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In -Silico Comparative Study of Camel Milk Protein and Insulin Secondary Structure

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Abstract
Protein secondary structure plays an important role to understanding metabolisms studies. Several studies describe that regular/partial consumption of camel milk for significantly improved the condition of diabetic patients and experimental animals. Moreover, various studies also found that camel milk more similar in comparison to other ruminants with human insulin. Primary protein structure similarity along with its physicochemicall evidence and various favorable hypothesis suggest that camel milk similar/ analog or contains unidentified small molecules of 'insulin-mimic' regulatory value or other properties to put off or slow trying to understand the secondary structure analysis of insulin and camel milk by using bioinformatics tools and techniques. The study revealed that the camel insulin itself is most likely not responsible for anti-diabetic properties of camel milk and due to low pH, good buffering agent and presence of metals therefore, camel milk contains 'insulin-like' small molecular substances that mimic insulin interaction with its receptor.

Keywords: *Anti- diabetic agent, Camel milk, Insulin, Secondary structure, Transmembrane proteins*

I. Introduction

One-humped camel (*Camelus dromedaries*) plays an important role in food and dairy products in gulf countries. In many parts of the arid world as well as arid regions, it valued for transportations and commercial purposes such as camel safaris, agricultural practices and source of hair and hides, (Sweet, 1965). Properties of camel milk are opaque white, normal odor and salty taste. The composition of its milk i.e. percent value of moisture (88.55-90.15), total solid (9.85-11.45), fat (2.60-3.20), Solid not Fat (SNF) (7.25.8.25), protein (3.73.389), casein (2.90-3.02), ash (0.82-085), acidity (0.12-0.14), and pH (6.36-6.58) respectively (Mal et al., 2006 and 2007). Such types of properties it's slightly diverse from other domestic ruminants moreover, camel milk does not form coagulum in an acidic environment (Wangoh, 1993 and Pareek *et. al.*, 2012). Many folkloric stories indicated that its medicinal properties including the treatment of diabetes mellitus (Hamers *et. al*,.1993). Worldwide researchers in a wide range of studies describe that regular/partial consumption of camel milk for significantly improved the condition of diabetic patients and experimental animals. These outcomes indicated that the effects of camel milk due to the presence of insulin in the milk or insulin-like growth factor/s which facilitated to change glucose level. Singh (2001) reported that concentration of insulin in camel milk is 52 units /liter therefore; it contains a higher level of insulin than milk from other animals (Sboui *et. al*,. 2010; Beg *et al*, 1986; Zagòrski *et. al*,. 1998; Agarwal *et. al*,. 2009 &2011, and Mohamad *et. al*,.2009). We hypothesized that camel insulin is protected from digestive enzymes in the stomach and thus absorbed in the intestine Yip, 2003 and Kristensen *et. al*,.1997). Various studies described that camel milk more similar in comparison to other ruminants with human insulin. He *et. al*,. 2011, developed an in vitro screening assay searching for insulin-mimetic. They found a compound (5, 8-diacetyloxy-2, 3-dichloro-1,4-naphthoquinone,) that activates insulin receptor directly binding to the receptor kinase domain, to trigger its kinase activity sensitizing insulin's action (He *et. al*,. 2011). Moreover, its physicochemical studies remark its therapeutic glycemic load regulation between human and camel milk insulin (Arora *et. al*,. 2016).

In this study we are trying to understand the secondary structure analysis of insulin and camel milk by using bioinformatics tools and techniques. Primary protein structure similarity along with its physicochemicall evidence and various favorable hypothesis suggest that camel milk similar/ analog or contains unidentified small molecules of 'insulin-mimic' regulatory value or other properties to put off or slow digestive enzyme activities.

II. Material And Method

Sequence retrieval

A homology searching done on public database viz. NCBI public database with the keyword “Camel Milk Protein” and search performed. Its result filter by default value and finally 8 template sequence found to depend on the maximum similarity. Insulin and Insulin like growth factor-1 (IGF-1) Protein Database Bank (PDB) and fasta format downloaded from PDB database. These 10 protein and fasta format files save in local hard drive for analysis point. Every PDB sequence has Unpot KB ID so that respective Uniport KB fasta file were also downloaded for further use in MSA. These are 5 Uniport sequences found after filtering the sequence. Finally 10 PDB and Fasta file for protein sequence and 5 Uniport KB file selected for homology modeling. These are (1DTZ (Khan *et. al*,.2001); 1GZZ (Brzozowski *et. al*,. 2002); 2J4U (Baalaji *et. al*,. 2007); 2R2K (Sharma *et. al*,.2007); 2Z9N (Sharma *et. al*,.2008); 3C93 (Sharma *et. al*,.2008); 3CG9 (Sharma *et. al*,.2008); 3COR (Sharma *et. al*,.2008); 3CXA (Balaji *et. al*,.2008) and 2HIU (Hua, *et. al*,.1995) as a PDB file and Q9TUM0; Q9GK12; Q1D297; PO1308; PO5019; PO6996 as Uniport KB file) (web source Uniport KB database).

Table 1. Some basic characterization of target protein sequences

PDB ID	Uniport KB ID	Classification	Structure Weight (Absence of Water Molecule)	Molecule	Length	Gene Symbol
2HIU	P01308	Harmon	5817.68	Insulin	21	INS
1GZZ	P05019	Growth Factor	8000.34	IGF-1	70	IBP1
2J4U	P06996	Member Protein/ Hydrolase	240426.63	Outer Membrane Protein C Precursor 1	356	OMPC meoA Par b2215 JW2203
2R2K	Q9GK12	Immune System	77645.65	Peptoglycan Recognition Protein	171	PGLYRP1
2Z9N			76496.66			
3C93			76417.70			
3CG9			76524.80			
3COR			76638.91			
3CXA		Antibiotic	76881.08			
1DTZ	Q9TUMO	Metal Transport	75452.70	APO Lectofreein	689	LTF

In Table 1, PDB ID:2HIU; UniportKB ID P01308 as human insulin, followed by1GZZ; P05019 as insulin like growth factor and rest sequences are camel milk protein.

Secondary structure analysis

Target sequence of protein analyzed by using different aspects. The target protein sequence was submitted to the following server se desire format from respective servers.

- All the target sequence (PDB ID and Uniport KB ID) as a input to Expasy server for secondary structure analysis. Expasy server gave a resulted in multidimensional outputs such has sequences composition, population and etc, all the target sequences are input and recorded result in template format.
- SSpro and SSpro8 is a server for protein secondary structure prediction based on protein evolutionary information.
- With the help of DOMpro tool, we can predict target proteins domain locations by using a specific algorithm i.e. 1D- recursive neural network. It is also predict sequence profile, secondary structure, and relative solvent accessibility.
- To identify whether target sequences are transmembrane protein therefore, ABTMpro server predicts whether sequence is a transmembrane protein or not.
- Motif finder (Both sequence and structure context) A conserved pattern of amino acids that is found in two or more proteins. And a combination of several secondary structural elements produced by the folding of adjacent sections of the polypeptide chain into a specific three-dimensional configuration.

III. Results And Discussion

To find secondary structure comparative analyses, Expasy server gave more meaningful information related to their structure composition.

Table (2) Frequency of secondary structure; in parenthesis showed number of secondary structure.

Protein ID	Beta Strand	Helix	Turn
P01308	26-29; 48-50; 74-76; 98-101**(5)**	33-40; 44-46; 79-81; 91-97; 102-106 **(5)**	59-66; 84-86; 107-109 **(3)**
P06996	23-27; 30-44; 56-85; 92-103; 107-115; 129-131; 138-140;143-155;164-171; 176-182;184-186; 200-209;212-222; 237-250; 253-264;271-273; 275-286; 291-305; 3112-340;358-367 **(22)**	119-122; 123-125; 156-159; 193-195;346-351 **(5)**	48-50; 104-106; 225-227; 308-310 **(4)**
Q9TUM0	23-31; 53-57; 75-78; 93-99; 104-106; 108-120; 132-136; 172-176; 178-180; 220-222; 224-229 **(11)**	32-46; 61-69; 80-87; 125-127; 145-150;152-154; 164-171; 186-189; 198-198; 210-219; 232-236; 240-243; 258-260; 283-297; 335-339; 341-348; 354-362; 371-384; 396-404; 415-422; 544-553 **(21)**	564-567; 600-605; 623-637; 676-680; 682-692; 698-705 **(6)**
Q9GK12	50-59; 94-67; 103-107; 109-111; 114-116; 124-131; 134-136; 158-167; 172-174 **(9)**	68-84; 117-120; 121-123; 140-155; 168-171;179-185 **(6)**	34-38 **(1)**
P05019	71-73; 79-81; 82-85; 96-98; 109-111; 112-116 **(6)**	52-66; 67-69; 90-95; 102-108 **(4)**	--

Results in Table 2 indicated that all target sequences are divers from their formation of its various structure types such as helix, beta-strand and turn similar in their secondary structure. It is instructing that insulin and milk protein sequences are very diverse in their molecular weight, length. However, the frequency of the helix structure are much similar in all target sequences. Protein ID of P01308 contain a number of 5 helix which are almost the same in P06996 (5), Q9GK12 (6) and P05019 (4). In the case of turn structure, all protein IDs number of clusters are not the same but differences are notable that it occurs in protein ID of P01308 (3) followed by P06996 (4) and Q9TUM0 (6), respectively.

For a better understanding of its protein secondary structure and relative solvent accessibility, it is very important to find about its evolutionary study and its functional aspect therefore, domain composition, motif and functionally stability is necessary for target sequence (Maganan, 2014).

Table 3: Result of Uniport KB IDs of target sequence in different server viz. SSProw, SSProw8, ABTMpro and Domprow.

Sequence ID	**Amino Acids:** MALWMRLLPLLALLALWGPDPAAAFVNQHLCGSHLVEALYLVCGERGFFYTPKTRREAEDLQVGQVELGGGP GAGSLQPLALEGSLQKRGIVEQCCTSICSLYQLENYCN
P01308	**Predicted Secondary Structure (3 Class):** CHHHHHHHHHHHHHHHHHCCCCCHHCCCCCCCHHHHHHHHHHHHHHHHCEEECCCCCCCCCCCCCCCCCCC CCCCCCCCHHHHHCCCCCCHHHHHHCCCCCCHHHHHHCEC
	Predicted Secondary Structure (8 Class): CCHHHHHHHHHHHHHHHHHCCCCHHHCCCHCCCHHHHHHHHHHHHHGGGCEEECCCCHHCSCTTHHSHCSTTT CTTTSCCCHHHHHSSSCCHHHHHHHTSSCCCHHHHHHTTBC
	ABTMpro Prediction: Non Transmembrane protein
	Predicted Probabilities: Non Transmembrane protein 0.617703 Alpha Helical Transmembrane protein 0.378706 Beta Barrel Transembrane protein 0.00359085
	Predicted Domains: Domain 1: 1 - 90 Domain 2: 91 – 110
q9tumo	**Amino Acids:** MKLFFPALLSLGALGLCLAASKKSVRWCTTSPAESSKCAQWQRRMKKVRGPSVTCVKKTSRFECIQAISTEKA DAVTLDGGLVYDAGLDPYKLRPIAAEVYGTENNPQTHYYAVAIAKKGTNFQLNQLQGLKSCHTGLGRSAGWN IPMGLLRPFLDWTGPPEPLQKAVAKFFSASCVPCVDGKEYPNLCQLCAGTGENKCACSSQEPYFGYSGAFKCLQ DGAGDVAFVKDSTVFESLPAKADRDQYELLCPNNTRKPVDAFQECHLARVPSHAVVARSVNGKEDLIWKLLV KAQEKFGRGKPSGFQLFGSPAGQKDLLFKDSALGLLRISSKIDSGLYLGSNYITAIRGLRETAAEVELRRAQVVW CAVGSDEQLKCQEWSRQSNQSVVCATASTTEDCIALVLKGEADALSLDGGYIYIAGKCGLVPVLAESQQSPESS GLDCVHRPVKGYLAVAVVRKANDKITWNSLRGKKSCHTAVDRTAGWNIPMGLLSKNTDSCRFDEFLSQSCAP GSDPRSKLCALCAGNEEGQNKCVPNSSERYYGYTGAFRCLAENVGDVAFVKDVTVLDNTDGKNTEQWAKDL KLGDFELLCLNGTRKPVTEAESCHLAVAPNHAVVSRIDKVAHLEQVLLRQQAHFGRNGRDCPGKFCLFQSKTK NLLFNDNTECLAKLQGKTTYEEYLGPQYVTAIAKLRRCSTSPLLEACAFLMR
	Predicted Secondary Structure (3 Class): CCHHHHHHHHHHHHHHHHHHCCCCCEEEEECCHHHHHHHHHHHHHHHHHHCCCCCEEEEECCCHHHHHHHHHHC CCCCEEEECHHHHHHHHCCCCCEEEEEEEEEECCCCEECEEEEEEEEEECCCCCCHHHCCCCEEEECCCCCCCCC

	CHHHHHHHHHHCCCCCCCHHHHHHHHCCEEECCCCCCCCCHHHHCCCCCCCCCCCCCCCCCCCHHHHH HHHHHCCCCCEEEEECCHHHHHCCHHHHCCEEEECCCCCEEEHHHHHHCCCEEEECCEEEEECCCCHHHH HHHHHHHHHHHCCCCCCCCCCCCCCCCCCCCCCCCCCCEEEECCCCCHHHHHCHHHHHHHHHHHCCHHH HHHHHHCEEEEEECHHHHHHHHHHHHHHCCCCEEEEEEECCHHHHHHHHHHCCCCEEEECHHHHHHHHHHCCCE EEEEEEECCCCCCCCCHHHCCCCCEEEEEEEEEECCCCCHHHCCCCEEEECCCCCCCCCCHHHHHHHHHHCCC CHHHCCCEEECCCCCCCCHHHCCCCCCCCCCCCCCCCCCCCCCHHHHHHHHHHCCCCCEEEEECCHHHHHC CCCCCHHCCCCCCHCCEEEECCCCCEEEHHHHHHCCCEEEECCEEEECHHHHHHHHHHHHHHHHHHHCCCCCC CCCCCCCCCCCCCCCCCCCCCECEEEECCCCCHHHHHCHHHHHHHHHHHHCCCCCHHHHHHHHHHHC
	Predicted Secondary Structure (8 Class): CCCHHHHHHHHHHHHHHHHHCCCCEEEEEEESHHHHHHHHHHHHHHHHHTTSCEEEEEECSSHHHHHHHHHHTT SCCBEEECHHHHHHHHSTTTCEEEEEEEEEECSSSEESEEEEEEEEEETTCCCCGGGCTTCEEEESCTTCIIIIIHHHH HHGGGGGCCSCCSSHHHHHHHHHSSEEECTTSCTTTCGGGGTTCCCCSCSTTCSSTTSTTCHHHHHHHHHHHTTSC SEEEEETTHHHHHCCSHHHHTTEEEECTTSCEEEGGGGGGSCSEEEECCEEEEESSSCCHHHHHHHHHHHHHHHH STTTCSSCCTTCCCTCSSSSSSCTTCCEEEECCTTCCHHHHHCHHHHHHHHHHHHHSCHHHHHHHHHHSEEEEEEESH HHHHHHHHHHHHHTTTSEEEEEESSHHHHHHHHHHHTSCCEEEECHHHHHHHHHHTTCEEEEEEEEECCSSCCSSCG GGSCCCCEEEEEEEEEETTCCCCGGGCTTCEEEESCTTCIIIIIHHHHHHHHHHHCCSCGGGTSSEEECTTSCTTSGGG TTCCCSTTSGSTTCSSTTSTTCHHHHHHHHHHHTTSCSEEEEETTHHHHHSTTSSCHHCCSTCCGTGEEEECTTSCE EEGGGGGGGSCSEEEECCEEEECGGGHHHHHHHHHHHHHHHHSTTCTTTTTTCCTTCSSSSCCSSCTTCEEEEECT TCCSHHHHHCHHHHHHHHHHHHHTTCCCHHHHHHHHHHHC
	ABTMpro Prediction: Non Transmembrane protein
	Predicted Probabilities: Non Transmembrane protein 0.943575 Alpha Helical Transmembrane protein 0.0549056 Beta Barrel Transembrane protein 0.00151992
	Predicted Domains: Domain 1: 1 - 258 Domain 2: 259 - 600 Domain 3: 601 - 708
po5019	**Amino Acids:** MGKISSLPTQLFKCCFCDFLKVKMHTMSSSHLFYLALCLLTFTSSATAGPETLCGAELVDALQFVCGDRGFYFN KPTGYGSSSRRAPQTGIVDECCFRSCDLRRLEMYCAPLKPAKSARSVRAQRHTDMPKTQKYQPPSTNKNTKSQ RRKGWPKTHPGGEQKEGTEASLQIRGKKKEQRREIGSRNAECRGKKGK
	Predicted Secondary Structure (3 Class): CCCCCCCCCCHHHHCCCCCCEEEEEEEHHHHHHHHHHHHHHCCCCCCCCCCCCCCCHHHHHHHHHHHHHCCCC CCCCCCCCCCCCCCCCCCCCEEHHHCCCCCCHHHHHHHCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC CCCCHCCCCCCCCCHHHHHHCHHHHHHHHCCCCCCCCHCCCCCCCCCCCCCC
	Predicted Secondary Structure (8 Class): CCCECCCCCHHHHHEECTTCEEEEEEEEHHHHHHHHHHHHHEECCHHCCCCCCCCHHHHHHHHHHHHHGGGCC CSCCCCSSSSCCSCCTTCCHHHHHETSCCCHHHHHHHHHCCCSCCCCCCCCCCCCCCCCCCTCCCCCCCCCCCCC CCHHCTTCCTCCHTHHHHHHHHHHHHHHHHTCCCCCHHHHHCHCCECCCTTCC
	ABTMpro Prediction: Non Transmembrane protein
	Predicted Probabilities: Non Transmembrane protein 0.660748 Alpha Helical Transmembrane protein 0.33153 Beta Barrel Transembrane protein 0.00772238
	Predicted Domains: Domain 1: 1 - 121 Domain 2: 122 - 195
q9gk12	**Amino Acids:** MTRHCVLLVWALLALLSLGAAREDPPACGSIVPRREWRALASECRERLTRPVRYVVVSHTAGSHCDTPASCAQ QAQNVQSYHVRNLGWCDVGYNFLIGEDGLVYEGRGWNIKGAHAGPTWNPISIGISFMGNYMNRVPPPRALRA AQNLLACGVALGALRSNYEVKGHRDVQPTLSPGDRLYEIIQTWSHYRA
	Predicted Secondary Structure (3 Class): CCHHHHHHHHHHHHHHHHHHHHCCCCCCCCCCCEECHHHHCCCCCCCCCECCCCEEEEEEEEECCCCCCCCHHHH HHHHHHHHHCCCCCCCCCCCCCCEEECCCCCEEECCCCCECCCCCCCCCCHHHEEEEEEECCCCCCCCCCHHHH HHHHHHHHHHHHHHCCEEEEEEEEEEHHHCCCCCCCCHHHHHHHCCCCCECC
	Predicted Secondary Structure (8 Class): CCHHHHHHHHHHHHHHHHHHHHHCCCCCCCCCCEECTGGGTCCCCCCCCBCCSSEEEEEEEEECCSCCCCSHHHHH HHHHHHHHIIIIISCCSSCSCSEEECTTSCEEESSTTTBCCSSSCTTTGGGEEEEEESSCCSSCCCCHHHHHHHHHH HHHHHHHTSEEEEEEEEEHGGHSSSCTTCHHHHHHHHTTSTTBCC
	ABTMpro Prediction: Non Transmembrane protein
	Predicted Probabilities: Non Transmembrane protein 0.755425 Alpha Helical Transmembrane protein 0.231141 Beta Barrel Transembrane protein 0.0134337
	Predicted Domains: Domain 1: 1 - 193
p06996	Amino Acids: MKVKVLSLLVPALLVAGAANAAEVYNKDGNKLDLYGKVDGLHYFSDNKDVDGDQTYMRLGFKGETQVTDQ

	LTGYGQWEYQIQGNSAENENNSWTRVAFAGLKFQDVGSFDYGRNYGVVYDVTSWTDVLPEFGGDTYGSDNF MQQRGNGFATYRNTDFFGLVDGLNFAVQYQGKNGNPSGEGFTSGVTNNGRDALRQNGDGVGGSITYDYEGF GIGGAISSSKRTDAQNTAAYIGNGDRAETYTGGLKYDANNIYLAAQYTQTYNATRVGSLGWANKAQNFEAVA QYQFDFGLRPSLAYLQSKGKNLGRGYDDEDILKYVDVGATYYFNKNMSTYVDYKINLLDDNQFTRDAGINTD NIVALGLVYQF
	Predicted Secondary Structure (3 Class): CCHHHHHHHHHHHHHHHHHHHHHCEEEEECCEEEEEEEEEEEEEEEECCCCCCEECCEEEEEEEEEEEECCCCEEEE EEEEEEEECCCCCCCCCCEEEEEEEEEEECCCEEEEEEEEEECCCHHHHCCCCCCCCCCCCCCCCCCCCCEEEEE EEEEECHHHHCCCCEEEEEEEEECCECECCCCCECCCECECCCCCCCCECCEEEEEEEEEECCEEEEEEEEEEECC HHHHCCCCECCCCCEEEEEEEEEEEEEECCEEEEEEEEEEEECCCEECCCEECCEEEEEEEEEEEECCCCCEEEEEEEEEE EEEEEECCCCEEEEEEEEEEEEEEEEEECCCCEEEEEEEEEEECCCCCHHHHHHCCCCECEEEEEEEEEC
	Predicted Secondary Structure (8 Class): CCHHHHHHHHHHHHHHHHHHHHHCEEEEETTEEEEEEEEEEEEEEEEECSSTTTCEECCEEEEEEEEEEEEECSSSEEEEE EEEEEEESSSCTTTTTCEEEEEEEEEEEETTTEEEEEEEEEECTTHHHHTTTCCCSSSCCTTCCTTSTTSSEEEEEEEEE ESHHHHTSTTEEEEEEEEECCBCBSSSTTBCTSBTBCCSSGGGCBCCEEEEEEEEEEETTEEEEEEEEEEEECCHHHHSS SCBCCCSEEEEEEEEEEEEETTEEEEEEEEEEEESCSEETTTEECSEEEEEEEEEEEECCTTSEEEEEEEEEEEEEEEESTT TEEEEEEEEEEEEEEEESSSSEEEEEEEEEEECCCTTHHHHHHCCCCBCEEEEEEEEEEC
	ABTMpro Prediction: Beta Barrel Transembrane protein
	Predicted Probabilities: Non Transmembrane protein 0.000536257 Alpha Helical Transmembrane protein 0.0075886 Beta Barrel Transembrane protein 0.991875
	Predicted Domains: Domain 1: 1 - 367

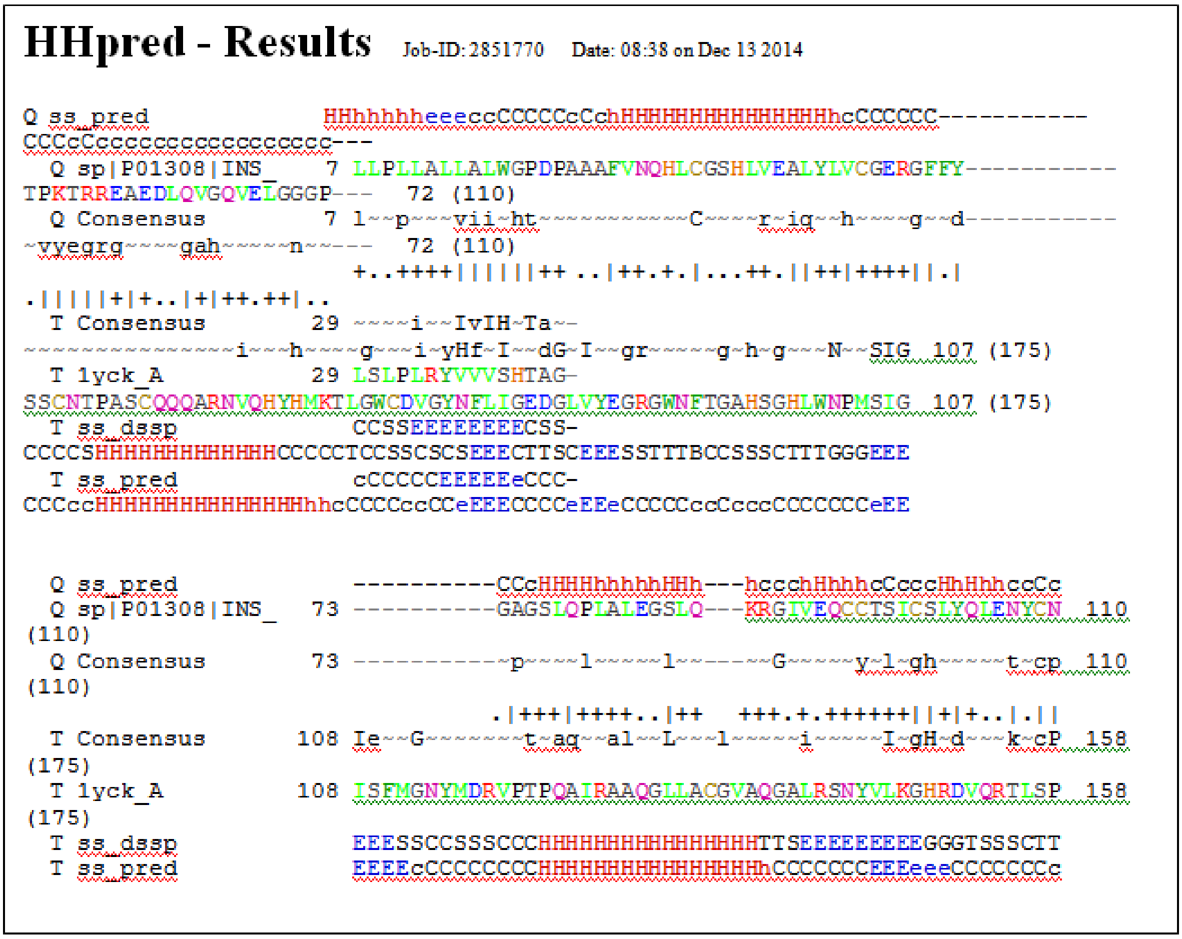
In Table 3, all target sequences are analyzed and the result showed in ABTMpro server resulted that all sequences are non- transmembrane protein except P06996, who are beta barrel trans-membrane protein. In other server results, probabilities of alpha helical transmembrane protein are very less than in comparison to beta barrel transemembrane protein. In this connection both type of protein present in all target sequences, it is very important concerning its functionally attributes because it is a major category of transmembrane proteins in humans, 27% of all proteins have been estimated to be alpha-helical membrane proteins (Almen *et. al*,.2009).

Table 4. PROSITE PATTERN of the PDB IDS and Uniport IDs

PDB IDs/ Uniport Ids	Found Motif	Position	Description	Related Sequences
1DTZ	TRANSFERRIN_LIKE_2	192..208 526..542	PS00206, Transferrin-like domain signature 2.	(YSGAFKCLQDGAGDVAF) (YTGAFRCLAENVGDVAF) 35
	TRANSFERRIN_LIKE_3	226..256		(QYELLCPNNTRKPVDAFQECH LARVPSHAV)34
	TRANSFERRIN_LIKE_1	92..101 93..101 433..442	PS00205, Transferrin-like domain signature 1.	(YYAVAIAKKG) (YAVAIAKKG) (YLAVAVVRKA) 34
1GZZ	INSULIN	47..61	PS00262, Insulin family signature.	(CCFRSCDLRRLEMYC) 222
2HIU	INSULIN	6..20	PS00262, Insulin family signature.	(CCTSICSLYQLENYC)222
2Z91	IG_MHC	191..197	PS00290, Immunoglobulins and major histocompatibility complex proteins signature.	(YTCEATH) 396
P01308	INSULIN	95..109	PS00262, Insulin family signature.	(CCTSICSLYQLENYC) 222
P06996	GRAM_NEG_PORIN	319..335	PS00576, General diffusion Gram-negative porins signature.	(VDVGATYYFNKNMSTYV) 44
P05019	INSULIN	95..109	PS00262, Insulin family signature.	(CCTSICSLYQLENYC) 222
Q9TUM0	TRANSFERRIN_LIKE_2	211..227 545..561	PS00206, Transferrin-like domain signature 2.	(YSGAFKCLQDGAGDVAF) (YTGAFRCLAENVGDVAF) 35
	TRANSFERRIN_LIKE_3	245..275 587..617	PS00207, Transferrin-like domain signature 3.	(QYELLCPNNTRKPVDAFQECH LARVPSHAVV) (DFELLCLNGTRKPVTEAESCH LAVAPNHAVV) 34

	TRANSFERRIN_LIKE_1	111..120 112..120 452..461	PS00205, Transferrin-like domain signature 1.	(YYAVAIAKKG) (YAVAIAKKG) (YLAVAVVRKA) 34

Above table (4) all target sequences are Transferrine –like motif 1,2, and 3 domain signature which is common to all target sequences. These sequences functions are clearly related to iron-binding and transport metals. lactoferrin domain groups act as antimicrobial function in mammals (Graham and Williams 1975; Anderson *et. al*,.1987). All targets sequence furthermore to find its functional similarity because sequence search methods such as BLAST, FASTA or PSI-BLAST (1–3) are most important and basic tools for biological, however, rather regularly no significant relationship between known function protein, therefore, HHpred search engine detected all homolog protein pattern which is functionally similar (Söding *et. al*,.2005). Obtained results from HHpred denoted that quality of column- column similarity ranged from more than 60% in some cluster and 40% in other clusters. Overall results indicated that insulin sequences functionally the same concerning target protein sequences.



```
HHpred - Results    Job-ID: 2851770    Date: 08:38 on Dec 13 2014

Q ss_pred             HHhhhhheeeccCCCCCcCchHHHHHHHHHHHHHHHHhcCCCCCC-----------
CCCcCcccccccccccccccc---
  Q sp|P01308|INS_    7 LLPLLALLALWGPDPAAAFVNQHLCGSHLVEALYLVCGERGFFY-----------
TPKTRREAEDLQVGQVELGGGP---   72 (110)
  Q Consensus         7 l~~p~~~vii~ht~~~~~~~~~~~~~~C~~~~~r~iq~~h~~~~g~~d-----------
~vyegrg~~~~gah~~~~~~n~~~---   72 (110)
                        +..++++||||||++ ..|++.+.|...++.||++|++++||.|
.|||||+|+..|+|++.++|..
  T Consensus        29 ~~~~i~~IvIH~Ta~-
~~~~~~~~~~~~~~~~~~~i~~~h~~~~g~~~i~yHf~I~~dG~I~~gr~~~~~~g~h~g~~~N~~SIG  107 (175)
  T 1yck_A           29 LSLPLRYVVVSHTAG-
SSCNTPASCQQQARNVQHYHMKTLGWCDVGYNFLIGEDGLVYEGRGWNFTGAHSGHLWNPMSIG  107 (175)
  T ss_dssp             CCSSEEEEEEEEECSS-
CCCCSHHHHHHHHHHHHHHCCCCCTCCSSCSCSEEECTTSCEEESSTTTBCCSSSCTTTGGGEEE
  T ss_pred             cCCCCCEEEEEeCCC-
CCCccHHHHHHHHHHHHHHHHhhcCCCCccCCeEEECCCCeEEeCCCCCccCcccCCCCCCCeEE


  Q ss_pred             -----------CCcHHHHhhhhhHHh---hccchHhhhcCcccHhHhhccCc
  Q sp|P01308|INS_   73 -----------GAGSLQPLALEGSLQ---KRGIVEQCCTSICSLYQLENYCN  110
(110)
  Q Consensus        73 -----------~p~~~~l~~~~~~l~~----~~G~~~~~~y~l~gh~~~~~~t~cp  110
(110)

                                   .|+++|++++..|++   +++.+.++++++||+|+..|.||
  T Consensus       108 Ie~~G~~~~~~~~~t~aq~~al~~L~~~l~~~~~~i~~~~~~I~gH~d~~~k~cP  158
(175)
  T 1yck_A          108 ISFMGNYMDRVPTPQAIRAAQGLLACGVAQGALRSNYVLKGHRDVQRTLSP  158
(175)
  T ss_dssp             EEESSCCSSSCCCHHHHHHHHHHHHHHHHTTSEEEEEEEEEGGGTSSSCTT
  T ss_pred             EEEEcCCCCCCCCHHHHHHHHHHHHHHHHhCCCCCCCEEEeeeCCCCCCCc
```

Figure 1. Output from HHpred of target sequence: Search results for taraget protein of camel milk In the summary hit list, column ‘Prob’ gives the probability that the hit is homologous to the query. This is the principle measure of statistical significance. In the alignments below, the sequences marked ‘Q’ (‘T’) refer to the query (template) alignment. Sequences ‘ss_pred’ and ‘ss_conf’ denote the PSI-PRED secondary structure prediction and confidence values, ‘ss_dssp’ is the secondary strcuture assigned by DSSP. Upper an lower case amino acids in the consensus sequences indicate high (≳60%) and moderate (≳40%) conservation, respectively. Symbols indicating the quality of the column–column match: ‘|’ very good, ‘+’ good, ‘·’ neutral, ‘–’ bad and ‘=’ very bad.

All search engines and tools indicated that camel milk protein and insulin protein secondary structure partially similar to their sequences and structure topology however, at the moment, protein is a mystery to their role for structures and function. Some domain and cluster which are shows his presence to indicate her homolog their structure and function.

Table 5: *Insilico* secondary structure comparison of human insulin and camel milk components

Sequence ID	**Amino Acids:** MALWMRLLPLLALLALWGPDPAAAFVNQHLCGSHLVEALYLVCGERGFFYTPKTRREAEDLQVGQVELGGGPGAGSLQPLALEGSLQKRGIVEQCCTSICSLYQLENYCN
P01308 (Human Insulin)	**Predicted Secondary Structure (3 Class):** CHHHHHHHHHHHHHHHHCCCCCHHCCCCCCCHHHHHHHHHHHHHHHHCEEECCCCCCCCCCCCCCCCCCCCCCCCCCCHHHHHCCCCCCHHHHHHCCCCCCHHHHHHCEC
	Predicted Secondary Structure (8 Class): CCHHHHHHHHHHHHHHHHCCCCHHHCCCHCCCHHHHHHHHHHHHHGGGCEEECCCCHHCSCTTHHSHCSTTTCTTTSCCCHHHHHSSSCCHHHHHHHTSSCCCHHHHHTTBC
Po5019 (IGF)	**Amino Acids:** MGKISSLPTQLFKCCFCDFLKVKMHTMSSSHLFYLALCLLTFTSSATAGPETLCGAELVDALQFVCGDRGFYFNKPTGYGSSSRRAPQTGIVDECCFRSCDLRRLEMYCAPLKPAKSARSVRAQRHTDMPKTQKYQPPSTNKNTKSQRRKGWPKTHPGGEQKEGTEASLQIRGKKKEQRREIGSRNAECRGKKGK
	Predicted Secondary Structure (3 Class): CCCCCCCCCCHHHHCCCCCCEEEEEEEHHHHHHHHHHHHHCCCCCCCCCCCCCCCHHHHHHHHHHHHHCCCCCCCCCCCCCCCCCCCCCCEEHHHCCCCCCHHHHHHHCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCHCCCCCCCCCHHHHHHCHHHHHHHHCCCCCCCHCCCCCCCCCCCCCC
	% identity = 47%
	Predicted Secondary Structure (8 Class): CCCECCCCCHHHHHEECTTCEEEEEEEEHHHHHHHHHHHHHEECCHHCCCCCCCCHHHHHHHHHHHHGGGCCCSCCCCSSSSCCSCCTTCCHHHHHETSCCCHHHHHHHHCCCSCCCCCCCCCCCCCCCCCTCCCCCCCCCCCCCCCHHCTTCCTCCHTHHHHHHHHHHHHHHHTCCCCCHHHHHCHCCECCCTTCC
	% identity = 49%
Q9gk12 **(a)** Immune system components (2R2K, 2Z9N, 3C93, 3CG9 and 3COR) **(b)** Antibiotic component (3CXA)	**Amino Acids:** MTRHCVLLVWALLALLSLGAAREDPPACGSIVPRREWRALASECRERLTRPVRYVVVSHTAGSHCDTPASCAQQAQNVQSYHVRNLGWCDVGYNFLIGEDGLVYEGRGWNIKGAHAGPTWNPISIGISFMGNYMNRVPPPRALRAAQNLLACGVALGALRSNYEVKGHRDVQPTLSPGDRLYEIIQTWSHYRA
	Predicted Secondary Structure (3 Class): CCHHHHHHHHHHHHHHHHHHHCCCCCCCCCCEECHHHHCCCCCCCCCECCCCEEEEEEEECCCCCCCCHHHHHHHHHHHHCCCCCCCCCCCCCCEEECCCCCEEECCCCCECCCCCCCCCCHHHEEEEEECCCCCCCCCCHHHHHHHHHHHHHHHHHCCEEEEEEEEEHHHCCCCCCCCHHHHH HHCCCCCECC
	% identity = 52%
	Predicted Secondary Structure (8 Class): CCHHHHHHHHHHHHHHHHHHHHCCCCCCCCCEECTGGGTCCCCCCCCBCCSSEEEEEEEEECCSCCCCSHHHHHHHHHHHHHIIIIISCCSSCSCSEEECTTSCEEESSTTTBCCSSSCTTTGGGEEEEEESSCCSSCCCCHHHHHHHHHHHHHHHHHTSEEEEEEEEEHGGHSSSCTTCHHHHHHHTTSTTBCC
	% identity = 39%

1. **3 class structures refers to: H: alpha-helix, E: extended strand and C: the rest.**
2. **8 class refers to: H: alpha-helix, G: 3-10-helix, I: pi-helix (extremely rare), E: extended strand, B: beta-bridge, T: turn, S: bend and C: the rest.**

Secondary structures are functional ports for proteins as their further folding leads to exposure of ligand and receptor binding sites. Protein structures are more stable in their form however, all the quarry structures except 1GZZ and 2HIU are no longer stable in their structure. It may be caused by their multi-functionally role in a lower energy case point of view. Other template protein structure i.e. 1DTZ, 2R2K, and 2Z4U, 2R2K, 3CXA, 3COR, 3CG9, 2Z9N and 3C93 are more stable in physical and chemical structure however it maybe their presence of legend and other side chain restudies which make a more stable structure. In the case of coiled structure, which is earlier discussed that many times it may be unstructured/ disorder of chain moreover, it may play a crucial role in its diverse functionality and structural stability in optimum condition. Frequencies of the coiled structure are maximum in all these templates structure and do not ignore coiled position on positively and negatively in B-factor normalized data. 1GZZ (IGF-1) and 2HIU (Human Insulin) both are partially similar to their functionality but in case of a structural point of view, both are quite diverse their structural similarity. Obtained results are indicated that in 2HIU (human insulin) positions of coiled structure, three clusters found one start from 23-26; 41-44; and 47-51. Out of which, it was several 13 coiled structures found in whole sequences. In the same manner, 1GZZ (IGF-1) position of the coiled structure are major three clusters i.e. 19-42; 47-53; and 61-70. The total numbers of the coiled structure are 40 out of which 70. Results indicated that even it's diverse in structure but their functionality is the same. It may be caused by their coiled structure because its play a hidden role in the binding site of legend and other foreign molecule interaction in the human body. Comparative studies of secondary structures in human insulin and camel milk components show resemblance only in immune-globulins po5019n and q9gk12 while all other components were structurally different. % identity for po5019n was 47% and 49% for 3 and 8 class while 52% and 39% for 3 and 8 class of q9gk12 (Table 5).

IV. Conclusion

In this study we are an attempt to find out the relation between camel milk and insulin by using bioinformatic tools. A previous study defined that camel milk us as treatment of diabetic type -1 and type -2 patients (Agrawal *et. al*,. 2005, El-Said El-Sherbini *et. al*,. 2010). Besides, studies also promote to use camel milk effective against several viral and bacterial Pathogens (Khitam, 2003), therapeutically used against dropsy, Jaundice, problems of the spleen, tuberculosis, asthma, anemia, and piles (Rao *et. al*,.1970) and other lung ailments and has proven beneficial in the treatment of tuberculosis (Akundov *et. al*,.1972). It is a strong part to attract researchers that camel milk was found to contain approximately 52 micro-unit/ml insulin and it may be the reason for a lesser requirement of insulin in diabetic patients consuming camel milk (Singh, 2001, Agarwal *et. al*,.2005).

Previous studies bridging the gap between clinical study and its associated research however, it not sure regarding camel milk behaves like insulin or insulin-like regulator. Secondary structure study clearly cut indicated that the frequency of helix structure is much similar in all target sequences moreover, protein ID of P01308 contains a number of 5 helix which are almost the same in P06996 (5), Q9GK12 (6) and P05019 (4). In the case of turn structure, all protein IDs number of clusters are not the same but differences are notable that it occurs in protein ID of P01308 (3) followed by P06996 (4) and Q9TUM0 (6), respectively. Frequencies of the coiled structure are maximum in all these templates structure and do not ignore coiled position on positively and negatively in B-factor normalized data. 1GZZ (IGF-1) and 2HIU (Human Insulin) both are partially similar to their functionality but in case of a structural point of view, both are quite diverse their structural similarity. All target sequences are not much significant similar but play a hidden role to act as an insulin mimic.

In other server results, alpha-helical transmembrane protein and beta-barrel transemembrane protein type of protein present in all target sequences, it is very important with its functionally attributes because it is a major category of transmembrane proteins in humans, 27% of all proteins have been estimated to be alpha-helical membrane proteins. These sequences functions are related to iron-binding and transport metals. lactoferrin domain groups act as antimicrobial function in mammals (Graham and Williams 1975; Anderson *et. al*,. 1987).

The study found that the camel insulin itself is most likely not responsible for anti-diabetic properties of camel milk and due to low pH, good buffering agent and presence of metals therefore, camel milk contains ‘insulin-like’ small molecular substances that mimic insulin interaction with its receptor.

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