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Toxicity of unwanted intermediates and products formed during accidental thermal decomposition of chemicals

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Abstract

The problem of the formation of unwanted substances that can occur during thermal decomposition of chemicals is studied from a toxicological point of view.

Two species, ethyl parathion (a widely used pesticide) and cumene hydroperoxide (an intermediate for the industrial production of phenol and acetone), are selected for this investigation. The hazards associated to their accidental thermal decomposition are estimated on the basis of the (known) intermediates and products formed by means of a computational tool (ECOSAR programme) and assessed experimentally by means of algal bioassays. Green alga *Pseudokirchneriella* is used as target organism for all the toxicological assessments. The results of these tests on the samples collected during the thermal decomposition of the two studied species indicate that in the case of ethyl parathion the decomposition process gives rise to a mixture of compounds which are more toxic than the parent species. On the other hand, the decomposition of cumene hydroperoxide in cumene results into the formation of different species whose toxicity towards the adopted organism is lower than that shown by the starting compound. A procedure is proposed to ascertain when it is necessary or it is avoidable to carry out further investigations that involve the analytical resolution of mixtures resulting from the thermal decomposition process.

This approach is suggested as a preliminary screening to identify the hazards associated with an accidental decomposition either of pure chemicals or of mixtures of compounds.

Keywords: Thermal decomposition; Accident; Toxicology; Calorimetry

1. Introduction

Incidental events in which unpredictable dangerous substances are released to the environment – as in the case of Seveso accident – forced the legislator to regulate this field. European Directive 96/82/EC (Better Known as Seveso-II Directive) and its recent modification (Directive 2003/105/EC, article 2) impose the knowledge of the substances which reasonably form during the loss of control of an industrial chemical process [1,2].

A literature survey indicated that some attempts have been done in the past to develop suitable procedures for the identification and prediction of hazardous substances which form during the loss of control of a chemical process [3,4]. Nevertheless, to date neither suitable experimental protocols nor theoretical tools devoted to assess or foresee the possible compounds that could be formed in such events have been still developed. This is principally due to the difficulties in the analytical resolution of the complex mixtures resulting from the thermal decomposition processes and the definition of the experimental conditions that could lead to samples representative of the worst scenario. Due to these difficulties for the most part of the chemicals the section of their Material Safety Data Sheet dedicated to the "decomposition products" contain no information or only scant data mainly for the evolved gases. The present paper aims at showing the importance to fill this gap of knowledge by demonstrating that the thermal decomposition of organic species may really give rise to the formation of intermediates and products which are more toxic than the starting compound and propose a new approach to face the problem. This is done by using some algal bioas-

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says in the case of the thermal decomposition of two chemical compounds, ethyl parathion and cumene hydroperoxide.

2. Experimental

Due to the large set of thermal aging methodologies of the samples that one can imagine (ranging from isothermal to dynamic and adiabatic conditions), and considering the explorative nature of the work, at present stage of the investigation it has been chosen to operate at different temperatures and fixed reaction time for ethyl paration and different reaction times at a fixed temperature for cumene hydroperoxide CHP. For the same reasons only the bioassays described below have been considered.

The calorimetric runs have been carried out by means of a PC Combilab (by Systag) equipped with a Radex oven operating in *quasi*-isothermal mode. Pressure stainless steel reactors have been used in all cases.

In the case of both ethyl parathion (98%, w/w technical purity grade) and cumene hydroperoxide (tech., 80%, w/w solution in cumene, Sigma–Aldrich), the samples withdrawn at the end of the calorimetric runs have been thermally quenched, dissolved in acetone and submitted to HPLC analysis for the determination of the reaction degree. This has been carried out by means of a 1100 Hewlett Packard HPLC equipped with a diode array detector. In the case of the ethyl parathion a Phenomenex Synergi 4 μ Polar-RP-80A column has been used. The mobile phase was (v/v-%) 50% of acetonitrile and 50% of a solution formed by 5% methanol, 0.4% H_3PO_4 and 94.6% H_2O, with a flow of 10^{-3} l min^{-1}. The oven temperature was set at 30 °C and the signals were acquired at λ = 210 and 280 nm.

For the cumene hydroperoxide, the instrument was equipped with a Synergi 4 μ Fusion RP-80 column and as eluent a solution 65% acetonitrile and 35% H_2O has been used, with a flow of 10^{-3} l min^{-1}, the signals being acquired at λ = 210 and 240 nm.

Preliminary dose–response experiments of ethyl parathion and cumene hydroperoxide toxicity towards *Pseudokirchneriella subcapitata* were carried out using either EPA medium [5] or BBM [6]. The results obtained (not shown) indicate that salt concentration in the medium does not influence the toxicity of the selected compounds and in 96-h end-point experiments algae grew at a faster growth rate with BBM. For this reason all the following experiments were performed with this latter medium.

For the algal bioassays [7], each solution of the selected compounds was prepared by dissolving a known quantity of compound in acetone to have a final concentration of 20 mg ml^{-1}. Then, the solution was stirred for 1 h and stored in the dark at 4 °C. The toxicity test was based on the measurement of the growth inhibition of the green unicellular alga *P. subcapitata*, strain UTEX 1648. Algal inocula corresponding to 10,000 cells/ml from laboratory cultures in mid exponential phase were grown in 100 ml Erlenmeyer flasks containing 50 ml of Bold Basal Medium (BBM) and the tested compound at different concentrations (0.25, 0.5, 1.0, 2.0 and 4.0 mg l^{-1} for ethyl parathion and at 0.5, 1.0, 2.0, 4.0, and 8.0 mg l^{-1} for cumene hydroperoxide). The flasks were incubated on a shaking apparatus, at 24 °C under continuous illumination at a light intensity of 90 μEs^{-1} m^{-2}. The tests were carried out in triplicate and in axenic conditions. A series of controls containing either BBM and the algal inocula, or BBM medium, the algal inocula and the same volume of acetone added to the test flasks were also prepared. The algal growth was followed after 96 h from the addition of the compounds, by measuring the optical density at 550 nm with a Secoman colorimeter. The concentrations that cause 50% of effect (EC_{50}) were determined by using the linear interpolation method [8].

3. Results and discussion

Generally speaking it can be easily recognized that the prediction of the capability of a species to exert toxic effects on some kind of living organism is a complex matter. In fact, it is necessary to choose reference organism(s) and a suitable "End Point" and to fix the duration of the experiments. The results herein considered refer to the environmental compartment (aquatic, terrestrial) in which the organisms actually live. In the present work both due to the preliminary character of this attempt and the possibility that unwanted species may really represent a hazard also for the environment, a software package (ECOSAR) has been previously used. It allows, whenever their structure is known, to select the species to be investigated on the basis of the predicted toxicity towards selected aquatic organisms of the intermediate and products of their thermal decomposition. ECOSAR has been developed and is freely available by US EPA [9]. This software allows evaluating some important ecotoxicological indicators considering as input the structure, in "smile" notation, of the target substance. The program is based upon structure–activity relationships (SARs). The aquatic toxicity of a chemical is estimated on the basis of the similarity of its structure to that of other chemicals for which the corresponding parameter is experimentally known.

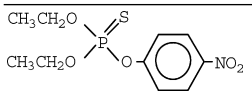
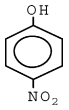
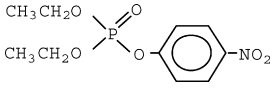
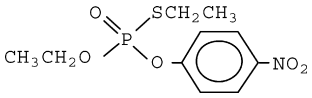
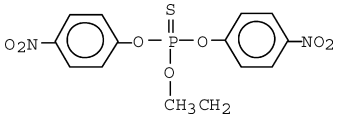
As an example of calculation the substances identified during the adiabatic thermal decomposition of ethyl parathion have been considered (Table 1) [10]. The decomposition process develops through a complex reaction network that involve at the initial stage an isomerization of the substrate followed by a series of nucleofilic substitutions at the phosphorus center that lead to the formation of the identified compounds.

In Fig. 1 the EC_{50} (Algae, 96 h) calculated by means of ECOSAR for the substances reported in Table 1 are shown.

It is evident from this figure that EC_{50} values for the compound IV and V are lower than that of ethyl parathion which means that – at least for the organism considered in the calculation – they are more toxic than the parent species.

It is worthy to observe that the results reported above just stress the importance to know the distribution of intermediates and products during the thermal decomposition of a chemical compound since this makes possible an estimation of the hazards associated to the process. In the example discussed above the calculations using ECOSAR have shown that more toxic species are formed during the decomposition process of the pesticide. It could be thus expected that an increase of an *overall toxicity*

Table 1
Substances identified during the adiabatic thermal decomposition of ethyl parathion

Structure	CAS number	ID
	56-38-2	I (substrate)
	100-02-7	II
	311-45-5	III
	597-88-6	IV
	7508-73-8	V

could be measured by means of proper experimental methods during the decomposition of the studied compound.

To this aim a series of bioassays have been performed both on the untreated compound and on the samples collected at the end of two different isothermal runs. These experiments have been performed at two different temperatures [175 °C (sample A) and 185 °C (Sample B)] in a Radex oven equipped with a stainless still reactor. The duration of the experiment at each temperature was of 2 h 20 min and in both cases a sample mass of 0.2280 g of ethyl parathion was used. At the end of the isothermal phase, the reactor was rapidly quenched and the decomposition products collected using acetone as solvent (100 ml) and submitted to the toxicological test and HPLC analysis to determine the conversion degree.

The toxicity of both ethyl parathion and its thermal decomposition products, has been assessed using the green alga *P. subcapitata*. Fig. 2 shows the dose–response curve of *P. subcapitata* exposed to different concentration of ethylparathion ranging from 0.25 to 4 mg l^{-1} with a 0.5 dilution factor in 96 h end-point experiments. Ethylparathion inhibited *P. subcapitata* growth in a typical dose-dependent manner; a toxic effect of the compound was observed at concentrations higher than 0.25 mg l^{-1}.

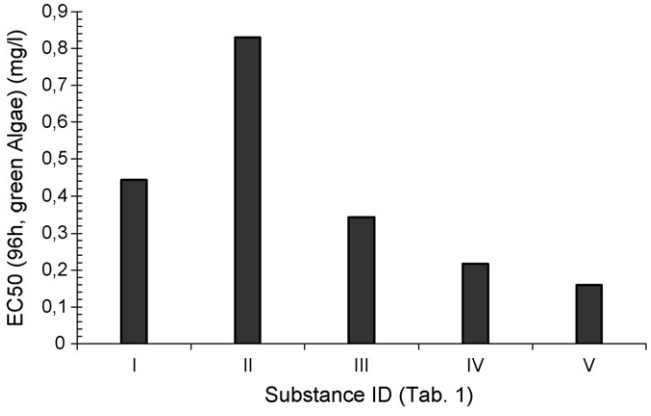


Fig. 1. EC_{50} (Green Algae, 96 h) calculated using ECOSAR for the compounds reported in Table 1 (the values reported for the compounds II and III are the real ones divided by 100 and 10, respectively).

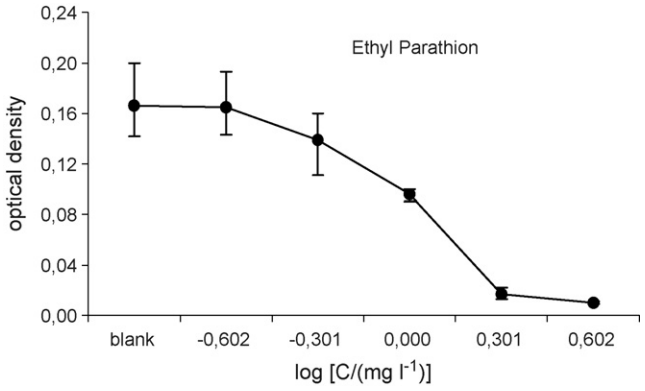


Fig. 2. Dose–response curve of ethylparathion on *Pseudokirchneriella subcapitata*.

In Table 2 the toxicity of untreated ethyl parathion is compared to that of the compounds originated through its heating. Toxicity was assessed in chronic end-point tests (96 h), by using the same previously indicated concentrations of ethyl parathion or of its decomposition products. EC_{50} values were calculated on the results from 96 h tests using the linear interpolation method [8]. As can be seen (Table 2) about the same values of EC_{50} were obtained when the tests were carried out on non-treated ethyl parathion (0.99 mg l^{-1}) and on the sample collected after exposition at 175 °C (0.98 mg l^{-1}). However after the thermal treatment at 185 °C, the recovered sample resulted much more toxic, the EC_{50} being 0.23 mg l^{-1}.

The approach described above has been successively adopted to study a second chemical substance, cumene hydroperoxide, an important intermediate in the production of phenol which has been involved in the past in more than one industrial accident [11]. The effect of different cumene hydroperoxide concentration on *P. subcapitata* was monitored at an end-point of 96 h to determine the dose–response curve (Fig. 3). As can be seen, inhibition effects were found only at concentrations ≥0.5 mg l^{-1} Then a series of experiments has been carried out in which a solution of cumene hydroperoxide in cumene (the substance in which CHP is generally dissolved during the storage and from wich it is normally produced by oxidation with air) has been kept at 130 °C for different reaction times (30, 60, 90, 120, 150, 180, 210 min). At the end of each of them a sample of the reacting solution has been collected for the analysis. In Fig. 4a and b the

Table 2
Toxicity of untreated ethyl parathion compared to that of compounds originated during its thermal decomposition

Sample	EC_{50} (mg l^{-1})	Conversion (mol/mol%)
Ethyl parathion (O)	0.99	0
Ethyl parathion 175 °C (A)	0.98	33
Ethyl parathion 185 °C (B)	0.23	65

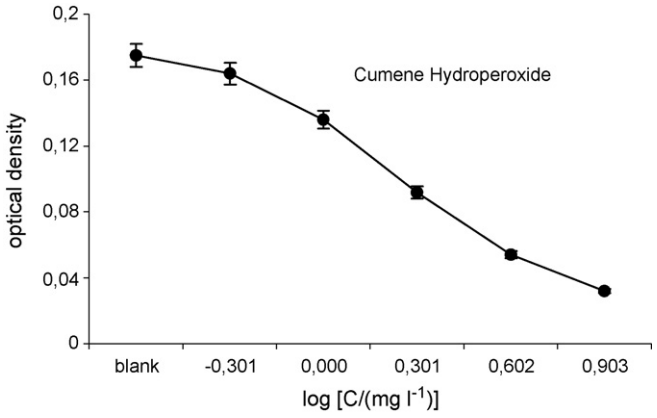


Fig. 3. Dose–response curve of cumene hydroperoxide on *P. subcapitata*.

distribution profiles of the species identified during the thermal decomposition of cumene hydroperoxide are shown.

On the basis of the information reported in this figure a calculation with the ECOSAR programme has been attempted. Unfortunately not for all the involved species the software was able to give the ecotoxicological information related to green algae. The only available calculations were related to EC_{50} (Algae, 96 h) for acetophenone, α-methylstirene cumene

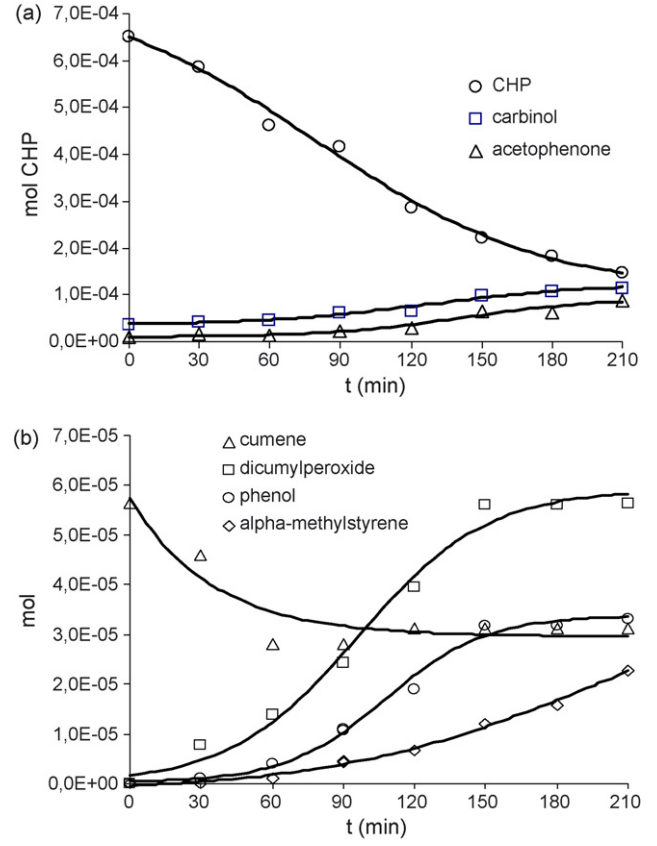


Fig. 4. (a) Distribution of the species identified during the thermal decomposition of cumene hydroperoxide kept in isothermal conditions (130 °C) and different reaction times. (b) Distribution of the species identified during the thermal decomposition of cumene hydroperoxide kept in isothermal conditions (130 °C) and different reaction times.

Table 3
Results of the bioassay carried out on the pure compounds found during the thermal decomposition of CHP

ID	Compound	CAS number	EC_{50} (mg l^{-1})
1	α-Methylstirene	98-83-9	>5.50
2	Cumene hydroperoxide (CHP)	80-15-9	1.70
3	Dicumylperoxide	80-43-3	>5.50
4	Cumene	98-82-8	>5.50
5	Acetophenone	98-86-2	>5.50
6	Carbinol	617-94-7	>5.50
7	Phenol	108-95-2	58

and phenol which resulted equal to 116.891, 3.120, 1.388 and 126.854 mg/l, respectively.

Therefore a first series of experiments to collect this information on each of the compounds reported in the Fig. 4a and b has been carried out.

In Table 3 the results obtained during these experiments are shown. It is evident from this table that none of the species formed during cumene hydroperoxide thermal decomposition is more toxic than the substrate. A similar conclusion can be also drawn for cumene (the solvent). On the basis of these considerations it could be expected that the degradation of cumene hydroperoxide would result into a reduction of the overall toxicity of the solution. To confirm this hypothesis, the samples collected for different reaction times at 130 °C have been also submitted to algal bioassays. In Table 4 the data obtained during these tests are shown. Algal growth inhibition due to the exposition to untreated cumene hydroperoxide was observed at concentrations ranging from to 05 to 8.0 mg l^{-1} and EC_{50} derived from the linear interpolation method [8] was 1.70 mg l^{-1}. The products arising from its thermal decomposition after a treatment at 130 °C, for reaction times longer than 150 min, yielded a lower toxicity, being the EC_{50} higher than 5.52 mg l^{-1}; for shorter reaction times slight differences have been observed for the ecotoxicity of the samples with respect to that on the initial solution.

These results are consistent with those shown in the Table 3. In fact, as previously pointed out, the decomposition of cumene hydroperoxide gives rise to the formation of chemical species which are less toxic towards the target organism than the substrate. Therefore the thermal conversion of cumene hydroperoxide invariably leads to a reduction of the overall toxicity of recovered solutions. The discussion reported above indicates that the measurement of an *overall toxicity* changes during the decomposition could represent – if properly used – a prelimi-

Table 4
Results of the bioassay carried out on the thermal decomposition product of CHP on samples collected at 130 °C and different duration of the isothermal phase

Reaction time (min)	EC_{50} (mg l^{-1})
0	1.70
30	1.34
90	1.50
150	>5.52
210	>5.52

nary approach to face the problem of the formation of hazardous unwanted species during the thermal decomposition. In fact in all the cases in which no changes of *overall toxicity* or a reduction are observed, the system could be no longer investigated. At the opposite, when an increase of the toxicity is recorded during the decomposition of a compound, the decomposition process has to be extensively investigated to achieve a complete chemical characterization that may be of great importance for planning the emergency response.

4. Conclusions

The results reported in the present work point out that in the case of a thermal decomposition of unstable compounds, the formation of species that are more dangerous than the initial substance is possible. It has been demonstrated the need to really fulfill the Seveso II directive by investigating the nature and the hazardous properties of unwanted thermal decomposition products to avoid an underestimation of the consequences of the explosive event in a real accident scenario that could lead to an inadequate planning of the emergency response.

A preliminary toxicological screening has been proposed to face the problem of the formation of unwanted compounds by measuring the change of an *overall toxicity* associated with the thermal decomposition of a species of interest. Interesting results have been obtained by applying this approach to the thermal decomposition of ethyl parathion and cumene hydroperoxide.

In the first case an increase of the *overall toxicity* of the recovered solutions has been observed during the decomposition at two temperatures (175 and 185 °C) whereas a decrease has been recorded in the case of the thermal decomposition of cumene hydroperoxide (at 130 °C).

Work is in progress to extend the investigation to other compounds by using both different thermoanalytical techniques and ecotoxicological tests.

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