Vol 11, Issue 6, November – December 2023 DOI: https://doi.org/10.31426/ijrpb.2023.11.6.11602

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef DOI: https://doi.org/10.31426/ijrpb Indexed in CAS and CABI, Impact Factor: 0.64

OCUSERTS

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ABSTRACT

A ocusert is an sterile, thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into the cul-de-sac or conjuctival sac, whose size and shape are specially designed for ophthalmic application. The ocular drug delivery system is one of novel drug delivery system which overcomes arise from the conventional dosage form. The domain "Ocuserts" comprises with 4 modules with different matters. Module one deals with Introduction, GMP and GLP. The second Module illustrated with preformulation, criteria for excipient selection, formulation and method of preparation. The third Module describes the evaluation and stability studies. The fourth Module includes package and labelling.

Keywords:

OCULAR DRUG DELIVERY SYSTEM

The novel approach in which drug can instilled into the cul-de-sac cavity of eye is known as ocular drug delivery system (ODDS). Ophthalmic preparations are specialized sterile preparation of dosage forms designed to be instilled onto the external surface of the eye(topical), administered insude (intraocular) or adjacent(periocular) to the eye or used in conjuction with an ophthalmic device. Various strategies for ocular drug delivery are consudered; from basic formulation techniques for improving bioavailability of drugs. ODDS can be mainly prepared as gels, ointments, microspheres, ocular inserts and nanoparticles etc.

ADVANTAGES

1. It increases accurate dosing
2. It provides controlled and sustained drug delivery
3. It provides better housing of drug delivery system

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DISADVANTAGES

1. It is difficult in placement and removal
2. It interferes with vision
3. Dosage form cannot be terminated during pregnancy

OCUSERTS

Ocular inserts are defined as sterile, thin, multilayered, drug-impregnated, solid, or semisolid consistency devices placed into the cul-de-sac or conjunctival sac, whose size and shape are specially designed for ophthalmic application. They are composed of polymeric support that may or may not contain drug. The drug can later be incorporated as dispersion or a solution in the polymeric support. The main objective of the ophthalmic inserts is to increase the contact time between the preparation and the conjunctival tissue, to ensure a controlled release suited for topical or systemic treatment.

Components of Couserts;

- "A central drug reservoir" in which the drug is incorporated in a polymer.
- "Rate controlling membrane" which ensures the controlled release of a medicament from the drug reservoir.
- "An outer annular ring" meant for easy handling and proper insertion.

ADVANTAGES

1. It increases ocular residence time, which results in prolonged drug activity.
2. Increases the bioavailability of the drug.
3. The release rate of drug is in acontrolled manner.
4. Reduction of systemic absorption.
5. Shelf life is increased when compared with aqueous solutions.
6. Improved patience compliance, due to the reduction of frequency of administration.
7. Reduction of visual and systemic side sffects.
8. Better stability.
9. Lack of explosion.
10. Ease of handling and insertion.

DISADVANTAGE

1. Initially discomfort due to their movement around the eye
2. Occasional accidental loss during sleep or while rubbing the eye
3. Difficult placement and intervention with vision
4. It is difficult in placement and removal
5. Interference with vision
6. Expensive

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7. The insert may be lost immediately
8. It may be inconvenient for the patient to retain the ocusert in the eye for the full 7 days
9. It must be checked periodically by the patient to see that the unit is still in place
10. A leakage may occur

CLASSIFICATION

The ocuserts are classified into three types according to their solubility. They are;

1. Insoluble
   a. Osmotic
   b. Diffusion
   c. Contact Lenses
2. Soluble
3. Bioerodible

Insoluble Ocuserts

a. Osmotic Inserts

The osmotic inserts are further divided into two types, in which the first one is the central reservoir compartment surrounded by a peripheral compartment. The reservoir is composed of the drug with or without an osmotic solute dispersed through a polymeric matrix so that the drug is surrounded by the polymer as discrete small deposits.

In the second one, the drug and the osmotic solutes are placed in two separate compartments. The tear fluid diffused into the peripheral compartment through the semi permeable polymeric membrane wets them and induces their dissolution. The solubilized deposits create a hydrostatic pressure against the polymer matrix and causeits rupture in the form of apertures. Then the drug is released through these apertures.

b. Diffusion Inserts

The diffusion systems are composed of a drug reservoir enclosed in a specially designed semi-permeable or microporous membrane, which allows the release of drug by diffusion method from the reservoir. The drug release is controlled by the lachrymal fluid, which permeates through the membrane. Sufficient internal pressure is achieved to drive the drug out from the reservoir. The drug delivery rate is controlled by diffusion through the membrane.

c. Soft Contact Lenses

These are made up of covalently cross-linked hydrophilic polymers. It forms a three-dimensional matrix capable of retaining water, aqueous solution or solid components. When the hydrophilic

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contact lenses is soaked into a drug solution, it absorbs the drug, but it does not deliver the drug as precisely as that provided by other non-soluble ophthalmic systems.

Soluble Ocuserts

Soluble inserts correspond to the oldest class of ocular inserts, which offer the advantage of being completely soluble at the application site. So, there is no need to remove from the site of application. It is prepared by using either natural polymers like collagen or synthetic/semisynthetic polymers. In this type, the therapeutic agent is absorbed by soaking the insert in a solution containing the drug, and drying and rehydrating it before use in the eye. The release of the drug will start when tears penetrate the ocular insert and the drug release is by diffusion technique.

Bioerodible Ocuserts

The bioerodible inserts are composed of homogeneous dispersion of a drug that can be included in or not included in the hydrophobic coat made of bioerodible polymers, which is impermeable to the drug. Drug release from such a system is due to the contact of the device with tear fluid, inducing superficial bioerosion of the matrix.

GOOD MANUFACURING PRACTICES

Current Good Manufacturing Practices (cGMP or GMP) regulations are established by the Food and Drug Administration (FDA) to ensure that the minimum standards are met for drug product quality in the United States. The cGMP regulations establish requirements for all aspects of pharmaceutical manufacture.

PRINCIPLES OF GMP

- Create Standard Operating Procedures (SOPs)
- Enforce / Implement SOPs and work instructions
- Document procedures and processes
- Validate the effectiveness of SOPs
- Design and use working systems
- Maintain systems, facilities, and equipment
- Develop job competence of workers
- Prevent contamination through cleanliness
- Prioritize quality and integrate into workflow
- Conduct GMP audits regularly

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ELEMENTS OF GMP

1) Quality management
2) Personnel
3) Contracts
4) Purchasing
5) Premises and equipment's
6) Documentation
7) Production
8) Quality control
9) Complaints and recall
10) Self-Inspection

COMPONENTS OF GMP

1. People

All employees are expected to strictly adhere to manufacturing processes and regulations. A current GMP training must be undertaken by all employees to fully understand their roles and responsibilities. Assessing their performance helps boost their productivity, efficiency, and competency.

2. Products

All products must undergo constant testing, comparison, and quality assurance before distributing to consumers. Manufacturers should ensure that primary materials including raw products and other components have clear specifications at every phase of production. The standard method must be observed for packing, testing, and allocating sample products.

3. Processes

Processes should be properly documented, clear, consistent, and distributed to all employees. Regular evaluation should be conducted to ensure all employees are complying with the current processes and are meeting the required standards of the organization.

4. Procedures

A procedure is a set of guidelines for undertaking a critical process or part of a process to achieve a consistent result. It must be laid out to all employees and followed consistently. Any deviation from the standard procedure should be reported immediately and investigated.

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5. Premises

Premises should promote cleanliness at all times to avoid cross-contamination, accidents, or even fatalities. All equipment should be placed or stored properly and calibrated regularly to ensure they are fit for the purpose of producing consistent results to prevent the risk of equipment failure.

GOOD LABORATORY PRACTICES

- In pharmaceutical laboratories, GLP should be followed. Following are the main points those should be considered under GLP:
- The laboratory should be located designed, customized and maintained to suit the performance of all Q.C. test and analysis required
- Conveniently located to service the manufacturing dept. but preferably separate to avoid vibration, dust, internal and external traffic to protect the delicate instruments.
- As far as possible there must be separate wings for analytical, instruments, microbiology and sterility etc. And all wings may be interconnected with the internal door
- There must be an effective air lock, provisions for A.C. and fumigation chamber, the laboratory should be so designed that not only adequate provision of space but provision for utility, water, solvent storage, extraction dust collection etc. were covered.
- Laboratory furniture so designed to provide for adaptability, tabletop must be covered properly resistant to acid, alkali and solvent. The floor should be smooth, easy to clean and adequate drainage facility.

Equipment

- There must be written SOP for each instrument. The instrument should be located with an adequate place in a separate room under controlled temperature. The instrument must be handled with care and should be cleaned.
- The calibration and maintenance record must be done periodically
- The glassware must be calibrated with certified one before use. Particularly the glassware which is supposed to be utilized for measuring purpose must need calibration before use. All the necessary instruction regarding operating, handling and care should be display near the instruments. The light should be adequate
- The electrical system in the laboratory must not be overloaded. Voltage stabilizer must be provided to protect delicate instruments.

Chemical Reagents

- Storage of chemicals and reagent should be done in a manner it involved in the use, the container of all chemicals and reagents must be properly labeled. Transfer of chemical must be done almost care. All analytical reagents and a prepared solution must be labeled. Records of Molar Solutions entered in the register prepared for the same.

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Organization And Personnel

- Every individual who is a part of the laboratory and engaged in the conduct of testing shall have the requisite educational qualification, training, and experience to enable the individual to perform the assigned function.
- There shall be sufficient and a number of personnel for the proper conduct of the studies in accordance with protocols. The personnel should take adequate precautions to avoid contamination of test and control article of the test systems.
- The personnel should be provided with appropriate clothing suiting to their needs and the clothing should be of nature, which will prevent microbiologically chemical contamination
- The personnel should be subjected to proper medical examination to ensure that there will not be a source of contamination and their health status.

Documentation

- The document is a critical factor of the good laboratory practice. Documentation is the accepted method of recording information for future reference. The major documents that need to be provided are protocols, logbook for usage, maintenance, and calibration of equipment there should be well established SOPs.

Quality Control

- There must be a well-defined procedure, which covers all the aspects pertaining to the sample i.e., receipt of the consignment, sampling techniques to be adopted, storage and handling of samples recording and reporting of analysis. Every sample that is received must have a distinctive number, which should appear on the label of the sample and should be stored in the prescribed conditions.
- There must be a well-defined sampling procedure in place, which should categorically specify in detail the sampling procedure. If the blending of the sample is permitted, how many can be blended together etc.

Protocol And Conduct of Laboratory

Each laboratory should develop a well –defined protocol to carry out the test and the protocol should categorically mention.

Records and Reports

Every laboratory should maintain records of all the tests performed any of the graphs pertaining to IR, HPLC, etc. should be stored along with the raw data. For a quick reference, the access to records should be restricted to an authorized person and these records are preferably stored under lock and key.

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Laboratory records are again classified as:

1. Batch Record

A batch record is a document that provides the complete manufacturing history of a pharmaceutical product. It aims to assure the safety and quality of the manufactured product by: Providing processing instructions to the operator during the execution of a manufacturing processes.

2. Master Batch Record

Master batch records provide drug development and manufacturing companies with step-by-step instructions for how to manufacture drugs. These records act as guidelines to help manufacturers maintain quality, safety, and reliability of a specific therapy.

3. Batch Manufacturing Record

A batch manufacturing record is a written record that documents the entire manufacturing process and the history of a product batch.

PREFORMULATION STUDIES

Pre formulation studies were performed on the procured drug samples and excipients with respect to the description, melting point, solubility, IR spectra, ultraviolet (UV) spectroscopic studies, and Differential Scanning Calorimetry.

NEED OF PREFORMULATION STUDY

Preformulation study is a phase which is initiated once the new molecule is seeded. In a broader way, it deals with studies of physical, chemical, analytical, and pharmaceutical properties related to molecule and provides idea about suitable modification in molecule to show a better performance.

A) IDENTIFICATION AND CHARACTERIZATION METHODS FOR DRUG

a) Organoleptic Properties

ocuserts were evaluated for the organoleptic characterization i.e. texture, appearance, odour and colour.

b) Melting Point Determination

Melting point of the drug sample was determined by using capillary tube method using melting point apparatus (Macro Scientific Works) by filling the drug sample in 3 separate capillaries. The samples were heated slowly and observed continuously for most accurate results. The melting range was recorded which begins when the sample first start to melt and ends when the sample is completely melted.

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c) Solubility Analysis

The solubility analysis for drug includes solubilization, thermal effect, common ion effect.

d) Stability Analysis

The stability analysis for drug includes solution-state stability testing, solid-state stability testing and drug-excipient compatibility study.

e) FTIR Spectrum

FTIR spectra of pure drug, polymer Sodium Carboxy Methyl Cellulose, and combination of drug and Sodium Carboxy Methyl Cellulose were carried out to check compatibility of drug with excipient. Solid powder samples were oven dried at around 3000 C, finely crushed, mixed with potassium bromide (1:10 ratio by weight) and pressed at 15000 psig to make disc. The pellets were then scanned using FTIR spectrophotometer . The wavelength ranged from 500 to 4500 cm-1 with a resolution of 4 cm-1. The FTIR spectra of mixture were compared with the FTIR Spectra of pure drug and pure polymer for important peaks.

B) EXCIPIENT-DRUG COMPATIBILITY STUDY

Studies of actual pharmaceutical drug and active excipient suitability represent a major stage in the design or development of the improvement of all dosage forms or drug delivery systems, one of which is the actual pharmaceutical drug or active pharmaceutical ingredient (API).

FTIR Spectroscopy

FTIR is another analytical technique used in compatibility assessment based on the same functional group change during drug-excipients interaction. If there is band shift and broadening in the functional groups as compared to the spectrum of the pure active drug in the FTIR spectrum, there is an interaction between active drug and excipients Fourier Transform Infrared Spectroscopy (FT-IR) Compatibility between the active drugs and worked excipients used were studied by using FTIR spectroscopy.

DSC Analysis

DSC is a highly sensitive technique, used widely in the pharmaceutical to determine the thermal transitions of API's and excipients. Drugs-excipient compatibility study was done on the stored mixture (kept at 50°C for 4 weeks) by the DSC curve of heat flux versus temperature or versus time at a rate of 50°C min-1 from 50 to 200°C temperature range under nitrogen flow of 25 ml min-1 to determine the melting temperature ™.

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SEM Analysis

The morphology of inserts was studied using a Quanta 200 ESEM scanning electron microscope (SEM). The samples were prepared by freezing the inserts in liquid nitrogen. Next, the surfaces of the inserts were analyzed. The devices were analyzed at suitable acceleration voltages using varying magnification for each sample. Representative micrographs were taken.

C) CRITERIA FOR EXCIPIENT SELECTION

The purpose of formulation development is to ensure that the drug is safe, effective, stable, and convenient to use. If the dosage form is improperly selected and if the prescription and process design are unreasonable, it will have a certain impact on the quality of the drug product, and even affect the drug's efficacy and safety. Therefore, formulation research occupies a very important position in drug development. Excipients are the general term for other materials in preparations except for the main drug, and are an important part of pharmaceutical preparations.

General Principles for The Selection of Excipients

Excipients can be selected according to the characteristics of the dosage form and the needs of the route of drug administration. The excipients used should not have an adverse interaction with the main drug, and should not affect the content determination of the preparation and the inspection of related substances. Also, the excipients required for the production of drugs must meet the requirements for medicinal use.

The ideal characteristics of an excipient are given as under: -

An excipient must be:

- Chemically stable
- Non-reactive
- Low equipment and process sensitive
- Inert to human body
- Non-toxic
- Acceptable with regards to organoleptic characteristics
- Economical
- Having efficiency in regards with the intended use

Some of the examples of excipients includes:

- Surfactants
- Buffers and pH regulation agent
- Isotonicity adjusting agent
- Antioxidants
- Preservatives

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D) FORMULATION OPTIMIZATION TECHNIQUES

Optimization is selecting the most suitable element from available decisions in any resources considering all the factors which in experiment. Various techniques of optimization Quality by Design enhances the assurance of safe and effective drugs to consumer and promise to improve manufacturing quality performance and also product free of t as in the label to the contamination and gives the desired benefits to consumer. Design of equipment is systemic planning and performing studies that change the experimental variables to determine their effect on a given response. Optimization techniques to examine various problems that occur design are used during the research. If the experiments in the production are carried out randomly then results obtained will be random, so we need to plan the experimental process such that relevant information is obtained.

Optimization is necessary because:

- It reduces the cost
- It provides safety and reduces error
- It provides innovation and efficacy
- It saves the time

PARAMETERS OF OPTMIZATION

Parameters of optimization is divided into two main types:

1. Problem Type

There are two general types are there in the problem type of optimization technique:

a) Constrained

These are the restrictions placed on the system by physical limitations.

Eg: Economical considerations

b) Uncontrained

In this system the problems involving uncomplicated or artless pharmaceutical preparations or processes.

2. Variables

Mathematically, they can be divided into two types:

a) Independent Or Primary Variables

This type of variable comes under the composition of the selected ingredients i.e; Excipients and drugs.

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b) Dependent or Secondary Variables

The formulator has no direct control over this type of variable. They are reliant on an unrelated variable. These are responses like flow property etc.

FORMULATION OF OCUSERTS

In addition to active ingredients, ocusert contains a number of inserts materials known as excipients.

Different excipients are:

EXCIPIENT	USE
Surfactant	It reducing the systemic drainage and improving the residence time, which further enhances the ocular bioavailability of drug.
Buffers	Buffers are needed to stabilize the pH at a level at which drugs are soluble, active and tolerable.
Isotonicity adjusting agent	To reduce the irritation
Antioxidants	To reduce the oxidation of specific substrates
Preservatives	It discourages growth of bacteria.

Formulation methods of ocuserts

- **Solvent Casting Method**

Due of its cost-effectiveness and simplicity, solvent casting is utilized to make ocuserts. In this procedure, rheological properties of polymer are examined since they impact ocusert thickness, drying rate, homogeneity, etc. De-aeration is needed because polymer mixing might create air bubbles. Polymers are casted onto the correct substrate after adequate mixing. After the mixture dries, the solvent evaporates, leaving the ocusert film. Then, ocusert films are trimmed to size.

- **Glass Substrate Technique**

Glass substrate technology is utilized to produce thin films. A transparent polymer solution is utilized to form a drug reservoir film. The polymer solution is vortexed to mix in the medication. Drug dissolution is followed by plasticizer addition. To make films, solution is added to a glass mould and dried. Drying at room temperature takes 24 hours. Dried films are then trimmed to size and then stored.

- **Melt Extrusion Technique**

Melt extrusion is an alternative for solvent casting. It is utilised for non-organic solvents. In this process, polymers and other components are melted and then passed through a die to prepare films. The films are then trimmed. This approach isn't for thermolabile substances.

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EVALUATION OF FORMULATION

Uniformity of Thickness

The ocusert's uniform thickness facilitates the even dispersion of components. A micrometer screw gauge is utilized to determine uniform thickness.

Uniformity of Weight

The ocusert's weight homogeneity shows how constant its constituents are. Three ocuserts are weighed from each batch. Mean weights are recorded.

Drug Content

Drug content measures active substances in each formulation. Ocusert is dissolved in 10 ml STF. UV visible spectrophotometer is used to estimate absorbance value after proper dilutions.

Swelling Index

Swelling index measures a formulation's swelling or water-absorption characteristics. Ocusert is weighed and added to 4 ml of STF. After 5 minutes, the ocusert is removed and excess simulated tear fluid is weighed.[38] The % swelling index can be calculated by the formula given below

%Swelling index = (Weight of swollen ocusert after time t – initial weight of ocusert) ÷ Initial weight of ocusert*100.

Sterility Test

This test uses Indian Pharmacopoeia. 2 ml of ocusert solution is aseptically transferred to fluid thioglycolate and soyabean-casein digest media. During 14 days, fluid thioglycolate media must be kept at 30 °C to 35 °C, and soyabean casein digest medium at 20 °C to 25 °C.

Stability Study

Stability study is done following ICH guidelines. Increasing a product's temperature speeds up its breakdown, determining its shelf life, variation in medication concentration, colour, folding endurance, etc. may be tracked during stability experiments.

In-Vitro Drug Release Studies

The in-vitro drug release from the different ocular inserts was studied using the classical standard cylinder tube fabricated in the laboratory. A simple modification of glass tube of 15mm internal diameter and 100mm height. The diffusion cell membrane was tied to one end of open cylinder which act as a donor compartment. An ocular insert was placed inside this compartment. The diffusion cell membrane acted as corneal epithelium. The entire surface of the membrane was in contact with the receptor compartment comprising of 12ml of simulated tear fluid ph (7.4) in a 50ml

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beaker. The content of receptor compartment was stirred continuously using a magnetic stirrer and temperature was maintained at 37±0. 5˚c.At specific intervels of time,1ml aliquot of solution was withdrawn from the receptor compartment and replaced with fresh buffer solution. The aliquot was analyzed for the drug content using UV spectrophotometer at 296nm after appropriate dilutions against reference using simulated tear fluid pH 7.4 as blank.

In-Vivo Drug Release Studies

Out of 5 batches of formulations F-5 and F-8 were taken for in vivo study on the basis of in vivo drug release studies. The ocuserts were sterilized by using UV radiation before in vivo study. The ocusert and other materials were exposed to UV radiation for 1 hour. After sterilization, occuserts were transferred into polyethylene bag with the help of forceps inside the sterilization chamber itself. The pure drug that was sterilized along with ocuserts was analyzed for potency by UV spectrophotometer at 254 nm after suitable dilution with pH 7.4 phosphate buffer.

Albino rabbits of either sex (New Zealand strain), weighing between 2.5-3.0 kg, were used for the experiment. The animals were housed on individual cages and customized to laboratory conditions for one day.

Percentage Moisture Absorption

The percentage moisture absorption test was carried out to check physical stability or integrity of ocular films. Ocular films were weighed and placed in a desiccator containing 100 ml of saturated solution of aluminium chloride, and 79.5% humidity was maintained. After three days the ocular films were taken out and reweighed. The percentage moisture absorption was calculated using the following equation:

Percentage moisture absorption=Final weight-initial weight*100

Percentage Moisture Loss

The percentage moisture loss was carried out to check integrity of the films at dry condition. Ocular films were weighed and kept in a desiccator containing anhydrous calcium chloride. After 3 days, the ocuserts were taken out and reweighed; the percentage moisture loss was calculated using the following equation:

Percentage moisture loss=Initial weight -Final weight*100

Ocular Irritation

The potential ocular irritation and damaging effects of the ocuserts under test were evaluated by observing them for redness, inflammation or increased tear production. Formulation was tested on five rabbits by placing the inserts in the cul-de-sac of the left eye. Both eyes of rabbits under test were examined for any signs of irritation before treatment and were observed up to 12 hours.

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STABILITY STUDIES

This is done to chek the physical stability or integrity of the ocuserts in humid conditions.

The selected ocuserts were stored at different temperature conditions which include,

- Refrigeration temperature (5 ± 0.5°C).
- Room temperature (30 ± 0.5°C) and a temperature of (40 ± 0.5°C) for 3 months to evaluate the physical stability according to ICH guidelines.

IMPORTANCE OF STABILITY STUDY

- Product instability of active drug may lead to under medication due to the lowering of the drug in dosage form.
- During the decomposition of the drug or product it may lead to toxic products.
- During the marketing from one place to another during the transportation the drug has the compatibility to change its physical properties.

STABILITY TESTING METHODS

1. Real time Stability Study

It is normally performed for a long duration of time to allow significant degradation of the product under the storage conditions recommended. The period of time for the test of the product depends on the stability of the product.

2. Accelerated Stability Study

The accelerated stability studies are carried out to predict the degradation that occurs over prolonged periods of storage, at normal conditions. The films of the insert are taken in a separate petri dish and are kept at three different temperatures 400˚C,500˚C and 600˚C, and the time taken for degradation of the ocular inserts is checked.

3.Retained Sample Stability Testing

These studies are done under room temperature and at refrigerator temperatures. In this type of testing, the stability is done by selecting one batch for a year. If the number of samples exceeds more than 50 the they are divided into two batches. The samples stability studies help to predict the shelf life. The maximum shelf life of every product predicted could be 5 years which is conventional to the test samples at 3,,9,12,18,24,3,48 and 0 months. This method of testing is also known as constant interval method.

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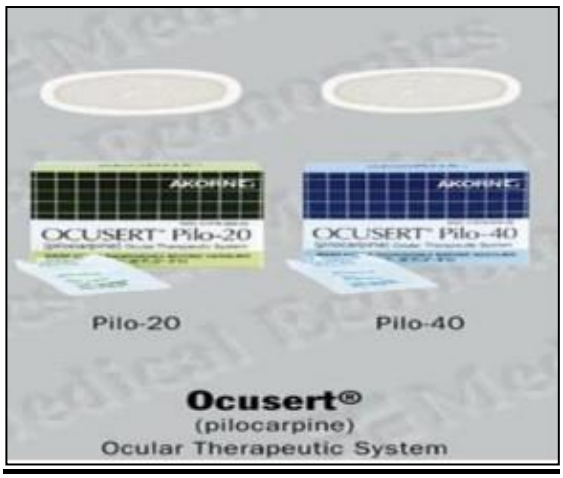
4.Cyclic Temperature Stress Testing

This method is not so much used to the sampling of the products. In this method, cyclic temperature stress tests are designed knowledge of the product so as to mimic likely conditions in the market place storage. In this testing the sampling is considered to be conducted by a cycle of 24 hours which is known as the rhythm of the earth is 24 hours.

PACKAGING OF OCUSERTS

- Ophtalmic inserts 5mg supplied in packages of 60 sterile unit dosage form.
- Each wrapped in an aluminium blister.
- With two reusable applicators.
- A plastic storage container to store the applicators for use.



LABELLING OF OCUSERTS

Labelling of ocuserts is crucial for proper identification, usage and regulatory compliance.it typically includes:

1. PRODUCT INFORMATION:
   Name of ocuserts, active ingredients, strength, dosage and formulation.
2. MANUFACTURER INFORMATION:
   Name, address and contact details of the company producing the ocusert.
3. BATCH OR LOT NUMBER:
   Unique identification for traceability and quality control.
4. EXPIRATION DATE:
   Indicates the end of the products shelf life.

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)
CrossRef DOI: https://doi.org/10.31426/ijrpb Indexed in CAS and CABI, Impact Factor: 0.64

5. USAGE INSTRUCTIONS:
   How to apply the ocusert, frequency and any specific instructions for use.
6. STORAGE CONDITIONS:
   Recommendations for proper storage to maintain efficacy.
7. WARNINGS/PRECAUTIONS:
   Important safety information or potential side effects.

   Adherence to regulatory standards and guidelines is essential in the labelling process to ensure accurate information for users and compliance with laws governing pharmaceutical product.

CONCLUSION

A detailed study was conducted on ocular drug delivery system (ocuserts). Ocuserts are defined as sterile, thin, multilayered, drug-impregnated, solid or semisolid consistency devices placed into the cul-de-sac or conjuctival sac, whose size and shape are specially designed for ophthalmic application. In this study we describe GMP and GLP requirements of ocuserts. The pre-formulation studies like identification and characterization method of drug, excipient drug compatibility studies, criteria for excipient selection, formulation and optimization techniques and formulation were also studied. The methods of preparation like solvent casting method, glass substrate technique, melt extrusion technique are studied. Evaluation of ocuserts was studied. And we studied stability studies, SOP's, packaging and labelling of ocuserts.

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