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COMPUTATIONAL APPROACH AGAINST MILK ALLERGY FOR HYPERSENSTIVITY AND MALNUTRITION IN NEWBORN

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ABSTRACT

The growth and development of a newborn largely depends on the nutrient content of mother's milk as diet intake. Milk is regarded as one of the most essential parts of a healthy diet in almost all over the world. It is the major source of all the nutrients required, especially to the neonates and infants for normal development. Cow milk is the second best source of nutrition for infants. Having said that, up to 6% children are unable to digest cow milk for those suffering from the hypersensitivity reaction, which is the reason for the CMA (Cow Milk Allergy). CMA leads to the necessity of an alternative to cow milk. In such case, sheep milk is regarded as the second possibility. Looking at the scenario where human, cow and sheep's milk are simultaneously required in a population; we study on the content analysis of each milk sample. The contents of various sources of milk for fibronectin, lactoferrin, lysozyme and alpha casein S1 protein were analyzed to identify the protein structure, functions and evolution of the concerned protein families. Further, the protein constituents with physical and chemical parameters for each protein were studied. The secondary structures were especially studied in this protein analysis for a higher level of understanding. The analysis from the study shows that the cow milk has better advantage of essential amino acids as compared to the human and sheep's milk. The current study shows remarkable results with greater similarity in terms of sequence identity and amino acid content of proteins in human and sheep milk as compared to the cow milk.

KEYWORDS: ***Milk Protein, Casein Alpha S1, Lactoferrin, Fibronectin, Lysozyme***

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INTRODUCTION

Human breast milk being a vital source of nutrient and supplement holds a prominent role in the diet of infants. Cases of allergy have been observed caused by human breast milk and the substitute milk from cows[1]. In such cases, the symptoms of cow milk allergy are IgE-mediated activation of mast cells, as well as activation of hyper allergen-specific T cells. Out of the twenty-five known proteins found in cow milk[2] to be harmful and allergy may lead to effect skin (Hives, Oedema, Eczema), Stomach and Intestinal Reactions (Abdominal pain and bloating, Diarrhea, Vomiting, Gas/wind, Cramps), Nose, Throat and Lung reactions (Running nose, sneezing, Itchy eyes, coughing, wheezing, shortness of breath. The proteins, which are mainly responsible for causing the allergy, are casein proteins and Lactoferrin. Lysozyme is responsible for developing the immune response against microbes present in the milk. To estimate the efficiency of lysozyme present in the cow milk, lysozyme was compared with the human milk and sheep milk. The casein is composed of alpha s1-s2, beta and kappa casein from which alpha S1 seems to be the major allergen[3-5]. Along with these proteins, few of the known microbial strains associated with various diseases were also found in milk[6]. In Asian countries like India, there is the unavailability of sheep milk compared to other countries in the Middle East. Therefore, the main alternative here is cow milk. However, the cases with symptoms of hypersensitivity including vomiting, diarrhea and gastrointestinal problems due to cow milk and are registered huge in number[7-8]. For the wellbeing and survival of infants, we need to analyze the alternative sources of milk that are being used. Hence, the present study is to establish a comparative analysis of milk from human, cow, and sheep to find the best source of nutrition and less allergic to the infants.

MATERIALS AND METHODS

Datasets

The data sets for the study were analyzed. The sequences are downloaded from NCBI (http://www.ncbi.nlm.nih.gov/protein) with accession number [refer Table 1 for the protein name, sources and their Gene Bank ID]. The dataset consist of casein alpha S1, fibronectin, lactoferrin and lysozyme in the human, cow and sheep.

Sequence analysis

The physiochemical analysis of the protein was done by using protparam (web.expasy.org/Protparam). It has a user-friendly interface to input protein sequence and can be used on a specific section of the sequence. The program calculates amino acid composition extinction coefficient, half-life, instability index and grand average of hydropathicity GRAVY9.

Multiple Sequence Alignment

CLUSTALW2 (www.ebi.ac.uk/Tools/msa/clustalw2) is a general purpose multiple sequence alignment tool to find the difference in the conserved domains of the proteins10. It calculates the appropriate possible match and lines them up to study the similarities and differences between the sequences using standard parameters11-12.

Secondary Structure Prediction

To predict the secondary structures from primary sequences GOR method was used. GOR is based on information theory and it was developed by J.Garnier, D.Osguthorpe, and B.Robson. The GOR method analyzes sequences to predict alpha helix, beta sheet, turn, or random coil secondary structure at each position based on 17-amino-acid sequence windows. There is no defined decision constant in GOR. Present version GOR-IV uses all possible fair frequencies of 17 amino acid residues13. The program provides a color-coded prediction, sequence length, percentage of each secondary element. GOR also gives two outputs; one is for better visualization of the prediction and the second depicts score curve for each predicted state.

RESULTS

Four protein sequences of alpha casein S1, fibronectin, lactoferrin, and lysozyme were analyzed [Table 1]. First, alpha S1 casein sequences were considered which helps in the transport of calcium phosphate in the milk14. It consists of 185aa, 214aa, 214aa in the case of Homo sapiens, Bostauras and Oviaries respectively. Second, fibronectin, a protein that helps in the growth and differentiation of cell were analysed15-16; its amino acid sequence length for Homo sapiens, Bostauras and Oviaries are 307aa, 320aa, 126aa respectively. The analysis of lactoferrin and lysozyme was also done as lactoferrin has the functionality of maintaining the innate immunity of the body17, its sequences for Homo sapiens, Bostauras and Oviaries are 711aa, 708aa, 708aa while lysozyme plays a vital role in protecting from microbial infection that is caused by staphylococcus, pseudomonas, streptococcus and campylobacter that are present in milk18. Lysozyme has 148aa, 147aa, and 148aa in Homo sapiens, Bostauras and Oviaries respectively. To calculate percentage similarity of the amino acid content PROTPARAM was used [Table 2.1]. It also computes the nutritional content and percentage composition of all essential amino acids19. Lysine, an essential amino acid is of great importance as body utilizes more than 50% of the dietary protein intake for protein synthesis and biosynthetic pathways20-and it is observed that in most cases Lysine is oxidized21. Lysine is the first limiting amino acid in the milk, which is needed to be fed to the mammalian neonates22, which makes it important to study. By the result obtained from PROTPARAM, it was observed that Lysine concentration is dramatically low in human compared with sheep and cow. Human milk contained only 3.9% of Lysine while sheep and cow showed 5.4% and 7% respectively. Using the GOR method the secondary structure was predicted for all the sequences and hydropathicity was observed [Table 3.1].

Table 1
Protein for comparison analysis

Genbank ID	Sources	Protein name
AAI28229	Homo sapiens	Casein alpha S1
P02662	Bostauras	Casein alpha S1
P04653	Oviaries	Casein alpha S1
AAD04751	Homo sapiens	Fibronectin
CAC86917	Bostauras	Fibronectin
ACJ24822	Oviaries	Fibronectin
AAA59511	Homo sapiens	Lactoferrin
AAA30610	Bostauras	Lactoferrin
AAV92908	Oviaries	Lactoferrin
P61626	Homo sapiens	Lysozyme
AAC37312	Bostauras	Lysozyme
AFP89959	Oviaries	Lysozyme

Table 2.1
Protparam results for amino acid composition of alpha S1 protein

AA	Homo sapiens	Bostauras	Oviaries
Ala (A)	5.90%	5.60%	7.00%
Arg (R)	6.50%	2.80%	2.80%
Asn (N)	8.10%	3.70%	4.70%
Asp (D)	1.60%	3.30%	3.30%
Cys (C)	2.20%	0.50%	0.50%
Gln (Q)	9.20%	6.50%	7.00%
Glu (E)	10.80%	11.70%	9.30%
Gly (G)	0.50%	4.20%	4.20%
His (H)	1.60%	2.30%	1.90%
Ile (I)	4.30%	5.60%	5.60%
Leu (L)	9.20%	10.30%	10.70%
Lys (K)	3.20%	7.00%	7.00%
Met (M)	4.30%	2.80%	2.80%
Phe (F)	2.20%	3.70%	3.30%
Pro (P)	7.60%	7.90%	7.90%
Ser (S)	8.60%	7.50%	8.90%
Thr (T)	2.70%	2.80%	1.90%
Trp (W)	1.10%	0.90%	0.90%
Tyr (Y)	4.90%	4.70%	5.10%
Val (V)	5.40%	6.10%	5.10%

Table 2.2
Protparam results for amino acid composition of Fibronectin protein

AA	Homo sapiens	Bostauras	Oviaries
Ala (A)	3.60%	5.00%	4.00%
Arg (R)	5.90%	5.90%	6.30%
Asn (N)	4.90%	3.80%	5.60%
Asp (D)	6.20%	5.90%	7.10%
Cys (C)	0.30%	2.80%	8.70%
Gln (Q)	2.60%	4.70%	7.10%
Glu (E)	5.90%	5.60%	8.70%
Gly (G)	6.50%	8.10%	11.10%
His (H)	2.60%	1.90%	4.00%
Ile (I)	5.50%	5.90%	1.60%
Leu (L)	6.80%	5.60%	2.40%
Lys (K)	2.00%	5.00%	4.00%
Met (M)	0.30%	0.60%	2.40%
Phe (F)	2.00%	2.20%	2.40%
Pro (P)	9.80%	7.20%	4.00%
Ser (S)	9.80%	7.20%	4.80%
Thr (T)	11.40%	10.60%	6.30%
Trp (W)	1.00%	1.90%	2.40%
Tyr (Y)	2.90%	4.10%	4.80%
Val (V)	10.10%	5.90%	2.40%

Table 2.3
Protparam results for amino acid composition of Lactoferrin protein

AA	Homo sapiens	Bostauras	Oviaries
Ala (A)	9.10%	9.70%	10.50%
Arg (R)	6.30%	5.40%	4.40%
Asn (N)	4.50%	4.10%	4.40%
Asp (D)	5.30%	5.10%	4.50%
Cys (C)	4.60%	4.90%	5.10%
Gln (Q)	4.10%	4.10%	4.40%
Glu (E)	5.90%	5.60%	5.80%
Gly (G)	7.70%	7.20%	7.60%
His (H)	1.30%	1.30%	1.30%
Ile (I)	2.30%	2.10%	2.00%
Leu (L)	9.30%	10.30%	10.00%
Lys (K)	6.50%	7.80%	7.30%
Met (M)	0.80%	0.70%	1.10%
Phe (F)	4.50%	4.00%	3.80%
Pro (P)	4.90%	4.40%	4.50%
Ser (S)	7.00%	6.40%	7.10%
Thr (T)	4.40%	5.20%	4.80%
Trp (W)	1.40%	1.80%	1.60%
Tyr (Y)	3.00%	3.10%	3.10%
Val (V)	7.00%	6.80%	6.80%

Table 2.4
Protparam results for amino acid composition of Lysozyme

AA	Homo sapiens	Bostauras	Oviaries
Ala (A)	10.10%	8.20%	10.10%
Arg (R)	9.50%	2.00%	6.10%
Asn (N)	6.80%	5.40%	5.40%
Asp (D)	5.40%	4.80%	5.40%
Cys (C)	5.40%	5.40%	5.40%
Gln (Q)	4.70%	2.70%	6.10%
Glu (E)	2.00%	4.80%	2.00%
Gly (G)	8.80%	6.80%	7.40%
His (H)	0.70%	2.70%	2.00%
Ile (I)	4.10%	4.80%	5.40%
Leu (L)	8.80%	8.80%	9.50%
Lys (K)	4.10%	8.20%	3.40%
Met (M)	2.00%	1.40%	2.00%
Phe (F)	1.40%	2.70%	2.70%
Pro (P)	1.40%	1.40%	1.40%
Ser (S)	4.70%	9.50%	8.10%
Thr (T)	4.10%	5.40%	4.70%
Trp (W)	3.40%	4.10%	4.10%
Tyr (Y)	4.10%	3.40%	2.70%
Val (V)	8.80%	7.50%	6.10%

Comparison of amino acid residues of the proteins giving specific position with change in secondary structure

Table 3.1
Alpha Casein S1 Comparison for Homo sapiens VS Cow

Base change	Change in primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Bostauras	Homo sapiens	Bostauras	Homo sapiens	Bostauras
28	E	Q	Hydrophilic		C	H
29	R	E	Hydrophilic		C	H
30	L	V	HYDROPHOBIC		C	H
31	Q	L	Hydrophilic	HYDROPHOBIC	C	H
32	N	N	Hydrophilic		C	H
33	P	E	HYDROPHOBIC	Hydrophilic	C	H
34	S	N	Hydrophilic		C	H
35	E	L	Hydrophilic	HYDROPHOBIC	C	H
36	S	L	Hydrophilic	HYDROPHOBIC	C	H
45	L	E	HYDROPHOBIC	Hydrophilic	H	C
46	E	V	Hydrophilic	HYDROPHOBIC	H	C
47	S	F	Hydrophilic	HYDROPHOBIC	H	C
48	R	G	Hydrophilic	HYDROPHOBIC	H	C
56	N	S	Hydrophilic		H	C
57	R	K	Hydrophilic		H	C
58	Q	D	Hydrophilic		H	C
59	R	I	Hydrophilic	HYDROPHOBIC	H	C

62	N	E	Hydrophilic		H	C
63	I	S	HYDROPHOBIC	Hydrophilic	H	C
64	L	T	HYDROPHOBIC	Hydrophilic	H	C
68	Q	A	Hydrophilic	HYDROPHOBIC	C	H
69	T	M	Hydrophilic		C	H
74	D	Q	Hydrophilic		C	H
75	T	M	Hydrophilic		C	H
76	R	E	Hydrophilic		C	H
77	N	A	Hydrophilic	HYDROPHOBIC	C	H
78	E	E	Hydrophilic		C	H
79	S	S	Hydrophilic		C	H
83	C	S	Hydrophilic		E	C
84	V	E	HYDROPHOBIC	Hydrophilic	E	C
85	V	E	HYDROPHOBIC	Hydrophilic	E	C
86	A	I	HYDROPHOBIC	HYDROPHOBIC	E	C
90	K	S	Hydrophilic		C	H
91	M	V	Hydrophilic	HYDROPHOBIC	C	H
92	E	E	Hydrophilic		C	H
93	S	Q	Hydrophilic		C	H
94	S	K	Hydrophilic		C	H
95	I	H	HYDROPHOBIC	Hydrophilic	C	H
96	S	I	Hydrophilic	HYDROPHOBIC	C	H
100	E	D	Hydrophilic		H	C
101	E	V	Hydrophilic	HYDROPHOBIC	H	C
102	M	P	Hydrophilic	HYDROPHOBIC	H	C
103	S	S	Hydrophilic		H	C
114	C	L	Hydrophilic	HYDROPHOBIC	C	H
115	R	R	Hydrophilic		C	H
116	L	L	HYDROPHOBIC	HYDROPHOBIC	C	H
117	N	K	Hydrophilic		C	H
118	E	K	Hydrophilic	HYDROPHOBIC	C	H
122	L	P	HYDROPHOBIC		H	C
123	Q	Q	Hydrophilic	Hydrophilic	H	C
124	L	L	HYDROPHOBIC		H	E
125	Q	E	Hydrophilic	Hydrophilic	H	E
126	A	I	HYDROPHOBIC		H	E
127	V	V	HYDROPHOBIC		H	C
128	H	P	Hydrophilic		H	C
140	E	E	Hydrophilic	Hydrophilic	C	H
141	N	G	Hydrophilic		C	H
142	S	I	Hydrophilic		C	H
143	H	H	Hydrophilic		C	H
144	V	A	HYDROPHOBIC		C	H
145	Q	Q	Hydrophilic		C	H
147	P	K	HYDROPHOBIC	Hydrophilic	H	C

Table 3.2

Alpha Casein S1 Comparison for Human and Sheep

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Oviaries	Homo sapiens	Oviaries	Homo sapiens	Oviaries
28	c	S	Hydrophilic		C	H
29	R	E	Hydrophilic		C	H
30	L	V	HYDROPHOBIC		C	H
31	Q	L	Hydrophilic		C	H
32	N	N	Hydrophilic		C	H
33	P	E	HYDROPHOBIC	Hydrophilic	C	H
34	S	N	Hydrophilic		C	H
35	E	L	Hydrophilic	HYDROPHOBIC	C	H
36	S	L	Hydrophilic	HYDROPHOBIC	C	H
45	L	E	HYDROPHOBIC	Hydrophilic	H	C
51	Y	N	Hydrophilic		H	C
56	N	S	Hydrophilic		H	C
57	R	K	Hydrophilic		H	C
58	Q	D	Hydrophilic		H	C
59	R	I	Hydrophilic	HYDROPHOBIC	H	C
62	N	E	Hydrophilic		H	C
63	I	S	HYDROPHOBIC	Hydrophilic	H	C
68	Q	A	Hydrophilic	HYDROPHOBIC	C	H
69	T	M	Hydrophilic		C	H
74	D	Q	Hydrophilic		C	H
75	T	M	Hydrophilic		C	H
76	R	K	Hydrophilic		C	H
83	C	S	Hydrophilic		E	C
84	V	E	HYDROPHOBIC	Hydrophilic	E	C
85	V	E	HYDROPHOBIC	Hydrophilic	E	C
86	A	I	HYDROPHOBIC		E	C
91	M	A	Hydrophilic	HYDROPHOBIC	C	H

92	E	E	Hydrophilic		C	H
93	S	Q	Hydrophilic		C	H
94	S	K	Hydrophilic		C	H
95	I	Y	HYDROPHOBIC	Hydrophilic	C	H
96	S	I	Hydrophilic		C	H
97	S	Q	Hydrophilic		C	H
100	H	D	Hydrophilic		H	C
101	H	V	Hydrophilic	HYDROPHOBIC	H	C
102	H	P	Hydrophilic	HYDROPHOBIC	H	C
103	H	S	Hydrophilic		H	C
114	C	L	Hydrophilic		C	H
115	R	R	Hydrophilic		C	H
116	L	L	HYDROPHOBIC		C	H
117	N	K	Hydrophilic		C	H
118	E	K	Hydrophilic		C	H
122	L	P	HYDROPHOBIC		H	C
123	Q	Q	Hydrophilic		H	C
124	L	L	HYDROPHOBIC		H	E
125	Q	E	Hydrophilic		H	E
126	A	I	HYDROPHOBIC		H	E
127	V	V	HYDROPHOBIC		H	C
128	H	P	Hydrophilic		H	C
146	V	Q	HYDROPHOBIC	Hydrophilic	H	C
147	P	K	HYDROPHOBIC	Hydrophilic	H	C
173	A	A	HYDROPHOBIC		H	C
177	A	G	HYDROPHOBIC		E	C
178	V	A	HYDROPHOBIC		E	C
182	P	L	HYDROPHOBIC		C	E
186	M	T	Hydrophilic		E	C
187	Q	Q	Hydrophilic		E	C
188	Y	Y	Hydrophilic		E	C

Table 3.3
Fibronectin Comparison for Homo sapiens and Cow

	Change primary sequence		**Change in properties**		**Change in secondary structure**	
Base change	Homo sapiens	Bostauras	Homo sapiens	Bostauras	Homo sapiens	Bostauras
42	R	L	Hydrophilic	HYDROPHOBIC	C	E
52	I	Q	HYDROPHOBIC	Hydrophilic	E	C
53	V	G	HYDROPHOBIC		E	C
54	N	V	Hydrophilic	HYDROPHOBIC	C	E
58	T	L	Hydrophilic	HYDROPHOBIC	C	E
67	H	A	Hydrophilic	HYDROPHOBIC	C	E
68	L	R	HYDROPHOBIC	Hydrophilic	C	E
69	E	V	Hydrophilic	HYDROPHOBIC	C	E
75	G	T	HYDROPHOBIC	Hydrophilic	E	C
81	W	S	Hydrophilic		C	E
82	E	W	Hydrophilic		C	E
91	G	T	HYDROPHOBIC	Hydrophilic	E	C
92	Y	G	Hydrophilic	HYDROPHOBIC	E	C
96	T	D	Hydrophilic		E	C
107	L	P	HYDROPHOBIC		E	C
108	E	I	Hydrophilic	HYDROPHOBIC	E	C
109	E	Q	Hydrophilic		E	C
112	H	I	Hydrophilic	HYDROPHOBIC	E	C
118	C	S	Hydrophilic		C	E
128	E	T	Hydrophilic		E	C
129	Y	D	Hydrophilic		E	C
130	N	Y	Hydrophilic		E	C
146	S	V	Hydrophilic	HYDROPHOBIC	C	E
147	D	V	Hydrophilic	HYDROPHOBIC	C	E
170	R	L	Hydrophilic	HYDROPHOBIC	E	C
184	F	G	HYDROPHOBIC		E	C
188	Y	K	Hydrophilic		C	E
189	S	Y	Hydrophilic		C	E
196	D	P	Hydrophilic	HYDROPHOBIC	H	C
197	V	R	HYDROPHOBIC	Hydrophilic	H	C
198	A	E	HYDROPHOBIC	Hydrophilic	H	E
199	E	V	Hydrophilic	HYDROPHOBIC	H	E
200	L	V	HYDROPHOBIC		H	C
201	S	P	Hydrophilic	HYDROPHOBIC	H	C
219	E	T	Hydrophilic		E	C
220	Y	E	Hydrophilic		E	C
221	V	Y	HYDROPHOBIC	Hydrophilic	E	H
222	V	T	HYDROPHOBIC	Hydrophilic	E	H
223	S	I	Hydrophilic	HYDROPHOBIC	E	H
224	V	Q	HYDROPHOBIC	Hydrophilic	E	H

225	S	V	Hydrophilic	HYDROPHOBIC	E	H
226	S	I	Hydrophilic	HYDROPHOBIC	E	H
227	V	A	HYDROPHOBIC		E	H
228	Y	L	Hydrophilic	HYDROPHOBIC	E	H
229	E	K	Hydrophilic		C	H
260	S	Y	Hydrophilic		C	E
261	D	T	Hydrophilic		C	E
262	I	V	HYDROPHOBIC		C	E
263	T	S	Hydrophilic		C	E
264	A	H	HYDROPHOBIC		C	E
265	N	Y	Hydrophilic		C	E
266	S	A	Hydrophilic	HYDROPHOBIC	C	E
267	F	I	HYDROPHOBIC		E	C
268	T	G	Hydrophilic	HYDROPHOBIC	E	C
269	V	E	HYDROPHOBIC	Hydrophilic	E	H
270	H	E	Hydrophilic		E	H
271	W	W	Hydrophilic		E	H
272	I	E	HYDROPHOBIC	Hydrophilic	E	H
273	A	R	HYDROPHOBIC	Hydrophilic	C	H
274	P	L	HYDROPHOBIC		C	H
284	R	Q	Hydrophilic		C	E
285	H	C	Hydrophilic		C	E
286	H	L	Hydrophilic	HYDROPHOBIC	C	E
287	P	G	HYDROPHOBIC		C	E
288	E	F	Hydrophilic		C	E
294	P	R	HYDROPHOBIC	Hydrophilic	C	E
313	R	K	Hydrophilic		C	E
314	E	W	Hydrophilic		C	E
315	D	D	Hydrophilic		C	E
323	S	M	Hydrophilic		C	E
331	P	N	HYDROPHOBIC	Hydrophilic	E	C
332	G	G	HYDROPHOBIC		E	C

Table 3.4
Fibronectin Comparison for Homo sapiens and Sheep

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Oviaries	Homo sapiens	Oviaries	Homo sapiens	Oviaries
186	V	E	HYDROPHOBIC	Hydrophilic	E	C
187	R	K	Hydrophilic		E	C
221	V	Q	HYDROPHOBIC	Hydrophilic	E	C
229	E	G	Hydrophilic	HYDROPHOBIC	C	E
263	T	K	Hydrophilic		C	E
264	A	T	HYDROPHOBIC	Hydrophilic	C	E
265	N	Y	Hydrophilic		C	E
266	S	H	Hydrophilic		C	E
268	T	G	Hydrophilic	HYDROPHOBIC	E	C
269	V	E	HYDROPHOBIC	Hydrophilic	E	H
270	H	Q	Hydrophilic		E	H
271	W	W	Hydrophilic		E	H
272	I	Q	HYDROPHOBIC	Hydrophilic	E	H
273	A	K	HYDROPHOBIC	Hydrophilic	C	H
274	P	E	HYDROPHOBIC	Hydrophilic	C	E
275	R	Y	Hydrophilic		C	E
277	T	L	Hydrophilic	HYDROPHOBIC	C	E
278	I	G	HYDROPHOBIC		C	E
279	T	A	Hydrophilic	HYDROPHOBIC	C	E
280	G	I	HYDROPHOBIC		C	E
283	I	C	HYDROPHOBIC	Hydrophilic	E	C

Table 3.5
Lactoferrin Comparison for Human and Cow

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Bostauras	Homo sapiens	Bostauras	Homo sapiens	Bostauras
12	G	G	HYDROPHOBIC		C	E
13	A	A	HYDROPHOBIC		H	E
14	L	L	HYDROPHOBIC		H	E
15	G	G	HYDROPHOBIC		H	E
16	L	L	HYDROPHOBIC		H	E
17	C	C	Hydrophilic		H	E
18	L	L	HYDROPHOBIC		H	E
19	A	A	HYDROPHOBIC		H	E
25	S	N	Hydrophilic		E	C
26	V	V	HYDROPHOBIC		E	C
32	S	S	Hydrophilic		C	E
36	A	W	HYDROPHOBIC	Hydrophilic	C	E

37	T	F	Hydrophilic		C	E
41	Q	R	Hydrophilic		C	E
42	W	W	Hydrophilic		C	E
43	Q	Q	Hydrophilic		C	E
44	R	W	Hydrophilic		C	E
45	N	R	Hydrophilic		C	E
46	M	M	Hydrophilic		C	E
47	R	K	Hydrophilic		C	E
55	E	T	Hydrophilic		C	H
56	E	C	Hydrophilic		E	H
57	C	V	Hydrophilic	HYDROPHOBIC	E	H
58	C	R	Hydrophilic		C	H
59	C	R	Hydrophilic		C	H
60	C	A	Hydrophilic	HYDROPHOBIC	C	H
61	C	F	Hydrophilic	HYDROPHOBIC	C	H
62	C	A	Hydrophilic	HYDROPHOBIC	C	H
63	C	L	Hydrophilic	HYDROPHOBIC	C	H
64	C	E	Hydrophilic		C	H
65	H	C	Hydrophilic		C	H
73	R	K	Hydrophilic		C	H
77	V	V	HYDROPHOBIC		H	E
78	T	T	Hydrophilic		H	E
79	L	L	HYDROPHOBIC		C	E
83	F	M	HYDROPHOBIC	Hydrophilic	H	E
84	I	V	HYDROPHOBIC		H	E
85	Y	F	Hydrophilic	HYDROPHOBIC	H	E
86	E	E	Hydrophilic		H	E
87	A	A	HYDROPHOBIC		H	C
96	P	P	HYDROPHOBIC		C	H
97	V	V	HYDROPHOBIC		C	H
125	Q	Q	Hydrophilic		H	C
126	L	L	HYDROPHOBIC		H	E
127	N	D	Hydrophilic		H	E
128	E	Q	Hydrophilic		H	E
129	L	L	HYDROPHOBIC		H	E
145	W	W	Hydrophilic		C	E
146	N	V	Hydrophilic	HYDROPHOBIC	C	E
147	V	I	HYDROPHOBIC		C	E
154	P	P	HYDROPHOBIC		E	C
155	F	Y	HYDROPHOBIC	Hydrophilic	E	C
156	L	L	HYDROPHOBIC		E	C
173	F	F	HYDROPHOBIC		C	H
189	L	L	HYDROPHOBIC		E	C
190	C	C	Hydrophilic		E	C
193	C	C	Hydrophilic		E	C
230	R	K	Hydrophilic		H	C
231	E	E	Hydrophilic		H	C
232	S	T	Hydrophilic		H	E
233	T	T	Hydrophilic		H	E
234	V	V	HYDROPHOBIC		H	E
235	F	F	HYDROPHOBIC		H	E
236	E	E	Hydrophilic		H	C
240	D	E	Hydrophilic		H	C
241	E	K	Hydrophilic		H	C
242	A	A	HYDROPHOBIC		H	C
243	E	D	Hydrophilic		H	C
250	L	L	HYDROPHOBIC		C	H
251	C	C	Hydrophilic		C	H
252	P	L	HYDROPHOBIC		C	H
260	D	D	Hydrophilic		C	H
261	K	A	Hydrophilic		C	H
262	F	F	HYDROPHOBIC		C	H
263	K	K	Hydrophilic		C	H
264	D	E	Hydrophilic		C	H
267	L	L	HYDROPHOBIC		E	C
268	A	A	HYDROPHOBIC		E	C
279	S	S	Hydrophilic		E	C
305	K	S	Hydrophilic		C	E
309	F	E	HYDROPHOBIC	Hydrophilic	E	C
316	K	R	Hydrophilic		H	C
322	D	D	Hydrophilic		C	H
323	S	S	Hydrophilic		C	H
324	A	A	HYDROPHOBIC		C	H
325	I	L	HYDROPHOBIC		C	H
328	S	L	Hydrophilic		C	E
329	R	R	Hydrophilic		C	E
336	S	S	Hydrophilic		C	H
337	G	A	HYDROPHOBIC		C	H

338	L	L	HYDROPHOBIC		E	H
339	Y	Y	Hydrophilic		E	H
340	L	L	HYDROPHOBIC		C	H
343	G	R	HYDROPHOBIC	Hydrophilic	C	H
344	Y	Y	Hydrophilic		C	H
366	V	V	HYDROPHOBIC		E	H
367	W	V	Hydrophilic		E	H
368	C	W	Hydrophilic		E	H
369	A	C	HYDROPHOBIC	Hydrophilic	E	H
370	V	A	HYDROPHOBIC		E	H
375	L	Q	HYDROPHOBIC	Hydrophilic	E	C
376	R	K	Hydrophilic		E	C
377	K	K	Hydrophilic		E	H
378	C	C	Hydrophilic		C	H
379	N	Q	Hydrophilic		C	H
380	Q	Q	Hydrophilic		C	H
381	W	W	Hydrophilic		C	H
382	S	S	Hydrophilic		E	C
383	G	Q	HYDROPHOBIC	Hydrophilic	E	C
388	S	N	Hydrophilic		E	C
393	S	T	Hydrophilic		C	E
394	A	A	HYDROPHOBIC		C	E
398	E	D	Hydrophilic		H	C
399	D	D	Hydrophilic		H	C
400	C	C	Hydrophilic		H	E
401	I	I	HYDROPHOBIC		H	E
402	A	V	HYDROPHOBIC		H	E
403	L	L	HYDROPHOBIC		H	E
404	V	V	HYDROPHOBIC		H	E
405	L	L	HYDROPHOBIC		H	E
406	K	K	Hydrophilic		H	E
413	S	N	Hydrophilic		H	C
414	L	L	HYDROPHOBIC		H	C
415	D	D	Hydrophilic		H	C
431	L	L	HYDROPHOBIC		C	E
432	A	A	HYDROPHOBIC		C	E
444	D	D	Hydrophilic		C	E
447	C	C	Hydrophilic		C	E
448	V	V	HYDROPHOBIC		C	E
449	D	L	Hydrophilic		C	E
456	L	L	HYDROPHOBIC		E	H
457	A	A	HYDROPHOBIC		E	H
458	V	V	HYDROPHOBIC		E	H
459	A	A	HYDROPHOBIC		E	H
460	V	V	HYDROPHOBIC		E	H
461	V	V	HYDROPHOBIC		E	H
462	R	K	Hydrophilic		E	H
463	R	K	Hydrophilic		E	H
587	K	N	Hydrophilic		H	C
588	L	R	HYDROPHOBIC	Hydrophilic	H	C
589	A	E	HYDROPHOBIC	Hydrophilic	H	C
590	D	D	Hydrophilic		H	C
591	F	F	HYDROPHOBIC		H	E
592	A	R	HYDROPHOBIC	Hydrophilic	H	E
593	L	L	HYDROPHOBIC		H	E
594	L	L	HYDROPHOBIC		H	E
595	C	C	Hydrophilic		H	E
603	V	V	HYDROPHOBIC		E	H
604	T	T	Hydrophilic		E	H
605	E	E	Hydrophilic		E	H
606	A	A	HYDROPHOBIC		E	H
607	R	Q	Hydrophilic		E	H
608	S	S	Hydrophilic		E	C
618	A	A	HYDROPHOBIC		H	C
619	V	V	HYDROPHOBIC		H	E
620	V	V	HYDROPHOBIC		H	E
621	S	S	Hydrophilic		H	E
622	R	R	Hydrophilic		H	E
623	M	S	Hydrophilic		H	C
624	D	D	Hydrophilic		H	C
686	Q	E	Hydrophilic		C	H
687	Y	Y	Hydrophilic		E	H
688	V	V	HYDROPHOBIC		E	H
689	A	T	HYDROPHOBIC	Hydrophilic	E	H
690	G	A	HYDROPHOBIC		E	H
691	I	I	HYDROPHOBIC		E	H
692	T	A	Hydrophilic	HYDROPHOBIC	E	H

Table 3.6
Lactoferrin Comparison for Human and Sheep

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Oviaries	Homo sapiens	Oviaries	Homo sapiens	Oviaries
12	G	G	HYDROPHOBIC		C	E
13	A	A	HYDROPHOBIC		H	E
14	L	L	HYDROPHOBIC		H	E
15	G	G	HYDROPHOBIC		H	E
16	L	L	HYDROPHOBIC		H	E
17	C	C	Hydrophilic		H	E
18	L	L	HYDROPHOBIC		H	E
19	A	A	HYDROPHOBIC		H	E
25	S	N	Hydrophilic		E	C
26	V	V	HYDROPHOBIC		E	C
32	S	S	Hydrophilic		C	E
38	E	K	Hydrophilic		E	C
42	W	W	Hydrophilic		C	H
43	Q	Q	Hydrophilic		C	H
44	R	R	Hydrophilic		C	H
45	N	R	Hydrophilic		C	H
58	K	R	Hydrophilic		C	E
62	P	A	HYDROPHOBIC		C	H
63	I	L	HYDROPHOBIC		C	H
64	Q	E	Hydrophilic		C	H
65	C	C	Hydrophilic		C	H
73	R	K	Hydrophilic		H	C
74	A	A	HYDROPHOBIC		H	C
75	D	D	Hydrophilic		H	C
76	A	A	HYDROPHOBIC		H	E
77	V	V	HYDROPHOBIC		H	E
78	T	T	Hydrophilic		H	E
79	L	L	HYDROPHOBIC		C	E
83	F	M	HYDROPHOBIC	Hydrophilic	H	E
84	I	V	HYDROPHOBIC		H	E
85	Y	F	Hydrophilic	HYDROPHOBIC	H	E
86	E	E	Hydrophilic		H	E
87	A	A	HYDROPHOBIC		H	C
97	V	V	HYDROPHOBIC		C	H
125	Q	Q	Hydrophilic		H	E
126	L	L	HYDROPHOBIC		H	E
127	N	D	Hydrophilic		H	E
128	E	Q	Hydrophilic		H	E
129	L	L	HYDROPHOBIC		H	E
130	Q	Q	Hydrophilic		C	E
131	G	G	HYDROPHOBIC		C	E
230	R	K	Hydrophilic		H	C
231	E	E	Hydrophilic		H	C
232	S	T	Hydrophilic		H	E
233	T	T	Hydrophilic		H	E
234	V	V	HYDROPHOBIC		H	E
235	F	F	HYDROPHOBIC		H	E
236	E	E	Hydrophilic		H	C
240	D	E	Hydrophilic		H	C
241	E	K	Hydrophilic		H	C
242	A	A	HYDROPHOBIC		H	C
243	E	D	Hydrophilic		H	C
250	L	L	HYDROPHOBIC		C	H
251	C	C	Hydrophilic		C	H
260	D	D	Hydrophilic		C	H
261	K	A	Hydrophilic	HYDROPHOBIC	C	H
262	F	F	HYDROPHOBIC		C	H
263	K	K	Hydrophilic		C	H
264	D	E	Hydrophilic		C	H
322	D	D	Hydrophilic		C	H
323	S	S	Hydrophilic		C	H
324	A	A	HYDROPHOBIC		C	H
327	F	F	HYDROPHOBIC		C	E
328	S	V	Hydrophilic		C	E
329	R	R	Hydrophilic		C	E
337	G	A	HYDROPHOBIC		C	H
338	L	L	HYDROPHOBIC		E	H
339	Y	Y	Hydrophilic		E	H
340	L	L	HYDROPHOBIC		C	H
456	L	L	HYDROPHOBIC		E	H
457	A	A	HYDROPHOBIC		E	H
458	V	V	HYDROPHOBIC		E	H

459	A	A	HYDROPHOBIC		E	H
460	V	V	HYDROPHOBIC		E	H
461	V	V	HYDROPHOBIC		E	H
462	R	K	Hydrophilic		E	H
463	R	K	Hydrophilic		E	H
588	L	N	HYDROPHOBIC	Hydrophilic	H	C
589	A	R	HYDROPHOBIC	Hydrophilic	H	C
590	D	E	Hydrophilic		H	C
591	F	D	HYDROPHOBIC	Hydrophilic	H	C
592	A	F	HYDROPHOBIC		H	E
593	L	R	HYDROPHOBIC	Hydrophilic	H	E
594	L	L	HYDROPHOBIC		H	E
595	C	L	Hydrophilic	HYDROPHOBIC	H	E
596	L	C	HYDROPHOBIC	Hydrophilic	H	E
603	V	V	HYDROPHOBIC		E	C
604	T	T	Hydrophilic		E	H
605	E	E	Hydrophilic		E	H
606	A	A	HYDROPHOBIC		E	H
607	R	Q	Hydrophilic		E	H
608	S	S	Hydrophilic		E	C
618	A	A	HYDROPHOBIC		H	C
619	V	V	HYDROPHOBIC		H	E
620	V	V	HYDROPHOBIC		H	E
621	S	S	Hydrophilic		H	E
622	R	R	Hydrophilic		H	C
623	M	S	Hydrophilic		H	C
624	D	D	Hydrophilic		H	C

Table 3.7
Lysozyme Comparison for Human and Cow

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Bostauras	Homo sapiens	Bostauras	Homo sapiens	Bostauras
9	L	F	HYDROPHOBIC		E	H
10	V	L	HYDROPHOBIC		E	H
11	L	F	HYDROPHOBIC		E	H
12	L	L	HYDROPHOBIC		E	H
13	S	S	Hydrophilic		C	H
14	V	V	HYDROPHOBIC		C	H
15	T	A	Hydrophilic	HYDROPHOBIC	C	H
16	V	V	HYDROPHOBIC		C	H
39	R	K	Hydrophilic		E	C
40	G	G	HYDROPHOBIC		E	C
41	I	V	HYDROPHOBIC		E	C
94	A	G	HYDROPHOBIC		E	C
95	C	C	Hydrophilic		E	C
96	H	H	Hydrophilic		C	E
97	L	V	HYDROPHOBIC		C	E
116	R	H	Hydrophilic		H	C
117	V	I	HYDROPHOBIC		H	E
118	V	V	HYDROPHOBIC		H	E
124	I	I	HYDROPHOBIC		H	E
125	R	T	Hydrophilic		H	E
126	A	A	HYDROPHOBIC		H	E
127	W	W	Hydrophilic		H	E
128	V	V	HYDROPHOBIC		H	E
129	A	A	HYDROPHOBIC		H	E
130	W	W	Hydrophilic		H	E
131	R	K	Hydrophilic		H	C

Table 3.8
Lysozyme Comparison for Human and Sheep

Base change	Change primary sequence		Change in properties		Change in secondary structure	
	Homo sapiens	Oviaries	Homo sapiens	Oviaries	Homo sapiens	Oviaries
8	G	G	HYDROPHOBIC			
9	L	L	HYDROPHOBIC			
10	V	L	HYDROPHOBIC			
11	L	L	HYDROPHOBIC			
12	L	L	HYDROPHOBIC			
13	S	S	Hydrophilic			
14	V	V	HYDROPHOBIC			
15	T	A	Hydrophilic	HYDROPHOBIC		
16	V	V	HYDROPHOBIC			
17	Q	Q	Hydrophilic			
18	G	A	HYDROPHOBIC			

52	W	W	Hydrophilic
61	T	T	Hydrophilic
62	N	N	Hydrophilic
63	Y	Y	Hydrophilic
72	Y	Y	Hydrophilic
73	G	G	HYDROPHOBIC
83	C	C	Hydrophilic
124	I	I	HYDROPHOBIC
125	R	R	Hydrophilic
126	A	A	HYDROPHOBIC
127	W	W	Hydrophilic
128	V	V	HYDROPHOBIC
129	A	A	HYDROPHOBIC
130	W	W	Hydrophilic
131	R	R	Hydrophilic

DISCUSSION

There are several different proteins in the human, cow and sheep's milk, but casein alpha S1 seems to be a major allergen. Similarly, fibronectin is involved in the pathogenesis of the infectious from the initiation of the infection through the final stages of wound healing, wound healing being the most salient features of fibronectin. The third protein Lactoferrin is considered, as this possesses various biological functions including antibacterial, antiviral and antiparasitic activity. Finally, Lysozyme, the first antibiotic, a small enzyme possess major antibacterial properties. The apt selection of the proteins helps categorize milk from different sources more efficiently. The current study involves the physiochemical analysis of the function of each protein. The function of any protein is altered by a slight change in its folding, which results in the change in the secondary and tertiary structure of the protein. The most common approach is to observe the changes in the primary sequences as the protein with similar sequences are ought to perform similar functions23. For most proteins, it is possible to predict the function and evolutionary changes by their sequences. Since the sequence similarity between Casein alpha S1 of Homo sapiens and Oviareis is very high which clearly depicts the reason for being sheep milk as the substitute for human milk24. In fibronectin, the sequence similarity between Homo sapiens and Oviaries is very less which makes Oviaries milk less hyper allergic. Similarly, lysozyme and lactoferrin single change in the amino acid sequence leads to a considerable change in the properties, which makes it hyper allergic to humans. The results of the protparam favored the same inference, as there was considerable change in the amino acid constituent for all the sequences [Table 3]. Results from PROTPARAM showed that cow milk has Lysine content roughly double than human milk, which concludes cow milk as the best source of nutrition compared to sheep and human. To have firmness for the outcome the secondary structure was studied using GOR method, which gave all the dramatic changes in the properties for the sequences when compared with one another. The detailed study of hydropathicity clearly shows the differences in the human, cow and sheep milk. In the PROTPARAM results of alpha casein S1, the Human and sheep milk share great similarity(with only 15 amino acid changes) as compared to the human and cow milk(43 amino acids changes)[see Table 3 part 3.1 and 3.2].Similarly, for fibronectin, the similarity between human and sheep(with only 12 amino acid changes) is higher than human and cow(with 35 amino acid changes) [see table 3 part 3.3 and 3.4].Also, for Lactoferrin, in the comparison of human and sheep similarity(with 9 amino acid changes) is higher as compared to human and cow[with 35 amino acid changes] [see table 3 part 3.5 and 3.6]. The Lysozyme shows maximum similarity with both cow and sheep milk with only one amino acid change in the comparison of human and cow as well as human and sheep milk. [See table 3 part 3.7 and 3.8].The hydropathicity analysis show sheep milk as the better substitute for human breast milk than the cow milk. There are many anecdotal proves of sheep milk being used as a substitute in place of human milk in the case of allergy, but to have a concrete conclusion, this study was done and the reasons for hyper-allergy due to human and cow milk are unveiled.

CONCLUSION

The study for four-protein sequences alpha casein S1, fibronectin, Lactoferrin and lysozyme, each of them plays a vital role in the human body has been done. It was deduced from the study that the changes in the sequences and secondary structures make the milk more or less allergic to the infants. Multiple sequence alignment proves sheep milk to be the better alternative in case of hypersensitivity and allergy towards milk from human and cow. The cases of malnutrition are also huge in numbers; less lysine intake in the body is a major reason for malnutrition in the babies. Cow milk has the highest percentage of lysine, which makes it best remedy in case of infant malnutrition. It can be concluded that cow milk should be used as a dietary supplement in the cases of malnutrition and to avoid the cases of hypersensitivity sheep milk should be preferred. It can also help the nutritionist and pediatrics in coping up with the cases of hypersensitivity and malnutrition by providing best available alternatives against hypersensitivity and malnutrition in infants.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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