Modification of PVC Film with Thiouronium and study the Effect of Biocompatibility

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Abstract— *Medical grade poly vinyl chloride surface modified with thiouronium by nucleophilic Substitution of thiouronium atoms in presence of a phase-transfer catalyst. Few of chloride group of PVC chain has replaced by basic thiouronium group and these thiouronium groups are further oxidized to sulfonate group. Surface modified PVC characterized with Fourier transforms infrared spectroscopy, scanning electron microscope, and differential scanning calorimetry. Migration or leaching of the plasticizer, di-(2-ethylhexyl) phthalate (DEHP), has examinined in petroleum ether followed by differential scanning calorimetry. The leaching test can also carry out with poly ethylene glycol-400 (PEG-400). The surface of modified PVC film can expect to be extremely migration resistant of DEHP in petroleum ether and PEG-400. Clotting time measurement performed on both modified and unmodified PVC, and observation has done. From that have to be observe the property of thrombogenicity. Further, blood compatibility of modified PVC has examinined through haemolysis assay and suggestion analyzed whether which produce nontoxic material for biomedical applications.*

KEYWORDS*: Poly vinyl chloride; plasticizer migration; surface modification, clotting time*.

1. INTRODUCTION

Poly vinyl chloride (PVC) is used in wide range of medical applications,[1] from intravenous bagsto catheters. The use has been grownconsiderably year by year, to the point where PVC represents more than 25 percent of all plastics used in medical devices. PVC is the second most used polymer in our day to day life and consumption is 26 million tons annually[2]. Other major uses of PVC in medical devices and health care industry include: blood bags, plasma collection bags, dialysis bags, catheters, and gloves. By nature, PVC is not a biocompatible material, so the specific characteristics of PVC medical applications are achieved through the addition of a wide variety of additives such as plasticizers, During this process, the properties improved physically and mechanically, otherwise the rigid polymer will generate harmful effects on biological systems[3,4]. In general, medical grade PVC devices are enhanced flexibility, and low temperature properties through addition of plasticizers. Hence, commercially available medical grade PVC contains around 40 percent of plasticizers with respect to the weight. The most familiar monomeric plasticizers are esters derived from phthalic acid and from different organic acids such as phosphates, citrates, sebacates, adipates, etc.[5,6]. But, di-ethylhexyl phthalate (DEHP or DOP) is the supreme plasticizer used in the production of medical devices for its processing advantages. However, studies have been alarmed that toxic phthalate esters are migrated from PVC based medical devices into physiological media such as blood, serum, plasma, saliva, and intravenous infusion fluids. Again, the leaching effect of plasticizer from PVC-based films into foods and direct ingestion into children body from PVC-based toys was reported [7-10]. The US Food and Drug Administration's Centre for Devices and Radiological Health and Health Canada was reported about the risk considerations of DEHP that migrated from PVC based product into human body. Different type of techniques were followed to resist the migration or leaching of plasticizer from PVC based devices, particularly PVC was coated with various polymers, crosslinking PVC using peroxides or by radiation, grafting hydrophilic monomers onto the surface, plasma treatment, substitution of chlorine on PVC with dialkyl dithiocarbamate followed by crosslinking, and azidation of PVC followed by photo cross linking. Again, highly migration resistant PVC was achieved by nucleophilic substitution of chlorine moieties on the PVC surface with thiosulphate anion. Based on previous report, the present study will involve the modification of PVC film surface by treating with thiouronium in presence of phase-transfer catalyst (PTC). The surface of the modified PVC was found to be extremely
Migration resistant in petroleum ether and PEG-400. Clotting time measurement was performed on both modified and unmodified PVC. Finally, modified PVC was examined for blood compatible through haemolysis assay. Our finding suggested the non toxic nature of modified PVC, and can be used for biomedical applications.[11]

2. CHARACTERIZATION

The gel content of modified PVC film was calculated by dissolving in THF at room temperature for 56 hours. The un-dissolved fractions were filtered, washed with THF, and dried in vacuum till constant weight. Gel content percentage was calculated based on initial weight of the films and found to be 99 percent. Surface morphology of modified and unmodified PVC films was examined using Scanning Electron Microscopy (SEM). Infrared spectra were recorded by using Fourier Transform Infrared (FTIR) spectroscopy. The thermal behavior of modified and un-modified PVC films was examined using differential scanning calorimetry (Perkin-Elmer DSC-7) under nitrogen atmosphere. Samples were scanned in the range of -20°C to 100°C with heating rate of 10°C per minute. Glass transition temperature was determined on the basis of thermograms collected during first heating scan.

3. LEACHING TEST

Leaching/migration of DEHP from modified and unmodified films were examined in petroleum ether at ambient temperature. The modified and unmodified PVC films were weighed individually and kept with petroleum ether in different volumetric flask. The amount of DEHP leached was studied gravimetrically. Again, leaching of DEHP from modified and un-modified PVC films was examined qualitatively by DSC. For qualitative analysis, the modified and unmodified PVC films were kept in petroleum ether. After six days, the DSC spectrum of the films was recorded. Further, the migration of DEHP from modified and unmodified PVC films were studied in poly (ethylene glycol)-400 (PEG-400) at 65°C by immersing the sample in 25ml of extraction medium. In pre-determined time intervals, samples were removed, and rinsed with 0.5 percent non-ionic soap solution followed by methanol and dried in an air oven at 55°C till constant weight. The amount of DEHP migrated from specimens was determined by measuring the change in weight of sample

4. CLOTTING TIME MEASUREMENT

Films (3cm x 3cm) were placed on different watch glass. Then fresh rabbit blood (0.1 mL) was placed directly on the PVC films. In pre-determined time interval, the sample was transferred into a beaker containing 5 ml distilled water. Blood cells (which are not trapped in thrombus) were haemolyzed, and free haemoglobins were distributed depressively in water. The concentration of free haemoglobinin water was measured at 540 nm using UV-Visible spectrophotometer.

5. HAEMOLYSIS ASSAY

Haemolysis assay was carried out using rabbit blood, anti-coagulated with acid citrate dextrose (ACD). 0.2 mL blood was added with 12.5 mL of phosphate buffered saline (PBS) containing modified and unmodified PVC films (0.5cm x 0.5cm) in different test tubes. A positive control (100% haemolysis induced by replacing PBS with 0.1% sodium carbonate solution) and negative control (0% haemolysis, PBS with no material added) were also set up. All test tubes were incubated at 37°C for 60 min. After incubation, the tubes were centrifuged at 300 rev/min. for five minute. The optical density of the above solutions was studied at 545 nm using a UVVisible spectrophotometer, and percentage haemolysis was calculated using the formula given below[12].

$$\text{Haemolysis (\%)} = \frac{\text{OD of the Test Sample} - \text{OD of the Negative Control}}{\text{OD of the Positive Control}} \times 100$$

6. RESULTS AND DISCUSSION

The reaction between alkyl halide and thiouronium was documented, and it forms a dialkyl Thiouronium. The halogen atoms of PVC are labile, so nucleophilic substitution of the halogen of alkyl by Thiouronium ions in presence of a suitable phase transfer catalyst occurs and forms S- type of linkages which causes the polymer chains to crosslink. Some loss of transparency was observed and it is due to some dehydrochlorination of PVC. The reaction between PVC and Thiouronium is expected to take place in a similar fashion, when PVC resin was reacted with ammonium thiosulfate in DMF, the product obtained was insoluble in THF, which is a good solvent for PVC [12]. Similarly, the resin reacted with an aqueous solution of Thiouronium in the presence of TBAH in the solid- liquid two phase system also resulted the formation of a product which is insoluble in THF [12]. Therefore, modification of plasticized PVC film with Thiouronium in aqueous medium in the presence of a suitable PTC would possibly due to surface crosslinking. time and it was found that the gel percentage was approximately 99 percent at around 5 h. Results suggested that, in PVC films the nucleophile i.e. Thiouronium ions were able to crosslink completely instead of surfaces. The possible reaction mechanism for the above discussion is given below [3].

The modified and un-modified PVC films were characterized by FT-IR spectroscopy. The IR spectra of PVC films before and after treatment with thiouronium were almost similar with slight variation of intensities, indicating that no reaction byproduct is formed when PVC film was treated with thiouronium in presence of TBAH in water. Again, in IR spectrum the C=O stretching frequency i.e. 1724 cm-1 remain unchanged. This suggested that the plasticizer is not affected through chemical crosslinking. Thus, only reaction between plasticized PVC film and sodium sulfide in the presence of TBAH is the nucleophilic substitution of chloride ions by thiouronium ions.

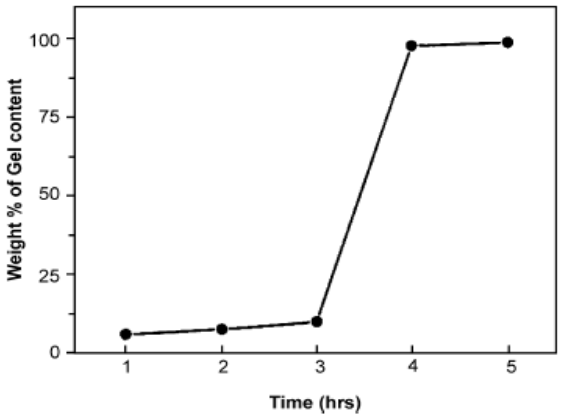

Fig.1 Percentage of gel formation in plasticized PVC film with different time intervals

7. CONCLUSION

The nucleophilic substitution of chloride ions in plasticized PVC by thiouronium ions offers an opportunity to restrict leaching out of Plasticizer. This phenomenon was proved by immersing modified and un-modified PVC films in various extraction media such as petroleum ether and PEG-400. Clotting time measurement and haemolysis assay was carried out for surface modified and un-modified PVC films and it was observed that the modified PVC film was blood compatible and non-toxic in nature. From these vital results,

we suggested that the surface modified PVC can be used for biomedical applications.

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