BINDING TO ACACIA CONTROLS DRUG RELEASE FROM MULTIPLE WALLED MICROCAPSULES

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Drugs microencapsulated by the multiple emulsion technique of Warburton (1982) display a characteristic release profile: an initial rapid release of approximately 50-80% of total drug content is followed by a much slower release of the remainder. Since these microcapsules consist of an acacia core, which contains the drug, surrounded by a layer of ethylcellulose we have sought to explain the two-stage drug release profile by examining the binding of drugs to acacia. The binding of crystal violet (CV) and quinine hydrochloride (QH) to acacia BP was investigated by dialysing increasing drug concentrations in double distilled water against 4% $^{W}/_{w}$ acacia in double distilled water at 25^{0}C. Microcapsules were prepared from multiple emulsion droplets by the method of Warburton (1982). Before extraction of the microcapsules by rotary evaporation the inner aqueous core of the multiple emulsion droplets contained 1.33% $^{W}/_{w}$ QH or 0.33% $^{W}/_{w}$ CV dissolved in 4% $^{W}/_{w}$ acacia. Release of drug from microcapsules was determined by a flow-through spectroscopic method using stirred suspensions containing 500 mg QH microcapsules (containing 50 mg QH) or 250 mg CV microcapsules (containing 7 mg CV) in one litre of double distilled water at 25^{0}C; maximum drug concentrations were less than 0.2% of solubilities.

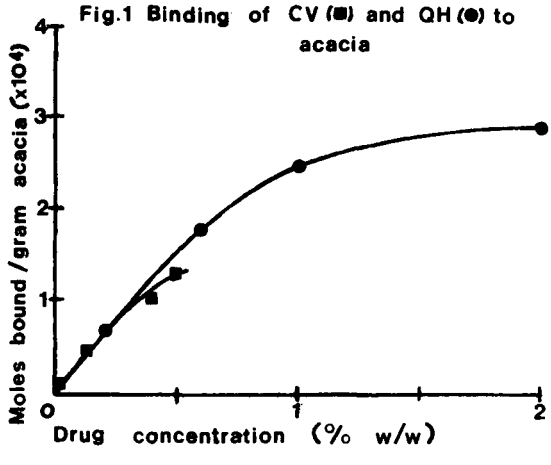

Fig.1 Binding of CV (■) and QH (●) to acacia

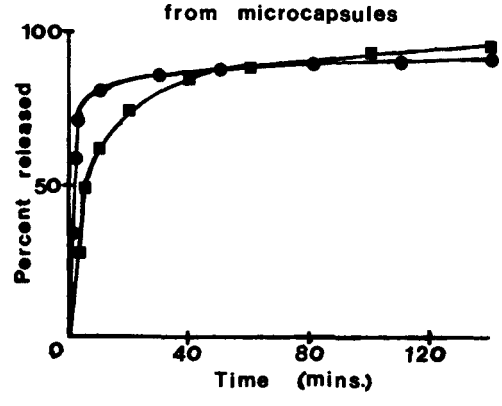

Fig.2 Release of CV (■) and QH(●) from microcapsules

The results (Fig 1) show that at the concentration of QH(1.33% $^{W}/_{w}$) present in the core of the multiple emulsion droplets, binding is almost saturated with respect to acacia concentration and the amount of QH bound is 2.66×10^{-4} mol g^{-1} acacia. Calculations show this represents 32% of the QH contained in the microcapsules. 68% QH is therefore free and available for immediate release. Fig 2 shows that this calculated quantity correlates well with that determined experimentally since the change in drug release rate occurs when 70% QH has been released. The remaining 30% of bound QH is then released at the slower rate. Similar calculations with CV showed that 47% was unbound, which once again agrees well with the experimentally determined figure of 50% (Fig 2). We have shown that the rate of drug release from microcapsules is determined by the extent of binding of the drug. Since the proportion of bound drug will be affected by the concentration of both drug and acacia it should be possible to control the drug release profile. Substitution of acacia by alternative macromolecules with differing binding capacities could also be used to alter release profiles.

Warburton, B. (1982) G. B. Patent 2,009,698