European Symposium on Computer Aided Process Engineering – 15
L. Puigjaner and A. Espuña (Editors)

A framework for product analysis: Modelling and design of release and uptake of pesticides

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Abstract

This paper presents a framework for chemical product (pesticide) design and analysis. The framework consists of a set of computer-aided methods and tools that have been integrated to tackle the needs with respect to solution of chemical product design problems related to pesticide formulations. Two of the mathematical models (controlled release and pesticide uptake) that provide the principal calculation options are highlighted together with selected results from case studies.

Keywords: Controlled release, Microcapsule, Uptake, Pesticide, Polymer.

1. Introduction

The agrochemical industry is under constant development in order to adjust to sustainability criteria, to achieve improved effectivity of the formulations and to optimize the doses of application into the crop. An important area of focus is the one of controlled release technology, which has been widely studied in the pharmaceutical industry and is nowadays also used for pesticide delivery. The advantages of, for example, having a pesticide compound encapsulated are numerous and related not only to improvements in the applications but also in minimizing health and environmental issues.

Once the pesticide has been delivered into the environment, it interacts with the plant. According to each type of pesticide (insecticides, fungicides, etc.) the desired behaviour regarding its uptake into the plant might be different (for example in the case of insecticides, little uptake is desired so they act as contact poisons from the leaf surface) and is therefore an important factor when considering the design of the pesticide formulation.

Mathematical models can provide a big help in the search for improved pesticide formulations and their uptake and delivery, as they can diminish the number of experiments that are needed to obtain the final product design. Research expenses as

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well as time to market can be considerably reduced with respect to product development.
The interest of this work is in the product design and analysis area, where the use of a framework that will allow the systematic study of the behaviour of the pesticide active ingredient (AI), including its delivery from microcapsules and its uptake into the plant, is being proposed. The framework consists of a collection of computer-aided methods/tools that guides the user through the various steps towards the problem solution. This paper describes the framework, its contents and highlights its use through a case study.

2. Framework for product and formulation design

The proposed framework includes tools such as, a database of plants, pesticide AI's, release devices, together with some of their characteristic properties; allows the selection of a candidate surfactant for a specific AI leading to a pesticide formulation that can be tested and evaluated using the appropriate release and uptake models (and their corresponding parameters).
In this section the framework for pesticide product design, illustrated in Fig.1, is presented in more detail.

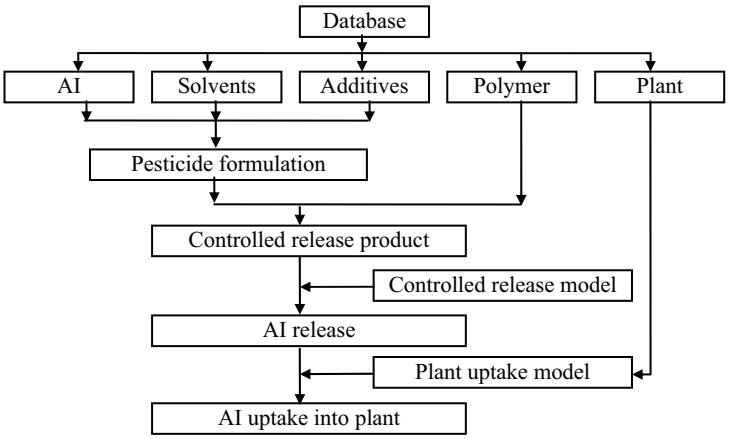

Figure 1. Framework for pesticide and product design.

The design of a pesticide product can be formulated as, given a pesticide active ingredient, we need to identify the optimal pesticide formulation to be sold as a product for application on specific crops. For that, we need to identify the compounds (surfactants) that must be added in order to meet the specified performance criteria. These criteria might be related to the release from the product (in case we are working with controlled release products) or with the pesticide uptake into the plant.
In order to solve the design problem the first step is the generation of candidates, that is, the selection of the additives (and the amounts) that together with the given AI, match the specific properties for the pesticide application. For that, a database is available that contains a selection of pesticide active ingredients, together with common solvents used in the formulations and surfactants, that combined give the pesticide formulation.

The next step involves the decision on which type of product needs to be designed. In the case that a controlled release product is desired, they consist of a polymer membrane that contains the pesticide formulation, therefore it is necessary to select a polymer that is also obtained from the database, as the material for the microcapsule. The controlled release product needs to be defined in terms of shape and dimensions, together with the formulation specifications given above. These specifications determine the pesticide system properties and constitute the input data required to evaluate the behaviour of the AI with the mathematical release model, which predicts the delivery of the AI to the environment as a function of time.

At this point, a controlled release product is available for the given pesticide and its performance can be evaluated with respect to the specified design criteria. On the other hand, if the interest is not in controlled release applications but in applications such as the pesticide being sprayed onto the crop, the analysis includes the study of the pesticide uptake into the plant. In order to do this, we need to know the plant to which the formulation will be applied. The necessary data, regarding the plant, that will be needed by the uptake model is obtained from the database, this is thicknesses of the different leaf layers, compositions and properties. From the preliminary definitions the pure component properties needed are available (water solubility, octanol-water partition coefficient, etc.) and after the plant data is introduced, the mixture properties are also defined (diffusivity and solubility into the leaf). Through the mathematical model the uptake of the AI into the plant is now calculated and the design criteria checked. In case the criteria are not matched, we go back to the first step and generate new alternatives, test their performance and check the design criteria until the proper formulation is found.

The proposed framework allows the user to produce several product alternatives and then take a decision based on either the desired release from a specific controlled release product or on the uptake behaviour needed for the pesticide into the plant. The main advantage of this framework is related to the predictive capabilities of the models and thus the simplification of the whole analysis of the formulation and product performance.

3. Controlled release model

A computer-based model that can predict the delivery of the AI from a fabricated device is required in this framework in order to optimize the design of the product (that contains the pesticide formulation) with respect to the amount of pesticide that will be available in the environment where it is released.

A mathematical model for the release of an AI from a microcapsule device (or solution of microcapsules) has been previously developed and validated (Muro-Suñé, 2004a). This model accounts for the number of microcapsules and their sizes through a normal distribution function of the microcapsule radii. The release is modelled with the equations for non-constant activity source (Comyn, 1985), that are derived from Fick's law of diffusion and provide the variation of the AI concentration with time, from which the percentage of release of the AI into the environment is obtained. This model applies for the case where the AI is available in solution below saturation.

The inputs to the model (represented by a set of DAE's) include the dimensions of the microcapsules (radii, membrane thickness), the initial concentration of AI inside the microcapsule and the properties related to the AI-polymer system, that is partition and diffusion coefficients. The geometric or physical shape parameters can be fixed according to the needs and reproduced accurately during the fabrication of the product. Therefore, the critical step is the estimation of the diffusion and partition coefficients through completely predictive models. These models have been developed.

The partition coefficients are calculated through activity coefficients, which are estimated with a group-contribution model, the GC-Flory EoS model (Bogdanic et al., 1994), developed for polymer systems. This is a predictive model, given that only the molecular structure of the compound and the system conditions are needed for the calculations, and it has been extended so that the complex pesticide molecules can be handled (Muro-Suñé, 2004b).

A prototype model for the diffusion coefficient has been developed based on the application of the free-volume theory (Vrentas and Duda, 1977 and Zielinski and Duda, 1992) in a completely predictive manner. This model can currently be applied to small solvents diffusing through polymers but from a pesticide product development point of view, it should be possible to predict the diffusion coefficients of large and complex pesticide molecules. For these compounds, the free-volume theory is, at the moment, only predictive in the way that by using data of diffusion coefficient as a function of temperature of a certain pesticide in a given polymer, the needed parameters can be estimated, and they can then, in principle, be used to predict the diffusion coefficient of the same pesticide in any other polymer.

In Table 1, predicted partition and diffusion coefficients are listed for a microcapsule consisting of a pesticide, Permethrin, that is encapsulated within a polyester polymer (Polyethylmethacrylate, PEMA), and where both the diffusion and partition coefficients have been estimated through the models described above. More details of the problem solution can be obtained from the authors.

Table1. Inputs for the microcapsule controlled release model

Parameter	Variable	Value	Data type
Geometric	Radius (m)	5e-6 – 2.25e-5	experimental
	Wall thickness (m)	2e-6	experimental
Partition coefficients	$K_{m/d}$	2.941	estimated
	$K_{m/r}$	$4.902 \cdot 10^{8}$	estimated
Diffusion coefficient	D (m^2/s)	1.02e-15	estimated

4. Pesticide uptake model

A generalized model that can reproduce and explain the behaviour of the pesticide uptake into the plant has been developed and included in this framework. The model is based on Fick's laws of diffusion and employs predictive constitutive models for some of the important parameters and properties. The main equations of the model are presented in Fig. 2 together with a schematic representation of the scenario modelled.

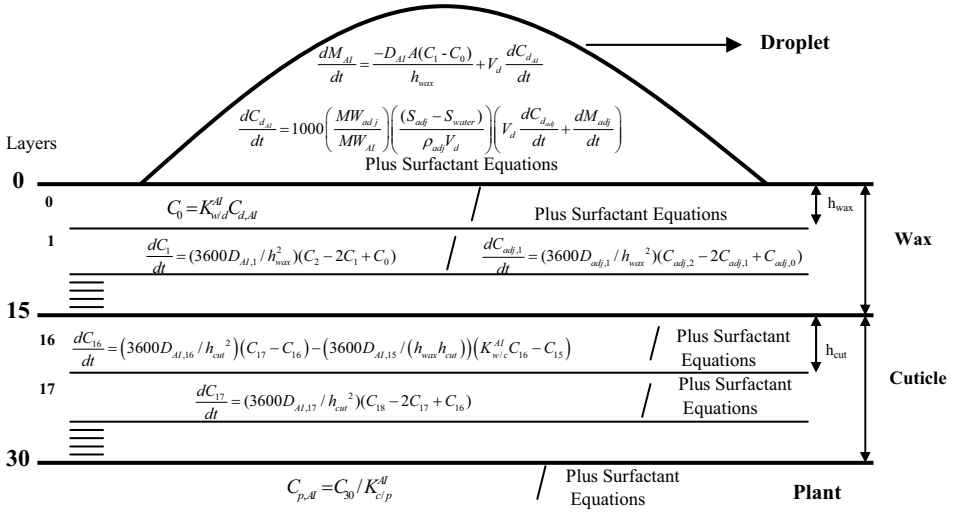

Figure 2. Pesticide uptake: scenario modelled and equations.

The plant leaf consists of distinct parts with different properties and functions. The outer layer is the cuticle, which is a barrier for penetration of water and gases into and out of plant that also protects the plant against diseases (Burghardt et al., 1998). This membrane consists of biopolymer cutin and associated cuticular waxes (Stock et al., 1993), which constitute the upper layer of leaf and provide the main barrier controlling the rate of transcuticular diffusion of active ingredients (Hess and Chester, 2000).

The model predicts the variation of the concentration of the AI in the different layers within the leaf (C_{AI}), as well as the adjuvant concentration (C_{Adj}) as a function of time (t), together with their concentrations in the droplet (C_d) and in the plant (C_p). The input data needed in the model regarding the description of the scenario includes the plant characterization (thickness of wax, h_{wax}, and cuticle, h_{cut}), the droplet dimensions (surface area, A, and volume, V_d), pure component properties (AI solubilities in water, S_{water}, and adjuvant, S_{adj}, adjuvant density, ρ_{adj} , and molecular weights, MW). Finally the system parameters needed are the partition coefficients (between the wax layer and the droplet, $K_{w/d}$, between the wax and the cuticle $K_{w/c}$, and between the cuticle and the plant, $K_{c/p}$) and the diffusion coefficients of the AI (D_{AI}) and the adjuvant (D_{adj}). The discretized PDAE model has 67 ODE's and 52 AE's.

The model for the diffusion coefficient estimation has been modified in order to account for different scenarios, such as the presence of a surfactant in the formulation that will have an accelerating effect on the AI diffusion into the plant. The model includes a diffusion coefficient that is a function of the type of surfactant and its concentration.

The use of the formulation framework is illustrated here with an example of how the pesticide uptake model can be applied for formulation design. The example used involves the pesticide Cyanazine, that is combined with two different surfactants, both linear alkane ethoxylates but of different chain length, to obtain a pesticide formulation that is sprayed onto wheat. The uptake of Cyanazine is predicted with the uptake model for each of the surfactants and the results are shown in Fig. 3 (a) and (b). In each of the plots, it is observed that the uptake increases significantly by adding a surfactant and is

a function of the concentration of the surfactant added. Also, the surfactant of the longer chain seems to have a greater effect on the uptake of the pesticide. These predictions help to make a decision on the choice of the surfactant and its amount in the formulation with respect to the desired uptake of the AI. More details on the problem solution can be obtained from the authors.

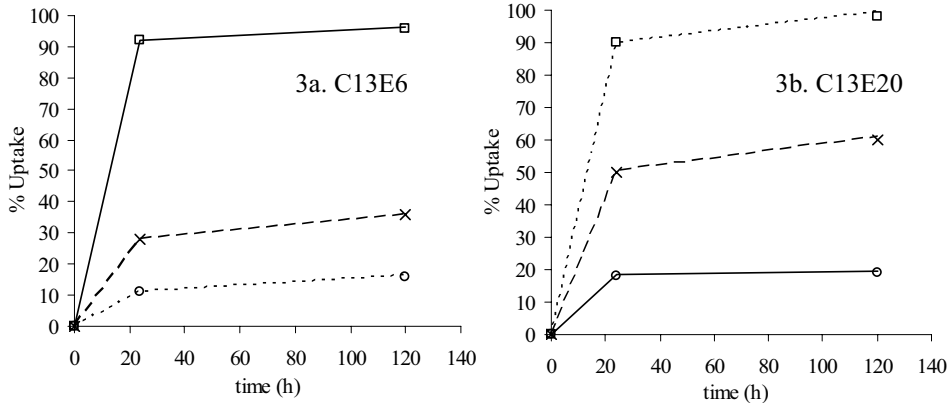

Figure 3. Uptake percentage of Cyanazine as a function of time for different surfactant concentrations, for surfactant C13E6 (a) and C13E20 (b). Where the symbols represent the experimental data: (○) 0.2 g/L of surfactant, (×) 1 g/L of surfactant, (□) 5 1 g/L of surfactant. And the lines represent the results from the model: (—) 0.2 g/L of surfactant, (− −) 1 g/L of surfactant, (---) 5 1 g/L of surfactant.

5. Conclusions

A general framework for computer-aided pesticide formulation and product design has been presented in this paper. A database containing a group of compounds, and their properties, has been combined with the needed mathematical models so that the behaviour of the pesticide product can be studied from the moment the AI is released from the product to its uptake into the plant. The mathematical models have been converted to their predictive forms through the development of predictive models for their parameters. Hopefully, the framework plus its resident tools will simplify and optimize the experimental work required in the complicated and time-consuming pesticide product design process by generating and testing a great number of feasible alternatives in an effective manner.

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