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Review on Mucoadhesive Buccal Patches

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ABSTRACT

When medication is administered buccal (via the internal jugular vein), it bypasses the hepatic first pass metabolism and enters the systemic circulation directly, offering excellent bioavailability. For the distribution of systemic medications, the buccal route is an ideal mode of administration. Because buccal bio adhesive films distribute topical drugs into the mouth cavity at a programmed, slow rate, they provide definite advantages over conventional dosage forms for the treatment of numerous disorders. Drug formulations known as buccal patches typically have an alternative delivery method that involves the buccal mucosa. By sandwiching the material between the cheek and upper gingiva, it can be utilised to treat both local and systemic conditions (gums). Buccal patches are easily accessible by the lining membranes of the oral cavity.

KEY WORDS : BUCCAL PATCHES

INTRODUCTION TO BUCCAL PATCHES

Buccal patch is a non-dispersible, thin-matrix modified release dosage form. composed of one or more polymer films or layers containing the drug and/or other excipients. The patch may have a muco adhesive polymer layer that sticks to the gingiva, teeth, or oral mucosa to allow for controlled release of the drug into the oral mucosa (unidirectional release), oral cavity (unidirectional release), or both (bidirectional release). The patch is removed from the mouth and disposed of after a set period of time.

TYPES

1. Matrix type (Bi-directional):

The buccal patch has a matrix pattern and contains the drug, adhesive, and additives. Medication is also administered into the oral mucosa by bi-directional patches. The buccal patch has a matrix pattern and contains the drug, adhesive, and additives. Medication is also administered into the oral mucosa by bi-directional patches.

2. Reservoir type (Unidirectional):

The buccal patch with reservoir design has a cavity where the medication and additives are maintained separate from the adhesive. An impermeable backing is inserted to prevent medication loss, reduce distortion and patch disintegration while in the mouth, and control the drug's distribution route.

ADVANTAGES

1. Increased patient compliance as a result of the injections' related pain being eliminated.
2. It is possible to attain a comparatively quick commencement of action in contrast to the oral route.
3. If it becomes necessary to stop therapy, the formulation can be eliminated.
4. Enhance the efficacy of numerous medications due to their extended duration of contact with the mucosa.
5. The dose form has a longer residence time at the absorption site, which raises the bioavailability.

DISADVANTAGES

1. The amount of surface area that can be absorbed is limited.

2. Drugs that irritate the mucosa, taste bitter or unpleasant, or have an offensive odour cannot be administered using this route.

3. For medications that are unstable at the pH of the buccal environment, this route is inappropriate.

4. The medication is subsequently diluted as a result of the saliva's constant secretion (0.5-2 l/day).

5. It is challenging to give drugs in big doses.

PREFORMULATION

The study of the chemical and physical properties of pharmaceuticals before formulations is known as preformulation, which comes from the terms "pre" for before and "formulation," for formulating or producing the substance.

A. IDENTIFICATION AND CHARECTERISATION METHOD OF BUCCAL PATCHES

There are several parameters that are to be studied before development of any formulation.

1. **Organoleptic properties** :

Basically, it refers to the process of identifying a substance through taste, sight ,and touch. Shape, colour ,and taste are the examples of qualities.

2. **Melting point determination**:

Includes determining the point in temperature at which a drug becomes a liquid instead of a solid. Once the sample is within the capillary, cover it with a flame for two to three minutes to seal the aperture. The sample was inserted into the capillary and placed inside the melting point apparatus. The melting point of a drug is the temperature at which it transitions from one state to another.

3. **IR for identification of drug**:

The drug molecule can be identified using the FTIR spectra of the sample and the standard. The drug was identified using the KBr pellet method.

4. **Determination of solubility**:

Measuring a drug's solubility in a range of solvents, including water, methanol, and chloroform. A beaker holding a little amount of medication was filled with 5–10 ml of solvent to create a saturated solution. The samples were stored for 24 hours at room temperature before being filtered, diluted, and examined for the presence of any undissolved particles.

5. **UV absorption maxima:**

The substance was identified using the UV spectrophotometric technique. From the drug's spectrum, the maximum was noted. The calibration curve was constructed using the spectral data from this scan.

B. EXCIPIENT DRUG COMPATIBILITY STUDY

When two or more chemicals are mixed, incompatibility results, which can be determined by physical, chemical, and/or medicinal properties. It might have an impact on the dosage form's appearance, efficacy, and safety.

Differential scanning calorimetry (DSC) :

There is a comparison between the DSC curves of pure components and those obtained from a 1:1 physical combination. Significant changes in the components' melting points, the emergence of a new exo- or endothermic peak, and/or adjustments to the associated enthalpies of reaction within the physical mixture indicate incompatibility..

Fourier –transform Infrared spectroscopy (FT-IR) :

FT-IR is another analytical technique that uses the same functional group change that takes place when the medication and excipient interact to determine compatibility. If the FTIR spectrum exhibits band shift and broadening in the functional groups relative to the spectrum of the pure active drug, there is an interaction between the excipients and the active drug. Fourier Transform Infrared Spectroscopy (FT-IR) The compatibility of the active drugs and the working excipients was examined using FTIR spectroscopy**.**

C. CRITERIA FOR EXCIPIENT SELECTION.

When choosing excipients for a patch, one should consider the intended formulation, method, qualities of the API, and any potential effects on the formulation.

The polymer matrix needs to meet these requirements.

The molecular weight and chemical activity of the polymer should allow a certain medication to diffuse and be released through it properly. It must be easy to create and fabricate into the necessary productive form, stable, and not react with the medication.

The adhesive needs to meet the following requirements.

- There shouldn't be any residue that can't be cleaned up.It ought to be simple to delete.
- Stick to the skin when the dose is being administered.
- Avoid irritating or oversensitizing the skin.
- It is necessary for the backing membrane to match the formulation3.

D. FORMULATION AND OPTIMIZATION TECHNIQUES

- • The definition of optimise is "to make perfect."
- In terms of formulation and processing, it is utilised in pharmacies. It is also involved in the development of drug products in many forms.
- It is the process of determining how best to use the resources already available while accounting for every aspect that affects the choices made during an experiment.
- It is necessary because of,

1. It reduces the cost.

2. It provides safety and reduces the error.

3. It provides innovation and efficacy.

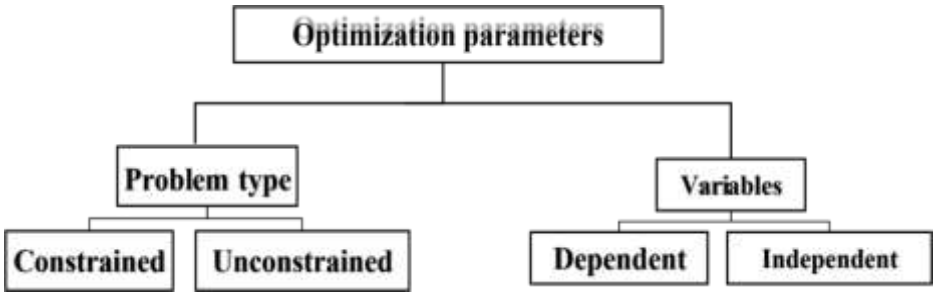

FIG.1: Optimization parameters

PROBLEM TYPE

1. Unconstrained

This approach does not impose restrictions based on tangible limitations. For example, one may want to allow an uncoated tablet to be used with a specific drug delivery system.

2. Constrained

The limitation in this system stems from physical constraints. Making the uncoated pill that won't dissolve in the stomach is hence the limited issue.

VARIABLE TYPE

1. Independent variables

This type of variable is come under the supervision of a formulator like the force of compression, lubrication level, binder level etc.

2. Dependent variables

The formulator has no direct control over this type of variable. They are reliant on an unrelated variable. These are responses like hardness, flow property, and friability, among others .

FORMULATIONS

The basic components of buccal bioadhesive drug delivery system are:

1. Active Pharmaceutical Ingredient

2. Mucoadhesive polymers

3. Backing membrane

4. Penetration enhancers

5. Plasticizer.

1. ACTIVE PHARMACEUTICAL INGREDIENT (API):

The interaction between API and mucosa must be expanded and improved in order to obtain the desired therapeutic effect for buccal medicine delivery. The degree to which the drug diffuses between the patch and the buccal mucosa depends on key pharmacological properties such as molecular weight, chemical functionality, and melting point.

2. MUCOADHESIVE POLYMERS:

Muco-adhesives, which are polymers, either natural or synthetic, interact with the mucus layer covering the mucosal epithelial surface and the main molecules that constitute a large component of mucus.

Eg. Natural polymers: Agarose, Chitosan, Gelatin, Hyaluronicacid, Various gums.

Cellulose derivatives: CMC,Thiolated CMC,sodium CMC, HEC, HPC,HPMC, MC, Methyl hydroxyl ethyl cellulose.

3. BACKING MEMBRANE:

The adhesion of bioadhesive devices to the mucous membrane is significantly influenced by the backing membrane. The backing membrane's components should be inert, impermeable to the medication, and enhancer of penetration.

Materials like carbopol, magnesium stearate, HPMC, HPC, CMC, polycarbophil, etc. are frequently employed in backing membranes.

4. PENETRATION ENHANCERS:

Substances that facilitate the permeation through buccal mucosa are referred as permeation enhancers.

Eg.Surfactants: IOINC: - sodium laurylsulfate, sodium laurate. NON IONIC: - Tween 80, sodium glycolate.

Bile Salts & Derivatives: Sodium deoxycholate, sodium glycocholate.

Fatty Acids & Derivatives: Oleic acid, caprylic acid, sodium caprate

5. PLASTICIZERS:

These are the substances that are utilised to give polymer blends or thin polymer films their pliability and softness.. Examples of common plasticizers used are glycerol, propylene glycol, PEG 200, PEG 400, castor oil etc.

METHOD OF PREPARATION

Mucoadhesive buccal patches can be prepared by the following methods:

1. **Solvent casting**:

Using a pestle and mortar, all components are precisely weighed and combined in this way. Subsequently, a magnetically stirred solvent system containing the plasticizer is gradually filled with the combination. Until a transparent solution is achieved, the stirring is kept up. Next, a quantitative transfer of the solution to Petridish is made. To allow the solvents to evaporate, inverted funnels are placed over the petri dish. They are stored for 24 to 48 hours, depending on the solvent system, at a temperature of 20 to 25 degrees Celsius. A thin layer of the protective backing material is laminated onto the coated release liner sheet following solvent evaporation to create a laminate that can be die-cut to create patches with the correct size and shape.

2. **Direct milling**:

This eliminates the need for solvents during the patch-making procedure. Drugs and excipients are mechanically mixed, usually without the use of liquids, by kneading or direct grinding. After mixing, the resultant material is rolled on a release liner until the desired thickness is achieved. Next, the coated release liner sheet is laminated with the backing material, forming a laminate that can be die-cut to produce patches that are the right size and shape.

EVALUATION OF BUCCAL PATCHES

The following tests are used to evaluate the Buccal Patches:

1. WEIGHT UNIFORMITY:

Each batch has five randomly chosen patches that are weighed, and the weight variation is computed..

2. THICKNESS UNIFORMITY:

Five randomly selected patches from each batch are weighed, and the weight variation is calculated.

3. FOLDING ENDURANCE:

Each patch's folding durability is measured by folding it repeatedly in the same spot until it breaks or reaches a maximum of 300 folds, which is deemed sufficient to disclose good film qualities.

4. SURFACE PH:

The buccal patches are made by dissolving 2% (w/v) agar in warm phosphate buffer (pH 6.8) while stirring, and then pouring the solution into a Petri dish and letting it gel at room temperature. The patches are then allowed to swell for two hours on the surface of an agar plate. By applying pH paper to the swollen patch's surface, the surface pH can be found. Three readings are averaged and recorded.

5. DRUG CONTENT UNIFORMITY:

For drug content uniformity, a 3 cm patch (without backing membrane) is separately dissolved in 100 ml of ethanol and simulated saliva solution (pH 6.2) mixture (20:80) for 12 h under occasional shaking. The resultant solution is filtered and the drug content of is estimated spectrophotometrically. The averages of three determinations are taken.

6. SWELLING INDEX:

Individual buccal patches (W1) are weighed and then placed in separate petri plates with pH 6.8 phosphate buffer. After removing the patches from the petri dishes, excess surface water is wiped away with filter paper.. The patches are reweighed (W2) and swelling index (SI) is calculated as follows:

$$SI = (W2-W1)/W1$$

7. IN-VITRO DRUG RELEASE:

The United States Pharmacopoeia (USP) XXIII-B rotating paddle method is used to test the drug release from the patches. The pH 6.8 phosphate buffer was used as the dissolving medium. The discharge occurs at 50 rpm of spin and 37°C ± 0.5°C. The backing layer of the buccal patch is attached to the glass disc using instant adhesive. The disc is attached to the bottom of the disintegration vessel. Five millilitre samples are removed and replaced with fresh medium at predetermined intervals. Following the appropriate dilution, Wattman filter paper is used to filter the samples, and their drug concentration is checked**.**

STABILITY STUDIES OF BUCCAL PATCHES

Pharmaceutical stability studies can be defined as the amount of time that a pharmaceutical product maintains its physical, chemical, microbiological, and pharmacokinetic features and characteristics during the course of its shelf life after it is manufactured.

The product's shelf life is determined by the substance's reduction to 90% of its initial concentration. The term "shelf life" refers to the product's stability and is commonly used interchangeably with "expiration date." Different medicinal preparations have different expiration dates.

STABILITY TESTING METHODS

Stability testing is a procedure performed for all the pharmaceutical products at various stages of the product development.

1. Real-time stability testing

Under the suggested storage settings, real-time stability testing is often carried out for an extended period of time to allow for notable product degradation.The duration of the product test is determined by its stability, which indicates unequivocally that it does not deteriorate or break down over an extended length of time.

2. Accelerated stability testing

Higher temperatures are used for this kind of stability testing, which determines how the product decomposes. The data is used to analyse the relative stability of different formulations or to forecast the shelf life. The Arrhenius equation predicts the accelerated stability studies with ease.

$$K = Ae^{-Ea/RT}$$

Where,

K= Specific rate constant

A= Frequency factor or Arrhenius factor

Ea= Energy of activation

R= Real gas constant 4.184 j/mol. k

T= Absolute temperature

In this method the drugs are stored at different temperatures such as 40°C, 60°C, 70°C,80°C, 100°C etc.

3. Retained sample stability testing

Both ambient temperature and refrigerator temperature are should be used for these investigations. To test for stability, a single batch is chosen and kept under observation for a full year. Samples are split into two batches if there are more than fifty of them. The shelf life is predicted in part by the stability assessments of the samples. Product shelf life predictions range from a maximum of five years to a typical three, six, nine, twelve, eighteen, twenty-four, thirty, forty, and sixty months. The constant interval approach is another name for this testing technique.

4. Cyclic temperature stress testing

This technique is not frequently used for product sampling. Using this approach, cyclic temperature stress tests are created with product knowledge to replicate possible market storage circumstances. The sampling in this experiment is thought to be done in cycles of twenty-four hours, or what is known as the earth's 24-hour rhythm.

PACKAGING AND LABELLING

PACKAGING

A device or material that holds a pharmaceutical product, whether or not it comes into direct touch with the substance, is called a pharmaceutical package container.

TYPES OF PACKAGES

1. Primary Packaging

Packages that come into direct contact with the pharmaceutical formulation are referred to as primary packaging. Protecting the formulation against mechanical, chemical, environmental, and/or other risks is the primary goal of the primary package.

2. Secondary Packaging

The secondary package is the one that is external to the primary package. In addition to offering extra security during storage, this packaging contains information on pharmaceutical products, such as leaflets..

3. Tertiary packaging

It is a supplemental packaging outer package that guards against product damage. It is employed in bulk transportation and handling. Barrel, crate, container, pallets, and slip sheet are a few examples.

There are numerous alternatives for packaging buccal films, including blister cards with multiple units, continuous roller dispensers, single pouches, and multiple-unit dispensers. For films, single packing is required. The most widely used packaging system technology is an aluminium bag.

LABELLING

A label is anything that is displayed on a container or the wrapper of a medication package that is written, printed, or visual.

LABEL REQUIREMENT

- Name of the medicine
- Name of the active ingredients
- Name of the dosage form
- Quantity or proportion of active ingredients Specific routes
- Batch number.
- Instructions for the use.
- Precautions & warnings.
- Registration number.
- Manufacturing & Expiry date.
- Price
- The name and address of pharmaceutical industry

CONCLUSION

A thorough investigation on buccal patches was carried out. Buccal patches are a type of modified release dosage form that has a non-dispersible thin matrix. Pre-formulation research encompassed the following areas: drug identification and characterization; drug compatibility of excipients; excipient selection criteria; formulation and optimisation techniques; and formulations. It was investigated how the buccal patch preparation procedure which comprised assessment, stability testing, packaging, and labeling was carried out.

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