

## EUROPEAN QUALIFYING EXAMINATION 2006

### PAPER B CHEMISTRY

This paper comprises:

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Patent application 2006/B(Ch)/e/1-6
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## **Annex 1 (Patent Application)**

### Controlled-release herbicide formulations

5 [0001] The present invention relates to herbicide formulations which slowly release the herbicide and therefore provide a long-term herbicidal effect. Such formulations are called controlled release formulations. Controlled-release herbicide formulations are particularly useful as pre-emergence herbicides (herbicides which are applied to a field before weeds are visible). The use of controlled-release formulations reduces the  
10 amount of herbicide required and minimises undesirable losses of the herbicide.

[0002] In order to obtain the controlled release of the herbicide, the herbicide is encapsulated in a microcapsule. A microcapsule as used in the present invention is a liquid droplet of herbicide solution (referred to as the core solution) covered with a  
15 porous polymeric shell material. The shell material used is an aminoplast resin. The term aminoplast resin as used in the present invention refers to a polymer made by condensing formaldehyde and at least one compound containing amine groups. The microcapsules of the present invention must have an average particle diameter of between 1 and 100 micrometers. The best microcapsules have a narrow size distribution  
20 and little variation in shell porosity. This combination of properties ensures that the capsules release the herbicide at a predictable and controlled rate.

[0003] A number of processes are known for forming microcapsules. It is also known to make microcapsules containing herbicides. The herbicide-containing microcapsules of the prior art have however been made using processes where the herbicide and a precursor for the polymeric shell were both dissolved in an organic solvent. These known processes have the disadvantage that the precursor often reacts with the herbicide to form undesirable side products. The present invention uses an in situ polymerisation process in an oil-in-water emulsion (a dispersion of an oil phase consisting of organic water-immiscible droplets in a continuous aqueous phase) to form the microcapsules. The precursor of the polymeric shell is dissolved in the aqueous phase and the herbicide is dissolved separately in the oil phase. This reduces the possibility of side reactions. The process used consists of the following steps:

- a) dissolving the herbicide in a water-immiscible organic solvent;
- b) forming an aqueous solution of a pre-polymer of the aminoplast resin shell material and a protective colloid;
- c) mixing the herbicide solution from step a) with the aqueous solution from step b) with rapid stirring to form an emulsion of droplets of the herbicide solution in the aqueous solution;
- d) adjusting the pH of the emulsion to a value between 3 and 4 to polymerise and precipitate the shell material around the droplets; and
- e) separating the microcapsules.

[0004] The present invention can be applied to any herbicide which can be dissolved in an organic solvent to provide a water-immiscible liquid. The present invention is particularly suitable for herbicides which are thiocarbamates or acetamides. Examples of thiocarbamate herbicides which can be encapsulated include S-ethyl diisobutylthiocarbamate, S-ethyl-N-cyclohexyl-N-ethylthiocarbamate, and S-ethyl hexahydro-1H-azepine-1-carbothioate. An acetamide herbicide which can be encapsulated is 2-chloro-N-ethoxymethyl-6-ethylacet-o-toluidide.

[0005] The solvent used in step a) may be any water-immiscible organic solvent, which does not react with any of the components used. The most appropriate solvents are typically xylene or kerosene.

5 [0006] In step b), an aqueous solution of a water-soluble pre-polymer of an aminoplast resin is formed. The aminoplast pre-polymer is a water-soluble product, of a condensation reaction between formaldehyde and a compound containing amine groups, which retains groups capable of further condensation polymerisation. The precise aminoplast pre-polymer used does not have a significant effect on the herbicidal  
10 properties of the final microcapsule. The aminoplast pre-polymer used is typically a urea-formaldehyde or a melamine-formaldehyde pre-polymer. Suitable commercially-available aminoplast pre-polymers include AMSHELL 135 or POLYMEM 204.

[0007] The aqueous solution used in step b) also contains a protective colloid. A  
15 protective colloid is a water-soluble polymer which stabilises an emulsion. The stabilisation of the emulsion results in microcapsules with a narrower distribution of sizes and a more uniform shell porosity. Overall the use of a protective colloid results in microcapsules which provide a more consistent herbicidal effect. The shell of the microcapsule contains the protective colloid. Polymers useful as protective colloids are  
20 well known. Suitable protective colloids include polyacrylic acid, acrylamide-acrylic acid copolymers, acrylic acid-styrenesulphonic acid copolymers, styrene-maleic anhydride copolymers, carboxymethyl cellulose and polyvinyl alcohol. The preferred protective colloids are polymers and copolymers containing acrylic acid monomer units. The use of an acrylic acid-styrenesulphonic acid copolymer is most preferred. The preferred  
25 protective colloids and especially the most preferred acrylic acid-styrenesulphonic acid copolymers, result in microcapsules with a particularly narrow size distribution and a particularly uniform shell porosity. The protective colloid is typically used at between 0.1 and 5 wt.% of the aqueous solution.

[0008] The weight ratio of the aqueous solution to the herbicide solution used to form the emulsion in step c) is not critical. Typically the herbicide solution will amount to between 10 and 60 wt.% of the emulsion in step c). A process using less than 10 wt.% herbicide solution is usually not economical. If the herbicide solution makes up more than 60 wt.% of the emulsion it is often difficult to form a stable emulsion.

[0009] In order to ensure that a uniform emulsion is obtained the mixture is stirred usually for between 10 and 45 minutes using a conventional high shear stirrer. The stirring conditions determine the droplet size of the herbicide solution in the emulsion and thus the size of the microcapsules. Suitable stirring conditions for a desired microcapsule diameter can be determined by routine experimentation. Typically stirring at between 1000 and 10000 revolutions per minute results in microcapsules with an average diameter between 1 and 100 micrometers.

[0010] In step d), the pH of the emulsion is adjusted to a value between 3 and 4. This causes the aminoplast pre-polymer to further polymerise by self-condensation. The polymer formed precipitates on the droplets of herbicide and forms the shell of the microcapsules. Any water-soluble acid can be used in this step. Hydrochloric acid and citric acid are particularly suitable. This step is preferably performed at a temperature of 40-60°C.

[0011] The microcapsules are separated in step e) by either filtration or spray drying.

[0012] Examples

[0013] Example 1: Preparation of microcapsules

5 [0014] An organic solution was prepared by dissolving 132 g of S-ethyl hexahydro-1H-azepine-1-carbothioate (a thiocarbamate herbicide) in 70g of kerosene. In a separate vessel an aqueous solution was prepared. The aqueous solution consisted of 180 g of water, 2 g of PROCOLL (an acrylic acid-styrene-sulphonic acid copolymer protective colloid) and 50 g of AMSHELL 135 (a 70% aqueous solution, pH 7.5 of a urea-

10 formaldehyde pre-polymer). The organic solution was emulsified in the aqueous solution by means of a high shear stirrer at 5000 revolutions per minute for 20 minutes. A stable emulsion was obtained.

[0015] The emulsion was heated to 50°C with gentle stirring and then hydrochloric acid

15 was slowly added to the emulsion to lower the pH to 3.5. Stirring was continued for 3 hours to obtain a microcapsule dispersion. The dispersion was allowed to cool to room temperature and was then filtered to separate the microcapsules. Microscopic observation confirmed that discrete microcapsules with an average diameter of 20 micrometers had been formed.

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[0016] Example 2: Test for pre-emergence herbicidal activity

[0017] A test plot at the Apple-Tree test farm was sown with a mixture of typical weeds. One half of the plot was then immediately treated with the microcapsules of example 1.

25 The other half of the plot was treated with an equivalent amount of a solution of 132 g of S-ethyl hexahydro-1H-azepine-1-carbothioate in 70 g of kerosene.

[0018] After 45 days, the plot, which had been treated with the microcapsules had considerably fewer weeds. This demonstrates the effectiveness of encapsulated

30 herbicides for pre-emergence application.

### Claims

1. Microcapsules having an average diameter of 1-100 micrometers consisting of a core of a herbicide dissolved in a water-immiscible organic solvent and an aminoplast resin shell containing a protective colloid.
2. Microcapsules according to claim 1 where the herbicide is a thiocarbamate or an acetamide.
3. A process for forming the microcapsules of claim 1 consisting of the following steps:
  - a) dissolving the herbicide in a water-immiscible organic solvent;
  - b) forming an aqueous solution of a pre-polymer of the aminoplast resin shell material and a protective colloid;
  - c) mixing the herbicide solution from step a) with the aqueous solution from step b) with rapid stirring to form an emulsion of droplets of the herbicide solution in the aqueous solution;
  - d) adjusting the pH of the emulsion to a value between 3 and 4 to polymerise and precipitate the shell material around the droplets; and
  - e) separating the microcapsules.
4. The use of the microcapsules of claims 1 or 2 as controlled-release herbicides.

## **Annex 2 (Communication)**

1. Document 1 (see claims, example 2 and paragraphs [0002], and [0005] to [0007]) discloses microcapsules with an aminoplast resin and protective colloid containing shell. In example 2 the average diameter was 40 micrometers and the material encapsulated was a solution of an acetamide herbicide in xylene. The process used to form the microcapsules was an in situ polymerisation process, where an amine-formaldehyde pre-polymer and the protective colloid are dissolved in the aqueous phase and the polymerization and precipitation of the shell material may be obtained by acidification to a pH of 3.5. The process may be used to form controlled-release formulations for herbicides.
2. Document 1 is thus novelty destroying for the subject-matter of claims 1-4 (Articles 52(1), 54(1) and 54(2) EPC).
3. Document 2 is comprised in the state of the art, in accordance with Articles 54(3) and (4) EPC for all the contracting states of the present application. This document is therefore relevant to the question of novelty for the present application. This document (see claims) also discloses microcapsules of an average particle diameter of 1 to 100 micrometers consisting of core solutions of thiocarbamate herbicides encapsulated in a shell consisting of a melamine-formaldehyde aminoplast resin and a protective colloid selected from styrene-maleic anhydride copolymers and acrylamide-acrylic acid copolymers. The microcapsules are made using the process claimed in the present application. Document 2 is thus also novelty destroying for the subject-matter of claims 1-4.



4. If the applicant wishes to maintain the application, new claims should be filed which take the above objections into account. Care should be taken to ensure that the new claims comply with the requirements of the EPC in respect of novelty, inventive step, clarity and if necessary unity (Articles 54, 56, 84 and 82 EPC). The applicant should also ensure that any amendments do not introduce subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).
5. In the letter of reply, the difference between the new claims and the state of the art disclosed in documents 1 and 2 as well as its significance should be identified. In addition the arguments of the applicant in respect of inventive step should be presented in such a way that in particular the technical problem being solved in view of the state of the art disclosed in document 1 and the solution proposed to this problem can be clearly understood (Rule 27(1)(c) EPC and Guidelines C-IV, 9.8).
6. An independent claim must specify all the technical features necessary to define the invention (Guidelines C-III, 4.4). Thus each independent claim must contain all the technical features essential to the solution of the problem on which the invention is based.
7. In order to facilitate the examination as to whether the new claims contain subject-matter which extends beyond the content of the application as filed, the applicant is requested to indicate precisely where in the application documents any amendments proposed find a basis (Article 123(2) EPC, Guidelines E-II, 1 and C-VI, 5.3). If a disclaimer is to be used in the claims, the letter preferably also makes it clear why this disclaimer is in accordance with the requirements set out in the Enlarged Board of Appeal decisions G 1/03 and G 2/03.
8. It is suggested that the adaptation of the description to any new claims be postponed until the Examining Division indicates that a set of claims is allowable.

**Annex 3 (Document 1)**

[0001] Microencapsulation of various core solutions is a common means of providing such materials with a protective environment. Forming microcapsules with, for example, a urea-formaldehyde resin shell, provides the core solutions with an external shell which insulates them from conditions which might lead to their loss or to loss of their desired, active properties.

[0002] Core solutions containing pharmaceuticals, pesticides, herbicides, anti-fouling agents, catalysts and the like may be encapsulated in order to provide for controlled release of such materials over an extended period of time.

[0003] The present invention provides a method for forming microcapsules which includes the steps of:

- A. Forming an organic core solution and separately an aqueous solution of pre-polymer for the shell material and a protective colloid;
- B. Mixing the two solutions and emulsifying the admixture to form fine droplets containing the core material;
- C. Polymerising and precipitating the shell-material by acidifying the emulsion to a pH of 3.2 to 4.5 using a water-soluble acid (for example citric or hydrochloric acid) and heating the emulsion to a temperature of 40-60°C; and
- D. Separating the resultant microcapsules from the remaining liquid.

[0004] In a first step, a core solution in an oily water-immiscible solvent such as for example kerosene or xylene and an aqueous solution of a protective colloid and a pre-polymer of the shell, which is most preferably a urea-formaldehyde pre-polymer, are prepared. The two solutions are then mixed. The core solution typically amounts to  
5 between 10 and 60 wt.% of the emulsion formed.

[0005] The mixture of the two solutions is stirred using a high-shear stirrer. The stirring conditions used determine the droplet size of the core solution and the size of the microcapsules formed. The average microcapsule diameter is typically 1 to 100  
10 micrometers. Microcapsules of an average particle diameter of 40 micrometers have been formed after stirring for 10 to 45 minutes at 3000 revolutions per minute. Higher and lower stirring speeds can equally be used.

The heating and acidification of the emulsion causes further polymerisation of the urea-formaldehyde pre-polymer. The polymer formed precipitates on the droplets to form the  
15 microcapsule shell. The shell usually makes up between 10 and 20 wt.% of the microcapsules. The pH conditions, acid used to acidify and the temperature must all be as specified above for successful microcapsule formation. A reaction time of 20 minutes is typically sufficient. Microcapsules with a urea-formaldehyde polymeric shell are then formed. The microcapsules are separated by spray drying or filtration.

20 [0006] Other aminoplast pre-polymers can be substituted for the urea-formaldehyde pre-polymer described above. Thus melamine-formaldehyde and thiourea-formaldehyde pre-polymers can be used as well as or instead of the urea-formaldehyde pre-polymer. The protective colloids used in accordance with the present invention are water soluble  
25 polymers selected from styrene-maleic anhydride copolymers, polyvinyl alcohol, carboxymethyl cellulose, starches and modified starches. These compounds stabilise the emulsion during the formation of the capsule shell wall.

[0007] The material to be encapsulated may include any material soluble in the organic solvent and insoluble in the water-immiscible solvent. The material encapsulated is most preferably an acetamide herbicide although other pesticides such as thiocarbamate herbicides, and organophosphate insecticides may also be used. The microcapsules formed are suitable for pre-emergence herbicidal application.

[0008] The following are examples of means for practicing the present invention:

[0009] Example 1 - preparation of the pre-polymer

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[0010] A mixture of 220 grams of 37% aqueous formaldehyde and 80 grams of urea was adjusted to a pH of 8 with sodium hydroxide and held at a temperature of 70°C for one hour to produce a urea-formaldehyde pre-polymer solution.

15 [0011] Example 2 - microcapsule formation

[0012] 100 g of the pre-polymer solution from example 1 were diluted with 200g of water and then 4 g of SEGURO (a polyvinyl alcohol protective colloid) was added. An organic solution of 120 g 2-chloro-N-ethoxymethyl-6-ethylacet-o-toluidide (an acetamide herbicide) in xylene 280 g was separately prepared. The two solutions were mixed and stirred for 30 minutes at 3000 revolutions per minute to form an emulsion. The pH of the emulsion was then adjusted to 3.5 using hydrochloric acid and the emulsion was heated to a temperature of 50°C. The reaction was allowed to proceed for 30 minutes and then the emulsion was spray dried. The microcapsules recovered were investigated under a microscope and shown to be of high quality with a narrow microcapsule size range and an average diameter of 40 micrometers.

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Claims

1. A process for forming microcapsules, which includes the steps of:

- a) forming an organic core solution and separately an aqueous solution of an amine-formaldehyde pre-polymer for the shell material and a protective colloid;
- b) mixing the two solutions and emulsifying the admixture to form fine droplets containing the core material;
- c) polymerizing and precipitating the shell material by acidifying the emulsion to a pH of 3.2 to 4.5 using a water-soluble acid and heating the emulsion to a temperature of 40-60 °C; and
- d) separating the resultant microcapsules from the remaining liquid.

2. The process of claim 1, wherein the core solution contains an acetamide herbicide.

**Annex 4 (Document 2)**

(prior art under Articles 54(3) and (4) EPC)

[0001] The present invention relates to formulations of thiocarbamate herbicides.

5 Thiocarbamate herbicides are very effective for suppressing weeds by the pre-emergence treatment of the fields upon which crops are to be grown. These herbicides however suffer volatilisation losses. The present invention addresses the problem of providing thiocarbamate herbicides in a formulation which is less subject to volatilisation losses. The problem is solved by incorporating a solution of the thiocarbamate herbicide  
10 in a microcapsule with a melamine-formaldehyde resin shell and an average particle diameter between 1 and 100 micrometers.

[0002] The present invention uses an in situ polymerisation process to form the microcapsules. The process used consists of the following steps:

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- a) dissolving the herbicide in a water-immiscible organic solvent;
- b) forming an aqueous solution of a pre-polymer of a melamine-formaldehyde resin and a protective colloid selected from styrene-maleic anhydride  
20 copolymers and acrylamide-acrylic acid copolymers;
- c) mixing the herbicide solution from step a) with the aqueous solution from step b) with rapid stirring to form an emulsion of droplets of the herbicide solution in the aqueous solution;  
25
- d) adjusting the pH of the emulsion to a value between 3 and 4 to polymerise and precipitate the shell material around the droplets; and
- e) separating the microcapsules.  
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[0003] Examples of thiocarbamate herbicides which can be encapsulated include S-ethyl diisobutylthiocarbamate, S-ethyl-N-cyclohexyl-N-ethylthiocarbamate, and S-ethyl hexahydro-1H-azepine-1-carbothioate. The solvent used for the herbicide is typically kerosene or xylene.

[0004] The pre-polymer used to form the shell may be any water-soluble melamine formaldehyde pre-polymer. The shell usually makes up 10 to 20 wt.% of the microcapsule. A suitable commercially available pre-polymer is POLYMEM 204. The aqueous solution used in step b) contains the pre-polymer and a protective colloid. The protective colloid is selected from styrene-maleic anhydride copolymers and acrylamide-acrylic acid copolymers. The protective colloid is typically used at between 0.1 and 5 wt.% of the aqueous solution.

[0005] The weight ratio between the aqueous solution and the herbicide solution used to form the emulsion in step c) is not critical. Typically the herbicide solution will amount to between 10 and 60 wt.% of the emulsion in step c). A process using less than 10 wt.% herbicide solution is usually not economical. If the herbicide solution makes up more than 60 wt.% of the emulsion, it is often difficult to form a stable emulsion. In order to ensure that a uniform emulsion is obtained it is necessary to stir the mixture for between 10 and 45 minutes using a conventional high shear stirrer.

[0006] In step d), the pH of the emulsion is adjusted to a value between 3 and 4. This causes the aminoplast pre-polymer to further polymerise by self-condensation. Any water-soluble acid can be used in this step. Hydrochloric acid and citric acid are particularly suitable. This step is preferably performed at a temperature of 40-60°C.

[0007] The microcapsules are separated in step e) by either filtration or spray drying.

[0008] Example

[0009] Microcapsules containing S-ethyl hexahydro-1H-azepine-1-carbothioate (a thiocarbamate herbicide) were prepared and isolated.

[0010] The microcapsules were placed in a sealed container and heated to 50°C. The container was flushed with nitrogen every 2 hours and the gas flushed from the container was passed to a gas chromatograph. The gas chromatograph is able to quantify the amount of herbicide lost by volatilisation from the capsules. After 24 hours the cumulative loss was 20 %. A solution of the same herbicide in kerosene, which had not been microencapsulated, when subjected to the same test, lost over 50 % of the herbicide to volatilisation.

### Claims

1. A process for forming microcapsules of thiocarbamate herbicides consisting of the following steps:
  - a) dissolving the herbicide in a water-immiscible organic solvent;
  - b) forming an aqueous solution of a pre-polymer of a melamine-formaldehyde resin and a protective colloid selected from styrene-maleic anhydride copolymers and acrylamide-acrylic acid copolymers;
  - c) mixing the herbicide solution from step a) with the aqueous solution from step b) with rapid stirring to form an emulsion of droplets of the herbicide solution in the aqueous solution;
  - d) adjusting the pH of the emulsion to a value between 3 and 4 to polymerise and precipitate the shell material around the droplets; and
  - e) separating the microcapsules.
2. Microcapsules having an average particle diameter of 1-100 micrometers consisting of a core consisting of a thiocarbamate herbicide dissolved in a water immiscible organic solvent and a melamine-formaldehyde resin shell containing a protective colloid selected from styrene-maleic anhydride copolymers and acrylamide-acrylic acid copolymers.
3. Microcapsules according to claim 2 where the herbicide is selected from S-ethyl diisobutylthiocarbamate, S-ethyl-N-cyclohexyl-N-ethylthiocarbamate, and S-ethyl hexahydro-1H-azepine-1-carbothioate.