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# Microencapsulation of Dichromate and Paracetamol with Eudragit Retard Polymers Using Phase Separation by Nonsolvent Addition

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## ABSTRACT

A coacervation technique for microencapsulation using Eudragit Retard polymers [poly(methyl methacrylates) substituted by quaternary ammonium groups] as wall material is described, based upon phase separation using a cold chloroform–cyclohexane mixture together with polyisobutylene as a stabilizer. The effect of various parameters on the nature and properties of the microcapsules of potassium dichromate and paracetamol has been studied, in particular the alteration in wall content and structure and release rate of contents. The microcapsules are discrete, their properties are reproducible, and various degrees of sustained release are obtained.

**Index Entries:** Microencapsulation, by phase separation; microcapsules, using Eudragit Retard [poly(methyl methacrylate) derivatives]; paracetamol microcapsules; dichromate, microencapsulation of; phase separation, in microencapsulation;

The coacervation method (*1*) was used for microencapsulation of potassium dichromate and paracetamol with poly(methyl ethyl methacrylate)—Eudragit Retart (Röhm-Pharma, Darmstadt)—to provide sustained release of the core material. The technique developed gave effective encapsulation that was complete and uniform.

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Coacervation was effected by nonsolvent addition. The coating material and polyisobutylene (PIB) were dissolved in chloroform and the core material was suspended in the solution. Cyclohexane containing PIB was added to the solution at a controlled rate. By decreasing Eudragit solubility in the chloroform (Table 1), cyclohexane caused phase separation, which, under the specified conditions of the work, yielded coacervate droplets that encapsulated the core material.

TABLE 1
Solubility of Eudragit RS in Chloroform-Cyclohexane

| Chloroform, % w/w | Eudragit in solution | |
|---|---|---|
| | mg/20 g | % w/w |
| 30 | 260 | 1.3 |
| 25 | 113 | 0.56 |
| 20 | 85 | 0.42 |
| 10 | 6 | 0.03 |

Fig. 1. SEM of paracetamol microcapsules coated with Eudragit RS polymer. Magnification 25:1.

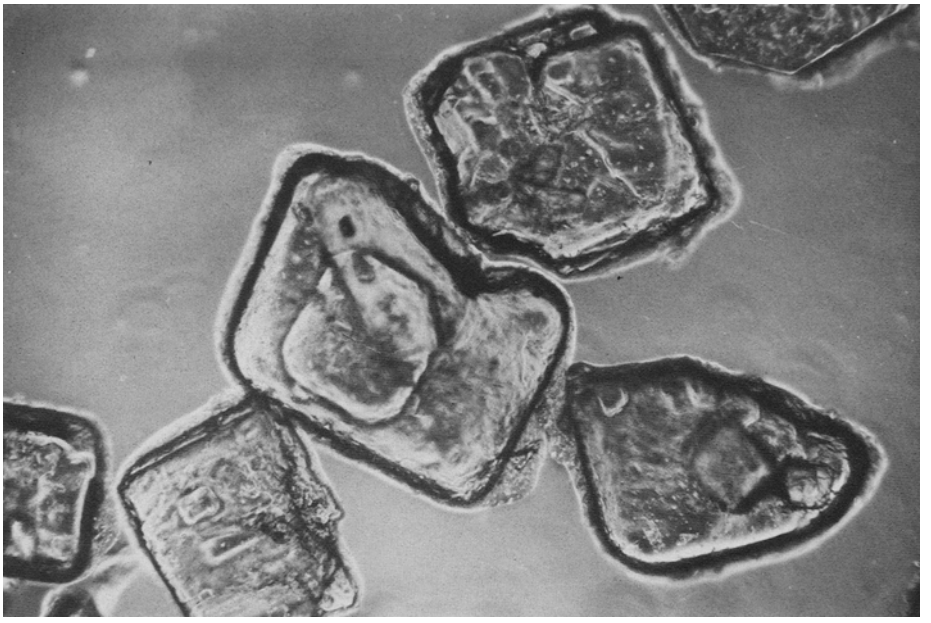

Fig. 2. Photomicrograph of potasium dichromate microcapsules coated with Eudragit RS polymer.

The PIB acted as a coacervate droplet stabilizer (2), ensuring formation of separate uniformly coated particles (Figs. 1 and 2) that, in its absence, aggregated into a mass.

Microcapsule quality was examined by microscopy and SEM and spectrophotometric analysis of core content and release rate using the modified rotating basket method (3).

Investigation of parameters revealed that change of the addition rate of the nonsolvent solution influenced the release properties of the microcapsules (Table 2). Since the core–wall ratios were not significantly

TABLE 2
Rate of Addition of Nonsolvent

| Addition rate, g $min^{-1}$ | Core material content, % | First-order rate constant $K$, $min^{-1} \times 10^3$ | Correlation coefficient $r$ |
|---|---|---|---|
| 10 | 78.6 | 14.5 | 1.000 |
| | 79.2 | 14.3 | 0.998 |
| 5 | 81.7 | 10.5 | 0.999 |
| | 81.0 | 10.7 | 1.000 |
| 0.9 | 79.3 | 3.2 | 1.000 |
| | 79.9 | 3.3 | 0.998 |

Fig. 3. SEM of paracetamol microcapsules containing solidified spheroid droplets of Eudragit RS polymer. Magnification 130:1.

different, structural changes were anticipated. Microscopy revealed that the microcapsules formed at high addition rates had polymer spheres attached at the surface (Fig. 3). In such clusters, the effective wall thickness is reduced, accounting for the enhancement of release.

The quantity of nonsolvent added controlled the amount of polymer separating till a negligible amount remained in solution. This was reflected in changes in the core–wall content and release rate (Table 3) between 60 and 90 g of nonsolvent, above which there was no dependence.

TABLE 3
Quantity of Nonsolvent Solution (Cyclohexane-PIB) Added

| Nonsolvent solution, g | Core material content, % | First-order rate constant $K$, $min^{-1} \times 10^3$ | Correlation coefficient, $r$ |
|---|---|---|---|
| 60 | 79.3 | 3.2 | 1.000 |
| | 79.9 | 3.3 | 0.998 |
| 90 | 77.5 | 1.57 | 0.995 |
| | 76.1 | 1.56 | 0.996 |
| 120 | 76.8 | 1.61 | 0.993 |
| | 77.1 | 1.58 | 0.999 |

The particle size of the core material also influenced the release rate, smaller particles giving faster release, whereas core–polymer ratio increase gave the expected thinner walls and faster rates.

Under optimum conditions, there was excellent control and reproducibility of coating and sustained-release characteristics (4).

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