

# DEVELOPMENT OF A NEW GRANULATION TECHNIQUE I.

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## Summary

The described drop technique allows to prepare spherical granules possessing high mechanical strength. The properties of the granules can be influenced — besides by the technological conditions — by varying their composition. The release rate of the active agent incorporated in the product can, e.g., be changed by varying the ratio and kind of the support and the polymer, resp.

## Introduction

The drop technique for encapsulation and microencapsulation has been described in the literature [1, 2, 3]. It consists in adding the solution of a polymer dropwise to a precipitating bath that does not dissolve the polymer and is not miscible with the solvent of the polymer. The polymer will precipitate in the bath and the droplet — owing to interface tension — will assume a spherical shape. Simultaneously, it will solidify either by cooling (the precipitating bath having a lower temperature than the solution of the polymer) or by the action of a curing (usually cross-linking) additive in the bath (e.g. formaldehyde in the case of gelatine solutions).

## Fundamental considerations and experimental

This technique, known from the literature, led us to the idea to utilize the drop process in a basically different manner to prepare spherical microgranules. The novel technique developed by us can be utilized in a wide range. Our experimental work indicated that the process can be applied for any system which satisfies the following four conditions:

- (i) A *polymer* soluble in the solvent and insoluble in the precipitating bath.
- (ii) A *solvent or solvent mixture* dissolving the polymer, and miscible with the precipitating bath. It is indifferent whether or not the active agent is soluble in the solvent.

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(iii) An *active agent* (or blend of agents) insoluble in the precipitating bath (either by its nature or by pre-saturation of the precipitating bath). As mentioned, it may or may not be soluble in the solvent.

(iv) A *precipitating bath* or mixture miscible with the solvent and not dissolving the polymer and the active agent.

Fillers and support materials may also be used in the process, with the condition that they be insoluble in the precipitating bath, and preferentially also in the solvent.

The essential features of the novel technique applied to produce pesticides, microgranules and capsules, including fillers, are described in the followings.

The active agent (or blend of agents) is combined with the filler in a manner depending on its physical, chemical etc. properties. (Powders are mixed mechanically, liquids are adsorbed on the support materials etc.)

The powder-like mixture of the active agent and the filler is mixed to a paste with the solution of a suitable polymer in a solvent miscible (preferably in all ratios) with the precipitating bath in which the polymer is insoluble.

If necessary, the paste is diluted with further solvent to a consistency that will allow easy dropping of the paste.

The paste is dropped into the precipitating bath through a capillary tube with a suitable diameter, by applying slight pressure. If the precipitating bath is water, it is expedient to lower its high surface tension by adding tensides; to promote the precipitation of the polymer (to reduce solubility) by mild cooling, e.g. adding ice will prove advantageous.

The experiments were performed in the apparatus shown schematically in Fig. 1. The viscous paste is pressed through the capillary end of the dropping funnel 1 by excess pressure from a buffer flask 4 filled with air, connected to the municipal water net.

The dropping height was determined experimentally. The drops assume a spherical shape in the bath; at the meeting of the drop and the bath, the polymer precipitates in the form of a thin film around the drop and its content (polymer, active agent and filler, all insoluble in the precipitating bath) remains in this shell. During the slow sinking of the drop, and after its reaching the bottom, two diffusion processes in reverse directions take place. On the one hand, the solvent diffuses from the interior of the drop into the precipitating bath with which it is miscible, and on the other hand, the precipitating bath diffuses into the drop, precipitating further layers of polymer. The final product of the two opposed diffusion processes is a solid containing some precipitating bath and very little solvent. It is expedient to apply gentle agitation during the process in order to prevent agglomeration of the drops sinking to the bottom.

The spherical microgranules (capsules) (Fig. 2) are separated from the precipitating bath by batchwise or continuous filtering and dried. To prevent

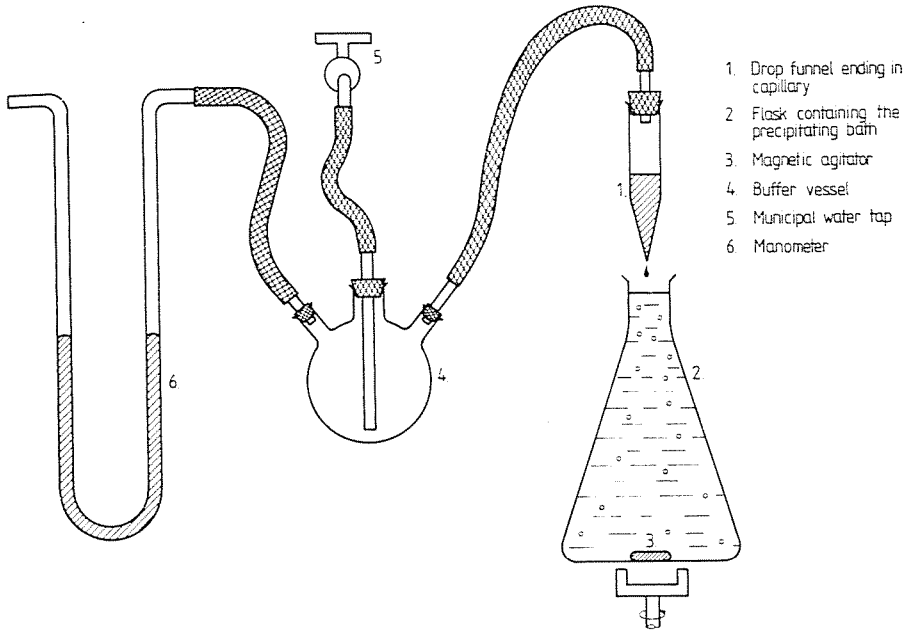


Fig. 1. Laboratory apparatus used in the drop technique

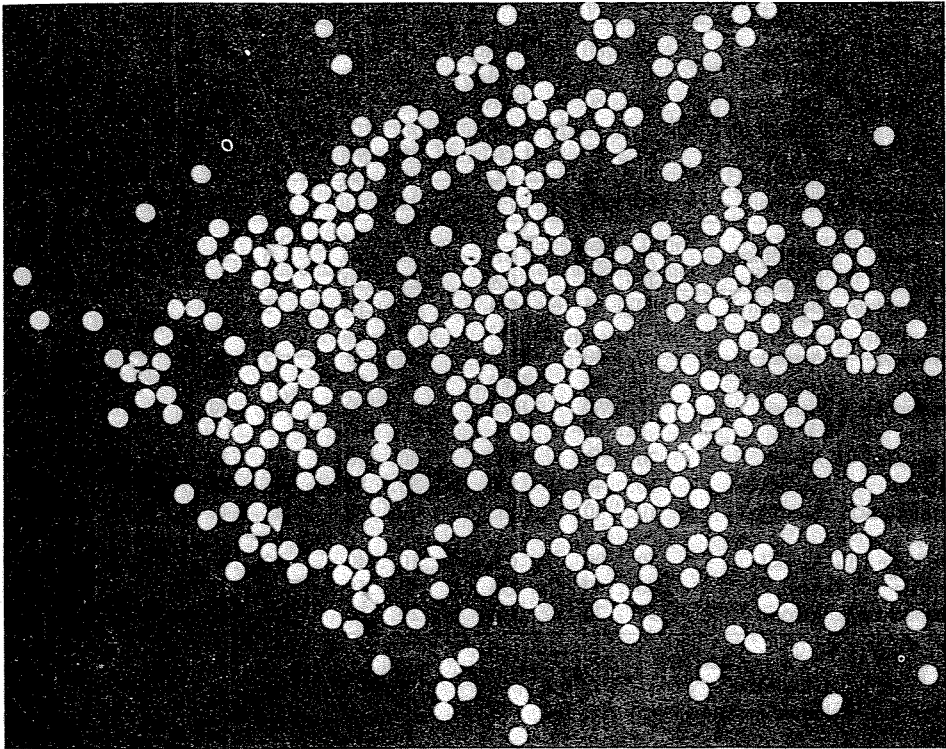


Fig. 2. Microgranules prepared with the drop technique

the accumulation of solvent in the precipitating bath, which would interfere with precipitation, it is serviceable to keep the bath in constant circulation and separate the solvent, e.g., by distillation or adsorption. In this manner the technique can be considered essentially continuous.

The active agents used in our experiments were Molinate (4'-chloro-2,2-dimethylvaleraniide), Propachlor (2-chloro-N-isopropylacetanilide) and Atrazin (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazin) [4]. The liquid Molinate can — in principle — be directly applied on the support, Propachlor, having a low melting point, in form of its melt or from solution. Atrazin, a powder with a high melting point and poor solubility can be applied as a mechanical mixture with the filler. (Actually, Propachlor was also applied in the powder form.) The nominal active agent content of the product was 10% in all experiments.

**Table 1**

Support material and polymer variations used in the experiments

Active agent, 10% by mass	Support (filler) material	% by mass in the final product	Polymer	% by mass in the final product	% by mass in the solution	Total % by mass of solids in the paste
Molinate	Bentonite	50...80	PVAc	10...40	22...38	42...58
Atrazin	Bentonite	40...85	PVAc	5...50	8...38	28...50
Propachlor	Bentonite	60...80	PVAc	10...30	11...31	42...49
Molinate	Bentonite	40...80	EC	10...40	28...49	21...53
Atrazin	Bentonite	30...80	EC	10...60	11...48	22...49
Propachlor	Bentonite	40...60	EC	30...50	28...42	29...44
Molinate	Bentonite	70...87	CA	2.5...20	3...8	24...51
Atrazin	Bentonite	70...87	CA	2.5...20	4...8	24...43
Propachlor	Bentonite	60...85	CA	5...30	5...8	16...47
Molinate	Aerosil	15...40	PVAc	50...75	13...38	10...36
Atrazin	Aerosil	10...40	PVAc	50...80	11...38	9...10
Propachlor	Aerosil	10...60	PVAc	30...80	5...30	10...12
Molinate	Aerosil	20...50	EC	40...70	9...39	13...14
Atrazin	Aerosil	10...40	EC	50...80	15...42	9...13
Propachlor	Aerosil	10...40	EC	50...80	11...42	8...10
Molinate	Aerosil	50...80	CA	10...40	2...8	14...36
Atrazin	Aerosil	40...60	CA	30...50	4...8	7...9
Propachlor	Aerosil	30...70	CA	20...60	3...8	5...11

PVAc = poly(vinyl acetate)

EC = ethylcellulose

CA = cellulose acetate

Bentonite or hydrophilic aerosil were used as filler-support materials. The precipitating bath was municipal water containing the tenside Tween 80 and cooled with ice.

The solvents (miscible with the precipitating bath) were ethanol and dimethylformamide, resp., the polymers (soluble in these solvents, but precipitated in water) were poly(vinyl acetate), ethylcellulose and cellulose acetate, resp.

It should be noted that the granular products obtained with our drop process can be used for various other purposes too. To demonstrate this fact, we prepared products free of active agents, which might be utilized as adsorbents.

We performed series of experiments with individual combinations of active agent — support — polymer — solvent, changing the concentrations of the polymer in the solution and of the solid support-filler material in the paste (Table 1). In the different phases of granule preparation we controlled their active agent content by gas chromatography (the experimental conditions are listed in Table 2). We wished to study how the nature and amount of the support and the polymer and the type of solvent affect the properties of granules with identical nominal active agent contents. The final products were appraised by their average grain size and grain mass, by their resistance to

**Table 2**

Conditions of gas chromatographic analysis of the final products  
Instrument: Hewlett-Packard 5750

Active agent	Molinate	Atrazin	Propachlor
Column	Glass, length 1.5 m internal diam. 2 mm	Steel, length 1.5 m internal diam. 2 mm	Glass, length 1 m internal diam. 2 mm
Packing	5% SE 30 on Chromosorb W	3% SE 30 on Chromosorb W	4% SE 30 on Chromosorb W
Temperature, °C			
of detection	210	250	240
of column	160	140–220	150–200
of injection	250	240	240
Flow rate, cm <sup>3</sup> /min			
of H <sub>2</sub>	12.5	10	14
of air	560	500	600
of N <sub>2</sub>	27	27	27
Recording rate, cm/h	30	30	30
Performance, number of theor. plates	8 · 10 <sup>3</sup>	32 · 10 <sup>2</sup>	128 · 10 <sup>3</sup>
Standard concentration, g/cm <sup>3</sup>	5 · 10 <sup>-2</sup>	7 · 10 <sup>-2</sup>	1 · 10 <sup>-2</sup>

**Table 3**  
Experimental conditions

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Application of the active agent: Molinate in the liquid state, Atrazin and Propachlor in powder form
Precipitating bath: water
Surface tension of precipitating bath: 48 mJ/m <sup>2</sup>
Tenside applied: Tween 80; 1 g/dm <sup>3</sup>
Sedimentation height of granules: 27 cm
Sedimentation time of granules: 2...3 s
Speed of magnetic agitator: 400...600 rpm.

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abrasion (in per cents) and by the rate constant  $k_0$  of the release of the active agent (a first-order reaction).

The technological conditions of the drop granulation process were established experimentally (pressure, drop height, drop rate). The final parameters are listed in Table 3. These experiments demonstrated the significant effect of the characteristics of the paste (e.g. its rheological properties) on the final product. The results of these experiments will be reported in a later paper.

The products which were accepted as successful are regularly spherical and possess high mechanical strength (Fig. 2).

We wish to note that the size of the granules can be readily varied (by the internal and external diameter of the capillary tube, by pressure etc.) and can exceed the usual size of pesticide granules. Hence the technique can be used in other fields apart from the formulation of pesticides.

## Discussion

Our experiments with the active agent Molinate showed that the drop granulation technique can be successfully applied with bentonite support and cellulose acetate polymer as well as with hydrophilic aerosil support and poly(vinyl acetate) polymer, both in dimethylformamide solvent. The product with the most favourable properties was obtained with bentonite and cellulose acetate (CA); as little as 25% polymer proved sufficient to prepare products with satisfactory characteristics.

With Propachlor as active agent, the support bentonite and the polymer cellulose acetate, in dimethylformamide as solvent, was found best. 5% polymer yields 94% active agent content, identical to the calculated value. When hydrophilic aerosil is applied as support, higher percentages of polymer (20...30%) are required.

Table 4

Rate constant of active agent release  $k_0$  vs. composition of the granules

Components	Nominal composition, %			Release rate constant $k_0$ , day <sup>-1</sup>
	active agent	support	polymer	
Molinate and poly(vinyl acetate)	10	20	70	37.0
	10	30	60	47.6
	10	40	50	62.5
Propachlor and cellulose acetate	10	60	30	61.9
	10	70	20	58.3
	10	80	10	58.0
	10	85	5	57.5

Bentonite — poly(vinyl acetate) — dimethylformamide is the most suitable combination for the active agent Atrazin. With 10% polymer, the obtained active agent content is close to the calculated value, and high resistance to abrasion is achieved.

The release rate of the active agent  $k_0$  depends on the ratio support to polymer (Table 4). In the case of poly(vinyl acetate) (PVAc),  $k_0$  increases with decreasing percentage of polymer, in the case of CA a slight decrease of  $k_0$  was found.

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