RESEARCH ARTICLE

Characterization and *In-vitro* Study of Polyethylene Glycol as Coating Material used as Drug Carriers on Coronary Stent for Treatment of Cardiac Diseases

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ABSTRACT

Background: The way coronary artery disease is treated has changed dramatically with the use of coronary angioplasty and stenting. Nowadays, acute coronary syndromes brought on by coronary artery disease are frequently treated using drug-eluting stents. A review of the literature reveals that the polymer coating's thickness affects the stent's safety; moreover, current computational studies suggest that larger coatings increase the risk of stent deformity. Polyethylene glycol is the preferred polymer coating material for coronary artery stents.

Objectives: Characterization of polyethylene glycol as a medication carrier coating for coronary stents used in cardiac disease therapy

Methods: Using UV-visible spectrophotometer, differential scanning calorimetry (DSC), fourier-transform infrared (FTIR), X-ray diffraction, thermogravimetric analysis, and surface morphology, polyethylene glycol was characterized.

Results: The calibration curves' linear regression results, as revealed by the UV-visible spectrophotometer investigation, showed a significant linear association between the concentration range of 10 to 60 µg/mL for polyethylene glycol Y = 0.0354X + 0.0212 (r2 = 0.999), was found. Polyethylene glycol's molecular miscibility, recrystallization, and phase separation were investigated using a DSC analysis. It was found that the material was physically stable because no recrystallization peaks were visible. According to the results of the thermogravimetric study, a ceramic sample cup with 4 to 6 mg of sample was heated to 400°C at a rate of 5°C every minute. Nitrogen gas was continuously supplied at a rate of 20 mL/min into the sample chamber during the analysis. The results of each batch were measured, and an average was determined. The study of surface coatings to examine the microstructure of the coatings produced both before and after the use of polymers is known as surface morphology. Within analytical imaging is the subset of surface morphology. Pure polyethylene glycol's morphology showed broad plate-shaped structures. Additionally, a strong band is detected between 1362 and 1287 cm^{-1}, which is comparable to the C-O stretching vibration seen in primary alcohol.

Conclusion: On base of the characterization results above shows that polymers were stable and included functional groups and structures throughout a range of conditions. It is possible to use polyethylene glycol as a coating material for coronary stents.

Keywords: polyethylene glycol, FTIR, DSC, TGA, XRD.

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INTRODUCTION

A common treatment for clogged arteries is coronary artery stenting, which involves inserting a coiled metallic mesh stent inside the affected area to increase blood flow. The buildup of calcified plaque in coronary arteries creates blockages, which results in a deficiency of oxygenated blood that is vital for the heart muscles. When examining coronary stents and their long-term mechanical properties, the impact of RBC contact has not been completely taken into account because prior research on stents and their mechanical qualities has mostly focused on the impact of arterial pulsation rather than RBC interaction.[1] RBC-RBC collisions can vary. RBC-RBC and RBC-polymer-coated stent collisions may differ. The human body mounts an immunological response to this disparity in the collision. In order to reduce the difference in the coronary stent's contact with RBC, an optimal polymer covering for the

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stent must be found. The best combination of polymer with stent qualities can be found by covering a polymer with varying concentrations or its derivatives. Vascular stenting has been utilized extensively in clinics because to its benefits of little trauma and efficient treatment. In order to improve stent coating and provide successful therapy, it is crucial to analyze how well the mechanical properties of the stent match the chosen polymer. The study found that polyethylene glycol is frequently used to prepare the digestive tract for examination or surgery.[2] Numerous pharmaceutical lotions, ointments, and medical solvents also include polyethylene glycol. These are essential to the drug delivery process because they can connect antibody-drug conjugates (ADCs). It can also be applied to nanoparticles as a surface coating to enhance systematic medication delivery. Polyethylene glycol can also be used in biomedicines to prevent coated proteins from being removed from the blood. Polyethylene glycol hydrogels are also used in drug delivery and tissue engineering. Polyethylene glycol hydrogels are gels that are resistant to adhesion and protein biodegradation. They are composed of networks of polymers with reactive PEG end groups that are cross-linked. These properties are beneficial to tissue engineering and drug delivery. Polyethylene glycol is a polymer that is widely used in the medical field. It is commonly found in products such as wound dressings, medical gloves, and catheters. Polyethylene glycol is also compatible with the human body. It is strong, resistant to abrasions, and chemically impermeable. Polyethylene glycol finds application in short-term implant devices, including feeding tubes, dialysis equipment, intra-aortic balloon pumps, and surgical drains. Because of its durability, polyethylene glycol is useful for devices that come into contact with other materials.[3]

MATERIAL METHODS

Materials

Polyethylene glycol polymer and all other chemicals and reagents were used in analytical-grade

Preparation of Stock Solution of Polyethylene Glycol

Ten milligrams of precisely weighed polyethylene glycol were moved to a 100 mL volumetric flask and manually shaken for ten minutes to dissolve it in 20 mL of distilled water. The volume was adjusted until it reached the desired final strength of 100 µg/mL.

Selection of Wavelength

The right amount of volume 10 mL volumetric flask was filled with 0.5 mL of the standard stock solution of polyethylene glycol. The solution was then diluted with distilled water and methanol to achieve a concentration of 5 µg/mL. UV (200–400 nm) scan was performed on the resultant solution. The greatest absorbance of polyethylene glycol was seen at 543 nm in the spectrum.

Linearity Study

A series of 10 mL volumetric flasks were filled to capacity with distilled water after various aliquots of polyethylene glycol in the range of 0.5 to 10 mL were placed into them. This allowed for concentrations of 5, 10, 15, 20, 25, and 30 µg/mL, respectively. A spectrophotometer was used to scan the solutions in the range of 200 to 400 nm. UV spectrum was obtained at 543 nm. The concentration vs. amplitude calibration plot was created.

Determination of Polyethylene Glycol in Bulk by UV-visible Spectrophotometer Analysis

About 1-mg of polyethylene glycol was dissolved in 100 mL of distilled water. The solution was then further diluted to obtain various concentrations. 10, 20, 30, 40, 50, 60 µg/mL, pour the solution into the cuvette. Take sample absorbance by inserting the cuvette into the sample holder, covering the cuvette chamber, and then run the spectra.[4]

Differential Scanning Calorimetry Study

Using differential scanning calorimetry (DSC) research, the degree of crystallinity and heat absorption property of polyethylene glycol was ascertained. Using a DSC loading puncher (Perkin, Massachusetts, USA), the dried sample of polyethylene glycol (about 1-mg) was loaded and sealed onto a DSC pan (Perkin Elmer, Massachusetts, USA). Under a nitrogen environment, the sample was heated at a rate of 10°C per minute while being scanned between 40 and 400°C. Nitrogen purging was utilized to preserve an inert atmosphere.[5]

Fourier Transform Infrared Spectroscopy

Using a Jasco FTIR spectrophotometer, infrared spectroscopy was performed, and the spectrum was obtained in the 3000 to 800 cm^{-1} wavelength range. The process involved scattering a sample in KBr (polymers alone or in combination with excipients) and compressing it into discs under pressure. After inserting the pellet into the light path, the spectrum was acquired. It is employed to verify if polyethylene glycol contain functional groups or not.[6]

X-ray Diffraction Study

Using X-ray diffraction (XRD), the physical characteristics of polyethylene glycol were examined. Using an X-ray powder diffractometer with a copper tube anode, the results of the powdered samples' XRD patterns were recorded over the range of 1–40° , 2θ–1. The operational parameters are: 45 kV of generator tension (voltage), 40 mA of generator current, 9 s scan step time, and 0.008° (2θ) scan step size was used.[7]

Thermogravimetric Analysis

Analysis of thermogravimetric data (TGA) TGA-50 Shimadzu thermo gravimetric analyzer (Tokyo, Japan) was used to measure the weight change of polymer powder samples as a function of temperature. A ceramic sample cup containing 4 to 6 mg of sample was heated to 400°C at a rate of 5°C per minute. During the analysis, nitrogen gas was continuously pumped into the sample chamber at a rate of 20 mL/min. Each batch's findings were measured and the average was calculated.[8]

Surface Morphology (Confocal Microscope from Olympus)

About 10 mg of each sample were gently placed onto a glass plate for morphological examination, which compared the morphologies and particle sizes of pure polyethylene

Table 1: Results of polyethylene glycol

Sr no	*Sample*	*Concentration*	*Instrument*	*Results*	*Standard as*	*Software used*	*% amount found*
1	PEG	10 µg/mL	Uv Specrto-photometer	Absorbance found = 543 nm	Absorbance= 543 nm*	Spectra-manager	99.12%

glycol. Using a 20 × objective lens and a 10 × eyepiece lens for microscopy, the morphologies of the two samples were investigated.[9,10]

RESULTS AND DISCUSSION

UV Spectra Analysis

Ultraviolet-visible spectroscopy is the area of study that looks into how matter and electromagnetic radiation interact. It is one of the most effective tools for studying atomic and molecular structure(s) and is applied to a variety of sample studies. The electromagnetic spectrum's range of 100 Å to 400 µm is included in optical spectroscopy. UV spectroscopy is used to measure the ratio of the intensity of two light beams in the UV-visible area.

Method for Typical Solution Preparation

To get the different concentration, 10 mg of polyethylene glycol was dissolved in distilled water, which is added to bring the volume up to 100 mL (100 ppm). Additionally, dilutions with varying concentrations of 10, 20, 30, 40, 50, and 60 µg/mL were prepared. In compliance with ICH principles, the suggested approach was validated. The drug solutions were made in accordance with the previously used protocol, which is provided in the experiment spectra displayed in Figure 1.

Linearity Studies

The calibration curves linear regression demonstrated a strong linear correlation between the concentration range from 10 to 60 µg/mL for polyethylene glycol, as depicted in Figure 2. The equation for the linear regression was determined to be Y = 0.0354X + 0.0212 (r^2 = 0.999). Figure 2 and Table 1 represents the outcome.

Determination of Polyethylene Glycol in Bulk

Equations for linear regression were used to determine the drug's concentrations. The amounts 99.12% was detected

Differential Scanning Calorimetry Study

DSC is frequently used as thermal analysis technique due to its capacity to offer comprehensive details about a substance's energetic and physical characteristics. The most popular thermal method for characterizing polyethylene glycol, it offers precise data on MP, glass transition temperature (Tg), energy changes related to phase transitions, such as the crystallization and fusing processes and more. As seen in Figure 3 the lack of a drug melting peak in the DSC thermogram of polyethylene glycol suggests that the drug is encapsulated or amorphous. According to literature reviews, the best polymer was a combination of polyethylene glycol with cardiac drug, resulting in a single phase of the mixture. After preparation and under accelerated stability circumstances, DSC was preferred to determine the molecular miscibility, recrystallization and phase separation of polyethylene glycol. Another peak in this investigation is demonstrating molecular miscibility was noted with polyethylene glycol also no recrystallization peaks was seen, hence polyethylene glycol was physically stable. The observation and results of differential scanning calorimetry (DSC) study are summarised in Table 2.

Thermo Gravimetric Analysis

One effective method for determining a material's heat stability, especially polymers, is thermo gravimetric analysis (TGA). The mentioned method measures a sample's weight changes when the temperature increases. It also measures the sample's

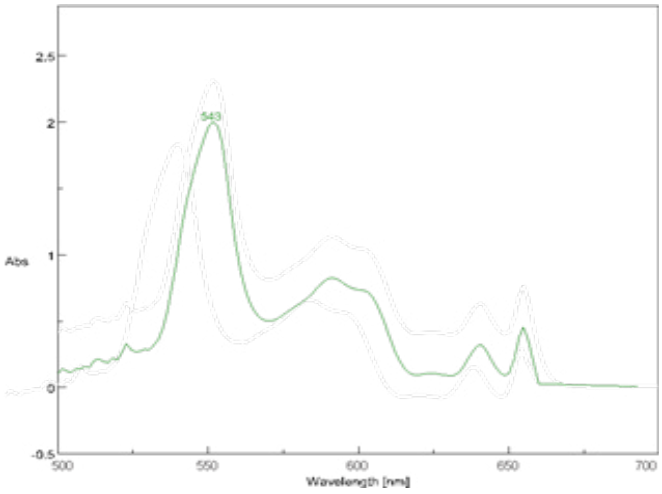

Figure 1: UV-visible spectra of PEG (10 µg/mL concentration)

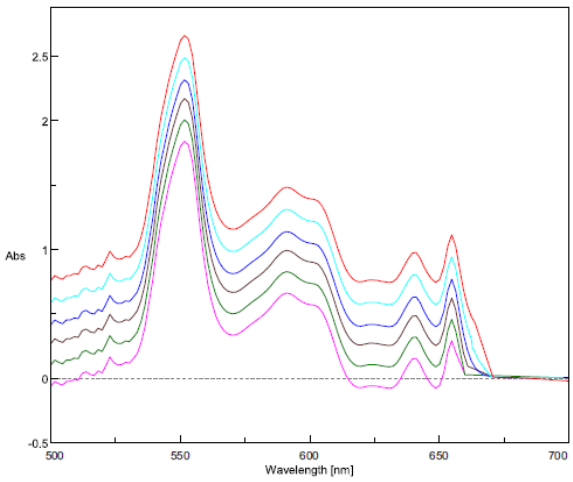

Figure 2: polyethylene glycol overlay of different concentrations

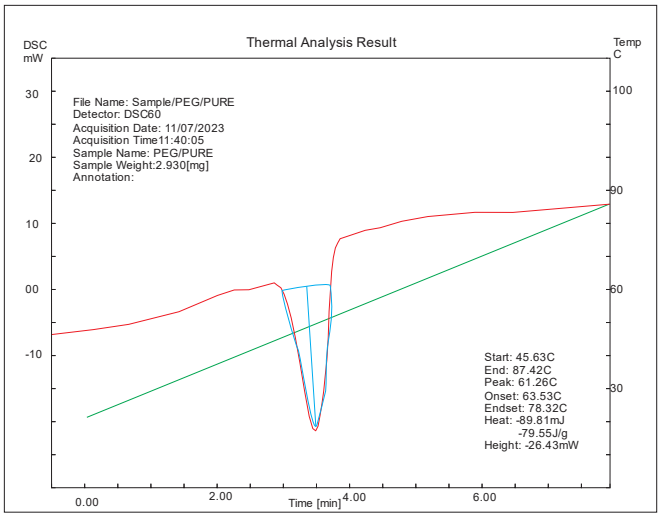

Figure 3: DSC graph of polyethylene glycol

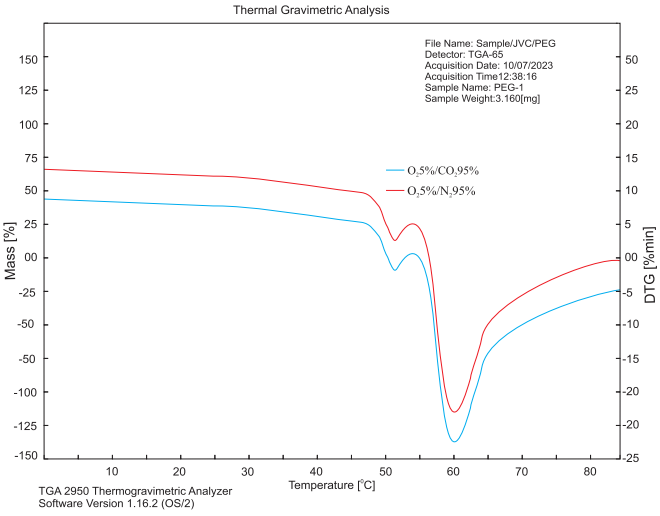

Figure 4: TGA of PEG

Table 2: Results of polyethylene glycol differential scanning calorimetry study

Parameter	*Observation*	*Standard value*
Detector	DSC60	DSC60
Sample Weight	2.930[mg]	Below 5[mg]
Reaction Start	45.63C	40–45 C
Reaction End	87.42C	80–90 C
Peak	61.26C	60–70 C
Onset Reaction	63.53C	60–70 C
Endset Reaction	78.32C	70–80 C
Heat absorb	-89.81	Below -100
Peak Height	26.43	Above 30
Nature of reaction conclusion	Endothermic	Endothermic

moisture and volatile contents. It helps determine whether or not a compound will react with other compounds in its environment after melting. It is a thermal analysis procedure that measures the weight loss of polymer due to temperature changes in the environment. Analysis of TGA-50 Shimadzu thermo gravimetric analyzer (Tokyo, Japan) was used to measure the weight change of polymer powder samples as a function of temperature. A ceramic sample cup containing 4 to 6 mg of content was heated to 400°C at a rate of 5°C per minute. During the analysis, nitrogen gas was continuously pumped into the sample chamber at a rate of 20 mL/min. Each batch's findings were measured, and the average was calculated results are shown in Figure 4 and results are summarised in Table 3.

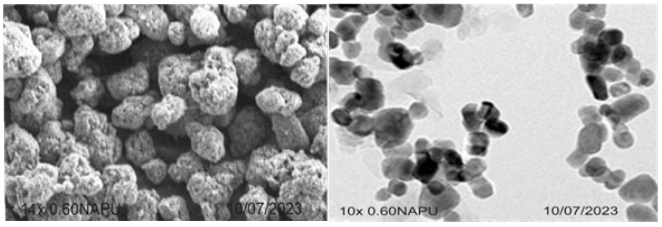

Figure 5: Images of PEG surface morphology 10 X Microscope

Surface Morphology (Confocal Microscope from Olympus)

Polymeric materials are defined by certain aspects of their surface morphology which influence their final surface properties like wettability and adhesiveness in biocompatible processes. Surface morphology is the study of surface coatings to analyze the microstructure of deposited coatings before and after using the polymers. Surface morphology is a subset of analytical imaging. The morphology of pure polyethylene glycol revealed formations with a broad plate shape, as seen in Figure 5. The nature of compounds is consistent with these results and findings align with the characteristics of substances shown in Figure 5.

Fourier Transform Infrared Study

FTIR spectroscopy is crucial for the study of polymer structure. Considering that it offers details on the complexation and interactions of the different components within the polymer electrolyte. Using a FTIR spectrophotometer SHIMADZU-8000 in the transmittance mode at room temperature, infrared spectra profiles were acquired. The

Table 3: Results of TGA

Atmosphere (Gas pass in %)	*M P of PEG (°C)*	*Heat absorb start (°C)*	*Melt at (°C)*	*Stable at (°C)*	*Conclusion*
$O_2$5%/$CO_2$95%	66	51	60	65	PEG is stable at meltiong point 60 to 65°C
$O_2$5%/$N_2$95%	66	52	60	65	

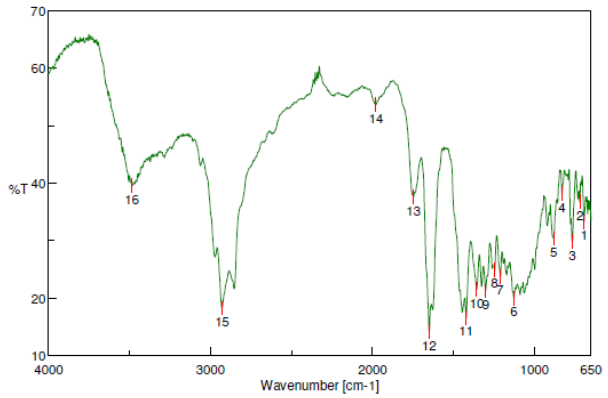

Figure 6: IR of PEG

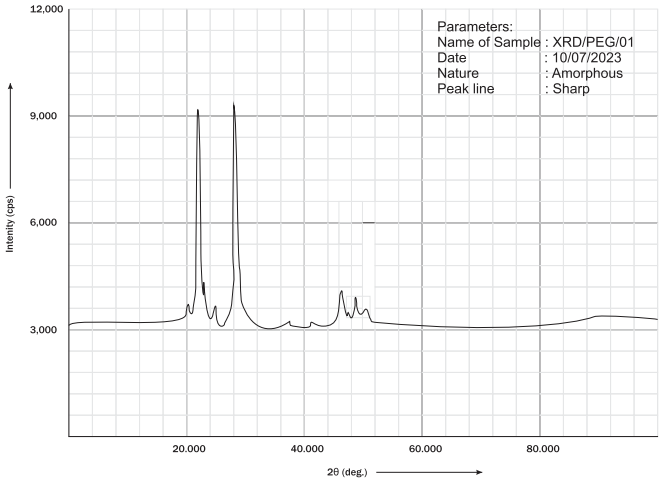

Figure 7: XRD of polyethylene glycol

Table 4: IR Functional group present

Functional group	*Observed wavenumbers*	*Standard wavenumbers*
OH	3450	3450–3490
CH	2868	2800–2900
C-O	1248	1200 –1250

preoccupations of the polyethylene glycol resemble those of a primary alcohol. This leads to these absorptions, which are limited to the C-C, C-O, CH, and C-H bending stretching and bending vibrations (methylene absorptions). With hydrogen bonding, the OH stretching vibration is seen in the range 3378 cm^{-1}. It is not possible to see the same absorption in any polymer combination. This demonstrates unequivocally that the action of NH_4Cl has an impact on the functional groups' absorption. It has been discovered that the methylene group in PEG vibrates in the stretching mode at a frequency of about 2803 cm^{-1}. The binding vibration of –CH2 is the cause of the absorption at about 1474 cm^{-1}. A strong band is also found about 1362 and 1287 cm^{-1}, similar to the C-O stretching vibration observed in primary alcohol. The results are displayed in Figure 6 and it has been summarised in Table 4.

The X-ray Diffractograms

The pure polyethylene glycol X-ray diffractogram's clear peaks at 2θ indicate that the material was amorphous in nature in the pure polyethylene glycol diffraction spectrum. Glacier 50/13 was used to prepare the polyethylene glycol spectrum. The results demonstrated a decrease in the overall number of peaks, a reduction in peak intensity and a broadening of the appeared peak in polyethylene glycol base, all of which provided strong evidence for the amorphous form of the polymer sample. The outcome shows that the polymers in the sample were amorphous. The results are displayed in Figure 7

CONCLUSION

A DSC thermal analysis study was conducted to investigate and define the matrix state involving polymer entrapment, component interactions and molecular miscibility and polyethylene glycol was physically stable. Using TGA to analyze the chosen polymers was a crucial step in the characterization process. This analysis approach will make it easier to choose the optimal drug-polymer mix and help select the optimum strategy for polymer stability. This will support the coating over the cardiac stent. It was possible to demonstrate needle-like crystallites with smooth surfaces and a range of particle sizes by using the surface morphology of polymers. There were spherical carriers of different sizes with smooth surfaces that were evidently present in the physical combination. However, no discernible needle-like crystallites resembling micrographs in the sample were seen; numerous tiny polymer-derived lamellae and particles covered the carrier's smooth surface. The investigation of surface morphology involved examining the coatings' microstructure both before and after the polymers were used as a coating material on the stent. The FTIR analysis was conducted, and the findings were examined and interpreted. Six bands were visible in the infrared (IR) spectra of the pure polyethylene glycol, which displayed a distinctive peak at because the original peaks in the spectrum remained consistent. It suggested the development of polyethylene glycol with carriers and it can identify the physiochemical interactions of drugs and carriers. It provides a flexible method for examining drug-carrier compatibility and intermolecular interactions. The polyethylene glycol base broadening and peak intensity reduction in XRD measurements provide strong support for the amorphous form of the polyethylene glycol sample. It can employ polyethylene glycol as coating materials for coronary stents because the characterization results above demonstrate that polymers are stable and include functional groups and structures under a variety of conditions.

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