IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON: INLAY TABLET

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ABSTRACT: The aim of present article to understand, what is Inlay tablet and its advantages over the conventional tablet dosage form. The inlay tablet improves the pharmacokinetic and pharmacodynamics principles in the design of drug delivery system and also improve therapeutic efficacy. Inlay tablet reduces the frequency of dose administration and improve the patient compliance. Review focused on a novel approach of drug delivery system in preparation of inlay tablets.

Keywords: Inlay tablets, Novel approach, Drug therapy Etc.

INTRODUCTION

Drug therapy has a profound influence on the health statistics all over the world. The effective and rational use of the drug constitutes one of the most important of the health program. Today all the world allopathic systems of medicine dominates the "Traditional medicine and healing art" due to its strong link with modern sciences & technology. Drug delivery has metamorphosed from the concept of pill to molecular medicine in the past 100 years. Better appreciation and integration of pharmacokinetic and pharmacodynamics principles in the design of drug delivery system has been developed a lead to improve therapeutic efficacy. Drug research has evolved and matured through phases beginning from pill to pharmaceutical dosage form [1].

Modified or controlled release oral drug delivery systems have, over the last few decades, been shown to offer advantages over conventional systems. These include increased patient compliance, selective pharmacological action; reduced side-effect profile and reduced dosing frequency. These systems may therefore have a significantly beneficial outcome in therapeutic efficacy. Controlled release offers prolonged delivery of drugs and maintenance of plasma levels within a therapeutic range Furthermore, by pairing drug administration rate with drug elimination rate, steady-state plasma levels can be maintained[2]. Currently most drug delivery systems exhibit first-order drug release kinetics where the plasma level of the drug is extremely high after administration and then decreases exponentially. This poses disadvantages such as minimal therapeutic efficacy due to reduced drug levels; or drug toxicity which can occur at high concentrations [3]. This type of drug release does not allow for appropriate plasma

drug level balance. Peak-to-trough fluctuations may occur with first-order drug release that may cause dose dependent side effects. Drug delivery systems should ideally exhibit zero-order drug release kinetics which allows for a constant quantity of drug to be released over an extended period of time, resulting in uniform and sustained drug delivery. Zero order is a desired drug release kinetic in antibiotic delivery, the treatment of hypertension, pain management, antidepressant delivery and numerous other conditions that require constant plasma drug levels.[5] Thus, various studies have been undertaken attempting to develop systems that are easily able to provide zero-order or near zero-order drug release[6] . The utilization of geometric principles have for many years been considered and employed in order to modify drug release behavior from non-linear to zero-order or near zero-order release kinetics. Thus far researchers have attempted to control dissolution behavior of drug delivery systems by modifying and controlling the geometry of the employed devices e.g., geometries such as spherical, cylindrical, holed cylindrical and biconvex devices [7].

ORAL ADMINISTRATION

Oral route is the most convenient and usually the safest and least expensive, it is the one most often used.

Advantages [8, 9]

1. Convenient - portable, no pain, easy to take.
2. Cheap - no need to sterilize (but must be hygienic of course), compact, multi-dose bottles, automated machines produce tablets in large quantities.
3. Variety - fast release tablets, capsules, enteric coated, layered tablets, slow release, suspensions, mixtures

Mechanism of absorption: [10, 11]

By passive diffusion through the lipid bilayer, neutral, liposoluble molecules but not those completely insoluble in water.

By secondary active transport, amino acids and sugars, certain peptides.

By complex mechanisms, elements in the form of ions, cations and anions, such as sodium, potassium, calcium, chlorine

The oral route can be used for a local or general treatment:

Local treatment: gastrointestinal protectants of the digestive tract itself, treatment of an intestinal infection or a parasitosis. In this case, one wishes, in general, that the drug will not be absorbed or only poorly absorbed.

General treatment: it is the usual route of administration of drugs and digestive absorption is followed of their diffusion in the body.

TABLET AS A DOSAGE FORM: [12]

Tablet is a solid dosage forms each containing a unit dose of one or more medicaments with or without suitable excipients.

Tablets may be swallowed whole or being chewed. Some are dissolved or dispersed in water before administration. Some are put in oral cavity, where the active ingredient is liberated at a predetermined rate. Implants or passeries may also be presented in form of tablet.

Tablet may vary in shape and differ greatly in size and weight depending on the amount of medicinal substance and the intended mode of administration[2].

Advantages:

Large scale manufacturing is feasible in comparison to other dosage forms. Therefore, economy can be achieved.

Accuracy of dose is maintained since tablet is a solid unit dosage form. Tailor made release profile can be achieved.

Longer expiry period and minimum microbial spillage owing to lower moisture content.

As tablet is not a sterile dosage form, stringent environmental conditions are not required in the tablet department.

Ease of packaging (blister or strip) and easy handling over liquid dosage form.

Easy to transport in bulk. Emergency supply supplies can be carried by patients.

Organoleptic properties (taste, appearance and odour) are best improved by coating of tablet.

Product identification is easy and markings done with the help of grooved punches and printing with edible ink.

Different types of tablets are available like buccal, floating, colon targeting, effervescent, dispersible, soluble, and chewable, etc.

In composition to parenteral dosage form, a doctor or a nurse is not required for administration. i.e. self administration is possible.

In comparison to capsules, tablets are more tamperproof.

Disadvantages:

It is difficult to convert a high dose poorly compressible API into a tablet of suitable size for human use.

Difficult to formulate a drug with poor wettability, slow dissolution into a tablet.

Slow onset of action as compared to parenterals, liquid orals and capsules.

The amount of liquid drug (e.g. Vitamin E, Simethicone) that can be trapped into a tablet is very less.

Difficult to swallow for kids, terminally ill and geriatric patients.

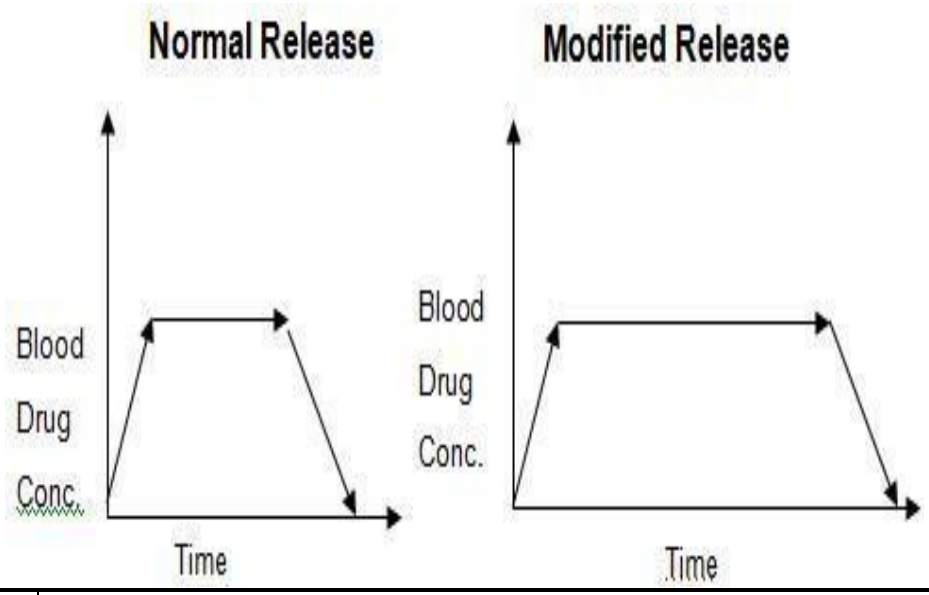
Patients undergoing radiotherapy cannot swallow tablet [13].

Classification of tablets:

To understand each dosage form, tablets here are classified by their route of administration and by the type of drug delivery system they represent within that route.

BENEFITS OF MODIFIED RELEASE TABLETS: [14]

- The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery or targeting the drug to desired site.
- Decreased in dosing frequency
- Reduced peak to trough ratio of drug in systemic circulation.
- Reduced rate of rise of drug concentration in blood.
- Sustained & Consistent blood level with in the therapeutic window.
- Enhanced bioavailability
- Customized delivery profiles
- Reduced side effects.



INLAY TABLETS:

- A type of layered tablet in which instead the core tablet being completely surrounded by coating, top surface is completely exposed. .
- Tablet compressing was done with core rod tooling in which only one surface of core is expose to outside and other drug is incorporated in cup portion.
- While preparation, only the bottom of the die cavity is filled with coating material and core is placed upon it [5].
- The main body portion may consist of an uncoated granulation which is compressed around the enteric coated inlay portion In this modification the main body portion of the tablet is first released and assimilated in the gastrointestinal tract while the enteric coating protects the inlay portion for a predetermined period of time so as to provide time delayed or sustained medication.
- Atoz is offering Inlay tablets with combinations like Metformin 500 mg sustained release (Outer coat) and Pioglitazone 15 mg (core tablet) which has a very unique advantage.
- Ursinos is the marketed inlay tablets containing aspirin.

Advantages of inlay tablets:

- Dosage form comprising of an active ingredient as modified release and an active ingredient as immediate release can be prepared.
- Plasma level can be maintained constant and within the therapeutic window throughout the period of treatment.
- Adverse effects due to sub therapeutic plasma concentration can be avoided.
- The burst effect, namely, large release within a short period of time, is common in highly soluble drugs, and shall be avoided, as it may lead to high concentration of active ingredients in the blood stream.
- Has the ability to release soluble and insoluble drugs at a zero-order rate of release in dissolution media .Dosage frequency of highly water soluble drugs con be reduced providing same efficacy.
- Tablets of different shape such as triangular, rectangular, or capsule shaped tablets can be manufactured.

Advantages of inlay tablets over other compressed tablets:

- Less coating material is required.
- Core is visible, so coreless tablets can be easily detected.
- Reduction in coating forms a thinner tablet and thus freedom from capping of top coating.
- The layered tablet is preferred over compression coated tablet as the surface contact is less and the production is simple and more rapid [15].

SUSTAINED RELEASE ORAL DRUG DELIVERY:

There is a continuously growing interest in the pharmaceutical industry for sustained release oral drug delivery systems. There is also a high interest for design a dosage formulation that allows high drug loading, particularly for actives with high water solubility.

This type of tablets are also called prolonged action tablet, repeat action tablet. In this type of dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response. The remaining fraction is released periodically and is required to maintain the maximum initial pharmacological activity for some desirable period of time in excess of time expected from usual single dose.

The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutic, Pharmacokinetic and Pharmacodynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route.

Sustained release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect.

The sustained plasma drug levels provide by sustained release products often times eliminates the need for night dosing, which benefits not only the patients but the care given as well.. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration.

Oral route has been the most popular and successfully used for sustained delivery of drugs because of convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost of such a system.

The sustained release systems for oral use are mostly solid and based on dissolution, diffusion or a combination of both mechanisms in the control of release of drugs.

They can often be taken less frequently than instant- release formulations of the same drug, and that they keep steadier levels of the drug in the bloodstream.

Advantages: [16, 17]

- Reduce the frequency of dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required, or providing uniform drug delivery.
- It would be a single dose for the duration of treatment whether it is for days or weeks, as with infection, or for the life time of the patient, as in hypertension or diabetes.
- It should deliver the active entity directly to the site of action, minimizing or eliminating side effects.
- This may necessitate delivery to specific receptors or to localization to cells or to specific areas of the body.
- The safety margin of high potency drug can be increase and the incidence of both local and systemic adverse side effects can be reduced in sensitive patient. Considerations for formulation of sustained release formulation:
- If the active compound has a long half-life (over 6 hours), it is sustained on its own.
- If the pharmacological activity of the active compound is not related to its blood levels, time releasing has no purpose.
- If the absorption of the active compound involves an active transport, the development of a time-release product may be problematic.
- Finally, if the active compound has a short half-life, it would require a large amount to maintain a prolonged effective dose. In this case, a broad therapeutic window is necessary to avoid toxicity; otherwise, the risk is unwarranted and another mode of administration would be recommended [8-10].

Problems:

- More complicated formulation may be more erratic in result. A sustained release product may contain a larger dose, i.e. the dose for two or three (or more) 'normal' dosing intervals. A failure of the controlled release mechanism may result in release of a large toxic dose.
- More expensive technology.

IMMEDIATE RELEASE ORAL DRUG DELIVERY: [18,19]

Immediate release formulations are designed to disintegrate and release the drug in absence of any controlling features such as coatings or other formulation techniques. Despite a rising interest in controlled-release drug delivery systems, the most common tablets are those intended to be swallowed whole, disintegrating and releasing their medicaments rapidly in the gastrointestinal tract. A *disintegrant* is a substance in a tablet formulation that enables the tablet to break up into smaller fragments upon contact with gastrointestinal fluids. Such a rapid rupture of the tablet matrix increases the surface area of the tablet particles, thereby increasing the rate of absorption of the active ingredient and producing the desired therapeutic action.

The proper choice of disintegrant and its consistency of performance are critical to formulation development of immediate release tablets. In the past, starch was one of the most widely used, inexpensive, and effective tablet disintegrants. A high concentration of starch is required to bring about effective disintegration. Scientists' search for disintegrating agents with efficient disintegrating properties at relatively low concentrations has led to the development of some new compounds with excellent disintegrating properties.

FORMULATION: [20]

Diluents:

Microcrystalline cellulose, lactose , mannitol , hypromellose , calcium phosphate , calsium sulphate , kaolin , dry starch etc.,

Binders:

Povidone, starch, stearic acid, hydroxyl propyl methyl cellulose, poly vinyl pyrrolidine etc.

Anti Oxidants:

Citric acid, propyl gallate, tocopherol, butyl hydroxyl toluene etc.

Disintegrants:

Starch, cross caramellose, cross povidone, sodium starch glycollate etc.

Coating Polymers:

Seal coat polymers: hydroxyl propyl methyl cellulose, hydroxyl propyl cellulose, poly vinyl pyrrolidine etc.,

Enteric coating polymers: Methyl methacrylate , eudragits , carboxy methyl cellulose , cellulose actate phthalate , hydroxyl propyl methyl cellulose phthalate etc.

Surfactants:

Polyoxy ethylene, castor oil, glycerin monostearate, sorbiton monostearate, polysorbates, macrogols, sodium lauryl sulphate etc.

Lubricants:

Magnesium stearate , zink stearate , calcium stearate , stearic acid , hydrogenated vegetable oil etc.,

Glidants: Talc , colloidal silicon dioxide , corn starch.

Coularants : Brilliant blue and other FDA approved colours

PREPARATION OF INLAY TABLETS: [21]

Preparation of inlay tablets can be done in three steps. They include

- **Preparation of core Tablet.**
- **Preparation of cup portion.**
- **Preparation of inlay tablet.**

EVALUATION OF INLAY TABLETS: [22]

The following standards or quality control tests should be carried out on compressed tablets:

- General appearance
- Content uniformity
- Mechanical strength of tablets
- Disintegration
- Dissolution
- Swelling and erosion test

GENERAL APPEARANCE: [23]

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, color, presence or absence of odor, taste etc.

A. Size & Shape:

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

B. Unique identification marking:

These marking utilize some form of embossing, engraving or printing. These markings include company name or symbol, product code, product name etc.

C. Organoleptic properties:

Color distribution must be uniform with no mottling. For visual color comparison compare the color of sample against standard color.

MECHANICAL STRENGTH OF TABLETS:

A. Hardness:

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes of handling in manufacture, packaging and shipping. Hardness generally measures the tablet crushing strength.

Friability:

Friability of a tablet can determine in laboratory by Roche friabilator. This consist of a plastic chamber that revolves at 25 rpm, dropping the tablets through a Distance of six inches in the friabilator, which is then operate for 100 revolutions. The tablets are reweighed. Compress tablet that lose less than 0.1 to 0.5 % of the Tablet weigh are consider acceptable.

CONTENT UNIFORMITY:[24]

Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablet assayed individually and none may fall out side of the 85 to 115% range.

Weight Variation test (U.S.P.):

Take 20 tablet and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

DISINTEGRATION TEST: [24]

The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screen at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 20 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. Disintegration time: Uncoated tablet: 5-30 minutes Coated tablet: 1-2 hours

DISSOLUTION TESTS: [24]

A) Apparatus-1 (Basket Type):

A single tablet is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor. The basket is immersed in a dissolution medium (as specified in monograph) contained in a 1000 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at 37±0.50C by a constant temperature bath. The motor is adjusted to turn at the specified speed and sample of the fluid are withdrawn at intervals to determine the amount of drug in solutions.

B) Apparatus-2 (Paddle Type)

It is same as apparatus-1, except the basket is replaced by a paddle. The dosage form is allowed to sink to the bottom of the flask before stirring. For dissolution test U.S.P. specifies the dissolution test medium and volume, type of apparatus to be used, rpm of the shaft, time limit of the test and assay procedure for. The test tolerance is expressed as a % of the labeled amount of drug dissolved in the time limit.

SWELLING AND EROSION TESTS [24]

Measurement of swelling and erosion rates of inlay tablets was carried out, after immersion of tablets in the test medium.Weighed tablets (W0) were placed in the closed plastic containers with the mesh underneath the tablets, rotating at specified rpm with the specified conditions of dissolution medium and time.

Each container was removed from the incubator, the tablet with the mesh was withdrawn from the medium and blotted to remove excess water and then weighed (W1) on an analytical balance .The wet samples were then dried in an oven at specified temperature for certain time, allowed cooling in a desiccators and finally weighed until constant weight was achieved (final dry weight, W2).

The experiment was performed in triplicate for each time point and fresh samples were used for each individual time point. The percentage increase in weight due to absorbed liquid or water uptake was estimated at each time point from following equation:

$$\%\text{weight change} = \frac{W_1 - W_0}{W_0} \times 100$$

The percentage remaining of tablets after erosion (ES) was calculated from following equation:

% Remaining = 100 - ES

where percentage eroded (ES) was estimated from the following equation:

$$ES = \frac{W_0 - W_2}{W_0} \times 100$$

Morphological examination of swollen tablets: [26]

Morphological examination of the swollen tablets was carried out using a digital camera equipped with zoom lens EF-S 18–55 mm. Photo imaging was performed on each tablet formulation after hydrating in 0.1 N HCl or pH 6.8 phosphate buffer for 30 min. The tablets were taken out from the medium and were imaged by a digital camera. Under the same optical conditions, an image of a linear scale was used to calibrate.

Measurement of axial swelling:

A single inlay tablet was placed on a glass slide in a petri dish (60 mm in diameter) containing 30 ml of medium specified maintained at given temperature in a thermostatic water bath. The lateral edge of the inlay tablet was photographed at 30 min time intervals for 360 min. The *swelling* distances were measured directly from the photographs using the thickness of the glass slide as a reference.

Measurement of radial swelling:

A inlay tablet was placed in identical conditions as described under axial swelling, but with a standard scale (in mm) placed underneath the petri dish. Visual measurements of the diameter were taken at 30 min time intervals for 360 min over the swelling period.

PATENTS REVIEW: [25]

U.S. Pat. No. 6,001,391 Similarly Jurgen Zeidler et al. described a process for producing solid combination tablets, which have at least two phases. The one of the two phases is processed by melt extrusion technique and contains a water soluble or swellable binder.

U.S. Pat. No. 3,336,200, George M. Krause et. al disclosed a compressed V-shaped center scored double layer tablet , one layer of which contains immediate release Active Ingredient and the other layer contains sustained release Active Ingredient. The tablet is divisible in two equal halves.

U.S. Pat. No. 4,503,031 Similarly Jacob A. Glassman described a super fast starting, slow release medicinal tablet, where in the tablet is comprised of two layers of compressed matrix that are fused together by means of readily dissolvable adhesive substance.

U.S. Pat. No. 6,238,699, Allan A. Rubin described a pharmaceutical dosage form of carbidopa and levodopa where both the Active Ingredients are present as immediate release and sustained release. The formulation is in the form of inlay tablet or bilayered tablet or a capsule containing pellets.

PCT application No. WO 01/72286 Block Jurgen et. al. described a formulation of vitamin composition whereas a beadlet comprises a slow release core coated by a controlled release coating. The sustained release core is coated with an immediate release layer.

U.S. Pat. No. 6,372,254 B1, Richard Ting and Charles Hscao described a press coated, pulsatile active ingredient delivery system which comprises a core of immediate release, enveloped by an extended release compartment.

Patented Inlay Tablet formulations

Pravastatin Sodium (10 mg) + Niacin (500mg)
Pravastatin Sodium (10 mg) + Niacin (1000mg)
Lamotrigine (25 mg) + Sodium Valproate (500 mg)
Lamotrigine (25 mg) + Sodium Valproate (1000 mg)
Rosiglitazone Maleate (2 mg) + Metformin Hydrochloride (500 mg)
Rosiglitazone Maleate (2 mg) + Metformin Hydrochloride (1000 mg)
Rosiglitazone Maleate (4 mg) + Metformin Hydrochloride (500 mg)
Rosiglitazone Maleate (4 mg) + Metformin Hydrochloride (1000 mg)
Glimipride (1 mg) + Metformin Hydrochloride (500 mg)
Glimipride (2 mg) + Metformin Hydrochloride (500 mg)

APPLICATIONS OF INLAY TABLETS: [25,26]

Formulation and development of modified release Inlayered tablet of glimpiride & metformin

The object of the present invention is to provide a dosage form comprising of an active ingredient as modified release and an active ingredient as immediate release.

Biguanides, particularly metformin, improve glucose tolerance but do not stimulate insulin secretion. Sulfonylureas lower blood glucose levels acutely by stimulating the release of insulin from the pancreas, an effect that is dependent upon properly functioning beta cells in the pancreatic islets.

A combination therapy of a biguanide and sulfonylurea has a synergistic effect on glucose control, since both agents act by different, but complementary, mechanisms.

The so-called burst effect, namely, large release within a short period of time, is common in highly soluble drugs, and shall be avoided, as it may lead to high concentration of active ingredients in the blood stream.

A new core-in-cup oral drug delivery system that has the ability to release soluble and insoluble drugs at a zero- order rate of release in dissolution media has been developed .

The core-in-cup tablets were manufactured with the aid of a novel adjustable punch that has the ability to produce cup-shaped tablets of various depth.

Novel Controlled Release Formulation for Highly Water Soluble Drug Tramadol HCl:

Tramadol, a synthetic opoid, is a dual action analgesic agent. Despite a good oral bioavailability (75%) and moderate elimination half life (5.5 hrs), Tramadol needs frequent oral dosing throughout the day (50 mg/4-6 hrs).

High aqueous solubility causes the rapid diffusion of drug from sustained release formulations.

A novel and robust controlled release formulation of Tramadol HCl to reduce the dosing frequency can be prepared.

Developed formulation of Tramadol HCl showed controlled release in-vitro behavior with a release profile of less than 15% for initial two hours (retarding initial burst) followed by a controlled complete release in controlled manner.

Developed formulation could be novel alternative to traditional immediate release formulations of tramadol is stable, convenient to manufacture and cost effective for commercial use.

Preparation of Compound pseudoephedrine hydrochloride sustained-release inlay tablets:

Compound pseudoephedrine hydrochloride sustained- release inlay tablets were prepared by twice-compressing technology using HPMC as the matrix of sustained-release part.

Compound pseudoephedrine hydrochloride sustained- release inlay tablets exhibite prominent sustained-release and rapid release characteristics in vitro.

Naproxen sodium released more than 75% in 0.5 hr, while pseudoephrine hydrochloride released 7%±3.6% in 0.5 hrs, 15.8%±2.3% in 1 hr, 49.5%±3.9% in 4 hr and more than 85% in 8 hr.

1. **A hypnotic tablet with Pentobarbital and Mephenesin**

The outer layer with uncoated granulations is promptly disintegratable for immediate hypnotic

effect and the inlay portion with an enteric coating or envelope around begins to disintegrate after three to four hours to maintain or continue the desired effect.

2. An appetite depressant tablet with Amphetamine sulfate and Amobarbital:

In the outer layer the particles of the granulation are enteric coated to provide slow release over a period of ten to twelve hours. The inlay portion is formed from an uncoated readily disintegratable granulation for immediate therapeutic effectiveness.

3. Inlay Tablets Containing Sumatriptan Succinate and Naproxen Sodium.

4. Rosiglitazone IR + Metformin SR Tablet.

5. An oral decongestant tablet containing Phenylpropanolamine hydrochloride , Pyrilamine maleate and Pheniramine maleate[27].

Fig 1. Drug Administered By Oral Route

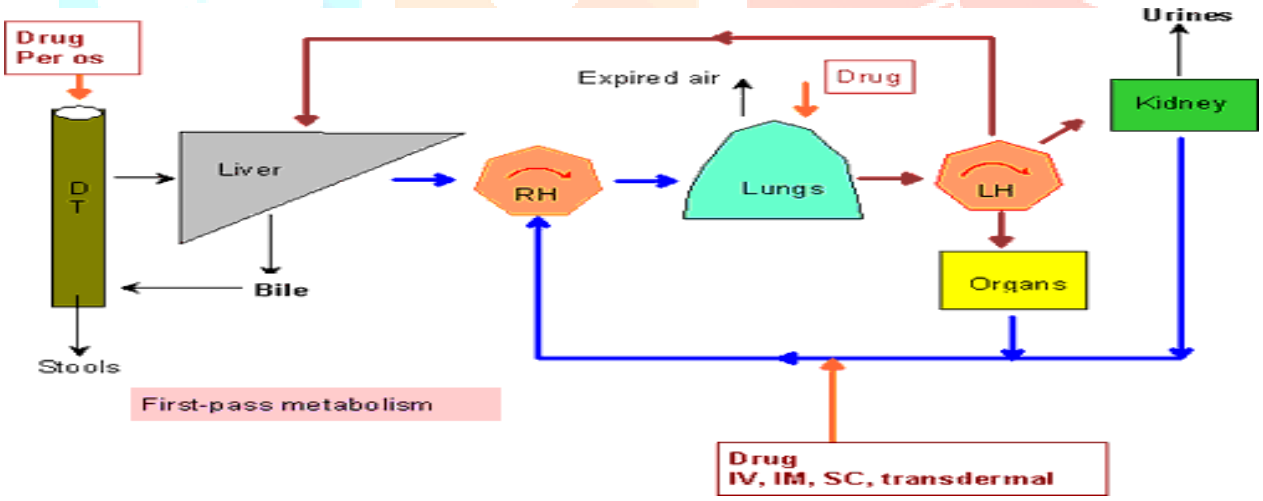


Fig 2. INLAY TABLETS

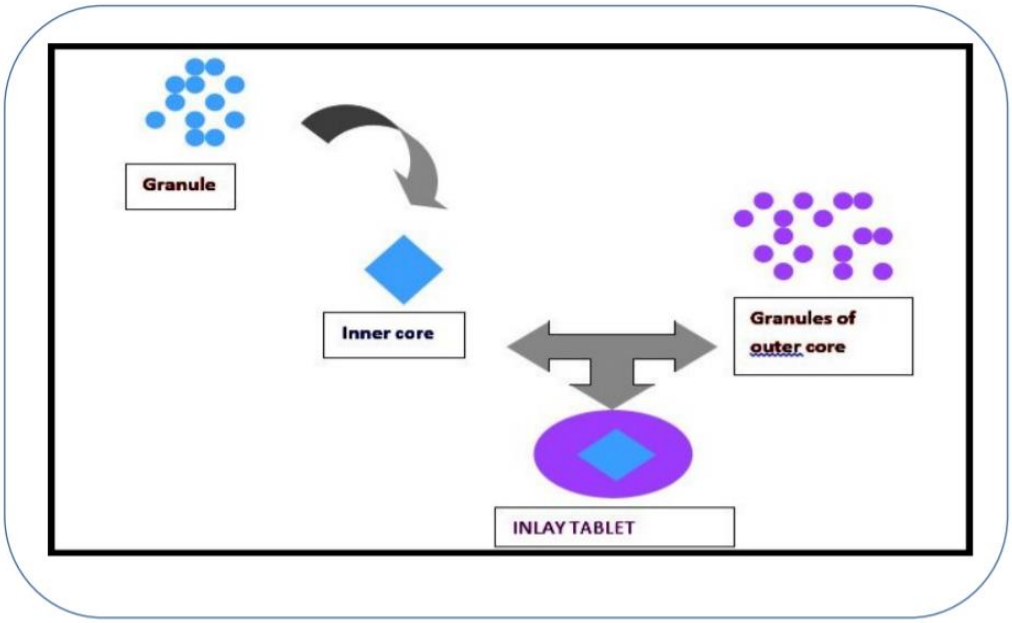


Fig 3. Preparation of Inlay tablet.

CONCLUSION: Inlay tablet is the dosage form consist of an one active ingredient as modified release and other active ingredient as immediate release with the ability to release soluble and insoluble drugs at a zero-order rate in dissolution media. Dosage frequency of highly water soluble drugs can be reduced providing same efficacy. Thus we can prepare any combinations drug with no interactions. Main problems of formulation of drugs like frequent dosing, interactions, burst effect can be reduced.

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