

Formulation and Evaluation Allopurinol Micro Encapsulation by Double Emulsion Solvent Diffusion Method

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ABSTRACT

The objective of the present study was to develop This study reports the micro capsulation of Allopurinol by the double emulsion solvent diffusion method and the release of the drug from the microcapsules. This sustained release of microcapsules is additionally influenced by the formulation of latest biodegradable polymer Ethyl cellulose, hence drug release pattern. The ready microcapsule was subjected to numerous pre and post formulation studies. Prepared microcapsule was evaluated for the partical size, percentage yield, entrapment efficiency, estimatin of drug content and in vitro drug release studies. Results of the present study indicate that allopurinol microcapsule can be successfully designed to develop sustained drug delivery that reduces the dosing frequency and their buy we can increase the patient compliance.

INTRODUCTION

Microencapsulation is a useful method which, prolongs the duration of the drug effect significantly and improves patient compliance. Eventually the total dose and few adverse reactions may be reduce since a steady plasma concentration is maintained.

Allopurinol is used to treat Gout and Tumor lysis syndrome, Inflammatory bowel disease. Its work its active metabolite, oxypurinol, inhibits the enzyme xanthine oxidase, blocking the conversion of the oxypurines

hypoxanthine and xanthine to uric acid. Elevated concentrations of oxypurine and oxypurine inhibition of xanthine oxidase through negative feedback results in a decrease in the concentrations of uric acid in the serum and urine. Microencapsulation is defined as the application of a thin coating to individual core materials that have an arbitrary particle size range between 5 μm to 5000 μm . Microencapsulation is widely used in the pharmaceutical and other sciences to mask taste or odors, prolong release, impart stability to drug molecules, improve bioavailability, and as a multi-particulate dosage form to produce controlled or targeted drug delivery. It is therefore, a rapidly expanding technology for achieving sustained release dosage form ^[1].

Double-emulsion droplets have found widespread applications in various engineering and biomedical fields because of their capability in encapsulating different components in each layer. The conventional double-emulsion method is the two-stage stirring emulsification method, which suffers from poor monodispersity and low encapsulation efficiency. With recent advances in micro fabrication, some novel methods for fabricating double-emulsion droplets have been developed, including micro fluidic emulsification (double-T-junction micro channel, double-cross-shaped micro channel and several three-dimensional micro channels), membrane emulsification and coaxial electro spraying.

MATERIALS AND METHOD

Allopurinol was obtained as a gift sample from Piramal healthcare, limited, Pithampur, Dhar. Ethylcellulose, SdFine-chem. Acetonitril, SdFine-chem. Dichloromethane, HiMedia Laboratories. Span 80 SdFine-chem. From SdFine-chem. limited (Mumbai).

For the determination of λ_{max} , Stock solution of drug was prepared by dissolving 100mg of drug in 0.1M HCL and make up the volume to 100ml (conc.1000 $\mu\text{g}/\text{ml}$). 10ml of stock solution was diluted to 100ml of 0.1M HCL and then 10ml of this solution was diluted to 100ml with 0.1M HCL. The resulting solution was examined in the range of 230nm to 360nm by UV-visible spectrophotometer. The resulting solution showed maximum absorptions.

Melting point of Allopurinol was determined by using open capillary method. The capillary was filled with small amount of drug powder and it was placed along with thermometer in melting point apparatus. The temperature was noted using thermometer. The average of three values was considered as the melting point of drug ^[2].

Samples of 1-2 mg of drug alone, each excipient alone, physical mixtures of allopurinol with the investigated excipients (1:1, w/w) prepared by physical and perfect mixing and solid dispersion were scanned from 4000-400 cm^{-1} . The spectrophotometer was of shimadzu. The results suggested that there was no interaction of between allopurinol and excipients. The IR Spectra of pure drug, carrier and formulations.

Preparation of standard calibration curve of etoricoxib

Standard calibration curve of allopurinol was prepared by taking accurately weighed 100 ml of allopurinol and dissolved in 100 ml of 0.1 N sodium hydroxide then make up the volume upto 1000 ml with 0.1 N sodium hydroxide. Then 1,2,3,4,5,6,7,8,9, and 10 ml of these solution was taken in 10 ml volumetric flask and make up the volume with 0.1 N sodium hydroxide up to 10 ml. The dilutions were analyzed by UV spectrophotometer at 250 nm and absorbance was noted. The standard curve was plotted with absorbance values against drug concentration.

Drug was added to 10 ml of different solvents. The solutions were sonicated for 1 hr at room temperature. The solutions obtained were filtered through a filter paper and the filtrate was diluted with distilled water. The diluted solutions were measured spectrophotometrically at a λ_{max} of 250 nm using the same medium as a blank and the resulting solubility.

Method of preparation micropencapsulation

The drug Allopurinol and the polymer, ethylcellulose were mixed and weighed amounts of ethylcellulose and drug were dissolved in mixture of acetonitrile and dichloromethane. The initial w/o emulsion was formed by adding of deionised water to the drug polymer solution with constant stirring at 500 rpm for 5 min. then slowly added to light liquid paraffin containing span 80 as a surfactant with constant stirring for 2 hrs. The n-hexane was added and the stirring was further for 1 hrs (Table 1) [3].

Table 1. composition of optimized liquisolid system.

Formulation Code	Drug (in mg)	Ethylcellulose (in gm)	Acetnitril (ml)	dichloromethane (in ml)
F1	500	2	10	10
F2	1000	2	-	-
F3	1.2	2	-	-
F4	1.3	2	-	-

Evaluation of microencapsulation

Partical size analysis: Determination of average particle size of the allopurinol microcapsules was carried out by the optical microscopy methods. A minute quantity of microcapsules were dispersed in liquid paraffin and then spread on clean glass slide and average size if microcapsules were determined in each batch:

- Bulk characterisation of microencapsulation
- Bulk characterisations of liquisolid system were estimated by Bulk density, Tapped density,

- Carr's index, and Hausner's ratio. The flow property was determined by Angle of repose.

Determination of saturation solubility of microencapsulation

Solubility study was performed according to method reported by Higuchi and Connors. The liquisolid compact system F1,F2,F3,F4,F5,F6 were added in 10 ml distilled water taken in stoppered conical flask and were shaken for 24 hrs at 37 °C in orbital shaker. 2 ml aliquots were withdrawn at 1 hr intervals and filtered through whatman filter paper. The filtered solution were analysed spectrophotometrically at nm against blank. The saturation solubility of liquisolid.

Drug content of microencapsulation

An amount equivalent to 10 mg of allopurinol was weighed from each resultant microencapsulate and in 50 mL 0.1 N sodium hydroxide using a 100 mL volumetric flask and then was stirred for 10 min. The volume obtained was completed to 100 mL with 0.1 N sodium hydroxide and shaken well. 2ml from the previous solution were taken and were completed to 10 ml with 0.1 N sodium hydroxide. The absorbance was measured using a UV spectrophotometer at 258 nm, using 0.1 N sodium hydroxide as a blank.

Fourier transforms infrared (FTIR) spectroscopy

The characteristic peak attributable to various functional groups present in the molecule of drug was assigned to establish the identity of drug. The results suggested that there was no interaction of between allopurinol and excipients. The IR Spectra of spure drug, carrier and formulations.

In vitro dissolution of allopurinol tablet from microcapsule. The rotating basket dissolution apparatus was used for the determination of dissolution rates of allopurinol solid dispersions. An accurately weighed amount of each solid dispersion equivalent to 100 mg of allopurinol tablet was placed into the basket of the dissolution test apparatus. The basket was rotated at 50 rpm in 900 mL of the dissolution medium (0.1 N HCl) and maintained at a constant temperature ($37 \pm 0.5^\circ\text{C}$). Each of 5 mL, were withdrawn from the dissolution medium at time intervals of 5, 15, 30, 45 and 60. The same volume of 0.1 N HCl was used to replace the withdrawn samples. The samples were suitably filtered, diluted, and measured spectrophotometrically at 258 nm. The *in vitro* release of various formulations.

RESULT AND DISCUSSION

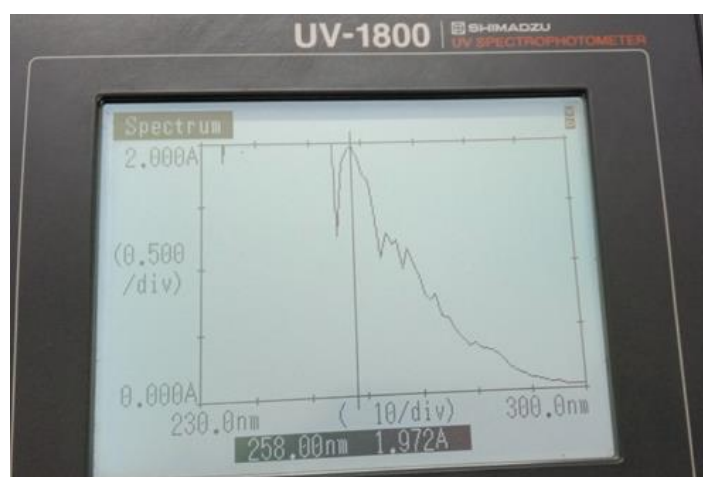
Melting point determination

The melting point of drug sample was determined by using melting point apparatus. The melting point was found between the range of 344-355 °C.

Standard curve of allopurinol

Standard calibration curve of allopurinol was prepared by taking accurately weighed 100 ml of allopurinol and dissolved in 100 ml of 0.1 N sodium hydroxide then make up the volume upto 1000 ml with 0.1 N sodium hydroxide. Then 1,2,3,4,5,6,7,8,9, and 10 ml of these solution was taken in 10 ml volumetric flask and make up the volume with 0.1 N sodium hydroxide upto 10 ml. The dilutions were analyzed by UV spectrophotometer at 250nm and absorbance was noted. The standard curve was plotted with absorbance values against drug concentration Calibration curve of Allopurinol in 0.1N NaOH (Figure 1) [4].

Figure 1. Lamda max of allopurinol



Drug was added to 10ml of different solvents. The solutions were sonicated for 1 hr at room temperature. The solutions obtained was filtered through a filter paper and the filtrate was diluted with distilled water. The diluted solutions were measured spectrophotometrically at a λ_{max} of 250 nm using the same medium as a blank and the resulting [5].

CONCLUSION

Formulation of microcapsule of allopurinol for the prolonged release of drug. Formulation F2 and F3 were found to be best among all other formulation. It was used in improve the solubility. It was used for controlled and targeted release bulk characterization and flow properties of liquisolid compact systems. It was also used for masking of taste or odors Allopurinol can be used as an Gout, Tumor lysis syndrome, Inflammatory bowel disease.

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