

“Preparation and Evaluation of Spray dried microsphere – Sumatriptan Succinate”

Diksha Pardeshi * Gitanjali Chavan, Naresh jaiswal, Krushna Zambre
, Tatwashil Kshirsagar

Department of Pharmaceutics SBSPM'S B- Pharmacy College Ambajogai Dr-
Babasaheb Ambedkar Marathwada University Aurangabad -4310

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ABSTRACT: The present research work was aimed at development and evaluation of poly lactic co-glycolic acid (PLGA) mucoadhesive microspheres of Sumatriptan Succinate for nasal delivery to avoid first pass metabolism and to improve the therapeutic efficacy in the treatment of Migraine. The microspheres were prepared by a spray drying technique. Particle size was analyzed by optical microscope technique and found to be in the range of 12-30 μm , which is favorable for intranasal absorption. The shape and surface characteristics were determined by scanning electron microscopy (SEM) which depicted the spherical nature and possess smooth surfaces of the microspheres. The percentage encapsulation efficiency was found to be in the range between 94-100%. *In vitro* mucoadhesion was carried out using sheep nasal mucosa and result obtained in 76.11-97.12. Differential Scanning Colorimetry, result indicated a molecular level dispersion of Sumatriptan Succinate in the microspheres. *In vitro* release studies in pH 6.2 phosphate buffer indicated an anomalous transport mechanism for drug release of Sumatriptan Succinate from the microspheres. On the basis of these results, Sumatriptan Succinate loaded PLGA microspheres may be considered as a promising nasal delivery system.
Keywords: Drug Release, Incorporation Efficiency, Poly Lactic Co Glycolic Acid, Particle Size, Swelling Index

I. INTRODUCTION -

Poly (lactic-co-glycolic acid) (PLGA), is significantly used biocompatible and biodegradable polymer for encapsulation of hydrophilic and hydrophobic therapeutic drug molecule^{1,2}. Moreover PLGA (50:50) polymer is nontoxic for human consumption and by choosing appropriate polymer composition predetermine drug release was obtained^{3,4,5}. Sumatriptan succinate is a class of drug for management of migraines. It aids to relieve pain, headache and other migraine symptoms. It selectively

binds with 5HT-1B receptors and thereby, stimulates 5-HT1B receptors and reduces the vascular pulsation and may provide relief in migraine headaches. Its absolute bioavailability is 15%^{6,7}. Various methods used for preparation of PLGA microspheres like phase separation, emulsion solvent evaporation and spray drying technique but spray drying is most advantageous method compared because it is one step method having high drug loading capability and reliability. The microspheres formed by this method have a high drug loading.⁹ Besides these spray drying technique is more precise and easy for scaling up compared to other methods⁸.

II. MATERIALS AND METHOD

Sumatriptan succinate is a kind gift from (Dr-Reddy's Laboratories, India). Poly (D, L-lactide-co-glycolide acid) (PLGA 50:50) gift sample from Resomer RG-502H, Inherent viscosity = 0.21 dl/g (Purac biomaterial, Gorinchem, Nederland). All different solvents and chemicals used were of analytical grade.

Preparation of Sumatriptan Succinate Loaded PLGA Microspheres –

Sumatriptan Succinate mucoadhesive microsphere was prepared using various drug and polymer ratios. PLGA 50:50 was dissolved in acetone solution, Sumatriptan Succinate was added to above polymer solution. The microspheres were obtained by spraying the feed in a spray dryer with a standard 0.7mm nozzle (LU-223 Advanced, Labultima, India). When the liquid was inserted to the nozzle with a peristaltic pump, atomization occurred by the force of the compressed gas, disrupting the liquid into tiny droplets. The droplets beside hot air were

blown into a chamber whenever the droplets were gaseous and discharge out through associated degree exhaust tube. The dry product was then collected in a collection pot. The spray drying conditions, inlet temperature, spray

Evaluation test -

Evaluation of Spray Dried Microspheres-In Vitro Taste Masking The study was conducted in accordance to the method adopted from Shukla et al.⁶⁾ The required amount of spray dried microspheres equivalent to 70 mg sumatriptan succinate was placed in a 25 ml beaker. A volume of 5 ml phosphate buffer solution pH 6.8 (United States Pharmacopeia (USP)) was added and the mixture was allowed to stand for 60 s. A 5 ml volume of phosphate buffer pH 6.8 was used to mimic the salivary fluid volume and pH. After the specified time, the suspension was filtered through 0.45 m m nylon membrane filter. The filtrate was analyzed for drug content using UV/Visible spectrophotometer (Hitachi, Japan) at 227 nm. The experiment was run in triplicate.

1) Thermal Analysis Differential Scanning Calorimetry (DSC) (Perkin Elmer, Pyris 6 DSC, California, U.S.A.) was used to evaluate the compatibility between sumatriptan succinate and Eudragit EPO. The DSC experiments were performed on plain drug, Eudragit EPO and spray dried drug loaded microspheres. Accurately weighed samples (5–7 mg) were sealed in flat bottom aluminium pans and thermograms were recorded at a constant rate of 10 °C/min over a temperature range of 30–300 °C. Inert atmosphere was provided by purging helium gas at a flow rate of 20ml/min .

3) Drug Entrapment Efficiency, Loading and Yield -The entrapment efficiency and drug loading in microspheres was estimated by dissolving 50 mg of spray dried powder in methanol and further diluted with 0.01 N HCl. The samples were analyzed using UV/Visible spectrophotometer (Hitachi, Japan) at a wavelength of 227 nm. Entrapment efficiency, drug loading and yield

2) Particle Size The analysis was performed using a Mastersizer S (Malvern Instruments, U.K.) fitted with MS1 small volume sample dispersion unit connected to a dispersion unit controller. The spray dried microspheres were dispersed in water and

sonicated for 2 min using bath sonicator (Branson 5200, Branson Ultrasonics, Danbury, U.S.A.) to prevent aggregation before measuring particle size. Samples were

III. RESULTS -

1. Product yield - Product yield was found in the range between 25 to 60 % These comparatively low values could also be owing to the low amount of feed used for the preparation of every batch and by the structure of the spray drier equipment that lacked a lure to capture the smallest and lightest particles .

2. Particle size - Average particle size of microspheres ranged from 10 to 35 µm, such particles are considered to be suitable for nasal administration It was found that increasing drug to polymer ratio will slightly increase the size of particle

3. Drug Loading and Incorporation Efficiency - Incorporation efficiency was high since it always exceeded 90 the result indicated that increasing the ratio of drug to polymer will increase drug loading

IV. DISCUSSION

Poly lactic co-glycolic acid (PLGA) is a biocompatible polymer, it does not cause any deleterious effect or toxic response in the nasal mucosal cavity even if used for prolonged periods was evaluated by histopathological studies. These results demonstrated that PLGA microspheres were potential to be used as a vehicle for the nasal delivery of Sumatriptan succinate. However extensive pharmacokinetics and pharmacodynamic studies are required to establish a correlation, if any, before establishing nasal delivery as an alternative.

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