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Editorial

Computer-Aided Formulation – Myth or Reality

The development of a commercial product whether it be a relatively simple formulation (eg a capsule, tablet or oral liquid) or a controlled release formulation (eg an implant) is always a time-consuming and complicated process. Generally an initial formulation consisting of one or more drugs mixed with various ingredients (excipients) is prepared, and, as development progresses, the choice of these and their levels as well as the manufacturing process are changed and optimized as a result of intensive, time-consuming experimentation. These iterations, in turn, result in the generation of large amounts of data, the processing and understanding of which is challenging. In reality, the formulator has to work in a design space that is multi-dimensional and virtually impossible to conceptualize.

Traditionally, formulators have tended to use their own experience in the generation of the initial formulation and statistical techniques such as a response surface methodology to investigate the design space but optimization by this method can be misleading especially if the formulation is complex. Nearly twenty years ago a small number of visionary scientists from both industry and academia started to address these problems by experimenting with what was then a relatively well developed field of computer science - artificial intelligence. The technologies included expert systems for the generation of the initial formulation; neural networks for modeling the design space; genetic algorithms for optimizing the formulation and manufacturing process and neuro-fuzzy logic and decision trees for exploring the relationships within the design space and generating understandable rules that can be used in future work.

Initial results with expert systems reported in the mid-1990s showed that the technology did work for tablets, capsules, parenterals, film-coatings and topicals. The formulations generated were comparable with those developed by experienced formulators with the added benefits of consistent decision making, decreased timelines and cost savings in drug and excipients[1]. Slightly later results with neural networks showed that they could be applied to any formulation, no matter how complex, provided there were sufficient data available covering the design space. They were able to model these data, in many cases better than statistics, with the added ability of being either combined with genetic algorithms to accommodate constraints and preferences in the optimization of a formulation and process or with fuzzy logic to generate understandable rules[2].

Of course, as with all new technologies, despite the benefits, there have been issues, not least related to software and lack of development skills (the initial problems related to computing power have been solved with the dramatic increase in the speed of new computer chips). These have recently been addressed and there are now neural computing software packages specifically aimed at formulators allowing them to easily apply the technology to problems without having to be an expert in it. These are increasingly being used in both industry and academia to model and understand even the most seemingly intractable problems, e.g., relating the *in vivo* response of an inhalation product to its formulation. A decision support software package for formulators has also been developed.

The next generation of formulators in the pharmaceutical industry is likely to find itself using artificial intelligence technology routinely and to an increasing extent. Several companies have already implemented some of the techniques and made them available either as stand-alone software or linked via an intranet. However, the largest benefit in the future will undoubtedly arise from the seamless integration of artificial intelligence with another advanced computer technique, that of computer simulation[3] into a common decision support system allowing the *in silico* generation of formulated products *ab initio.*

References

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