by a factor of 1.1 when carboxymethylated BCD was used as chiral discriminator. In this work the chiral
discrimination energetics was modeled by an inclusion complex of MT in BCD and of MT in Cel7A using molecular
dynamics(MD) simulation. With software SYBYL6.5 the aromatic ring of MT was inserted into the BCD cavity
corresponding to the NMR structure. And MT was inserted into Cel7A binding pocket corresponding to X-ray
structure of (S)-propranolol–Cel7A complex. Starting Coordinate from this structures performed 1ns MD
simulations in water using GROMACS 3.0 program package with GROMOS96 (43a1) force field, respectively.
In the normal MD phenox oxygen atom. OH and NH group of both MT enantiomers were involved in intensive H-
bonding with O2 groups of glycosidyl rings of BCD. Furthermore free energy calculation for the transition of (S)–
to (R)–form was performed using slow–growth, to yield a free energy change from (S)–MT–BCD to (R)–MT–BCD
of 2.73kJ/mol, which rationalizes the bigger stability of (R)–MT–BCD complex than that of (S)–isomer. Also a
relative free energy difference is 4.23 kJ/mol from (S)–MT–Cel7A to (R)–MT–Cel7A. Cel7A was confirm a chiral
discriminator for the separation of beta–blocker theoretically.

[PD1–51] [10/17/2002 (Th) 09:30 – 12:30 / Hall C]
The 3–D QSAR study of antitumor arylsulfonylimidazolidinone derivatives by CoMFA and COMSIA

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Three–dimensional quantitative activity relationship (3D–QSAR) study for a series of arylsulfonylimidazolidinone
derivatives with antitumor activity was conducted using comparative molecular field analysis (CoMFA) and
comparative molecular similarity indices anaysis (CoMSIA). The in vitro cytotoxicity against human lung carcinoma
(A549) exhibited a strong correlation with steric and electrostatic factors of the molecules. However the
contribution of steric factor was high and compounds with bulky side chain on indoline nitrogen are expected to
have antitumor activity. The statistical result, cross–validated q2 (0.577 and 0.581) and conventional r2 (0.901
and 0.917) values, gave reliability to the prediction of the antitumor activities of this series.

[PD1–52] [10/17/2002 (Th) 09:30 – 12:30 / Hall C]
Synthesis and in vitro/in vivo properties of prednisolone 21–sulfate sodium as a colon–specific
prodrug of prednisolone

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Corticosteroids have been used most frequently for inflammatory bowel disease. They are well absorbed and only
a limited fraction of the dose is delivered to the inflammatory site in the colon. To reduce side effects by the
systemic absorption, colon–specific delivery is highly desirable. We prepared prednisolone 21–sulfate sodium
(PDS) and investigated its suitability as a colon–specific prodrug of prednisolone(PD). If PDS is nonabsorbable and
stable in the upper intestine, it will be delivered to the colon, where the sulfate group may hydrolyze to
release PD by the sulfatase originated from microbes. METHOD: PDS was obtained by reacting PD and
sulfatriloxide triethylamine, and subsequently treating the product with NaCl solution. Stability in pH 1.2 and 6.8
buffer solutions and apparent partition coefficient in 1–octanol/pH 6.8 buffer were determined. Prodrug
conversion was determined by incubating PDS with the contents of various segments of gastrointestinal(GI) tract
of rats. After oral administration, rats were sacrificed at predetermined time interval, and PD and PDS in the
contents of GI tract and plasma were determined. RESULTS: PDS was stable and apparent partition coefficient of
PD and PDS was 21.8 and 0.11, respectively. PDS was chemically stable on incubation with the contents of the
stomach or small intestine (SI). With the cecal contents, PDS was decreased to 54% to give PD 29% of the dose
in 6 h. The amount of PD was always less than the decreased PDS, which suggested that reduction of steroid
took place by the cecal contents. After oral administration of PDS, neither PDS nor PD was detected from the
plasma, and small amount of PD was recovered from the cecal contents but not from the SI. CONCLUSION: PDS
is stable and nonabsorbable in the upper GI tract and release PD in the cecum. which implies that sulfate ester of
glucocorticoid can be a promising colon–specific prodrug.