Study of Serum Vitamin Profiles in Diabetes Mellitus Patients by using Artificial Neural Networks in a District, Andhra Pradesh, India

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Abstract: ***Diabetes mellitus is a universally prevalent disorder leading to death rooted from various issues of which under nourishment is a major reason in which Micronutrients have been investigated as potential preventive and treatment agents for both type 1 and type 2 diabetes and for common complications of diabetes. At this point, we focused to analyze methodological differences in the profiles of both fat-soluble vitamins and water soluble vitamin in patients with diabetes mellitus from urban and rural areas to know the possible role of these substance(s) in the pathogenesis of diabetes mellitus and an attempt has been done to optimize the serum vitamin concentrations. In both male and female subjects of vitamin supplemented group, slightly lower concentrations of vitamins A, E, C, B_1, B_2, B_6 and B_{12} were observed when compared to the control group. By using ANN, the vitamins showing the maximum decline effect on the A and E.***

Keywords: Diabetes Mellitus, Vitamins concentrations, Artificial Neural Networks, Andhra Pradesh

1. Introduction

Diabetes is the most prevalent endocrine disorder in the world. The total estimated number of people with diabetes worldwide is 347 million. WHO predicts that diabetes would emerge as seventh leading cause of death by 2030. It is a multi-factorial complex disease which is caused due to genetic and environmental factors of which malnutrition has been suggested as one of the major causes of diabetes mellitus in certain geographic areas. More than 80% of total diabetes deaths are estimated to happen in countries with low and middle income.

Over the last 20 years, numerous studies have found alterations in micronutrient status of patients with diabetes mellitus, and in some studies deficiency of certain minerals or vitamins is correlated with presence of diabetic complications. However, these findings have not been comprehensively evaluated. In view of this, depending upon the essentiality of vitamins especially in human body; it is proposed to understand their profiles in diabetic populations But many studies have verified the status of individual vitamins in a particular disease condition.

At this point, we focused to analyze methodological differences in the profiles of both fat-soluble vitamins A (Retinol), D (Cholecalciferol), E (α-Tocopherol) and K (Menaquinone) and water soluble vitamin C and B-complex vitamins: B_1 (Thiamin), B_2 (Riboflavin), B_3 (Nicotinic acid), B_6 (Pyridoxine), B_9 (Folic acid) and B_{12} (Cyanocobalamin) in patients with diabetes mellitus from urban and rural areas to know the possible role of these substance(s) in the pathogenesis of diabetes mellitus and an attempt has been done to optimize the serum vitamin concentrations. The key factor to optimize a process is to understand the system's dynamics which can be obtained by using an accurate mathematical model i.e., non-linear statistical data modeling tool, Artificial Neural Networks (ANN).

In previous studies, authors developed various statistical models to evaluate the vitamin status and noticed that the complexity of vitamin levels in the body in diverse pathological conditions was not well understood due to their inadequate accuracies. To overcome this drawback, a methodology based on ANN was adopted.

These days, usage of ANN is becoming popular in the research field especially in medical and clinical research. ANN offers a new dimension for this study, due to its unique advantages such as non-linearity complex behavior and ability to model poorly understood biological systems. It is suitable for optimizing the exact study of systems from all points of view, without performing additional experiments. With the remarkable ability to derive meaning from complicated or imprecise data, ANN can be used to extract patterns and detect trends that are too complex to be noticed by either humans or insilico methods. Development of suitable models, allows optimization and implementation in the process which is highly desirable.

2. Materials and Methods

In the present study, two groups of diabetic subjects from urban and rural areas of about 42 sample was taken from East Godavari district, AP, India were selected where one group was Supplemented Group (SG) that received one multivitamin capsule per day under medical supervision while the other group was Non supplemented group (NSG) that did not receive any supplementation. Non-diabetic subjects from same geographical area were considered as Control group (CG) and their physical, personal and clinical parameters details were recorded.

Blood samples (2 mL) were collected under medical supervision from the subjects with an informed consent at diabetic care unit, GSL general hospital, Rajahmundry, AP, India.

3. Results and Discussion

Subjects with diabetes mellitus having age between 50 – 60 yrs were considered for this study. The baseline data on physical and clinical characteristics among subjects did not show significant differences. The serum vitamin concentrations of subjects with the diabetes mellitus were presented in Table 1. Gender-wise differences were not found with respect to the concentrations of vitamin A, E, K and B-Complex. However, measurable differences were observed in case of vitamin D and C concentrations. This study was initiated to compare the vitamin (A, D, E, K, C, B_1, B_2, B_3, B_6, B_9 and B_{12}) levels in diabetic subjects of vitamin supplemented group (SG) and non-supplemented group (NSG) with non-diabetic subjects of control group (CG). In both male and female subjects of vitamin supplemented group, slightly lower concentrations of vitamins A, E, C, B_1, B_2, B_6 and B_{12} were observed when compared to the control group. In case of non supplemented group subjects, very low concentrations of A, E, C, B_1, B_2, B_6 and B_{12} vitamins were observed when compared to subjects of control group as well as supplemented group. Thus, the above vitamins were found to be low in diabetic subjects. Diabetes appears to have great effect on the decline of vitamin concentrations. Vitamin supplementation under medical supervision could have prevented sharp fall in the vitamin concentrations.

Table 1: Vitamin levels of subjects with diabetes mellitus.

S. No	Batch No.	Group	VITAMIN CONCENTRATION (ng/mL)										
			Fat soluble				Water soluble						
			A	D	E	K	C	B_1	B_2	B_3	B_6	B_9	B_{12}
1	1*	S.G	238.2	41.082	610.4	0.165	2304.8	2.469	2.952	3.325	5.359	0.730	12.414
2	2*		226.4	39.069	643.0	0.190	2274.2	3.362	2.861	3.055	6.047	0.714	13.413
3	3*		205.2	40.187	635.8	0.195	2317.3	3.563	2.765	2.812	5.898	0.753	13.445
4	4*		238.2	41.082	610.4	0.165	2304.8	2.469	2.952	3.325	5.359	0.730	12.414
5	5*		226.4	39.069	643.0	0.190	2274.2	3.362	2.861	3.055	6.047	0.714	13.413
6	6*		205.2	40.187	635.8	0.195	2317.3	3.563	2.765	2.812	5.898	0.753	13.445
7	7*		238.2	41.082	610.4	0.165	2304.8	2.469	2.952	3.325	5.359	0.730	12.414
8	1		176.9	6.412	605.6	0.175	3055.1	3.171	2.828	2.947	5.698	0.675	12.997
9	2		214.6	6.039	617.1	0.182	3175.3	3.499	2.815	3.109	6.083	0.793	13.117
10	3		200.5	6.859	624.3	0.170	3155.6	3.380	2.615	3.271	5.893	0.750	13.381
11	4		176.9	6.412	605.6	0.175	3055.1	3.171	2.828	2.947	5.698	0.675	12.997
12	5		214.6	6.039	617.1	0.182	3175.3	3.499	2.815	3.109	6.083	0.793	13.117
13	6		200.5	6.859	624.3	0.170	3155.6	3.380	2.615	3.271	5.893	0.750	13.381
14	7		214.6	6.039	617.1	0.182	3175.3	3.499	2.815	3.109	6.083	0.793	13.117
15	1 *	N.S.G	122.7	21.398	506.3	0.082	1935.0	1.786	2.336	1.595	4.917	0.335	7.210
16	2*		151.0	28.407	526.9	0.119	1836.3	1.936	2.191	1.703	4.454	0.601	11.350
17	3*		165.1	25.499	503.9	0.135	1868.6	2.264	2.224	2.352	4.372	0.625	11.702
18	4*		122.7	21.398	506.3	0.082	1935.0	1.786	2.336	1.595	4.917	0.335	7.210
19	5*		151.0	28.407	526.9	0.119	1836.3	1.936	2.191	1.703	4.454	0.601	11.350
20	6*		165.1	25.499	503.9	0.135	1868.6	2.264	2.224	2.352	4.372	0.625	11.702
21	7*		122.7	21.398	506.3	0.082	1935.0	1.786	2.336	1.595	4.917	0.335	7.210
22	1		54.3	5.145	405.2	0.100	2593.7	0.378	0.554	0.324	3.180	0.031	7.218
23	2		136.8	3.952	530.8	0.121	2570.4	1.941	2.139	2.109	4.485	0.238	11.406
24	3		148.6	4.921	525.5	0.139	2780.4	1.827	2.245	1.784	4.454	0.366	11.390
25	4		54.3	5.145	405.2	0.100	2593.7	0.378	0.554	0.324	3.180	0.031	7.218
26	5		136.8	3.952	530.8	0.121	2570.4	1.941	2.139	2.109	4.485	0.238	11.406
27	6		148.6	4.921	525.5	0.139	2780.4	1.827	2.245	1.784	4.454	0.366	11.390
28	7		136.8	3.952	530.8	0.121	2570.4	1.941	2.139	2.109	4.485	0.238	11.406
29	1*	C.G	1068.5	45.034	1125.8	0.937	5356.2	12.077	13.429	6.326	29.531	1.328	31.533
30	2*		990.7	48.612	1236.1	1.024	4482.1	10.911	9.027	5.353	24.928	1.471	38.783
31	3*		837.3	73.217	1322.9	0.991	6250.1	14.842	12.305	6.867	17.904	1.407	34.035
32	4*		1068.5	45.034	1125.8	0.937	5356.2	12.077	13.429	6.326	29.531	1.328	31.533
33	5*		990.7	48.612	1236.1	1.024	4482.1	10.911	9.027	5.353	24.928	1.471	38.783
34	6*		837.3	73.217	1322.9	0.991	6250.1	14.842	12.305	6.867	17.904	1.407	34.035
35	7*		990.7	48.612	1236.1	1.024	4482.1	10.911	9.027	5.353	24.928	1.471	38.783
36	1		462.3	14.614	1029.0	0.469	7556.9	15.740	11.026	6.326	31.925	1.488	31.533
37	2		820.8	25.947	1134.9	0.730	8991.1	8.633	13.328	5.839	22.009	1.364	33.244
38	3		587.3	33.253	1282.1	0.699	6217.8	7.531	8.954	6.623	16.173	1.205	27.625
39	4		462.3	14.614	1029.0	0.469	7556.9	15.740	11.026	6.326	31.925	1.488	31.533
40	5		587.3	33.253	1282.1	0.699	6217.8	7.531	8.954	6.623	16.173	1.205	27.625
41	6		820.8	25.947	1134.9	0.730	8991.1	8.633	13.328	5.839	22.009	1.364	33.244
42	7		587.3	33.253	1282.1	0.699	6217.8	7.531	8.954	6.623	16.173	1.205	27.625

The observed vitamin profile of all subjects was fed as input to the artificial neural network. The network used in this study is fully connected, feed forward and supervised network with back propagation learning rule which is an excellent network for prediction and classification tasks. Here, the input variables were age, disease condition (0 - 3)

and concentration of vitamins. All three parameter groups are considered as three different single data set points.
All the data points were used during training, weights and biases were adjusted to minimize the error. While the network was been optimized, the testing data evaluates the trained network. This process was repeated till the maximum number of fixed epochs or minimum root mean squared error was reached. Then the predicted values of the vitamin concentrations of all the sets of data points were obtained as output of the network
The coefficient of determination (R^2) was used as a measure of the predictive ability of the network and gives an evidence for a satisfactory correlation between the inputs and the predicted outputs. Decision on the optimum topology was based on the minimum error of testing. Each topology was repeated five times to avoid random correlation due to the random initialization of the weights .The statistical indicator R^2 values in the present study remain above the benchmark value of 0.95 for the best fit and well above 0.8 required to meet the minimum criteria.

ANN was used to construct a response surface for the complete experimental plan considering the variables as disease condition (diabetes mellitus), age and vitamin profiles of the subjects. Three dimensional response surface and contour plots for serum vitamin profiles were shown in Figure(s) 1-11.

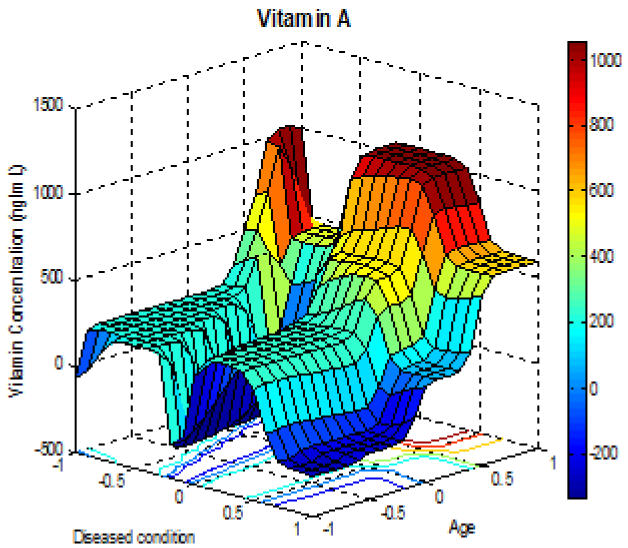

Figure 1: Response Surface plot of vitamin A.

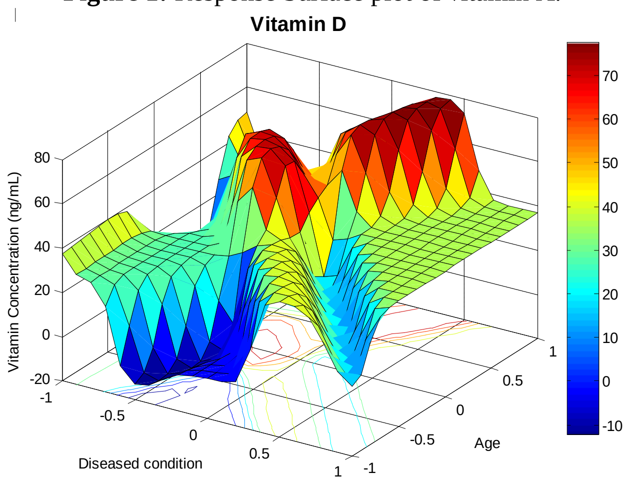

Figure 2: Response Surface plot of vitamin D

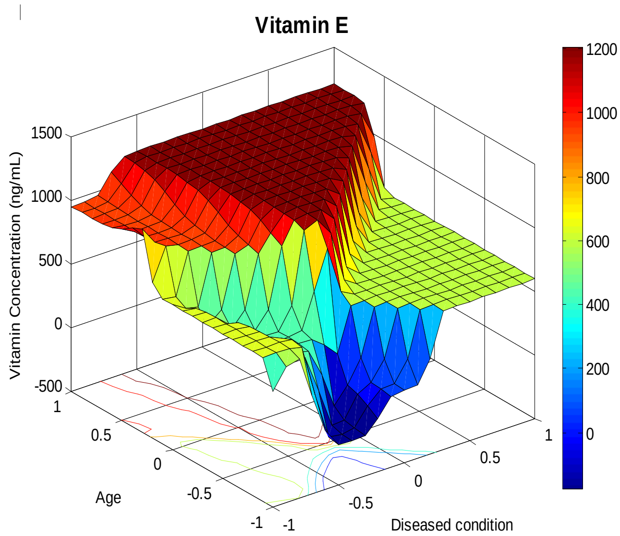

Figure 3: Response Surface plot of vitamin E

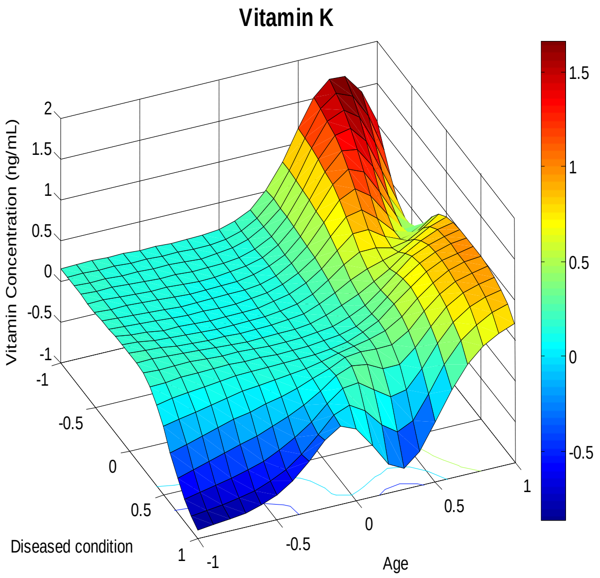

Figure 4: Response Surface plot of vitamin K

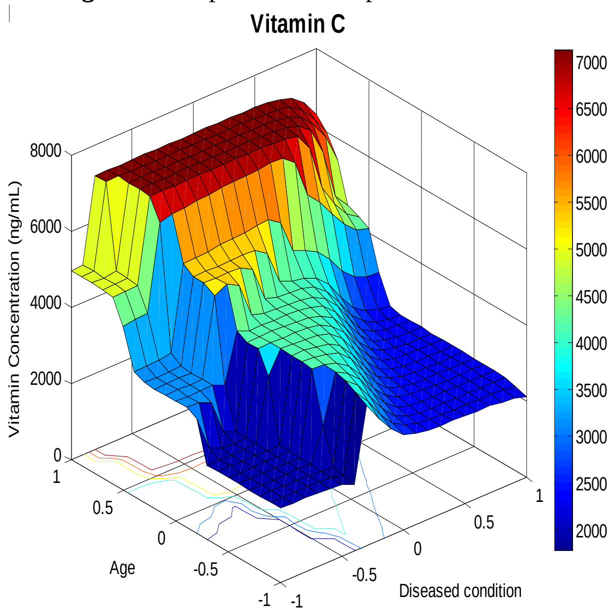

Figure 5: Response Surface plot of vitamin C

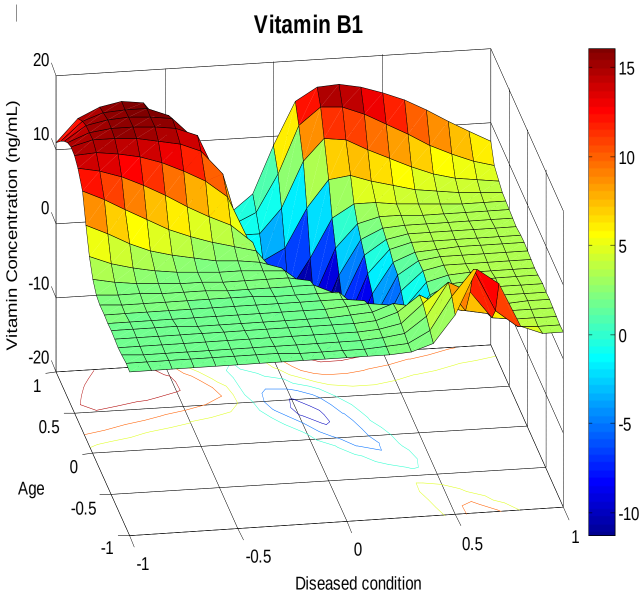

Figure 6: Response Surface plot of vitamin B1

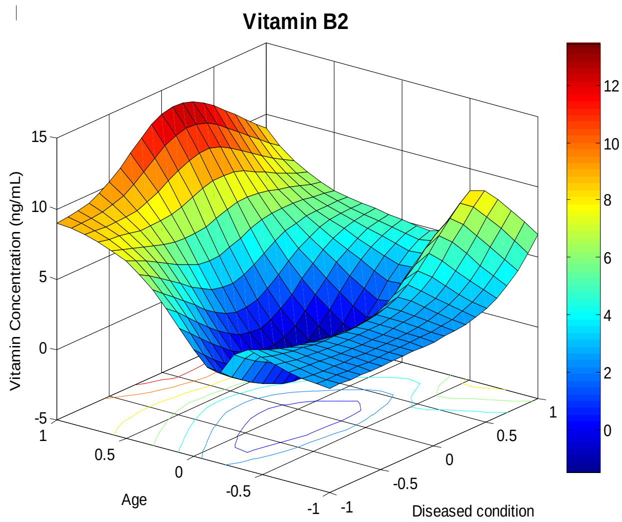

Figure 7: Response Surface plot of vitamin B2

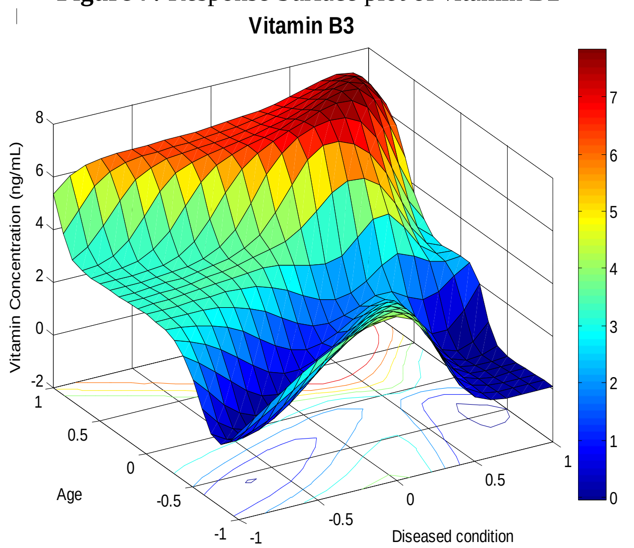

Figure 8: Response Surface plot of vitamin B3

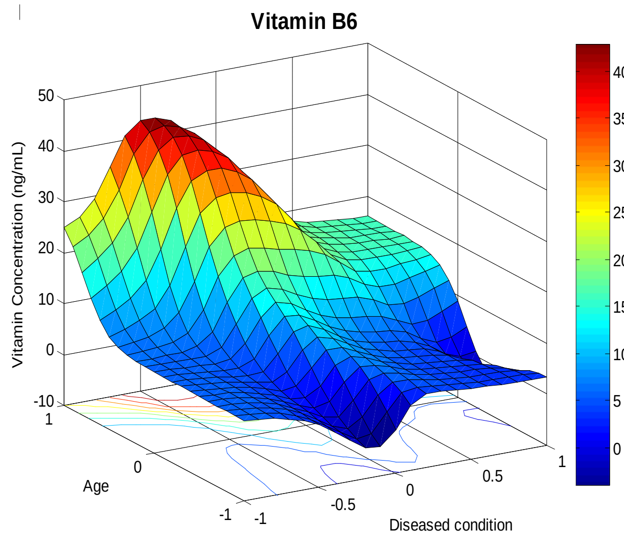

Figure 9: Response Surface plot of vitamin B6

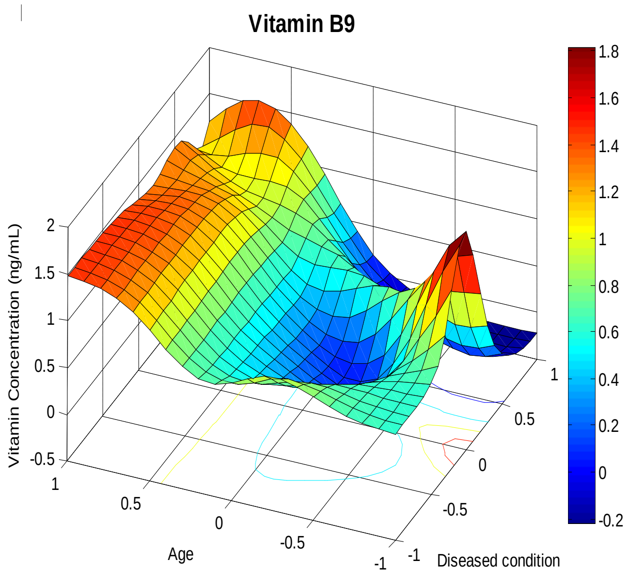

Figure 10: Response Surface plot of vitamin B9

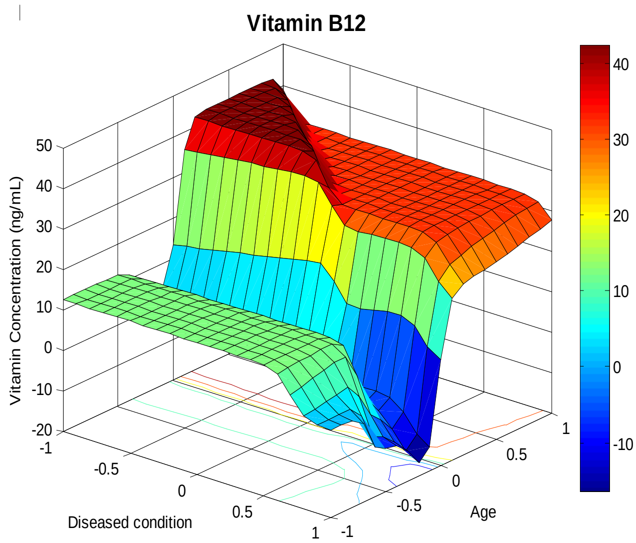

Figure 11: Response Surface plot of vitamin B12

The optimum concentration of vitamin D and K were investigated using the plots and found that the variables are moderately influencing the vitamin concentration since the nature of the plot was almost uniform, excluding some areas where the peaks were formed. The vitamin A and E were greatly affected by the disease condition variable as the optimum value was again found with the control subjects.

The plot of vitamin C has affirmed that the disease condition was positively influencing the vitamin concentration until an optimum value was reached. The response surfaces of B_3 and B_6 reached the optimum level uniformly due to sufficient supplementation however at some areas the response surface is reduced to low levels even under unfavorable conditions. The plots of vitamin B_1, B_2 and B_{12} were uniform at several conditions but at the central point of the age of subjects, the vitamin levels were reduced to a greater extent. The predicted levels of vitamin concentration were reached at the most favorable conditions.

The yield values for different concentrations of the variable can also be predicted from the respective response surface plots. The maximum predicted value is indicated by the surface confined in the response surface plot. The best predicted values were depicted in the Table 2.

Table 2: Permissible levels of vitamins given by ANN:

S. No.	Vitamin	Vitamin value (ng/mL)
1	A	1064.5
2	D	♂−73.22, ♀−45.03
3	E	1217.6
4	K	1.024
5	C	7177.9
6	B_1	15.732
7	B_2	13.390
8	B_3	6.619
9	B_6	31.927
10	B_9	1.481
11	B_{12}	38.786

4. Conclusion

Diabetes mellitus appears to have great effect on the decline of vitamin concentrations in both male and female Diabetes patients who are having vitamin supplements are slightly lower concentrations of vitamins A, E, C, B_1, B_2, B_6 and B_{12} were observed when compared to Non diabetic control group. By using ANN in the Diabetes mellitus patients showing that the maximum decline effect on the A and E vitamins. That shows a planned dietary intake and supplementation of deficient vitamins (500 – 1000 IU vitamin/day) help to reduce the risk of the diabetes in patients.

References

[1] Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet*, 2011, 378(9785):31–40.

[2] WHO report. Global status report on noncommunicable diseases 2010. Geneva, World Health Organization, 2011.

[3] Golden BE, Golden MHN: Malnutrition and diabetes mellitus: a case study. Wis Med J 32:241-247, 1983.

[4] Oh JM: Diabetes mellitus in Africans. J R Coil PhysiciansLond l7:224-227, 1983.

[5] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*, 2006, 3(11):e442.

[6] Jenkins DJA: Dietary fibre, diabetes and hyperhipidemia. Lancet 2:1287-90, 1979.

[7] Biju Thomas, Suchetha Kumari, Ramitha K., M. B. Ashwini Kumari : Comparative evaluation of micronutrient status in the serum of diabetes mellitus patients and healthy individuals with periodontitis. Journal of Indian Society of Periodontology - Vol 14, Issue 1, Jan-Mar 2010

[8] Anderson JW, Ferguson SK, Karounos D, O'Malley L, Sieling B, Chen WJ: Mineral and vitamin status on high-fiber diets: long-term studies of diabetic patients. Diabetes Care 3(1):38-40, 1980.

[9] Muhammad Akmal Sapon , Khadijah Ismail and Suehazlyn Zainudin : Prediction of Diabetes by using Artificial Neural Network 2011 International Conference on Circuits, System and Simulation IPCSIT vol.7 (2011) © (2011) IACSIT Press, Singapore.

[10] Pavlos Chatzimichalakis F, Victoria Samanidou F, Loannis Papadoyannis N: Development of a validated liquid chromatography method for the simultaneous determination of eight fat soluble vitamins in biological fluids after solid phase extraction. J Chromatogr B 805:289-296, 2004.

[11] Pavlos Chatzimichalakis F, Victoria Samanidou F, Robert Verpoorte, Loannis Papadoyannis N: Development of a validated HPLC method for the determination of B-complex vitamins in pharmaceuticals and biological fluid after solid phase extraction. J Sep.Sci. 805:289-296, 2004.

[12] Lobanov V: Using artificial neural networks to drive virtual screening of combinatorial libraries. *DDT Biosilic*, 2:149–156, 2004.

[13] Rumelhart DE, Hinton GE, Williams RJ: Learning representations by back-propagating errors. Nature 323:533–536, 1986.

[14] Hussain, Mukhtar, Bedi, Jatinder S, Singh, Harpreet: Determining number of neurons in hidden layers for binary error correcting codes. In: Proceedings of Applications of Artificial Neural Networks III – SPIE:1015-1022, 1992.

[15] Ahmed, Farid E: Artificial neural networks for diagnosis and survival prediction in colon cancer. Molecular Cancer 4:29, 2005.

[16] Song, Xiaowei; Mitnitski, Arnold; Macknight, Chris and Rockwood, Kenneth: Assessment of individual risk of death using self-report data: An artificial neural network compared with a frailty index. Journal of the American Geriatrics Society 52(7):1180-1184, 2004.

[17] Mandal, Sumantra, Sivaprasad PV, Venugopal S, Murthy KPN: Artificial neural network modeling to evaluate and predict the deformation behavior of

stainless steel type AISI 304L during hot torsion. Applied Soft Computing 9(1):237-244, 2009.

[18] Kose, Erdogan: Modelling of colour perception of different age groups using artificial neural networks. Expert Systems with Applications 34(3):2129-2139, 2008.

[19] Kasiri MB, Aleboyeh H, Aleboyeh A: Modeling and optimization of heterogeneous photo-fenton process with response surface methodology and artificial neural networks. Environmental Science & Technology 42(21):7970-7975, 2008.

[20] Franz MJ, Bantle JP, Eds.: *American Diabetes Association Guide to Medical Nutrition Therapy for Diabetes.* Alexandria Va., American Diabetes Association, 1999

[21] Mooradian AD, Failla M, Hoogwerf B,Marynuik M, Wylie-Rosett J. Selected vitaminsand minerals in diabetes. *Diabetes Care* 17:464-479, 1994