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RESEARCH ARTICLE

DEVELOPMENT OF THINFILM FOR TRANSDERMAL DELIVERY OF HERBAL OILS

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Abstract

Wound healing is a complex biological process, results in the restoration of tissue integrity. Allopathy uses drugs and sometimes surgery to treat ailments related to bone and joint disorders. To overcome the drawbacks associated with current treatment methodologies herbal therapies such as herbal oils, tablets, yoga, meditation, special diets, etc are followed. To enhance the herbal delivery several nanomaterials are used. In the current study Poly (vinyl alcohol)/Chitosan (PVA/CTS) thin films of approximately 4 mm in thickness were synthesized by stirring using acetic acid and Glutaraldehyde. The prepared thin film with a high crosslinking density and a dense inter-porous structure were utilized with oil for the formation of herbal oil thin film. The composite films were characterized by Fourier-transform infrared spectroscopy (FTIR), and biocompatibility assays. The results confirmed that highly stable and uniformly distributed herbal thin film obtained over the entire thin film networks. The tensile test revealed that the effective incorporation of herbal oil within the hydrogel networks rendered the composite films more elastic. Due to its inter-porous structure, uniform distribution of oil and biocompatibility, the herbal oil-loaded PVA/CTS thin film may be utilized as a biomaterial in medical applications.

keywords

Thin films, nanomaterial, herbal oil, PVA, Chitosan

Introduction:

Wound healing is a complex biological process, results in the restoration of tissue integrity. General medicines are concentrating on the symptoms of a disease and not on the causes of those symptoms (Bennadi, D. 2013, Alonso-Castro *et al*., 2018). Herbal medicine has a long history of evolution in styles and practice worldwide (Srivastava, J. K *et al*., 2010). In its early stage, herbal or animal medicines were widely utilized over many different countries, including Greece, as allopathic medicine, Ayurvedic medicine in India (Han, G and Ceilley R., 2017, Zhang, J., *et al* 2012). In today's time, nanotechnology is being utilized to develop efficient products in the cosmetic and pharmaceutical industries (Pandey, A., & Pandey, G. 2013). The application of nanotechnology in transforming bioactive material into nanoscale products substantially improves their biocompatibility and enhances their effectiveness, even when used in lower quantities (Ansari, S. H. *et al*., 2012, Bonifacio, B. V *et al*., 2014). There is a significant global market potential for these nanoparticles because of which research teams around the world are interested in the advancements in nanotechnology. (Abdullah, O. G, *et al*., 2015).

Wounds can be categorized into acute and chronic types Acute wounds are the outcome of traumatic or surgical events that heal predictably following a regular healing process (Ellis, S., *et al*., 2018, Young, A., & McNaught, C. E. 2011). Burn wounds are another class of wounds that are caused by heat, chemicals, electricity, sunlight, radiation or friction Burns can be classified into superficial, partial-thickness and full-thickness burns. The materials used in the treatment of chronic wounds are used for two different purposes scaffolding materials that can host the endogenous cells and facilitate their growth and wound closure; temporary dressings that cover the wound area and maintain a suitable condition supporting the healing process. The ideal wound dressings are supposed to cover the wound, preserve the body water content, be oxygen permeable to allow oxygen access to growing tissue, and prevent the growth of environmental pathogens without interfering with the wound healing (Harper, D., *et al.,* 2014, Guo, S. A., & DiPietro, L. A. 2010). The utilized materials should be immunocompatible, non-degradable, and should not support cell ingrowth and cellular adhesion so to avoid complications during their removal. Dressing delivering drugs and biological factors

should preserve the activity of the drugs and should be able to release the drugs at the desired rate. Scaffolding materials used for the treatment of chronic wounds, should facilitate the tissue regeneration, restore the tissue function, and promote a rapid healing process preventing chronic wounds. The material should possess a degradation rate that matches the rate of tissue growth. In addition, neither the material nor the by-products of the degradation process should induce immunogenicity and toxicity. The scaffolding material should adhere properly to the surrounding tissues and its mechanical properties should match those of native skin to avoid the detachment and breakage over the course of healing (Saghazadeh *et.al*., 2018). They should have a limited swelling capacity and maintain their shape over time. These scaffolding materials can also be used as a depot of growth factors and the drug that are directly being delivered to the healing tissue (Murphy, P. S., & Evans, G. R. 2012).

Polyvinyl alcohol (PVA) was created about 90 years ago as the first synthetic colloid and it has been used for various applications since then. PVA is prepared in two steps due to the unstable form (readily tautomerized into acetaldehyde) of vinyl alcohol as monomeric units he free-radical polymerization of vinyl acetate in an alcoholic solution and partial hydrolysis of poly vinyl acetate (Noushini, A *et al*., 2013) By controlling hydrolysis step, different grades as degree of hydrolysis of PVA polymer can be prepared and finally affect the behaviour of polymer material, solubility, crystallinity, and chemical properties (Thong *et al*., 2016). Chitosan is a deacetylated product of chitin, which is an abundant natural resource that features less storage than cellulose (Aranaz, I., *et al*., 2021) Chitosan is a renewable natural alkaline polysaccharide that has no toxicity and no side effects, and it features good moisturizing and adsorption properties (El Hadrami, A *et al*., 2010). The United States Food and Drug Administration (FDA) has approved that chitosan is safe in the use of foods and drugs (Wang *et.al*., 2020). The current study aims to develop thinfilm for herbal oil delivery.

1. MATERIALS AND METHODS

1.1. Materials

Chitosan, PVA, acetic acid, glutaraldehyde, Dulbecco's modified Eagle's medium (DMEM), Fetal Bovine Serum (FBS), sodium chloride, sodium bicarbonate, di-sodium hydrogen phosphate dihy drate, 3-(4,5-dimethyl thiazolyl-2)-2,5-diphenyl tetra zolium bromide (MTT) and other chemicals were obtained from Himedia, Mumbai, India. All the chemicals used were of analytical grade without any further purification.

1.2. Cell culture

The cultures were maintained in the medium containing DMEM, FBS (10% v/v), penicillin (100 units/ml), and streptomycin (100 mg/ml). The cells were incubated at 37 °C with 5% CO2 throughout the study. The cells were detached after the plates reached 100% confluency using trypsin and seeded at a density of 1 9 103 cells/well (Park, S *et al*., 2017).

2.3. Thin film preparation

0.25 g of chitosan is dissolved in 25 ml of acetic acid, and an equal volume of pva solution is mix which contains 0.25 g of pva and 25 ml of distilled water. The two mixtures are mixed for one hour in a magnetic stirrer at 1000 rpm at 60 degrees Celsius. 1ml of 2% Glutaraldehyde solution in water was added to the solution, and the chitosan-pva blend mixture was immediately transferred to an aluminium covert glass plate and air dried for 4 hours in an oven at 80 ℃. (Jiang, S *et* al., 2011, Hu, Y *et al.*, 2020)

2.4. Oil incorporation in thin film preparation

0.25 g of chitosan is dissolved in 25 ml of acetic acid, and an equal volume of pva solution is mix, which contains 0.25 g of pva and 25 ml of distilled water. The two mixtures are mixed for one hour in a magnetic stirrer at 1000 rpm at 60 degrees Celsius. 1 mL of 2% Glutaraldehyde solution in water has been added to the solution, along with 2 mL of murivenna herbal oil. The chitosan-pva-oil mixture was immediately transferred to an aluminium covert glass plate and air dried for 8 hours in an oven at 80 ℃ (Kudaibergenov, S. E *et* al., 2012, Kumar, H. N. *et al*., 2010).

2.5. Fourier transform infrared (FTIR) spectroscopy:

The vibrational structural characteristics analysis of the chemical functional group in the thin films was done using Fourier transform infrared (FTIR) spectroscopy (Ng, Y.C *et al*., 2013). FT-IR spectrophotometer was used to record the IR spectra of between 500–4000 cm−1(Transmittance range).

2.6. Skin irritacy assay – Pig skin protocol:

Ex-viva pig skin irritation study:

Fresh porcine skin was purchased from a local slaughterhouse within 6 hours of animal slaughter. Initially the skin is washed thoroughly with tap water and then with distilled water. The skin was shaved carefully to remove hair and subcutaneous fat using scalpel, then washed with sterile phosphate-buffered saline (PBS, pH 7.4). The tissue was cut into uniform pieces of roughly 2 × 2 cm were mounted on Petri dishes with the epidermal surface facing upward (Moniz T *et al*., 2021).

Control films containing PVA and Chitosan, and test films containing PVA, Chitosan and Murivenna herbal oil were gently placed on the skin surface and covered with thin parafilm to ensure uniform

contact. The skin samples were incubated at 37 °C for 24 hours in a humidified chamber.

After incubation, the thin films were carefully removed, and each skin sample was examined visually for signs of redness, swelling, or any other allergic irritation. The tissues were then fixed in 10% neutral buffered formalin, processed through graded alcohols to remove water, embedded in paraffin. The tissue is cut to a thickness of 5 µm slice. The sectioned slice was stained with hematoxylin and eosin (H & E) and examined microscopically to assess the condition of the epidermis and dermis layer of skin for erythema (Lakshmi, C. 2014, Mojumdar, E.H *et al*., 2021).

2.7. Cytotoxicity assay:

In a 96-well plate, the cells were seeded on the thin films with a density of 1000 cells/well and incubated for 24 h in a 5% CO2 incubator. The sample with media solution was removed after 24 h incubation and the cells were washed with phosphate-buffered saline (PBS) before the cell culture assays (Seah, M.Q *et al*., 2020). Further cell proliferation and viability referred to as MTT (3-(4,5- dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay was carried out.

2. RESULTS AND DISCUSSION

3.1. Preparation of Thin Film

The thin film was successfully developed using polyvinyl alcohol (PVA) and chitosan in a 1:1 ratio, with the incorporation of selected herbal oils. The film developed (Fig. 1) was smooth, flexible, transparent, and non-sticky, indicating good miscibility between the polymers and uniform distribution of the oil. The developed thin film was assessed further for studying the thin film properties.

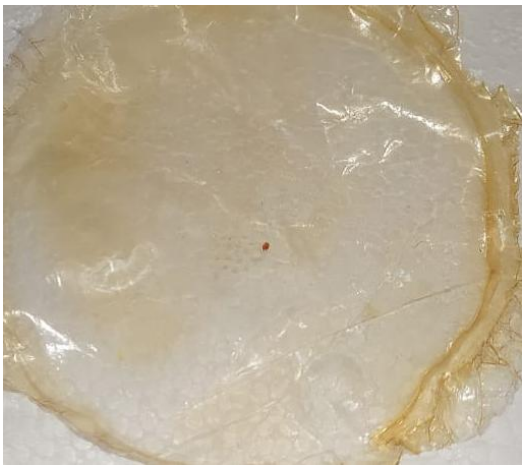
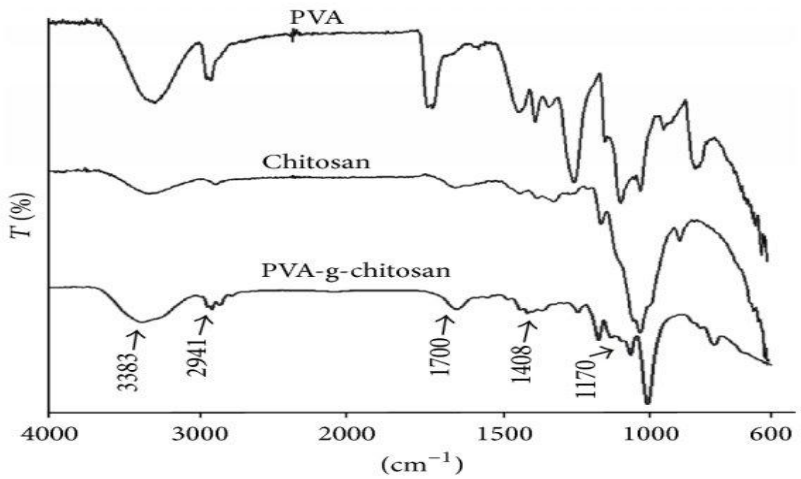


Fig 1: Developed thin film incorporated with herbal oil

3.2. FTIR (Fourier Transform Infrared Radiation)

Fourier transform infrared spectroscopy also known as FTIR analysis is an analytical technique used to identify organic, polymeric, and inorganic materials. FTIR analysis method used infrared light to scan test sample and observe chemical properties

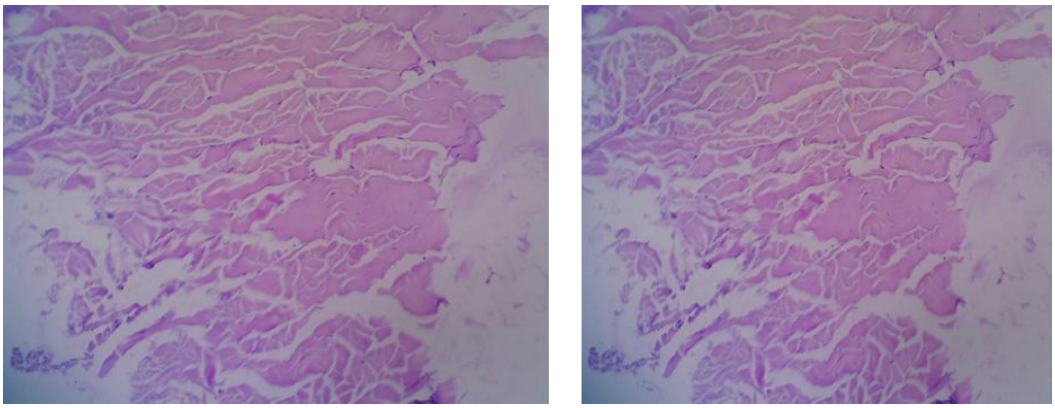
The identification of oil and polymers molecules in the combined solution of pva, chitosan was studied at the range 4500-500 cm-1 using FTIR spectroscopy by thin film. FTIR is the most powerful tools for identifying the types of chemical bonds (functional groups) present in the compounds.



The peak of 3383 and 2941 cm-1 in the spectra correspond to O-H stretching vibration indicating the presence of Alchol. The peak at 1700 cm-1 was assigned as C=O stretching indicates the presence of Conjugated aldehyde. The peak at 1408cm-1was assigned S=O stretching indicates the presence of Sulfonyl chloride. The peak of 1170cm-1 was assigned as C-O stretching indicates the presence of Ester.

3.3. Skin irritacy test – pig skin

The skin irritancy test was performed using pig skin, which closely resembles human skin in histological structure. The control film (without herbal oil) and herbal oil-incorporated film were applied to the pig skin and observed for any signs allergic irritation or inflammation.



Control thin film Thin film with oil

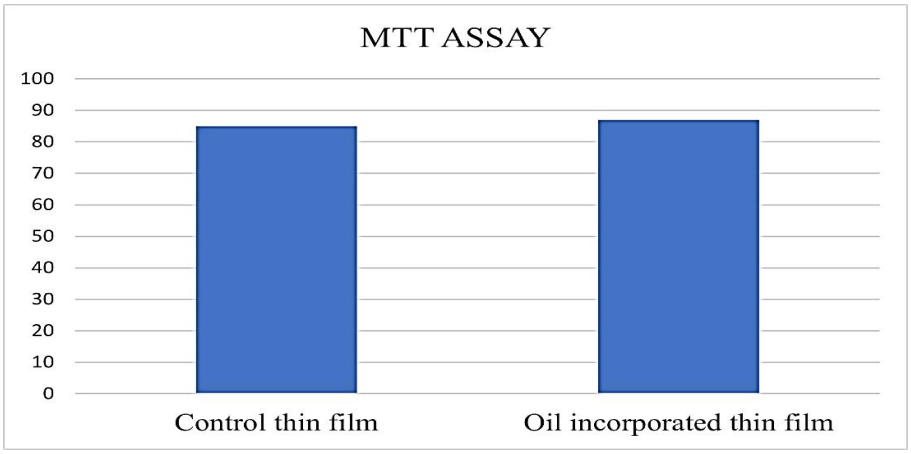
Fig 3: Skin Irritacy test

Samples	Observation
Control film	Normal appearance of epidermis and dermis, no signs of inflammation and allergic irritations
Film with herbal oil	Mild skin reaction observed in the muscle and adipose tissue, indicating minimal irritation

The invitro study shows (wound healing) no irritation and allergy; thin film 10 x muscle bundle, thin film shinned out epidermis with dermis shows normal, thin film 10 x shoes deep adipose tissue of animal tissue by using this thin film. In the incorporation thin film with oil there is a slit skin irritation in the muscle, and adipose tissue

3.4. Cytotoxicity Assay – MTT

The MTT assay was carried out to assess the cytotoxic effect of the developed thin film on living cells. The result indicated that the film extract showed no significant cytotoxicity when compared to the control (untreated) cells. The cell viability remained above 85%, indicating that the polymer-oil matrix is non-toxic and did not interfere with normal cellular metabolism. The result confirmed that the formulated film is non-toxic and suitable for biomedical applications such as wound healing or transdermal drug delivery.



3. CONCLUTION

In this study thin film was formulated and developed using polyvinyl alcohol (PVA) and chitosan in equal proportions for the incorporation and delivery of herbal oil (Murivenna) which has significance in pain relief. The FTIR analysis was performed and determine the drug in thin film which indicate the successful blending of polymers and herbal components. The MTT assay showed cell viability greater than 85%, indicating the film is non-toxic and biocompatible. Furthermore, the ex vivo pig skin irritation assay showed no significant tissue damage, confirming its dermal safety and compatibility. The thin film may allow potential to be used as biomaterials for medical applications, like wound dressing, pain-relief patch etc. In previous work PVA and chitosan were used for the preparation of hydrogel, in this study these polymers were successfully employed as "Thin Film" with the incorporation of herbal oils.

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