small intestine. Accordingly, formulating this kind of drugs with too much release time resulted in very low bioavailability.
So, we tried to formulate the matrix tablet containing CFT with short-term sustained release so that we should minimize the portion of the unabsorbed drug through the small intestine. We chose various hydroxypropylmethylcelluloses (HPMC) as a matrix carrier and estimated how the drug to polymer ratio and polymer type had an influence on the release of the drug. In more, we evaluated not only the effect of various diluents and lubricants, but also the influence of granulation on the release of the drug.
As a result of our research, we could formulate the robust short-term sustained release tablet with the duration time of about 2 hours. It is supposed to make other similar drugs, which has the narrow absorption window, a sustained release form with relatively high bioavailability than ever since.

[PE1-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

PREPARATION AND EVALUATION OF MICROEMULSION CONTAINING IBUPROFEN

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PREPARATION AND EVALUATION OF MICROEMULSION CONTAINING IBUPROFEN
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Oleic acid, linoleic acid, and several kinds of glycerides and triglycerides were used as an oil phase with several surfactants, which consist of saturated polyglycolized glycerides (Labrasol) , diethylene glycol monoethyl ether(Transcutol) , and polyoxyethylene(4) lauryl ether(Brij 30). The solubilities of ibuprofen in oils and surfactants were about 100 times higher than that of water. The three phase diagrams show o/w microemulsion domain. When oleoyl macroglycerides EP(Labrafil) or caprylic/capric triglyceride polyethylene glycol-4 complex(Labrafac) as oil phase and diethylene glycol monoethyl ether(Transcutol) or saturated polyglycolized glycerides (Labrasol) as surfactant were used, the domain of microemulsion was wide. In dissolution test, it was showed 23.7 %, 24.3%, 19.1 % and 15.4 % for caprylic/capric triglyceride polyethylene glycol-4 complex (Labrafac), oleoyl macroglycerides EP(Labrafil), linoleic acid and suspension, respectively. Following oral administration of microemulsion containing ibuprofen, the Cmax was more increased and the Tmax was more rapid than these of suspension. The relative bioavailability of microemulsion was increased as 165.5 %, 166.1 % and 134.8 % for caprylic/capric triglyceride polyethylene glycol-4 complex(Labrafac), oleoyl macroglycerides EP(Labrafil), linoleic acid and suspension, respectively.

[PE1-5] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Synthesis and characterization of a ketoprofen prodrug

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The objective of this study is to prepare ketoprofen (KP) - polyethylene glycol (PEG) conjugate and to study its degradation kinetics and solution behavior. KP-PEG conjugate were synthesized from ketoprofen and PEG methylester by esterification in the presence of DCC. The KP-PEG conjugate (KPEG750) was characterized by IR, ^{1}H-NMR spectroscopy. The quantitation and separation of KPEG750 were performed by HPLC with mobile phase consists of acetonitril/ammonium phosphate buffer (pH 3.0). The conjugation between KP and PEG could be observed by the disappearance and appearance of some specific IR bands: ① the disappearance of very broad peak by hydrogen

bonding of -OH in KP ② the shift of carbonyl band from 1697cm^{-1} to higher frequency (1732 cm^{-1}) ③ the appearance of larger and sharper aliphatic C-H stretching band at 2872cm^{-1}The result of ^{1}H-NMR (300 MHz, $CDCl_3$) is δ1.75 (d, 3H, J=7.1Hz), 3.59 (s, 3H), 3.74-3.92 (m, 64H-72H), 4.02-4.09 (m, 1H), 4.38-4.52 (m, 2H), 7.65-8.03 (m, 9H). The hydrolysis rate constant was high at low and high pHs, and showed minimum at pH 4 and 5. Increase in pH from 1 to 4 resulted in a linear decrease in rate (slope=-0.90) and further increase in pH from 6 to 10 resulted in a linear increase in rate (slope=0.88). These slopes are close to unity, indicative of specific hydrogen/hydroxide ion catalysis. When the concentration was above 1 mg/ml (1x10^{-3}M), micelles with average size of 90-140 nm were observed, suggesting that CMC is about 1x10^{-3}M.

[PE1-6] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

The preparation of O/W microemulsion and micelle containing propofol

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Propofol, the recently marked intravenous injection agent for anaesthesia, is highly lipophilic agent. The purpose of this study is to develop O/W microemulsion and micelle system containing propofol (1%) for intravenous injection. To make the best system, we used various oils, surfactants, and water-phase. The o/w microemulsion systems were made from oil(soybean oil or ethyl oleate) and nonionic surfactant such as polyoxyethylene castor oil derivatives(Cremophore RH 40, Cremophore EL), polyoxyethylene sorbitan fatty acid esters(Tween 20,80), poloxamer and polyethylene glycol 660 12-hydroxystearate(Solutol HS 15). In addition, pH 7.4 phosphate buffer solution that contained propylene glycol, Kollidon 17 PF(Pyrogen Free) or Glycerin used as water phase.
We investigated the Oil- and Surfactant-related changes at the microemulsion system and observed particle size using dynamic light scattering, transmittance at 540nm, and viscosity. The release pattern of propofol is performed by the Dialysis test(MWCO 12000) and is quantified using HPLC.

[PE1-7] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Sustained release of L-arginine from nanospheres for prevention of restenosis

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Recurrent luminal narrowing, restenosis, as a result of excessive intimal hyperplasia remains a major limiting factor for the long-term success of vascular surgery. For prevention of restenosis, various devices, such as polymeric matrices, microspheres and circumferential wraps, have been developed for perivascular local delivery. And many pharmacologycal agents have been tested to reduce restenosis.In order to inhibit vascular smooth muscle cell proliferation, drugs must be delivered at a high concentration for a prolonged period of time. Nanoparticles could be delivered more efficiently to the arterial tissue than microarparticles because they are capable of cellular internalization and connective tissue permeation. In this study, biodegradable nanospheres containing L-arginine (antiproliferative agents) were formulated using poly(D,L-lactic-co-glycolic acid)(PLGA) as a sustained drug delivery systems for the prevention of restenosis. The drug loaded PLGA nanospheres were prepared by an emulsion-solvent extraction method. As a result of particle size distribution, the size of nanospheres was average 200-300nm. The release of the drug was sustained in vitro, and the nanospheres showed an antiproliferative effect.