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THE EFFECT OF SELECTED VARIABLES ON THE PREPARATION AND OXIDATIVE DECOMPOSITION OF MICROENCAPSULATED BENZALDEHYDE

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The decomposition of the essential oils used in the pharmaceutical, food and cosmetic industries proceeds by an oxidative chain reaction involving the intermediate formation of hydroperoxide free radicals. The oxidative decomposition eventually results in the formation of objectionable odours and tastes, but, possibly of greater importance, the products of oxidation besides being highly reactive may also be toxic. It follows that drugs and other materials which are associated with the oil may themselves be subject to decomposition.

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Many ways have been suggested in order to overcome this problem and for most purposes the inclusion of an antioxidant is a sufficient protection. The choice of antioxidants for use in the pharmaceutical industry is limited and even when effective problems of odour and taste may intrude. The decomposition products of the antioxidants themselves also exhibit the same problems with regard to toxicity as shown by the original decomposing oil. Instances exist in all three fields, pharmacy, food and cosmetics, where the use of antioxidants as a means of preservation may not be acceptable.

From work conducted in the late 1950s (2) and early 1960s (2,3) using reference compounds it was found that reducing the bulk volume of the individual entities in the form of emulsion droplets or micelles could lead to a slowing down of the oxidation rate. Variations did exist in this protective effect and it appeared that the more viscous, water insoluble, fixed oils which did not contain an oxidisable aldehyde group could actually oxidise faster under certain emulsified conditions (1). Although the overall pattern was extremely complicated once solubilised most oils were protected to a maximum degree.

One of the problems associated with the preservation of 'oils' in an emulsified form was that the surface of the emulsion droplet presented little or no barrier to the diffusion of oxygen from the

surrounding media. If the droplets could be prepared with an impervious wall this problem would no longer exist and a more complete protection from oxidation should be obtained. It is suggested that these conditions may be approached and possibly fully realised by microencapsulation of the oil.

The preparation of microcapsules containing liquids as the core material is now a well documented technique (1) and, depending on the properties, many methods are available. A number of advantages have been claimed, including stability to oxidation, but little detailed evidence has been reported. Unsupported statements have been made to the effect that the oil, or core contents, were still present after long periods, although the condition of the contents was not specified nor was the amount which had remained unencapsulated during the processing. The oxidation behaviour of this non-microencapsulated oil, which tends to be associated with the outer wall, appears to be ignored.

The walls of most commercially available microcapsules are composed of gelatin-acacia or one of the celluloses and as such are not completely impervious to the passage of oxygen and it is obvious that oxidative decomposition, whilst it is slowed down, will not be completely prevented.

The friable nature of the wall will also allow the gradual passage of the core content out so that the formation of a diffusion gradient of the

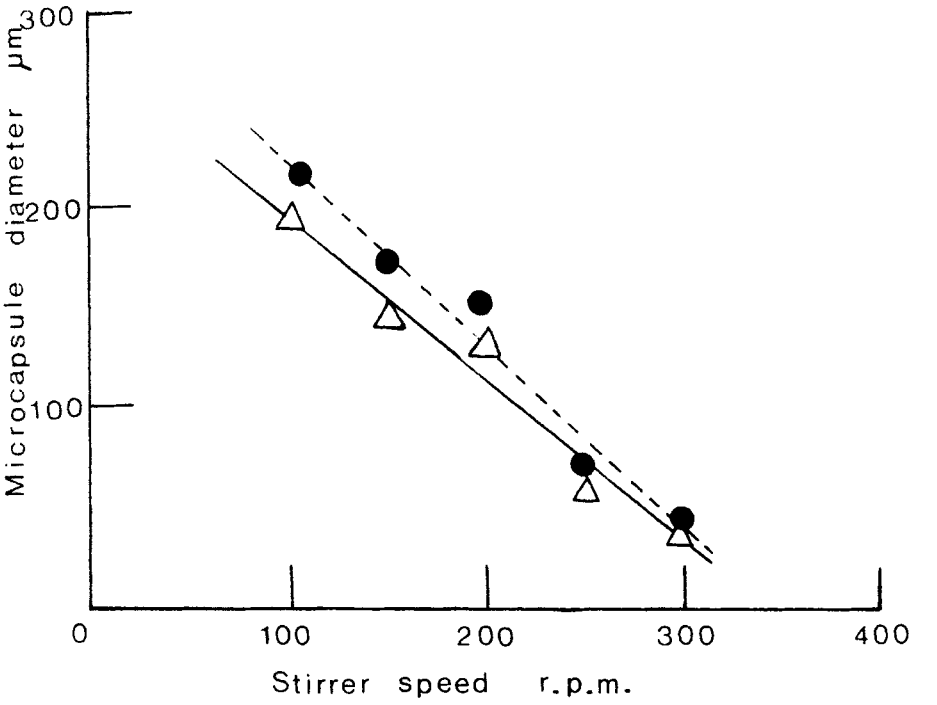

FIGURE 1 The effect of stirrer speed on the mean number microcapsule size. ●, Formalin hardened, Δ unhardened.

oil through the wall will also take place. That this occurs can be detected by odour. Many commercial oil containing microcapsules retain an odour of their contents which tends to become more pronounced with time suggesting that this diffusional process is taking place.

The present work forms part of a major study of the stability of microencapsulated drugs and in the present instance is concerned with the oxidation of the liquid core contents. Benzaldehyde has been

chosen because its oxidative behaviour is well documented and relatively simple. The microcapsules have been prepared by a variation of the well known N.C.R. gelatin-acacia complex coacervation process, as being the process with the greatest commercial application at present. The benzaldehyde was emulsified in the 2% gum acacia solution and whilst this was stirred the 2% gelatin solution was added slowly and the mixture maintained at 40° ± 0.1°. The pH was adjusted to 4.1 to give the optimal conditions for coacervation. The speed of stirring can be used to control the size of the microcapsule and was carefully maintained at the approximate r.p.m. Formaldehyde was added to harden the outer wall and the temperature reduced to 5° c. After filtration the microcapsules were washed with isopropanol and dried with nitrogen at room temperature. The size distribution of the microcapsules was determined microscopically.

A Warburg respirometer was used to measure the oxygen uptake of suspended microcapsules. The microcapsule charge, distributed in 2ml of triple distilled water, was shaken at 25° ± 0.1°; the speed and period being adjusted so that diffusion of oxygen into the triple distilled water was not a limiting factor. Changes in atmospheric pressure were corrected by means of a thermobarometer, the flask of which contained a similar microcapsule dispersion but minus the benzaldehyde core.

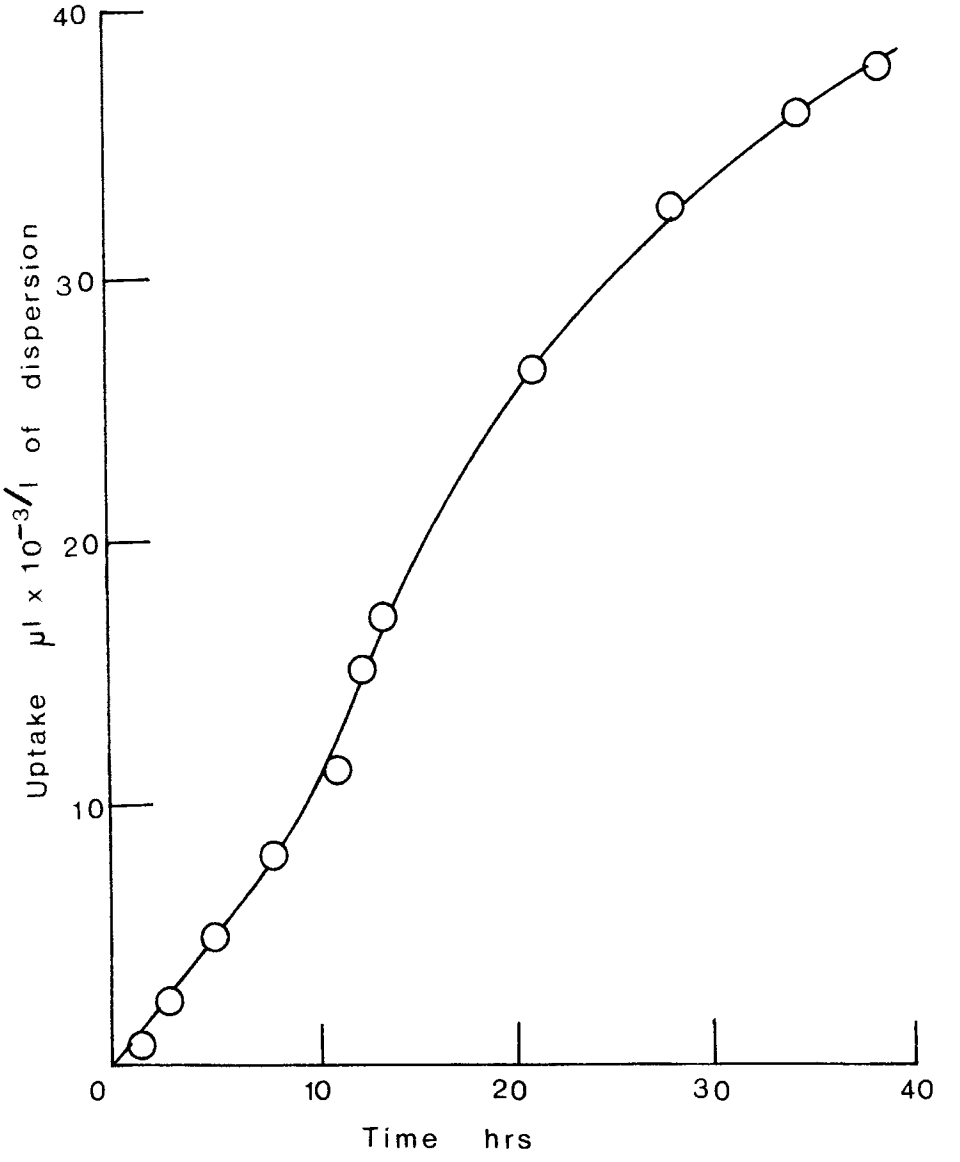

FIGURE 2 The oxidation of benzaldehyde dispersed in triple distilled water. Temp. 25° ± 0.1°, benzaldehyde 3.75 mg ml $^{-1}$.

Within the limits imposed by the microscopic measurement of microcapsule size, re the tendency to underestimate the very small microcapsules, an increase in the stirrer speed during preparation produces a linear reduction in the mean size of the microcapsule, the size for a given stirring speed being slightly larger for the hardened material. Stirrer speeds lower than 100 r.p.m. or greater than 300 did not allow the formation of microcapsules with our system. The effect of stirring speed can be attributed to the smaller benzaldehyde emulsion droplets produced at the higher r.p.m.: the emulsion droplet size controlling that of the final microcapsules. At these high stirring speeds the initial coacervate droplets are also small and so cannot engulf more than one benzaldehyde droplet which also tends to form small microcapsules. The reason for the difference in hardened microcapsule size is obscure. If the unhardened material hydrated to a greater extent than the hardened capsules then the reverse picture would have been expected to occur. It is possible that the hardened material is held in place in a more rigid fashion in the liquid state and on extraction still retains its more extended state of dispersion at the wall.

The effect of microencapsulation and in particular the effect of size, core: wall ratio and preparative conditions on the oxidation are complicated. As a reference the oxidation of non microencapsulated

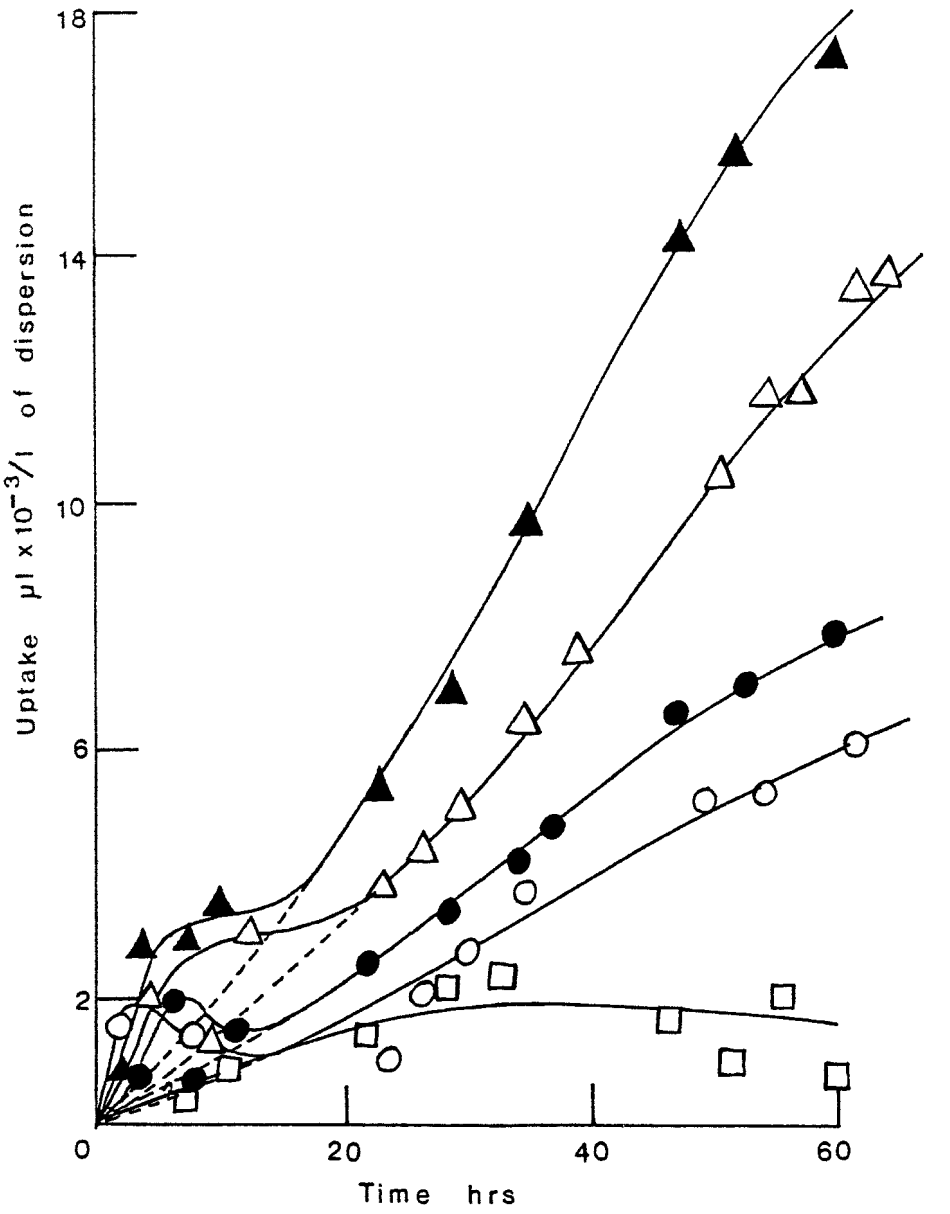

FIGURE 3 Effect of size on the oxygen uptake of formalin hardened microcapsules.

Temp. 25° ± 0.1, Microcapsules 100 mg in 2 ml of triple distilled water, Mean microcapsule size µm, 44, ○ 69, ● 147, △ 177, ▲ 220.

benzaldehyde was determined showing the normal sigmoidal curve. It is difficult to determine an induction period for this system and an empirical figure of 200 µl oxygen uptake was used. The time taken for this amount of oxygen to be taken up by microencapsulated benzaldehyde is difficult to assess because of the complication caused by the rapid oxidation of unencapsulated benzaldehyde associated with the surface. As assessment of the 'induction period' with these graphs is produced by extrapolating the main portion of the curve towards zero. With both the hardened and unhardened samples this produced a linear decrease in the induction period with respect to increased microcapsule size the slope being greater with the hardened microcapsules (Figure 4).

Once the induction period has been passed the steady oxidation rate attained by the microencapsulated benzaldehyde shows an almost linear increase with respect to microcapsule size but these oxidation rates are very much slower than that of non encapsulated material (Figure 5). The oxidation must take place in individual microcapsules and, whilst the overall surface area available for diffusion of oxygen into the microcapsules will be larger with the systems containing smaller microcapsules, the individual bulk volumes per microcapsule which are oxidising will be greater with larger microcapsules and

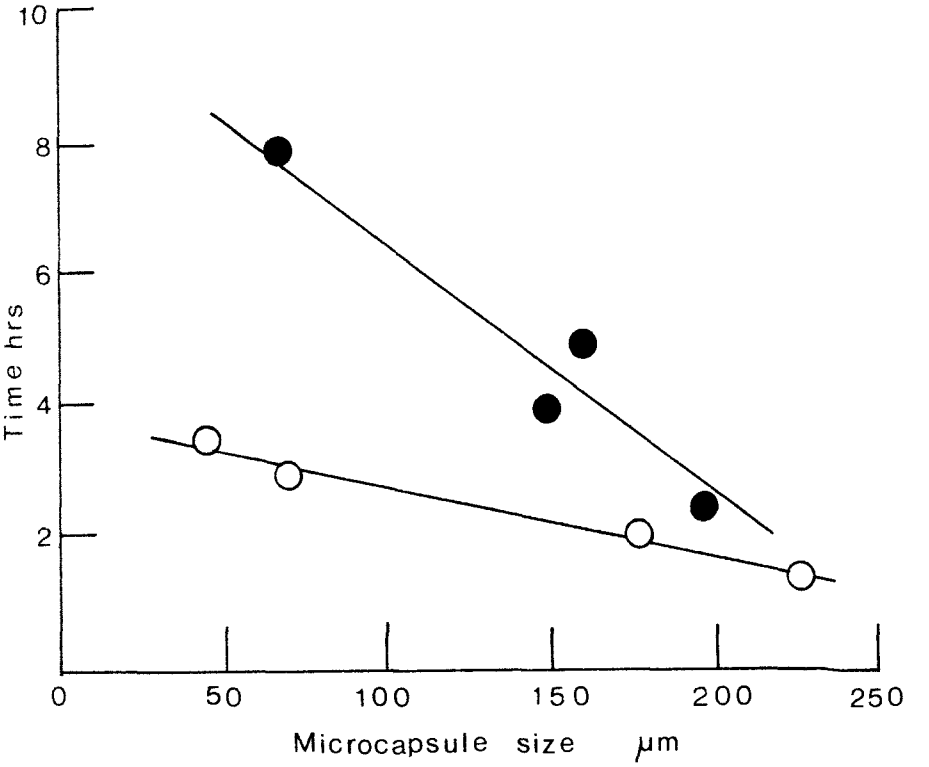

FIGURE 4 Effect of microcapsule size on the 'induction period' of oxidising encapsulated benzaldehyde.

Temp. 25° ± 0.1°, ● unhardened microcapsules, ○ Formalin hardened microcapsules.

these will also have a smaller tendency to allow termination reactions to take place.

A feature which is present in the oxidation of microencapsulated oils is the primary peak (Figure 3). This is due to the oxidation of the unencapsulated oil associated with the outer wall and occurs

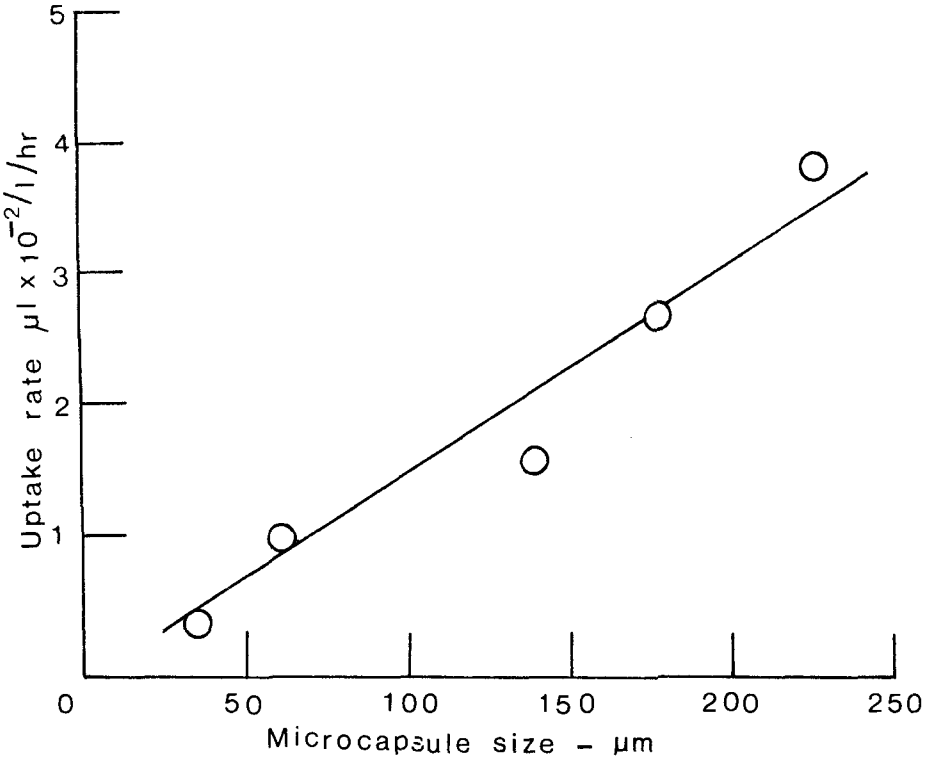

FIGURE 5 Effect of microcapsule size on the oxidation rate of formalin hardened microcapsules of benzaldehyde at 25° ± 0.1°.

rapidly. Once this is complete the benzaldehyde diffusing through the microcapsule wall has a tendency to cause an increase in pressure within the flask system resulting in a peak on the graph, until, as the oxidation of the microencapsulated oil increases, the curve starts to rise again. The amount of surface free benzaldehyde appears to be inversely proportional to microcapsule size.

The oxidation with unhardened microcapsules is much slower than with the corresponding hardened material (Figure 6). Again the preliminary peaks are present but even with this non encapsulated material the rate of oxidation is decreased. It is suggested that the

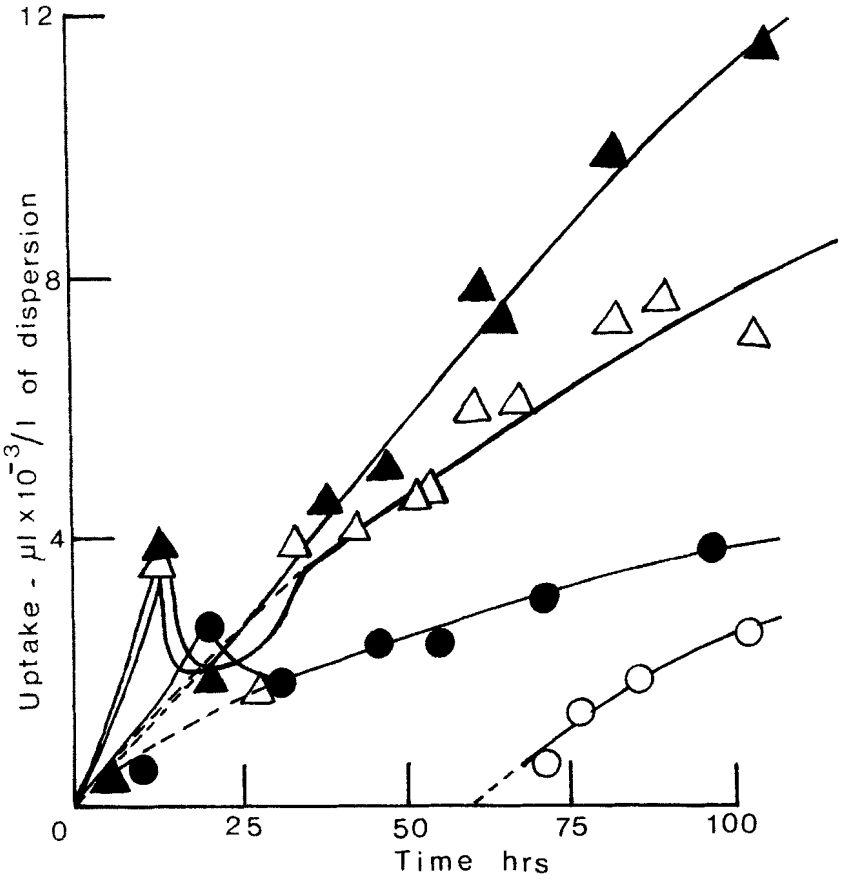

FIGURE 6 The effect of size on the oxygen uptake of hardened microcapsules.

Temp. 25° ± 0.1°, Microcapsules 100 mg in 2 ml of triple distilled water, Mean microcapsule size µm, ○ 68, ● 154, △ 183, ▲ 198.

walls of the microcapsules hydrate and form a gelatinous barrier to the diffusion of oxygen due to the loss of the friable nature of the wall. This rigid friable wall, present in the hardened microcapsules, allowed the ready passage of oxygen.

From the results presented it is evident that whilst micro-encapsulation will afford a degree of protection to oxidisable materials this will not be absolute. The core: wall ratios involved are important and this is being further investigated. As would be expected thicker walls afford greater protection but do not cause the absolute suppression of oxidation. The effect of pH on preparation also causes changes in both microcapsule size and the susceptibility to oxidation and this is under active study. It would appear that in order to fully protect micro-encapsulated oils it will be necessary to include an antioxidant into the formulation.

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