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Application of Artificial Neural Network (ANN) for the Extraction of a Non-Steroidal Anti-Inflammatory Drug through Emulsion Liquid Membrane

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ABSTRACT

In the present work, a non-steroidal anti-inflammatory drug (NSAID), Diclofenac (DCF) is removed with the help of emulsion liquid membrane and an artificial neural network is applied to predict the percentage extraction of Diclofenac at different levels of various parameters. The emulsion liquid membrane (ELM) was prepared using n-heptane as an organic solvent, Di-2-ethylhexyl phosphoric acid (D2EHPA) as a carrier, and span 80 as a surfactant. An artificial neural network (ANN) model is proposed in the present study to examine the effect of stripping phase concentration, surfactant concentration, carrier concentration, homogenizer speed and stirring speed. Multilayer perceptron (MLP) model is used to predict the percentage extraction at different parameters conditions. The neural network proved as a very promising method for the purpose of process simulation. At optimum conditions of all parameters the maximum 96 % extraction is possible within 30 minutes.

Keywords

Diclofenac, Emulsion Liquid Membrane, Artificial Neural Network.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the drugs which are responsible for reducing pain, fever and inflammation [1]. Diclofenac (DCF) is one of the common NSAIDs commonly used as analgesic, antiarthritic and antirheumatic drug. Diclofenac sodium is the most commonly prescribed anti-inflammatory drug with paracetamol or alone for the treatment of various inflammatory disorders. The presence of even small amounts of these drugs in environment water body is responsible for chronic toxicity, endocrine disruption and other toxic effects [2].

Various methods have been proposed to remove DCF from the aquatic environment such as adsorption, advanced oxidation processes, membrane filtration, photo-degradation and micro-extraction [3-6]. ELM proves to be promising method for separation of compounds from waste water. Recently, Zahra Seifollahi and Ahmad Rahbar-Kelishami studied and optimized different parameters for the extraction of DCF through ELM using response surface methodology [7].

ANN (ARTIFICIAL NEURAL NETWORK)

The present work involved the study of an emulsion liquid membrane process by an artificial neural network (ANN) for the extraction of diclofenac from its aqueous solutions. ANN is used in various fields such as agriculture, medicine, robotics, material science, weather forecasting, finance and economics, chemistry and chemical engineering, etc. Lots of application of ANN improved in the chemical engineering since 1988[8]. Considering the use of ANN in ELM process, Chakraborty et al., 2003 studied the applicability of ANN in ELM to predict nickel concentration in feed during extraction operation and ultimate % extraction [9]. The obtained ANN model could be used to predict the response at any operating conditions of initial solute concentration in feed phase, internal reagent concentration, treat ratio, volume fraction of internal aqueous phase in emulsion and time. Later on, ANN approach was used in the modeling and optimization of the reactive extraction of tartaric acid from aqueous solutions in which a comparison between response surface methodology and artificial neural network was shown where ANN was proved to be as a good model to predict % extraction. [10].

ANN consists of groups of extremely interconnected process elements referred to as neurons. The connections between neurons incorporate weights and biases. Each neuron comprises of summing junction and transfer function. The pattern of interconnection among neurons is termed the network topology. The neurons of a network are organized into many groups termed as layers. A multi-layer neural network consists of hidden and output layers. The multi-layer feed-forward neural network is the most common neural network architecture used for solving non-linear regression problems and known as multi-layer perceptron (MLP). A feed forward-type neural network in MLP topology has good model performance and it is most widely used model in membrane processes [11].

ANN involves three important steps training, validation and testing. In training step network is trained by adjusting the weights. Second step is validation, it is necessary to avoid over fitting the network and also provide fine-tuning to the model. Validation set directly not used for weights adjustment but it is used for optimum number of hidden layers and also decide stopping point. Third step i.e. testing used to check the prediction ability of the network [11].

MATERIALS AND METHODS

Chemicals

All chemicals used in this study for the extraction of DCF by emulsion liquid membrane were of analytical grade. n-Heptane (density 0.6795g/L and viscosity 386µPaS) was purchased from Finar chemicals, Ahmedabad, India and used as membrane (organic) phase. Dilute solutions of H_2SO_4, HCl and HNO_3 were purchased from Finar Chemicals Ahmedabad, India (99 % pure) and used as stripping phase. SPAN 80 (Sorbitan monooleate) was used as surfactants and purchased from National Chemicals. D2EHPA was purchased from Finar Chemicals, Ahmedabad, India (99 % pure) and used as carrier. Diclofenac was purchased from Sigma-Aldrich. Experimental conditions of the ELM process is presented in Table 1.

Experimental Procedure

The extraction of Diclofenac using liquid emulsion membrane involves three steps

1. Preparation of stable white w/o emulsion at high homogenizer speed in which organic phase will act as membrane phase

2. Extraction of the solute from feed by contacting with the prepared w/o emulsion to the membrane phase and the to the internal stripping phase in a ELM reactor equipped with a mechanical stirrer

3. Separation of liquid emulsion from the external feed phase.

During the experiment, the volume ratio of stripping phase to membrane phase was kept at 1:1, stirring speed was varied from 100-300rpm for the extraction of Diclofenac. Samples of about 10mL were withdrawn from the reactor at different time intervals and filtered to separate the emulsion and the aqueous feed phase, and then analyzed. The concentration of Diclofenac in the solutions was determined using a HACH make UV–visible spectrophotometer (Germany) with the help of calibration curve constructed at 276 nm (maximum absorption wavelength) on the basis of beer's law. R^2 value of calibration curve was 0.99.

RESULTS AND DISCUSSION

Effect of types of stripping phase

To examine the effect of different types of stripping phase on the extraction of diclofenac, a series of experiments was performed keeping stripping phase as sulfuric acid(H_2SO_4), hydrochloric acid (HCl) and nitric acid (HNO_3) of 0.01 M, surfactant concentration of 2 w/v % , carrier of 2 w/v %, stirring speed 300 rpm

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and w/o emulsion was prepared at 6500 rpm. It was found from the Fig. 1, that nitric acid gave best results than sulfuric and hydrochloric acid. This is because due to an activity coefficient of nitric acid which is due to its higher activity coefficient [12].

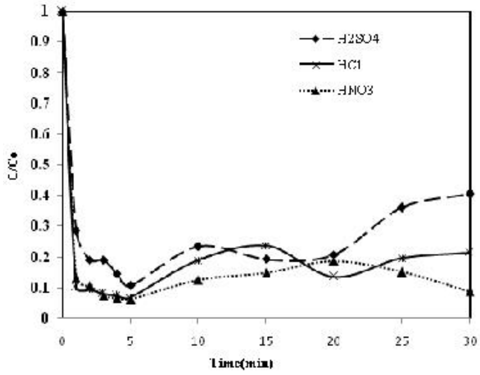

Fig 1: Extraction of DCF using 2 w/v % D2EHPA, 2 w/v % Span 80, homogenizer speed 6500 rpm and stirring speed 300rpm with stripping phase concentration of 0.01 M .

Effect of concentration of stripping phase

After fixing HNO_3 as an internal phase (stripping phase) of w/o/w emulsion, it is required to optimize its concentration in the stripping phase to get the maximum extraction of diclofenac from the external phase (feed phase). For this purpose, a series of experiments was carried out at different concentration of stripping phase (i.e. 0.1, 0.01 and 0.001M) and keeping rest of the parameters same as in previous experiments. It was observed from Fig. 2 that the % extraction was decreasing with the increase in acid concentration. This might be due to two facts that at higher acid concentration diclofenac will not be released from the complex formed with the carrier within the membrane phase as diclofenac is weak organic acid [13]. And also on increasing the acid concentration in the internal phase there will be an increase in the partial loss of the properties of the surfactant which will be responsible for the instability of the w/o emulsion.

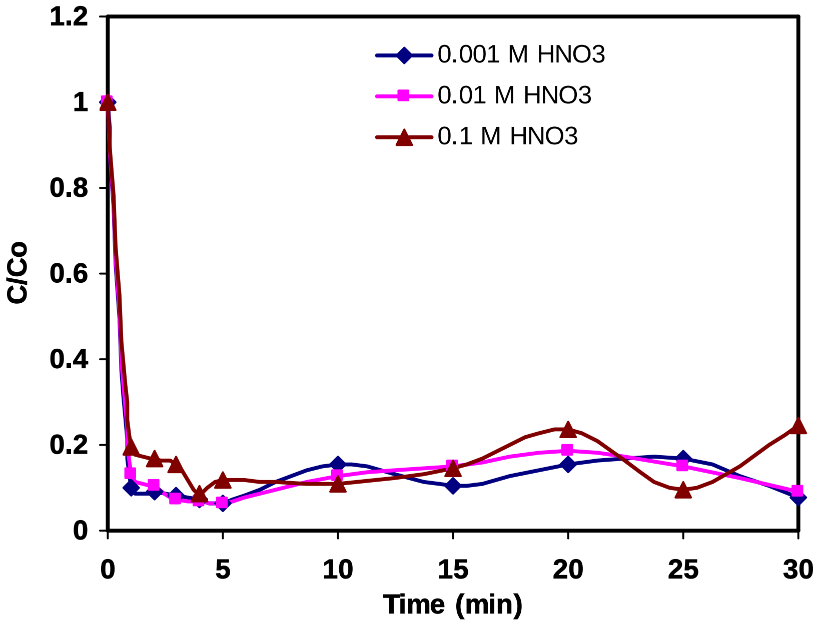

Fig 2: Extraction of DCF using 2 w/v % D2EHPA, 2 w/v % Span 80, homogenizer speed 6500 rpm and stirring speed 300rpm at different concentration of stripping phase.

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ANN Approach

In this section, a mixed level orthogonal array (4 factors having 3 level and 1 factor has 2 levels) was used which was selected from Minitab software. Total 18 experiments (showed in Table 1) were performed and from that ANN model was built up. ANN model was developed by using STATISTICA 17 software. Multi-layer perceptron feed forward topology and the Broyden–Fletcher–Goldfarb–Shanno (BFGS) algorithm was used to construct an ANN model. Sum of square error function was used and minimized the squared error between network's output and target value.

To build a multilayer network experimental data was divided into three subsets 70% for training (14 experiments), 15 % for testing (2 experiments) and 15 % for validation(2 Experiments). Before the network training to minimize the redundancy, inputs and target data were normalized between 0 (minimum) and 1 (maximum) by using a following equation.

$Y_n=(Y-Y_{min})/(Y_{max}-Y_{min})$

where Y_{min}= Minimum of all data, Y_{max}=Maximum of all data and Y_n= Normalized Y. After training testing and validation, output data are de-normalized using following equation [14]:

$Y=Y_{min}+ Y_n(Y_{max}-Y_{min})$

A mode MLP 5-8-1 is selected, training error 0.000157, test error 0.00008 and validation error 0.014. Training algorithm BFGS-45, error function is sum of square and hidden activation logistic and output activation is identity.

Table 1: ELM experiments for the development of ANN model

Exp. no.	Acid (M)	Surfactant(%)	Carrier(%)	Homog.Spd. (rpm)	Stirrer speed (rpm)	Extractn (%)	Normalized value
1	0.001	1	1	6500	100	79.57	0.1868
2	0.001	2	2	6500	200	93.81	1
3	0.001	3	3	6500	300	88.22	0.6808
4	0.01	1	1	6500	200	87.24	0.6248
5	0.01	2	2	6500	300	87.72	0.6522
6	0.01	3	3	6500	100	87.58	0.6442
7	0.1	1	2	6500	100	81.04	0.2707
8	0.1	2	3	6500	200	89.33	0.7442
9	0.1	3	1	6500	300	87.67	0.6494
10	0.001	1	3	9500	300	88.89	0.719
11	0.001	2	1	9500	100	82.04	0.3278
12	0.001	3	2	9500	200	87.77	0.6551
13	0.01	1	2	9500	300	90.69	0.8219
14	0.01	2	3	9500	100	76.3	0
15	0.01	3	1	9500	200	87.88	0.6613
16	0.1	1	3	9500	200	86.95	0.6082
17	0.1	2	1	9500	300	91.99	0.8961
18	0.1	3	2	9500	100	77	0.0400

Table 2: Summary of active networks

Network name	**Training error**	**Test error**	**Validation error**	**Training algorithm**	**Error function**	**Hidden activation**	**Output activation**
MLP5-11-1	0.001717	0.003530	0.020089	BFGS	SOS	Tanh	Tanh
MLP5-5-1	0.000218	0.000021	0.008941	BFGS	SOS	Logistic	Identity
MLP5-5-1	0.007795	0.000283	0.021877	BFGS	SOS	Exponential	Exponential
MLP5-8-1	0.000157	0.000080	0.014060	BFGS	SOS	Logistic	Identity
MLP5-10-1	0.010965	0.001819	0.048022	BFGS	SOS	Identity	Logistic
MLP5-5-1	0.002049	0.000098	0.003350	BFGS	SOS	Tanh	Exponential
MLP5-7-1	0.014176	0.004481	0.101693	BFGS	SOS	Identity	Identity
MLP5-7-1	0.014153	0.004544	0.095438	BFGS	SOS	Identity	Identity

from above 8 models 4th one is selected which is 5-8-1 because training perfection is maximum and error is less out of all so 5-8-1 means 5 input layers, 8 hidden layers and 1 output layer network is selected for better performance (Fig. 3). Fig. 4 is a graph for normalized output (experimental) V/S normalized target (predicted by model). Based on 18 experiments, the combined effect of surfactant concentration and carrier concentration on the % extraction of diclofenac through ELM is shown in Fig. 5. From Fig. 5, it was observed the maximum extraction of diclofenac was achieved with 2 % w/v of surfactant concentration and 2 % w/v of carrier concentration.

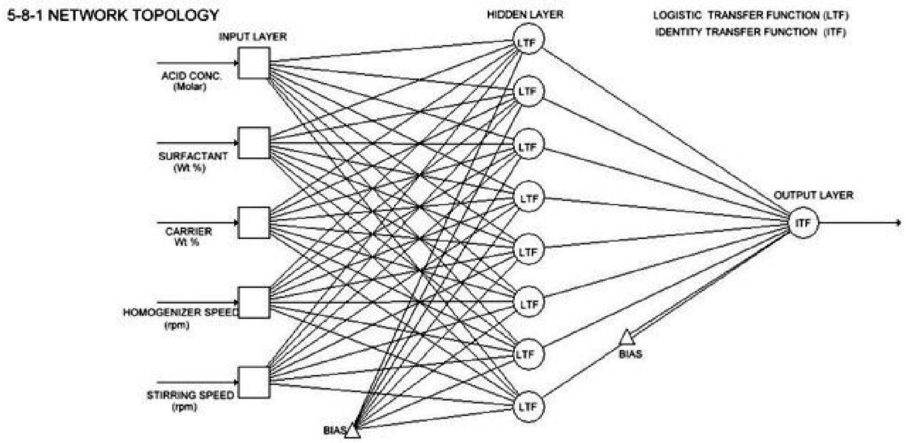

Fig 3: Network analogy for ANN model 5-8-1

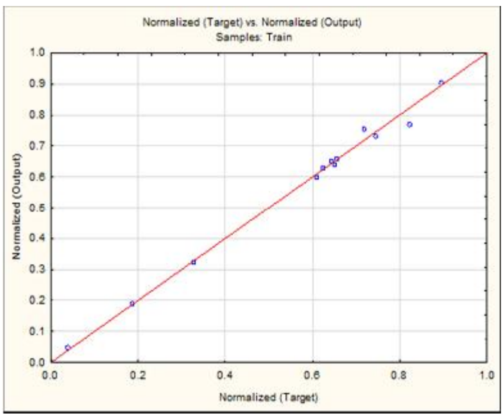

Fig 4: Output prediction of model 5-8-1.

Confirmation Experiments

After model built up we performed some extra experiment to check the accuracy of model and we performed 5 experiments at different parameter values and compare the experimental output and output given by model 5-8-1 and predictions are shown in Table 3.

Table 3: Output of custom prediction in terms of % extraction.

S. No.	Acid (M)	Surfactant(w/v %)	Carrier (w/v%)	Homogenizer Speed (rpm)	Stirrer speed (rpm)	Normalized Predicted Output	Denormalized Predicted Output (%)	Experimental Output(%)
1	0.001	2.0	2.0	9500	300	1.093968	95.45	94.95
2	0.001	2.0	2.0	9500	100	0.183183	79.50	81
3	0.001	2.0	2.0	6500	200	1.001634	93.83	91.11
4	0.001	1.0	2.0	9500	300	0.79243	90.17	89.55
5	0.001	2.0	3.0	9500	300	1.040965	94.52	94.88
6	0.1	2.0	2.0	9500	300	0.868121	91.50	90.78

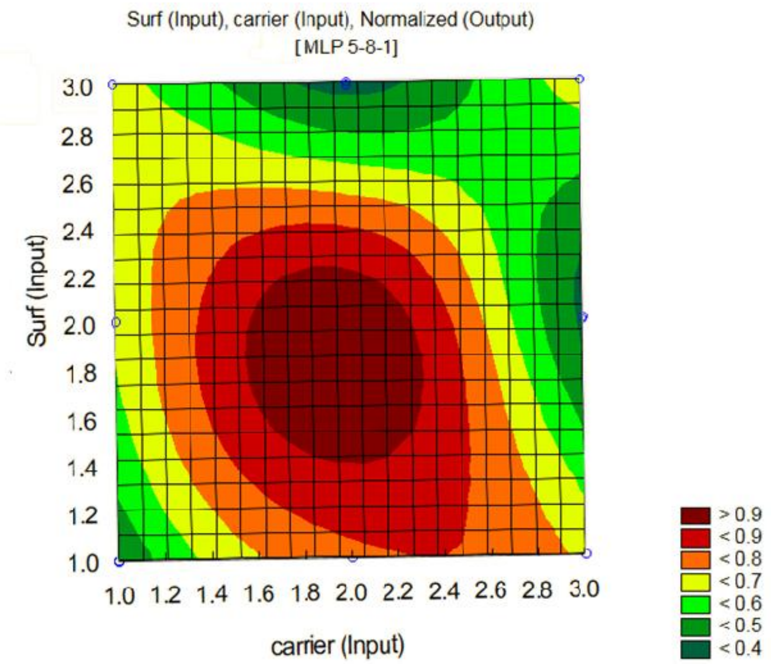

Fig 5: Combine effect of carrier and surfactant concentration on percentage extraction of DCF.

CONCLUSIONS

This study demonstrated an artificial neural network approach to find the real optimum conditions for extraction of diclofenac from waste water using emulsion liquid membrane. Different parameters like surfactant concentration, carrier concentration, homogenizer speed, stirring speed and acid concentration were chosen as controlling parameters. ANN model can be used to predict the percentage extraction accurately. ANN modeling method has many useful properties such as rapidity and robustness. It also has fault tolerance, adaptability, generalization. Because due to simplicity of ANN model makes it an interesting choice for modeling of complex systems such as wastewater treatment processes. Maximum 96% extraction of Diclofenac is possible with good stability of membrane. Optimum condition obtained was 2 w/v % Surfactant, 2 w/v % D2EHPA as carrier, HNO_3 as a stripping phase having concentration of 0.001M, homogenizer speed 9500 rpm and stirring speed 300 rpm.

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