制御可能な薬物送達を目的とした多孔質生体内分解性マイクロスフィア．Ⅰ．調製条件および溶媒除去法の評価

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Porous Biodegradable Microspheres for Controlled Drug Delivery. I. Assessment of Processing Conditions and Solvent Removal Techniques

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ABSTRACT Microspheres containing methylene blue and prednisolone acetate were prepared by one of three methods: freeze-drying, evaporation, and solvent-extraction-precipitation. An extremely porous structure was obtained by the freeze-dry and solvent-extraction-precipitation procedures. The specific surface ares of 6.33-μm particles was 20.6m^2/g, or 35 times that of a particle devoid of pores, and the void space was 59-61%. The sphericity, size, and yields of the microspheres were influenced by the preparation procedure, surfactant type and concentration, temperature of the continuous phase, polymer concentration in the dispersed phase, and ratio of marker to polymer. The most suitable processing conditions were a polymer concentration of 5-10%, a marker loading of 10%, 0.1% sorbitan sesquioleate as the surfactant, and temperature adjustment of the continuous phase from 15 to 50℃ following the addition of the dispersed phase. Complete release of the highly water soluble methylene blue occurred within 72 hr, while the less soluble prednisolone acetate released much more slowly, i.e., 90% after 7 days. The microspheres remained relatively intact during the *in vitro* release of methylene blue, confirming that the incorporated agent was confined to the walls of the porous network. Collapse of the polymer structure was evident after 7 days. The release therefore was believed to be governed principally by the solubility of the drug and the porosity of the matrix.

抄録　薬物含有マイクロスフィアを次の3種の方法で調製した：凍結乾燥法，蒸発乾固法，液中乾燥法。その結果，凍結乾燥法と液中乾燥法で調製した場合に多孔質マイクロスフィアが得られることがわかった。形状，粒状，回収率は，調製法，界面活性剤の種類と濃度，連続相の温度，分散相中のポリマー濃度，薬物：ポリマー比などの影響を受けることがわかった。最適の調製条件を決定した。*in vitro* で，マイクロスフィアからの薬物放出を測定し，放出が，薬物の溶解度と，マイクロスフィアの多孔性の程度により影響されることがわかった。

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