FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES FOR JOINT PAIN

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ABSTRACT:

Joint pain is a common issue caused by aging, poor nutrition, or health disorders. This study developed a herbal transdermal patch containing camphor,mustard oil, and clove oil for effective pain relief. Polymers like eudrajit RL, HPMC, and Tween-80 were used, with Glycerine as a plasticizer. The patch was evaluated for thickness, moisture content, folding endurance, weight uniformity, drug content, pH, and in-vitro permeation. Results showed stable, effective, and sustained drug release. The formulation proved to be a safe, non-invasive, and efficient alternative for managing joint pain and improving patient compliance.

Keywords: Transdermal patches, joint pain, Folding Endurance, Herbal, Eggshell membrane.

Objective:

The goal of this study is to create and evaluate a transdermal patch using natural chemicals to safely, effectively, and painlessly relieve joint pain.

1. INTRODUCTION:

Transdermal patches are a cutting-edge drug delivery technique that enables medications to reach the bloodstream through the skin. This approach has numerous benefits over traditional administration channels like oral or intravenous methods. By providing a controlled and sustained release of medication, transdermal patches ensure consistent therapeutic levels in the bloodstream, which can increase efficacy and reduce the frequency of doses. Furthermore, by avoiding the gastrointestinal tract and the liver's first-pass metabolism, this drug administration method increases bioavailability and reduces systemic side effects (Reddy & Guy, 2010).[(1)]

Transdermal Patches:

Often called "patches," transdermal drug delivery systems (TDDS) are dosage forms designed to disperse a medicament across a patient's skin in a therapeutically effective amount. When administering medications for systemic effects, the entire morphological, biophysical, and physicochemical properties of human skin must be considered. Transdermal delivery provides a major advantage over injectables and oral approaches by increasing patient compliance and avoiding first pass metabolism, respectively. In addition to providing controlled, continuous drug administration, transdermal delivery eliminates pulsed entry into systemic circulation, which usually leads to adverse side effects, and allows continuous input of drugs with short biological half-lives. One of the most cutting-edge ways to distribute new medications is through transdermal patches. One advantage of transdermal drug delivery systems is that they are a painless way to administer medication. These days, transdermal patches are frequently used as topical, transdermal, and cosmetic delivery systems.[2]

1.2Advantages of TDDS:

1. To avoid first-pass metabolism, transdermal administration ensures a material's prolonged and continuous penetration.
2. Increase patient compliance.
3. The intestinal and stomach fluids are unchanged.
4. Provides long-term control by keeping blood levels constant and steady.
5. Reduced levels of medication plasma concentration.[3]

1.3The disadvantages of TDDS:

1. The drug needs to have favorable physicochemical properties in order to cross the stratum corneum.
2. The daily dosage of medication should not exceed 5 mg; if the daily dosage surpasses 10–25 mg, transdermal drug distribution becomes challenging.
3. The patch's adhesive, medicine, and other ingredients may cause local irritation.
4. There should be a clear clinical need for the transdermal delivery mechanism.
5. High drug levels in blood or plasma were not achievable.[3]

2. TRANSDERMAL PATCH TYPES:

2.1 Adhesive with a single layer of medication:

The sticky layer of this system also contains the drug. This type of patch's adhesive layer controls the release of the drug in addition to holding the various layers and the overall system to the skin. A backing and a temporary liner encircle the adhesive layer.[2]

2.2 Drug layer in multi-adhesive:

The multi-layer drug in an adhesive patch and the single-layer device are similar in that the drug
is released by the two layers of glue. In contrast, the multi-layer technique incorporates an extra layer of drug-inadhesive, usually (but not always) separated by a membrane.
This patch also has a temporary liner layer and a permanent backing.[2]

2.3 Reservoir:
Unlike single-layer and multilayer drug adhesive systems, the reservoir transdermal system contains a separate drug layer. A liquid compartment holding a medication solution is called the drug layer.
suspension that the sticky layer separates. This patch is also supported by the backing layer. The rate
of release is zero order in this type of system.[2]

2.4 Matrix:
A drug solution or suspension is contained in a drug layer of a semisolid matrix in the Matrix system. The sticky layer in this patch partially covers the pharmaceutical layer.[2]

2.4 Vapour Patch:
In this type of patch, the adhesive layer releases vapor in addition to holding the several layers together. The vapor patches are brand-new and can release essential oils for up to six hours. The main purposes of the vapor patches are essential oil release and congestion. Other vapour patches include controller vapour patches that improve the quality of sleep. There are also vapor patches on the market that reduce the number of cigarettes a person smokes each month.[2]

3.JOINT PAIN:

Pain in the joints Joint pain is a widespread symptom rather than a specific sickness, with numerous causes, including autoimmune disorders, degenerative diseases, traumas, and inflammatory issues [4]. Understanding the complexities of joint pain, from its nuanced spectrum of symptoms to its structural reasons, is essential for both those experiencing discomfort and medical professionals looking to provide effective therapies.[5]

3.1 Joint pain causes:

Inflammation: Rheumatoid arthritis and lupus are two inflammatory joint disorders that can cause chronic joint discomfort. Inflammation caused by conditions like Lyme disease or viral arthritis can also affect the joints. [6]

Degeneration: Pain and bone-on-bone contact are caused by osteoarthritis, a common form of joint discomfort caused by cartilage degradation.

Injury: Acute injuries such as fractures, dislocations, or sprains can cause immediate joint discomfort. Overuse injuries are common in sports and can lead to chronic joint discomfort.

Autoimmune disorders: In conditions like rheumatoid arthritis and ankylosing spondylitis, the immune system attacks the joints, causing pain and inflammation.

Metabolic disorders: Gout is a kind of arthritis that results in severe pain and inflammation due to the accumulation of uric acid crystals in the joints.[7]

Infectious diseases: Septic arthritis is one type of infection that can cause joint pain and swelling.

4. MATERIAL AND METHOD:

Camphor, mustard oil, and clove oil were procured from the local market in Shahada. Hydroxypropyl methylcellulose (HPMC), Eudragit RL, Tween 80, glycerine, chloroform, and ethanol were obtained from the laboratory. All chemicals used were of analytical grade.

5.HERBAL PARTS:

5.1 CAMPHOR:

Physical attributes:

Color: colorless to white
Smell: The smell of arrogance
Taste: Aromatic flavor
Boiling point: 760 mmHg at 399F
Melting point: 345 degrees Fahrenheit; soluble in ethanol but insoluble in water

Uses:

a. It can be added to explosives, lacquers, varnishes, insecticides, fungicides, medications, cosmetics, and flavorings in addition to being used as a chemical intermediate and plasticizer.
b. It eases muscle aches and pains as well as rheumatism.
c. It also helps reduce cholesterol levels in the body.[8]

Camphor's pharmacological action:

Anti-inflammatory:

It lowers cholesterol and relieves aches and pains in the muscles, chest congestion, and rheumatism. Camphor oil is widely used in vapor rubs, balms, and liniments due to its anti-inflammatory qualities. Acute inflammation, a vital defense mechanism against invasive microbes, is characterized by swelling, heat, redness, and pain. The mediators produced by the cyclooxygenase (COX) cascade and the role of physiologically active prostaglandins in the inflammatory process and body homeostasis have been the subject of several investigations.
Strong anti-inflammatory drugs called cyclooxygenase inhibitors reduce prostaglandin levels and important markers of inflammation by stopping prostaglandin synthesis . [9]

5.2 MUSTARD OIL:

Alternatives: Vegetable oil
Biological source: Musterd oil derived from the natural seeds of Brassica juncea L. czern or Brassica nigra Koch
Chemical components:
Musterd oil includes roughly 21% polyunsaturated fats and 60% monounsaturated fats (42% erucic acid and 12% oleic acid).

Applications:

- use of mustard oil as a
- An analgesic for teeth
- Carminatives
- Stimulants
- Fragrant [8]
- Relieve your aches and pains.
- Decrease the inflammation brought on by respiratory conditions including bronchitis and pneumonia.
- Lessens bodily discomfort [10]

5.3 CLOVE OIL:

Synonym: Eugenia cariophylata

Biological source: Eugenia caryophyllus flower buds that have been dried make up cloves. (Myrtaceae family).

Chemical components:

Clove oil contains roughly 15–20% volatile oil, 10%–13% tannis, resins, chromosomes, and eugenics. The drug's volatile oil contains 89% eugenol, 5–15% eugenol acetate, and betacairofileno.

Applications:

• Reduces discomfort in the muscles.• Encourages quicker recovery.

• Diminish agitation.[8]

6.FORMULATION OF TRANSDERMAL PATCHES:

Sr.No	Ingredients	F1
1	Herbal API mixture	10ml
2	HPMC	2.5gm
3	Eudrajit RL	1gm
4	PVA	1gm
5	Tween 80	1ml
6	Glycerine	2ml
7	Ethanol	25ml
8	Chloroform	25ml
9	Distilled water	q.s

Table: Formulation of transdermal patches

7. PREPARATION OF TRANSDERMAL PATCHES:

To make the active therapeutic ingredient, 1 gram of camphor was mixed with 8 milliliters of mustard oil and 1 millilitres of clove oil. Mix 25 milliliters of ethanol and 25 milliliters of chloroform to create the organic solvent. After that, add one gram of eudrajit RL and stir the mixture with a mechanical stirrer until a clear solution is formed. The drug matrix was made by dissolving HPMC in distilled water. This mixture was stirred until a transparent solution developed after PVA was added. To form a homogenous viscous mixture, gradually incorporate the organic phase into the drug matrix and stir continuously for 30 to 45 minutes.Add 1 ml of tween 80 and 2 ml of glycerine to the liquid after it is consistently thick, and mix well.Add the herbal API to the mixture and gently whisk to prevent it from evaporating.The homogenous dispersion that was produced was placed on a petri dish and let to cure at room temperature for a whole day. The dried films were removed, wrapped in aluminum foil, and kept in a desiccator before being used. An adhesive bandage layer purchased from the local market was used to adhere the created films.[10]

8. EVALUATION PARAMETERS:

1. Visual Appearance

It was noted that the created patches had a frightening, uniform, and smooth physical appearance.They have a flexible physical appearance and are not confined by air bubbles.[10]

2. The thickness of the patch

Using a digital micrometre, traveling microscope, and dial gauges, the thickness of the drug-loaded patch is computed in many prints to ensure that the prepared patch will have an equal thickness at every place. The average thickness and standard deviation for the same are then determined. The thickness variation within and between patches can be computed.[8]

3. Moisture content:

Individually weighed patches are kept in desiccators with fused calcium chloride at room temperature for an entire day. After a day, the patches need to be weighed again and their moisture % determined.

The content is calculated using the following formula:

% Moisture content = (Initial weight- Final weight) x 100/initial weight. [10]

4. Endurance in Folding:

To ascertain this, the film was repeatedly folded in the same location until it broke. The length of time the films could be folded in one spot without cracking or breaking was used to calculate the folding endurance value. [10]

5. Weight uniformity:

After the patches were carefully split into different portions, a preset portion was weighed using a digital balance. The average weight and standard deviation data were calculated using the individual weight. [10]

6. Evaluation of drug content assessment:

To determine how much medication was trapped in a 2x2 cm2 patch, it was totally dissolved in 100 milliliters of phosphate buffer solution (PH 7.4). To ensure total disintegration, the patch-containing solution was shaken for around twenty-four hours.

Spectrophotometry was used to assess the drug content at 210 nm after the solution had been filtered and suitably diluted. [10]

7. The pH of the patch:

A standard buffer solution was used to calibrate the pH meter.One patch was dissolved in fifty milliliters of phosphate buffer, and its pH was then tested. Using a wash bottle, stirrer, pH meter, and baker.[10]

8. In Vitro Drug Release Studies:

Diffusion was performed using a Franz Diffusion cell to determine the percentage of a drug released from the patch into the receptor medium. The trials were conducted for six or nine hours in order to determine the percentage of medicine release from the patch. In order to provide a sink environment for the drug's release, cellulose parchment paper, which resembles skin, was in contact with the patch. A pH 7.4 buffer was utilized, and the contents were constantly swirled using a magnetic stirrer.[11]

9. Flatness

The patches of each formulation were divided into lengthy strips. One from the middle of the patch and one from the other side. The length of each strip and the variation in length brought on by the uneven flatness were measured. 0% constriction was the definition of 100% flatness. Flatness was calculated using the given formula.[8]

% Constriction = I1 (the original length of each strip)-I2 (the length of the trimmed film)I2 (length edit of the film)

10. Moisture Uptake:

For a whole day, the manufactured patches were kept at room temperature in silica gel desiccators.Following that, they were weighed and transferred to various desiccators where a saturated sodium chloride solution at 25°C was used to expose them to 75% relative humidity. The moisture uptake capacity was calculated using the formula

% Moisture uptake = Initial weight – Final weight/Initial weight ×100.[8]

11. Stability analysis (per ICH guidelines):

Formulations were stored for three months at 40 °C and 75% relative humidity in accordance with ICH guidelines in order to conduct stability experiments. After thirty, the samples were taken out. 60 and 90 days, and their drug content and physical attributes were evaluated. An ex vivo permeation study was carried out after 90 days and contrasted with a fresh batch.[12]

9. RESULT AND DISCUSSION:

1. Physical Appearance

Colour – Yellowish

Flexibility – Flexible

Texture – Smooth
Entrapment of air bubbles – Absent

2. Patch Thickness:
Average thickness of the patch = 0.30+0.28+0.29+0.31+0.30÷5
= 1.48÷5 = 0.296

The thickness of the patch = 0.296

3. Moisture content:
Initial weight = 0.70
Final weight = 0.68
% moisture content = Initial weight – Final weight/ Initial weight ×100
0.70 – 0.68/0.70×100 = 0.02/0.70 × 100
0.0285×100 = 2.85%
% Moisture content = 2.85 %

4. Folding Endurance: 86 +-(1)

5. Uniformity of Weight:
0.94+0.70+1.05+0.86+0.62+0.87+0.69+0.70+1.60+0.87 ÷ 10
Weight of 10 patches = 8.9 ÷ 10 = 0.89
Weight of patches = 0.89gm

6. Assessment of drug content determination:
Drug content (mg) = C×V×D
Where,
c = Concentration from calibration curv
V= Volume of solution
D= Dilution factor
C= 0.085mg
V= 100ml
D= 1 (no dilution)
Calculate actual drug content = 0.085×100 ×1
=8.5mg
% drug content t= Actual drug content/Theoretical drug content ×100
% drug content = 8.5/9×100 = 94.4%
Actual drug content – 8.5mg
% Drug content – 94.4%

5. pH Test:
PH of patches = 5.6

6. Drug release studies in vitro:

Time (min)	Release Drug (%)
0 min	0
10 min	5.84
20 min	9.11
30 min	24.30
40 min	32.58
50 min	42.90
60 min	54.66
120 min	65.52

Table no.2: Drug release studies in vitro

9. Flatness test:

Initial weight = 8 gm

Final weight= 7.7 gm

% constriction=

Initial weight – Final weight / Final weight ×100

= 8 – 7.7 / 8 × 100

= 0.3/8 × 100 = 0.0375× 100

% constriction = 3.75

The patch shows 3.75 % constriction indicating it is 96.25% flat

10. Moisture uptake:

Moisture uptake= Initial weight – Final weight/Initial weight × 100

0.68- 0.65/ 0.68× 100

0.03/0.68×100 = 0.0441×100

Moisture uptake = 4.41%

11. Stability analysis (in accordance with ICH recommendations):

The formulation showed no physical changes, good stability under accelerated ICH conditions, with only a slight decrease in drug content and permeation after 90 days. The formulation was found to be stable and suitable for transdermal drug delivery.

9. CONCLUSION:

For the purpose of relieving joint discomfort, the study created a herbal transdermal patch including camphor, mustard oil, and clove oil. It demonstrated consistent drug content, good physicochemical characteristics, and prolonged release. The patch provided a practical, non-invasive, and patient-friendly substitute for treating musculoskeletal conditions since it was stable, skin-friendly, and effective.

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