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Formulation and Development of Naproxen Loaded Polymeric Nanoparticles using the Solvent Evaporation Method

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Abstract
Oil in water (O/W) emulsion solvent evaporation was used to develop polymeric drug nanoparticles for this study. Water served as a non-solvent and the polymer's solvent was acetone. The emulsion solvent evaporation method will be used in this study to prepare nanoparticles and to analyze the effects of different processing parameters on the properties of the nanoparticles. We use two different types of acrylic polymers in this study: Eudragit E100 and Eudragit RS100. It was observed that various factors, including the polymer content in the organic solvent, the concentration of the surfactant, and the volume ratio of the oil and water phases, affect the size of the nanoparticles. By using a transmission electron microscope, the morphological structure is examined (TEM). The production of spherical nanoparticles with an average size of 90 nm was verified by TEM pictures. By using laser dynamic light scattering, the size distribution is determined. The range of the nanoparticles' size distribution, from 50 to 150 nm, was found. Fourier transform infrared spectroscopy analysis revealed no interactions between the medication and polymer. The amorphous structure was visible in the X-ray diffraction patterns of nanoparticles containing naproxen, eudragit E100, and eudragit RS 100.
Keywords: Nanoparticles, Eudragit E100, Polymer

Introduction

Nanoparticle drug delivery involves creating drug-loaded particles with 1–1000 nm in diameter. Solid, submicron-sized medication carriers known as nanoparticles may or may not be biodegradable[1,2]. Based on their structure, drug nanoparticles can be further divided into nanocapsules and nanospheres[3]. In vesicular systems called nanocapsules, the medicine is contained in a hollow with an inner liquid core and a polymeric membrane around it. Nanospheres are built like a matrix. Drugs may be contained within the particle or absorbed at the surface of the sphere. The medication is either incorporated as crystallites in the polymer matrix or solubilized in the polymer matrix to create an amorphous particle [4].

There are numerous microencapsulation techniques available to produce drug nanoparticles. The drug is dissolved, dispersed, or emulsified in an organic polymer solution in the typical microencapsulation approach employing oil in water (O/W) emulsion system, which is subsequently emulsified in an external aqueous or oil phase. The drug and polymer precipitate in the droplets as the organic solvent is evaporated, generating the nanospheres or nanocapsules. A variety of biocompatible polymers, including poly (D,L-lactide-co-glycolide) [5&6,] and eudragit [7], have been utilised to successfully create microspheres using the emulsion solvent evaporation technique, which was fully developed by the end of the 1970s. Kawashima et al. [8, 9] proposed an emulsion solvent diffusion method more recently. The process

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of emulsion solvent evaporation has a number of benefits, and it is preferred to other preparation techniques like spray drying, sonication, and homogenization because it just calls for moderate conditions like room temperature and continual stirring. With the drug's activity unaffected, a stable emulsion can be created. The general emulsification solvent evaporation method, which is used to create nanoparticles, involves a number of processing and material parameters, including the amount of energy used, the power and duration used, the volume of the aqueous phase, the concentration of polymers and drugs in the organic phase, the molecular weight and end groups of the polymers, the volume of the solvent, and the concentration of surfactants. The size and/or drug content are influenced by each of these processing and material characteristics.

Nanoparticles for drug delivery should be easily biocompatible and biodegradable. The choice of nanoparticle material and surface modification can have an impact on these qualities, as well as targeting and controlled release. Nanoparticles are created using substances like protein, synthetic polymers, and other natural macromolecules. In the administration of therapeutic molecules, drug nanoparticles may be used for tissue targeting in cancer therapy, controlled release, carrier action for peptide transport, and an improvement in drug solubility.[10]

In this study, two different types of acrylic polymers, Eudragit E 100 and Eudragit RS 100, are used to create nanoparticles using the emulsion solvent evaporation method in order to examine the impact of different processing parameters on particle size and nanoparticle properties. The concentration of polymers in the organic phase, the concentration of polyvinyl alcohol (PVA) in the aqueous phase, and the volume ratio of the oil to water phases are among the processing parameters. Non-prescription naproxen is used to treat minor discomfort from toothaches, backaches, menstrual cramps, arthritis, headaches, muscular pains, and the common cold. Naproxen belongs to the group of drugs known as NSAIDs.

Experimental

Materials/Methods

Naproxen is a methoxynaphthalene that is 2-methoxynaphthalene substituted by a carboxy ethyl group at position 6. Naproxen is having white to creamy white, crystalline powder; soluble in water and sparingly soluble in alcohol.

In this investigation, Eudragit NE 30 D and Eudragit NM 30 D polymers were used. They are soluble in organic solvents like acetone, ethanol, and others but insoluble in acid and water.

Bi-distilled water was used as non-solvents. PVA was used as an emulsifying agent.

All materials were obtained from commercial sources and used as received: naproxen (USP-30; Dr. Reddy's Laboratories) Eudragit E 100, Eudragit RS 100 (Merck, Germany), PVA, acetone (Merck, German).

Preparation of the Drug Nanoparticles

In this study, emulsification solvent evaporation technique with sonication is used to create nanoparticles. An organic phase made up of drug (naproxen) and polymer (Eudragit E 100 or RS 100) dissolved in acetone (10 mL). An O/W type emulsion is created by mixing this organic phase with an aqueous phase that already contains a surfactant (PVA, concentration 0.5%, 90 mL). Oil and water phases had a volume ratio of 1:9. By using outside energy through a sonicator, this emulsion is broken down into nanodroplets. When the extremely volatile organic solvent is evaporated, these nanodroplets turn into nanoparticles. During magnetic stirring at 300 rpm under atmospheric conditions for 2 hours, the organic solvent evaporates.

We evaluated at how different processing settings affected particle size. The concentration of polymers in the organic phase, the concentration of PVA in the aqueous phase, and the volume ratio of the oil and water phases are the processing parameters.

Characterisation of Nanoparticles

We examine on the morphology, crystallinity, and particle size and size distribution of nanoparticles.

Dynamic light scattering was used to determine the particle size distribution (HORIBA LB-550-Japan).

A Fourier transform infrared (FT-IR) spectrometer (TEMSORTM37 - Bruner, USA) was used to record

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the infrared (IR) absorption spectra of raw materials and nanoparticles in the wavelength range 4000-400 cm-1.

Using a transmission electron microscope (TEM; JEM-1400, Japan) and an acceleration voltage of 100 kV, particle morphology was examined.

Utilizing X-ray diffraction, the particles' crystallinity was investigated (XRD; D8 Advance – Bruker, German).

Results and discussion

Effect of Various Processing Parameter on the Size of Particles

1. Effect of Polymer Concentration in the Organic Phase

The polymer Eudragit E100 was used to produce the naproxen nanoparticles. The volume ratio of the oil to water phases was 1:9, and the PVA concentration in the aqueous phase was 0.5%. The polymer concentration ranges from 3% (w/v) to 15% (w/v). The impact of polymer content on particle size in the organic phase is shown in Figure 1. The diameter of the nanoparticles gradually grows as the amount of polymer in a fixed volume of organic solvent increases. The viscosity increases with increasing polymer concentration, increasing the emulsion droplet size. The organic phase shear stresses are opposed by the viscous forces, and the ultimate particle size and size distribution rely on the net shear stress that is available to the droplet. Previous studies using different poly (lactic-co-glycolic acid)/poly lactic acid (PLGA/PLA) systems have shown the significance of polymer content in regulating the size of particles produced by the general emulsification process.

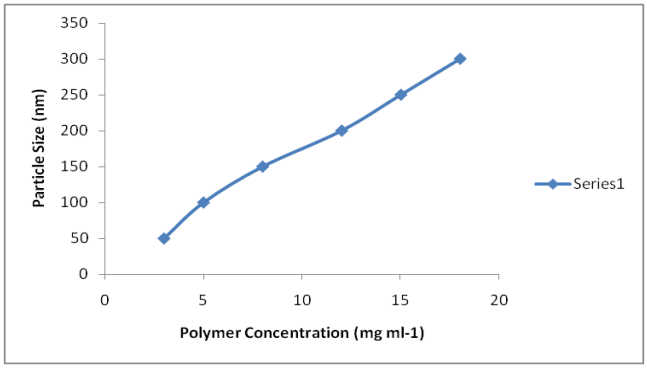

Figure No.1: Effect of Polymer Concentration in the Organic Phase on the Particle Size

2. Effect of PVA Concentration in the Aqueous Phase

The polymer Eudragit E100 was used to make the naproxen nanoparticles; the oil to water volume ratio was 1:9 and the polymer content was 5%. PVA is present in the aqueous phase at concentrations ranging from 0.5% (w/v) to 2% (w/v). The effects of PVA content in the aqueous phase on particle size are depicted in Figure 2. Due to the high aqueous phase viscosity caused by increasing PVA concentration, particles gradually grow in size, which decreases the net shear force that may be used to break apart droplets. At high PVA concentrations, Zweers et al. [11] reported that PLGA nanoparticle size increased.

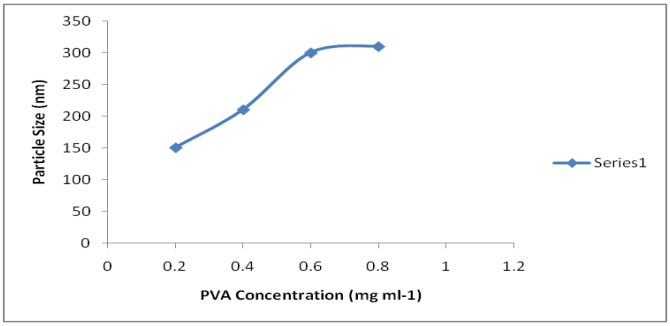

Figure No.2: Effect of PVA Concentration in the Aqueous Phase on the Particle Size.

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3. Effect of the Volume Ratio of oil and Water Phases

The polymer Eudragit E100 was used to create the naproxen nanoparticles; the polymer concentration was set at 5% (w/v), and the PVA concentration in the aqueous phase was set at 0.5% (w/v). The volume ratio of the water to oil phases was different. The effects of the volume ratio of the oil and water phases on particle size are depicted in Figure 3. The size of the particles increases quickly as the volume ratio of the oil and water phases rises above 0.6.

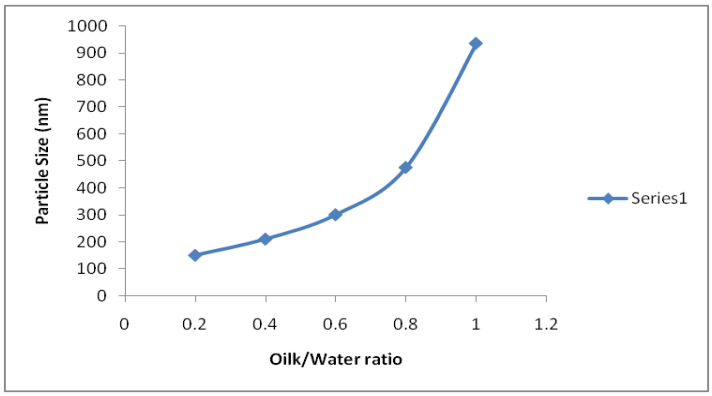
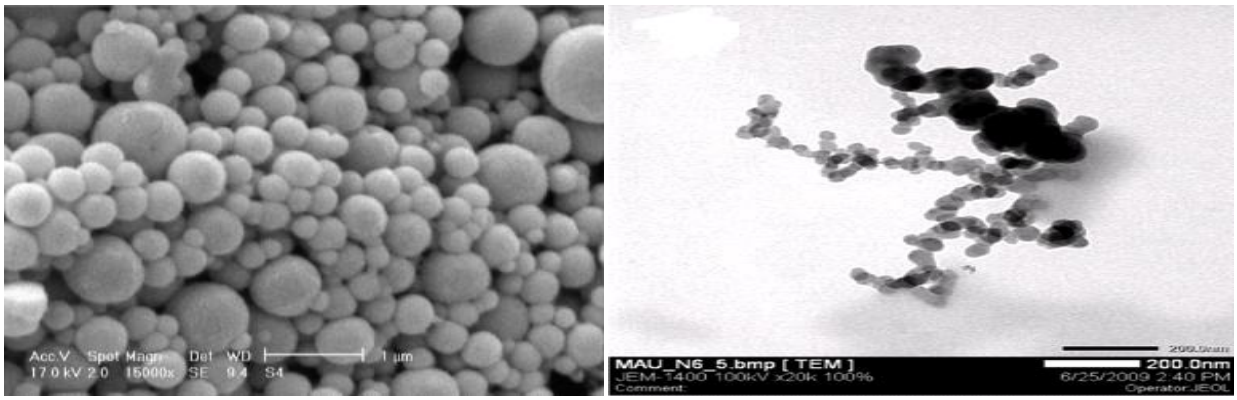


Figure No.3: Effect of the Volume Ratio of oil and Water Phases on the Particle Size.

4. The Characteristics of Nanoparticle

A TEM was used to study the morphology of the prepared nanoparticles. Naproxen nanoparticles containing 10% (w/w) and 90% (w/w) Eudragit E100 are displayed in Fig 4(a) using TEM images. Nanoparticles with 10% (w/w) naproxen and 90% (w/w) Eudragit RS 100 are shown in TEM images in Figure 4(b). Grain boundaries or crystallinity were not visible in Figure 4(a) or (b). The nanoparticles were round, amorphous, and smooth, according to TEM pictures. The particles had an average size of 90 nm. There has been evidence of the emergence of a drug-amorphous polymer structure.



(a) **(b)**

Figure 4: TEM images of the Nanoparticles Containing: 10% (w/w) Naproxen and 90% (w/w) Eudragit NE (a) and 10% (w/w) Naproxen and 90% (w/w) Eudragit NM (b).

The interactions of the drug with the polymers were studied using IR spectroscopy. Figure 5 displays the nanoparticles' IR spectra in the 4000 to 400 cm-1 wavenumber region. Naproxen possesses a carboxylic acid group that can interact with the polymer's function groups.

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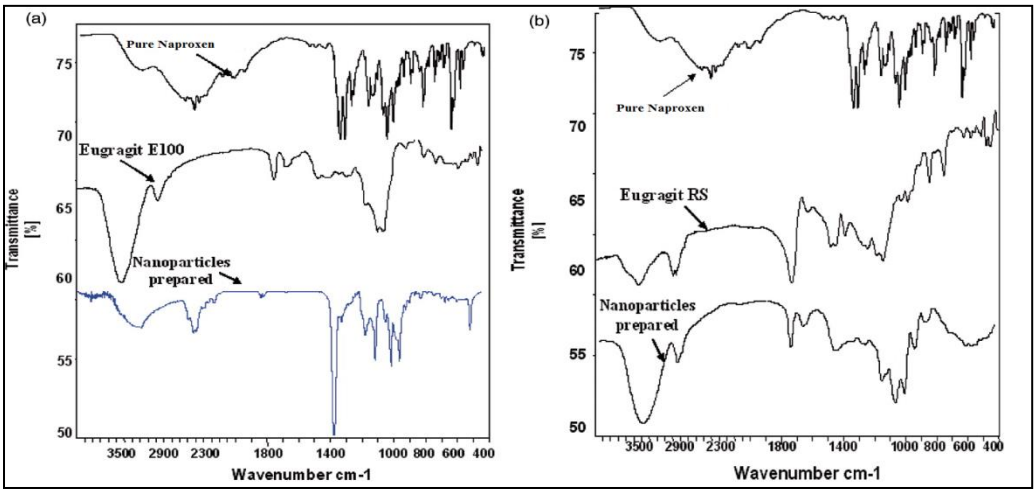

Figure No. 5: Infrared Spectra at Wavenumber of 4000 to 400 cm^{-1} of the Nanoparticles Containing: (a) 10% (w/w) Naproxen and 90% (w/w) Eudragit E100 and (b) 10% (w/w) Naproxen and 90% (w/w) Eudragit RS.

FT-IR patterns of naproxen, naproxen/eudragit® RS100/ eudragit E100 physical mixtures as well as the related nanoparticles are demonstrated in Fig. 5. Matching up to FT-IR spectrum of naproxen with the physical mixtures revealed no distinctive changes indicating that eudragit® RS100 and eudragit E100 was not involved in intermolecular interaction with naproxen in physical mixtures.

Figure 6 shows the particle size distribution of nanoparticles containing: naproxen and Eudragit E100 (Figure 6(a)), naproxen and Eudragit RS (Figure 6(b)). Size distribution were determined by dynamic light scattering in aqueous solution, the size of the particles was in the range from 50 to 150 nm and the mean diameter was 90 nm. Based on these results, we can see the sonication method is suited to produce small size nanoparticles (<300 nm diameter) with narrow size distribution.

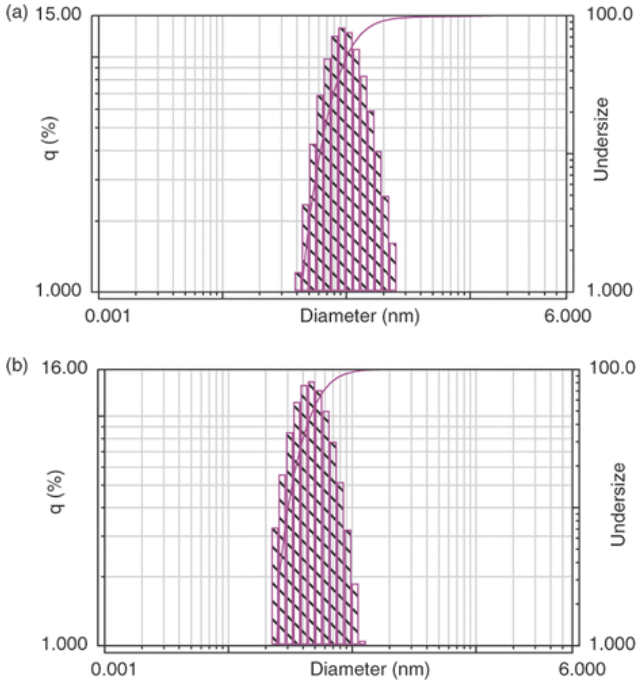

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Figure 6: The Particle Size Distribution of Nanoparticles Containing: (a) 10% (w/w) Naproxen and 90% (w/w) Eudragit E100 and (b) 10% (w/w) Naproxen and 90% (w/w) Eudragit RS

The nanoparticles' XRD patterns are shown in Figure 7: 10% naproxen and 90% eudragit rs (Figure 7(a)), and 10% naproxen and 90% eudragit e100 (Figure 7b). The amorphous structure and lack of crystallinity in Figure 7(a) and (b) were shown by the XRD diffraction pattern.

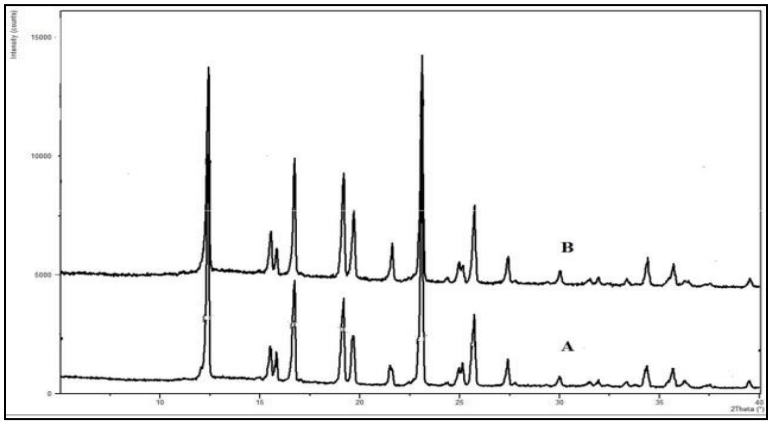

Figure 7: XRD Patterns of the Nanoparticles Containing: 10% (w/w) Naproxen and 90% (w/w) Eudragit E100 (a) and 10% (w/w) Naproxen and 90% (w/w) Eudragit RS (b).

The absence of peaks corresponding to diffraction from the drug crystal lattice leads us to the conclusion that the nanoparticles generated were amorphous.

Conclusion

Emulsion solvent evaporation was used to produce polymeric drug nanoparticles. We examined into just how different processing variables affected nanoparticle properties and particle size. Particle size increased as a result of changes in various factors, including the concentration of polymers in the organic solvent, the concentration of surfactants, and the volume ratio of the oil to water phases. The TEM observation reveals the surface morphological characteristics; the particle morphology was spherical and homogeneous. The nanoparticles were discovered to have a size distribution in the 50 to 150 nm range, with a mean diameter of 90 nm. FT-IR was used to analyze how the medication and polymer interacted. We found that the naproxen molecule's carboxylic group interacts with the eudragit. Nanoparticle XRD patterns revealed the amorphous structure.

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