Determine the effect of giving a patient multiple drugs at the same time by using neural network

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Abstract:

The aim of this study is to construct a neural network for drug-interaction to facilitate the task of finding the interaction which occur between multiple drugs given to the patient at the same time.

The suggested system used to enable physicians and pharmacists to find the interaction which occur between multiple drugs prescribed to patients to get the safe, beneficial and effective therapy. The suggested system may be considered as practical approach that can be implemented in general hospitals, pharmacies, also in colleges as educational and teaching system. It was a good practice for physician pharmacists to use the computer for prescribing a safe therapy to patients and for learning.

Keywords: neural network,

المستخلص

الهدف من هذا البحث هو تكوين شبكة عصبية باستخدام خوارزمية Back-propagation من اجل تسهيل اكتشاف التداخل بين الادوية عندما يتناول المريض أكثر من دواء بنفس الوقت .

الطريقة المقترحة تساعد الاطباء و الصيادلة في المستشفيات و كليات المجموعة الطبية لتحديد نوع الضرر الذي يصيب المريض نتيجة تناوله اكثر من دواء بنفس الوقت.

1. Introduction :

Today there is much concern about drug –interaction because many patients receive more than one drug at the time. Many doctors are unaware of risks to which their patients are exposed when treated with multiple drugs. So drug –interactions occur when two or more drug are given simultaneously or concurrently. The therapeutic response of drug is concurrently. The therapeutic response of drug is normally response on an adequate concentration of the drug at the sites of action of the drug [1].

So when a drug is administered a response is obtained, if a second drug is given and response of first drug is altered, drug interaction is said to have occurred. Thus one drug may antagonize or potentate the effect of another. The outcome may be harmful if the interaction causes an increase in the efficacy or toxicity of the drug . for example patients already taking WARFARINE may begin to bleed if given PHENYLBUTAZONE unless the WARFARIN dosage is reduced appropriately [2].

A reduction in efficacy as a result of an interaction may also be harmful. Thus patients an WARFARIN given RIFAMPICIN will need an increase in dosage of WARFARIN to maintain adequate anticoagulation [3]. So some drug be life threatening.

Consultative advise is often required in the hospitals because the large number of potential drug interaction precludes physicians and

pharmacists either from remembering the majority of them or from looking them up manually on routine basis. To deal with this problem, it is necessary to design a neural network (NN) model that can solve this problem and help the physicians to make decision about any combination of drugs which should be avoided or can be used.

2. Neural Network:

Many successful applications of neural network have raised the interest of researchers from differ scientific disciplines in the NN area. Various and complex problems have been treated successfully using NN.

Instead of executing step-by-step programs to carry out the required transformation, the NN produces its internal rules that controlling the transformation, and comparing the result of these rules to the examples. Through trial and error, the NN learned how to do the required task [4].

The NN is a collection of processing elements or nodes, the output of each node has two basic parts:

1. Summation function that receives the various input activation through input connections (synapses) and sums them into a single activation.
2. Threshold function which transfers the summation of input activation into output activation through output connection as shown in fig.(1)

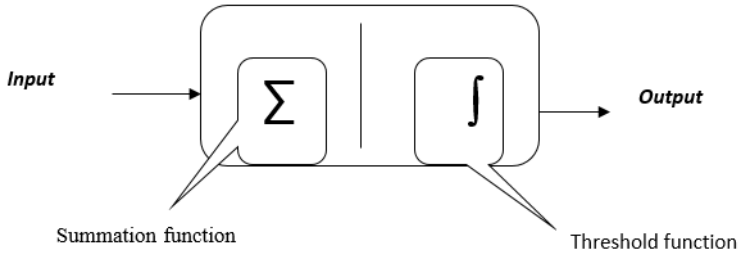

Fig. (1) Artificial neuron

Instead of programming a NN, we teach it to give a correct output. Entering the input and desired output patterns, assigning the initial weight values to the connections within the network, then it will adjust those weights over and over until it gives a correct output.

Back-propagation (BP) is the most widely used learning algorithm in the NN and can be applied to handle any problem that requires pattern mapping from input pattern to output pattern.

BP network is considered to consist of three layers or more of processing elements, the input layer, hidden layers and the output layer. Each neuron is connected to every unit in the layer above and the layer below, so the network is fully connected. The activation function in BP algorithm is typically a sigmoid function.

The sigmoid compresses the range of the neuron output so that it lies between $(0,1)$ or $(-1,1)$.

The operation of the BP algorithm involves two phases, the forward phase and the backward phase. During the forward phase the input is presented and propagated toward the output, while during the

backward phase, the errors are formed at the output and back propagated toward the input.[6]

3.Neural network for drug –interactions:

An attempt is made to develop NN for drug–interaction to assist the physician to determine which combination of drugs is adverse and should be avoided. So the proposed project is to design and built NN which will referred to as NNFDI(Neural Network For Drug–Interactions) that assists in resolving the main problem of treatment by multiple drugs.

The characteristics of NNFDI which is designed can be summarized as follows:

- NNFDI can act as a personal consultant to the physicians and pharmacist who deal with more complex problems when prescribing two drugs to the patients.
- NNFDI can be used in general hospitals, pharmacies and in collages as an educational and teaching system [1].

4.NNDFI Utility:

NNFDI enables a physician and pharmacist to determine which combination of drugs is adverse and should be avoided through finding the interactions between drugs at the same time.

5.The NNFDI Architecture:

The NNFDI architecture as shown in fig.2 is based on the concepts of data base and neural network system. A description of the functions of the various system components are shown below in fig.2:

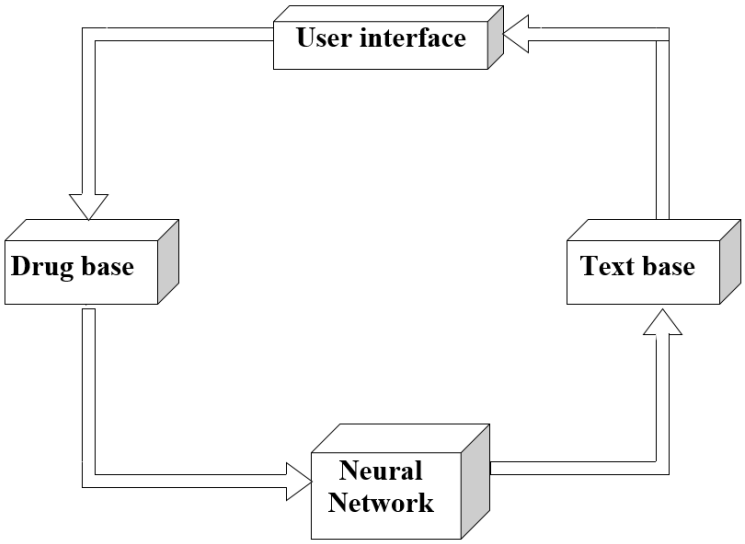

Fig (2) NNFDI Architecture.

5.1 User Interface:

User interface performs the task of communicating with the user by receiving human questions and providing the results and displaying the message to the user. NNFDI user interface uses menus that contains the three drugs and their numbers as shown below in fig.3:

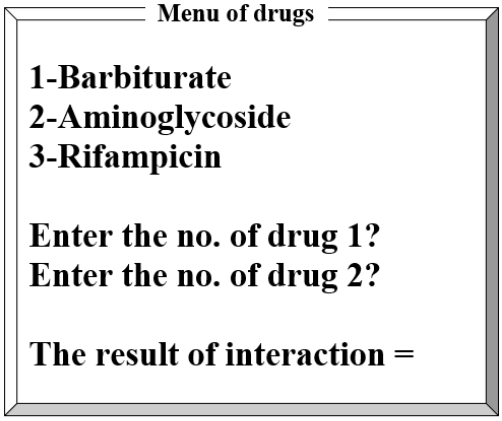

Fig.3 drugs menu.

When this menu appear will ask the user to enter the number of first and second drugs which are given to the patient at the same time to find if there is an interaction between them to get the safe, beneficial and effective therapy. When the user enter the numbers of two drugs.

These numbers will be entered to the drug base(second stage) to obtain the code of these drugs.

5.2 Drug base:

This base consists the number of two drugs and code of these drugs as shown below in table (1):

Table (1) codes of the drugs combination

No. drug 1	no. of drug2	Code
1	2	000
2	1	001
1	3	010
3	1	011
2	3	100
3	2	101

Where:

1 is a number refers to Barbiturate.

2 is a number refers to Aminoglycoside.

001 is a code refers to two drugs are given at the same time.

This code of the drug combination will be enter to the NN. So this base used to convert the no. of two drugs into the code that represent the combination of these drugs.

The table above take only three drugs and the possibilities of entering two drugs at the same time. Three bits are used in the code, because we have three drugs so there are 2 different drug

combinations. The drug in this base are either particular drug or group of drugs.

5.3 The neural network model:

To solve any problem using NN, we need the input–output pattern and the initial weight values to the connections within the network. The number of nodes in the input layer is equal to the number of bits in inputs of the pattern, while the number of nodes in the output layer is equal to the number of bits in the outputs of the pattern, and the number of nodes in the hidden layer is varied according to the complexity of the applied pattern. when all input–output pairs have been presented to the network, one iteration has been completed, then running the network as many iterations as desired in order to minimize the cost criteria and get approximate result.

The problem now is to construct a NN model to realize the following input–output pattern in table (2):

Table (2) input–output pattern

Inputs	outputs
drug combination	Interaction type
000	000
001	000
010	101
011	100
100	011
101	011

The input to this pattern is the last output from the drugs base. A binary number is assigned to each drug combinations. For example when two drugs are used, the number(000) means using barbiturate as drug1 and aminoglycoside as drug2, while (001) means using aminoglycoside asdrug1 and barbiturate as drug2. The two states have the same type of interaction is (000) which means no interaction. Another example, the number (001) means using barbiturate as drug1 and cyclosporine as drug2, while (011) means using cyclosporine as drug1 and barbiturate as drug2. The two states in this case have different interaction, since in the first state the type of interaction is (101), which means decrease the effect of drug1, because the cyclosporine has been entered as drug1 and so on.

A NN model is constructed to realize the previous pattern as shown below in fig. 4:

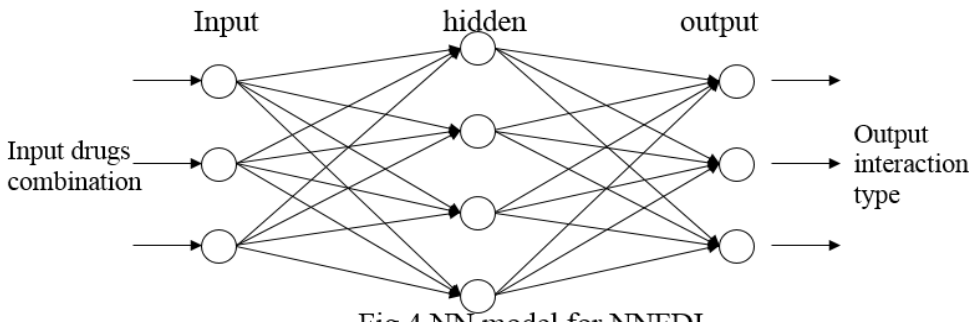

Fig.4 NN model for NNFDI

This model is consisting of the input layer with three nodes, one hidden layer with four hidden nodes, and the output layer with three nodes. Back- propagation algorithm is used as a learning tool to realize the pattern.

This model has reached the desired output after (265) iterations through six input- output patterns with a learning rate $\eta=0.3$ and MSE= 0.032 . When the learning phase is completed, the NN model can accept any of the inputs that have been learned to get the desired output directly. The output of this model will be applied to the text base in the next stage.

5.4 Text base:

This base is used to convert the code output from NN that represent the type of the interaction to text as shown below in table (3) :

Table (3) text conversion

Code	text
000	no interaction
001	enhanced effect of drug1
010	enhanced effect of drug2
011	toxic interaction
100	decrease effect of drug1
101	decrease effect of drug2
110	increase effect of drug1 and decrease effect of drug2
111	increase effect of drug2 and decrease effect of drug1

These codes are applied to this base in order to be converted to a text that represent the type of interaction and then sent this text to user interface.

A practical example is shown in fig.5 below:

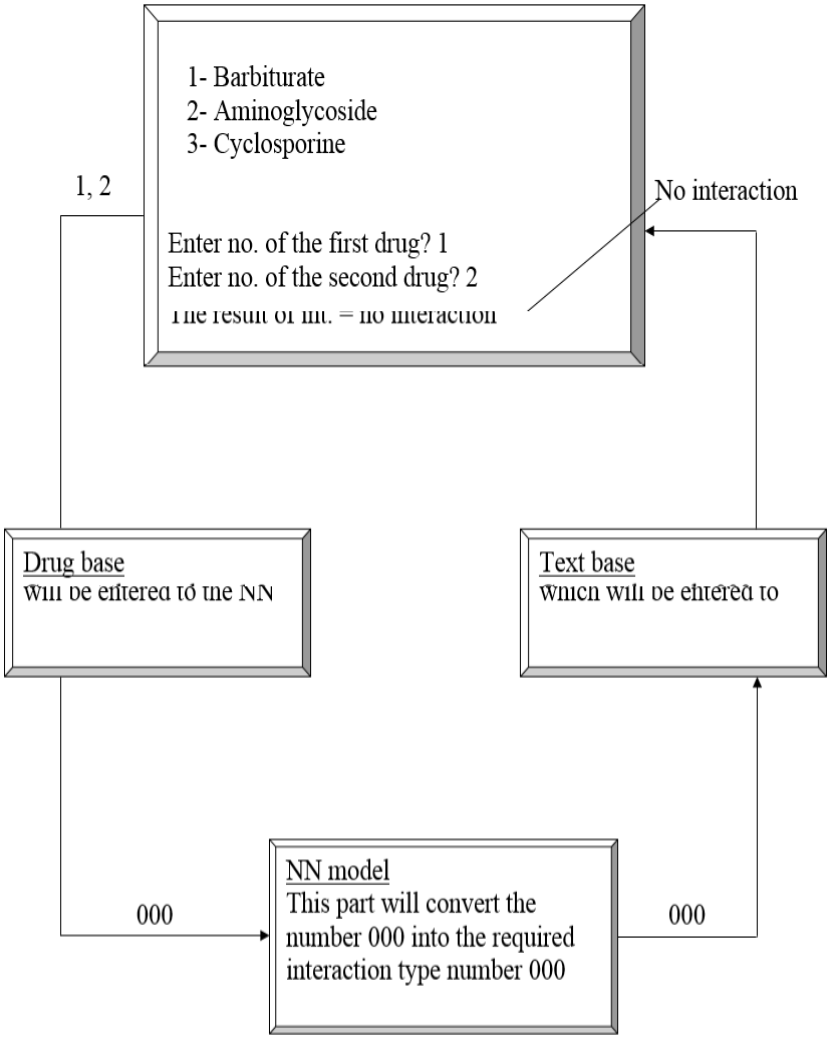

Fig.5 practical example

6. Conclusion:

1- It can be concluded that using neural network in this paper plays a major role in speeding- up the searching in drug interaction problem. The time of the searching has been reduced significantly compared to the traditional methods, because the NN model is used to learn the desired input-output patterns off-line, so during the searching process, the NN model submits the desired output directly without needing to search for all inputs to get the desired output.

2- The NN gives the required interaction type directly after applying two drugs at the same time.

3- the suggested system was a good practice for physicians and pharmacist to use the computer for prescribing a safe therapy to patients and for learning.

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