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their common K^+ channel opening activity. Like pinacidil, the geometries of the latter molecules were also optimized by Tripos force field starting from their respective X-ray conformations. The isopotential maps of the optimized structure of diazoxide, cromakalim and the four low energy conformers of pinacidil were compared. The isopotential map of diazoxide shows a good analogy with that of two calculated conformations of pinacidil (both different from that in crystal). Recent studies (Schwanstecker, M., Brandt, C., Behrends, S., Schaupp, U. and Panten, U., Br. J. Pharmacol., 1992, 106, 295-301) have suggested that diazoxide and pinacidil could exert their activity on the pancreatic K_{ATP} channel after interaction with a common binding site. We tentatively conclude that the moderate activity of pinacidil on the insulin release from pancreatic B-cells could be explained by adoption for pinacidil of a low energy conformation which can be reasonably fitted on diazoxide both from the point of view of atom positions and of stereoelectronic properties.

PS-05.01.07 MODELLING OF SOME RETROVIRAL ASPARTYL PROTEINASES. STUDY OF THE SHORTER SEQUENCE REQUIRED FOR THE *IN VITRO* ENZYMATIC ACTIVITY. By S. Geoffre*, R. Léonard, S. Llido, P. Picard and G. Précigoux, Lab. de Cristallographie, University Bordeaux I, 33405 - Talence, France.

The Bovine Leukaemia Virus (BLV) and Human T-cell Leukaemia Virus (HTLV) aspartyl proteinases are reported as putative proteins made of 126 and 125 amino acids respectively ("long sequences"). Since all known aspartic proteinases contain a conserved active site and core structure, it is reasonable to attempt to use them to model the unknown structure of another aspartic proteinase. The crystal structures of Rous Sarcoma Virus (RSV PR) and Human Immunodeficiency Virus (HIV-1 PR) were used to align the sequences of BLV and HIV-1 PR and to construct models. These models show that BLV and HTLV-I proteinases made of only 116 and 115 amino acids respectively ("short sequences") display three dimensional structures similar to that observed for other retroviral proteinases. The ten amino acids of the carboxyl extremities of the BLV and HTLV-I "long sequences" do not have any equivalent residue in the alignment of the active RSV and HIV-1 PR and would not act in the catalysis process.

The real value of our models is underlined by the *in vitro* activity and inhibition of the synthetic BLV proteinase made of only 116 amino acids.

PS-05.01.08 DIRECTIONAL PREFERENCES OF BINDING OF FUNCTIONAL GROUPS. J.P. Glusker, C.W. Bock*, L. Shimoni, A. Kaufman, A.B. Carrell, H.L. Carrell, The Institute for Cancer Research 7701 Burholme Avenue, Philadelphia, PA 19111, USA, *Philadelphia College of Textiles and Science, Philadelphia, PA 19144, USA.

The directional preferences for binding of functional groups to different molecules are studied by use of the Cambridge Structural Database (CSD). Data on intermolecular interactions to a selected functional group and large numbers of small-molecule crystal structures are analysed. These are analyzed in a statistical manner by use of contoured scatterplots in order to determine the variability in such binding. The results can then be used for macromolecules, studied to lower resolution, in order to suggest modes of ligand binding. Two types of interactions will be described here.

Hydrogen bonding and metal binding to nitrogen-containing heterocycles has been studied in this way to give ranges within which such binding deviates from the plane of the ring system and from the line disecting the C-N-C angle. The results are compared with X-ray structural data at lower resolution for some acridine-oligonucleotide complexes and the surroundings of histidine rings in some protein crystal structures .

Additionally, the stereochemistry of binding of functional groups to metal cations, such as divalent magnesium, manganese and cobalt, will be described, and the relevance of such binding to enzyme mechanisms will be discussed.

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PS-05.01.09 MOLECULAR SIMULATION OF HUMAN INSULIN-LIKE GROWTH FACTOR I B. Xiao, C. Verma and G. G. Dodson
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Molecular modelling on human insulin-like growth factor I (IGF) has been carried out based on the X-ray structures of mini proinsulins and the IGF-I NMR structures using the computer system - Protein Workbench. Searches for equivalents to the C domain linking the A and B chains and to the D domain as an extension of the A chain C-terminal were made in the protein data bank. Molecular dynamics and minimization were carried out (using CHARMM) on a solvated system to determine the final model. The model of IGF's three-dimensional structure was compared with the X-ray structure of the mini proinsulin. It has been found that the A- and B- domains of the three dimensional model of IGF-I are consistent with molecule 1 of the mini proinsulin but not with the C-loop where the molecule of the proinsulin has only a short connection. The high mobility of D-domain was observed - not surprisingly. However, the geometry of the model is fairly good enough and the result was used to interpret the binding sites of IGF binding proteins.

