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Characterization of Nanogel for Transdermal Drug Delivery System

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Abstract : Transdermal drug delivery system is an alternative to conventional drug delivery methods such as oral delivery of drugs and is poised to provide an alternative to hypodermic injection. It is designed to deliver a therapeutically effective amount of drug across a patient's skin. In recent years the use of nanogel have been increased enormously in biomedical due to its advantageous properties such as biocompatibility, bioavailability, degradability, ability to load drug in nanogel and high stability in aqueous solution makes them more attractive in transdermal drug delivery. PVA/1-vinylimidazole complex nanogel is synthesized by polymerization of PVA nanoparticles with vinylimidazole monomer in the presence of MBA, TEMED and KPS as cross-linking agent and initiator. The SEM image shows the size and morphology of the nanogel. The swelling behaviour and the batch/in-vitro studies will be conducted for the trans-dermal drug delivery application.

Introduction

Nanogel can be termed as dispersion of hydrogel by physical and chemical cross-linking polymer at nanoscale size[1]. Nanogel has ability to control size, composition depending upon the application. Nanogel also has unique properties such as biocompatibility, bioavailability, degradability, ability to trap a large amount of water[2]. Polymeric nanogel has been used as a carrier for gene delivery such as oligonucleotide and DNA[3]. Nanogel is used to study the isolation of bacteria and fungi from aquatic environment[4]. Nanogel is also used as protection efficiency for mid steel in HCL as cathodic inhibitor in corrosion[5]. Nanogel can be used as additives in various applications such as paint, cosmetics, medical and etc. Nanogel is used to load drugs and followed by stimuli-sensitive, multi-responsive, magnetic and targeted drug delivery application and also in bioimaging[2].

The main aim of this work is to synthesis and analyse the nanogel sample in two different concentration using SEM chacaertization technique. Further the in-vitro studies of nanogel behaviour in trans-dermal drug delivery application are discussed. Transdermal drug delivery is the way of application of medications to the skin to ease ailments is a practice that has been utilized by humankind over the millennia and has included the

application of poultices, gels, ointments, creams, and pastes. These applications were basically used for local topical effect. The use of adhesive skin patches to deliver drugs systemically is a relatively new phenomenon[6]. Transdermal drugs are generally poorly absorbed with very controlled depot effect. It is only effective in only some drugs. To date, transdermal drug delivery for systemic effects is limited to very few drugs, all of which have low molecular weights and high to moderate lipophilicity. Transdermal drug delivery offers controlled release of the drug into the patient, it helps in steady blood-level profile, resulting in reduced systemic side effects and improved efficacy over other dosage forms. In addition transdermal patches are user-friendly, convenient, painless, and offer multi-day dosing, it is generally accepted that they offer improved patient compliance. The first-pass effect (or first-pass metabolism) is a phenomenon of drug metabolism. Transdermal delivery of a drug product allows for the avoidance of first pass metabolism by the liver and the delivery of a more even level of the therapeutic agent over the course of 24 hours. Dermal patches are the most common form of transdermal delivery of drugs. Transdermal gels are designed to deliver sustained drug amounts, resulting in systemically consistence levels. They represent an improvement compared with transdermal delivery by patches because they offer more dosage flexibility, less irritation potential and a better cosmetic appearance. Advanced transdermal delivery gel technology was developed in order to provide enhanced passive skin permeation of various active drugs for the treatment of many conditions. A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a time released dose of medication through the skin and into the bloodstream. Transdermal patches are used to deliver a wide variety of pharmaceuticals. The most well-known skin patch nowadays is the nicotine patch which releases nicotine to help quitting the habit of tobacco smoking. Other skin patches administer estrogen for menopause and to prevent osteoporosis after menopause, nitroglycerin for angina, and lidocaine to relieve the pain of shingles (herpes zoster). Recent developments expanded their use to the delivery of hormonal contraceptives, antidepressants and even pain killers[7] The first adhesive transdermal delivery system patch was approved by the Food and Drug Administration in 1979. Nitroglycerine patches were approved in 1981. This method of delivery became widely recognized when nicotine patches for smoking cessation were introduced in 1991[6].

Polyvinyl alcohol (PVOH, PVA, or PVAl) is a water-soluble synthetic polymer (not to be confused with polyvinyl acetate, a popular wood glue). It has the idealized formula $[CH_2CH(OH)]_n$. It is used in papermaking, textiles, and a variety of coatings. It is white (colourless) and odorless. It is sometimes supplied as beads or as solutions in water. PVA has a melting point of 230 °C and 180–190°C (356-374 degrees Fahrenheit) for the fully hydrolysed and partially hydrolysed grades, respectively. It decomposes rapidly above 200 °C as it can undergo pyrolysis at high temperatures. PVA is close to incompressible. The Poisson's ratio is between 0.42 and 0.48. PVA is nontoxic. It biodegrades slowly, but solutions containing up to 5% PVA are nontoxic to fish. Imidazole is an organic compound with the formula $(CH)_2N(NH)CH$. It is a colourless solid that dissolves in water to give mildly alkaline solution. In chemistry, it is an aromatic heterocycle, classified as a diazole and as an alkaloid. It is highly soluble in water. The compound is classified as aromatic due to the presence of a sextet of π-electrons, consisting of a pair of electrons from the protonated nitrogen atom and one from each of the remaining four atoms of the ring.

Experimental

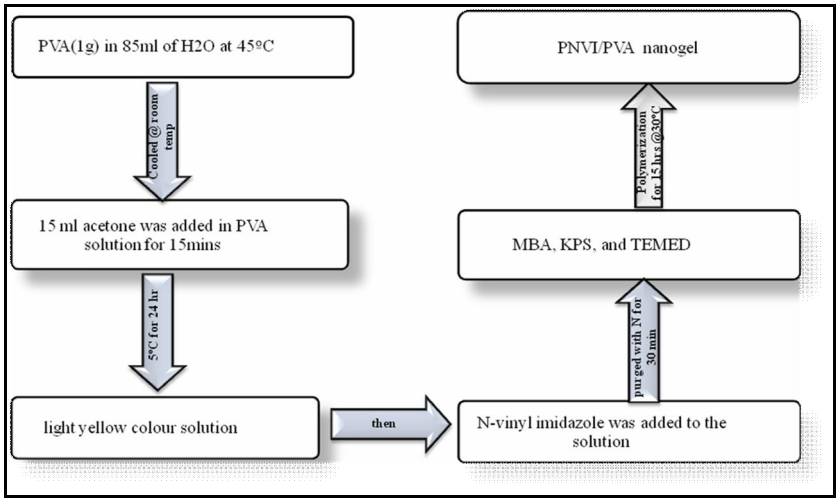
Chemicals required

Poly vinyl alcohol (PVA) with average molecular weight 40,500g/mol and 1-(vinyl imidazole) are purchased from Sigma-Aldrich Corporation. Methylenebisacrylamide (MBA) and Potassium persulfate (KPS) are purchased from Sudagar Biological & Chemicals. Tetramethylethylinediamine (TEMED) is purchased from southern India Chemicals Corporation.

The 1-vinyl imidazole/PVA complex nanogel is synthesized with two different concentration of PVA. PVA of 1g and 0.5gconcentration is dissolved in 85ml of water at 60ºC for 2 hours. After cooling at room temperature 15ml of acetone was added dropwise to the PVA solution in a magnetic stirrer to form 1% of PVA solution respectively. Then the PVA solution is placed at 4ºC for 24 hours. Then 0.5% of 1-vinyl imidazole is added to the PVA solution. Then this solution is purged with Nitrogen gas for 30mins. 4mM of MBA, 0.4mM of KPS and 0.67mM of TEMED is added to the solution to carryout polymerization for 15hrs at 30ºC then the nanogel is formed. Same procedure was repeated for 0.5% concentration of PVA.

Synthesis Protocol

The synthesis part is followed by the following flow chart [5].



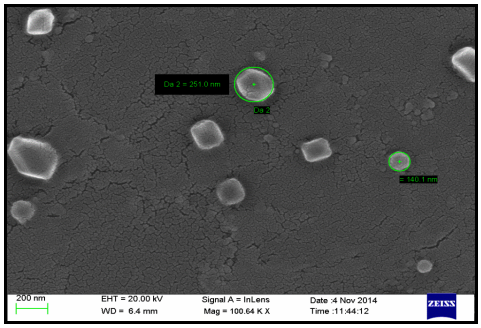
Synthesis protocol for PVA/Vinyl imidazole nanogel

Results and Discussion

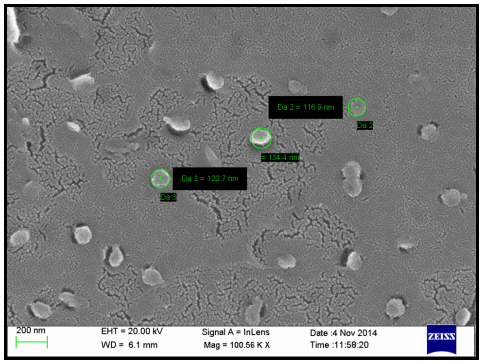
SEM

Sample preparation

The nanogel sample is prepared for the SEM chacertization by using few drops of nanogel solution is added to 2ml of acetone and then some amount of the prepared sample is placed in glass plate followed by drying. The following prepared sample is used for SEM characterization.



Fig(a)



Fig(b)

The Fig(a) shows nanogel with 1% of PVA and 0.5% of vinyl imidazole, Fig(b) shows nanogel with 0.5% of PVA and 0.5% of vinyl imidazole.

Nanogel with 1% of PVA and 0.5% of vinyl imidazole shows the size of about 241nm, 140nm and the average size 196nm. Nanogel with 0.5% of PVA and 0.5% of vinyl imidazole shows the size of about 116nm, 134nm, 122.7 and the average size 124nm.

Conclusion

Nanogel is synthesized using the above mentioned method with two different concentrations and the size of the nanogel is well studied using SEM characterization technique, which shows the 1% of PVA and 0.5% of vinyl imidazole nanogel has about average size of 196nm and 0.5% of PVA and 0.5% of vinyl imidazole nanogel has about average size of 124nm. It concludes that as the size of the nanogel decreases with the decrease in concentration of PVA. Further nanogel will be characterized with dynamic light scattering technique to find overall average particle size and charge of the particle and followed by FTIR to study the chemical bonding and cross-linking polymerization. Then nanogel will be used for batch studies and in-vitro studies for trans-dermal drug delivery.

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