Rosin, a Polymer for Microencapsulation of Diltiazem Hydrochloride for Sustained Release by Emulsion - Solvent Evaporation Technique

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Microcapsules of diltiazem hydrochloride with rosin were prepared by an emulsion-solvent-evaporation technique. Different amounts of drugs were added in order to obtain various drug to polymer ratios. The physical properties, loading efficiency and release rate depended on the drug to polymer ratio. The low drug content of microcapsules may be due to the interaction between the hydrochloride form of diltiazem and rosin in acetone, where as non-hydrochloride drug like sulphamethoxpyridazine showed complete loading efficiency. Span 80 was used to prevent aggregation. The mean size of the microcapsules decreased as the drug/polymer ratio increased. Since microcapsules were very small they were embedded into a tablet. The microcapsules produced a typical 24 h sustained release pattern. *In vitro* dissolution studies showed that first-order release characteristics were exhibited.

As not much work has been done on rosin as a coating material, we have attempted to study the effectiveness of rosin as a polymer in microencapsulation of various drugs. Rosin (colophony) is a resin and it is the residue left after the distillation of the oil of turpentine from the crude oleo- resin of various species of Pinus (Tourn) linn., family: Pinaceae[1].

In the present study, diltiazem hydrochloride was microencapsulated using rosin as a polymer with a view to sustain release. The microcapsules were evaluated for size distribution, flow properties, drug content and drug release properties.

Diltiazem Hydrochloride was a gift sample from Parke-Davis, Hyderabad, while ephedrine hydrochloride and sulphamethoxypyridazine were gift samples from Emkay Labs, Bangalore and I.D.P.L., Hyderabad, respectively. Rosin N-grade was locally purchased. Acetone was supplied by NICE Chemicals, Cochin while hexane was supplied by E. Merck (I) Ltd., Mumbai. Liquid paraffin was supplied by Loba Chemie Pvt. Ltd. and Span 80 was supplied by GSC, Mumbai respectively. A Remi make paddle stirrer was used in the dissolution studies. Dissolution apparatus by Campbell electronics, Mumbai was used for the dissolution studies. A Shimadzu make UV VIS spectrophotometer was used for estimation of the drugs in dissolution studies.

Microcapsules were prepared by emulsion solvent-evaporation technique[2]. Acetone was used as the polymer solvent, light mineral oil as the microcapsulating vehicle, span 80 as the surfactant and n-hexane as the decanter of paraffin oil. To prepare microcapsules with various drug to polymer ratios such as 1:8 and 1:10, an amount of 100 mg of diltiazem hydrochloride was weighed and either 800 or 1000 mg of rosin was added respectively. The drug to polymer ratio was varied keeping the amount of drug constant in both cases and increasing the amount of polymer used.

An amount of 800 mg of rosin was completely dissolved in 30 ml of acetone. Weighed amounts of diltiazem hydrochloride, depending on the desired ratio, were dispersed in this solution. The dispersion was poured into 100 ml of liquid paraffin containing 1% of Span 80 and stirred for 45 min at 2500 rpm at room temperature. Stirring was carried out using a paddle stirrer, during the 45 min stirring period. Acetone used as a solvent for rosin, was completely removed by evaporation. The light mineral oil was decanted and the collected microcapsules were washed twice with 100 ml of n-hexane at room tem-

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TABLE 1 : DRUG CONTENT OF THE MICROCAPSULES

Drug	Drug polymer ratio	Theoretical yield (mg)	Practical yield (mg)	% yield	Theoretical drug content (mg)	Practical drug content* (mg)	% Drug content
Diltiazem	1:8	900	460	51.11	100	5.00	5.00
hydrochloride	1:10	1100	598	54.36	100	4.06	4.06
Ephedrine	1:8	900	473	52.55	100	5.03	5.03
hydrochloride	1:10	1100	608	55.27	100	4.08	4.08
Sulphamethoxy-	1:8	900	456	50.66	100	86.0	86.0
pyridazine	1:10	1100	576	52.36	100	82.0	82.0

*Whole microcapsules of practical yield was used

perature, after which the microcapsules were separated by vacuum filtration and air dried for 12 h.

The size of the microcapsules was measured by using a calibrated microscope, not less than 200 particles in a single plane were measured. The bulk density (Pb) was determined by the formula (Pb) = M/V_b, where M is the mass of the particles and V_b is the total volume of packing. The angle of repose was calculated using the equation, $\tan \alpha = H/R$, where α is the angle of repose, H is the height of the pile and R is the radius of the base of the conical pile. Values for angle of repose $\leq 30^\circ$ usually indicate a free flowing material and angles $\geq 40^\circ$ suggest a poorly flowing material.

The porosity value was determined experimentally by measuring the volume occupied by a selected weight of a powder. This volume is called the V_{bulk}. The true volume V, of a powder is the space occupied by the powder exclusive of spaces greater than the intramolecular space. The bulk volume is the sum of True volume and Porosity.

For drug content determination, a sample from each batch of microcapsules was taken, crushed and 100 ml of distilled water was added to it and kept in a shaker bath for 2 h. It was then filtered and then solution was analysed by U.V. Spectrophotometer at 237 nm. The USP paddle method was used to determine release of diltiazem hydrochloride from the microcapsules embedded into tablet. As dissolution medium, 900 ml of distilled water at 37°±1° was used with stirring at 100 rpm (USP XXIII dissolution method)[3], Samples were taken at appropriate intervals up to 24 h and then filtered. Diltiazem hydrochloride content was determined spectrophotometrically at λ_{max} 237 nm.

Microcapsules of diltiazem hydrochloride prepared by emulsion solvent-evaporation technique were found to be very small, mononuclear and spherical in shape. But an important aspect, that is, polymer ratio and stirring rate altered the shape and size. As the stirring rate was increased, the size of microcapsules decreased.

As the drug to polymer ratio was increased, the microcapsule size was also found to increase. The probable reason could be the increase in viscosity of the internal phase as a result of an increase in the concentration of solids in the polymer solution. But as mentioned earlier, the stirring rate also plays a very important role in the resultant size of the microcapsules. So even if the drug to polymer ratio is increased, a slight increase in the stirring rate reduced the size. The drug to polymer ratio was varied keeping the amount of polymer constant and varying the amount of drug to be used. The bulk density, angle of repose and porosity with drug to polymer ratios of 1:8 and 1:10 were 0.2g/ml, 23.19° 9% and 0.16 g/ml, 25.20°, 12.5% respectively.

The percentage drug content was determined in diltiazem hydrochloride, ephedrine hydrochloride and sulphamethoxypyridazine microcapsules prepared using different drug to polymer ratios. The mean practical drug content of diltiazem hydrochloride and ephedrine chloride microcapsules was drastically decreased to about 4-5% of the theoretical values, whereas for sulphamethoxypyridazine microcapsules, it was within acceptable limits, about 85-90%. The practical yield of microcapsules was between 50-60%, indicating the loss of polymer during the process Table 1. The dissolution

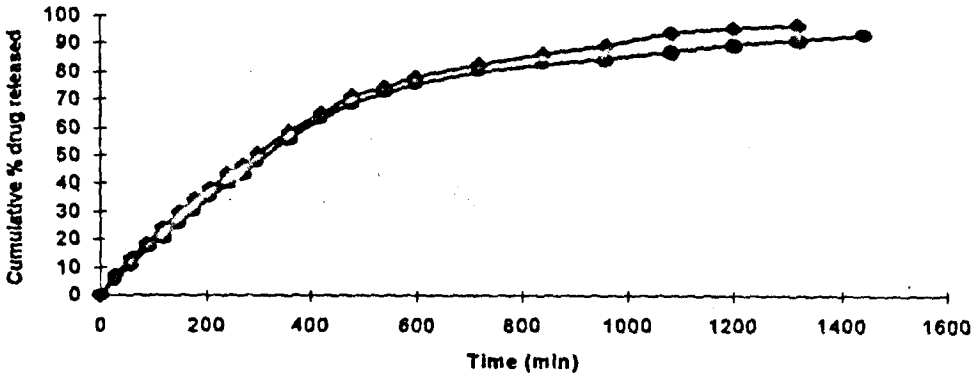

Fig. 1 : Drug release from diltiazem-rosin microcapsules.
Drug release was studied from microcapsules containing diltiazem and rosin in the ratio of 1:8 (–♦–) and 1:10 (–●–), over a period of 24 h using USP method.

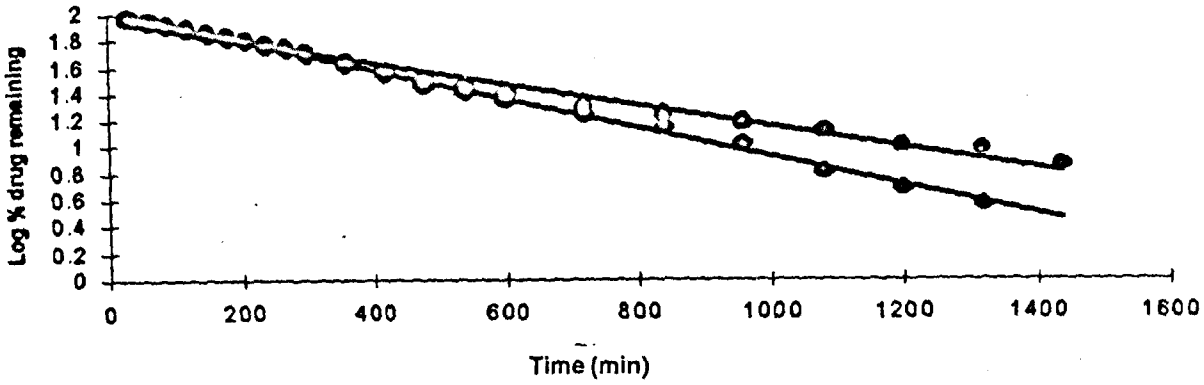

Fig. 2 : First order release plot of diltiazem microcapsules.
First order release kinetics for microcapsules containing diltiazem and rosin in the ratio of 1:8 (♦) and 1:10 (●), over a period of 24 h using USP method.

rate profile curves of diltiazem hydrochloride-rosin at 1:8 and 1:10 ratios shows that cumulative drug release was very slow, giving a sustained release of 22-24 h. However, it was also noted that the drug release from drug to polymer ratio 1:10, was slower as compared to 1:8 Fig. 1. Fig. 2 shows that the release of diltiazem hydrochloride from all microcapsules prepared follows the first order kinetics.

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