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(54) **Title**: IMPROVED POWDEROUS FORMULATIONS OF ORGANIC ACIDS OR ESTERS HAVING AN AROMATIC RING SYSTEM

(57) **Abstract**: The present invention relates to improved powderous formulations of organic acids or esters having an aromatic ring system, as well as to the production of such formulations.

IMPROVED POWDEROUS FORMULATIONS OF ORGANIC ACIDS OR ESTERS HAVING AN AROMATIC RING SYSTEM

The present invention relates to improved powderous formulations as well as to the production of such formulations.

Powderous formulations of organic acids or esters having an aromatic ring system are very common and useful formulations.

Examples of such organic acids or esters are niacin and benzoic acid.

Niacin (also known as vitamin B3, nicotinic acid and vitamin PP) is an essential human nutrient.
A lack of niacin in the diet can cause the disease pellagra, which is characterized by diarrhea, dermatitis, and dementia, as well as "necklace" lesions on the lower neck, hyperpigmentation, thickening of the skin, inflammation of the mouth and tongue, digestive disturbances, amnesia, delirium, and eventually death, if left untreated. A lack of niacin can also cause psychiatric symptoms such as irritability, poor concentration, anxiety, fatigue, restlessness, apathy, and depression.

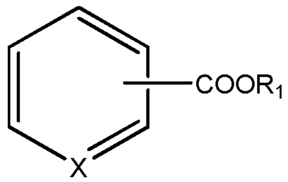
Benzoic acid and its salts are used as food preservative.

When these organic acids are used in powder form, these formulations do unfortunately have a tendency to explode.

Even when the powder has a prominent amount of larger particles, there is always a certain amount of small particles present. These small particles are responsible for the explosion risk.

Dust explosions are a huge risk in any processes wherein powders are used. Therefore there is a need for powderous formulations with low explosion hazard. But nevertheless the powderous formulations must still have the essential (and advanta geous) features of a powder, such as free flowable, easy to transport, easy to dosage etc.

Surprisingly it was found that powderous formulations comprising at least one compound of formula (I)

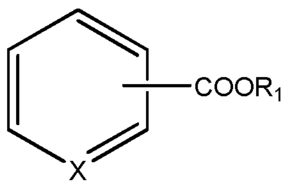


(I)

wherein
X is –N- or –CH- and
R_1 is H or a C_1-C_4 alkyl moiety, and
comprising one or more specific compounds (auxiliary compound), and
at least one carrier material
do have a low risk of explosion.

Therefore the present application relates to powderous formulations (I) comprising

(i) 0.5 to 60 weight-% (wt-%), based on the total weight of the powderous formulation, of at least one compound of formula (I)



(I)

,

wherein
X is –N- or –CH- and
R_1 is H or a C_1-C_4 alkyl moiety, and

(ii) 0.5 – 50 wt-%, based on the total weight of the powderous formulation, of at least one auxiliary compound selected from the group consisting of aluminum ammonium sulphate, aluminum potassium sulfate, ammonium acetate, ammonium bisulphite, ammonium carbonate, ammonium chloride, ammonium dihydrogen phosphate, ammonium hydrogen carbonate, bentonite, montmorillonite, calcium aluminates, calcium carbonate, calcium silicate, synthetic calcium sulphate dihydrate, calcium sulfate, kaolinitic clays (such as Kaolin), diatomaceous earth, perlite, potassium bisulphite, potassium hydrogen carbonate, potassium sulphate, potassium carbonate, sepiolitic clays, silicic acid, synthetic sodium aluminosilicate, sodium aluminosulfate, sodium bisulphate, sodium carbonate, sodium chloride, sodium hydrogen carbonate, sodium sulphate, vermiculite, calcium carbonate, magnesium carbonate, calcareous marine algae, magnesium oxide, magnesium sulphate, dicalcium phosphate, tri-calcium phosphate, mono-dicalcium phosphate, defluorinated rock-phosphate, monocalcium phosphate, calcium-magnesium phosphate, mono-ammonium phosphate, magnesium phosphate, sodium-calcium-magnesium phosphate, mono-sodium phosphate, glycerol, propylene glycol (E 1520), glyceryl triacetate (E1518), sorbitol (E420), polydextrose, lactic acid and urea, and

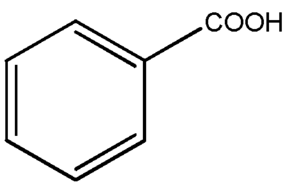
(iii) up to 40 wt-%, based on the total weight of the powderous formulation, of a carrier material.

Preferably, R_1 in the definition of formula (I) is H, CH_3, CH_2CH_3, $(CH_2)_2CH_3$ and $(CH_2)CH_3$. More preferably R_1 is H or CH_3.

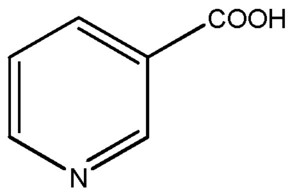
It is clear that the addition of all the wt-% always adds up to 100.

In the context of the present invention the specific compounds (ii) are also defined as auxiliary compounds.

Compounds of formula (Ia) and (Ib) are preferred



(Ia) and



(Ib) .

Preferably, the auxiliary compounds have an average particle size (d 0.5) (in the powder formulation) of 10 μm – 100 μm.

Furthermore preferred are formulations (I'), which are formulations (I), wherein the auxiliary compound has an average particle size (d 0.5) of 10μm – 100μm.
The average particle sizes are measured by a Malvern Master Sizer 2000. During this laser diffraction measurement, particles are passed through a focused laser beam. These particles scatter light at an angle that is inversely proportional to their size. The angular intensity of the scattered light is then measured by a series of photosensitive detectors. The map of scattering intensity versus angle is the primary source of information used to calculate the particle size. For the measurement of dry materials such as the applied additives, a dry powder feeder (Malvern Scirocco) was used.

The explosion hazard of powders (dusts) is usually measured by a standardized method (EN 13821:2002 (Determination of minimum ignition energy of dust/air mixtures)). This is the method which is used for the determination of all MIE values in this patent application. This method allows to determining the minimum ignition energy (MIE) of a powder. The MIE is the minimum amount of energy required to ignite a combustible vapor, gas or dust cloud, for example due to an electrostatic discharge. MIE is measured in joules (J).

The average size of the powder particles for the measurement according to the procedure in EN 13821:2002 is ≤ 63μm.

All the MIE values in this patent application are determined by using a modified Hartmann tube (type MIKE 3) available from Adolf Kühner AG (Birsfelden, CH).
This equipment is specially designed to allow the measurement of very low ignition energies. This is achieved by having different capacitors installed. The capacitors are designed to store the energy of 1 mJ, 3 mJ, 10 mJ, 30 mJ, 100 mJ, 300 mJ and 1000 mJ.

When measuring the MIE of commercially available powderous formulations comprising at least one compound of formula (I), they are usually in the range of 1-3 mJ. This means that a very low amount of energy is sufficient to initiate an explosion.

On the other hand, the formulations according to the present invention have MIE values in the range of 10 - 1000 mJ (or even more than 1000 mJ).

Therefore the present invention relates to formulations (II), which are formulations (I) or (I') with MIE values of 10 – 1000 mJ (determined by the method of EN 13821:2002). It can be even higher than 1000 mJ.

The formulations according to the present invention are dry powders. But depending on the process of production as well as the storage conditions, the formulations can comprise some water. The water content is usually below 5 wt-%, based on the total weight of the formulation.
Therefore a further embodiment of the present invention relates to formulations (III), which are formulations (I), (I') and (II), wherein 0 to 5 wt-%, based on the total weight of the formulation, of water is present.

Preferably the powderous formulations do not comprise other ingredients/compounds than as disclosed above. They do not contain any commonly used stabilisers, surface active ingredients or sugars.

The compounds of formula (I) can be from a natural source or they can be synthesised. Due to the nature of either the isolation process or the process of production, it is possible that traces of side products are present.

The carrier material used in the formulations according to the present invention are commonly known and used carrier material. A suitable carrier material is synthetically produced precipitated silica or formiate (such as calcium formiate). This carrier material consists of porous particles. Other suitable carrier materials are proteins, starches, lignosulfonates and gums.

Preferred formulations of the present invention are formulations (IV), wherein formulations (I), (I'), (II) and/or (III) comprise

(ii) 20 - 60 wt-%, based on the total weight of the formulation, of at least one compound selected from the group consisting of ammonium dihydrogen phosphate, (purified) diatomaceous earth, potassium hydrogen carbonate, potassium sulphate, potassium carbonate, sodium chloride and sodium hydrogen carbonate.

More preferred are formulations (IV'), which are formulations (IV) with MIE values of 10 – 1000 mJ (determined by the method of EN 13821:2002). It can be even higher than 1000 mJ.

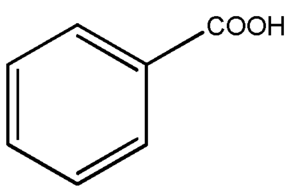
Furthermore preferred are formulations (IV''), which are formulations (IV') wherein the auxiliary compound has an average particle size (d 0.5) of 10μm – 100μm.

Also preferred are formulations (V), which are formulations (I), (I'), (II), (III), (IV), (IV') and (IV''), which comprise

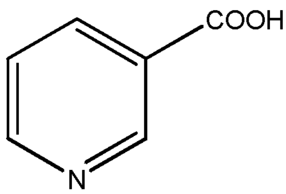
(iii) up to 40 wt-%, based on the total weight of the formulation, of at least one carrier material chosen from the group consisting of synthetically produced precipitated silica, formiate (such as calcium formiate), proteins, starches, lignosulfonates and gums.

An especially preferred embodiment of the present invention relates to formulations (V), consisting of

(i) 20 - 60 wt-%, based on the total weight of the powderous formulation, of



(Ia) and/or



(Ib), and

(ii) 25 - 50 wt-%, based on the total weight of the powderous formulation, of at least one auxiliary compound selected from the group consisting of ammonium dihydrogen phosphate, (purified) diatomaceous earth, potassium hydrogen carbonate, potassium sulphate, potassium carbonate, sodium chloride, sodium sulphate and sodium hydrogen carbonate,

(iii) up to 40 wt-%, based on the total weight of the powderous formulation, of at least one carrier material chosen from the group consisting of synthetically produced precipitated silica, formiate (such as calcium formiate), proteins, starches, lignosulfonates and gums, and

(iv) 0 to 5 wt-%, based on the total weight of the powderous formulation, of water.

To produce a powder according to the present invention (formulations (I), (I'), (II), (III), (IV), (IV'), (IV'') and (V)) it is possible that at least one compound of formula (I) is sprayed onto the carrier material and then at least one auxiliary compound is added and the formulation is blended.
It is also possible that at least one compound of formula (I) is sprayed onto a mixture of at least one carrier material and at least one auxiliary compound.

All the above disclosed formulations (I), (I'), (II), (III), (IV), (IV'), (IV'') and (V) can be used as such or in food products, feed products and personal care products.

All the above disclosed formulations (I), (I'), (II), (III), (IV), (IV'), (IV'') and (V) can be used as such in the production of food products, feed products and personal care products.

Furthermore the invention also relates to food products, feed products and personal care products comprising at least one formulations (I), (I'), (II), (III), (IV), (IV'), (IV'') and/or (V).

The invention is illustrated by the following Examples. All temperatures are given in °C and all parts and percentages are related to the weight.

Examples

<u>Example 1</u>

900 g benzoic acid (purity 99.9%) was filled into an appropriate blender (Nauta) and 700 g sodium chloride having a particle size, analysed by laser diffraction, of 54 µm

were added. Then 150 g silicon dioxide and 150 g calcium formiate were added and the mixture was blended for 10 minutes. The obtained free flowing white powder was filled into a container.
The blend was then air classified in an appropriate apparatus (Alpine Multiprocess unit 100 AFG/50ATP), using an air flow of 60 m^3/h and rotation speed of the sifter wheel of 2200 rpm, and the fines collected.
Assessed by laser diffraction, the particles averaged 27 μm, sodium chloride content was 38.3 wt-% and benzoic acid content was 56.1 wt-%. The fines were analyzed according to the above mentioned EN 13821:2002 and minimum ignition energy was found to be 10 – 30 mJ.

Example 2:

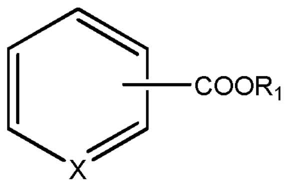
600 g Niacin (Rovimix® Niacin from DSM) and 600 g sodium chloride were mixed for 20 minutes in a Turbula mixer. The material was sifted (1 mm sieve) and mixed again in the Turbula mixer for another 10 minutes. The median size of this material was 328 μm. The material was the transferred to a Retsch Grindomixer and milled (10'000 rpm/1 min.). The median size of this material was 68 μm. This material was sifted (125 um sieve) and a final product with a median particle size of 59 μm was obtained. This material was analyzed according to the above mentioned EN 13821:2002 and minimum ignition energy was found to be > 1000 mJ.

Example 3:

300 g benzoic acid (purity 99.9%) was filled into an appropriate blender (Turbula) and 300 g sodium chloride having a particle size, analysed by laser diffraction, of 54 μm was added, the mix then blended for 10 minutes. The obtained free flowing white powder was filled into a container.
The powder was analyzed according to the above mentioned EN 13821:2002 and the minimum ignition energy was found to be over 1000 mJ.

Claims

1. A powderous formulation comprising
   (i) 0.5 to 60 wt-%, based on the total weight of the powderous formulation, of at least one compound of formula (I)



(I)

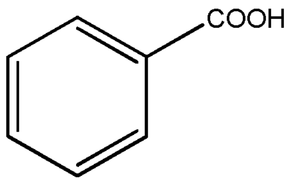
,

wherein
X is –N- or –CH- and
R_1 is H or a C_1-C_4 alkyl moiety, and

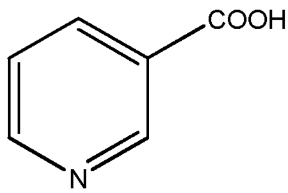
   (ii) 0.5 – 50 wt-%, based on the total weight of the powderous formulation, of at least one auxiliary compound selected from the group consisting of aluminum ammonium sulphate, aluminum potassium sulfate, ammonium acetate, ammonium bisulphite, ammonium carbonate, ammonium chloride, ammonium dihydrogen phosphate, ammonium hydrogen carbonate, bentonite, montmorillonite, calcium aluminates, calcium carbonate, calcium silicate, synthetic calcium sulphate dihydrate, calcium sulfate, kaolinitic clays (such as Kaolin), diatomaceous earth, perlite, potassium bisulphite, potassium hydrogen carbonate, potassium sulphate, potassium carbonate, sepiolitic clays, silicic acid, synthetic sodium aluminosilicate, sodium aluminosulfate, sodium bisulphate, sodium carbonate, sodium chloride, sodium hydrogen carbonate, sodium sulphate, vermiculite, calcium carbonate, magnesium carbonate, calcareous marine algae, magnesium oxide, magnesium sulphate, dicalcium phosphate, tri-calcium phosphate, mono-dicalcium phosphate, defluorinated rock-phosphate, monocalcium phosphate, calcium-magnesium phosphate, mono-ammonium phosphate, magnesium phosphate, sodium-calcium-magnesium phosphate, mono-sodium phosphate, glycerol, propylene glycol (E 1520), glyceryl triacetate (E1518), sorbitol (E420), polydextrose, lactic acid and urea, and

(iii) up to 40 wt-%, based on the total weight of the powderous formulation, of a carrier material.

2. A powderous formulation according to claim 1, wherein the compound of formula (I) is a compound of formula (Ia) and/or (Ib)



(Ia) and



(Ib) .

3. A powderous formulation according to any of the preceding claims, wherein the auxiliary compounds have an average particle size (d 0.5) (in the powder formulation) of 10 μm – 100 μm.

4. A powderous formulation according to any of the preceding claims, wherein the formulations have MIE values of 10 – 1000 mJ.

5. A powderous formulation according to any of the preceding claims 1 – 3, wherein the formulations have MIE values of more than 1000 mJ.

6. A powderous formulation according to any of the preceding claims, comprising 0 to 5 wt-%, based on the total weight of the formulation, of water.

7. A powderous formulation according to any of the preceding claims, wherein the formulations comprise

(ii) 20 - 60 wt-%, based on the total weight of the formulation, of at least one compound selected from the group consisting of ammonium dihydrogen phosphate, (purified) diatomaceous earth, potassium hydrogen carbonate, potassium sulphate, potassium carbonate, sodium chloride and sodium hydrogen carbonate.

8. A powderous formulation according to any of the preceding claims, wherein the formulations comprise

(iii) up to 40 wt-%, based on the total weight of the formulation, of at least one carrier material chosen from the group consisting of synthetically produced precipitated silica, formiate (such as calcium formiate), proteins, starches, lignosulfonates and gums.

9. Use of at least one formulation according to any of claims 1 – 8 in food products, feed products and personal care products.

10 Food products, feed products and personal care products comprising at least one formulation according to any of claims 1 – 8.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/052281

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23P1/06 A23L1/302 A23L3/3508 A23L3/3517 A61K8/67
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A23L A23P A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, FSTA, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 102 078 631 A (ZHUAN ZHUANG) 1 June 2011 (2011-06-01) abstract; examples 1-5	1,2,4-6, 8-10
X	DATABASE WPI Week 201054 Thomson Scientific, London, GB; AN 2010-K02588 XP002681499, & CN 101 766 268 A (WENG X) 7 July 2010 (2010-07-07) abstract; claims 2-3; examples 1-2	1,2,4-6, 8-10
A	US 5 100 592 A (SPARKS ROBERT E [US] ET AL) 31 March 1992 (1992-03-31) column 1, line 42 - line 49 column 2, line 36 - line 43 example 6	1-10

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search

13 May 2013

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 188 298 A1 (STAMICARBON [NL]) 23 July 1986 (1986-07-23) page 1, line 19 - line 30 page 2, line 12 - line 17 examples 1-2	1-10
A	NL 8 503 102 A (STAMICARBON) 1 June 1987 (1987-06-01) page 1, line 5 - line 8 page 1, line 22 - line 25	1-10
A	US 4 617 294 A (KRIVAK THOMAS G [US] ET AL) 14 October 1986 (1986-10-14) column 1, line 56 - column 2, line 23 column 3, line 49 column 3, line 62 - line 65 claim 1	1-10

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2013/052281

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 102078631 A	01-06-2011	NONE	
CN 101766268 A	07-07-2010	NONE	
US 5100592 A	31-03-1992	AU 9166591 A	22-07-1992
		CA 2098600 A1	21-06-1992
		EP 0563302 A1	06-10-1993
		JP H06507571 A	01-09-1994
		US 5100592 A	31-03-1992
		WO 9211120 A1	09-07-1992
EP 0188298 A1	23-07-1986	CA 1268477 A1	01-05-1990
		DE 3663941 D1	20-07-1989
		EP 0188298 A1	23-07-1986
		JP S61165347 A	26-07-1986
		NL 8500060 A	01-08-1986
		US 4675440 A	23-06-1987
NL 8503102 A	01-06-1987	NONE	
US 4617294 A	14-10-1986	US 4617294 A	14-10-1986
		US 4717561 A	05-01-1988