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PREPARATION OF CARBAPOL COATED NANOPARTICLES BY EMULSION POLYMERIZATION TECHNIQUE

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ABSTRACT

Nowadays there has been considerable interest in developing new routes alternative to injection for delivering macromolecules such as proteins and peptides. However, peptides and protein drugs are degraded before they reach the blood stream and can not cross the mucosal barrier. The mucoadhesive polymer coated nanoparticles can solve these problems. They were prepared by emulsion polymerization. Methyl methacrylate polymerized in the presence of polysaccharide such as carbapol leads to formation of mucoadhesive polymer coated nanoparticles. The mucoadhesive polymers could interact with the mucus glycoproteins which allow the mucoadhesive system to remain adhesive for an extended period of time. Coating nanoparticles with them improved their mucoadhesion. These mucoadhesive polymer coated nanoparticles are suitable for carrying hydrophilic drugs. In present study carbapol coated nanoparticles are prepared by emulsion polymerization technique. Particle size was measured by Scanning electron Microscope. The effect of polymer concentration and chemical initiator concentration on the resultant nanoparticles was studied.

INTRODUCTION: Nanoparticles used as drug delivery vehicles are generally < 100 nm in at least one dimension and consist of different biodegradable materials such as natural or synthetic polymer lipids or metals. Nanoparticles are taken up by cells more efficiently than larger micromolecules so can be used as effective transport and delivery systems [1, 2].

For therapeutic applications drugs can either be integrated in the matrix of the particle attached or to the particle surface. A dug targeting system should be able to control the fate of drug entering the biological environment. An effective approach for achieving efficient drug delivery would be to rationally develop nanosystems based on the understanding of their interactions with the biological environment, target cell population, target cell surface receptors, changes in cell receptors that occur with progression of disease, mechanism and site of drug action, drug retention, multiple drug administration, molecular mechanisms and pathobiology of disease under consideration. Reduced drug efficacy could be due to multiple drug targeting, chemical properties of delivering molecules, alterations in genetic makeup of cell surface receptors, over expression of efflux pumps, changes in the signalling pathways with the progression of disease or drug degradation. Most of the nanoparticles prepared from water insoluble polymers are involved heat, organic solvent or high shear force that can be harmful to the drug stability. In contrast water soluble polymers offer mild and simple preparation methods without use of organic solvent and high shear force [3, 4, 5].

Carbapol is a high molecular weight Poly(acrylicacid) copolymer ,loosely cross linked with allyl sucrose [6, 7, 8].

This mucoadhesive polymer could interact with mucus glycoproteins by forming physical entanglements followed by hydrogen with sugar residues on oligosaccharide chains resulting in the formation of a strengthened mucus gel network, which allows the mucoadhesive system to remain adhesive for an extended period of times. It was also showed that coating nanoparticles with them improved their mucoadhesion [9, 10, 11].

MATERIALS AND METHODS:

Materials:

- Methylmethacrylate
- Carbapol
- Ammoniumpersulphate

Preparation of Carbapol coated nanoparticles: Carbapol coated nanoparticles were prepared by emulsion polymerization technique in a closed 100ml flask. Carbapol was dissolved in 100 ml water under magnetic stirring at 400-500 rpm. One percent (w/v) of the monomer methylmethacrylate was dissolved in the above mixture at 75^0c and APS solution was added. The reaction was completed after 24 hrs. Different batches were prepared according to the following reaction conditions.

1) Concentration of chemical initiator (APS) was varied keeping monomer concentration and polymer concentration constant.

2) Concentration of carbapol was varied keeping monomer concentration and chemical initiator (APS) concentration constant.

The effect of carbapol concentration and initiator (APS) concentration on the resultant nanoparticles size was studied.

RESULTS AND DISCUSSION: In order to perform the SEM observation, nanoparticle suspension was fist diluted with ultrapure water (1/5), and then a drop of the diluted nanoparticle suspension was then directly deposited on a polished aluminium sample holder. Samples were dried in vacuum. The morphology of nanoparticles was observed at 15 kV using a scanning electron microscope (SEM; S-3700 N, Hitachi, Japan).

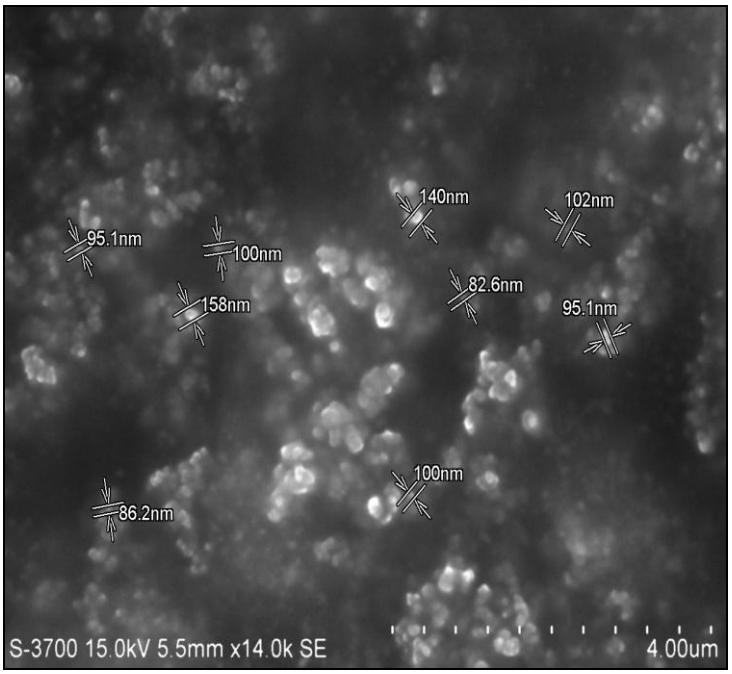

FIG. 1: SEM IMAGES APS (1%)

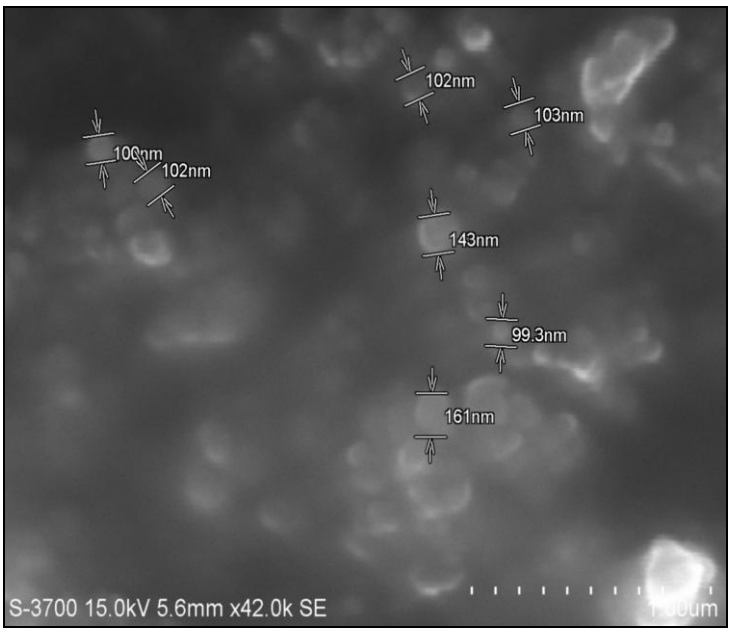

FIG. 2: SEM IMAGES APS (3%)

Determination of carbapol nanoparticles by X-ray diffraction study:

Physical status of carbapol nanoparticles: An X-ray diffractometer (Philips, Xpert-Pro, Netherlands) was used to determine the physical status of carbapol in the nanoparticles. The diffraction angle (2ϑ) was recorded from 3° to 80° with a scanning speed of 5°/minute. CuKa radiation was used as the X-ray source at 40 kV and 30 mA. Particle size of carbapol is also conformed by X-ray diffraction study. Particles are found be crystalline in nature.

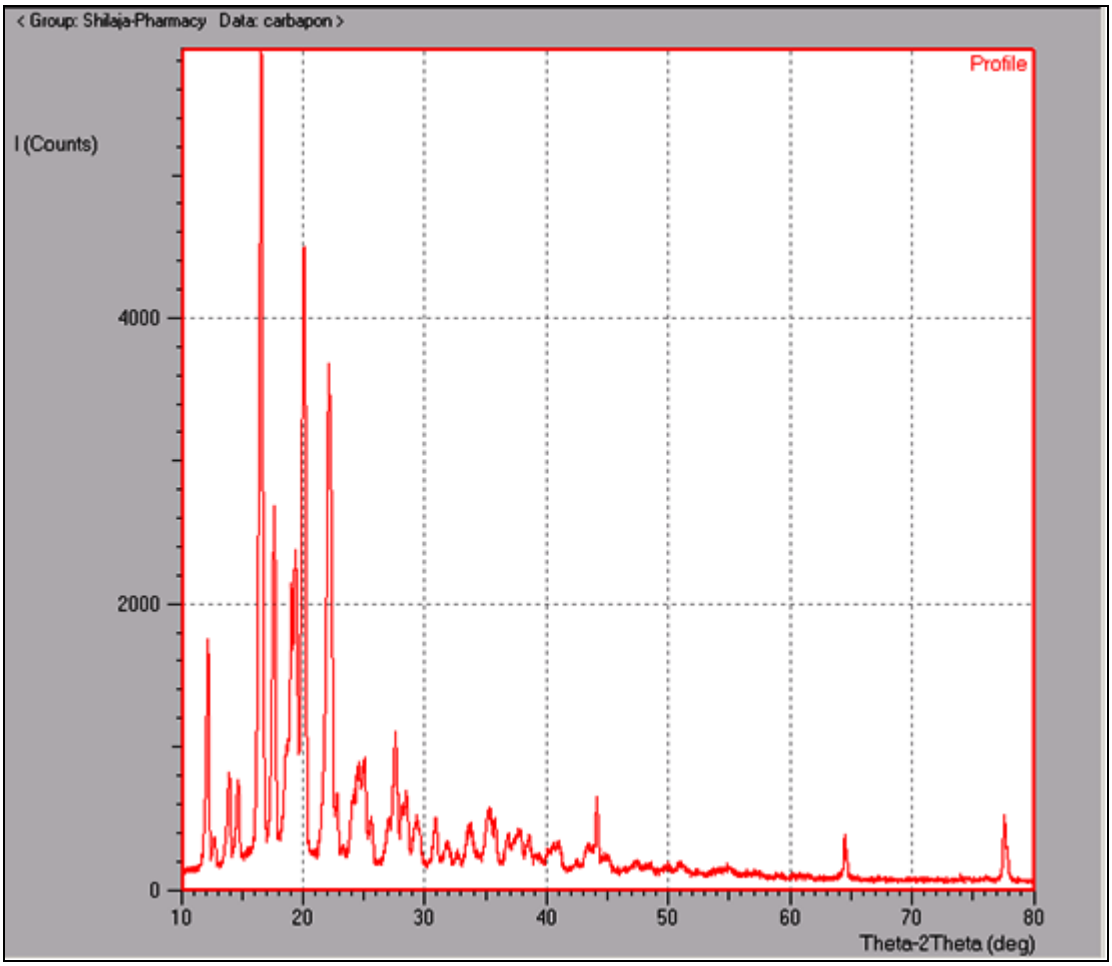

FIG. 3: XRD FOR CARBAPOL NANOPARTICLES

The mean size of the ordered domains is determined by the following formula;

$T = K\chi/B \cos\theta$

K=shape factor; χ= X-ray wavelength; B= FWHM (Half the maximum intensity in radium; θ= angle; T= mean size of the ordered domains (crystalline)

K=0.9 (typical value) varies with the actual shape of the crystallite

Scherrer equation: It is not applicable to grains larger than about 0.1 µm.

χ =1.5406

T value for carbapol (2g, 1%APS) = 0.9×1.5406÷0.32130 × 3.15×cos16.5343 = 14.2×10-9 = 14.2 nm.

Carbapol nanoparticles were prepared using Ammonium per sulphate as an initiator for polymerization reaction. Different batches were prepared using APS at 1%, 2% and 3% concentrations. All the three batches were evaluated for particle size and crystallinity. It was observed that the batches prepared by using 3% and 1% APS were shown to fall in a range of 100-200nm.Uniformity was obtained at 3% APS concentration. The particles prepared with 3% APS were falling in the range of 100-150nm. The particles prepared with 1% APS were falling in the range of 80-160nm.Particles at 2% APS were formed as aggregates.

CONCLUSIONS: The mucoadhesive polymer-coated nanoparticles could be developed through polymerizing methylmethacrylates in the presence of mucoadhesive polymers. The resulting nanoparticle suspension could incorporate the hydrophilic drugs greatly due to the hydrophilicity on the surface of the nanoparticles. They possessed mucoadhesive polymers which interacted with mucus to prolong the residence time of the drug carriers at the drug absorption sites and protected the entrapped drugs from enzymatic degradation.

Therefore bioavailability of the drug may be improved. Therefore they are promising for transmucosal drug delivery.

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