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Review Article

Celecoxib Mucoadhisive In-Situ Gel for Transmucosal Drug Delivery System

Dipayan Purakayastha*, Anup Pramanik, Tuman P. Rai, Madhvi Ghadge, Shiv Garg, Piush Sharma

Dept. of Pharmaceutical Sciences, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302039, Rajasthan, India

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ABSTRACT

Transmucosal routes are most efficient route to achieve the effective therapy. The anatomical structure and physiological structure of transmucosal route improve the bioavailability of formulation. In case of In-situ gel, formulations are solution in form but when in administrated into human body it converted into gel form which is directly reached to the systemic circulation without fast pass effect. In transmucosal routes (Vaginal, Rectal, buccal etc) stratum corneum epidermis is absent, which is considered to be a major barrier for drug absorption so it goes to systemic circulations directly and increase bioavailability of drug and improve the effectiveness of formulation. Comparison to other route transmucosal route has better bioavailability and effectiveness.

Keyword: Transmucosal route, In-situ gel, celecoxib, stratum corneum.

Address for Correspondence: Dr. Shiv Garg, Asso. Professor Head, Dept. of Pharmaceutics Maharishi Arvind College of Pharmacy Ambabari, Jaipur. E-Mail: gargshiv81@yahoo.co.in

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INTRODUCTION

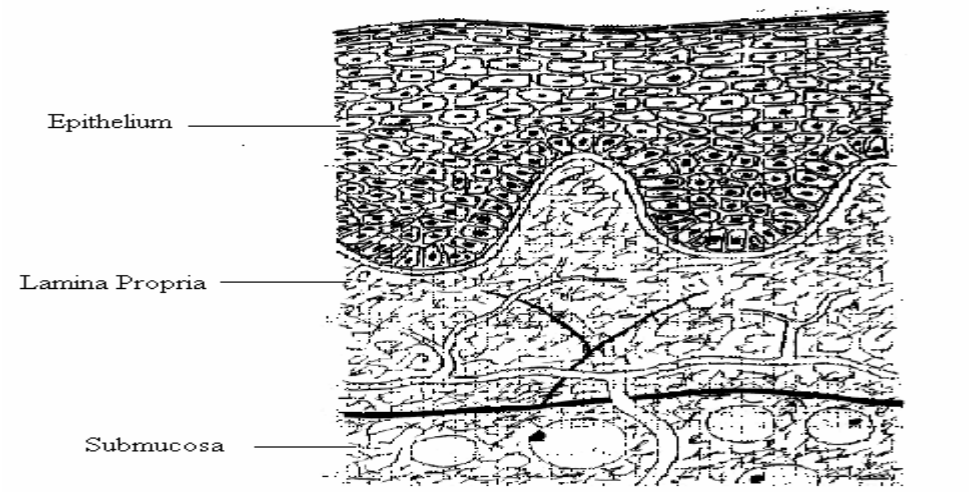
Last 20 years advances in drug formulations and innovative routes of administration have been made. Drug transport across tissues has increased. The administration of drug by transmucosal routes offers the advantages like painless administration, convenient termination of threrapy, Localization of drug action of the delivery system, and it has the potential for greater flexibility in different situation. Different types of transmucosal routes are vaginal , rectal , nasal, oral, urethral. Transmucosal drug delivery is a popular method because mucous membranes are relatively permeable, allowing for rapid uptake of a drug into the systemic circulation and avoiding the first pass metabolism. Efficient uptake offers several benefits over other methods of delivery.

Insitu is a Latin phrase which translated literally as In position. Insitu gel are drug delivery system that are in solution form before administration in the body, but once administered to human body it become gel . In situ gel formulations used in form of solutions or suspensions that undergo gelation after instillation. These systems are more acceptable for the patients. Increased bioavailability due to increased precorneal residence time.Insitu gel can administrated easily and it targeted directly to the site of action without fast pass metabolism. It has better bioavailability than oral formulations.Insitu gel is introduced in early 1970s.Insiu gel is most prominent among novel drug delivery.It reduce patient compliances .

Celecoxib was the first synthesized non-steroidal anti-inflammatory drug (NSAID) able to selectively inhibit COX-2 activity.It is used in treatment of dysmenorrhea, mentrual symtoms and it also reduce number of colon and rectum polyps in human body which is reason polyposis and rheumatoid arthritis and acute pain. Transmucosal route improve the bioavailability of celecoxib. Mucosal surface are generally important absorption site because of the absence of stratum corneum epidermidis, which are considered to be a major barrier for drug absorption. Mucosal surfaces are rich in blood supply providing a better chance for the drug to transport in systemic circulation.Dosage form is one which attains the desired therapeutic concentration of drug in plasma and maintains a constant for the entire duration of treatment. It is possible through administration of a conventional dosage form in a particular dose and at a particular frequency.

Transmucosal drug delivery:

Mucosa is composed of outermost layer squamous epithelium, below which lies a lamina propria followed by the submucosa as the innermost layer. Epithelium is similar to stratified squamous epithelia found others part of human body in that it has a mitotically active basal cell layer, advancing through a number of differentiating intermediate layers to the superficial layers, where cells are shed from the surface of the epithelium. Epithelium of the buccal mucosa is about 40-50 cell layers thick.



Advantages of Transmucosal drug delivery:

1. Ease of administration.
2. Convenient termination of therapy.
3. Medications can administrat easy to the unconsious patient.
4. Localization of drug action.
5. Targeted to the site of action.
6. Rapid systemic absorbation.

Need of transmucosal drug delivery:

Transmucosal route is prominent and efficient route ,in transmucosal route stratum corneum is absent which is big barrier of absorbtion because of its absence it drug can easily reached to systemic circulationand avoid the fast pass metabolism .it also improve bioavailibility of drug so that's why

transmucosal routes are important and more effective than any others route.

Different advantages of insitu gel:

1. In-situ gels show ease of administration.
2. It shows increased gastric retention with slow drug release.
3. It reduces dosing frequency.
4. It shows onto the targeted local action and site specificity by acting directly site.
5, it shows less adverse effects compared to other pharmacological dosage forms

Different approaches of In-situ gel:

There are six approaches for insitu gel which are mention below:

1. Temperature- sensitive hydrogels
2. P^{H}-sensetive gels
3. ion – sensitivre gels
4. Enzyme- sensitive gels
5. Light- sensitive gels
6. Dilution sensitive gels

Temperature sensitive gels: Temperature sensitive insitu gels are probably the most commonly studied class of enviroment sensitive polymer systems in drug delivery research. The use of biomaterial which transits from solution gel is triggered by increase in temperature, is an attractive way to approach in-situ formation .The ideal critical temperature range for such system is surrounding physiologic temperature, such that clinical manipulation is facilited and no external source of heat other than that of body is required for trigger gelation. Temperature sensitive gels are classified into three parts which are mention below:

A.Negatively thermo sensitive
B.Positively thermo sensitive
C. Thermally reversible gels

2. P^{H} Sensitive gels: In this type of formation gel is induced byP^{H}changes.All the p^{H} sensitive polymers contain pendent acidic or basic groups that either accept or release proton in reponse to changes in enviromental $P^{H.}$The swelling of insitu gel increases in the case of weakly acidicgroups but deceasees if polymer contains weakly basic groups.polymers used in this type of gel are chitosoan, polyacrilic acid (carbopol) etc. it convert ed solution to gel when p^{H}rise from 4.2 to 7.4.At higher P^{H}.At higher polymer level .

3. Ion sensitive gels: Ion-sensitive system produce gel of the polymer when it get specific ion in contact . Gelrite gellan gum a novel opthalmic vehicle that gels in the presence of mono or divalent cation present in the lachrymal fluid can be used alone and in combinations with sodium alginate as gelling agent.

4. Enzyme sensitive gel: Insitu formation catalysed by natural enzymes has not been investigated widely but seems to have some advantages over chemical and photochemical approaches. For examples an enzymatic process opeates efficiently under physiologic conditions without need for potentially harmful chemicals such as monomers and intiator. cationic p^{H} sensitive polymers containing immobilize insulin and glucose oxidase can swell in response to blood glucose level releasing the entrapped insulin in a pulsatile fashion.

5. Light sensitive gels: Phtopolymerisation is commonly used for in-situ formation of biomaterials. A solution of monomers or reactive macromer and initiator can be injected into a tissues site and the application of electromagnetic radiation used to form gel. acryate or similar polymerizable functional group are typically used as the polymerizable grops on the individual monomers and macromers because they rapidly undergophoto-polymerisation in the presence of suitable photo initiator. Typically long wavelenghth are used. Short wavelengenth utraviolate is not used often because it has limited penetration of tissue and biologically harmful.

6. Dilution sensitive gels: This type of insitu gel contains polymer that undergoes phase transition in presence of higher amountof water., by having asystem undergoing phas transition as a consequence of dilution with water a higher amount of polymer can be used,eg lutrol.

DRUG AND EXCIPIENTS

1. Celecoxib(Drug)
2. Methyl cellulose
3. Sodium chloride(NaCL)
4. Potassium chloride(KCL)
5. Sodium biacarbonate
6. Sodium lauryl sulphate(SLS)
7. PEG 400
8. Methanol

Method:

The in-situ gel formulations were prepared by simple mixing of drug solution in polymer solution. weighed quantity of polymer, surfactant, salt were dissolved in water in beaker one. beaker two drug was dissolved in PEG 400. The drug solution added to the polymer solution with continuous stirring using magnetic stirrer for 30 minutes at 150-200 rpm

Evaluation Parameter:

A. Rheological property (viscosity):

In rheological studies, viscosity determination of sample was done using Brookfield model

viscometer using spindle no 62. At angular velocity of 30 rpm.

B. Gelling Capacity:

1. Gelling temperature: The prepared formulation taken in transparent vial. It kept in a water bath maintained at constant temperature (starting at 30°C). The vials were inverted and visually evaluated. The temperature of the water-bath gradually increased till the sample started gelling.

2. Gelling time: Gelling time of the formulation determined by taking 2 ml of the formulation into a vial, which placed in the water bath maintained at temperature 37+2°C. The time for gel formation was noted.

3. Gelling strength: Gel strength performed by noting down the time up to which it remains in the form of gel at constant temperature of (37°C) using water bath.

C. Drug content: 1 ml of formulation in methanol taken in vial and shake for few minutes. The concentration of celecoxib was determined using UV spectrophotometer after suitable dilution against blank formulation treated in same manner and by this process gelling strength determined.

D. Bioadhesive strength: The bioadhesive strength measured using a modified two arm balance. Biological membrane fixed to the outer surface of the bottom of a 50 ml beaker with cynoacrylate adhesive and then placed in a 100 ml beaker. Accurately measured 1 ml formulation and converted into gel by gelling temperature. Formed gel transferred between the bottom of modified stainless steel pan and beaker. Initially, 50 gm preload applied for the establishment of adhesion between gel and biological membrane. For all the formulations, preload time was kept constant. At preload time another beaker was placed on the opposite pan. Water was added drop by drop into the beaker until the membrane gets detached at the opposite end. The weight in grams required to detach the pan from membrane gives the measure of bio-adhesive strength.

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