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An intelligent system for the characterization of hyperlipidemic blood and a comparative study on the efficacy of statins

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ABSTRACT

Elevated lipid level is supposed to be one of the main risk factors for cardiovascular diseases. Therefore lipid lowering is one of the major target in cardiovascular treatment and prevention. Hence hyperlipidemic blood has to be identified and lipid level has to be lowered. Atorvastatin and simvastatin are the lipid lowering agents, they lower the low density cholesterol. For the characterization of hyperlipidemic blood, the FTIR spectra of blood sera of 20 healthy people and 20 hyperlipidemic patients of the same age group were recorded and fed as input to our system.To study the efficacy of statins, the FTIR spectral data of blood sera of the 20 hyperlipidemic patients of the same age group and blood group were recorded and fed as input to our system. Our system is trained to distinguish between the healthy and hyperlipidemic blood. Some remarkable differences are identified by our system. Both the statins were well tolerated and it is concluded from the results that Atorvastatin is more efficacious than simvastatin in modifying lipids in patients with hyperlipidemia and a high coronary heart disease risk. FTIR spectroscopy allows accurate lipids concentration determination. The results obtained from our System are well supported by both spectroscopic data and clinical data. Since our system is trained to distinguish the hyperlipidemic blood with the fine details of FTIR spectra, it can improve the diagnostic accuracy and rate of cardiovascular treatment and also it can analyze the efficacy of statins at a faster rate with more accuracy.

Key words: Lipids, hyperlipidemia, atorvastatin, simvastatin, Efficacy of statins.

INTRODUCTION

Hyperlipidemia is a risk factor for coronary heart disease (CHD). Clinical studies have shown that lowering elevated serum total cholesterol levels (TC) and particularly low density lipoprotein cholesterol(LDL) levels, reduces the frequency of coronary morbidity and deaths, whereas high serum level of high density lipoprotein cholesterol (HDL) protect against CHD. Therefore hyperlipidemic blood has to be identified and lipid level has to be lowered for cardio vascular treatment and prevention (A-D).

Neural network (NN) processes information in a similar way the human brain does. To capture the essence of biological neural systems, an artificial neuron is defined as follows:

- It receives a number of inputs. Each input comes via a connection that has strength (weight), which corresponds to synaptic efficacy in a biological neuron. Each neuron also has a single threshold value. The weighted sum of inputs is formed, and the threshold subtracted, to compose the activation of the neuron.
- The activation signal is passed through an activation function to produce the output of the neuron.

The NN is composed of a large number of highly interconnected processing elements (neurons) working in parallel to solve a specific problem. NN learns by examples. It can be trained according to our need. The examples must be selected carefully (H).

Even though investigations on characterization of hyperlipidemic blood and efficacy

of atorvastatin and simvastatin have been done by many, not much work is done on automation of this investigation. In cardiac analysis it is found that TGL, TC to HDL ratio and LDL to HDL ratio are good indicators of potential cardiac problems (E). The goal of this study is to design a system that can identify whether the given blood sample is hyperlipidemic or not, across the dose range on TC, HDL, LDL, triglycerides(TGL) and also to examine prospectively the effects of atorvastatin and simvastatin in patients with hyperlipidemia in the statin therapies, using the system which is already trained to identify the hyperlipidemic blood (F,G).

MATERIAL AND METHODS

For the characterization of hyperlipidemic blood, the FTIR spectra of blood sera of 20 healthy people and 20 hyperlipidemic patients of same age group were recorded and fed as input to train our system (F) which is a three-layer feed-forward back-propagation network. During the training iteration of our System, we modified the weights at the output layer and then we proceeded backwards on the hidden layer to reach the input layer (G). Our NN consists of 3 layers namely (i) input layer with 4 neurons each corresponding to TC, HDL, LDL, TGL (ii) hidden layer with 3 neurons and (iii) output layer with 1 neuron. The value of the output neuron varies from .5 to 1 for the hyperlipidemic blood and 0 to < .5 for the healthy blood (value 0 indicates the most healthy blood and value 1 indicates the most diseased blood). The calculated Weight $_{IH}$ x–y which is the strength/weight of the connection between unit x in the input layer and unit y in the hidden layer and Weight $_{HO}$ x–y which is the weight of the connection between unit x in the hidden layer and unit y in the output layer are given in Table 1.

Table 1

Weight	Value
$Weight_{IH}$ 1 – 1	-0.754152
$Weight_{IH}$ 1 – 2	-1.043419
$Weight_{IH}$ 1 – 3	-3.909459
$Weight_{IH}$ 2 – 1	-0.862884
$Weight_{IH}$ 2 – 2	-1.982549
$Weight_{IH}$ 2 – 3	-9.440568
$Weight_{IH}$ 3 – 1	1.285868
$Weight_{IH}$ 3 – 2	0.992494
$Weight_{IH}$ 3 – 3	10.830954
$Weight_{IH}$ 4 – 1	-0.229326
$Weight_{IH}$ 4 – 2	-0.220465
$Weight_{IH}$ 4 – 3	-1.667688
$Weight_{HO}$ 1 – 1	1.299790
$Weight_{HO}$ 2 – 1	-0.283240
$Weight_{HO}$ 3 – 1	-9.579176

Table 2

No. of neurons in hidden layer	No. of iterations
1	9,63,701
2	7,83,522
3	2,30,983
4	8,39,228

Table 4: Testing - Random Samples

Sample 1	
Give the input(TGL)	-.4960
Give the input(TCL)	-.4904
Give the input(HDL)	-.7420
Give the input(LDL)	-.4499
Result :	.000001
Sample 2	
Give the input(TGL)	-.6952
Give the input(TCL)	-.7111
Give the input(HDL)	-.6434
Give the input(LDL)	-.6158
Result :	.670587
Sample 3	
Give the input(TGL)	-.7395
Give the input(TCL)	-.7588
Give the input(HDL)	-.6799
Give the input(LDL)	-.6398
Result :	.665383
Sample 4	
Give the input(TGL)	-.4870
Give the input(TCL)	-.4700
Give the input(HDL)	-.7255
Give the input(LDL)	-.4488
Result :	.000001

The learning parameters 'eta 'component that is the gradient descent and 'alpha' component that is a 'momentum' term which effectively keeps a moving average of the gradient descent weight change contributions, were carefully chosen to speed up the training(I). 40 training samples were repeatedly fed to the NN in a random order for each iteration to minimize the weight oscillation.

To study the efficacy of statins, the blood samples were collected from the adult patients with their consent. Twenty patients of the same age group and blood group were chosen for the investigation. The patients were divided into two groups A and B. To access the lipid lowering effects of the two statins, group A is prescribed with atorvastain and group B with simvastatin.

Table 3: Testing-training samples

Sample No.	TGL	TC	HDL	LDL	Output
1.	0.715200	0.755500	0.665700	0.625800	0.500137
2.	0.689400	0.729800	0.639300	0.599700	0.499730
3.	0.678700	0.718500	0.628800	0.588900	0.499806
4.	0.729500	0.769800	0.679800	0.639800	0.499917
5.	0.698500	0.738400	0.648800	0.606900	0.500060
6.	0.707000	0.748300	0.659300	0.617300	0.500079
7.	0.723500	0.765900	0.674100	0.634800	0.500082
8.	0.684500	0.724300	0.636900	0.597200	0.499485
9.	0.708600	0.746400	0.659400	0.617300	0.500014
10.	0.669700	0.707200	0.618500	0.579800	0.499762
11.	0.533800	0.527200	0.768600	0.488300	0.000000
12.	0.507000	0.503000	0.741700	0.462600	0.000000
13.	0.496900	0.490500	0.731700	0.453300	0.000000
14.	0.547800	0.542400	0.784600	0.502200	0.000000
15.	0.516500	0.511600	0.752400	0.472500	0.000000
16.	0.527000	0.519700	0.762400	0.482800	0.000000
17.	0.543900	0.508500	0.775600	0.499200	0.000000
18.	0.503000	0.495800	0.735700	0.459600	0.000000
19.	0.526300	0.521600	0.764400	0.483400	0.000000
20.	0.487000	0.476800	0.721300	0.449200	0.000000
21.	0.626200	0.660600	0.551700	0.532500	0.500139
22.	0.684600	0.719900	0.609700	0.591300	0.500186
23.	0.712300	0.747600	0.638300	0.619300	0.499976
24.	0.693900	0.728700	0.619500	0.601400	0.499986
25.	0.724400	0.759300	0.649400	0.631600	0.500018
26.	0.711300	0.746700	0.636800	0.618200	0.499573
27.	0.692600	0.726700	0.616600	0.598400	0.499998
28.	0.647300	0.682600	0.573700	0.554100	0.500316
29.	0.693700	0.728400	0.618300	0.617200	0.499809
30.	0.727800	0.762700	0.652600	0.634900	0.499738
31.	0.493700	0.475200	0.611300	0.426000	0.000009
32.	0.556800	0.538900	0.671800	0.485400	0.000136
33.	0.584800	0.562600	0.698400	0.513700	0.000325
34.	0.561400	0.546500	0.679100	0.497100	0.000182
35.	0.592900	0.574600	0.709700	0.524600	0.000472
36.	0.579400	0.561200	0.697300	0.513800	0.000264
37.	0.559100	0.547400	0.677400	0.494200	0.000206
38.	0.471700	0.494200	0.633500	0.448900	0.000004
39.	0.562300	0.543700	0.679100	0.496700	0.000146
40.	0.596400	0.577500	0.713400	0.528800	0.000508

atorvastatin 20mg. (Aztor) and simvastatin 20mg. (Zocor) were taken once daily with the evening meal for a period of six months by patients of group A and B respectively. An interim and final check up was performed over a period of 3rd and 6th months respectively, after the treatment was initiated. Before the drug therapy, the FTIR spectra of blood sera of both the groups were recorded and the spectral data were fed as inputs to our system and the outputs were noted down (pre-treatmental). To find the efficacy of atorvastatin and simvastatin, the FTIR spectra were recorded at regular interval of 3 months and the spectral data were fed as inputs to our System and the outputs were noted down (post treatmental) (A-G).

RESULTS AND DISCUSSION

The maximum number of iterations that the input samples can be repeated for training is 1,000,000. Our System will stop learning when the error term that is the difference between network's actual output and the desired output is less than 0.000001 or when it reaches the maximum number of iterations, 1,000,000. Fixing the eta value and alpha value to 0.9, the network is trained by varying the number of neurons in the hidden layer (Table 2). We found that the system is trained effectively with 3 neurons in the hidden layer.

Table 5: Lipid lowering effect of Group A

Sample No.	TGL	TC	HDL	LDL	Output
			Pre		
1	0.715200	0.755500	0.665700	0.625800	0.666663
2	0.689400	0.729800	0.639300	0.599700	0.668872
3	0.678700	0.718500	0.628800	0.588900	0.669932
4	0.729500	0.769800	0.679800	0.639800	0.665273
5	0.698500	0.738400	0.648800	0.606900	0.668300
6	0.707000	0.748300	0.659300	0.617300	0.667726
7	0.723500	0.765900	0.674100	0.634800	0.665570
8	0.684500	0.724300	0.636900	0.597200	0.669849
9	0.708600	0.746400	0.659400	0.617300	0.667774
10	0.669700	0.707200	0.618500	0.579800	0.670689
			Post 1		
1	0.617600	0.644700	0.724000	0.556100	0.553023
2	0.591900	0.618900	0.697800	0.531300	0.515143
3	0.580800	0.607700	0.687400	0.519600	0.490732
4	0.631700	0.658500	0.737300	0.571300	0.573656
5	0.604700	0.627500	0.706600	0.562000	0.547390
6	0.609700	0.635100	0.719600	0.548100	0.521076
7	0.625700	0.628600	0.731400	0.565300	0.476128
8	0.586800	0.613700	0.693900	0.526500	0.500311
9	0.613900	0.638200	0.713700	0.548700	0.560269
10	0.571400	0.599600	0.677800	0.512400	0.480787
			Post 2		
1	0.533800	0.527200	0.768600	0.488300	0.000004
2	0.507000	0.503000	0.741700	0.462600	0.000002
3	0.496900	0.490500	0.731700	0.453300	0.000001
4	0.547800	0.542400	0.784600	0.502200	0.000006
5	0.516500	0.511600	0.752400	0.472500	0.000003
6	0.527000	0.519700	0.762400	0.482800	0.000003
7	0.543900	0.508500	0.775600	0.499200	0.000001
8	0.503000	0.495800	0.735700	0.459600	0.000002
9	0.526300	0.521600	0.764400	0.483400	0.000003
10	0.487000	0.476800	0.721300	0.449200	0.000001

Table 6: Lipid lowering effects of Group B

Sample No.	TGL	TC	HDL	LDL	Output
			Pre		
1	0.626200	0.660600	0.551700	0.532500	0.669628
2	0.684600	0.719900	0.609700	0.591300	0.664242
3	0.712300	0.747600	0.638300	0.619300	0.661791
4	0.693900	0.728700	0.619500	0.601400	0.663522
5	0.724400	0.759300	0.649400	0.631600	0.660396
6	0.711300	0.746700	0.636800	0.618200	0.661752
7	0.692600	0.726700	0.616600	0.598400	0.663429
8	0.647300	0.682600	0.573700	0.554100	0.667926
9	0.693700	0.728400	0.618300	0.617200	0.662587
10	0.727800	0.762700	0.652600	0.634900	0.660011
			Post 1		
1	0.564300	0.568400	0.583500	0.471900	0.643281
2	0.623200	0.638700	0.642400	0.532600	0.670534
3	0.651700	0.655400	0.672600	0.558500	0.669220
4	0.632000	0.639400	0.651400	0.539100	0.668017
5	0.663800	0.667400	0.683600	0.578400	0.671960
6	0.653500	0.658500	0.669400	0.557600	0.671915
7	0.631800	0.634500	0.649300	0.539700	0.666506
8	0.586500	0.593600	0.604600	0.493800	0.656501
9	0.632500	0.636500	0.651200	0.539400	0.666655
10	0.668500	0.673800	0.685300	0.575600	0.673765
			Post 2		
1	0.493700	0.475200	0.611300	0.426000	0.017883
2	0.556800	0.538900	0.671800	0.485400	0.103387
3	0.584800	0.562600	0.698400	0.513700	0.153656
4	0.561400	0.546500	0.679100	0.497100	0.118791
5	0.592900	0.574600	0.709700	0.524600	0.179107
6	0.579400	0.561200	0.697300	0.513800	0.140763
7	0.559100	0.547400	0.677400	0.494200	0.125899
8	0.471700	0.494200	0.633500	0.448900	0.007908
9	0.562300	0.543700	0.679100	0.496700	0.106624
10	0.596400	0.577500	0.713400	0.528800	0.184212

Table 7: Efficacy of Atorvastatin

Sample No.	Percentage
1	99.999345
2	99.999655
3	99.999781
4	99.999037
5	99.999603
6	99.999517
7	99.999837
8	99.999709
9	99.999536
10	99.999854

Table 8: Efficacy of Simvastatin

Sample No.	Percentage
1	97.329459
2	84.435352
3	76.781815
4	82.096903
5	72.878811
6	78.728693
7	81.022921
8	98.816070
9	83.907897
10	72.089623

Our system is able to identify the training samples (40) correctly, the result of which is summarized in Table 3. It is also able to identify any random sample correctly which is evidenced by Table 4.

In order to find the efficacy of atorvastatin and simvastatin, the outputs of pre-treatment (Pre), post-treatment1 (Post 1), post-treatment 2 (Post 2) for Group A are given in Table 5 and for Group B in Table 6. The % of efficacy of the statins is calculated using the formula (Pre-Post) / Pre * 100 and the results are given in Table 7 and Table 8. It is concluded from the result that atorvastatin is more efficacious than simvastatin in modifying lipids in patients with hyperlipidemia.

CONCLUSION

NNs are being used in the detection of various diseases. A variety of health-related indices can be monitored. The onset of a particular medical condition could be associated with a very complex combination of changes on a subset of the variables being monitored in medicines. NNs have been used to recognize this predictive pattern so that the appropriate treatment can be prescribed. FTIR spectroscopy allows accurate lipids concentration determination. The results obtained from our system are well supported by both spectroscopic data and clinical data. Since our system is trained to distinguish the hyperlipidemic blood with the fine details of FTIR spectra, it can improve the diagnostic accuracy and rate of cardiovascular treatment and also it can analyze the efficacy of statins at a faster rate with more accuracy.

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