Finding Rules for AntibacterialPolyherbal Gels with FormRules

Background

Traditional medicines have proved efficacious as antibacterials, but it can be difficult to ensure that they are delivered to the right site and that they stay in intimate and prolonged contact with diseased tissue. Gel formulations can be one way of achieving this goal, particularly if the gelation occurs *in situ* e.g. because of a change in pH or temperature.

Chopra *et al*, publishing in 2007 in *European Journal of Pharmaceutics and Biopharmaceutics*, have designed a system using a mixture of

Carbopol (range 0.25% to 1%)
Honey (range 3% to 5%)
Aerosil (range 0.5% to 2%)

where the Aerosil serves as an in-situ thickener because of its ability to absorb water. This mixture is used to deliver a mixture of 250 g of antibacterials derived from a mixture of four different herbal sources.

The properties measured included

Storage modulus (in Pa)
Gel Index
Maximum Detachment Force (g)

The study that Chopra et al undertook involved a Box Behnken design, with the weight/weight percentage of each of the three ingredients being varied. The limitations of statistical models meant that only three variables could be investigated, so the amount of the drug, and the processing conditions, were held constant in their study.

The present document describes the use of neurofuzzy logic to understand in detail how the three ingredients affect these properties of mucoadhesive gels, using the data reported by Chopra *et al*.

Models for Polyherbal Gels

The Structural Risk Minimization model selection criterion (the default within FormRules) was used to develop models for each of the properties. ANOVA statistics for these models indicated that they were of excellent quality (indicating, incidentally, that the data points were very reliable). R^2 values

for the ANOVA statistics were between 0.96 and 0.99.

The models developed indicate that for each property, the polymer concentration made the most important contribution to the model. The amount of honey was also important. Figure 1 shows the graphical representation of the model for the storage modulus.

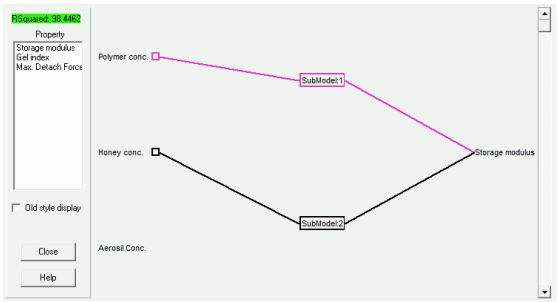

Figure 1. Graphical representation of model for storage modulus

The rules underlying this model are as follows:

IF Polymer conc. is LOW THEN Storage modulus is LOW (1.00)
IF Polymer conc. is MID THEN Storage modulus is LOW (1.00)
IF Polymer conc. is HIGH THEN Storage modulus is HIGH (1.00)

which can be represented graphically as shown in Figure 2.

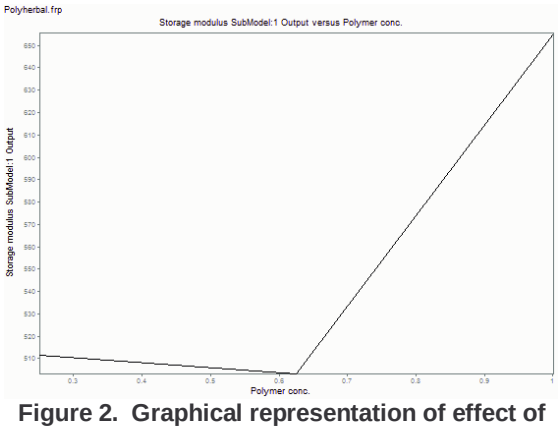

Figure 2. Graphical representation of effect of polymer concentration on storage modulus

Clearly from this plot, when the polymer concentration is below about 0.62%, it has virtually no effect on the storage modulus.

Intelligensys Ltd, Springboard Business Centre, Stokesley Business Park, Stokesley, N. Yorks. TS9 5JZ, UK
Tel: (+44) 1642 715380 Fax: (+44) 1642 715301 e-mail postmaster@intelligensys.co.uk

The second contribution to the storage modulus comes from the honey concentration, where the rules are

IF Honey conc. is LOW THEN Storage modulus is LOW (0.73)
IF Honey conc. is HIGH THEN Storage modulus is HIGH (0.80)

So, higher honey concentrations tend to lead to a higher storage modulus, following a simple linear relationship.

The total model represents the experimental data well, as shown by Figure 4 which gives the actual vs. predicted values.

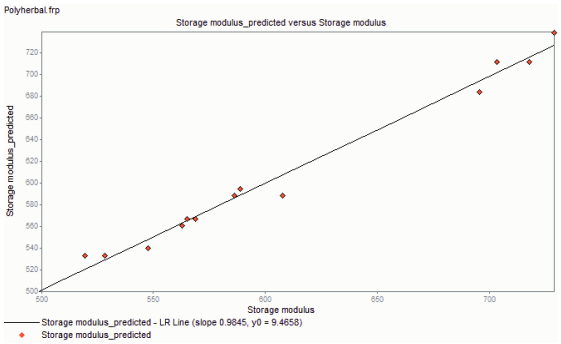

Figure 4. Actual vs predicted values for storage modulus.

Gel index is also affected by the polymer concentration in a linear fashion, following the rules

IF Polymer conc. is LOW THEN Gel index is LOW (1.00)
IF Polymer conc. is HIGH THEN Gel index is HIGH (1.00)

while a lesser contribution comes from the amount of honey, described by the rules

IF Honey conc. is LOW THEN Gel index is LOW (0.90)
IF Honey conc. is HIGH THEN Gel index is HIGH (0.77)

The maximum detachment force is affected most strongly by the polymer concentration, following the rules

IF Polymer conc. is LOW THEN Max. Detach Force is LOW (1.00)
IF Polymer conc. is MID THEN Max. Detach Force is HIGH (0.84)
IF Polymer conc. is HIGH THEN Max. Detach Force is HIGH (0.80)

The behaviour is illustrated graphically in Figure 5, which shows that as polymer concentration increases up to about 0.6%, the maximum detachment force increases. Above this point, it remains substantially unaffected by higher concentrations of polymer. This is consistent with the results from the statistical treatment of Chopra *et al*, who found that the highest values for this property occurred only when the concentration of 0.5% or greater.

As for the other properties, the honey concentration was the next most important variable, with simple linear behaviour encapsulated in the rules

IF Honey conc. is LOW THEN Max. Detach Force is LOW (0.65)
IF Honey conc. is HIGH THEN Max. Detach Force is HIGH (0.87)

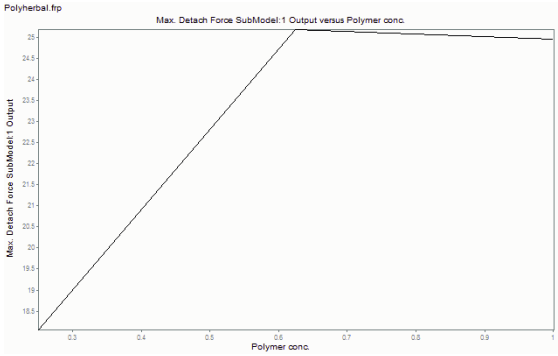

Figure 5. Effect of polymer concentration on maximum detachment force

Interestingly, the Aerosil concentration appeared not to affect any of the properties significantly; it was not required to use this variable in order to develop excellent models.

Conclusions

The high quality of the data means that excellent models could be developed for all three properties. Polymer concentration was the most important variable for each of the properties, with the honey concentration being next in importance. Aerosil concentration did not feature in any of the models.

At least two of these models showed that the behaviour was approximately linear over only part of the range.

The models developed were simpler than those from the statistical treatment, highlighting more clearly exactly which variables were most important for each of the properties.

For further information on FormRules, and applying neurofuzzy logic to your problems, contact us at the address below.

Intelligensys Ltd, Springboard Business Centre, Stokesley Business Park, Stokesley, N. Yorks. TS9 5JZ, UK
Tel: (+44) 1642 715380 Fax: (+44) 1642 715301 e-mail postmaster@intelligensys.co.uk