Effect of Leuteinizing Hormone –Releasing Hormone Analogue, Lorelin depot on Testostoerone Suppression and Biochemical Study in Rat

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Leuprolide acetate is a potent leuteinizing hormone-releasing hormone analogue (leuprorelin, (des-Gly[10]-D-Leu[6]-Pro-NHEt[9])-LHRH acetate). It has been used anticancer drug by suppression the blood level of testosterone in prostate cancer. Lorelin depot, which was composed of leuprolide acetate, was designed for one-month release injectable and biodegradable microsphere of multiple high doses. Here we examined the effect of microsphere lorelin depot, in comparison with Takeda microsphere (Lucrin Depot). Lorelin (leuprolide 3.75 mg/kg of body weight) was administered s.c. to male rat and serum was obtained from rat tail vein. Enzyme immunoassay (EIA) for testosterone was carried out to investigate the effect of lorelin depot. A transient initial high peak (5-7 ng/ml) in serum testosterone level resulting from an initial burst of drug release was observed and the lorelin maintained sustained serum testosteorne levels below 0.5 ng/ml for one month. In addition, the rats were sacrificed after 42 days, morphological changes of brain and testis were observed by LM (light microscopy) and electrophoresis performed to reveal the protein changes of brain and testis.

[PC1-9] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Computer-aided molecular docking of ligands into target proteins using FlexiDock

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Prediction of the binding mode of a ligand to its target protein is an important problem in rational drug design. A computer program, FlexiDock with genetic algorithm was used in this study to carry out the molecular docking operation automatically. The program allows for the full flexibility of ligands in the docking calculations, allowing the user to define the flexible bonds during the docking process.
Dihydrofolare reductase which is an attractive target for antiproliferative drug design because of its key role in the synthesis of DNA was used as a target protein. Ligands were docked into the protein active sites and the energy of the protein-ligand complexes were calculated. The results agree well with the X-ray complex structures with very small rms deviations. Docking searches also demonstrated that a new inhibitor with biological activity proven experimentally docks well into the active site of the enzyme. This program may be used to predict the precise binding mode of ligands to target proteins to discover novel lead compounds.

[PC1-10] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Powerful flexible docking of inhibitors into target enzymes with QXP

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