[PE3-1] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Pharmacokinetics and liver targetability of methotrexate-lactosylated albumin conjugates

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Purpose. To study whether we could enhance the liver targeting of anticancer agent via asialoglycoprotein receptors using conjugates of MTX-variously lactosylated bovine serum albumin.
Methods. methotrexate (MTX) was conjugated with albumin previously substituted with varying content of lactose (L0, L5 and L24). The uptake of MTX by rat hepatocyte in vitro and the MTX level in the plasma and various organs was determined by counting the radioactivity of MTX and by HPLC assay, separately to monitor the in vivo fate of MTX not only as total, regardless of forms of MTX, but also as free/intact MTX level.
Results. Conjugation of MTX with albumin alone provided the enhanced delivery of MTX to the liver, accompanied by decreased accumulation in the kidney, but by increased accumulation in other non-target organs such lung, heart and spleen. Lactosylation of albumin conjugates further enhanced the delivery of MTX to the liver in a lactose content-dependent manner, accompanied by decreased accumulation of MTX in the lung and heart as well as kidney. The total MTX level accumulated in the liver was 2.9-, 4.1- and 11.0- fold higher at 1 h and 5.4-, 7.0- and 16.5- fold higher at 4 h after injection of MTX-L0, L5, L24 albumin conjugates compared with MTX alone. MTX conjugates with lactosylated albumin provided low but prolonged level of free/intact MTX in the liver.
Conclusions. The pharmacokinetics and liver targetability of MTX could be favorably modulated by controlling the lactose content on the albumin conjugates. Lactosylated albumin conjugation might also provide a potential for the prolonged and targeted delivery of other drugs for the treatment of liver diseases.
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Dissolution Behaviors of Various Commercial Preparations in Different Dissolution Medium Compositions

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The differences in dissolution behaviors of commercial preparations using different compositions of dissolution media were investigated. The immediate release itraconazole (ITR-IR) and acyclovir(ACV-IR) and sustained release nifedipine (NIF-SR) preparations were chosen. The composition of dissolution media used was simulated gastric fluid (SGF) or simulated intestinal fluid(SIF) with tween 80, sodium lauryl sulfate(SLS), pepsin, pancreatine, and 3.5% fat milk, respectively. The dissolution behaviors were evaluated using USP dissolution method II (paddle). In case of ITR-IR, addition of SLS and pepsin