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# Study on Oral Osmotic Tablet

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## ABSTRACT

The oral route is that the most typical and most acceptable route of drug administration. this article tries to supply data on Oral osmotic Drug Delivery .For treatment of chronic diseases recurrent dose administration is needed, the osmotic drug delivery system function a tool for management unharness of medication in these conditions and avoid the recurrent administration. Novel drug delivery systems (NDDS) represent the mainstay of pharmaceutical analysis and development. A big milestone in oral NDDS is that the development of the diffusion drug delivery system, associate innovative and extremely versatile drug delivery system. diffusion drug delivery systems utilize the principle of osmotic pressure, as an energy supply, for the delivery of medication. Oral diffusion drug delivery systems with their skillfulness and their extremely certain drug unharness rates provide numerous medicine benefits.

***Keywords:*** Osmotic, ODDS

## Introduction[1, 2]

Tablet has long been used as an efficient dosage for its stability and ease of administration .It contains a mix of active substances and excipients, typically in powder type, compressed or compacted from a powder into a solid dose. "Tablets is also defined as solid pharmaceutical dose forms containing drug substances with or while not suitable diluents and prepared by either direct compression or molding methods". they're simple to use for many individuals and low-cost for makers to supply.

## Advantages

Tablets are historically circular or disk formed however will correspond any form.

•They are a unit doses form and provide the best dose precision and also the least content variability, their price is lowest of all oral indefinite quantity forms, they're the lightest and most compact of all oral indefinite quantity forms, they're normally the best and most cost-effective to package and ship of all oral indefinite quantity forms,

•They may give the best simple swallowing with the least tendency for "hang-up" higher than the abdomen, particularly once coated, only if tablet disintegration isn't too fast, They lend themselves to bound special release profile products, like enteric or delayed-release products,

•They are higher suited to massive scale production than different unit oral forms and that they have the best-combined properties of chemical and mechanical and microbiologic stability of all the oral forms.

## Disadvantages of tablet.

A number of the disadvantages of tablets embrace the following include,

Some medicine resist compression into dense compacts thanks to their amorphous nature or flocculent density character,

Drugs with poor wetting, slow dissolution properties, intermediate to giant dosages or any combination of these options is also tough or not possible to formulate

Manufacture as a pill that might still give adequate or full drug bioavailability associated bitter tasting medicine with an objectionable odour may need coating.1.[1]

**Types of tablet.**

There are many types of tablets are available in the market such as, sugar-coated tablets, film-coated tablets, enteric-coated tablets, multiple-coated tablets, layered tablets, press-coated tablets, controlled release tablets, buccal or sublingual tablets, tablets for solution, molded tablets or tablet triturates and fast dissolving / disintegrating tablets.[2]

**Methods of manufacturing**.

Generally tablets are manufactured by wet granulation, dry granulation and direct compression method.

***Wet Granulation***.

Wet granulation is the process in which a liquid is added to a powder in a vessel equipped with any type of agitation that will produce agglomeration or granules. These granules are then compressed to form tablets.

**CONTROLLED DRUG DELIVERY SYSTEM.[3-4]**

Therapeutic efficacy and safety of drugs, administrated by conventional methods, can be improved by more precise spatial and temporal placement within the body, thereby reducing both the size and number of doses by using controlled drug delivery system. An ideal controlled drug delivery system is the one which delivers the drug at predetermined rate, locally or systemically for a specified period of time. An ideal targeted drug delivery system delivers the drug only to its site of action.

Controlled delivery of drugs, proteins and other bioactive agents can be achieved by incorporating them either in dissolved or dispersed form in polymers.

In general controlled delivery attempts to,

- Sustain drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body.
- Localize drug action by spatial placement of a controlled release system (rate controlled) adjacent to or in the diseased tissue or organ.
- Target drug action by using carriers to deliver drugs to particular target cell type.

**Objectives of controlled drug delivery systems.**

The chief objective of most products should be controlled delivery to reduce dosing frequency to an extended that once daily does is sufficient for therapeutic management though a uniform plasma concentration at a steady state. The major objectives include

- Predict drug release rated form and drug diffusion behavior through polymers, thus avoiding excessive experimentation.
- Elucidate the physical mechanism of drug transport by simply comparing the release data mathematical models.
- Design new drug delivery system based on general release expressions.

**OSMOTIC PRESSURE ACTIVATED DRUG DELIVERY SYSTEM INTRODUCTION.[5]**

Osmotic drug delivery system utilizes Osmosis as the major driving force for drug release. Adequate water solubility of the drug is a prerequisite for osmotic drug delivery system. Osmotic drug delivery devices are composed of an osmotically active drug core, which is surrounded by a rate controlling membrane. Osmotic drug delivery system differs from diffusion based systems in that the delivery of the active agents is driven by an osmotic gradient rather than the concentration of drug in the device.

**Advantages.**

- Desired zero order delivery rates is achieved with osmotic systems.
- Delivery rate osmotic greater as compared to diffusion based systems.
- Delayed or pulsed drug delivery is obtainable with osmotic system.

- Release rate is predictable.

**Disadvantages.**

- High cost.
- Chances of dose dumping.
- Reduced potential for dosage adjustments.
- Increased potential for first pass clearance.
- Poor systematic availability in general.

**Principle of Osmosis.**

Osmosis refers to the process of movement of solvent from lower concentration of solute towards higher concentration of solute across a semi permeable membrane.

**Parameters**

***Orifice size.***

To achieve an optimal zero-order delivery profile, the cross-sectional area of the orifice must be smaller than a maximum size to minimize drug delivery by diffusion through the orifice.

***Solubility.***

The release rate depends on the solubility of the solute inside the drug delivery system. Therefore, drugs should have sufficient solubility to be delivered by osmotic delivery. In the case of low solubility compounds, several alternate strategies may be employed. Broadly, the approaches can be divided into two categories.

***Osmotic pressure***.

The osmotic pressure π directly affects the release rate. To achieve a zero-order release rate, it is essential to keep π constant by maintaining a saturated solute solution.

***Semipermeable membrane***.

Since the semi permeable membrane is permeable to water and not to ions, the release rate is essentially independent of the pH of the environment. Additionally, the drug dissolution process takes place inside the delivery system, completely separated from the environment.

**Basic Components of Osmotic Systems.[6]**

***Drug.***

It has short biological half-life and which is used for prolonged treatment are ideal candidate for osmotic systems. Various drug candidates such as Diltiazem HCl, Carbamazepine, Metoprolol, Oxprenolol, Nifedipine, Glipizide etc are formulated as osmotic delivery.

***Semipermeable membrane.***

An important part of the osmotic drug delivery system is the semi permeable membrane housing. Therefore, the polymeric membrane selection is key to the osmotic delivery formulation. The membrane should be inert and maintain its dimensional integrity to provide a constant osmotic driving force during drug delivery e.g. Cellulose esters like cellulose acetate, cellulose acetate butyrate, cellulose triacetate and ethyl cellulose and Eudragit.

***Osmotic agent***.

Osmotic agents maintain a concentration gradient across the membrane. They also generate a driving force for the uptake of water and assist in maintaining drug uniformity in the hydrated formulation. Osmotic components usually are ionic compounds consisting of either inorganic salts or hydrophilic polymers. Osmotic agents can be any salt such as sodium chloride, potassium chloride, or sulfates of sodium or potassium and lithium. Additionally, sugars such as glucose, sorbitol, or sucrose or inorganic salts of carbohydrates can act as osmotic agents.

***Flux regulator***.

Delivery systems can be designed to regulate the permeability of the fluid by incorporating flux regulating agents in the layer. Hydrophilic substances such as poly ethylene glycols, polyhydric alcohols, polyalkylene glycols, and the like improve the flux, whereas hydrophobic materials such as phthalates substituted with an alkyl or alkoxy (e.g., diethyl phthalate or

dimethoxyethylphthalate) tend to decrease the flux. Insoluble salts or insoluble oxides, which are substantially water-impermeable materials, also can be used for this purpose.

***Wicking agent.***

A wicking agent is defined as a material with the ability to draw water into the porous network of a delivery device. A wicking agent is of either swellable or non-swellable nature. The function of the wicking agent is to carry water to surfaces inside the core of the tablet, thereby creating channels or a network of increased surface area. Materials, which suitably for act as wicking agents include colloidal silicon dioxide, kaolin, titanium dioxide, alumina, sodium lauryl sulphate (SLS), poly vinyl pyrrolidone (PVP), magnesium aluminium silicate, polyethylene.

***Pore forming agent.***

These agents are particularly used in the pumps developed for poorly water soluble drug and in the development of controlled porosity or multi particulate osmotic pumps. These pore forming agents cause the formation of micro porous membrane. For example, sodium chloride, sodium bromide, potassium chloride, potassium sulphate, calcium chloride, sucrose, glucose, fructose, mannose, lactose, sorbitol, mannitol, polyvinyl pyrrolidone can be used as pore forming agents.

***Solvents.***

Solvents suitable for making polymeric solution that is used for manufacturing the wall of the osmotic device include inert inorganic and organic solvents that do not adversely harm the core, wall and other materials. The typical solvents include methylene chloride, acetone, methanol, ethanol, isopropyl alcohol, butyl alcohol, ethyl acetate, cyclohexane, carbon tetrachloride, water etc.

***Plasticiser.***

Different types of plasticizers used in coating membrane also have a significant importance in the formulation of osmotic systems. They can change visco-elastic behavior of polymers and these

changes may affect the permeability of the polymeric films. Some of the plasticizer used is as follows:

- Polyethylene glycols.
- Triethyl citrate.

***. Surfectant***.

Surfactants are particularly useful when added to wall forming material. The surfactants act by regulating the surface energy of materials to improve their blending in to the composite and maintain their integrity in the environment of use during the drug release period. Typical surfactants such as polyoxyetylenated castor oil having ethylene oxide, glyceryl laureates, glycerol (sorbitonoleate, Stearate or laureates) etc.

***Solubilising agent.***

Non-swellable solubilizing agents are the agents that inhibit crystal formation of the drugs or otherwise act by complexation with the drugs (e.g., PVP, poly (ethylene glycol) [PEG 8000] and α, β, γ- cyclodextrins).

**Preformulation studies of the drug.**

**Physico-chemical characterization of Ramipril.**

The following physico-chemical properties of Ramipril were evaluated by employing the prescribed standard techniques.

***Density measurement.***

Different types of density calculation were done to characterize the drug. In generally two types of density are determined i.e. bulk density and tapped density. The following methods were followed for the determination of densities.

- **Bulk Density (Db).**

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder i.e. 2gm of drug sample (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

Db (g/ml) = M/ Vb

Where, M is the mass of powder in gm.

Vb is the bulk volume of the powder sample [53].

- **Tapped Density (Dt).**

Tapped density of drug was determined by pouring gently 5mg of sample through a glass funnel into a clean dried graduated glass cylinder. The cylinder was tapped from a height of 2 inches until a constant volume was obtained.

Dt (g/ml) = M / Vt , Where, M is the mass of powder in gm. And Vt is the tapped volume of the powder.

***Flow property.***

- **Angle of Repose (θ).**

The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane [55].

**$\tan(\theta) = \tan^{-1} h / r$,** Where, θ is the angle of repose, h is the height in cm. and r is the radius in cm.

**Carr's index (or) % compressibility.**

It indicates powder flow properties. It is expressed in percentage by comparing the bulk density and tapped density. A useful empirical guide is given by Carr's compressibility. Table 13 shows the relationship between the compressibility and flow properties [25].

$$\text{Carr's index} = \frac{\text{Tapped desnity} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

**Table 1: Standard values of angle of repose and flow property.**

| % Compressibility | Flow property |
|---|---|
| 5-12 | Excellent |
| 12-16 | Good |
| 18-21 | Fair passable |
| 23-35 | Poor |
| 33-38 | Very poor |
| <40 | Very very poor |

**Table 2: Compressibility and flow property relationship.**

- **Hausner's ratio.**

| % Comp. Index | Properties |
|---|---|
| 5-12 | Free flowing |
| 12-16 | Good |
| 18-21 | Fair |
| 23-35 | Poor |
| 33-38 | Very poor |
| >40 | Extremely poor |

It indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density

Hausner's Ratio = Tapped density/Bulk density.

**Table 3: Flow property by Hausner's ratio.**

| Sl. No | Hausner's Ratio | Property |
|---|---|---|
| 1 | <1.25 | Better flow ability |
| 2 | >1.25 | Poor flow ability |

**Table 4: Physico-chemical characteristics of Ramipril.**

| Experiment | Result |
|---|---|
| **Bulk density** | 0.2173 g/cc |
| **Tapped density** | 0.3125 g/cc |
| **Carr's index** | 30.46 % |
| **Hausner's ratio** | 1.438 |
| **Angle of repose** | $28^0$ |

**Formulation of osmotic tablets of Ramipril.**.

The drug was selected for the formulation of osmotic tablets. Different polymers like PVP-K30and Ethyl cellulose were used in the present study. Diluents like microcrystalline cellulose (MCC), Potassium chloride, Mannitol & lubricants like Magnesium stearate were used in all the formulations. All the formulations were formulated by wet granulation of tablet compression method. The procedure employed for each formulation is given below.

- **Preparation of core tablets**.

Accurately weighed quantities of ingredients along with drug mentioned were passed through sieve No. 60 (aperture size 250 μm). All the ingredients, except lubricant (magnesium stearate), glidant talc and binder poly vinyl pyrrolidone (PVP), were manually blended homogeneously in a mortar by way of geometric dilution. The mixture was moistened with solution of 10% (m/V) PVP and methanol to get wet mass and these wet mass granulated through sieve No. 16 (aperture size 1000 μm) and dried in a hot air oven at 60 $^0$C for sufficient time (3 to 4 hours) so that the moisture content of the granules reached 2–4%. The dried granules were passed through sieve No. 44 (aperture size 325 μm) and blended with talc and magnesium stearate. The homogeneous blend was then compressed into tablets (500 mg each) using 12-mm diameter, deep concave punches. The compression force was adjusted to give tablets with approximately 5 kg/cm$^2$ hardness on a Monsanto tablet hardness tester .

- **Coating of core tablets.**

Core tablets were film coated with a semi permeable membrane of cellulose acetate (CA) in methylene chloride with methanol.. This coating solution was applied on the core tablets using a conventional laboratory grade spraying instrument. The manual coating procedure used was based on an intermittent spraying and drying technique.

## PHYSICO-CHEMICAL EVALUATION OF PREPARED OSMOTIC TABLETS.[7-9]

The prepared compressed tablets were evaluated for their important parameters that affect the release of the drug. The parameters include weight variation, thickness, hardness, friability, drug content and in-vitro drug release pattern. All the physic-chemical evaluation results of prepared osmotic core tablets and coated tablets are presented below.

### Weight variation.

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table No 10.

**Table 5: Weight Variation Specification as per IP.**

| Average Weight of Tablet | % Deviation |
|---|---|
| 80 mg or less | ±10 |
| More than 80 mg but less than 250 mg | ±7.5 |
| 250 mg or more | ±5 |

**Hardness.**

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in $kg/cm^2$.

**Size & Shape.**

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by Vernier caliper or by other device. Tablet thickness should be controlled within a ± 7.5% variation of standard value.

**Friability (F).**

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

**Drug contents.**

About 20 tablets randomly selected from each formulation. They were finely powdered and powder equivalent to 100 mg of Ramipril was accurately weighed and transferred to 100ml volumetric flasks containing 50 ml of phosphate buffer pH-6.8.

***In vitro* release studies.**

*In vitro* dissolution studies were designed to carry out in such a way that they simulate *in-vivo* conditions. The purpose of *in vitro* release study was to provide a fast, easily performed and in-expensive method that correlates with the performance of dosage form in human subjects. The conditions of *in vitro* dissolution test were well defined, standardized and enable comparison among various results.

- *Dissolution Parameters*:

- Apparatus: USP XX Apparatus II (PADDLE TYPE)
- Medium: 900 ml pH 6.8 phosphate buffer
- RPM:100
- Temperature: $(37 \pm 0.5)^0$C
- Sample collection volume: 1 ml
- Replacement: 1 ml of pH 6.8 phosphate buffer was added.
- Sampling intervals: After every one hour till 24 hrs.
- Absorbance was measured at λ max 271 nm.

**Mechanism of drug release.**

To find out the mechanism of drug release from hydrophilic matrices, the dissolution data of tablets of each batch was treated with different kinetic equations, namely zero order, 1st order, Higuchi, Hixon-crowell, etc.

- **Zero order Kinetic Model.**

According to this model, under standard conditions of temperature and agitation in the dissolution medium, the dissolution rate model can be described by the following equation.

$dq/dt = K_0$ or in an integral form

$Q = K_0t$ , Where q = amount of drug released / unit surface area.

$K_0$ = Zero-order release rate constant and T = Time.

- **First order Kinetic Model.**

According to Noyes Whitney, under standard condition of agitation and temperature the dissolution rate process for solids can be described by the following equation.

$Dq/dt = K_1 (Cs – Ct)$

Under sink condition, i.e. when $Ct < 0.15 Cs$, the equation becomes $dq / dt = K_1Cs$ Or an integrated form.

$\ln q_0/q_t = k_1t$

Where, qt = amount drug released per unit surface area, $k_1$ = 1st order release rate constant, $q_0$ = Initial amount, Cs = Saturation stability, Ct = concentration at time 't'.

The Log percentage amount remaining to be released in different time intervals of different formulations are given in the Table-23. The plots of log % amount remaining to be released vs. time of different formulations are given the Figures-21. The $R_2$ (regression) values and rate constants of all the formulations are depicted below.

- **Hixon – Crowell Kinetic Model.**

As solid dissolved, the surface area changed with time. The Hixon-Crowell cube root equation for dissolution kinetics is based on the assumption that:

- Dissolution occurs normal to the surface area of the particles.
- Agitation is uniform on overall exposed surface and there is no stagnation.
- The particles of solute retain its geometric shape.

For a non-dispersible powder with spherical particles, a bit mathematical derivation leads to the kinetics equation.

$Wo^{1/3} - Wt^{1/3} = K_{Hc}t$

Where, Wo = Initial weight of the particles, Wt = Weight of the particle at't', $K_{HC}$ = Hixon – Crowell release rate constant and t = time.

- **Higuchi kinetic Model.**

For a coated or matrix type dosage form, the dissolution medium enters the dosage form in order the drug to be released by diffusion. In such cases, the dissolution follows the equation by Higuchi (Q) .

Or Q = KHG t0.5

Where, Q = Amount of drug released per unit area of the dosage form, D = Diffusion coefficient of the drug, E = Porosity of the matrix, A = Area, Cs = Saturation solubility of the drug in the surrounding liquid, KHG = Higuchi Release rate constant and t = time.

The cumulative percentage amounts of drug released with respect to square root of time of various formulations are given.

- **Korsmer-pappas kinetic model.**

Korsemer developed a simple semi imperial model, relating exponentially the drug release to the elapsed time, which was verified by Peppas & Franson, Peppas & Sachlin ·

The model relates the fractional release with potency time and described as,

$$M_t/M_\alpha=K_m t^n$$

2010; 1(1): 1-8.Log $M_t/M_\alpha$=log $K_m$ +Nlog t

Where, $M_t/M_\alpha$ = Fraction release of drug, T= Release time, $K_m$= Constant incorporating geometric and structural characterization off release device, n = Release exponent indicative of release mechanism.

If one, plot the logarithm of fractional release Vs the logarithm time then the slope of graph gives the values of 'n'.

**Conclusion**

Oral osmotic tablets are being attempted on certain drugs with aview to provide constant release of the drug to achieve the desired therapeutic efficacy in clinical disorders.The delivery rate was found to increase at a constant rate throughout the dissolution study.

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