Formulation And Evaluation of Transdermal Patch for Arthritis

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***Abstract*— The formation of Celecoxib Transdermal patch to avoid first pass metabolism and to overcome the problems associated with its biological short half-life and fluctuations in plasma concentration upon oral administration. The patch was prepared using Solvent Casting Method, using HPMC as polymer, Ethanol: distilled water as solvent. The physical evaluation of the prepared patch include Organoleptic observation, moisture uptake, moisture loss, content uniformity test, stability studies, swelling index, folding endurance. The drug release was determined using Franz diffusion cells in phosphate buffer (pH 7.4).**

***Index Terms*— Celecoxib , Transdermal patch and conventional dosage form**

I. INTRODUCTION

Transdermal drug delivery system – TDDS are topically dosage form, which deliver the drug through the skin. They are define as the self contained dosage form which are also known as 'Patches' are applied to the intact skin , deliver the drug through the skin at a controlled rate to the systemic circulation.[1]

Patch - A patch is adhesive substance which contain medicament that attaches to your skin. The drug from the patch is absorbed through skin in your body over a period of time .A patch is more comfortable option for taking some medication.[2]

Principle- The drugs initially penetrate through the stratum corneum and then passes through the deeper epidermis and dermis without drug accumulation in the dermal layer. When drug reaches the dermal layer, it becomes available for systemic absorption via the dermal microcirculation.[3]

Transdermal patches have been in existence for a long time. In 1979, the FDA approved the first transdermal patch, which administered scopolamine for motion sickness.Since last decade, TDDS acquired a lot of interest due over the conventional dosage formsand oral controlled release delivery, specifically for the avoidance of hepatic first pass Effect Optimization of drug release through the skin directly into the systemic circulationand parallel minimize the retention and metabolism of the drug in the skin is the major goal of trans dermal products.[4] A Trans dermal patch is a medicament adhesive patch which when applied to the skinutilizes passive diffusion of drug at controlled rate through the skin and into the bloodstream.[5-8]

Administration of drugs in the conventional dosage forms as compare to the controlled orsustain release form usually results in large scale fluctuations in plasma drug concentrationsleading to unwanted toxicity or poor effectiveness along with limitations such as repetitivedosing at certain time interval and unpredictable absorption, led to the concept of thecontrolled drug delivery system or therapeutic system.[6]The successful development of transdermal therapeutic system mainly depends on choice of drug, which should be non-irritant, non-toxic and must cross the various skin layer to produce the desired therapeuticeffect at specific period of time. Drugs which produce these effects in small amounts withmolecular weight range of 100-800 Da are ideal candidates for TDDS.[9-10]

NSAIDs (Non-steroidal anti-inflammatory drugs) are mostly used for the preparation oftransdermal patches for the treatment of inflammation or pain. The NSAIDs patches are saferand convenient to use than its oral dosage form. NSAIDs tablets for rheumatism

leads tovarious side effects like internal stomach bleeding, increased acidity, ulcers can be avoidedby using transdermal patches of NSAIDs.[11-13] On the other hand, the analgesic patchof NSAIDs can be used on the site of sprain or strain. These patch when applied on the skinin form of transdermal patch, without reaching higher plasma drug concentrations the drugpenetrate the various layer of skin in sufficient amount to exert local therapeutic effect.Hence NSAIDs transdermal patches offers advantages of painless drug delivery, is easy toapply, provides faster and longer relief, and have no or few gastrointestinal side effects from the drug itself. That's the reason now a days patients are advised to take the NSAIDs patch over the other route because of its minimal side effects related to systemic toxicity and GIT irritation.[14]

Celecoxib is an NSAID category of drug which is used to treat osteoarthritis, rheumatoid arthritis, acute pain, menstrual symptoms, and to reduce polyps is familial adenomatous polyposis. Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor, it is a non steroidal anti-inflammatory drug (NSAID) which is also known for its reduced risk of causing gastrointestinal bleeding compared to other NSAIDS. It is used to control symptoms of different types of arthritis pain and in familial adenomatous polyposis (FAP) to reduce precancerous polyps in the colon. It is marketed by Pfizer under the brand name Celebrex, and was initially granted FDA approval in 1998.[15-17] Celecoxib weakly inhibits COX-1 and, therefore, may affect platelet function less than aspirin.Celecoxib also has anticancer properties discussed below and exerts its anticancer properties by binding cadherin-11 (CDH11), which likely plays a significant role in the malignant progression of cancerous cells. Celecoxib is extensively metabolized through cytochrome P450 2C9 (CYP2C9) and may have interactions with other medications that are substrates of CYP2C9.[18-25]

II. MATERIAL AND METHEDOLOGY OF TRANSDERMAL PATCH

2.1 Materials

The chemical which are used in this procedure were of standard analytical or pharmaceutical grade. Celecoxib was a gift sample which is obtained from Pharmaceutical industry. Formulation of patch include-

Active ingredient- It is consider as API (active pharmaceutical ingredient) means the active ingredient which is contained in medicine which gives therapeutic effect.

Backing agent- It is act as a protector. It protect the patch from the outer environment, is impermeable to the Transdermal patch components and provide the patch with its flexibility.

Plasticizer- Plasticizer are low molecular weight substance added to a polymer solution to promote its plasticity and flexibility.

Penetration enhancer – They are the agent that penetrate into the skin and interact with skin constituent to promote drug flux or reversibly decrease the barrier resistance .These agent can increase drug solubility in the subcutaneous by altering the solvent properties of the SC, resulting in improvement of drug partitioning.[26-30]

Table 1: Ingredients table of celecoxib patch

Sr.no.	INGREDIENTS	ACTIVITY
1.	Celecoxib(mg)	Active ingredient
2.	Hydroxypropyl methylcellulose (mg)	Backing agent
3.	PG 400(ml)	Plasticizer
4.	Pyrrolidone , Glycol(ml)	Penetration enhancer
5.	Ethanol (ml)	Solvent

2.2 Methodology of Transdermal patches-Following methods considered to prepare Transdermal patches .

1. Circular Teflon Mould method
2. Asymmetric TPX membrane method
3. Mercury substrate method
4. Solvent casting method
5. EVAC membrane method

Solvent casting method

Transdermal patches were produce using methyl cellulose as a polymers containing Celecoxib drug by solvent casting method. According to the formula, HPMC were accurately weighed and dissolved in mixture of ethanol as a solvent. The drug Celecoxib

was then dispersed in the polymeric solution and plasticizer PG400 was added with continuous stirring using a magnetic stirrer to obtain homogeneous mixture. Lastly, the bottom of petri dish were covered with an aluminium foil and the resulting solution was poured into levelled mercury surface in a petri dish covered with a funnel.The solvent will allowed to evaporate and left undisturbed at room temperature for the next 24 hour.The patch will obtained by slowly lifting from the petri dish and transdermal patches were cut into appropriate radius.[31-40]

Table 2: Composition of Celecoxib containing Transdermal Patch

Sr. No.	INGREDIENTS	QUANTITY
1.	Celecoxib drug(mg)	Was taken
2.	HPMC(mg)	Was taken
3.	PG 400(ml)	Was taken

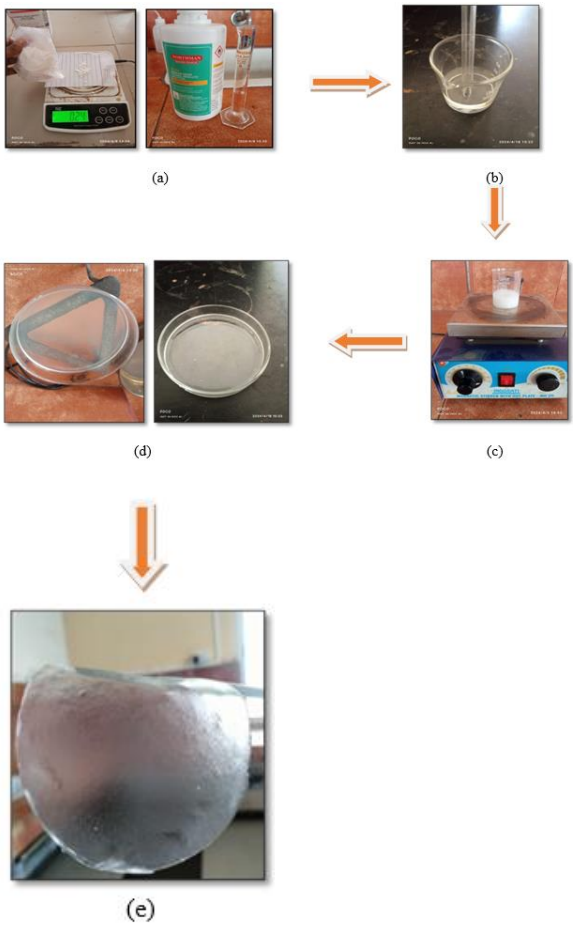

Figure 1: Preparation of Transdermal Patch by Solvent Casting Method (a)Weighing process of drug and ingredient (b) Mixture containing drug and other excipients (c) Stirring on magnetic stirrer (d) Solution poured into petridish (e) Prepared patch by solvent casting method.

III. CHARACTERIZATION AND EVALUATION OF MEDICATED PATCH

After preparing the formulation, it was further studied for its physical, mechanical and permeability of the drug. We find out the physical and mechanical properties of medicated transdermal patch such as thickness, surface pH, content uniformity, folding endurance, moisture loss, moisture uptake, weight uniformity, and stability studies. Also medicated patch were evaluated for drug content, in-vitro drug release

3.1 Physical Appearance

Prepared transdermal film were inspectedOrganoleptically where colour, transparency, shape, texture of the surface, homogeneity of thickness, film formation (no collapse or shrinkage)upon drying.

Figure 2: Transdermal Patch

Table 3: Physical Appearance of Patch.

Sr. No.	Physical Appearance	Result
1.	Colour	Transparent
2.	Surface texture	Smooth
3.	Shape	Round

3.2 Surface pH

Prepared film was allowed to swell by adding 0.5mL of distilled water on the film surface for 1hr at room

temperature. Then, pH was noted by bringing the electrode into contact to the surface of the film and allowing it to equilibrate for 1 min.

Table 4: Determination of surface pH

Sr. No.	Sample	pH
1.	S1	5.5
2.	S2	6.8
3.	S3	6.6

Figure 3: pH Determination

3.3 Thickness of Patch

The thickness of the patch is determined by screw gauge and micrometer at different point and average of readings were calculated.

Figure 4: Thickness Testing

Table 5: Determination of Thickness of Patch

Sr. No.	Sample	Thickness(mm)
1.	S1	0.295
2.	S2	0.245
3.	S3	0.254

3.4 Moisture uptake

For finding moisture uptake the prepared films were placed in a desiccator containing activated silica gel for 24 hr. Then, they were weighed (Wd) and then transfer to another desiccator containing saturated sodium chloride (75%). The films were weighed daily until they showed constant weight (Wu). The percentage of moisture uptake was calculated by.

The formula used for finding moisture uptake is –

Moisture uptake capacity% = Wu-Wd ÷ Wd × 100

3.5 Folding Endurance

This test is performed to determine the elasticity and fragility of Transdermal patch. The test was conducted by folding of patch at the same point n number of times till the patch is broken. The number of fold is considered to be the value of resistance to folding.

CONCLUSION

The application of Transdermal is one of the most promising method over the conventional form. Patch of Celecoxib was successfully prepared with different polymers by solvent casting method. The present studies were helped in understanding the effect of formulation process. This study is further aimed to perform in-vivo studies for the concentration of Celecoxib drug reaching into the skin and to study its effect, which will help to avoid the first pass metabolism and to make novel transdermal dosage form.

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