SHORT COMMUNICATIONS

Preparation and Evaluation of Alginate-Chitosan Beads

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Chitosan was reacted with sodium alginate in the presence of tripolyphosphate for bead formation. Diltiazem hydrochloride was used as the model drug. Spherical beads were produced with diameter in the range of 440-660 µm. The encapsulation efficiency was found to be 80-90%. There was a rapid initial drug release phase followed by a second release phase. But when glutaraldehyde or pectin is added the burst effect disappeared and they also decreased the percentage release of drug from the beads.

Chitosan [α-(1,4)2-amino-2-deoxy-β-D-glucon] is a unique polysaccharide derived from chitin. Chitosan has a variety of promising pharmaceutical uses and is presently considered as a novel carrier material in drug delivery systems, as indicated by the large number of studies published over the last few years[1]. Chitosan is a poly cationic polysaccharide that forms gel beads with multivalent counter ion[2]. For more stable alginate beads, complex coacervation between two oppositely charged polysaccharides is required[3]. Cross-linking agents like sodium alginate, glutaraldehyde and pectin can be used to control the release rate of the drug[4]. In this study alginate chitosan beads were prepared using glutaraldehyde and pectin as cross-linking agents and the resulting beads were evaluated. Diltiazem hydrochloride, a water-soluble drug with a short half-life was used as the model drug.

Chitosan, tripolyphosphate and glutaraldehyde were obtained from Sigma-Aldrich Chemicals, USA, Mo. Diltiazem hydrochloride was a gift sample from M/s Anglo French Pharmaceutical, Bangalore. Sodium alginate and pectin were procured from M/s Loba Chemie, Mumbai.

Alginate-treated chitosan beads containing diltiazem hydrochloride were prepared as per the method of Bodmeier[5]. Diltiazem hydrochloride (90 mg) was dissolved in water. To this, 2% W/V of chitosan in acetic acid was added. This mixture was dropped through a syringe into gently agitated tripolyphosphate -1% W/V solution containing sodium alginate. The formed beads were separated and washed with distilled water three times. Beads were filtered and dried at room temperature. Glutaraldehyde and pectin were added to the external phase to study the effect on bead properties. A number of formulations were prepared with varying concentrations of sodium alginate, glutaraldehyde and pectin as shown in Table 1.

Optical microscopy technique was used to determine the size of the beads. Average and standard deviation of 100 particles was estimated. The results are given in Table 1. Fifty milligrams of beads were digested with 5 ml of phosphate buffered saline at room temperature for 12 h and filtered. Then 1 ml of the filtered solution was diluted to 50 ml with distilled water and the absorbance was measured at 236 nm using a blank. Fifty milligrams of beads were weighed and suspended in 5 ml of phosphate buffered saline (pH 7.4) contained in a dialysis bag. The medium was stirred at 100 rpm on a laboratory shaker and maintained at 37±1° in a water bath. Sample was removed periodically, suitably diluted and assayed spectrophotometrically at 236 nm for diltiazem hydrochloride content.

Roughly spherical and regular shaped beads were ob-

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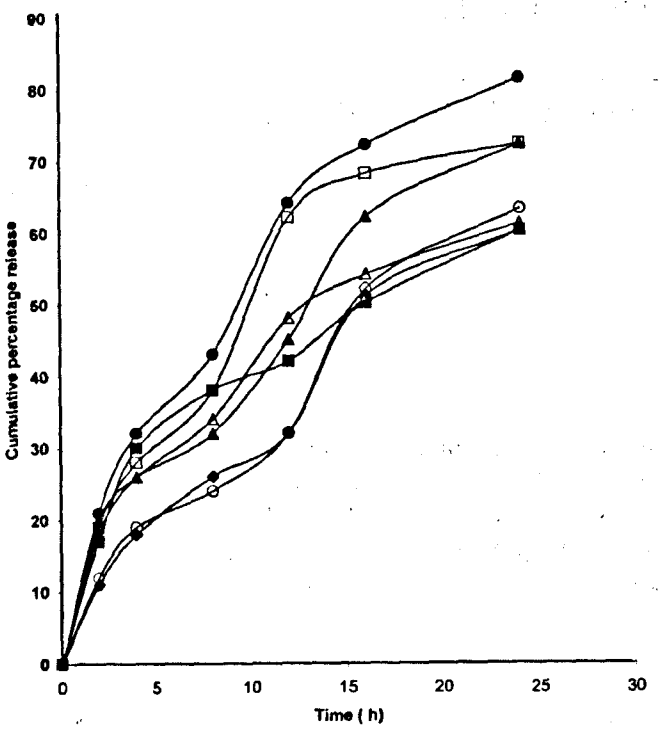

fig. 1: C_1 (-□-), C_2 (-●-) and C_3 (-▲-) contain sodium alginate in increasing concentration of 0.5, 1, 1.5%. C_4 (-△-), C_5 (-■-), C_6 (-O-) and C_7 (-◆-) contains 1% of sodium alginate. C_4 contains 2.5% of glutaraldehyde and that of C_5 contains 5% glutarldehyde. C_6 and C_7 contain 1 and 2% pectin, respectively. In C_4-C_7 burst effect disappears. C_3 shows decrease in percent of drug release.

tained. The beads were about 440-660 nm in diameter. The bead size increased with alginate concentration. If the concentration of sodium alginate is more than 1.5%, the beads were not formed which could be due to high viscosity. The encapsulation efficiency varied from 80-90% (Table 1). The higher solubility of diltiazem hydrochloride in the aqueous phase, resulted in higher encapsulation efficiency of all the formulations.

As per the release profile studies, (fig. 1) there was a rapid initial drug release phase followed by a second release phase. But when glutaraldehyde or pectin is added the burst effect disappeared. Increase in the concentration of sodium alginate, glutaraldehyde and pectin resulted in decrease in the percentage of drug release. This may be due to altered membrane permeability of chitosan beads.

In chitosan beads, the polyelectrolyte complex occurs between chitosan and tripolyphosphate. The complex also occurs between chitosan and alginate, which protect the gel matrix from environmental conditions. Better cross-linking was obtained in chitosan beads with glutaraldehyde or pectin, which helps in controlling the release rate of the drug. Thus alginate chitosan beads can be used as a potential delivery system.

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TABLE 1: COMPOSITION AND DIAMETER OF CHITOSAN BEADS.

Formulation	Sodium alginate (%)	Glutaraldehye (%)	Pectin (%)	Diameter (μm±S.D.)	Encapsulation Efficiency (%)
C_1	0.5	-	-	440.3±3.6	80.3
C_2	1.0	-	-	467.4±8.5	84.6
C_3	1.0	-	-	540.3±3.2	82.1
C_4	1.0	2.5	-	535.4±4.8	84.2
C_5	1.0	5.0	-	533.6±7.2	83.4
C_6	1.0	-	1.0	660.2±5.3	90.1
C_7	1.0	-	2.0	632.3±4.9	86.3

C_1, C_2 and C_3 contain sodium alginate in increasing concentration of 0.5, 1, 1.5%. C_4, C_5, C_6 and C_7 contains 1% of sodium alginate. C_4 contains 2.5% of glutaraldehyde and that of C_5 contains 5% glutarldehyde. C_6 and C_7 contain 1 and 2% pectin, respectively.

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Rapid Spectophotometric Determination of Sulphonamide Derivatives with Resorcinol

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A rapid and simple spectrophotometric method for the determination of sulpha drugs is described. The method is based on the formation of a red coloured azo product by the diazotisation of sulphonamides, sulphamethoxazole, sulphadiazene and sulphacetamide followed by a coupling reaction with resorcinol. Absorbance of the resulting red azo product is measured at 500 nm. Beer's law is obeyed in the concentration range of 0.25-7.0 µg/ml at the wavelength of maximum absorption. The method is successfully employed for the determination of sulphonamides in various pharmaceutical preparations.

Sulpha drugs are widely used in the treatment of infections, especially for patients intolerant to antibiotics. The vast commercial success of these medicinal agents has made the chemistry of sulphonamides to become a major area of research and an important branch of commercial importance in pharmaceutical sciences[1]. A survey of literature reveals that there are various methods available for the determination of sulphonamide derivatives. The official method of BP[2,3] and USP[4] describes nitrite titration method for the analysis of sulpha drugs. Among the number of spectrophotometric methods available the most prominent methods are chloramine-T[5], o-chloranil[6], metol-periodate[7], 4-dimethylaminecinnamaldehyde[8,9] and acetylacetone-formaldehyde[10] but all have certain limitations.

The present work describes the diazotisation reaction of sulphanomide derivatives followed by coupling with resorcinol to yield a red azo product with a maximum absorption at 500 nm. The method offers the advantages of rapidity, sensitivity and simplicity without the need for extraction or heating.

A JASCO model UVIDEC-610 UV/VIS spectrophotometer with 1.0 cm matched cells was used for electronic spectral measurements. Sulphonamide derivatives were all purchased from Sigma Chemical Co, St. Louis, MO, and were used without further purification. Sodium nitrite and resorcinol were purchased from BDH and AR sulphuric acid was used. All other reagents were of analytical grade. Commercial dosage forms were purchased from Burroughs Wellcome, Rhone-Poulnec, Nicholas Piramal India Ltd and East India Ltd. Deionized water was used to prepare all solutions. Standard solutions of sulphonamides (1000 µg/ml) were prepared by dissolving 100 mg of each sulphonamide in 2.0 ml of 10 M H_2SO_4 and then diluting to the mark in a 100 ml standard flask. A working standard solution of each sulphonamide containing 25 µg/ml was prepared by further

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