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Abstract
An oral suspension could a suitable dosage form for the geriatric patients. The calcium alginate coated ion exchange resinate of propranolol hydrochloride were prepared using Amberlite IR-120 by solvent evaporation. Microcapsules of propranolol hydrochloride resinate were prepared by solvent evaporation technique, the suspensions were prepared by using deionised water as the vehicle. Methyl cellulose and Tween 80 were used as suspending agents in four different concentrations: 0.5, 1, 1.5 and 2%. The suspensions were evaluated for physical stability, redispersibility and in vitro release patterns. Microcapsules of propranolol hydrochloride corresponding to drug polymer ratios of 1:1.0, 1:1.5, 1:2.0, 1:2.5 and 1:3.0 were evaluated for physical stability, percentage yield, particle size, and in vitro drug release profile. The drug loading capacity of ion exchange resine was found to be 41% (w/v). The suspensions were prepared with 1.5% Tween 80 had good physical stability and redispersibility and in vitro release patterns, and were also suitable for sustained release formulation. Therefore, calcium alginate coated propranolol hydrochloride formulation as oral sustained suspension is an effective system, which can be suitable dosage form for geriatric use.

Keywords: Amberlite IR120; Calcium alginate; Microcapsules; Propranolol.
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1. Introduction
The goal of any drug release systems is to provide a therapeutic amount of drug to the proper site in the body to achieve and maintain the desired drug concentration at the site of action [1]. This objective points to the most important aspects of drug delivery, namely spatial placement and temporarily delivery of the drug. The sustained release system produces a slow release of drug over an extended period of time. If the system is successfully maintaining a constant drug level in blood or targeted tissue, it is considered as controlled release system. An oral suspension could be a suitable dosage form for the geriatric patients, because of its easy
consumption and flexibility in the dosage administration. Many therapeutic benefits could be gained by incorporating functions of sustained drug release into suspension dosage forms. They include improvement of rate and extent of drug absorption and a higher patient compliance [2, 3]. Propranolol hydrochloride has a great utility as a therapeutic agent in the treatment of hypertension. It has a short plasma half-life (2-3.5 h) and is metabolized extensively by first pass metabolism. Different methods for sustaining the release of drugs are described by Riens [4]. One of the methods to sustain the drug release is the use of ion exchange resins. In the present work, propranolol hydrochloride was absorbed on cationic exchange resin, Amberlite IR-120 and later a coating of Calcium alginate was given. Then, these resinates were formulated into a suspension form, which can release the drug in a slow controlled manner. The dissolution rate and bioavailability from suspensions are reported to be adversely affected by the suspending agents, which are used to increase the viscosity of the media to maintain uniform dispersion during storage [5, 6].

Hence, in the present study an attempt is made to evaluate different suspending agents for their stability for the formulation of sustained release suspension containing propranolol hydrochloride microcapsules.

2. Materials and methods
2.1. Materials
Propranolol hydrochloride was obtained as free samples from Ranbaxy, Bangalore. Amberlite IR120 was from BDH, UK. Calcium alginate, Tween 80 and methyl cellulose were from SD fine Chemicals Chennai, and all of them were of analytical reagent grade.

2.2. Preparation of drug resonates
The resin beads were grounded and passed through sieve number 120 to get a uniform size distribution. One g of resin was added to 25 ml of propranolol hydrochloride solution (20 g/ml) and was stirred for 4 h, and then filtered and dried.

2.3. Determination of ion exchange capacity
The ion exchange capacity of the resin was determined by a known quantity of drug resinates with 50 ml of 0.2 M hydrochloric acid for 4 h. It was then filtered and the amount of drug in the filterate was determined by UV spectrophotometer (Shimadzu 160-A Japan) at 290 nm against a blank which was prepared under similar conditions using a plain resin.

2.4. Preparation of microcapsules
Microcapsules of propranolol hydrochloride resinates were prepared by the solvent evaporation techniques [4]. A known quantity of the drug resinate was dispersed in

![Figure 1](image_url)  
*Figure 1. In vitro release profile of different batches of microcapsules.*
100 ml of cyclohexane containing 3% polyisobutylene, and then 35 ml of light liquid paraffin was added to the mixture and stirred. A sufficient quantity of calcium alginate was dissolved in 100 ml of ethyl acetate separately and this polymeric solution was added to the drug resinate dispersion and stirred at 100 rpm to evaporate the solvent to half of its original volume (120 ml). The microcapsules formed were washed with 25 ml of cyclohexane to remove the excess of polyiso-butylene, and followed by washing with 25 ml of petroleum ether to remove the liquid paraffin. The mass was dried and passed through a standard sieve, packed in a well-closed container and stored in desiccators.

Five batches of microcapsules corresponding to drug resinate polymer ratios of (1:1, 1:1.5, 1:2, 1:2.5 and 1:3), coded as S1, S2, S3, S4 and S5, respectively, were prepared and evaluated for the drug content, particle size and in vitro drug release.

<table>
<thead>
<tr>
<th>Batch code</th>
<th>Drug resinate polymer ratio</th>
<th>Nature of microcapsules</th>
<th>%Yield</th>
<th>Drug content (%)</th>
<th>Average particle size (μm) ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>1:1</td>
<td>Free flowing</td>
<td>78.54</td>
<td>41.06</td>
<td>233.4±0.1</td>
</tr>
<tr>
<td>S2</td>
<td>1:1.5</td>
<td>Free flowing</td>
<td>83.33</td>
<td>40.86</td>
<td>232.9±0.1</td>
</tr>
<tr>
<td>S3</td>
<td>1:2</td>
<td>Free flowing</td>
<td>89.27</td>
<td>40.96</td>
<td>239.5±0.1</td>
</tr>
<tr>
<td>S4</td>
<td>1:2.5</td>
<td>Free flowing</td>
<td>91.27</td>
<td>41.65</td>
<td>194.9±0.3</td>
</tr>
<tr>
<td>S5</td>
<td>1:3</td>
<td>Free flowing</td>
<td>94.31</td>
<td>40.57</td>
<td>227.0±0.4</td>
</tr>
</tbody>
</table>

2.5. Determination of drug content in microcapsules

A known quantity (100 mg) of the microcapsules was stirred with 100 ml of 0.2 M hydrochloric acid for 6 h, filtered and the absorbance of the filtrate was measured at 290 nm. The drug content was calculated using the calibration curve.

2.5. Determination of the particle size of microcapsules

A small amount of prepared microcapsules was diluted with petroleum ether. Using this suspension, the particle size was determined by optical microscopic method.

2.6. In vitro drug release from microcapsules

For the determination of in vitro drug release USP dissolution apparatus 2 (paddle method) was used. Half dilution method was employed to maintain different pH conditions in the dissolution studies [6-8]. The prepared microcapsules equivalent to 40 mg of propranolol were added to 500 ml of 0.1 M hydrochloric acid at a stirring rate of 50 rpm. At predetermined time intervals, 5 ml samples were withdrawn and replaced with fresh buffer to maintain the volume. The absorbance of the filtrate at 290 nm was determined.

![In vitro dissolution profile of different batches of suspensions.](image)
propranolol hydrochloride were added in 900 ml of buffer solution with pH 1.2, contained in the dissolution flask and the temperature was maintained at 37±1 °C. Stirring was done at 100 rpm using the paddle. Aliquots of 5 ml were withdrawn at specific time intervals and an equal amount of fresh media was replaced after each sampling. At the end of 3 h, half of the medium was removed by filtering through a membrane of 0.45 mm pore size, and it was replaced by buffer of pH 9.3, to get a pH of 6.8 in the dissolution medium. The dissolution was continued in this medium up to 12 h. The amount of drug dissolved was determined by diluting the samples and measuring the absorbance at 290 nm using UV spectrophotometer (Shimadzu160-A Japan) [9].

2.7. Preparation of suspensions

The suspensions were prepared by using de-ionized water as the vehicle. Other ingredients added to the formulation were liquid glucose (30%) and sodium salts of methyl paraben (0.18%). Eight batches of suspensions were prepared using methyl cellulose, a suspending agent, and Tween 80, a surfactant, in four different concentrations, 0.5, 1, 1.5 and 2%. These suspensions were coded from F1 to F8 (Table 2). In all the suspensions, the dose level of propranolol hydrochloride was kept 40 mg per 5 ml of suspension (microcapsules of drug resinates equivalent to 40 mg of the drugs were suspended in each 5 ml).

2.8. Physical stability and redispersibility of suspensions

The formulated suspensions were evaluated for physical stability by determining the sedimentation volume [8-10]. A 50 ml sample of each suspension was taken in a 50 ml stopped graduated measuring cylinder. The suspensions was dispersed thoroughly by moving up and down three times. Later, the suspensions were allowed to settle for 2 min., and the volume of each sediment was noted. This is the original volume of sediment (H0). The cylinder was kept undisturbed for 7 days. The volume of sediment read on the seventh day was considered as final volume of sediment (H0). The redispersibility of the suspensions was checked by moving the stopper cylinders upside down until there was no sediment at the bottom of the cylinder.

2.9. Drug leaching into the suspensions

The amount of the drug leaching into the vehicles after storage of suspensions at room temperature for three months was determined by filtering the suspension and measuring the absorbance at 290 nm, using a suspension prepared without microcapsules as a blank. The drug leached into vehicle was calculated using calibration curve.

2.10. In vitro release from drug suspension

In vitro release studies for the suspensions were carried out by dialysis bag method [4], and half dilution method was employed to maintain different pH conditions in the dissolution studies. The suspensions were placed in a dialysis bag, and it was held in a position in the dissolution fluid by a heavy clamp with the stirring element (paddle), which was rotated at 50 rpm. The sampling was done at different intervals and fresh medium was added as replacement for sample quantity. The dissolution was carried out for 12 h; for the first 3 h under gastric pH (1.2 pH) followed by 9 h under intestinal pH (pH 6.8) the sample were withdrawn and diluted, and the absorbance was measured at 290 nm.

3. Results and discussion

Five batches of microcapsules (S1-S5) propranolol hydrochloride, corresponding to drug polymer ratios of 1:1, 1:1.5, 1:2, 1:2.5 and 1:3 were evaluated for the percentage of yield, the drug content, particle size and in vitro drug release profile. The drug loading capacity of ion exchange resin was found to
be 41.7% (w/v). The uniformity of drug content was observed in all of the batches and the values of drug content were found to be satisfactory. These values are shown in Table 1. The average particle size for S1-S5 was found to be suitable for suspensions.

The in vitro drug release studies for different batches for microcapsule (Figure 1) showed that increase in methylcellulose proportion reduces the rate of release. The batch S5, in which the maximum calcium alginate was used, showed minimum drug release (60%) at the end of 12 h. The batch S1, in which minimum proportion of calcium alginate was used, showed maximum drug release (94.9%). Among the 5 batches, batch S2 showed uniformity of drug release up to 12 h and was considered as ideal for formulation of sustained release suspensions and the batch was selected for further studies.

### 3.1. Evaluation of suspensions

Eight batches of suspensions of propranolol hydrochloride microcapsules were prepared (F1-F8) and evaluated for physical stability, drug leakage, viscosity and in vitro drug release. The ‘H/u/H0’ values for the suspensions are shown in Table 2. Tween 80 showed a better physical stability than methyl cellulose. The maximum physical stability was obtained with 2% concentration of both suspending agent. All of the suspensions, except those prepared with 2% of both of the suspending agents, could be redispersed easily after the seventh day of settling and gave a uniform dispersion upon checking. The suspensions prepared with 2% concentration of methylcellulose and Tween 80 could not be redispersed because of their higher viscosity. In all of the suspensions, the drug leaching was found to be less than 0.1% after storing at room temperature for 3 months, which provide the protection offered by calcium alginate.

The results of in vitro studies are shown in Figure 2. The release data showed that the rates of drug release from the suspension was reduced with increasing the concentrations of suspending agents. This is because an increase in the concentration of suspending agent increases viscosity, which in turn reduces the rate of diffusion. The suspension prepared with 2% concentration of Tween 80 and methylcellulose showed maximum sustaining effect and released only 79.0% and 71.4% of drug at the end of 12 h. But the physical characteristics of those suspensions were not ideal. The suspensions were prepared with 1.5% of suspending agents had good physical stability and redispersability. The release pattern was also suitable for a sustained release preparation. Hence, they were considered as ideal.

### 4. Conclusion

Ion exchange resinates of propranolol hydrochloride coated with calcium alginate and formulated, as oral suspension is an effective system for sustained release of propranolol hydrochloride and this can be a

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Table 2. Physical characteristics of and drug leaching in different batches of suspensions prepared using propranolol hydrochloride resinates.

<table>
<thead>
<tr>
<th>Batch code</th>
<th>Suspending agent</th>
<th>Concentration %w/v</th>
<th>Viscosity (cps)</th>
<th>H/u/H0</th>
<th>Amount of drug released into vehicle (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>Methyl cellulose</td>
<td>0.5</td>
<td>200</td>
<td>0.20</td>
<td>0.02</td>
</tr>
<tr>
<td>F2</td>
<td>Methyl cellulose</td>
<td>1.0</td>
<td>290</td>
<td>0.60</td>
<td>0.03</td>
</tr>
<tr>
<td>F3</td>
<td>Methyl cellulose</td>
<td>1.5</td>
<td>240</td>
<td>0.73</td>
<td>0.07</td>
</tr>
<tr>
<td>F4</td>
<td>Methyl cellulose</td>
<td>2.0</td>
<td>350</td>
<td>0.60</td>
<td>0.06</td>
</tr>
<tr>
<td>F5</td>
<td>Tween80</td>
<td>0.5</td>
<td>230</td>
<td>0.40</td>
<td>0.07</td>
</tr>
<tr>
<td>F6</td>
<td>Tween80</td>
<td>1.0</td>
<td>280</td>
<td>0.74</td>
<td>0.02</td>
</tr>
<tr>
<td>F7</td>
<td>Tween80</td>
<td>1.5</td>
<td>300</td>
<td>0.85</td>
<td>0.08</td>
</tr>
<tr>
<td>F8</td>
<td>Tween80</td>
<td>2.0</td>
<td>380</td>
<td>0.83</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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Microcapsules of sustained release propranolol suspensions
suitable dosage form for geriatric use. This formulation improves the rate and extent of drug absorption and higher patient compliance.

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Reference


