Determining the maximum residue level (MRL) for oxalic acid in honey

Anton Imdorf[1] and Eva Rademacher[2]
European Working Group for Integrated Varroa Control
[1] Agroscope Liebefeld-Posieux, SwissBee Research Center, CH-3003 Bern
[2] Freie Universität Berlin, Institut für Biologie/Neurobiologie, Königin-Luise-Strasse 28-30, DE-14159 Berlin

It is imperative to combat the Varroa mite continuously. Due to the biology of both the host and the parasite, integrated treatment, carried out with various means throughout the year, is crucial. This is especially true because in recent years in various parts of Europe Varroa has become resistant to treatments used so far. The pharmaceutical industry is not interested in developing new varroacides, due to the small size of the market and the enormous costs involved in developing and obtaining government approval for these substances.

In this situation, bee scientists from all over Europe have taken on the task of developing substances for controlling Varroa. A European Union Task Force on „Integrated Varroa Control" was founded for this purpose. One of its achievements is the development of oxalic acid all the way to the final application stage as a medicament (Nanetti et al. 2003). Oxalic acid is indispensable for the late fall/winter phase of the integrated treatment concept against Varroa infestation. Government approval for its use was held up by the requirement that the maximum allowed residue level (MRL) first be officially determined.

Why is it necessary to determine the MRL?

In EU countries, government approval is only given to a new veterinary medicament for use in treating animal diseases after the EMEA, the European Union's Agency for Evaluating Medical Products, has determined the maximum residue level of the active ingredient allowed in the final food product. This procedure is meant to protect consumers from toxicologically critical residue in foods resulting from medicines used on animals.

Procedure for determining an MRL

The MRLs already existed for formic acid, lactic acid and thymol, substances also used in alternative Varroa treatment (these substances were included in Annex II of the Council Regulation (ECC) 2377/90), however the MRL had not yet been established for oxalic acid. In order to achieve the legal use of oxalic acid as a key substance for winter treatment within the framework of this concept, the members of the European Working Group for Integrated Varroa Control initiated the procedure to have the EMEA determine the MRL.

To do so, it was necessary to create a dossier of the current knowledge about oxalic acid's toxicity and its potential residue in bee products (in this case, honey). A team of EMEA experts then evaluates the dossier, judging the substance's potential for danger and, if required, setting the maximum residue level for the final food product.

Financing the MRL procedure

Establishing an MRL is normally a very expensive undertaking, costing approximately 100,000 Euros. Half of this amount is needed to create the MRL dossier, half for it for processing at EMEA. Our work in managing the project was contributed for free, as part of our general efforts to support beekeepers. The European Working Group for Integrated Varroa Control has no financial means. Therefore beekeeper associations in various EU countries were contacted with the request that they help finance this project, with the amount to be allotted according to each countries number of bee colonies.

Austria, Belgium, Denmark, Finnland, France, Germany, Italy, The Netherlands and Sweden joined together to finance the project, some of them with amounts quite above their proportional share of the total. Special thanks go to the French Beekeepers, who covered about 45% of the budget with money from the European Union's Beekeeper Fund. In Italy apart from the beekeeper associations U.N.A. API also two bee science institutions made financial contributions to help the project. Although not a member of the European Union, Norway, on its own initiative, contributed a considerable amount.

Unfortunately, several countries never responded to our repeated requests for financial participation (Great Britain, Greece, Luxembourg, Portugal, and Spain). We had no contact person in Ireland. Because these countries didn't finance their share of the work, the project ran into financial difficulties, and would have had to be cancelled if the EMEA had not, at the last minute, granted our request to waive the processing fee of 58,000 Euros. After numerous discussions and letters, the EMEA acknowledged the honeybee's importance for the general public, the necessity to keep bee populations strong, and the problem of the small market for developing drugs for these animals. This meant that the bee was de facto treated like the other „Minor Species" (i.e., as an animal group for which no commercial profit is expected from developing medicaments), even though the bee was not mentioned in the relevant Note of Guidance. An additional aspect was the fact that the Free University of Berlin was deeply involved in this procedure, but had no financial interest in it. It was the combination of all these factors that meant that enough financial means were finally available to pursue the project.

Organising the financing was a complex and thankless job. It would have been ideal if the beekeeper organisations in the various EU countries had joined together, to function as a competent contact person for the scientists working on a project that would, in the end, benefit the beekeepers. Even one qualified contact person would have saved us quite a lot of work.

Creating the MRL Dossier

The MRL dossier is made up of two parts: the toxicology of oxalic acid, and oxalic acid residues in honey. The first part summarizes existing information about the substance, its pharmacology, human and general toxicology. Dr. Jean-Michel Poul from the French Agency for Food Safety, AFSSA (Agence Française de Sécurité Sanitaire des Aliments, Laboratoire d'Etudes et de Recherches sur les Médicaments Vétérinaires et les Désinfectants, Unité de Toxicologie Alimentaire, F-35302, Fougeres Cedex, France), prepared the dossier (129 pages) in cooperation with the authors. The report on residue was 75 pages long and contained detailed information about the chemical composition of the substance, a summary of all publications about the residue problem in bee products, and the relevant analysis methods. This report was prepared by Dr. Alex Wibbertmann from the German Fraunhofer Institute for Toxicology and Experimental Medicine (Nikolai-Fuchs-Strasse 1, D-30625 Hannover), again in cooperation with the authors. The two independent experts, after evaluating the toxicological risks and the residue situation, proposed that oxalic acid be added to Annex II of the Council Regulation (EEC) 2377/90, to be used in combatting Varroa destructor. Subtances in Annex II do not have a definite amount listed as an MRL, that means that there are no predetermined maximum amounts of oxalic acid allowed as residues in bee products. The experts argued thusly: first, the natural level of oxalic acid in honey would, if at all, be increased only very minimally by the correct use of oxalic acid in fighting parasites. Secondly, the amount of oxalic acid a person would consume by eating honey every day is toxicologically insignificant and a minute fraction of the amount consumed as residue in other foods.

Evaluation and Decision by the EMEA

The submitted dossier was evaluated by the EMEA commission responsible for veterinary medicines (CVMP). In this procedure, the dossier was evaluated and commented on in detail by the Rapporteur (from Germany) and the Co-Rapporteur (from Denmark). Their report formed the foundation for the Commission's decision, made on Dec. 9 and 10, 2003 in London, which included oxalic acid for use with bees in Annex II of the Council Regulation (EEC) 2377/90 (as was already the case for formic acid, lactic acid and thymol). That means that no maximum limit exists for oxalic

acid residues in honey. However, this does not mean that beekeepers are allowed to use an inappropriate amount of oxalic acid in treating their bees, thereby causing high amounts of residue in their honey. According to European honey standards, honey may have up to 50 milliequivalents of free acids. If higher residues of oxalic or other acids are produced, this limit is soon exceeded, and the beekeeper risks having problems if his honey is checked by authorities. If oxalic acid is used properly, there is absolutely no risk of problems with the honey.

What does this mean for beekeepers?

Now that the EMEA has made this decision, which is certainly good news for beekeepers everywhere, each individual country can apply for national approval of oxalic acid (or products containing it) to be used to combat Varroa destructor in bee colonies. This means that oxalic acid will soon be available for legal use as an ecological winter treatment in fighting Varroa. This is an important milestone on the path to establishing alternative Varroa treatments.

A Word of Thanks

Our special thanks go to Jean-Michel Poul and Alex Wibbertmann, the very dedicated experts who created the MRL dossier, and once again to Jean-Michel Poul for his support in submitting the dossier. Marc Subirana from the French Bee Development Center CNDA (Centre National de Développement Apicole, F-45595 Paris) was most helpful in facilitating the generous funding provided by the French beekeepers – we are very grateful for that. We also want to thank all our colleagues from the European Working Group for Integrated Varroa Controll, each of whom, in his/her home country, worked to secure the financial basis for the project.

Literatur

Nanetti A, Büchler R, Charrière J D, Fries I, Helland S, Imdorf A, Korpela S, Kristiansen P (2003) Oxalic acid treatments for varroa control (Review). Apiacta 38 (1) 81-87.