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A COMPREHENSIVE REVIEW ON SUSTAIN RELEASE DRUG DELIVERY MATRIX SYSTEM DEVELOPMENT STRATERGIES

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Abstract:-

Sustained Release Drug Delivery System (SRDDS) is designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effect. Sustain Release of drugs in GI tract following oral administration is not affectected by the absorption process. The current work was focused to formulate & evaluated sustained release formulations Hydroxypropyl & Ethyl cellulose, air matrix polymer can be used in formulation of sustained release dosage forms of slightly water soluble drugs. Drugs excipients compactibility studies have been performed & the tablets have been prepared in seven different formulations with the change in the ratio of excipients. These tablets are evaluated for various parameters including the release of drug by using dissolution.

Key word: SRDDS, Matrix Method, hydrophobic polymer, Hydrophilic polymer, and control release.

Introduction:-

It is refer to the technology utilized to present the drug to the desired body site for drug the desired body site for drug release & absorption. Never discoveries & advancement in technology has led to various new technology has led to various new techniques of delivering the drug for maximum patient compliance at minimum dose & side effects. Sustain release describes the release of drug substance from a dosage or delivery system over an extended period of time. Sustain release systems, which only prolong therapeutic blood or tissue levels of the drug for an extended period of time. In the conventional aliquot quantities of drugs are introduced into the system at specified intervals of the time with the result that there is considerable fluctuation in drug concentration levels.

However, an ideal dosage regimen would be one, which the concentration of the drug, nearly coinciding with minimum effective concentration (M.E.C.)is maintained at a constant level throughout the treatment period. To reduce the frequency of administration and to improve patient compliance, a one daily sustained release formulation of Nefedipine is desirable. Most commanly used method of modulating the drug release is to include it in a matrix system, because of their flexibility hydrophilic polymer matrix system are widely used in oral control controlled drug delivery to obtain a desirable drug release profile, cost-effectiveness and board regulatory acceptance. The natural material have been extensively used in in the field of drug delivery because they are readily available, cost-effective, eco-friendly, capable of multiple of chemical modifications potentially degradable and compatible due to their natural origin. Gum copal (GC) and Gum Damar (GD) are natural resinous material of plant Burseraceous and Shorea wiesneri family Dipterocarpaceae, respectively. The wide applications of GC and Gd propose their strong hydrophobic nature, substantial binding property, compactibility with the physiologic environment and their sustaining property. More ever, melt granulation is one of the most widely applied processing techniques in the array of pharmaceutical manufacturing operations due to its simplicity and easy scale up. In recent year, melt granulation also has been successfully employed to improve the dissolulation rate of poorly soluble compounds increasing the bioavailability of these kinds of drugs and in the development of CR formulation and masking the bitter test of an active drugs.

Need of developing sustained release:

1. Extension of the duration of action.

2. To reduce the frequency of the dose.

3. To improve the Bioavailability of the drug.

4. To minimize the fluctuation in plasma level.

5. To improve the drug utilization.

6. Less adverse effect.

Advantages of the sustained release Dosage form:

1. Control drug therapy is achieved.

2. The rate and extend of drug absorption is achieved.

3. The frequency of drug administration is reduced.

4. Patient compliance is increases.

5. Reduction of the cost of treatment.

6. Improvement of deficiency in treatment.

Disadvantages of the sustain release dosage form:

1. More cost that conventional dosage form.

2. Increase potential of the First pass metabolism.

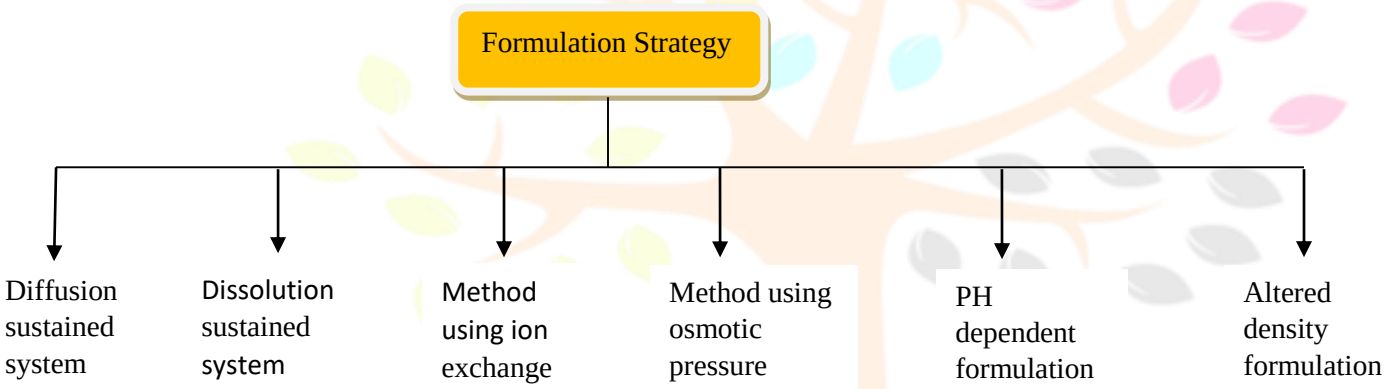
3. Poor invivo and invitro correlation.

4. Possibility of the reduction of the Bioavailability.

5. Dose dumping may occur.

6. Reduce potential for dose administration.

Formulation strategy for development of the oral sustain release drug delivery system:



1. Diffusion sustained system;

It involve passage of the drug molecule from the higher concentration to the lower concentration it give as,

$$J = -Ddc/dx$$

Where, D is the diffusion coefficient area.

dc/dx is the change of conc.

2. Dissolution sustained system:

It contain the polymer which are incorporated along with the drug which releases the drug at slow rate and reduced the dissolution rate by sufficient formation of the drug derivative for drug with high water solubility. Generally that method used to formulate the enteric coated tablet and it get release at the suitable media.

3. Ion exchange method:

In that method drug delivery depend upon the ionic environment of the drug containing resin.

4. Altered density:

Not releasing of all the drug content in GIT causes a limited use, to overcome this method are developed to increase the resident time in the GIT.

5. PH dependent formulation:

Maintain the constant PH, help to make PH-dependent drug release substituent like amino acid, citric acid, tartaric acid. In that method preparation of the buffered sustain release formulation of the simple compound with the one or more buffering agent.

Matrix tablet:

It is the oral solid dosage form in which the drug is homogeneously dispersed or dissolved within the hydrophilic and the hydrophobic polymer. In this system drug are released in a continuous manner by dissolution control and the diffusion control mechanism.

Advantages of the Matrix system:

1. Easy to manufacture.

2. It is versatile, effective and having lower cost.

3. It is implemented for the drug having high molecular weight.

4. Accidently leakage of the drug is less likely occur.

Disadvantage of the matrix system:

1. Delay the onset of action.

2. Increase potential for the First pass metabolism.

3. The release of the drug is affected by the food.

4. The remaining matrix must be removed after the release of the drug.

5. The drug release rate vary with the square root of time.

Classification of the Matrix Tablet:

A. On the basis of retardant material used:

1. Hydrophilic matrix tablet:

It is formulated by the wet granulation of the drug and the hydrophobic matrix material or by the direct

compression of the blended mixture of the active ingredient and the certain hydrophobic carrier.

2. Hydrophobic Matrix:

In this method usually drug release is delayed because of the dissolved drug has to diffused through the capillary network between the compacted polymer particle. In that system drug is directly dispersed within the tablet by the compression of the drug with the plastic material e.g. polyvinyl chloride, ethylcellulose, cellulose acetate and polysterine.

3. Fat-wax matrix tablet:

In this method the drug are incorporated into the fat wax granules by the spray congealing technique, then blend the congealing in an aqueous media with or without aid of the surfactant

4. Biodegradable polymer:

It consist of the biodegradable polymer that are degraded by the enzymatic and the non-enzymatic process into by product is eliminated from the body e.g. polyanhydrides, protein and the polysaccharide.

6. Mineral matrix:

It contain the polymer which are obtained from the various species of seaweeds e.g. alginic acid.

Mechanism of the drug release:

The mechanism involved in the release of the drug include either diffusion or the dissolution. On exposure of the matrix to the aqueous solution leads to hydration take place results to swell the pore, results into dissolution of the content take place and formation of the gel which give rises oppose the liquid entry and causes the disintegration of the matrix.

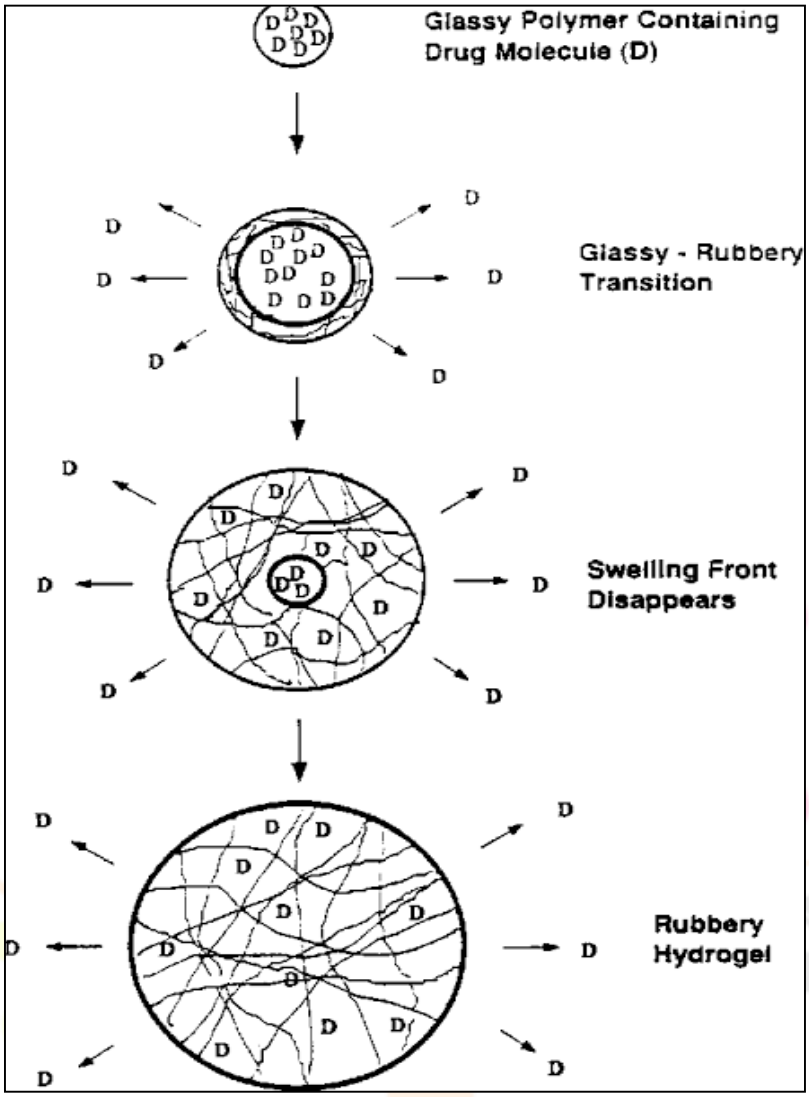


Fig 1 : mechanism of drug release

Material and method:

Polymer used in matrix tablet:

Polymer	**Example**
Hydrogel polymer	Polyhydroxyethylmethylacrylate, cross linked polyvinyl e, polyacrylamide.
Soluble polymer	Polyethylene glycol, polyvinyl alcohol, polyvinylpyrrolidone, Hydroxypropyl methyl cellulose.
Biodegradable polymer	Polylactic acid, polyglycolic acid, polycaprolactone, polyanhydrides, polyorthoester
Non-biodegradable polymer	Polyethylene vinyl acetate, polydimethylsiloxane, polyether urethane, polyvinyl chloride, cellulose acetate, ethyl cellulose.

Mucoadhesive polymer	Sodium carboxy methyl cellulose, polyacrelic acid, tragacanth, methyl cellulose, pectine.
Natural polymer	Xanthum gum, gaur gum, sodium alginate, pectin, chitosan.

Tab no 1: polymer used in the matrix

Methods:-

1. Wet granulation:-Wet granulation technique, drug, PVP and other dry mix materials were passed through 40#sieve.All ingredients were mixed for 15-20 min for uniform distribution of API. Sifted mixture is grousing required amount of water for granulation. The granules obtained were size through #20 mesh. Required amount of Stearic acid, Magnesium stearate and Talc were weighed, passed through #40 mesh and blended with the granules for 5 min. The granules obtained were compressed with 21.00*10.50mm Caplet shaped contains 800 mg of drug and other pharmaceutical ingredients.

2. Melt granulation:-Accurately weigh drugs was melted in a porcelain dish at 55-60 C on heating metal and the accurate quantity of excipient was added to melted of drugs. Then mass was removed from the hot plate and subjected to scrapping until it attained room temperature. The coherent mass was passed through 22 mesh, and the resulting granules were resifted over 44 meshes to separate granules and fines. The % loss of mass during melt granulation was found between 15 and 20 % of total weight. The granules were collected and mixed with talc and magnesium stearate.

3. Method of preparation of Nano sponges:-Each batches of nanospongesnamed as F1-F8 were synthesized, using different ratios of ethyl cellulose and PVA as suggested by the fractional design software by emulsion solvent diffusion method. In this method, two phases were taken into consideration, one being continuous phase consisting required quantity of PVA dispersed in distilled water and required quantity of ethyl cellulose dispersed in dichloromethane, The disperse phase was then added drop by drop into the continuous phase at room temperature and the entire mixture was sonicated for 30 min using ultrasonicator at the predicted sonication intensity given by the factorial design software. Care was taken maintain the temperature conditions using water bath, as sonication for longer period of time dissipated heat which might affect the formulation properties. The solution obtain was then centrifuged using bench top centrifugation at 300rpm for 10 min. Formed Nano sponges were collected and placed in a vacuum oven at 45c for 24 h for solvent evaporation and stored in a desiccator.

4. Direct compression method:

In this process powder material are directly compressed without changing the property of the drug like physical and chemical properties.

Drug	Polymer
aceclofenac	Carbopol 971O, carbopol
Captopril	HPMC, K4M, Ethyl cellulose
Nicorandil	HPMC, Ethylcellulose, Gaur gum, Zanthum Gum, PVP
Tramdol	Xanthum gum, Gaur gum
Ibuprofen	Ethylcellulose, cellulose acetate phthalate.
Nifidipine	HPMC K15M, HPMC E10 PCR premium, sodium alginate, MCC.

Table no 2: some drug formulation with excipient

EVALUTION:-

A) Evolution parameters of Granules:-

1) Angle of Response:-Funnel method was used for Angle of Response of powder. Accurately weight powder blend were taken in the funnel. Funnel height was adjusted in such way that the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel on to the surface diameter of the powder cone was measured and Angle of repose was calculated using the following equation 1.

Tan=h/r..... (1)

2) Density:-

a)Bulk Density(BD):-Weight accurately 25 gm of drug, which passed through 20# sieve, transferred in 100 ml graduated cylinder and read the unsettled apparent volume (Vo) and calculated BD in gm/ml by following equation 2

BD=weigh of powder/bulk volume..... (2)

b)Tapped Density(TD):-Weight accurately 25 gm of drug which passed through 20# sieve, transferred in 100ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 14+-2 mm at a nominal rate of 300 drops per min. Tapped the cylinder for 500 tines initially and measure the tapped volume and read the unsettled apparent volume and calculate TD in gm/ml by following equation 3

TD=weigh of powder/tapped volume..... (3)

3) Carr's index:-It is determined by, simple test to evaluate the BD & TD of powder and rate at which it packed down. The formula for Carr's index is a as below equation 4

Carr's index (%) = [(TD-BD) 100]/TD..... (4)

4) Hausner's ratio:-Hausner's ratio as a number that is correlated to the flow ability of a powder. The formula for Hausner's ratio is below equation 5

Hausner's ratio=TD/BD..... (5)

B. Evaluation parameter for Tablet:

1. Dimension:

The dimension parameter like thickness and diameter are determine using the digital vernier caliper, and it must within range of 0.01.

2. Hardness:

The hardness of the tablet are measured using the Monsanto type. It is in the range of 4-5 kg/cm^{-3}.

3. Friability:

The friability of the tablet was measured by a Roche friabilator. It is amount of powder loss is calculated by the following formula. And it should be not more than 1%. It required the 20 tablet to calculate friability.

% friability = W_0-W/W_0×100.

Where, W_0 is the initial weight of the tablet

W is the final weight of the tablet.

4. Weight of variation:

It is the official method of the evaluation parameter of the tablet. It required the twenty tablet to calculate the weight variation.

5. Uniformity of weight:

Every individual tablet have the uniform weight and weight variation in within the permissible limits. Weight control on the basis of the twenty tablet. The weight are within range of ±1mg.

6. In-Vitro dissolution study:

The release rate of the matrix tablet was determined using the United States pharmacopoeia dissolution testing apparatus II. This test performed using the 900ml suitable solvent and set RPM. Sample withdrawal with the specific time of the interval. This sample are measured under the UV spectroscopy to calculate the amount of drug to be release.

Conclusion:

This article mainly based on the matrix sustain release drug system. From the above discussion of the matrix delivery system it is concluded that these system is more convenient with respect to the patient compliance, drug bioavailability and the with respect to the reducing the dosing frequency, this method is the future scope for the development of the various formulations. It became the large implemented technique.

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