SIMULATION OF BETAMETHASONE RELEASE PROFILES FROM IN SITU FORMING SYSTEMS BASED ON PLGA

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ABSTRACT SUMMARY

In this study, *In Situ Forming* Betamethasone delivery system based on PLGA, drug release profiles were modeled and ability of the model in designing the drug delivery system is shown.

INTRODUCTION

Drug release profile is a specific curve according to kind of disease and physical conditions of patient. *In Situ Forming* drug delivery systems are novel systems that in these systems initially by mixing a drug with a solvent and polymer as a carrier make a liquid solution then is injected to the target issue. After some hours, solvent gets out of system and a jelly heap is formed that contains drug and polymer. Polymer is gradually degraded and the drug is released, the drug release rate is proportional to the polymer degradation rate.
This drug delivery system has many applications to cure diseases and specific release profile designing depends on disease and patient condition to get the best result. There are different variables in these systems such as type and concentration of drug, type of polymer, presence or non-presence of additive , etc. that help formulator to design a proper drug release in terms of patient's needs. In terms of existence different variables, it is essential to do various experiments to design a specific release profile and obtain the favorite one. Doing these experiments is time and expense consumer; therefore, modeling the drug release treatment helps to make it applicable, inexpensive and accurate formulation design in terms of system entrance variables. In this study, by the usage of practical experiments data of *In Situ Forming* Betamethasone delivery system based on PLGA, release profiles were modeled by use of artificial neural networks and ability of the model in designing the drug delivery system is shown.

EXPERIMENTAL METHODS

At first, we should present the symbols used in this paper. Polymer H: RG 756, L: RG 504H, M: RG 504H 1:1 RG 756. Additive E: Ethyl heptanoate. Drug A: Betamethasone acetate. B: Betamethasone.
Primary experimental data for modeling *In Situ Forming* Drug delivery system for Betamethasone (5, 7, 10 and 15%), Ethyl heptanoate additive and PLGA polymer was considered. A neural network was designed by Feed Forward Back Propagation method with two hidden layers and primary data classified in two sets, 41 trains and 9 test data, then network trained and tested by using of these data. On the basis of obtained results, trained network has proper accuracy in MSE (Mean squared error performance function) = 7.1008e-006 and MAE
(Mean absolute error performance function) = 0.0018. Repeatability of the network by use of networks' errors variance calculations that have been repeated 10 times was confirmed and it was equal to 1.3358e-011.

RESULTS AND DISCUTION

This study proves that modeling the drug release profile by use of artificial neural

networks has ability to offer a proper method for drug release profile designing in accurate method. The network base on adequate recognition of primary data has ability to anticipate system's treatment in the span of entrance data. According to this ability, we can design patient's required drug release profile by changing variables for access the favorite release. Three Case studies as follows present its application as sample:

Case 1: Effect of drug loading measurement on drug release profile:

We know that increase in the Betamethasone amount of loading causes the decrease in burst release and release speed reduction in system, but the amount of this affect of loading increase on drug release reduction must calculate quantitatively and accurately for designing the drug release profile. On the other hand, presence or non presence of additive also has effect on drug release type. Therefore, for designing a release profile by consideration to these two parameters and fixing the other parameters, various experiments are needed. Modeling by neural network offers an ability of this designing with minimum error. Figure1 illustrates the release type in favorite condition with concentration and additive variables.

Now by consideration to this result, by use of neural network model we can design a favorite release profile. Attention to this point is so important that obtaining these profiles from software is so fast and doesn't have the real experiments' expense and long time duration.

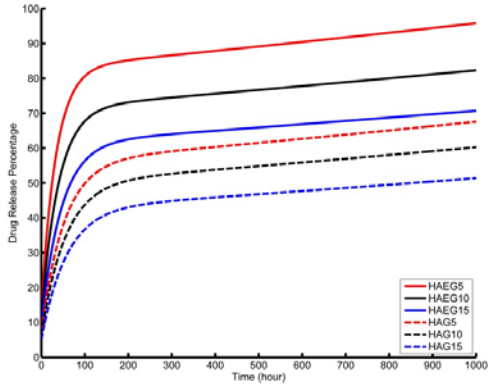

Figure 1: Effect of drug loading by showing 8 profiles release

Case2: Effect of polymer type:

One of the system's features that has affect on drug release profile is type of the polymer. For example, three types of polymer RG 504H (H), RG 756 (L) and their 1:1 proportion (M) were considered in experiments performance and related data was used for modeling.

As it can be seen, effect of polymer type is too much in release and using of designed model offered a possibility to formulator to design a favorite release profile. (Figure 2)

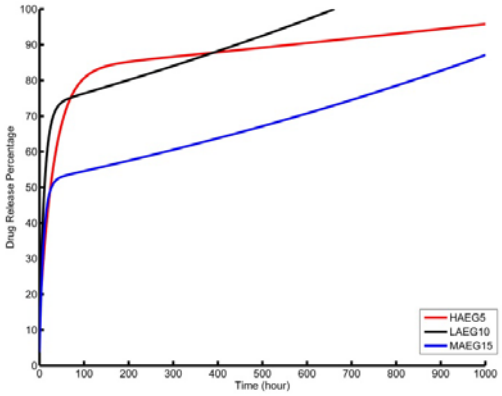

Figure 2: Effect of polymer type by showing 3 profiles release

Case 3: Effect of drug's type:

In figure 3, profile release for Betamethasone drug and Betamethasone acetate has been drawn for samples including 5% drug loading and base on H polymer and Ethyl Heptanoate and gamma radiation.

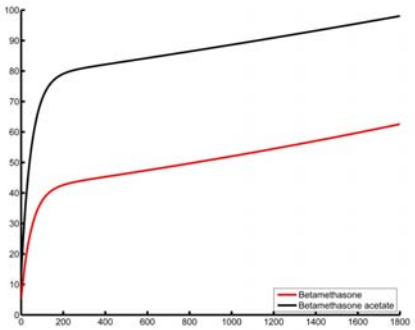

Figure 3: Profiles release of HAEG5%, HBEG5%

In figure 4, profiles release of two drugs for samples with 5% drug based on M polymer and above conditions have been drawn.

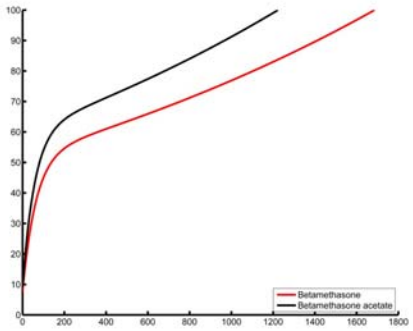

Figure 4: Profiles release of MAEG5%, MBEG5%

Figure 5 shows the release profiles of two drugs for samples with 5% drug and base on L polymer and above conditions.

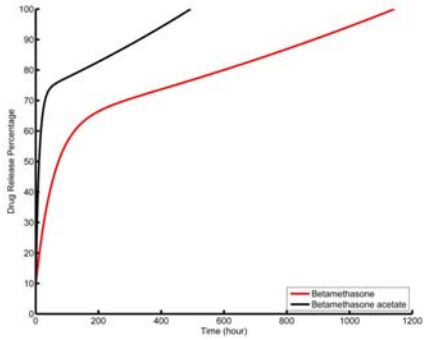

Figure 5: Profiles release of LAEG5%, LBEG5%

From all of above figures can be conclude simply that Betamethasone acetate drug release from our system is more than Betamethasone.

CONCLUSION

By use of artificial neural networks, designing and accurate performing a set of experiments, we can anticipate drug delivery systems treatment and utilize it for drug release profiles designing. This modeling let formulator using of these systems more easily and less expensively.

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