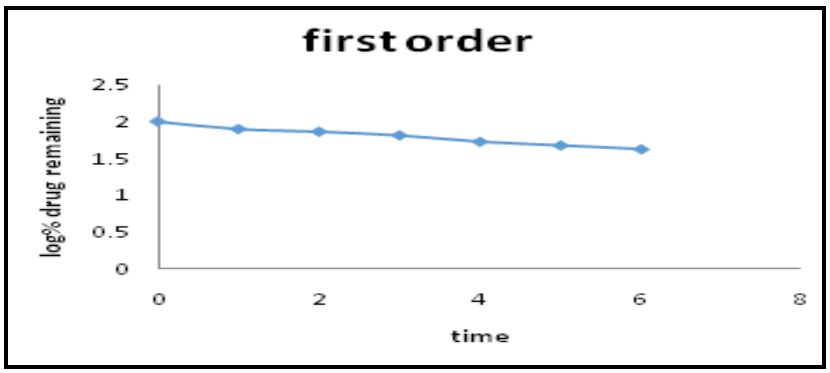
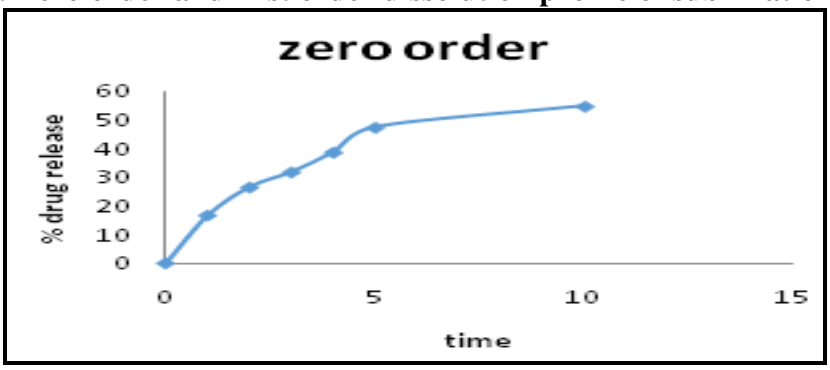


Figure No.20: Zero order and first order dissolution profile of sublimation method (F5)



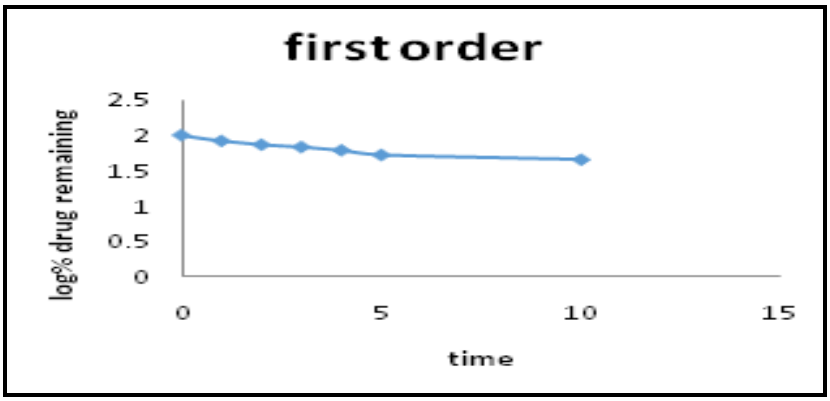
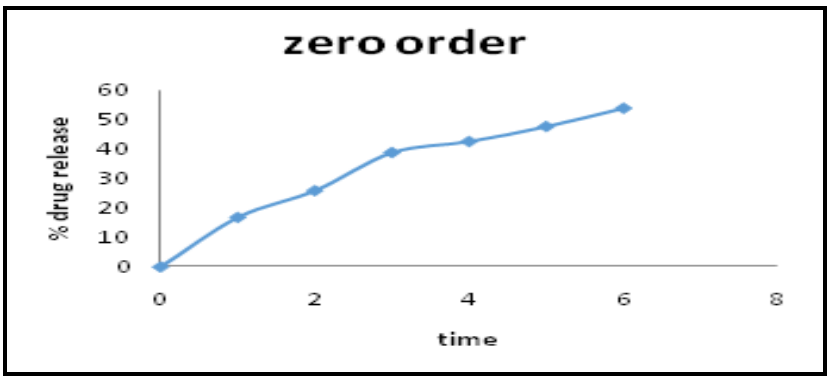


Figure No.21: Zero order and first order dissolution profile of sublimation method (F6)



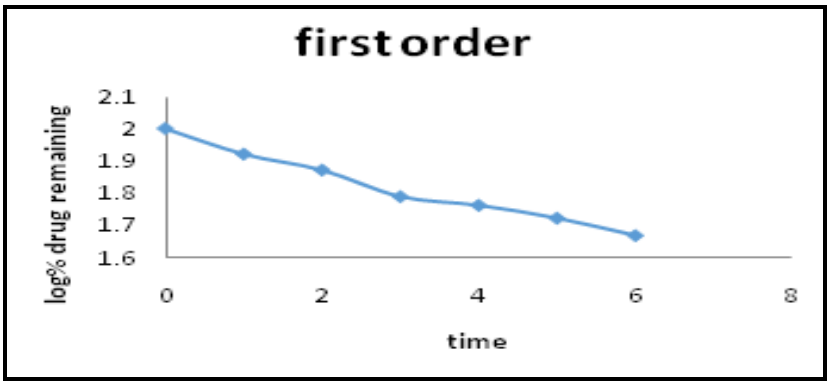
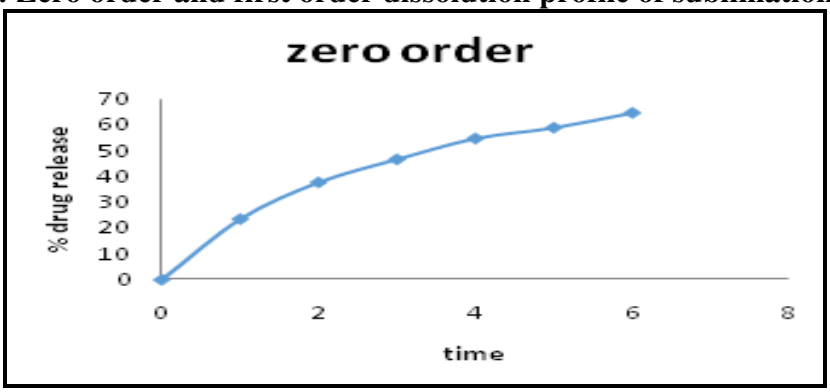


Figure No.22: Zero order and first order dissolution profile of sublimation method (F7)



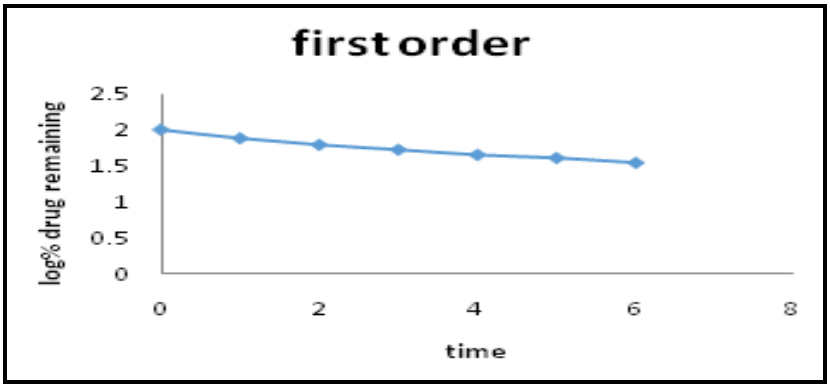


Figure No.23: Zero order and first order dissolution profile of sublimation method (F8)

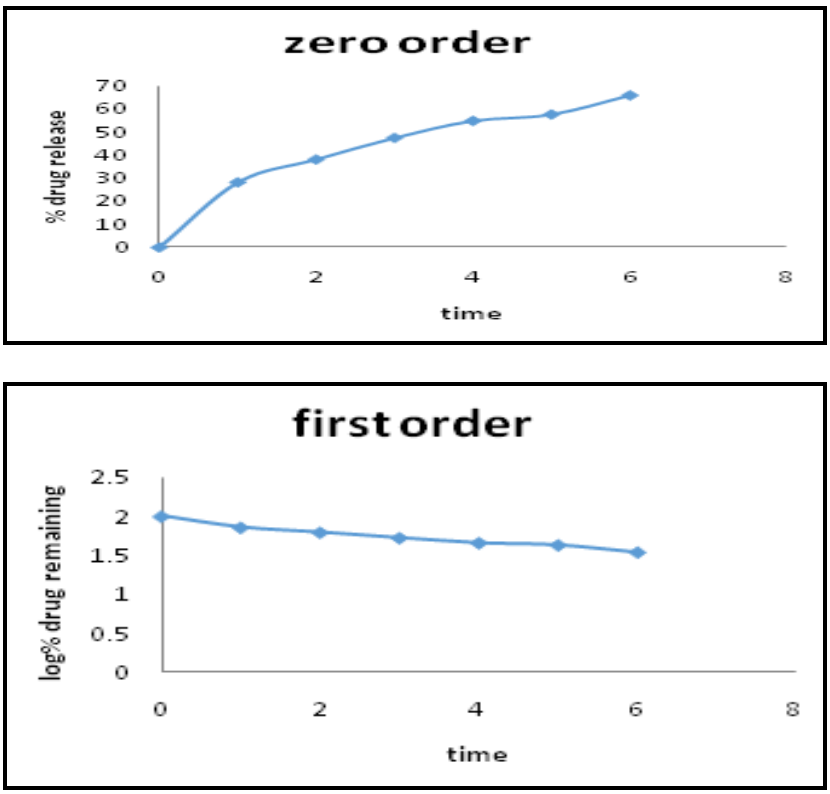


Figure No.24: Zero order and first order dissolution profile of sublimation method (F9)

Figure No.25: Zero order and first order dissolution profile of direct compression method (F9)

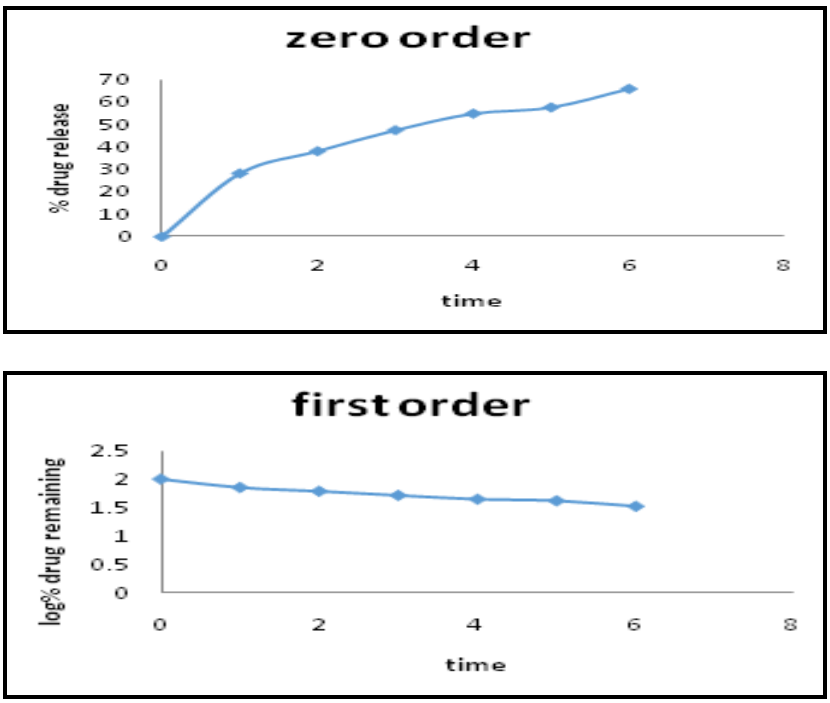


Figure No.26: Zero order and first order dissolution profile of sublimation method (F9)

CONCLUSION

In the presents study various formulation of fast dissolving tablets were prepared by direct compression method and sublimation method. To perform Pre-formulation studies like Micromeritics, melting point, partition coefficients, FTIR spectroscopy, UV spectroscopy, % assay, thin layer chromatography, loss on drying. In direct compression method tablet was prepared by using super disintegrates (crosscarmellose and sodium starch glycolate), lubricant (magnesium stearate), diluents (lactose), surfactant (sodium lauryl sulphate), sweetening agents (sucrose), binder (starch 20%). Total nine formulations were prepared. Tablets were evaluated for various parameter like hardness, thickness, weight variation, friability, % drugs content, water absorption time, wetting time, disintegrating time, % in vitro dissolution study. The *in-vitro* release profile depends upon type and concentration of superdisintegrant and drug release was increase with Superdisintegrants concentration. In sublimation method tablet was prepared by using super disintegrates (crosscarmellose and sodium starch glycolate), volatizing agents (camphor), lubricant (magnesium stearate), diluents (lactose), surfactant (sodium lauryl sulphate), sweetening agents (sucrose), binder (starch 20%) and total nine formulation were prepared. Tablets were evaluated for various parameter like hardness, thickness, weight variation, friability, % drugs content, water absorption time, wetting time, disintegrating time, % *in vitro* dissolution study. Amongst all the formulation F9 containing superdisintegrant (sodium starch glycolate 20mg, croscarmellose 40mg) and camphor (50mg) fulfilling all the parameter satisfactory and as shown fasted disintegration (55±1.2), wetting time (37±2.5) and higher % drug release (88.3%) as compared to other formulation. Over all, the results suggest that the suitably formulated fast dissolving tablet of Enalapril maleate containing super disintegrating and camphor as a volatizing/ subliming agents (F9) can be achieved. Over sublimation method is better than direct compression method, because the release of faster rate of dissolution is due to high porosity created by sublimation technique.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Goel Institute of Pharmacy and Sciences, Lucknow affiliated to Dr. APJ Abdul Kalam Technical University, Lucknow, Uttar Pradesh, India for providing necessary facilities to carry out this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Murrell W. Nitroglycerin as a remedy for insomnia, *Lancet,* 1(80), 1879, 113, 225, 284, 642-646.
2. Harris D, Robinson J R. Drug delivery via the mucous membranes of the oral cavity, *J Pharm Sci,* 81(1), 1992, 1-10.
3. Aulton's E. Michael, aulton pharmaceutical the design and manufacture of medicine, *Churchill Livingstone,* 3rd Edition, 2007, 347.
4. Indian pharmacopeia 2007, *Published by the Indian pharmacopeia commission, Ghaziadad,* 1, 2007, 480.
5. British pharmacopeia, *Published by the Stationary Office on the Behalf the Medicine And Health Care Product Regulatory Agency,* 1, 2013, 807-808.
6. Martin alferd physical pharmacy physical chemistry pharmaceutical sciences, *Varganes Publishing House,* 3rd Edition, 1991, 237-242.
7. Rowlins E A. Bentileys text book of pharmaceutics, *Elsevier,* 8th Edition, 2010, 19-22.
8. Asija R, Asijia S, Hemlata. A review on fast dissolving drug delivery system, *International Journals of Research in Pharmacy and Science,* 4(3), 2014, 7-12.
9. Patel Parag, Pateltejal, Patelrajesh. Formulation and evaluation of mouth dissolving tablet for anti-hypertensive drug, *Pharmagene,* 1(2), 2013, 10-20.
10. Lokesh B V S, Naidu S R. New dissolution method of enalapril maleate by UV spectroscopy, *JASA,* 2007, 31-35.
11. Kapil Kumar Goel, Nidhi Goel, Smita Gajbhiyea. Development of new UV spectrophotometer method for the estimation of Enalapril maleate in bulk and tablet dosage form, *The Asian Journals of Experimental Chemistry,* 3(1-2), 2008, 92-93.
12. Prasad Neelkant, Kumar Rajeev, Kumarvipin and Roy Ram Kumar. A simple UV spectrophotometric method for quantitative estimation of enalapril maleate, *Current Research in Pharmaceutical Science,* 6(1), 2016, 21-26.
13. Lindgren S, Janzon L. Dysphagia. Prevalence of swallowing complaints and clinical findings, *Medical Clinics of North America,* 77(1), 1993, 3-5.
14. Avery S W, Dellarosa D M. Approaches to treating dysphagia in patients with brain injury, *Am. J. Occup. Ther,* 48(3), 1994, 235-239.
15. Logoyda Liliya, Korobko Dmytro, Saprun Stanislav, Zarivna Nadia. Development of methods for the chromatographic identification of active pharmaceutical ingredient from group of angiotensin-converting enzyme inhibitors in pharmaceuticals, *International Journal of Green Pharmacy*, 11(4), 2017, 737-741.
16. Jain C P and Naruka P S. Formulation and evaluation of fast dissolving table of valsartan, *International Journal of Pharmacy and Pharmaceutical Sciences,* 1(1), 2009, 219-226.
17. Raviteja Penjarla, Muralidhar S, Ramesh R, Narayana T V, Kumar P. Vasantha, Kumar G. Vijay. Formulation and evaluation of valsartan fast disintegrating tablets using solid dispersion technique, *International Journal of Innovative Pharmaceutical Research,* 4(1), 2013, 274-280.

18. Peter Ronald, Nayak N. Shashank, Shwetha S, Kamath K, Shabaraya A R. Formulation and evaluation of fast dissolving tablets of flunarizinehcl by sublimation method using treated agar as superdisintegrant, *International Journal of Pharmaceutical and Chemical Science,* 3(2), 2014, 552-562.
19. Buddhadev Sheetal, Buddhadev Sandip. Formulation and evaluation of fast dissolving tablets of albendazole by sublimation method, *International Journal of Applied Pharmaceutical and Biological Research,* 2(4), 2017, 35-47.
20. Anievijetha K, Padmaja B, Kumarg Sravan, Swethaj Hima, Sravanthi D. Formulation and characterization of fast dissolving tablets of isradipine by using different technologies, *International Journal of Pharmaceutical Research and Biomedical Analysis,* 1(2), 2012, 1-10.

Please cite this article in press as: Karunakar Prasad Dwivedi and Amresh Gupta. Development and characterization of fast dissolving tablet of Enalapril maleate, *International Journal of Research in Pharmaceutical and Nano Sciences,* 10(3), 2021, 205-239.