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FORMULATION AND EVALUATION OF TRANSDERMAL PATCH USING ANTIOXIDANT PHYTOCONSTITUENT

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Abstract

Conventional drug delivery system has many problems so bulk of research has now shifted from synthetic drugs to herbal drugs. This is possible because of the vast variety of bioactive molecules in the plants and their higher safety margin. This present study is focused on the use of curcumin, the active constituent of Curcuma longa (haldi), and belonging to family Zingiberaceae as an antioxidant agent. The main objective of present work was to develop the transdermal patch of curcumin using polymer blends so that minimize the side effects and maximize the therapeutic efficacy. The formulations were also evaluated for weight variation, moisture uptake, thickness, moisture content, and folding endurance. Shows satisfactory results.

Keywords: Curcumin, Poly Vinayl Pyrollidone, Ethyl Cellulose, Transdermal Patch.

INTRODUCTION

A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative way for administrating medication. This device allowed for pharmaceuticals to be delivered across the skin barrier (Chin, Y.W. et al 1992). Simple theory behind transdermal permeation is that a drug is applied in a relatively high dosage at the surrounded by of a patch or other system, which is worn on the skin for an extended period of time. Throughout a diffusion course, the drug inters in the blood stream directly through the skin. Since there is elevated concentration on the patch and small concentration in the blood, the drug will keep diffusion in to the blood for a long episode of time; maintain the unchanging concentration of drug in the blood flow (Ancel, H.c. et al 2002).

A transdermal patch is defined as medicated adhesive patch which is placed above the skin to deliver a specific dose of medication through the skin with a predetermined rate of release to reach into the bloodstream.

Curcumin has antioxidant, anti-inflammatory, antiviral and antifungal actions. Studies have shown that curcumin is not toxic to humans. Curcumin exerts anti-inflammatory activity by inhibition of a number of different molecules that play an important role in inflammation. Turmeric is effective in reducing post-surgical inflammation. Oral bioavailability 1% and half-life 2 to 4 hours. Curcumin has been shown to inhibit certain epigenetic enzymes (the histone deacetylases: HDAC1, HDAC3, and HDAC8) and transcriptional co-activator proteins (the p300 histone acetyl transferase). Curcumin also inhibits the arachidonate 5-lipoxygenase enzyme *in vitro*, as well as the enzyme cyclooxygenase. The free radical mediated peroxidation of membrane lipid and oxidative damage of DNA and protein are believed to be associated with a variety of chronic pathological complication such as cancer, atherosclerosis, and neuro degenerative disease, curcumin is thought to play a vital role against this pathological condition.

ANTIOXIDANT

Antioxidants are an inhibitor of the process of oxidation, even at relatively small concentration and thus have diverse physiological role in the body. Antioxidant constituents of the plant material act as radical scavengers, and helps in converting the radicals to less reactive species.Antioxidants that have traditionally been used to inhibit oxidation in foods also quench dreaded free radicals and stop oxidation chains *in-vivo*, so they have become viewed by many as nature's answer to environmental and physiological stress, aging, atherosclerosis, and cancer. The nutraceutical trend towards doubling the impact of natural antioxidants that stabilize food and maximize health impact presents distinct challenges in evaluating antioxidant activity of purified individual compounds, mixed extracts, and endogenous food matrices and optimizing applications.It is well known that Mediterranean diet, which is rich in natural antioxidants, leads to a limited incidence of cardio- and cerebrovascular diseases (Hertog M. G. L. et al). It is known that compounds belonging to several classes of phytochemical components such as phenols, flavonoids, and carotenoids are able to scavenge free radical such as $O2^{\cdot}$, $OH^{\cdot}$, or lipid peroxyl radical $low^{\cdot}$ in plasma (Kaur C et al 2001). [38]. The effective intake of single food antioxidants and their fate in the human body have been defined only for a few compounds (Larson R. A.et al 1988). It is

reasonable that the higher the antioxidant content in foods is, the higher the intake by the human body will be.

Natural antioxidants occur in all parts of plants. These antioxidants include carotenoids, vitamins, phenols, flavonoids, dietary glutathione, and endogenous metabolites (Manach C..et al 1998,). Plant-derived antioxidants have been shown to function as singlet and triplet oxygen quenchers, free radical scavengers, peroxide decomposers, enzyme inhibitors, and synergists (Saba Maanvizhi et al 2015). The most current research on antioxidant action focuses on phenolic compounds such as flavonoids. Fruits and vegetables contain different antioxidant compounds, such as vitamin C, vitamin E and carotenoids, whose activities have been established in recent years. Flavonoids, tannins and other phenolic constituents (Boddupalli Bindu Madhavi, et al 2013). Multiple pathways are involved in photocarcinogenisis so mixture of several botanical antioxidents working through various mechanisms in conjuction with the use of sunscream could also be an effective approach reducing ultravailet generated reductive oxigens species mediated photodamage immunosuppressen and skin cancer in human (Chanchal deep kaur 2012).

MATERIAL AND METHODS

Curcumin was procured as a gift sample of hi media. All chemicals and reagents used were of analytical grade and obtained from ideal chemical company. All other ingredients used were of analytical grade of our institute.

Method of Preparation

Solvent Evaporation Method

Preparation of backing membrane

The 4 gm polyvinyl alcohol (PVA) is dissolve in 100 ml of distilled water to prepare 4% of polymeric solution with continuous magnetic stirring. After the 4% polymeric solution is pour in 4 open glass mould at same proportion and transfer in hot air oven at 60 ^{o}C for 6 hrs. Before pouring of polymeric solution in open glass mould few drop of glycerine is pour in glass mould. (Saba Maanvizhi et al 2015)

Preparation of casting solution

Casting solution is prepared by the using suitable solvent (ethanol), ethyl cellulose, polymer (polyvinyl pyrolidone) and plasticizer (dibutylpthalate) is added slowly-slowly with

continuous stirring. The selected drug is also added slowly with continuous stirring of casting solution up to 45 min.

The dried backing membrane glass Petridis is removed from hot air oven after overnight. The prepared casting solution pour in open glass contain dried backing membrane and transfer in to hot air oven at 60 ºC for 6 hrs. After the complete drying of transdermal film the dried film is removed from glass mould (Kumar. PD et al 2011)

Table 1 Formulation Design

S.N.	INGREDIENTS	WORKING FORMULA
1.	Curcumin	20 mg
2.	Poly vinyl pyrolidone	860 mg
3.	Ethyl cellulose	140 mg
4.	Di butyl phthalate	30 mg
5.	Poly vinyl alcohol	4 gm/100ml

EVALUATION

Physical appearance

The prepared patches are physically examined for colour, clarity and surface texture.

Thickness of the patch

The thickness of the drug loaded patch is calculated in different points by using a digital micrometre, or travelling microscope, dial gauge, screw gauge, and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch. Patch will have an equal thickness at every point. The variation of thickness within the patch and patch to patch can be calculated (Radhika Gadekar et al 2012)

Moisture content

Individually weighed patches are kept in the desiccators having fused calcium-chloride at room temperature for 24 hours. After 24 hrs the patches are to be reweighed and percentage moisture content is calculated by the formula.

$$\% \text{ Moisture content} = \frac{\text{(Initial weight – Final weight) X 100}}{\text{Final weight}}$$

Moisture uptake

The weighed films are to be kept in desiccators at room temperature for 24 hrs containing saturated solution of potassium chloride in instruct to maintain 84% RH. After 24 hrs the films are to be reweighed and determined the percentage moisture uptake from the mentioned formula.

$$\% \text{ Moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Folding endurance

This was determined by repeatedly folding the film at the same place until it broke. The number of period the films could be folded at the same place without breaking/ cracking gave the value of folding endurance **(**Payal Khamora et al 2014).

RESULT AND DISCUSSION

Physical evaluation

All the transdermal patches were visually inspected for colour, clarity, flexibility and smoothness.

Thickness

Patch thickness was measured using Vernier calliper at three different places, and the mean value was calculated.

Table 2 Thickness determination of formulation

S.N.	Thickness(mm)	Average(mm)
1	0.33	
2	0.37	0.35
3	0.37	

Moisture content

Individually weighed patches are kept in the desiccators having fused calcium-chloride at room temperature for 24 hours. After 24 hrs the patches are to be reweighed and percentage moisture content is calculated by the formula.

Table 3 Moisture content determination of formulation

S.N.	Moisture content %	Average %

1	0.87	
2	1	0.956
3	1	

Moisture uptake

The weighed films are to be kept in desiccators at room temperature for 24 hrs containing saturated solution of potassium chloride in instruct to maintain 84% RH. After 24 hrs the films are to be reweighed and determined the percentage moisture uptake from the mentioned formula.

Table 4 Moisture uptake determination of formulation

S.N.	Moisture uptake %	Average %
1	1.11	
2	1.36	1.32
3	1.49	

Folding endurance

Folding endurance test results indicated that the films would not break and would maintain their integrity with general skin folding when applied.

Table No.11 Folding endurance determination of formulation

S.N.	Folding Endurance	Average
1	18	
2	25	23.3
3	27	

CONCLUSION

Transdermal patches of curcumin were successfully prepared by using ethyl cellulose and poly vinyl pyrollidone. Prepared patches were found to have smooth and uniform surface when they are functional onto skin. TDDS of curcumin were prepared by solvent evaporation method and evaluated for different parameters. Evaluated for, physical appearance, thickness was found to be 0.35mm, moisture content was found to be 0.956%, moisture uptake was found to be 1.32%, and folding endurance was found to be 23. Shows satisfactory results.

This research work highlights that curcumin may be incorporated into the transdermal drug delivery system for their suitable and convenient use. Studies have shown promising results. Hence there is a scope for further pharmacodynamics and pharmacokinetic evaluation.

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