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# Bioefficacy and Controlled Release Performance ofMicroencapsulated Hexaconazole against Powdery Mildew Disease on Field Pea

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## Abstract

Hexaconazole is a Broad-spectrum systemic triazole fungicide used for the control of many fungi particularly Ascomycetes and Basidiomycetes. The hexaconazole were microencapsulated in polyurethane shell by interfacial polymerization. Themicrocapsules were characterized by the particle size analysis, Scanning Electron Microscope (SEM), thermogravimetric analysis, and High-Performance Liquid Chromatography (HPLC). The particle size of the prepared microcapsules was found in the range 1-15 µm in diameter with excellent encapsulation efficiency in the range 85-95%. The SEM micrographs shows microcapsules were approximately spherical in shape and ruptured microcapsule confirms the formation of the core and shell structure. The maximum sustained release content of Hexaconazole was found to be 98% for the sample of S3 after interval of 30 days. While slower release was obtained for the ratio of S1 (65.46%) for the same time interval, i.e. 30 days. The release mechanism non-Fickian diffusion may be due to combine effect of diffusion and erosion mechanism.The microencapsulation improves the sustainability and controlled release property of hexaconazole which is useful to control the disease over period of time.

## 1. Introduction

Pea (*Pisum sativum)* is most widely cultivated crop and is one of the important vegetable crops of subtropical and temperate areas [1,2]. Among the several fungal diseases, powdery mildew caused by *Erysiphe pisi* and downy mildew caused by *Peronospora viciae f. sp. pisi* are two major diseases of pea and cause severe damagewithin short period of time throughout the globally [1,3,4]. Powdery mildew causes serious deseases affecting nearly 10,000 species of angiosperms [5].To protect the peas from the loss in crop yield caused by the fungal damage and to maintain their nutritional composition, different fungicides are applied [2]. The fungicides are hexaconazole, tebuconazole, carbendazim, thiram are applied indiscriminately to prevent losses [6,7].

As a systematic fungicide, hexaconazole can prevent and treat disease caused by ascomycetes, basidiomycetes and imperfect fungi. It especially can eradicate the diseases as powdery mildew, rust, scab, brown blotch and anthracnose caused by basidiomycetes and ascomycetes. Additionally, this crop protection chemical has excellent preventative effect for the sheath blight of paddy rice. Hexaconazole is an effective pesticide in fruit and vegetable disease control. It is applicable to apples grapes, bananas, vegetables (likes melons, peppers, etc.), peanuts, coffee, cereal crop and ornamental plants. Hexaconazole is widely used throughout the world because of its high antifungal activity and a relatively low resistance risk. However, since hexaconazole is used as an agricultural fungicide, there is concern for potential human and wildlife exposure to its residues in the environment, including plants, soil, and water receiving soil runoff [8]. There are still serious problems with emulsifiable concentrate and suspension concentrate formulations due to immediate release of active ingredients, which reduces the efficacy and activity of active ingredients. Therefore excessive quantities of active ingredients are applied to compensate the losses, also resulting in sever economic losses. Thus the developing the formulation which enhances the efficacy as well as minimizes the environmental impact are interesting. Among the other technologies, microencapsulation has the great potential to control the both, efficacy and environmental impact and widely practiced today in various sector.

Microencapsulation technology has received much attention in the past decades and process has been significantly used in various fields including fragrance oils [9], cosmetics [10], self-healing agents [11,12], Phase change materials [13,14], immobilized extraction reagents, and pesticides [15][16]. If a plant is treated with microencapsulated active agents such as insecticides, fungicides and herbicides, higher effectiveness and longer durability are expected [17–19]. Microencapsulation process involves encapsulating or surrounding the tiny droplets or particles with a polymer as outer Shell [20,21].

In this study, we used toluene diisocyanate asa precursor and ethylene glycol as a curing agent to prepare polyurethane shelled hexaconazole microcapsules by using an interfacial polymerization method. Prepared microcapsules were characterized by FTIR spectroscopy. The particle size and shape were characterized by particle size analyzer and optical microscope. The controlled release rate evaluated by HPLC method.

## 2. Material and Methods

### *2.1. Materials*

Technical grade Hexaconazole with purity 97% obtained from Gharda Chemicals Limited. Toluene diisocyanate (Purity ≥ 99.0%) was obtained from Bayer Material Science. Ethylene Glycol was purchased from the SD Fine chemicals. Polyvinyl alcohol (PVA) (Degree of hydrolysis-86-89%, molecular weight-85000-124000) as stabilizers in the aqueous phase, Chloroform as a solvent in the oil phase, and methanol as an extractant were obtained from SD Fine. All chemicals were of reagent grade and used without further purification. Xanthan gum used as stabilizer for capsule suspension.

### *2.2. Preparation of Microcapsules*

Polyurethane microcapsules prepared by using interfacial polymerization in an oil-in-water emulsion technique. Briefly, the organic phase was obtained by dissolving 6.167 g Hexaconazole and 1.54 g of TDI in 12.33 g chloroform and stirred till the homogeneous mixture is obtained. Simultaneously an aqueous phase was prepared comprised of the 1 % poly (vinyl alcohol). Then, the organic phase was added dropwise to the aqueous phase under constant stirring. This mixture was emulsified using a high-speed mixer at approximately2500 rpm for 10 min. After emulsifying the mixture at room temperature, the oil in water emulsion was then transferred to a three-neck flask and stirred at 300 r/min.Next, the ethylene glycol was added dropwise as a 20% aqueous solution while stirring at a reduced speed at 300rpm that maintained good mixing at a temperature of 60°C. Following the completion of the ethylene glycol addition the resulting capsule suspension was stirred for an additional four hours to complete the preparation of the capsule suspension. Formation ofmicrocapsules was checked by observing reaction mixturetime to time under optical microscope. Then microcapsules from the suspension was recovered by filtration, washed with ethanol (30%) and distilled water anddried in an oven at 50°C for 48 hrs.

**Table 1.** Batch Formulation for 10% loading of Hexaconazole

| Sr. No. | Sample Code | Hexaconazole | Isocyanate | Shear Rate | Shear Time (min) |
|---|---|---|---|---|---|
| 1 | S1 | 6.167 | 1.54 | 2500 | 10 |
| 2 | S2 | 6.167 | 1.23 | 2500 | 10 |
| 3 | S3 | 6.167 | 0.617 | 2500 | 10 |

### *2.3. Characterization*

#### *2.3.1. Fourier Transform Infrared (FTIR) Spectroscopy*

Fourier Transform Infrared spectroscopy (FTIR) was used for identification of dried microcapsules measuring transmittance from 500 to 4000 cm-1. All the measurements were recorded on a Bruker-Alpha's Zn-Se ATR model.

#### *2.3.2. Thermo-gravimetric Analysis*

The thermogravimetric analysis (TGA) of polyurethane microcapsules was performed using Pyris-1-TGA Perkin Elmer thermogravimetric analyzer at scanning rate of 20°C/min nitrogen atmosphere with 20 ml/min nitrogen flow rate from temperature 40 to 700°C.

#### *2.3.3. Morphology and Structure Analysis*

The surface morphology of the hexaconazole polyurea microcapsules analyzed by SEM (scanning electron microscopy) using FEI Quanta 200 ESEM model.

*2.3.4. Mean particle size and span*

To determine the diameter of the Hexaconazole/polyurethane microcapsules 1 g of microcapsules suspension was diluted by the 5 ml of distilled water. It was measured by dynamic light scattering technique using Nanoplus (Micromeritics, USA).

*2.3.5. Measurement of the Encapsulation Efficiency*

The Hexaconazole microcapsules suspension was dispersed in a certain amount of n-hexane. Then, the mixture was shaken upside down for one minute, followed by standing for 1 min for stratification. The supernatant was filtered and the concentration of unencapsulated Hexaconazole was determined. The supernatant was analyzed by high-performance liquid chromatography (HPLC, Waters) with a UV/Visible (Waters 2489) detector. The HPLC separation of Hexaconazole was carried out on a Cosmosil-5C18-MS-II packed column (4.6 mm ID x 250 mm, 5µ, Cosmosil) with an isocratic elution of acetonitrile: water (85:15vol/vol) as the mobile phase at a detection wavelength of 210 nm. The encapsulation efficiency (EE) was calculated according to the following Eq. (1):

$$EncapsulationEfficiency,\% = \frac{massofhexaconazoleinmicrocapsules}{initialmassofhexaconazole} * 100$$

*2.3.6. Determination of the Release Rate of the Microcapsules*

The release rate of hexaconazole from Polyurethane microcapsules in water was determined through dissolution experiment. A certain quantity of hexaconazole loaded microcapsules placed in 500 mL of distilled water and the media were stirred at 35+2°C and 50 rpm as shown in figure. Thereafter, 1 mL of the media was obtained for hexaconazole concentration analysis at specific time intervals. Subsequently, 1 ml of fresh distilled water was added to the media to maintain a constant volume and unsaturated conditions. The concentration of released Hexaconazole was determined through HPLC. The release mechanism of the hexaconazole from the polyurea microcapsules was investigated by the Korsmeyer–Peppas model[22,23].

$$\frac{M_t}{M_\infty} = kt^n$$

Where Mt is the amount of drug released in time t, M∞ is the initial amount of drug in the microcapsule sample, k is the release constant and n is the diffusion exponent.

*2.4. Field Trails*

The experiment was conducted at Plant Pathology and Agricultural Microbiology, Mahatma Phule Krishi Vidyapeeth, Rahuri during the Rabi 2018-2019 season to evaluate the efficacy of the polyurethane microcapsules loaded with the hexaconazole formulation having hexaconazole 5% CS. The trials were laid in the completely randomized block design with seven treatment including untreated control and three replications. Popular green peas variety, golden Mahabeej which is highly susceptible to the powdery mildew. A spacing of 15x15 cm was adopted in the gross plot size of 12 $m^2$. The microencapsulated hexaconazole formulation evaluated at three different dosage (0.5 ml/L, 0.6 ml/L and 0.7 ml/L). the single spray was taken up till the flowering stage. The data on the disease incidence of powdery mildew and subsequent spread were collected from the date of first incidence of the disease till 30 days after final spray. The percent disease incidence and severity was calculated from the data collected from 5 plant in each replication in each treatment.

## 3. Results and Discussion

*3.1. FTIR Spectroscopy*

To ensure the successful encapsulation of the Hexaconazole in the polyurethane the FTIR spectra of Hexaconazole and microcapsules formed was recorded and shown in the figure 1. The spectrum of polyurea shell showed the strong band at 3311 cm−1, which is assigned to N-H stretching vibration. The C=O stretching frequencies for –CONH- are present in polyurea microcapsules observed at 1640 cm−1. The absorption peak at 1548 cm−1 corresponds to -C=C-present in the aromatic ring. Furthermore, absorption band for –N-H bending of N-substituted amide in polyurea can be observed at 1515 cm−1.The characteristicabsorptionpeaks of hexaconazole observed at 670, and 1020 were assigned as C–Cl (Py–Cl) stretching and P–O–C stretching respectively.

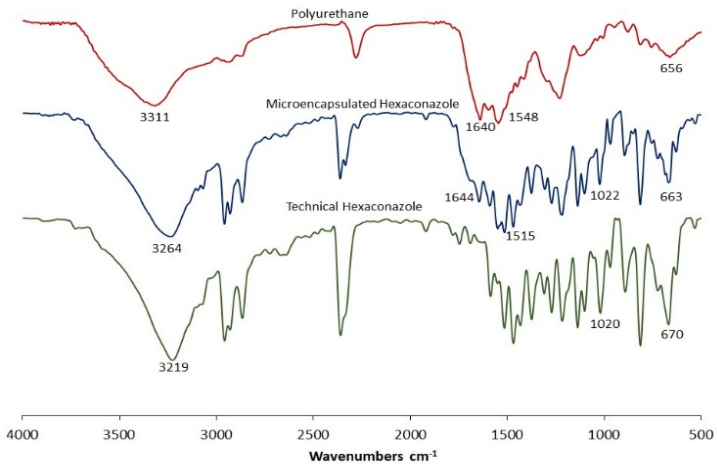


**Figure 1.** FTIR Spectra for technical Hexaconazole, Polyurethane and Hexaconazole/polyurethane Microcapsules

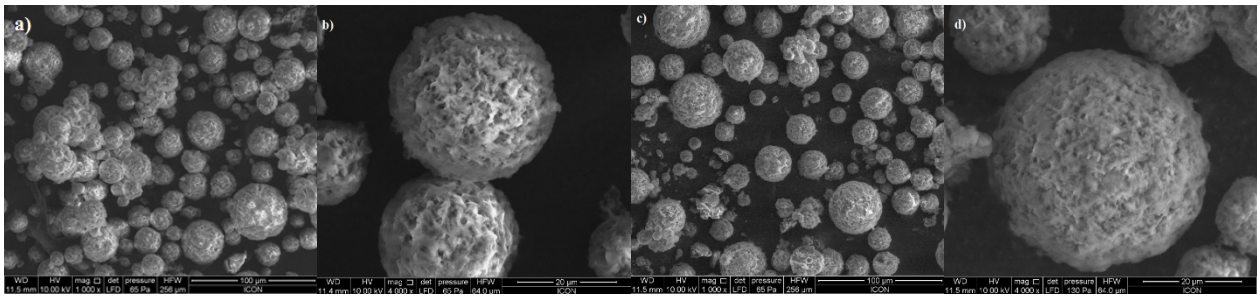


**Figure 2.** The SEM images of Hexaconazole/polyurea microcapsules. a) and b) for S1 and c) and d) for S2

*3.2. Morphology*

The morphology and dispersion of Hexaconazole/polyurethane was investigated by the optical microscope and presented in Figure 2. The microcapsules of Hexaconazole/polyurethane are evenly dispersed without aggregation. The morphology of the microcapsules is approximately spherical, and the surface is uneven and compact. From the SEM images, it was cleared that the spherical shape microcapsules with a porous compact shell wall were obtained.

*3.3. Particle Size Analysis*

The particle size analysis of the microcapsule suspension was investigated by the particle size analysis and represented in figure 3 and Table 2. The average particle size was found in the range of 1-15 µm. For sample S1, D50was 3.294 µm, whereas the D10and D 90 were 2.279and 6.853 µm, respectively. While for sample S3, S1 D50was 7.377 µm, whereas the D10and D 90 were 5.44 and 11.057 µm. The encapsulation efficiency was determined and found in the range 85-95%.

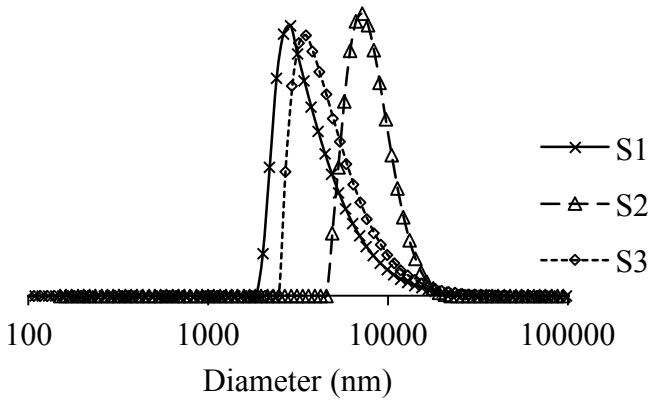


**Figure 3.** Particle Size Distribution of Hexaconazole/Polyurethane Microcapsules

**Table 2.** Characteristic properties of Hexaconazole/Polyurethane microcapsules

| Core to Shell Ratio | Average Diameter, (μm)[(a)] | D10, (μm) | D50, (μm) | D90, (μm) | Span(a) | EE, %[(b)] |
|---|---|---|---|---|---|---|
| S1 | 4.357 + 3.066 | 2.279 | 3.294 | 6.853 | 0.813 | 95.23 |
| S2 | 5.267 + 3.266 | 2.843 | 4.107 | 8.149 | 0.852 | 95.38 |
| S3 | 8.198 + 2.411 | 5.44 | 7.377 | 11.057 | 1.159 | 85.81 |

Note: a) Particle Size Distribution Calculated by DLS method
b) Content of Chlorpyrifos determined by HPLC

*3.4. Controlled release kinetics*

Figure 4 represents the release behavior of the hexaconazole form the polyurea microcapsules in the dissolution medium i.e. water. From the fig. Figure 4 it was observed the controlled release behavior of the hexaconazole through microcapsules. the emulsifier has no effect on the controlled release properties of the microcapsules.
The microsphere formulations exhibited burst release at the beginning of the release experiments. The burst effect may be attributed to the fact that some of the raw hexaconazole were not encapsulated; hexaconazole that were not encapsulated easily leached into water. Slow release occurred after the burst release owing to diffusion and erosion. Mainly the release of the active ingredients from the microcapsule was observed due to the diffusion and erosion of the wall materials.

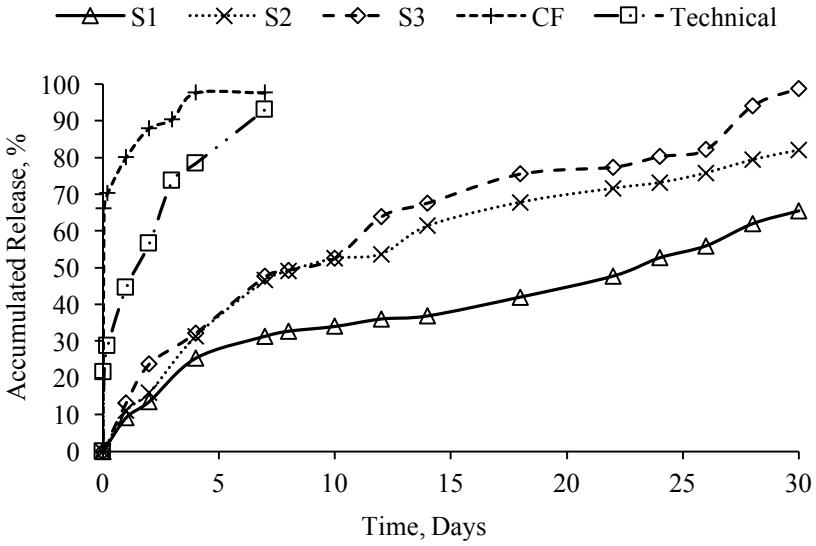


Figure 4. Release behavior of hexaconazole/polyurethane microcapsules in water for different core to shell ratio.

**Table 3.** Parameters Characterizing Fitting of the Model Equation on Hexaconazole Gradual Release Data

| Batch Name | k | n | R | Kinetic Equation of release curve of Hexa/PUr Microcapsule | t50 (days) |
|---|---|---|---|---|---|
| S1 | 0.101 | 0.527 | 0.9858 | $Mt/M\infty = 0.101*t^{0.527}$ | 20.80 |
| S2 | 0.168 | 0.471 | 0.9775 | $Mt/M\infty = 0.167*t^{0.471}$ | 10.13 |
| S3 | 0.166 | 0.514 | 0.9842 | $Mt/M\infty = 0.166*t^{0.514}$ | 8.54 |
| CF | 0.829 | 0.087 | 0.5496 | $Mt/M\infty = 0.829*t^{0.087}$ | 0.00 |
| Technical | 0.483 | 0.337 | 0.944 | $Mt/M\infty = 0.483*t^{0.337}$ | 1.11 |

A sustainable release profile for hexaconazole was investigated over 30-day for the different core to shell ratio. Faster release was observed for core to shell ratio of S3 which produces the thinner shell material which results in the high amount of release of the hexaconazole through shell into water. The maximum amount of the hexaconazole release in water was found to 98% for 30 days. The slower hexaconazole release followed by the

core to shell ratio (5:1) S2 in which the amount of hexaconazole reach to 81%. While slower release behavior was obtained for the sample of S1 (65%). This performance may be explained by the different characteristics of the hexaconazole microcapsules as a result of different core to shell ratios used in microencapsulation. The commercial emulsifiable concentrate and technical hexaconazole shows the faster release compared to the microencapsulated hexaconazole. The 50% release of the hexaconazole observed on day 1 for both formulation and all release were observed within the 7 days.

### *3.5. Field Experiment*

The data from the field experiment was recorded and presented in the table 4. results indicated that the test microencapsulated hexaconazole at dosage rate of 60 g a.i./ha was found highly effective against the powdery mildew compared to the untreated control, wherein the maximum disease incidence was reached to the 7.07% in untreated control plot. There is significant difference among the treatments with respects to powdery mildew. Lowest incidence was recorded with the microencapsulated hexaconazole at dosage rate of 60 g a.i./ha, 25.69%. Similarly, for the treatment with dosage rate of 50 g a.i./ha was found to be 31.36% and for the treatment at dosage rate of 40 g a.i./ha was recorded 31.67%. wherein for the convention suspension concentrate formulation of the hexaconazole was similar to T1 i.e. 31.65%.

**Table 4.** Efficacy of the microencapsulated hexaconazole against powdery mildew.

| Treatment | DBS | 7 DAS | 15 DAS | 21 DAS | 28 DAS | 35 DAS |
|---|---|---|---|---|---|---|
| T1 | 10.86 | 14.568 | 19.498 | 25.88 | 29.116 | 33.356 |
| T2 | 9.32 | 13.90 | 20.77 | 25.16 | 28.84 | 32.12 |
| T3 | 7.12 | 11.98 | 16.00 | 20.53 | 22.32 | 23.37 |
| SC | 6.056 | 9.516 | 15.626 | 18.728 | 30.580 | 31.657 |
| CR | 8.346 | 20.486 | 37.402 | 44.258 | 56.540 | 70.072 |
| SEd | 0.865 | 1.297 | 0.807 | 1.125 | 1.291 | 0.840 |
| CD @5% | 2.401 | 3.601 | 2.240 | 3.123 | 3.583 | 2.331 |
| CV | 0.733 | 0.651 | 0.261 | 0.296 | 0.273 | 0.156 |

T1: Hexaconazole 5% CS @ 50 g a.i./ha.
T2: Hexaconazole 5% CS @ 60 g a.i./ha.
T3: Hexaconazole 5% CS @ 70 g a.i./ha.
SC: Hexaconazole 5% CS @ 60 g a.i./ha.
CR: Untreated Control

## Conclusions

Microencapsulation is the promising technology to protect and to improve the life of the pesticides. Microencapsulation of the Hexaconazole was successfully carried out by the interfacial polymerization by using polyurethane and Polyurethane. The particle size of the prepared microcapsules was found in the range 1-15 µm in diameter. Obtained microcapsules were confirm by FTIR spectroscopy and optical microscope. The encapsulation efficiency was determined and found in the range 85-95%. The microcapsules were approximately spherical in shape and ruptured microcapsule confirms the formation of the core and shell structure. The microencapsulation helps in the controlled release of the hexaconazole which can be programmed by the core to shell ratio. The maximum sustained release content of Hexaconazole was found to be 98% for the sample of S3 after interval of 30 days. While slower release was obtained for the ratio of S1 (65.46%) for the same time interval, i.e. 30 days. The release mechanism non-Fickian diffusion may be due to combine effect of diffusion and erosion mechanism. The field trail studies show the effect of microencapsulated hexaconazole on the green peas infected by the powdery mildew. The microencapsulation improves the durability and controlled release property which is useful to control the disease over period of time.

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