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[Lab. of Pharm. Anal. Chemistry]

**Non-aqueous Capillary Electrophoresis of p-Quinone Anion Radicals.**

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The electrophoretic detection of two kinds of *para*-quinone anion radicals arising from the electrolysis of benzoquinone and chloranil was achieved by employing an acetonitrile medium. Sufficient dehydration of a running solution was necessary for the detecting of the benzoquinone anion radical. Oxygen in the running solution also caused a serious decrease in the amount of the benzoquinone anion radical during electrophoresis. The addition of methanol as a hydrogen-donor decreased the electrophoretic mobility of the benzoquinone anion radical significantly, while that of the chloranil anion radical was little changed. This result is interpreted in terms of hydrogen-bonding interaction between the *para*-quinone anion radicals and methanol, reflecting the magnitude of their proton-accepting ability (benzoquinone anion radical > chloranil anion radical).

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[Lab. of Pharm. Anal. Chemistry]

**Polyacrylamides as Hydrophilic Selectors in Non-aqueous Capillary Electrophoresis.**

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Polyacrylamides (PAAms) were investigated as hydrophilic selectors in non-aqueous capillary electrophoresis (CE). Separation of 10 substituted benzoates and unsubstituted benzoate as model samples was greatly improved by addition of PAAms in acetonitrile-CE. The migration behavior indicates that the carbonyl moiety of PAAms works as a good hydrogen-accepting site toward hydrogen-donating analytes such as 4-hydroxybenzoate anion (4OH-BA) in acetonitrile. The overall mode of the interaction is similar to that of polyethylene glycol (PEG 20000) reported previously, but the complex formation constant of poly(*N-tert.*-butyl)acrylamide (PBAAm) with 4OH-BA estimated here was 130-fold larger than that of PEG 20000. This would be ascribed the the strong basicity of the carbonyl oxygen atoms of PBAAm as compared with the ether oxygen atoms of PEG. Furthermore, a copolymer of (*n-tert.*-butyl)acrylamide-acrylamide [70:30 in feed] exhibited a complex formation constant of about four-fold larger toward 4OH-BA than PBAAm, most probably due to decrease in steric hindrance from the *tert.*-butyl groups. Adrenaline and its six precursors have been separated successfully using PAAms.

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[Lab. of Pharm. Engineering]

**Passive Targeting of Doxorubicin with Polymer Coated Liposomes in Tumor Bearing Rats.**

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The purpose of this study was to reveal the effectiveness of the polymer coated liposomes as a carrier of the anticancer drug doxorubicin in intravenous administration. The size controlled doxorubicin-loaded liposomes were coated with hydrophilic polymers having a hydrophobic moiety in the molecules (PVA-R, HPMC-R). The polymer coating effects on the tumor accumulation of the drug encapsulated in the liposomes were evaluated in Walker rat carcinoma bearing rats. The doxorubicin-loaded liposomes coated with PVA-R and HPMC-R showed higher drug accumulation into the tumor site by prolonging the systemic circulation. The targeting efficiency of the polymer coated liposomes calculated with the total and tumorous clearance of the drug was ca. 5 times larger than that of non-coated liposomes. We ascertained that polymers having a hydrophobic moiety in the molecule such as PVA-R and HPMC-R are suitable materials for modifying the surfaces of the doxorubicin-loaded liposome to improve its targeting properties.

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[Lab. of Pharm. Engineering]

**Evaluation of circulation profiles of liposomes coated with hydrophilic polymers having different molecular weights in rats.**

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The purpose of this study was to evaluate the circulating properties of liposomes coated with modified polyvinyl alcohol (PVA-R) having different molecular weights (6000, 9000 and 20000). Polymer coated liposomes were prepared by just mixing the resultant liposomal suspension and a polymer solution. The effects of polymer coating were evaluated by measuring the circulation time of the injected liposomes after i.v. administration in rats and the dispersing property of the liposomes in a biological condition. The circulation of the PVA-R coated liposomes was prolonged with increasing the molecular weight of PVA-R. The aggregation and/or fusion of the liposomes in the presence of serum *in vitro* was also depressed more by coating the liposomes with PVA-R having higher molecular weight. There was a good correlation between the circulation time and the physical stability of non-coated and the various PVA-R coated liposomes. The prolonged circulation time of PVA-R (molecular weight: 20000) coated liposomes (ca. 1.3 mol% coating) was comparable to that of a stealth liposome prepared with 8mol% of DSPE – PEG (molecular weight of PEG: 2000).