



## FORMULATION OF ALBUMIN NANOPARTICLES CONTAINING AN ANTICANCER DRUG OXALIPLATIN

**Barnabas Wilson<sup>1,4,\*</sup>, Brahmani Priyadarshini S. R.<sup>1,4</sup>, Geetha K. M.<sup>2,4</sup> and Murugan V.<sup>3,4</sup>**

<sup>1</sup>Department of Pharmaceutics, Dayananda Sagar College of Pharmacy, Kumaraswamy Layout, Bangalore, Karnataka-560078, India.

<sup>2</sup>Department of Pharmacology, Dayananda Sagar College of Pharmacy, Kumaraswamy Layout, Bangalore, Karnataka-560078, India.

<sup>3</sup>Department of Pharmaceutical Chemistry, Dayananda Sagar College of Pharmacy, Kumaraswamy Layout, Bangalore, Karnataka-560078, India.

<sup>4</sup>College of Pharmaceutical Sciences, Dayananda Sagar University, Kumaraswamy Layout, Bangalore, Karnataka-560078, India.

**\*Corresponding Author: Dr. Barnabas Wilson**

Department of Pharmaceutics, Dayananda Sagar College of Pharmacy, Kumaraswamy Layout, Bangalore, Karnataka-560078, India.

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### ABSTRACT

Cancerous cells divide without any control in an abnormal way. Oxaliplatin, a platinum derivative, is used for treating colorectal cancer. It is soluble in water and having a molecular weight of 399.31 g/mol. Oxaliplatin exhibits its activity by specifically inhibiting the synthesis of deoxyribonucleic acid. It is well known that anticancer drugs affect normal cells. Nanoparticles are able to deliver the anticancer drugs into the cancerous tissues in a controlled manner. The present study objective was to prepare and evaluate albumin nanoparticles of oxaliplatin. The albumin nanoparticles were prepared by desolvation method. The particles were characterized for their size and drug loading. The *in vitro* release studies showed initial burst effect followed by a sustained release.

**KEYWORDS:** Oxaliplatin; albumin nanoparticles; anticancer.

### INTRODUCTION

Cancerous cells divide without any control in an abnormal way. Further, cancer cells can enter into other tissues and organs through the blood and lymph. The exact cause of cancer is difficult to specify. Many factors increase the risk. In 2030, it is estimated that globally over 13.1 million people will be suffered by cancer.<sup>[1]</sup> The treatment of cancer patients could be improved by controlling the pharmacokinetics of anticancer drugs by delivering more drugs into the tumour while minimizing drug concentration into the normal cells.<sup>[2]</sup> Nanocarriers such as nanoparticles can be used to increase the therapeutic index of anticancer drugs.<sup>[3]</sup>

Nanoparticles, for drug targeting, can be prepared using various natural and synthetic polymers in which the active principle (drug) is dissolved, entrapped, or encapsulated. They have a particle size in the range of 1nm to 1000 nm. It has been reported that nanoparticles prepared using proteins like albumin are nonimmunogenic, biodegradable and biocompatible. They are comparatively easy to prepare. Further, drugs can physically adsorb on the surface of the protein.<sup>[4]</sup> Both bovine and human serum albumins are widely used

for the preparation of nanoparticles.<sup>[5]</sup> Various drugs and diagnostic agents can be incorporated into nanoparticles and administered by various routes including oral, intravenous, intranasal and ophthalmic routes.<sup>[6]</sup> Albumin nanoparticles can be prepared by desolvation method.<sup>[7]</sup> Oxaliplatin is a platinum analogue used for treating colon cancer. Oxaliplatin exhibits its activity by specifically inhibiting the synthesis of deoxyribonucleic acid.<sup>[8]</sup> It is well known that anticancer drugs affect normal cells. Oxaliplatin also causes various side effects including acute neuropathy.<sup>[9]</sup> The present study objective was to prepare and evaluate albumin nanoparticles of oxaliplatin. The albumin nanoparticles were prepared by desolvation method. The particles were characterized for their size and drug loading. The *in vitro* release studies showed initial burst effect followed by a sustained release.

### MATERIALS AND METHODS

Oxaliplatin was purchased from Sigma-Aldrich, St. Louis, USA. Bovine serum albumin was purchased from Central Drug House, India. All the other chemicals used were analytical grade.

### Preparation of bovine serum albumin nanoparticles containing oxaliplatin

Oxaliplatin loaded bovine serum albumin nanoparticles were prepared by desolvation method.<sup>[10]</sup> For this, 100 mg polymer was dissolved in 10 mM sodium chloride solution. 100 mg oxaliplatin was added to the bovine serum albumin solution and the pH was made up between 7-8. Acetone was added to this (1 ml/min) under continuous magnetic stirring at 500 rpm. The bovine serum albumin nanoparticles obtained were cross linked with 100  $\mu$ l of 4% glutaraldehyde-ethanol and stirring continued for another 3 h. 100 mg glucose was added into the nanosuspension and continued the stirring. The nanosuspension was subjected to centrifugation and dried by lyophilization.

### Characterization

#### Percentage yield and particle size determination

The percentage yield was determined by using the following formula: (practical yield / theoretical yield)  $\times$  100. The particle size of drug loaded bovine serum albumin nanoparticles was determined by Scanning Electron Microscopy (JEOL-JSM-6100, Japan).

#### Determination of drug loading capacity of nanoparticle

The percentage of oxaliplatin loading into the albumin nanoparticles were analyzed by the following way. The drug was completely extracted from 100 mg of nanoparticles in pH 7.4 phosphate buffer.<sup>[11]</sup> The amount of drug present in the solution was determined spectrophotometrically (Shimadzu 160A, Japan) at a wavelength of 210 nm against blank.

### In vitro drug release study

Oxaliplatin release from the bovine serum albumin nanoparticles was done by dialysis method.<sup>[12]</sup> For this, 5 mg drug equivalent nanoparticles were placed into a dialysis bag containing 2 ml of dissolution media (pH 7.4 phosphate buffer). The dialysis bag was immersed into the dissolution medium. The buffer was stirred at 100 rpm and maintained at 37°C. At different time intervals samples were collected and the same were replaced with fresh medium. The amount of drug present in the samples was determined spectrophotometrically (Shimadzu 160A, Japan) at a wavelength of 210 nm against blank.

### RESULT AND DISCUSSION

Bovine serum albumin nanoparticles of oxaliplatin were prepared by desolvation method. Acetone was used as desolvating agent to form nanoparticles. Glutaraldehyde-ethanol solution was added for cross linking and to harden the coacervates. The average particle size was determined by scanning electron microscope (JEOL-JSM-6100, Japan). The mean particle size was found to be 642 nm (Figure 1). It is known that nanoparticles can alter the biodistribution pattern of the incorporated drug. This is important to deliver the drugs at the specific sites. Further, the size of the particles plays an important role to internalize the particles into the cells by the interaction between the particles and tissue surface. Nanoparticles prepared with hydrophilic polymers increase the circulation time in the blood which in turn enhances site specificity.<sup>[13]</sup>

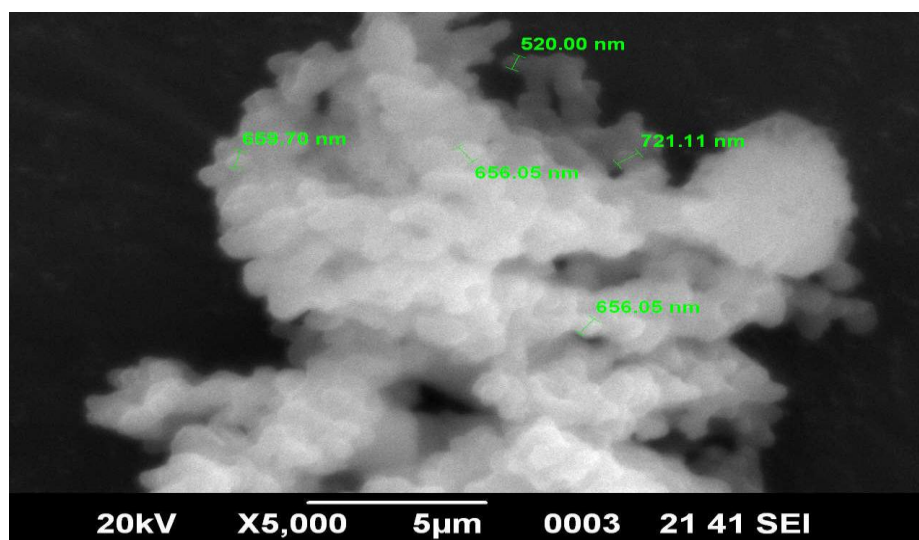


Fig. 1: Scanning electron microscope image of oxaliplatin loaded bovine serum albumin nanoparticles.

The nanoparticles showed  $24 \pm 72\%$  process yield and a drug loading capacity of  $9.189 \pm 1.3\%$  w/v. Higher drug loading is always desirable as it minimize the solid content per ml during injection.<sup>[14]</sup> The *in vitro* drug release from the nanoparticle formulation was carried out

by using dialysis method in 7.4 pH phosphate buffer for 24 h. The drug release from the nanoparticles was 78.48% and the particles were able to release the drug in a sustained manner (Fig. 2).

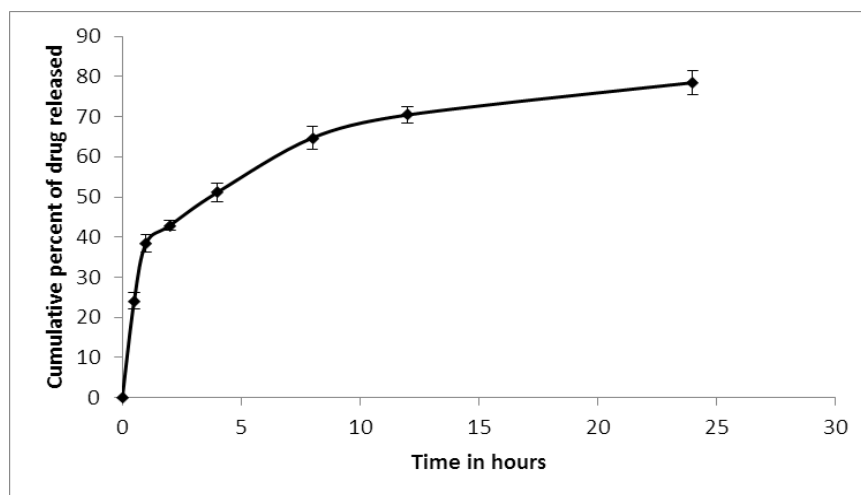


Fig. 2: *In vitro* release of oxaliplatin from albumin nanoparticle formulations.

## CONCLUSION

New platinum-based drugs like oxaliplatin were introduced to provide better therapeutic activity with lesser side effects than cisplatin. Oxaliplatin did not show considerable nephrotoxicity. But it produces ototoxicity and sensory and motor neuropathy.<sup>[15]</sup> In the present study, we prepared bovine serum nanoparticles containing the anticancer drug oxaliplatin. Bovine serum albumin nanoparticles containing the drug oxaliplatin were prepared by desolvation method. The nanoparticles showed good drug loading efficiency and were able to sustain the drug release for 24 h. It can be concluded that this preliminary study may provide an insight to take up further studies.

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