In Silico Physico-Chemical Comparative Study of Human And Camel Insulin

Arora Asha¹, Kamlesh Pareek² And Sonam Shah³

¹ Department Of Biotechnology, B N P G College, B N University, Udaipur (Raj.) India
²,³ Pacific Academy Of Higher Education And Research University, Udaipur (Raj.) India

Abstract:-The Physical, Chemical, Conformational, And Energetic Properties Of Amino Acid Residues In Turn Alter The Physiological Properties Of The Activating Protein Molecules. The Sequence Comparison Of Insulin Chain A And Chain B Of Camelus Dromedaries Was Compared To Homo Sapiens . Although The Sequences Differed Only In Four Amino Acids But Their Physico-Chemical Properties Stretched Apart. Camel Milk Insulin Had Large Mutable Affinity For Alanine Which In Turn Is Responsible For –I. High Thermo-Stability II. High Aliphatic Index And Iii. High Hydropathicity. Due To This Altered Behavior Of Insulin Molecule In Camel, It Does Not Forms Coagulum And Is Resistant To Proteolysis During Digestion. In Gut Part This Indigestible Insulin Peptide Enters Circulatory System And Regulates Glycemic Loads In Diabetic Patients.

Keywords: Aliphatic Index, Camel Milk, Flexibility, Grand Average Of Hydropathicity, Instability Index, Insulin, Polarity, Relative Mutability.

I. INTRODUCTION


II. MATERIALS AND METHODS


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III. RESULT AND DISCUSSION

In Silico Local Alignment Of Human Insulin And Camel Insulin Residues Reveals That Both Are Nearly Identical With Four Substitutions With Equally 2 Residual Substitutions In Both The Chain A And Chain B. 90 % Identity And 95 % Positives Were Obtained While Comparing Chain A While Chain B Had 93 % Both Identity And Positives .All The Three Primary Receptor-Binding Surface Of Insulin: (I) The N-Terminal And C-Terminal Segments Of The A Chain (Gly A1 -Ile A2 -Val A3 -Glu A4 And Tyr A10 -Cys A20 -Asn A21 ), (II) The Central A-Helix Of The B Chain (Especially Val B12 ) And (iii) And The C-Terminal Segment Of B Chain (Phe B24 -Phe B25 -Tyr B26 ) Were Conserved In Camel Insulin As Akin To Human Insulin. These Surfaces Are Classified As Its “Site-1” Related Binding Surface In Relation To “Site-2” Related Surface. The Putative Site-2 Related Surface Of Insulin, Is Proposed To Correspond To Its Hexamer-Forming Surface Which Includes Residues His B10 , Leu B17 , Val B18 , Ser A12 , Leu A13 And Glu A17 . Substitutions In Any Of The Residues At Site 2 Affects The Kinetic Properties Of Hormone Binding Disproportionately To Effect On Its Affinity. Such Kinetic Properties (Related To The Residence Time Of The Hormone-Receptor Complex) Correlate With Relative Post-Receptor Signaling Pathways; Prolonged Residence Times Also Favor Mitogenic Signaling Relative To Metabolic Signaling. This “Site-2” In Camel Insulin Was Identical To That Of Human Insulin Pointing Similar Dimer And Hexamer Structural Affinities [11] (Fig.1).

Physico-Chemical Comparison Of Human And Camel Insulin Chain A And Chain B Reveal Identical Isoelectric Point, Total No Of Negative Charge Residue (Asp + Glu) And Total No Of Positive Charge Residue (Arg + Lys). Aliphatic Index, Which Is Also Defined As The Relative Volume Of The Protein Occupied By Aliphatic Side Chains I.E. Alanine, Valine, Isoleucine, And Leucine Of Proteins Is Significantly Higher In Camel Chain B Than That Of Human Insulin Chain B. This Index Is A Positive Factor For The Increase Of Thermostability Of Globular Proteins [12]. Instability Index Was Similar For Chain B While For Chain A It Was Comparatively Lower In Camel Insulin Referring Its More Stability. The Stability Of Any Peptide Is A Result Of An Increased Alanine Residues Although It Does Not Affect The Secondary Structure [13,14] . Grand Average Of Hydropathicity Differed For Both The Chains In Both The Organisms. Gravy Was Higher In Both Insulin Component Chain A And Chain B Of Camelus Dromedaries As Compared To Homo Sapiens. In Both The Insulin Components Chain A Had More Hydrophobicity As Compared To Chain B (Table 1). Various Forces Are Involved In Unique Conformations Of Polypeptide Chains. This Resulting Pattern Allows Hydrophilic Side-Chains Access To The Aqueous Media While Consequentially Minimizes Contact Between Water And Hydrophobic Side-Chains [15]. It Also Reveals The Extent Of Residual Depth In Tertiary Structures Signifying Hydrophobicity Of The Molecule [16]. The Structural Conformations Are The Result Of Both Hydrophobicity And Steric Effects That Determine Packing Between The Secondary Structures In The Crowded Interior Of The Macromolecule [17]. Minimum Polarity/Ganathm Values And Relative Mutability For Insulin Molecule Were Similar In Both Camelus Dromedaries And Homo Sapiens While In Terms Of Maximum Value Camel Insulin Molecule Is More Polar And Mutable Than Human Insulin (Fig 2). The Relative Mutability Of Each Amino Acid Is Proportional To The Ratio Of Changes To Occurrences. In Camel Insulin Chain A And B The Ala Residue Is The Mutable Choice Directing Thermo-Stability To The Molecule [18,19]. Average Flexibility Was Identical For Both Minimum And Maximum Values In Both The Studied Molecule. This Flexibility Is A Dynamic Character Of A Insulin Molecule. Among The Non-Polar Residues Tyr And Ala Fluctuate More Than The Others While In Polar Types His Tends To Be Less Flexible. The Bend-Forming Residues Gly And Pro Are Equally Flexible Akin To Highly Flexible Polar Amino Acid Residues. The Residues Lys, Asp And Ser Of The Polar Group Are Exceptionally Flexible. The Buried Effect Of The Non-Polar Residues Is Indicates Less Flexible Trends Of Phe, Met And Trp [20].

IV. CONCLUSION

Ingestion Of Camel Milk As A Therapeutic Source In Diabetes Has Been Practiced In Various Parts Of The World. The Underneath Mechanism Of Its Intact Insulin During Digestion Process Is An Probable Outcome Of Alanine Incorporation In Camel Insulin During Molecular Evolutionary Process Due To Which It Does Not Forms The Coagulum And Leads To Resistance Of Insulin Molecule In Digestive Proteolysis. Alanine Increases Hydro-Pathicity And Aliphatic Index Due To Which The Insulin Has More Thermo-Stability Index And Hence It Enters The Circulatory System Without Degeneration. It Can Be One Of The Major Routes For Its Therapeutic Glycemic Load Regulation.
REFERENCES


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\begin{align*}
\text{Chain A} \\
\text{Cd:} & \text{ FANNQHLCGSVLVEALYLCGERGFFYTPKA} \\
\text{Hs:} & \text{ FVNQHLCGSVLVEALYLCGERGFFYTPKT} \\
\text{Chain B} \\
\text{Cd:} & \text{ GIVEQCCASYCSDLQLENYC} \\
\text{Hs:} & \text{ GIVEQCCASYCSDLQLENYC}
\end{align*}
\]
### Table 1: *In Silico* Physico-Chemical Comparison Of Human And Camel Insulin Chain A And Chain B Using Prot Pram

<table>
<thead>
<tr>
<th>S.No</th>
<th>Pcp</th>
<th>Chain A</th>
<th>Chain B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hs</td>
<td>Cd</td>
</tr>
<tr>
<td>1</td>
<td>Naa</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>Mw</td>
<td>2383.71</td>
<td>2339.65</td>
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<tr>
<td>3</td>
<td>Pi</td>
<td>3.79</td>
<td>3.79</td>
</tr>
<tr>
<td>4</td>
<td>Tnrs (D + E)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Tnpr (R + K)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>Ii</td>
<td>22.54**</td>
<td>7.02**</td>
</tr>
<tr>
<td>7</td>
<td>Ai</td>
<td>88.10</td>
<td>88.10</td>
</tr>
<tr>
<td>8</td>
<td>Gravy</td>
<td>0.214</td>
<td>0.319</td>
</tr>
</tbody>
</table>

1. Hs- Homo Sapiens And Cd- Camelus Dromedarius
2. Pcp- Physicochemical Parameter; Naa- Number Of Amino Acids; Mw- Molecular Weight; Pi- Isoelectric Point; Tnrs (D + E) - Total Number Of Negatively Charged Residues (Asp + Glu); Tnpr (R + K) - Total Number Of Positively Charged Residues (Arg + Lys); Ii- Instability Index; Ai- Aliphatic Index And Gravy- Grand Average Of Hydropathicity

*.- Unstable; **.- Stable

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![Graph showing comparison of polarity, relative instability and average flexibility of insulin molecule in Camelus dromedarius (Cd) and Homo sapiens (Hs).]