



A Review On Transdermal Patches Using Ginger And Neem Oil

MS. Chavan Dipali Vilas, Ms.Khilare Manjusha Balaso, MS. Chavan Shweta Bibhishan,

Ms.shinde KavitaVishnu, Ms.Chormale Tejal Bapurav

Quality Assurance,

ABSTRACT: -

Innovations in transdermal delivery system (TDDS) have made important contributions to medical practice by providing advances in the delivery of treatment with existing and novel drugs. Today about 74% of drugs are taken orally and are found not to be as effective as desired.

To improve such character's transdermal drug delivery system was emerged Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery system

The study aimed to formulate a pure herbal transdermal patch and to evaluate its physicochemical properties. The Herbal transdermal patch was formulated by adding the extract of neem in the form of oil and ginger powder. Several test such as visual inspection, pH, thickness, weight variation, folding endurance etc. were performed to determine the physiochemical Properties of prepared transdermal patch. It showed clear appearance, standard surface ph and thickness. The result indicated the formulated transdermal patch is having excellent appearance and surface PH.

Key words: - Herbal transdermal patch, Systemic absorption, Neem oil patch, herbal combination patch, Antifungal patch.

Introduction: -

HISTORY:

In 1980 a US patent disclosed a transdermal patch for hypertension therapy. The first commercially available prescription patch was approved by the US food and drug administration in December 1979. These patches administered scopolamine for motion sickness. A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the blood stream. The FDA has approved till 2003 more than 35 transversal patch products spanning 13 molecules. The US transdermal market approached \$1.2 billion in 2001. Two new recently approved transdermal patch products contraceptive patch containing ethinyl estradiol and nor elgestromin

Transdermal patches are now widely used as cosmetic, topical and transdermal delivery system. These patches represent a key outcome from the growth in skin science technology and expertise developed through trial and error clinical observation and evidence based studies that date back to the first existing human records. The earliest documentation of neem mention fruit, seeds ,oil for their medicinal properties .first recorded indication that neem was being used in medicinal treatment about 4,500 years ago .Ginger was known dates back about 5000 years its native home southeast Asia ,India ,China it is tonic root to treat many ailments.

1.Overview of Transdermal Patches:

- A transdermal patch is medicated adhesive patch which is placed on skin to deliver/release the dose of medication in blood stream.
- Transdermal drug administration refers to substance that is absorbed through skin.
- Transdermal drug delivery can deliver drugs via the skin portal to systemic circulation at a predetermined rate and maintain clinically effective concentration over a prolonged period of time.
- These are designed to support the passage of drug substance from the surface of skin, through its various layers and into the systemic circulation.
- The main route for penetration of drug is generally through the epidermal layers.
- Many people's feel difficulty in swallowing tablets or getting injection, patches are active for longer period of time than tablet, so patients do not have to remember and follow the frequent schedule for taking medication at specific time.
- Currently the patches are used in therapeutic area for reduction of irritation, treating fungal infection on skin.
- **Selection of drug for Transdermal drug delivery system:**
 - Non-irritant , potent, non ionic
 - Narrow therapeutic index
 - Low molecular weight, i.e. 400-1000 Daltons
 - Melting point <200 degree Celsius
 - Water solubility>1mg/ ml
 - Oil solubility>1mg/ml
 - Dose<20mg/day
 - PH between 5-9
 - Preferably for drug undergo extensive first pass metabolism
 - Half life <10hrs
 - Log p1-3
 - Less oral bioavailability

2. Role of Skin in Transdermal drug delivery system:

- The skin is one of the largest organs of the human body.
- It is one of the tissues in our body that duplicates the most and the fastest.
- The drug initially penetrates through the stratum corneum and then passes through the deeper epidermis and dermis with ought to drug accumulation in the dermal layer.
 - At the point of application, adhesive secures the patch to the skin
 - This allows the drug access to the skin, where permeation begins
 - Once applied, a patch administers the drug until either the drug is fully absorbed or the patch is removed.

3. Drugs used in Transdermal Patches:

A. GINGER POWDER: (PEPPINESS , GINGERROOT)

- The ginger powder is prepared from dried Rhizomes of Ginger (Zingier Officinalis).
- It belongs to family zingiberaceae.
- It helps in reduction of irritation, treat Stomach upset, Diarrhea , Nausea , arthritis , migraines ,Hypertensions .

B. NEEM OIL: (NIM TREE, MARGOSA, ARISHTH)

- It is used as medicine for some skin diseases.
- Pure neem oil is in creditably potent.
- It is used to treat Acne, fungal infection.
- Used undiluted neem oil to spot treat affected areas.
- Neem is member of mahogany family, Meliaceae with botanical name Azadirachta indica.



Neem Oil



Neem Plant

Advantages:

- Topical patches are a painless non-invasive way to deliver substances directly into the body.
- Topical patches are a better way to deliver substance that are broken down by the stomach acid, not well absorb from the gut or extensively degraded by Liver.
- Topical patches over a controlled, steady delivery of medication over long period of time.
- Topical patch have Fever side effect than other route.
- Topical patches are easy to use and remember.
- Topical patches are useful for those patients who are unable to prefer the oral medication.
- Topical patches are cost effective.
- People prefer topical patches.

LIMITATION:

- TDDS cannot deliver ionic drugs.
- TDDS cannot achieve high drug levels in blood /plasma.
- It cannot develop for drugs of large molecular size.
- TDDS cannot deliver drugs in pulsatile fashion.
- TDDS cannot develop if drug or formulation causes irritation to skin.
- May cause allergic reaction.

- Long term adherence is difficult

WHEN TRANSDERMAL PATCH IS USED?

- When the patient has intolerable side effect (including constipation) and who is unable to take medication (dysphasia) and is requesting an alternative method of drug delivery.
- Where the pain control might be improved by reliable administration. This might be useful in patient with cognitive impairment or those who for other reasons are not able to self-medicate with their analgesia.
- It can be used in combination with other enhancement strategies to produce synergistic effect.

REVIEW OF LITERATURE

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Traditionally, the well-known and widely used herb, which is ginger having scientific name "Zingiber officinale" that contains several bioactive constituents, has been extensively used for a number of medicinal purposes like to cure pain, lowers cholesterol level in the body and to fight arthritis and act as a stimulant for digestion and absorption, also provide alleviation from constipation and flatulence by enhancing activity of muscles in the digestive tract. For over one thousand years, China has been using ginger as an herbal medicine, it is used as Materia Medica that helps to improve body fluids flow and also by diluting blood and producing strong stimulating effect on heart muscle, and it stimulates the blood circulation in the body. Ginger is considered an aphrodisiac in Arabian medicine. In 19th century, the Electric physicians were used to rely on ginger to improve appetite, cure nausea, induce sweating and lower topical irritation. In India it has been estimated that the average daily consumption of fresh ginger root is -10g

2.S. S. Patil Associate Professor,

Department of Pharmacognosy, Prin. K. M. Kundnani College of Pharmacy. Mumbai University. Cuffe Parade. Colaba, Mumbai-400005,

The potential of transferosome formulation for transdermal delivery of Ginger constituents was investigated. The aim was to reduce the dosage and improve patient acceptance. Transferosomes were formulated by ethanol injection technique using Phospholipids (Lipoid P-100), cholesterol, various edge activators (tween 80, Span 80), and other excipients. Transdermal patches were prepared by solvent casting method using polymers (Ethylcellulose, HPMC). penetration enhancers (Oleic acid, Tween 80) and PEG 400 as a plasticizer. Transferosomes were evaluated for in-vitro release, particle size, zeta potential, entrapment efficiency, and stability. Patches were evaluated for folding endurance, uniformity of weight, drug content, and thickness. Transferosomes with 1:2:0.25 ratio of Phospholipid: ginger extract: Tween 80 showed particles of 318.8nm, the zeta potential of - 6.3mV and 74.4% entrapment efficiency and 67% in-vitro release. Optimized batch of patches showed folding endurance 7, 0.134 0.0012 mm thickness, 97.18 0.78% drug content. Thus, transferosomes with transdermal delivery is a better approach to deliver ginger constituents.

3. Ming Shuang Ding Matthew Leach Helen Bradley

The use of ginger as a topical intervention is widely advocated in the popular media. However, there has been no attempt to date to synthesize the evidence for topically administered ginger. To systematically review and synthesize the best available evidence of effectiveness for topical ginger in any condition. CAM on PubMed, CINAHL, Google Scholar, MEDLINE, National Library of Australia, The Cochrane Library, TRIP, pertinent texts, and bibliographies of relevant papers. Data sources were systematically searched for studies investigating the clinical effectiveness of topical ginger, in any form and for any condition, regardless of study design. Studies were limited to those published between 1980 and 2010, and published in English, Mandarin, Cantonese, or Taiwanese. Data were extracted by two authors, independently, using standardized templates. Four studies met the inclusion criteria, including three

randomized controlled trials and one non-randomized controlled trial. All studies differed in terms of study population, outcome measures, comparative interventions, and dose and form of ginger used, and thus, were not amenable to metaanalysis. Findings from all trials favored usage of ginger for most outcomes. However, the small sample sizes and inadequate methodological reporting indicate a high risk of bias and the need for caution when interpreting these results. Few studies have investigated the effectiveness of topically administered ginger for any condition. Until the findings of these studies are corroborated by more robust research, and the safety of ginger is adequately established, clinicians should remain cautious about using topical ginger in clinical practice.

4. International journal of pharmaceutical sciences and research

An International Journal published monthly Development and evaluation of ginger transdermal patch and its implications in migraine therapy. The potential of transferosomal formulation for transdermal delivery of Ginger constituents was investigated. The aim was to reduce the dosage and improve patient acceptance. Transferosomes were formulated by ethanol injection technique using Phospholipids (Lipoid P-100), cholesterol, various edge activators (tween 80, Span 80), and other excipients. Transdermal patches were prepared by solvent casting method using polymers (Ethylcellulose, HPMC), penetration enhancers (Oleic acid, Tween 80) and PEG 400 as a plasticizer. Transferosomes were evaluated for in-vitro release, particle size, zeta potential, entrapment efficiency, and stability. Patches were evaluated for folding endurance, uniformity of weight, drug content, and thickness. Transferosomes with 1:2:0.25 ratio of Phospholipid: ginger extract: Tween 80 showed particles of 318.8nm, the zeta potential of -6.3mV and 74.4% entrapment efficiency and 67% in-vitro release. Optimized batch of patches showed folding endurance 7, 0.134 ± 0.0012 mm thickness, 97.18 ± 0.78% drug content. Thus, transferosomes with transdermal delivery is a better approach to deliver ginger constituents.

5. Medically reviewed by Sade Meeks, MS RD-written by Jenna Fletcher updated on March 27 2022

Mariangela Rondanelli, Federica Fossari, Viviana Vecchio,
Clara Gasparri, Gabriella Peroni, Daniele Spadaccini, Antonella Riva, Giovanna Petrangolini, Giancarlo Iannello, Mara Nichetti, Vittoria Infantino, Simone Pe

Ginger may have anti-inflammatory, antibacterial, and antiviral properties. Ginger has a pain-reducing effect and it can modulate pain through various mechanisms: inhibition of prostaglandins via the COX and LOX-pathways, antioxidant activity, inhibition of the transcription factor $\text{nf-}\kappa\text{B}$, or acting as an agonist of vanilloid nociceptor. This narrative review summarizes the last 10-year of randomized controlled trials (RCTs), in which ginger was traditionally used as a pain reliever for dysmenorrhea, delayed onset muscle soreness (DOMS), osteoarthritis (AO), chronic low back pain (CLBP), and migraine. Regarding dysmenorrhea, six eligible studies suggest a promising effect of oral ginger. As concerned with DOMS, the four eligible RCTs suggested a reduction of inflammation after oral and topical ginger administration. Regarding knee AO, nine RCTs agree in stating that oral and topical use of ginger seems to be effective against pain, while other did not find significant differences. One RCT considered the use of ginger in migraine and suggested its beneficial activity. Finally, one RCT evaluated the effects of Swedish massage with aromatic ginger oil on CLBP demonstrated a reduction in pain. The use of ginger for its pain-lowering effect is safe and promising, even though more studies are needed to create a consensus about the dosage of ginger useful for long-term therapy.

AIM AND OBJECT

Aim: To prepare and Evaluate the Herbal Transdermal Patch

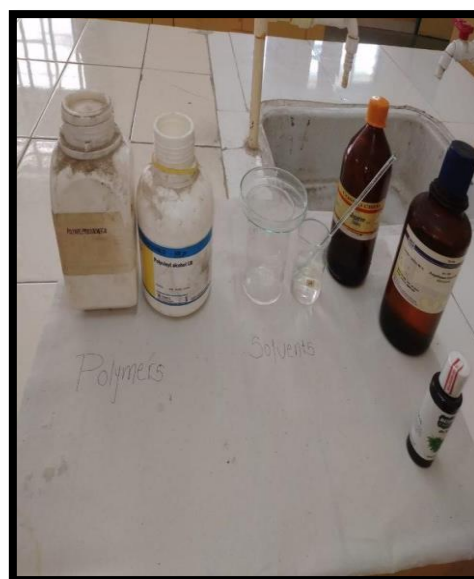
Objectives:

- To explore skin as site for drug administration.
- To stability study.
- To study drug excipients interaction.
- Propylene glycol was used in preparation of patches.
- Ginger was used as stain remover and to improve health of skin.
- Self administration is possible.
- Easy to prepare and transport.
- It avoids first pass metabolism effect.
- Topical patches are painless.
- It improves bioavailability.
- Possibility of terminating the drug administration by the simple removal of the patches.
- Reduction in the frequency of dosing.

MATERIAL AND METHOD MATERIAL

Material- Apparatus:

Petri plate, beaker, stirrer, water bath, hot air oven, tripod stand, wire gauge, Vernier caliper, digital balance, Thermometer



Chemicals:

Neem oil, Ginger powder, distilled water, methanol, polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol 400, dimethyl sulfoxide, glycerine.

Formulae:

Chemical	Quantity	Role
Neem oil	5 ml	API antifungal action
Ginger powder	2 mg	API anti-inflammatory action
Polyvinyl Pyrrolidone	2mg	Polymer
Polyvinyl alcohol	3mg	Polymer
Distilled water	10 ml	Solvent
Methanol	10 ml	Solvent
Polyethylene glycol 400	0.2 ml	Plasticizer
Dimethyl sulfoxide	0.2 ml	Penetration enhancer

Method of preparation:

1. The equal amount of water and methanol taken and make the solution of solvents.
2. The given quantity of PVP and PVA polymers are taken, dissolve and clear solution is produced.
3. To dissolve polymers and make clear solution it heated at 60 degree Celsius.
4. Add required drops of Neem oil and given quantity of Ginger powder.
5. At the last add polyethylene glycol 400 and dimethyl sulfoxide in given quantity.
6. Apply glycerin to Petri plate.
7. Pour solution into petri plate at all equal thickness.
8. Place Petri plate without disturbance in hot air oven for 20 minutes.
9. After drying, striped patch with the help of knife.
10. Cut the patches into (2*2) cm. Packed in polythene bags and submitted.



Evaluations tests for transdermal patch –

1. Physical appearance :

All the prepared patches were visually inspected for color, clarity, flexibility, and smoothness.

2. Thickness of the patch:

The thickness of the drug loaded patches was measured by using a Vernier caliper. The thickness of 10 patches is measured.

3. Uniformity of weight:

The patches were subjected to weight variation test by weighing all the patches on a digital weighing balance.

4. Folding endurance:

This test was carried out to check the efficiency of the plasticizer and the strength of the patch prepared using different polymers. The folding endurance is defined as the number of folds required to break any polymeric patch. The folding endurance was measured manually by repeatedly folding a small strip of the film (2×2 cm) at the same place until it broke. The number of times the patch could be folded at the same place without breaking/cracking gave the value of folding endurance.

5. Surface pH

Patches were kept in contact with 0.5 ml of double distilled water for 1 h in glass tubes and were allowed to swell. A combined glass electrode was brought near the surface of patch and pH readings were taken after allowing an equilibration period of 1 min.

Vernier Caliper:



Result and conclusion –

Ayurvedic systems of medicine have described specified methods and natural drugs. TDDS was ideally suited for drugs that undergoes hepatic first-pass metabolism with a short elimination half-life.

Transdermal patches are prepared by using PVP and PVA as a polymer. Methanol and water both used as solvent. Polyethylene glycol 400 acts as plasticizer in patch. Dimethyl sulfoxide used for penetration enhancer.

The combination patch of Neem and ginger is prepared and submitted. The physical appearance is light brown color, translucent and little bit rough. The flexibility is high. The thicknesses of patches are varied. The standard thickness of patches is form 0.12mm to 0.20mm.

Patches	Thickness (mm)
1	0.182
2	0.155
3	0.184
4	0.164
5	0.105
6	0.182
7	0.102
8	0.186
9	0.184
10	0.102

Average Thickness of patches is 0.148mm. Uniformity in weight of patches check by comparing it with average weight.

Patches	Weight (gm)	Deviation from average weight
1	0.120	0.015
2	0.130	0.025
3	0.140	0.035
4	0.090	-0.015
5	0.080	-0.025
6	0.120	0.015
7	0.070	-0.035
8	0.100	0.005
9	0.140	0.035
10	0.060	-0.045
Average weight	0.105	0.039

The average weight of patch with deviation is 0.105 ± 0.03 Folding endurance of patches is around 200.

Patches	Folding endurance
1	180
2	145
3	225
4	150
5	155
6	160
7	150
8	188
9	210
10	170

Surface pH of the patches was found in between 6.8 to 7.1 and it is acceptable.

Patch	Surface pH
1	7.1
2	6.9
3	7.0
4	7.2
5	7.1
6	6.8
7	6.9
8	7.0
9	7.1
10	7.0

The average pH value of patches 7.01.

SUMMARY AND DISCUSSION

- ✓ The aim of the present investigation was to develop and evaluate transdermal patch.
- ✓ PVP and PVA used as polymers.
- ✓ Glycerine was used as permeability enhancer.
- ✓ The final formulation found satisfactory.
- ✓ There was no interaction between drug and excipient.
- ✓ Trial A1-A14 was initiated using different polymers in formulation.
- ✓ The prepared patches are transparent and smooth in nature.
- ✓ The weight variation found well within acceptable range.
- ✓ The thickness of patches was found uniform and variation is satisfactory.
- ✓ The drug content, folding endurance and % elongation were found well within acceptable range.
- ✓ Initially patches are prepared without drug for checking compatibility with each other.
- ✓ Hence combination of these polymers are taken and found better result than single polymer used.

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