Journal of Computational Intelligence in Bioinformatics
ISSN: 0973-385X Volume 3 Number 1 (2010) pp. 127–131

http://www.ripublication.com/jcib.htm

Computational Model of Synthetic Construct of Monellin-A Chain

PK. Ragunath[1], Anand Krishnamuthy*[2], Sindhuja[3], D. Anusha[4] and D. Sudarshanam[5]

[1,3,4]Department of Bioinformatics, Sri Ramachandra University , Chennai , India
[2,5]Loyola College, Chennai, India
**E-mail: spibet@gmail.com*

Abstract

Most proteins are tasteless and flavorless, while some proteins elicit a sweet-taste response on the human palate. Six proteins, thaumatin, monellin, mabinlin, brazzein, egg lysozyme, and neoculin (previously considered as curculin) have been identified as sweet-tasting proteins. Information on the structure-sweetness relationship for these proteins would help not only in the clarification of the mechanism of interaction of sweet-tasting proteins with their receptors, but also in the design of more effective low-calorie sweeteners. We have modeled the three dimensional structure of monellin synthetic construct using swiss model server and studied the conformation of the secondary structure using Ramachandran plot statistics. It is observed that the structure coincides with its berry counterpart 1MOL_B chain and, the rmsd distance of is 1.61 A is observed. The structure is deposited at the protein databank and id is 2GPK.

Introduction

Monellin is isolated from the fruit of the tropical plant Dioscoreophyllum cumminsii Diels (1). It consists of two noncovalently associated polypeptide chains the A and B chains, which consist of 44 amino acids and 50 amino acids, respectively. It is approximately 90,000 times sweeter than sucrose on a molar basis and 3000 times sweeter than sucrose on a weight basis (1,2). Monellin has no disulfide bond and is thermally less stable than thaumatin (3). The three-dimensional structure of monellin has two polypeptide chains that interact closely through hydrogen bonds as well as Van der Waals contacts (4). Since the N-terminus of the A chain is close to the C-terminus of the B chain, two polypeptides were joined by genetic engineering to produce covalently linked single-chain monellin (3,5). Eight comparative modeling

groups at CASP4 were roughly similar (6,7). Obtaining good alignments appears to be the key element of success; loop modeling and further refinement are futile without a reasonably accurate initial alignment. The best predicted regions are often biologically important (8), because these are the most structurally conserved by evolution. Thus, comparative modeling often predicts accurately 'the parts that matter'.

Materials and methods

Protein modeling

Protein sequences used in modeling are derived from the genbank entry AAG21344. The sequence of synthetic monellin is used to predict three-dimensional (3D) models according to the homology modeling strategy by using the template models from serendipity berry Monellin A and monellin B (PDB code: 1MOL_B chain from natural Monellin at 1.7 angstroms. As the sequence identities between each target protein sequence and the homologous template model are 100% identities and positives, we used an accurate procedure described previously (9). The search for sequence similarity within databases and the alignment of the selected sequences were performed with the BLAST program (10), which was part of swiss model structure prediction. The programs swiss model (11) were used to build a full-atom models for protein under prediction. The program Swiss pdb viewer (12) was also used to evaluate the occurrence of conformation of secondary structure by plotting the Ramachandran plot. The model was minimized using swiss pdb viewer and the lowest energy of stable conformation predicted

Results and discussion

We used comparative modeling techniques to generate a single and stable model for sequence with genbank id AAG21344 and is shown in Figure 1. The protein structure prediction is based on templates 1MOL B chain as PDB entry. The pdb entry is sequentially identical to extracted sequence from the genbank.

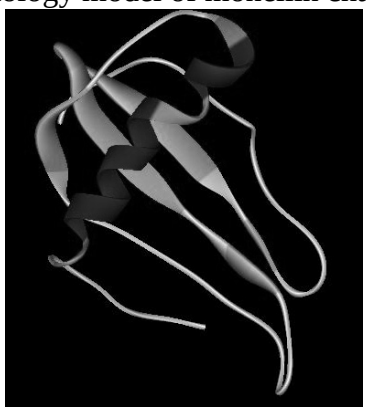
The Structural similarity between Monellin chain B and the swiss modeled structure 2GPK illustrates a closeness between the two structures and is found to have a RMSD distance of 1.61 A for chain B. The figure 2 shows the extent of superimposition between the two structures and is represented as solid ribbon.

The conformation of the secondary structure of the protein is predicted Insilico using Discovery studio and the result shows that the modeled structure has well agrees with structure stability norms. There is an nearly equal distribution of amino acids in both alpha helix as well as beta sheet conformation and many amino acids fall in the turn region or loop region corresponding to a right handed helix conformation. These results suggest that the amino acids have more conserved regions. The results are tabulated in table I and the Ramachandran plot is shown in figure 3.

Table I: Statistical perspective of the Ramachandran plot.

Slno.	**Regions**	**Expected percentage of residues for stability**	**Number of residues in region**	**Percent of residues in region**
1	Favoured region	98 %	66	73.3%
2	Allowed region	2 %	19	21.1%
3	Outlier region	-	5	5.6%

Homology model of monellin chain-A



Figureure 1: Homology Model of the genbank ID AAG21344 as predicted by Swiss model with PDB code: 2GPK.

Superimposed model of predicted monellin Chain-a with its template 1mol chain-B

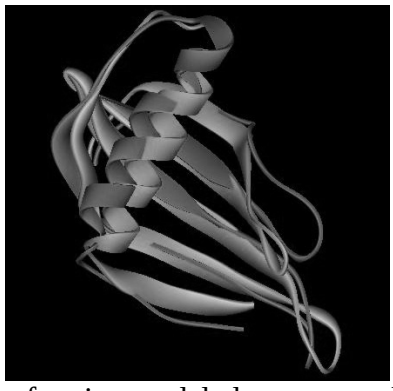


Figure 2: Superimposition of swiss modeled structure along with templates 1MOL chain B.

Ramachandran plot statistics for the predicted model 2GPK

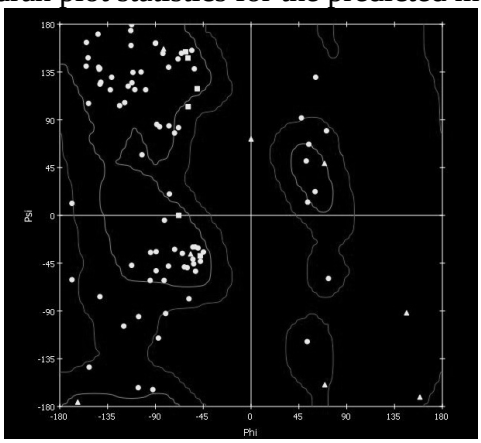


Figure 3: Ramachandran plot diagram for PDB id: 2GPK Statistical perspective of the Ramachandran plot.

Acknowledgements

I sincerely acknowledge the principal Reverend Father Albert Muthumalai of Loyola College, Mr. Ambrose Head of the Department of animal biotechnology and advance zoology and other research colleagues for their support in the research investigation.

References

[1] Moris JM and Cagan, RH., 1972, “Purification Of Monellin, The Sweet Principal For Dioscoreophyllum Cumminsii, Biochim. Biophys,” Acta., 261: 114-122,.

[2] Moris JM and Cagan RH., 1973, “Chemostimulatory Protein: A New Type Of Taste Stimulus,” Science, 181: 32-35.

[3] Kim SH, Kang CH, Kim R, Cho JM, Lee YB, Lee TK., 1989, “Redesigning A Sweet Protein: Increased Stability And Renaturability”, Protein Engg, 2: 571-575.

[4] Ogata C, Hatada M, Tomlinson G, Shin WC, Kim SH., 1987, “Crystal Structure Of The Intensely Sweet Protein Monellin’, Nature, 328:739-742.

[5] Tancredi T, Iijima H, Saviano G, Amodeo P, Temussi PA., 1992, “Structural Determination Of The Active Site Of A Sweet Protein, A 1H NMR Investigation Of Pmnei”, FEBS Lett, 310: 27-30.

[6] Tramontano, Leplae R, Morea V., 2001, “Analysis And Assessment Of Comparative Modeling Predictions In CASP4”, Protein, 45: 22-38.

[7] Marti-renom, Madhusudhan MS, Fiser A, Rost B, Sali A., 2002, “Reliability of Assessment of Protein Structure Prediction Methods,” Structure, 10: 435-440.

[8] Bates PA, Kelley LA, Maccallum RM, Sternberg MJ., 2001, "Enhancement Of Protein Modeling By Human Intervention In Applying The Automatic Programs 3D JIGSAW And 3D-PSSM", Proteins 45, Suppl 5: 39-46.

[9] Facchiano AM, Stiuso P, Chiusano ML, Caraglia M, Giuberti G, Marra M, Abbruzzese A, Colonna G., 2001, "Homology Modeling Of The Human Eukaryotic Initiation Factor 5A (Eif-5A)", Protein Engg, 14: 881-890.

[10] Altschul SF, Gish W, Miller W, Myers E, Lipman DJ., 1990, "Best Local Alignment Search Tool", J Mol Biol, 215: 403-410.

[11] Guex N, Peitsch MC., 1997, "SWISS-MODEL And The Swiss-Pdbviewer: An Environment For Comparative Protein Modeling", Electrophoresis, 18: 2714-2723.

[12] Guex N, Peitsch MC., 1996, "Swiss-Pdb Viewer: A Fast And East-To-Use PDB Viewer For Macintosh And PC", Protein Data Bank Quaterly Newsletter, 77: 7.