Original Article

Investigation of Solubility of Mebendazole Drug using Linear Prediction and Multilayer Feed Forward Neural Network

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ABSTRACT

Objectives: A systematic *in-vitro* study has been achieved to decide the stability of a selection of three presidential hydrotropes to decorate the obvious aqueous solubility of the sparingly water- soluble drug, mebendazole drug. This study is that the ANN model to be prediction the solubility of the mebendazole drug among the chemical substances. **Methodology:** These experimental data, together with a selection of recounted and estimate physico-chemical consequences of the hydrotropes are after that utilizing *in-silico* to set up a counterfeit neural system (ANN) to engage for desires mebendazole drug solubilization. These trial information, along with a determination of described and gauge physico-chemical outcomes of the hydrotropes are after that using *in-silico* to set up a counterfeit neural system (ANN) to engage for desires mebendazole tranquilize solubilization. The readied ANN transformed into once determined to exist particularly correct predictions of mebendazole drug solubilization in the presence of hydrotropes and was once for that purpose validated to provide a precious capacity through which hydrotrope sensibility could in like way be screened computationally. The readied ANN transformed into once resolved to exist especially address forecasts of mebendazole tranquilize solubilization within the sight of hydrotropes and was once for that reason approved to give a valuable limit through which hydrotrope sensibility could in like way be screened computationally. The artificial neural network for predicting the solubility properties of the hydrotropic-ester combination was once developed the utilization of MATLAB 2011. For growing the ANN, solubility records that changed into obtained from the experiments had been used. **Results:** The interest of the hydrotropic will become set as input to the neural network and thus, the precise solubility turn out to be set as target records. The set of rules used to prepare the community modified into the Levenberg Marquardt algorithm. **Conclusion:** Two hidden layers were expressed. Randomly chosen 80% of the data became used to train the network, It's far is inferred that *in-silico* screening of drug/hydrotrope structures the utilization of artificial neural networks presents specifically possible to decrease the want for large laboratory testing of those systems and will thus flexibly an economy in expressions of diminished costs and time in tranquilize framework improvement.

Key words: Mebendazole Drug, Solubility, Hydrotropes, Mathematical Model, Artificial Neural Networks.

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INTRODUCTION

Mebendazole is a benzimidazole anthelmintic used in the cure of ascariasis, oxyuriasis, trichuriasis and greater than one worm contamination at a time. It's active against intestinal nematodes and hydatid disease when administered in high doses (2.4 g/day, for 1 to 6 months), molecular structure of Mebendazole.

Nevertheless, its poor aqueous solubility limits its bioavailability and in case of an acceptable systemic effect, improving its solubility should be an alternative to the

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use of excessive doses, usually related with adverse side effects. MBZ is inclined to high first-pass elimination and poor the water-soluble drug, it can exhibit a range of poor clinical effects such as potentially serious issues of inter-patient variability, erratic absorption (2-10% of an oral dose absorbed) and limited efficiency against tissue-dwelling helminthes. So, it requires innovative approaches to attain a sufficiently excessive bioavailability when administered by using the oral route.

Fast dissolving drug shipping system as a novel drug delivery system and a patient-oriented pharmaceutical training is designed to enhance the protection and efficacy of the drug molecule by formulating a dosage structure which disintegrates or dissolves in a few seconds after placement in the mouth. It can be administered without difficulty to geriatrics, pediatrics and patients struggling from dysphasia. It can ignore first-pass elimination by undergoing pre-gastric absorption. This improves the bioavailability of the drug and reduces dosing frequency and dose-related untoward effects.

An artificial neural network, usually called neural networks, maybe a mathematical model and computational model as much as expected, is stimulated with the help of the configuration and/or practical factors on technological neural networks.[1-5] A neural network is consists concerning connected team concerning artificial neurons. Modern-day neural networks are non-linear statistical facts modeling equipment.[6-7] They are typically persistent in conformity with version complex relationships among inputs then outputs but after find patterns of data.[8] ANNs are applied effectively among a variety of fields about science, designing, medicine, financial aspects, meteorology, psychology, neurology and climate or want developments forecasting.[9-12]

Input layer from ANN's that acquire uncooked data and remarks network. Input nodes are unbiased variables that together have an impact on the output parameter value. The records accumulated at the enter nodes represent the most important situation problem.[12,13] An output layer represents the response of the network to give input conditions. ANN's system has a hidden layer that connects the input layer and output layer. Consequently, the process depends on the interest of the enter layer and circumstance value or weights.[14-16] The input, hidden and output layer nodes are interconnected through tuned connection weight to refer to particular problems or samples of data.[17,18] Inside the technique, learning until the perceived pattern involves determining network parameters, like connection weights, threshold values and the most beneficial range of hidden nodes.[19] The advantages of ANNs in assessment to classical techniques are pace, simplicity and capacity to investigate from examples.[20-23] In the remaining decade, a few works approximately using ANNs in strength systems had been published. This method may stand used to inward the modeling of complicated physical phenomena.[24] So, engineering strive may be reduced. Additionally, a synthetic artificial neural is advanced to predict the residences and therefore, the values are in comparison with the experimental records.[25]

Experimental

The Artificial neural networks variety beyond the ordinary modeling techniques in as they can also be knowledgeable in imitation of investigating alternatives instead regarding life programmed according to model an absolutely special problem inside the everyday techniques. They're usually used in accordance with address issues so are refractory then difficult after the remedy with normal techniques. They are ready to study beside examples, are faulty-tolerant within the experience that they're capable to manage noisy then imperfect records are prepared in imitation of affect non-linear problems and, as much soon as trained, may operate predictions at entirely excessive speed. ANNs have been utilized of many engineering applications along inside control systems, of type then into modeling complex approach modifications.

Selection of Variables

The temperature and pressure are employing to lie the experimental variable models a high-quality way to ensure the robustness of the models. The whole concerning the mean solubility properties is placed to on keeping with the stay the independent variables. Take the temperature (T) prediction version due to the fact an instance, for this reason making sure the robustness about the prediction model.

Training Process of the Neural Network

The ANN calculation model is made by means of manner of the Neural Tools Software (Trial Version, Palisade Corporation, NY, or USA). We pick the General Regression Neural Networks (GRNN) module and Multilayer Feed Forward Neural (MLFN) module due to the fact the training modules. Solubility over mebendazole drug at unique temperatures is tabulated. The references need in accordance with being consulted for records on the uncertainties and therefore the attention states due to E, H and S. The education results

are showed as follows (Data deliver: CRC guide of Chemistry and Physics).

RESULTS AND DISCUSSION

The artificial neural network for predicting the solubility properties of the hydrotrope-drug mixture was developed using MATLAB 2011. For developing the ANN, solubility data that become obtained from the experiments had been used shown in Table 1-3. The concentration of the hydrotrope was set as input to the neural network and thus the particular solubility was set as target data. The inevitable solubility is that the output. The algorithm wants to train the network was Levenberg Marquardt algorithm. One hidden layer was unique. Randomly selected 60% of the data was used to train the network, 20% of the data was used for validation and remaining 20% was used for testing as shown in the Figure 1.

Solubility Prediction by ANN: Prediction for sodium salicylate hydrotrope concentration on the solubility of mebendazole at various temperatures.

The training, validation and testing of the sodium salicylate- mebendazole drug using ANN is shown in Figures 2-7. In the following Figures,

Target data = Actual Solubility

Output = Predicted Solubility

The training on the network became as soon as decided to be 99%, 98%, 100% efficient at 298K, 303K and 310K respectively. The validation on the data was once observed according to stand 100%, 93%, 91% efficient at 298K, 303K and 310K respectively. The testing of the data was once found consistent with stay 91%, 100% and 100% efficient at 298K, 303K and 310K respectively. The functional fit regarding the input (concentration), target (mebendazole proper solubility), then outturn (predicted solubility) for sodium salicylate-drug mebendazole at various temperature is shown between Figures 2-7.

Prediction for sodium benzoate hydrotrope concentration on the solubility of mebendazole at various temperatures

The training, validation and testing of the sodium benzoate-drug mebendazole using ANN is shown in Figures 8-13. In the following Figures. The training of the network was found to be 94%, 96%, 91% efficient at 298K, 303K and 310K respectively. The validation of the data was found to be 91%, 91%, 100% efficient at 298K, 303K and 310K respectively. The testing of

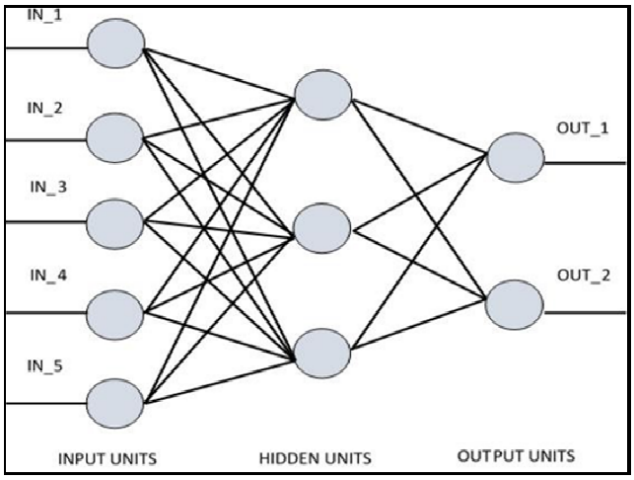

Figure 1: Schematic Representation of Artificial Neural Network.

Table 1: Predicted values for sodium salicylate hydrotrope concentration on the solubility of mebendazole in water at various temperatures by ANN.

C, mol/L	10^4S (mol/L)		
	T=298 K	T=303K	T=310K
0.1	3.47	3.65	5.50
0.3(MHC)	4.10	4.86	5.65
0.6	5.32	6.42	6.06
0.9	6.85	7.71	6.87
1.2	8.56	8.98	8.24
1.5	10.28	10.65	10.15
1.8	11.81	12.72	12.15
2.1	13.04	14.27	13.72
2.4(C_{max})	13.94	14.99	14.69
2.7	14.57	15.28	15.22
3.0	14.99	15.40	15.47

Table 2: Predicted values for sodium benzoate hydrotrope concentration on the solubility of mebendazole in water at various temperatures by ANN.

C, mol/L	10^4S (mol/L)		
	T=298 K	T=303K	T=310K
0.1	3.81	3.39	3.10
0.3(MHC)	6.55	6.55	6.87
0.6	10.63	11.25	12.47
0.9	13.27	14.29	16.08
1.2	14.64	15.85	17.90
1.5	15.80	17.13	19.27
1.8	18.04	19.57	21.71
2.1	21.47	23.27	25.36
2.4(C_{max})	23.86	25.84	27.90
2.7	24.73	26.78	28.83
3.0	24.97	27.04	29.08

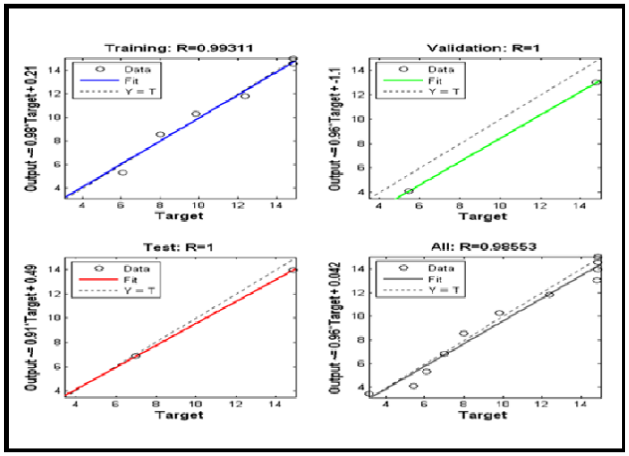

Figure 2: Plot fit for sodium salicylate and mebendazole solubility at 298 K.

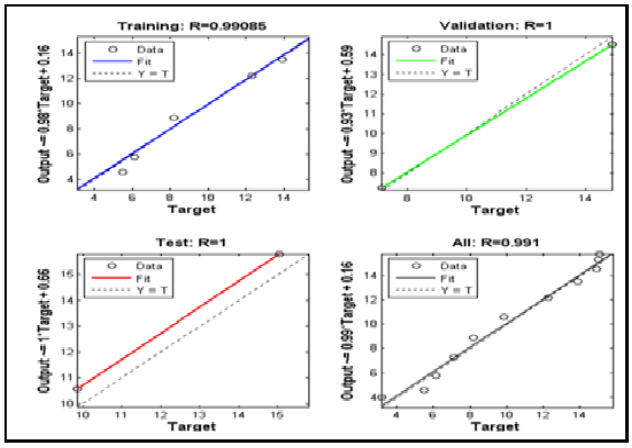

Figure 4: Plot fit sodium salicylate and mebendazole solubility at 303 K.

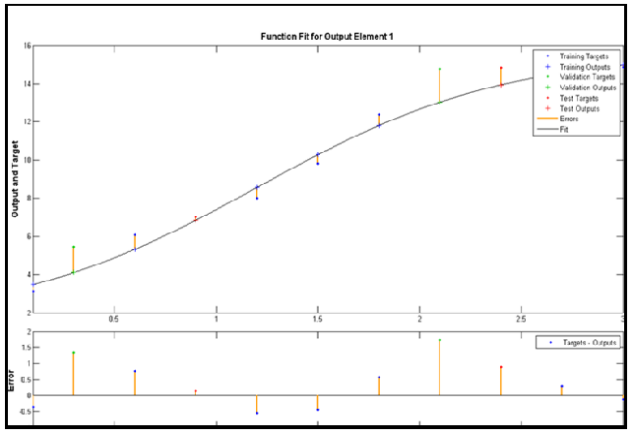

Figure 3: Function fit for sodium salicylate and mebendazole solubility at 298 K.

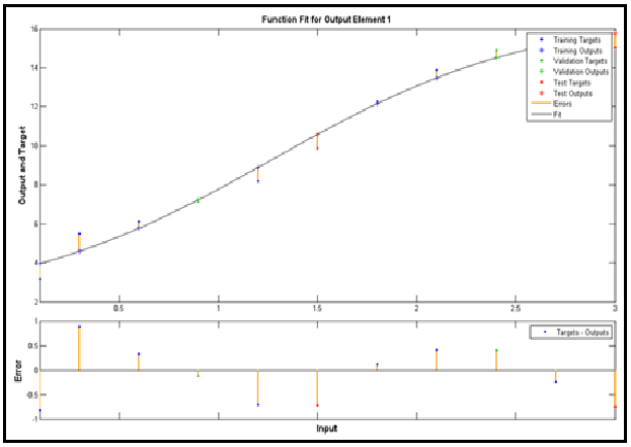

Figure 5: Function fit for sodium salicylate and mebendazole solubility at 303 K.

Table 3: Predicted values for resorcinol hydrotrope concentration on the solubility of mebendazole in water at various temperatures by ANN.

C, mol/L	10^4S (mol/L)		
	T=298 K	T=303K	T=310K
0.1	2.46	2.46	2.31
0.3(MHC)	2.59	2.56	2.66
0.6	2.88	2.79	3.38
0.9	3.34	3.17	4.38
1.2	4.03	3.77	5.66
1.5	5.01	4.68	7.13
1.8	6.28	5.95	8.64
2.1	7.79	7.53	10.02
2.4(C_{max})	9.37	9.27	11.14
2.7	10.82	10.91	11.98
3.0	12.00	12.26	12.56

the data was observed to be 98%, 98%, 100% efficient at 298K, 303K and 310K respectively. The functional fit of the input (concentration), target (mebendazole actual solubility) and output (predicted solubility) for sodium benzoate- drug mebendazole at various temperature is shown in Figures 8-13.

Prediction for resorcinol hydrotrope concentration on the solubility of mebendazole at various temperatures

The training, validation and testing of the sodium resorcinol-drug mebendazole using ANN is shown in Figures 14-19. In the following Figures. The training of the network was found to be 91%, 100%, 91% efficient at 298K, 303K and 310K respectively. The validation of the data was observed to be 91%, 93%, 100% efficient at 298K, 303K and 310K respectively. The testing of the data was observed to be 100%, 95%, 100% efficient at 298K, 303K and 310K respectively.

Sodium salicylate, Sodium benzoate and Resorcinol were used in the experiments to study the solubility at

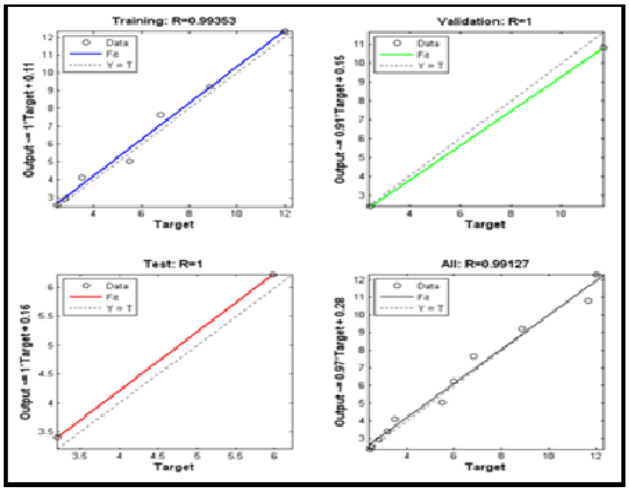

Figure 6: Plot fit sodium salicylate and mebendazole solubility at 310 K.

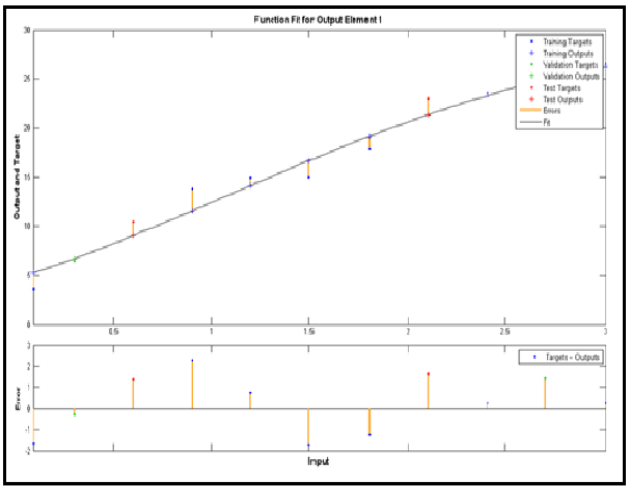

Figure 9: Function fit for sodium benzoate and mebendazole solubility at 298 K.

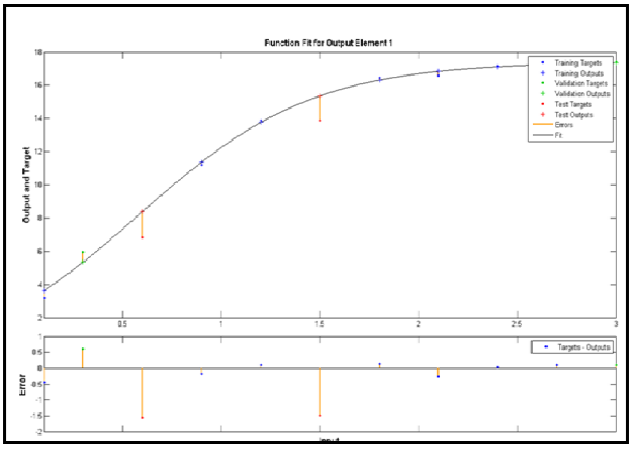

Figure 7: Function fit for sodium salicylate and mebendazole solubility at 310 K.

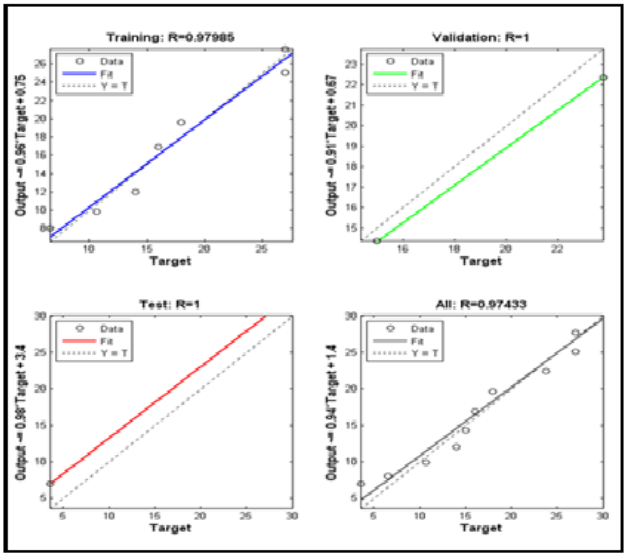

Figure 10: Plot fit for hydrotrope of sodium benzoate at 303 K.

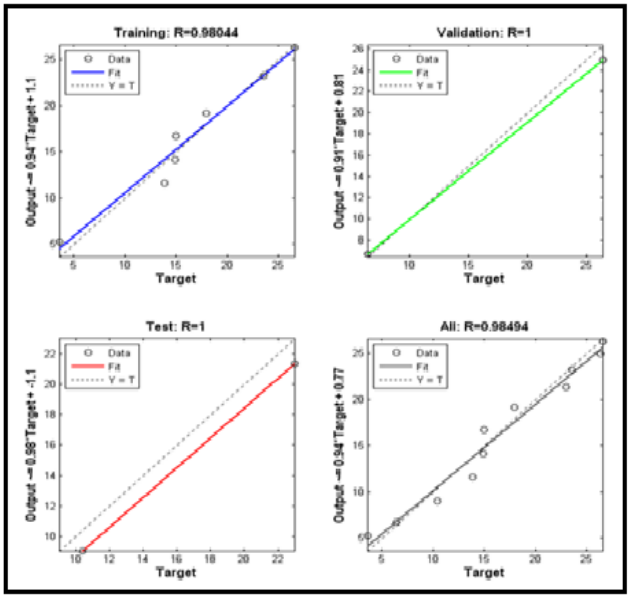

Figure 8: Plot fit for sodium benzoate and mebendazole solubility at 298 K.

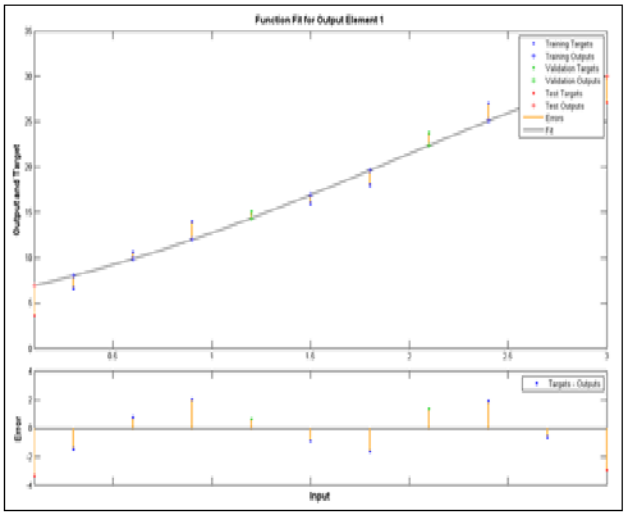

Figure 11: Function fit for sodium benzoate and mebendazole solubility at 310 K.

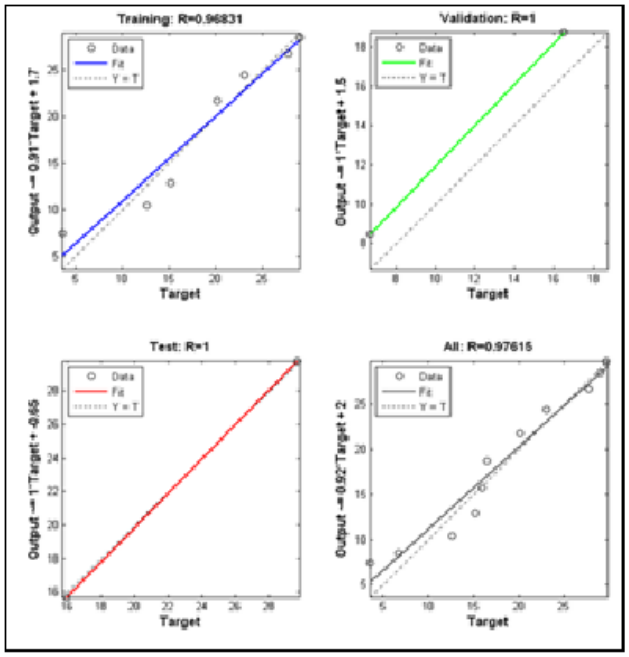

Figure 12: Plot fit for sodium benzoate and mebendazole solubility at 310 K.

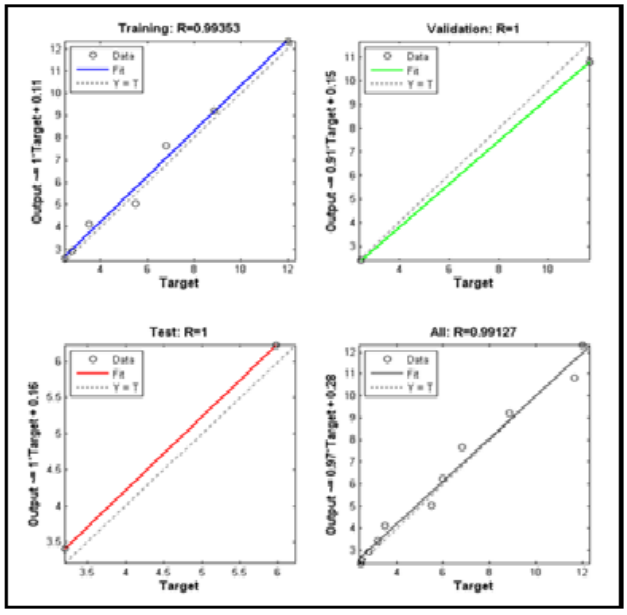

Figure 14: Plot fit for the resorcinol and mebendazole solubility at 298 K.

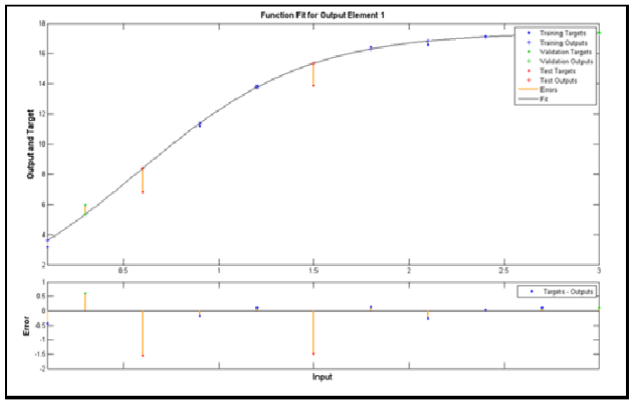

Figure 13: Function fit for sodium benzoate and mebendazole solubility at 310 K.

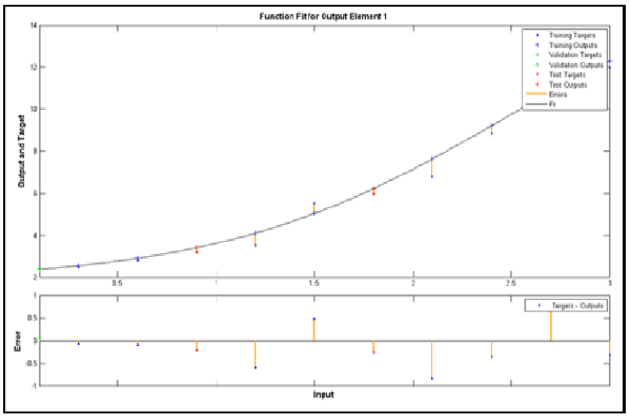

Figure 15: Function fit for resorcinol and mebendazole solubility at 298 K.

different temperatures (298 K, 303 K and 310 K). Out of these three hydrotropes, mebendazole drug is more soluble in sodium salicylate hydrotrope. Because it is molecular structure is more suitable to soluble in water. This reality should be explained by mebendazole affinity minimize for the hydrophobic cavity, in ionized form and therefore, greater hydrophilic form.

CONCLUSION

We considered a solubility regarding mebendazole anticipating model supported on a multi-layer feed-forward neural network with the mutual records function selection. We also evaluated the performance of our model on solubility data collected from mebendazole. The ANN educated on the premise of the reported mebendazole/hydrotrope solubilization records changed into utilized now not simplest to expect–with excessive accuracy–the growth inside the aqueous solubility of the mebendazole, however also allowed an informative exploration of the relative importance of diverse physico-chemical properties of the hydrotropes in imparting such certain enhancements. The designed ANN became as soon as moreover proven to be precious into figuring out instantaneous capability hydrotropes due to mebendazole.

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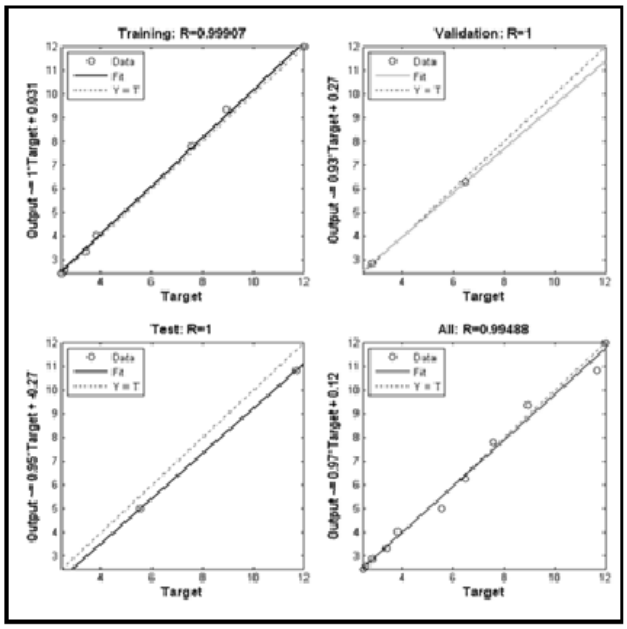


Figure 16: Plot fit for the resorcinol and mebendazole solubility at 303 K.

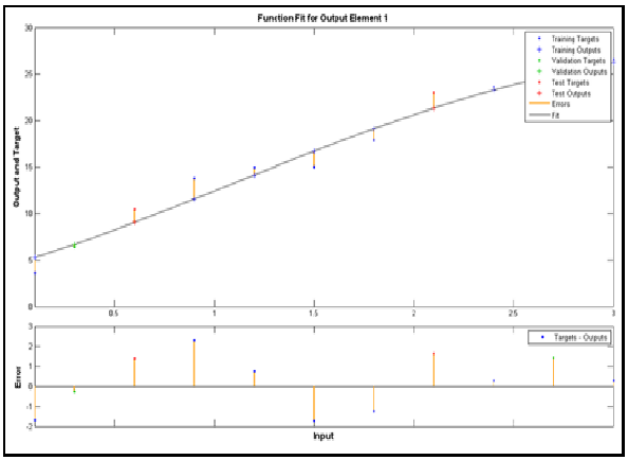


Figure 17: Function fit for resorcinol and mebendazole solubility at 303 K.

University for providing the infrastructure and support to carry out the research work.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ABBREVIATIONS

ANNs: Artificial neural networks; **GRNN:** General Regression Neural Networks; **MLFN:** Multilayer Feed forward Neural; **MATLAB:** Matrix laboratory.

REFERENCES

1. Neuberg C. Hydrotropy. Biochem Z.1916;76:107.

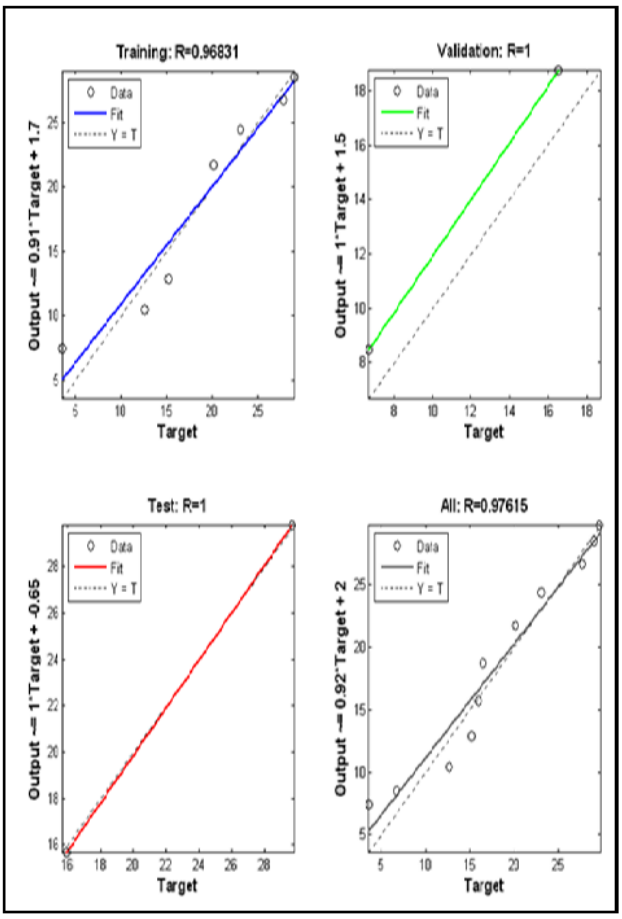


Figure 18: Plot fit for resorcinol and mebendazole solubility at 310 K.

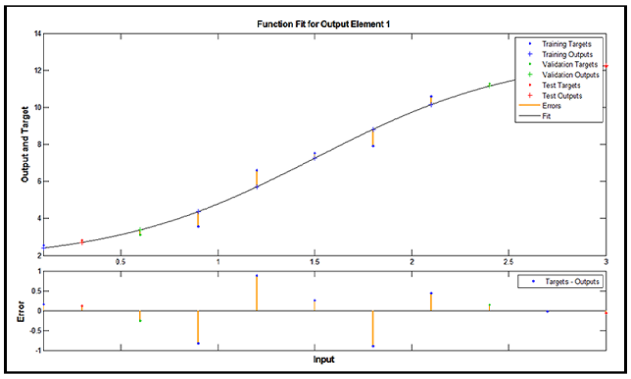
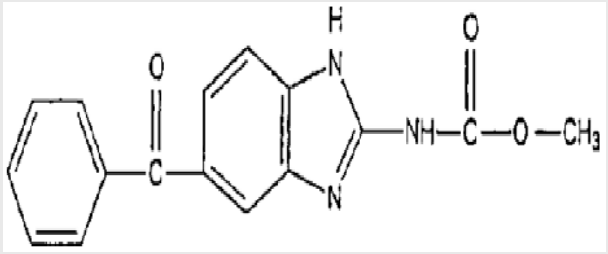


Figure 19: Function fit resorcinol and mebendazole solubility at 310 K.

2. Srinivas V, Balasubramanian D. When Does the Switch from Hydrotropy to Micellar Behavior Occur. Langmuir. 1998;14(23):6658-61.
3. Shanthi D, Sahoo G, Saravanan N. Designing an Artificial Neural Network Model for the Prediction of Thromboembolic Stroke. International Journals of Biometric and Bioinformatics. 2009;3(1):10-8.
4. Sundari N, Radhika T, Saranya V, Jayakumar C. Quantitative analysis of salbutamol bulk sample using nicotinamide hydrotrope. International Journal of Pharmacy and Pharmaceutical Science Research. 2012;2(1):16-9.
5. Reddy PDM, Senthilkumar R, Lakshmana RG, Saravanakumar K, Naveen PBS. A critical review on thermal energy storage materials and systems for solar applications. AIMS Energy. 2019;7(4):507.

6. Balasubramanian D, Srinivas V, Gaikar VG, Sharma MM. Aggregation Behaviour of Hydrotropic Compounds in Aqueous Solution. J Phys Chem. 1989;93(9):3865.
7. Senthilkumar R, Reddy PDM, Lakshmana RG, Saravanakumar K, Naveen PBS. Improved sorption of reactive black 5 by date seed-derived biochar: Isotherm, kinetic and thermodynamic studies. Separation Science and Technology. 2019;54(15):2351.
8. Kim S, Kim JY. Papp M. Hydrotropic solubilization of poorly water-soluble drugs. J Pharm Sci. 2010;99(9):3955-65.
9. Akhilesh KJ. Solubilization of indomethacin using hydrotropes for aqueous injection. European Journal of Pharmaceutics and Biopharmaceutics. 2008;68(3):701-14.
10. Jayakumar C, Antony BM, Rajasekhar RG. Quantitative analysis of famotidine bulk sample using sodium Salicylate hydrotrope. International Journal of Institutional Pharmacy and Life Sciences. 2012;2:2249.
11. Kan T, Shimada Y, Sato F, Ito T, Kondo K, Watanabe G, *et al*. Prediction of Lymph Node Metastasis with use of Artificial Neural Networks Based on Gene Expression Profiles in Esophageal Squamous Cell Carcinoma. Ann Surg Oncol. 2004;11(12):1070.
12. Jayakumar C, Deepak KK, Nesakumar D. Quantitative analysis of Theophylline bulk sample using Sodium salicylate hydrotrope. Indian J Pharm Sci. 2010;2:0975.
13. Jayakumar C, Sampath KV, Raja C. Thermodynamic Study On Hydrotropic Aggregation Behavior Of Mebendazole. International Journal of Research. 2020;7: 540.
14. Jayakumar C, Mansa DV, Reddy PDM, Sridar R. A study on the extraction of bioactive compounds from *Capparis zeylanica*. AIP Conference Proceedings. 2020;2225(1):70002.
15. Coffman RE, Kildsig DO. Effect of Nicotinamide and Urea on the Solubility of Riboflavin in Various Solvent. J Pharm Sci. 1996;85(9):951-4.
16. Reddy PDM, Nur SBR, Huei RO, Chin KC, Maksudur RK, *et al*. Preparation and Characterization of Photocatalyst for the Conversion of Carbon Dioxide to Methanol. International Journal of Chemical, Molecular, Nuclear, Materials and Metallurgical Engineering. 2016;10(5): 515.
17. Jayakumar C, Mansa DV, Reddy PDM, Sridar R. Oil Extraction from *Trichosanthes tricuspidata* Seed using Conventional Soxhlet Apparatus. Asian Journal of Chemistry. 2019;32:9.
18. Miguel GN, Carla CS, Katia RP, Beatriz EG. The Photophysical Determination of the Minimum Hydrotrope Concentration of Aromatic Hydrotropes. J Colloid Interface Sci. 2007;315(2):810-3.
19. Taki S, Badens E, Charbit G. Controlled Release System Formed by Supercritical Anti-Solvent Co-precipitation of a Herbicide and a Biodegradable. Polymer J Supercrit Fluids. 2001;21(1):61-70.
20. Krishnaiah D, Reddy PDM, Sarbatly R, Bono A, Anisuzzaman SM, Krishnaiah KK. Solid–Liquid Mass Transfer Coefficients in an Ultrasound-Irradiated Extraction of Iota-Carrageenan. Developments in Sustainable Chemical and Bioprocess Technology. 2013;10:249.
21. Rubino JT, Yalkowsky SH. Co-solvency and deviations from log linear solubilization. Pharm Res 1987;4(3):231.
22. Strickley RG. Solubilizing excipients in oral and injectable formulations. Pharm Res. 2004;21(2):201-30.
23. Reddy PDM, Nur SBR, Huei RO, Chin KC, Maksudur RKD. Preparation and Characterization of Photocatalyst for the Conversion of Carbon Dioxide to Methanol. International Journal of Chemical, Molecular, Nuclear, Materials and Metallurgical Engineering. 2016;10(5):515-8.
24. Reddy PDM, Nur SBR, Huei RO, Chin KC, Maksudur RK, Sathiyamoorthy D. Preparation and Characterization of Photocatalyst for the Conversion of Carbon Dioxide to Methanol. International Journal of Chemical, Molecular, Nuclear, Materials and Metallurgical Engineering. 2016;10(5):515-8.
25. Reddy P, Duduku K, Awang B, Paulraj P, Rosli BMY, Naveena L. Estimation of Carrageenan Concentration by using ultrasonic waves and Back propagation Neural Networks. Journal of Applied Science. 2010;10(21):2729-32.

PICTORIAL ABSTRACT



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SUMMARY

In the present research work, the ANN model to predict the solubility regarding the mebendazole remedy amongst the chemical substances. These empirical data, mutually including a range of acknowledged then computed physico-chemical properties concerning the hydrotropes are like after using among silico to train an artificial neural network (ANN) in imitation of allow because of predictions regarding mebendazole drug solubilization. The trained ANN used to be as soon as determined according to exist incredibly accurate predictions about mebendazole drug solubilization inside the presence of hydrotropes then used after be for so purpose validated in imitation of provide a treasured potential through who hydrotrope faculty should additionally be screened computationally. The artificial neural community because predicting the solubility properties on the hydrotropic-ester mixture was once developed the utilization of MATLAB 2011. For developing the ANN, solubility records up to expectation modified within obtained from the experiments had been used.

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