Diclofenac Transdermal Patches used in analgesic (NSAID) condition

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Abstract: Patch formulation is the novel drug delivery system formulation in that drug are given in patch formulation in that drug is absorb through skin and produce the action on that particular area part of body Diclofenac is Non-steroidal anti-inflammatory (NSAID) category type drug in these article discuss about various type of diclofenac patch such as transdermal patch, Transbuccal Patch , Diclofenac patch in women. In that also study of mechanism of action of diclofenac inhibit the activity of cyclooxygenase enzymes (COX-1 and COX-2). And Inflammation indices., in these article also discuss evaluation of diclofenac patch such as Thickness of patch, Weight uniformity Patches, Folding endurance. Percentage moisture content .Percentage moisture uptake .Drug content

Keyword: nonsteroidal anti-inflammatory drugs NSAIDs, cyclooxygenase enzymes COX-1, COX-2 diclofenac

INTRODUCTION

Prevention of postoperative pain remains an arena for never ending research with better formulations and modalities constantly replacing the obsolete ones. Pain following surgery is one of the most important factors causing morbidity and mortality, two causes prolonging the hospital stay[1]. Generally, a specific group of drugs called nonsteroidal anti-inflammatory drugs (NSAIDs) which is used for the treatment of local muscular pain and inflammation. The NSAIDs inhibit the activity of cyclooxygenase enzymes (COX-1 and COX-2), thereby controlling the synthesis of thromboxanes and prostaglandins [2], transdermal delivery of DS hydrogel patches has been developed in recent years. However, previous research has reported that DS loaded hydrogel patches encountered the problems of burst release, non-responsive drug release profile and heterogeneous drug distribution, since DS is partially soluble in water[3]. NSAIDs could also cause certain cardiac side effects, such as myocardial infarction, heart failure, atrial fibrillation, arrhythmia and sudden cardiac death. Rofecoxib was withdrawn from the market in 2004 due to its serious thrombotic risk [4] Nevertheless, the successful application of most TDDSs in clinic is still limited by poor skin permeability and uncontrollable drug delivery process. Normally, to increase the transdermal absorption of drugs, chemical or physical enhancers are employed to help the drugs across the skin barriers[5]. The magnitude of heat-induced enhancement in drug permeation can be affected by the physical and chemical nature of the formulation, drug load, and physicochemical properties of the drug molecule. This can result in altered pharmacokinetic profiles in both patch and semisolid topical or transdermal formulations [6] Voltage-gated sodium channels (VGSCs), important transmembrane proteins, participate in the generation and conduction of action potentials and maintain cell homeostasis. VGSCs mainly distributed on the membranes of myocardium, skeletal muscle and nerve cells, and are responsible for regulating the initial ascending phase of action potentials. Cardiac sodium channel plays an important role in cardiac electrical excitability. Gain-of-function and loss-of-function of Nav1.5 will lead to the generation and development of a series of diseases, such as Long-QT syndrome (LQTS), Brugada syndrome (BrS), Sick sinus syndrome (SSS), Progressive cardiac conduction disease (PCCD) and Dilated cardiomyopathy (DCM). Nav1.5 determines cardiac excitability and is currently recognized as the most abundant and important cardiac sodium channel [7].

METODOLOGY

Effective information is taken from pubmed, science hub and science direct . in these article we study Pharmacokinetics And Pharmacodynamics of action of diclofenacpatch with diagrammatically

mechanism of action in that also study the what kind of side effect of the diclofenac patch, Adverse drug reaction in that also included chemical structure of diclofenac patch is the novel drug delivery system in which study about patch application, dose size, toxic effect, effective dose concentration, therapeutic dose ,toxic dose c-max and t-max also study in this article Transbuccal Patch Transbuccal diclofenac patch [TBDP] is one of the few drugs given through the novel route, i.e. administration via buccal mucosa. Between two polymer layer that is hydroxyl propyl methyl cellulose HPMC patch is made and it contain I, 20 mg diclofenac sodium . The thickness of the patch is 0.308 ± 0.049 mm, shape is circular with a diameter of 1.5 cm, and colour of the patch is off white, packaged in foil-lined packets. It is used to relieve mild to moderate postoperative pain. It is applied on the buccal mucosa with a dry finger, and thereafter, digital pressure is applied over the patch for 30 s and the patch adheres to the buccal mucosa[8]

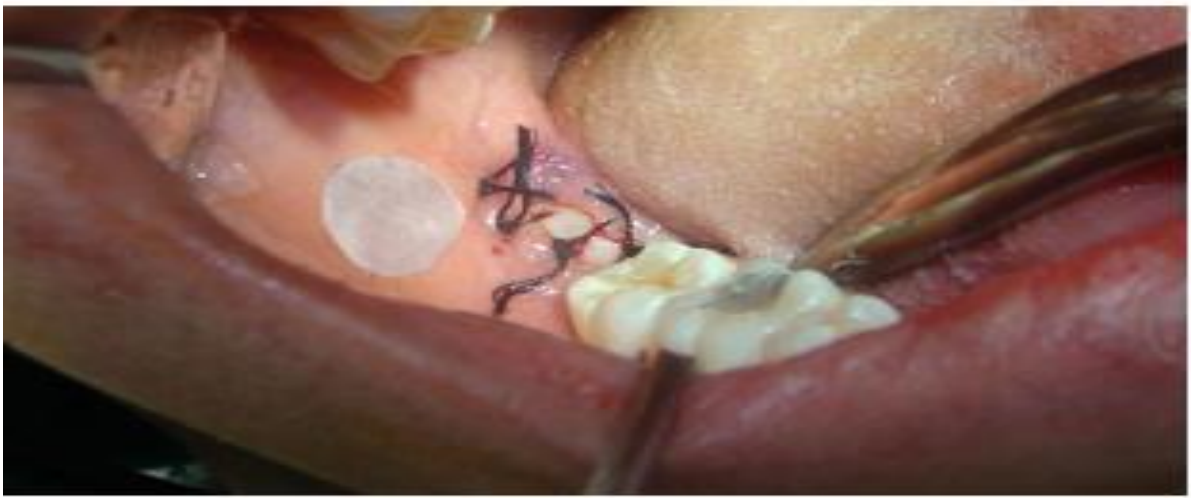


Figure 1

INFLAMMATION INDICES

Indices including serum uric acid, WBC, CRP and ESR were examined before treatment and directly after treatment. Before collecting blood samples, all patients underwent 10 hr of overnight fasting. The serum uric acid, WBC, CRP and ESR were evaluated by experienced technicians blinded to the study using standard enzymatic procedures on an automated bioanalyser (Hitachi, Tokyo, Japan)[9] use . Actually, these release values are similar to those reported for BNC membranes loaded with DCF and plasticized with glycerol Still, this rapid release profile is adequate for the therapeutic effect intended in this study. In fact, a rapid local analgesic and anti-inflammatory [10]

Diclofenac sodium patch contains 140 mg/14 g diclofenac sodium gel, and when applied topically, passes through the skin to the underlying tissue and weakens acute and chronic inflammatory reactions. The plasma concentrations of diclofenac sustain the uptake of diclofenac from the patch, irrespective of the time the patch is applied (morning or evening), and without causing any gastrointestinal upset. The metabolism of topical diclofenac is reported to be equivalent to oral intake[11]

DICLOFENAC PATCH IN WOMEN

A pilot study to test the uniformity of transdermal drug delivery to the breast using diclofenac epolamine patch was approved by the Northwestern University Institutional Review Board. Non-pregnant women scheduled for mastectomy to prevent or treat breast cancer were recruited through the Lynn Sage Comprehensive Breast Center of Northwestern Medicine. All participants were randomized to patch application to one surgical breast (per participant) or the abdominal skin. The diclofenac patch (Flector patch, 10 cm × 14 cm) is a semi-occlusive, bioadhesive patch containing 129.7 mg of diclofenac acid. After baseline evaluation, the participants were instructed on site of patch application and to replace patch every 12 h over 72 h prior to surgery[12].

FORMULATION OF TRANSDERMAL PATCH

Matrix type monolithic polymeric transdermal patches were prepared by solvent casting method. The various formulation compositions .Eudragit RL 100 (ERL) was dissolved in isopropyl alcohol

during 24 h. The Resveratrol-phospholipid complex (RSVP)or Resveratrol (1:0.75), polyvinyl chloride PVP K30, and plasticizer (PEG 400) were mixed in the ERL solution under magnetic stirring for 15 min for uniform dispersion. The mixture was poured into aluminum Petri dish (12 cm2) (fabricated with aluminum sheet, thickness 0.4 mm) covered with pre-shaped aluminum foil (thickness 0.2 mm) to serve as impermeable backing and left for drying at room temperature for 24 h. The patches were then dried in a hot air oven at 60°C for 2 h to reach a stable drug-polymer matrix. The presence of plasticizer in the dried drug-polymer matrix imparts adhesive property to the prepared patch (36), and no additional adhesive material was applied in the formulation. The formulation along with the backing was removed from the Petri dish after drying, so that patch formulation was protected from one side by the impermeable[13]

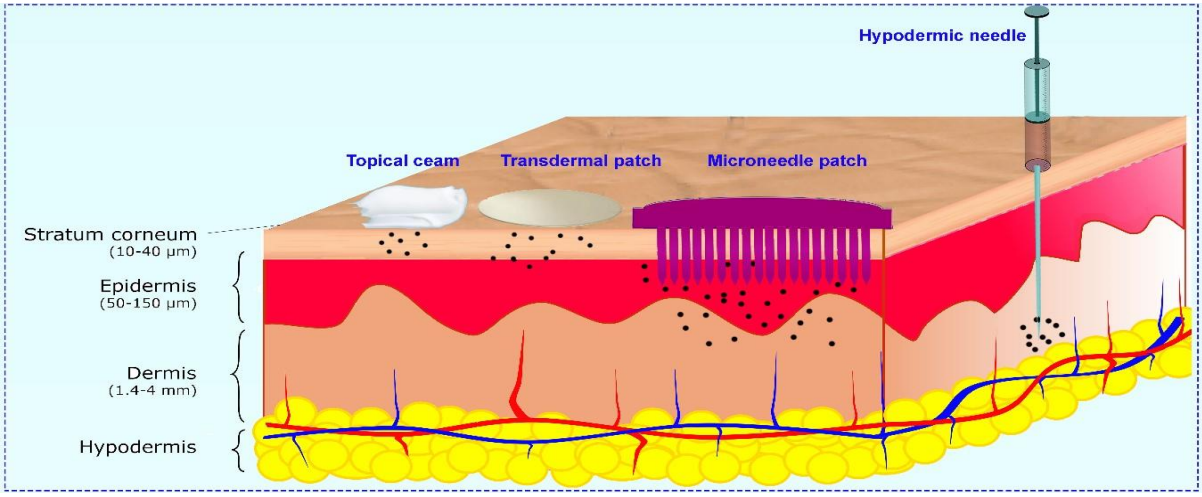


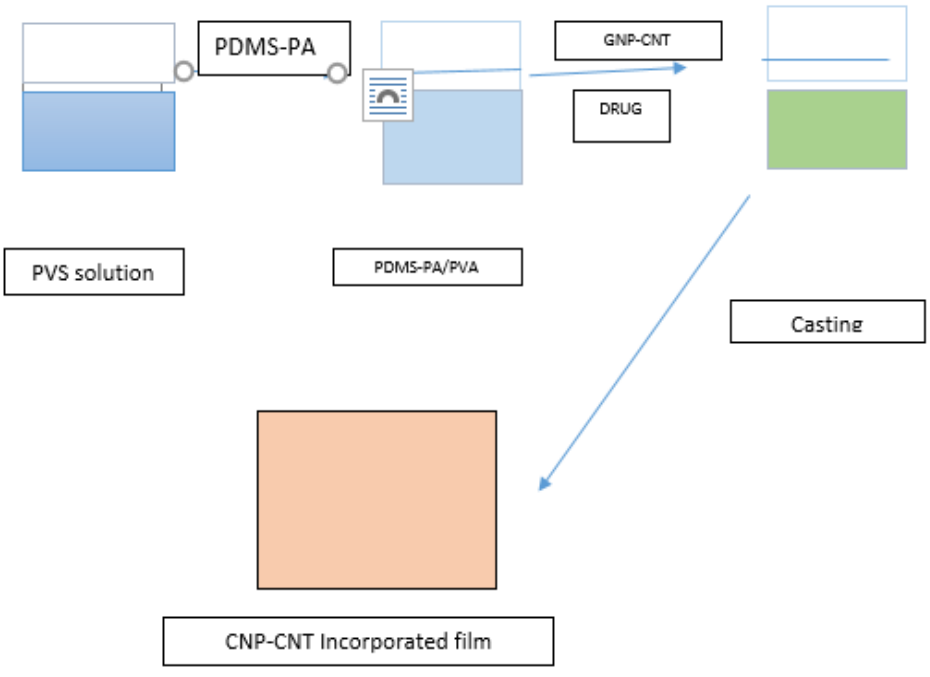
Figure 2

METHODS

Ethyl Cellulose was generally used for the formulation of Transdermal Patch. Polyethylene glycol (PEG 400) was used as a plasticizer. Dibutylphthalate is used as penetration enhancer. The polymer was dissolved in chloroform: methanol (1:1) solvent. The drug was dispersed uniformly in the viscous solution with continuous stirring. The resulting mass was poured into leveled mercury surface in a Petri dish covered with inverted funnel. The Petri dish was left undisturbed at room temperature for one day. The patch was obtained intact by slowly lifting from the Petri dish and transdermal patches were cut into radius of 2cm2[14] Preparation of topical patches The formulation of DS-loaded topical patches was performed by the solvent casting method . The first step consisted of the preparation of the backing membrane by pouring 10 ml of a PVA solution (3%, w/v) in a Petri dish. The obtained film was left to dry in ambient air for 24 h. Subsequently, solutions of CTS and KC (1.0%, w/w) with PG (2.0%, v/v) as plasticizer were prepared separately in an aqueous solution (1%, v/v) of acetic acid and distilled water, respectively. The resulting solutions were then filtered and stored for 24 h until it was needed. Both solutions were mixed at different proportions and vigorously stirred at 75 °C with magnetic agitation until the mixture reached room temperature. Later on, T80 (1.0%, v/w) was added as a permeation enhancer. The loading of the drug (1.3%, w/w) was carried out by homogeneous dispersion, with slight mechanical stirring, to obtain matrix patches containing 6 mg/cm2 of DS. The dispersion was poured onto the backing membrane and dried at 40 °C for 12 h. Finally, a gummy tape was then adhered to the support membrane keeping the matrix side up. The drug matrices were kept in desiccators until their characterization [15]

Preparation of diclofenac loaded transdermal films First an aqueous solution of PVA was prepared by dissolving 1.0 g PVA in 20.0 mL distilled water and stirred at 70 °C for 2.0 h. Varying content of PDMS-PA from 0, 2.0, 4.0, 6.0, 8.0,10.0 and 12.0 wt% of the solid PVA mass was then added into the solution. The mixture was further stirred for 3.0 h. The resulting suspensions were casted in a petri dish and dried at room temperature. The obtained membranes were stored in desiccator to remove the remaining moisture. The peel adhesion force of the membranes was determined to optimize the film in terms of adhesion behavior based on method detailed elsewhere. The DS loaded GNP-CNT reinforced membranes were prepared by solution cast method (Fig. 1). Briefly, to an aqueous solution of PVA (1.0 g in 20.0 mL), optimized amount of PDMS-PA was

added and stirred for 2.0 h. Schematics of the synthesis of GNP-CNT. T.S. Anirudhan and S.S. Nair Materials Science & Engineering C 102 (2019) 437–446 438 suspension containing 0, 0.5, 1.0, 1.5 and 2.0 wt% (of the mass of solid PVA) GNP-CNT, followed by adding 5.0 wt% DS. After continuous stirring at room temperature for 2.0 h, the suspension was sonicated for another 5.0 min. The obtained mixture was cast on petri plates, dried and stored in desiccator. The film incorporated with 0, 0.5, 1.0, 1.5 and 2.0 wt% GNP-CNT is abbreviated as PV0, PV0.5, PV1.0, PV1.5 and PV2.0. The drug encapsulation efficiency (DEE) of the prepared membranes was evaluated spectrophotometrically based on our previous investigation [16]



Systematic representation of the preparation of TRD devise

Figure 3

evaluated the analgesic efficacy of patch and intramuscular injection of diclofenac in immediate post-operative period of bi-jaw surgery for correction of dentofacial deformities in 60 patients and concluded that a single dose of 100 mg transdermal diclofenac was more efficient than the diclofenac injection with a significantly higher mean duration of analgesia and better adverse effect profile. Similarly, demonstrated in their study of 153 subjects with myofascial pain syndrome of upper trapezius that diclofenac patch had significantly better VAS score, range of motion with no adverse effects when compared with placebo. This study is singular in comparing three different routes of diclofenac administration using a standardized model and evaluated not only analgesic efficacy but overall global assessment indicating the patient compliance levels, which forms the basis for efficient management for any post-operative pain. This study accepts the null hypothesis that the diclofenac patch group was as efficacious in pain control as oral and parenteral routes. The present study has its demerits though. Blinding has not been done as is desirable in an analgesic assay[17]

EVALUATION AND CHARACTERIZATION

Thickness of patch

The thickness of each patch was measured by using screw gauge at five different positions of the patch and the average was calculated [18]

Weight uniformity Patches

sizes of 2cm radius (4cm diameter) was cut. The weights of five patches were taken and the weight variation was calculated [20]

Folding endurance

A patch of 2cm radius (4cm diameter) was cut evenly and repeatedly folded at the same place till it

brakes. The numbers of times the film was folded at the same place without breaking give the value of the folding endurance [21 22]

Percentage moisture content

The prepared films were weighed individually and kept in a desiccators containing fuse calcium chloride at room temperature for 24h. After 24h, the films were reweighed and determined the percentage moisture content from the mentioned formula [23 24]

Percentage moisture uptake

The weighed films were kept in desiccators at room temperature for 24h containing saturated solution of potassium chloride in order to maintain 84% RH. After 24h, the films were reweighed and determined the percentage moisture uptake from the below mentioned formula [25 26]

Drug content

A specified area of patch was dissolved in a phosphate buffer solution. The content was stirred to dissolve the film. The content was transferred to a volumetric flask. The absorbance of the solution was measured at wavelength 284nm and determines the drug content [27]

ADVANTAGES OF PATCH

- Avoidance of first pass metabolism and GI tract variability in drug delivery
- Administration directly to desired site of action.
- Topical administration may be more acceptable to patients and therefore increase adherence.
- Allowance of medication administration when patients are unable to take/tolerate oral formulations.
- May be more cost-effective due to ease of administration compared with other routes of administration.
- Avoidance of drug-drug interactions. Potentially decreased time to efficacy due to elimination of dosage titration[18]

PREDICTING THE SKIN APPLICATION

The optimal drugs found in this study for inclusion into our designed PDMS matrix, to be released over a period of several days, were and diclofenac most non-steroidal anti-inflammatory (NSAID) can also lead to an increased risk of gastrointestinal and cardiovascular adverse events. The superiorities of TDD, as described in the Introduction section, can avoid the side effects of NSAID [28]Efficacy and safety of a transdermal patch, which is incorporated with diclofenac diethylamine, which releases the medication in sustained doses over a period of time, hence effective in pain control. Diclofenac in a transdermal patch form is know[29]

DISCUSSION

In that we study about the various type of patch which is used for local as well as systemic action is produce . In that basically discus about diclofenac patch type of diclofenac patch such as Transbuccal Patch , Diclofenac patch in women ,Formulation of Transdermal Patch . use of patch to manage the post-operative pain. in that discuss about the evaluation parameter of patch with applications of patch

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