The Microencapsulation of Terbinafine via *In Situ* Polymerization of Melamine-Formaldehyde and Their Application to Cotton Fabric

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Received 6 August 2009; accepted 28 March 2010
DOI 10.1002/app.32525
Published online 15 July 2010 in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: In this study an antifungal pharmaceutical agent, terbinafine, was microencapsulated by using *in situ* polymerization. The polymerization was carried out at four mole ratio level and preparations were applied to the 100% cotton fabric. X-ray diffractometry, DSC, FTIR, BET, contact angle measurements, particle size distribution and imaging techniques were performed. Best results were obtained in the case of 8 : 1 mole ratio. Strength of microcapsule applied fabrics to washing and fungus were also determined. After 25 washing cycle, microcapsules were still in the fabric and had antifungal properties against *A. niger*. Antifungal strength against *T. rubrum* was observed up to 15 washing cycles. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 118: 3707–3714, 2010

Key words: terbinafine; fibers; melamine-formaldehyde; *in situ* polymerization; microencapsulation

INTRODUCTION

Microencapsulation is a technique that allows liquid or solid agents, such as drugs, proteins, hormones, fertilizers, pesticides, herbicides, dyes, cosmetics and fragrances, to be encapsulated by a suitable barrier wall. Liquid or solid agents that are encapsulated are called core material. Therefore the core material is isolated from reactive, corrosive, and hostile environments and also their releasing behavior is controlled. The barrier wall can be built using monomers to form polymers or polymers that are polymerized elsewhere, or readymade capsules such as liposome, cyclodextrin derivatives or microorganisms' cells.[1–4]

The functional finishes importance have been increasing rapidly in textile market because of competition, gaining added values and increasing market share. The consumers' demands are not only defined by aesthetic properties, but also functional properties have been playing an increasing role. Microencapsulation has appeared an alternative way to achieve the functional finishes because of their unique properties, such as controlled release, protection against to hazardous and destructive media, and providing higher surface area. Especially, microcapsules contained fragrances,[4–8] phase change materials,[9–13] flame retardants,[14–17] dyes,[4,18–20] and insecticides[4] were applied to the textiles.

Terbinafine is an allylamine based novel and newly developed antifungal drug, which inhibits squalene epoxidase, the enzyme which catalyzes the conversion of squalene to squalene-2,3 epoxide, a precursor of lanosterol, which in turn is a direct precursor of ergosterol. A deficiency of ergosterol is detrimental to the integrity of the cell membrane resulting in a fungistatic effect similar to that seen with the azole antifungal compounds.[21]

Terbinafine (Fig. 1) is a very broad spectrum antifungal agent, exhibiting the best activity against the dermatophytes of the entire antifungal agent, and also demonstrates reasonable *in vitro* activity against many *Aspergillus* species including *A. fumigatus, A. flavus, A. niger,* and *A. ustus*.[21]

Mycoses include Candidiasis, *Cryptococcosis, Tinea pedis, Tinea corporis*, and *Tinea cruris* cause serious health problems. Also they are very contagious and easily spreads out. Treatment of mycoses needs long-term and systematic antifungal agents curing. Microencapsulated antifungal agents can be applied to textiles. Therefore treatment can be achieved in long-term and systematic.

In this study terbinafine was microencapsulated by using *in situ* polymerization. The preparations were applied to the 100% cotton fabric by padding method. X-ray diffractometry, thermal analyses, FTIR, imaging techniques, and antifungal tests, were also applied.

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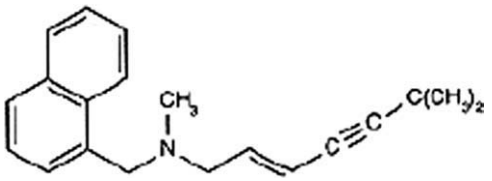

Figure 1 Terbinafine.

MATERIAL AND METHOD

Materials

Terbinafine (Nobel Ilaç Sanayi (pharmaceutical industry); Turkey) was used as core material. Melamine (Fluka) and formaldehyde (Fluka, 37%) were used as wall material. Citric acid (Riedel-de-Haën) and sodium hydroxide (Merck) were used to adjust the pH. Tween 20 (polyethylene glycol sorbitan monolaurate, Sigma) was used as emulsifier. Chloroform (Sigma, spectrophotometric grade) was used as organic solvent. All chemicals were used without any purification.

Preparation of microcapsules

Preparation of microcapsules was carried out by using *in situ* polymerization method. 50 mL prepolymer of melamine and formaldehyde (5 : 2, 3 : 1, 5 : 1, and 8 : 1 mole ratios of melamine/formaldehyde) was prepared at 70°C, pH 8 for 10 min. Terbinafine (4 g) and chloroform were well mixed to form organic phase. After that the organic phase was added into aqua phase, which contained distilled water (100 mL) and Tween 20 (2% w/w). The system was vigorously stirred by Eurostar Digital mixing device (overhead stirrer - IKA), equipped with centrifugal stirrer, at 55°C and 2000 rpm until the stable emulsion was obtained. When a stable emulsion was formed, the prepolymer solution was added to the emulsion. After addition of prepolymer, stirring was reduced to 600 rpm and pH of system was gradually decreased to 4–5.5 by addition of citric acid at 65°C. Reaction was completed after 3 h. Then solution was filtered to obtain microcapsule slurry and then dried at room temperature and at oven at 105°C for 4 hours.[5,7,22] pH was adjusted by 0.01 *M* citric acid and 0.01 *M* sodium hydroxide.

Application to textiles

Melamine-formaldehyde microcapsules were applied to cotton fibers by using a suitable crosslinking agent (KNITTEX® FFRC - Huntsmann), which is consist of modified dihydroxyethylene urea. First preparations (25 g L^{-1}) were dissolved in water and then 150 g L^{-1} crosslinking agent KNITTEX® FFRC was added. pH of solution was adjusted to pH5 by acetic acid (Merck). Application was occurred according to impregnating method at 80% pickup in vertical type foulard (Rapid-Labortex). The volume of trough was 200 mL. Drying was carried out at 130°C. Curing was performed at 130°C for 3 minutes.[22]

Characterization

Differential scanning calorimeter (DSC)

Measurements of melting point and melting heat of the microcapsules obtained were performed in a differential scanning calorimeter (DSC) Perkin–Elmer DSC apparatus. The samples were compared with Al pan at nitrogen flow. The measurements were performed varying the temperature in the range from 20 to 250°C with heating rate of 10°C min^{-1}.

X-ray diffraction (XRD)

XRD patterns of the samples were obtained using an X-ray diffractometer (Rigaku D/Max-2200/PC). The observations were carried out at 2°θ and the copper source was employed.

Scanning electron microscope (SEM)

Microstructural features of the prepared capsules were analyzed by scanning electron microscopy (SEM) by using JSM–6060 JEOL microscope. Before imagining, the samples were coated by Au-Pd.

Particle size distribution

Particle size distribution was carried out at Malvern Mastersizer 2000 particle size analyzer. The analyzer performs based on Mie scattering. The apparatus equipped with red light (Forward scattering, side scattering and back scattering) and blue light (wide angle forward and back scattering), which are produced by helium neon laser and solid state light source respectively. Microcapsules were dispersed in a sonicator before testing.

Strength to washing

Strength of cotton fabrics to washing were performed by using Atlas Linitest apparatus according to TS EN ISO 105 C06 Test for color fastness- Part C06: Color fastness to domestic and commercial laundering 2001.

Fourier transform infrared (FTIR)

FTIR spectra of melamine-formaldehyde microcapsules at different mole ratios were obtained using Perkin–Elmer Spectrum BX FTIR (wave-numbers 400–4000 cm^{-1}) at room temperature, according to KBr tablet method.

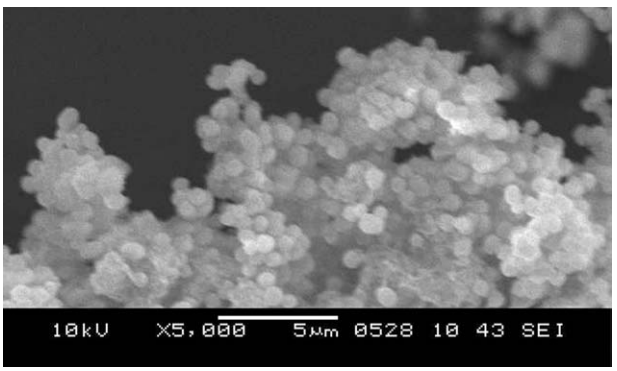

Figure 2 SEM micrographs of melamine-formaldehyde microcapsules.

Antifungal test

Antifungal tests were performed according to AATCC Test Method 30 Antifungal activity, assessment on textile materials: Mildew and rot resistance of textile materials. However test method was modified based on study of Gregory at al.[23] *A. niger* and *Trichophyton rubrum* were used as test cultures. *A. niger* growth media was prepared according to AATCC Test Method 30 and malt extract peptone agar was used as growth media of *T. rubrum*.

Contact angle measurements

Samples were uniformly coated onto a glass slide and then pressed slightly with another a glass slide to ensure a flat surface. Contact angle measurements of a drop of glycerin on polymer blocks were carried out using the sessile drop method with a CAM 100 KSV (KSV, Finland). Recording the drop profile with a CCD video camera allowed monitoring changes in contact angle. All reported data were the average of at least five measurements at different locations of the polymer block surface. The experiments were conducted at ambient temperature. The volume of the drops was always about 2 μL.

Bet analysis

BET analysis was performed using BET analyzer, Quantachrome Corporation, Autosorb-1-C/MS. The samples were dried at 100°C, for 4 h. The analyzer calculates BET parameters using software, which is integrated. The surface area was determined from nitrogen adsorption isotherm by the BET method and determination of the pore size distribution from adsorption branch by the BJH method.

RESULTS AND DISCUSSION

Characterization of Microcapsules

SEM photograph of surface morphologies of the microcapsules, which were formed in 8 : 1 mole ratio, are shown in Figure 2. As can be seen in figure, microcapsules have spherical shape and smooth surface. However an agglomeration can be seen, which may be caused by drying process.

Figure 3 depicts particle size distribution of microcapsules. 5 : 2 mole ratios of melamine/formaldehyde microcapsules had particle sizes of around 1 μm and also had a small distribution around 100 μm. Although all mole ratios were shown more or less distribution around 1 μm, mass of the distribution was observed around 10 μm for 8 : 1 mole ratio, between 1 and 10 μm for 3 : 1 mole ratios and between 10 and 100 μm for 5 : 1 mole ratio. The greater sizes may be caused by agglomeration. Agglomeration can be occurred during the drying process.

Figure 4 shows FTIR spectra of melamine resin microcapsules containing terbinafine and melamine resin microcapsules alone. An intensity peak was observed for all samples around 3350 cm^{-1} due to stretching of O—H and N—H bonds. Asymmetric stretching vibration of methylene groups of melamine-formaldehyde wall material was observed around 2950 cm^{-1}. After polymerization of melamine and formaldehyde, triazine ring of melamine still remains. Hence observed peaks around 1570 and 1490 cm^{-1} may due to in-plane —C=N— vibrations of triazine ring system. The sharp band around 810 cm^{-1}, which is characteristic band for melamine based polymers, can be assigned to the out-of-plane deformation vibration of triazine ring system. The band around 1360 cm^{-1} can be assigned to C—H

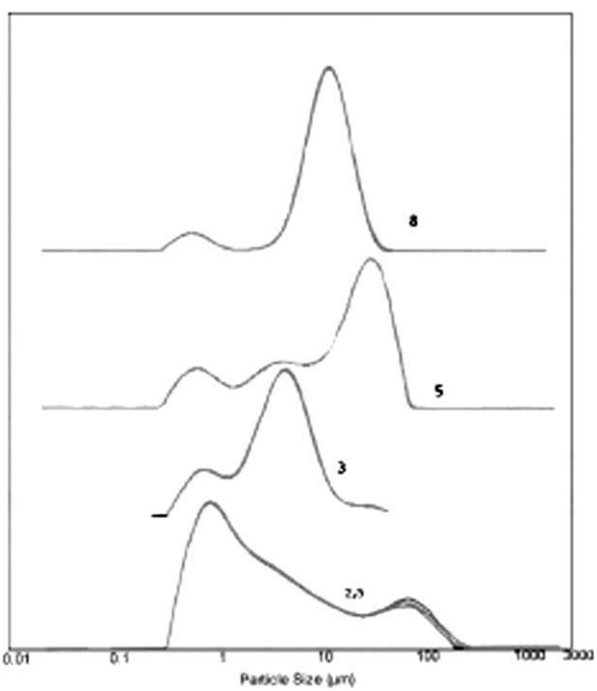

Figure 3 Particle size distribution of melamine-formaldehyde microcapsules.

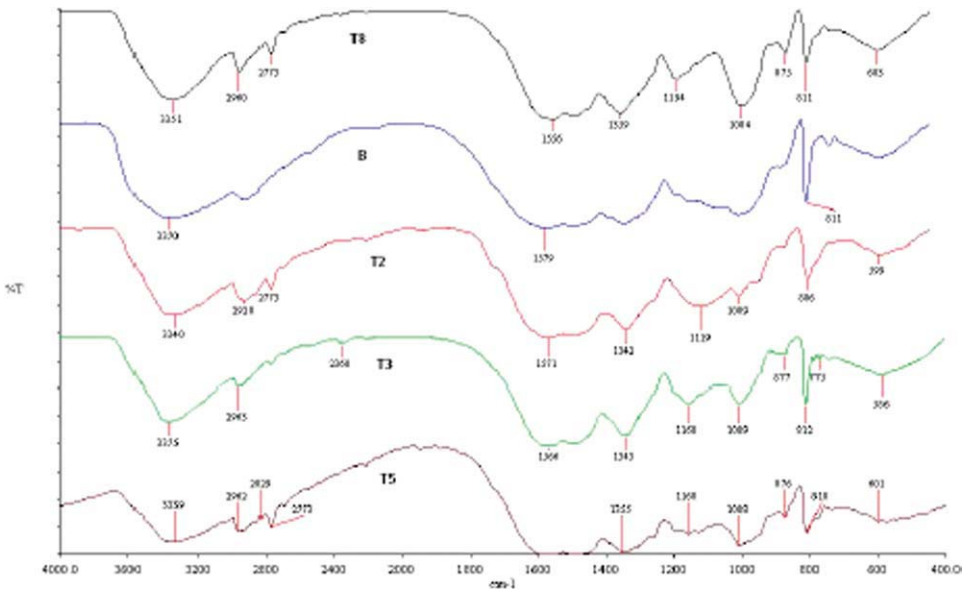

Figure 4 FTIR spectra of melamine-formaldehyde microcapsules: (K2) 2.5 mole ratio (K3) 3 mole ratio (K5) 5 mole ratio (K8) 8 mole ratio (B) Blank microcapsules. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

bending vibration due to methylene bridges. The absorption bands of aliphatic C—N vibration appeared between 1200 and 1160 cm^{-1}. N—CH_3 stretching of terbinafine was observed at 2773 cm^{-1}. However C≡C stretching bands between 2260 and 2100 cm^{-1} can not be observed due to overlap of melamine-formaldehyde polymer.

XRD patterns of melamine-formaldehyde microcapsules are shown in Figure 5. Terbinafine is naturally crystalline; however besides terbinafine, the empty melamine-formaldehyde microcapsule shows amorphous structure due to its lattice nature of polymer. Terbinafine have characteristic peaks around 5, 10, 16, 18, 19.5, 21, 24, 30, and 38° 2θ due to its crystalline structure.

In Figure 5, characteristic peaks of terbinafine were observed at 5 : 2, 3 : 1, and 5 : 1 mole ratio, in spite of amorphous graph of melamine-formaldehyde microcapsules. Especially in 5 mole ratio these peaks were clearly appeared. Other mole ratios gave more amorphous XRD patterns respect to 5 : 1 mole ratio. Decreasing of intensities of peaks was observed, when compared 3 : 1 mole ratio with 5 : 2 and 5 : 1 mole ratios. However in the case of 8 : 1 mole ratio, the characteristic peaks of terbinafine disappeared and amorphous structure of blank melamine-formaldehyde microcapsules was observed. It can be inferred that microencapsulation of terbinafine was molecularly homogeneity.

DSC thermographs of different mole ratios of melamine-formaldehyde microcapsules are shown in Figure 6. When thermographs examined, an endothermic peak appears around 43°C for all mole ratios. One possible explanation for the reason of

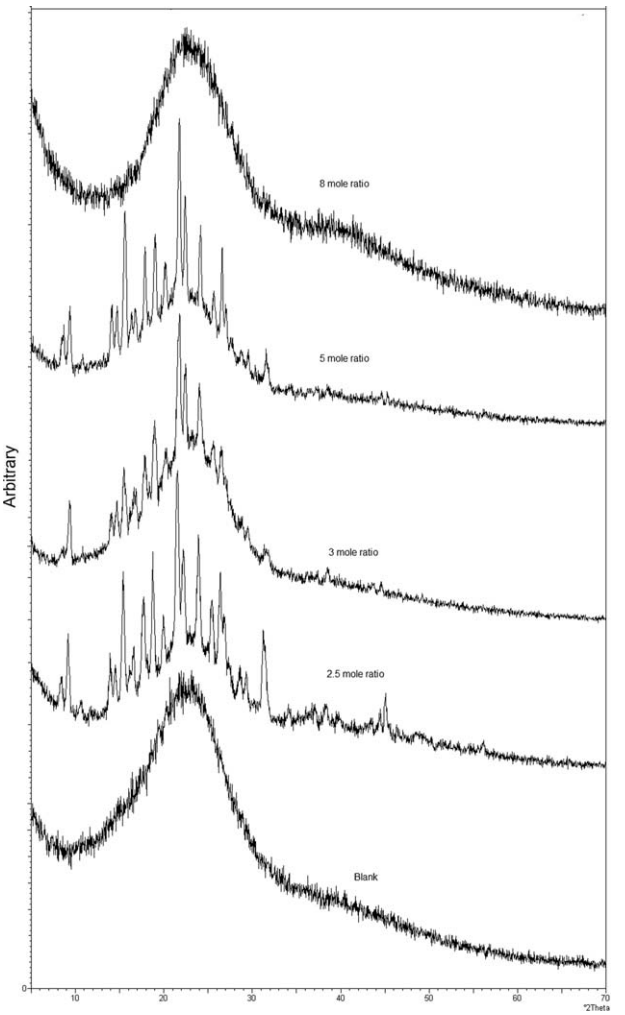

Figure 5 XRD patterns of melamine-formaldehyde microcapsules.

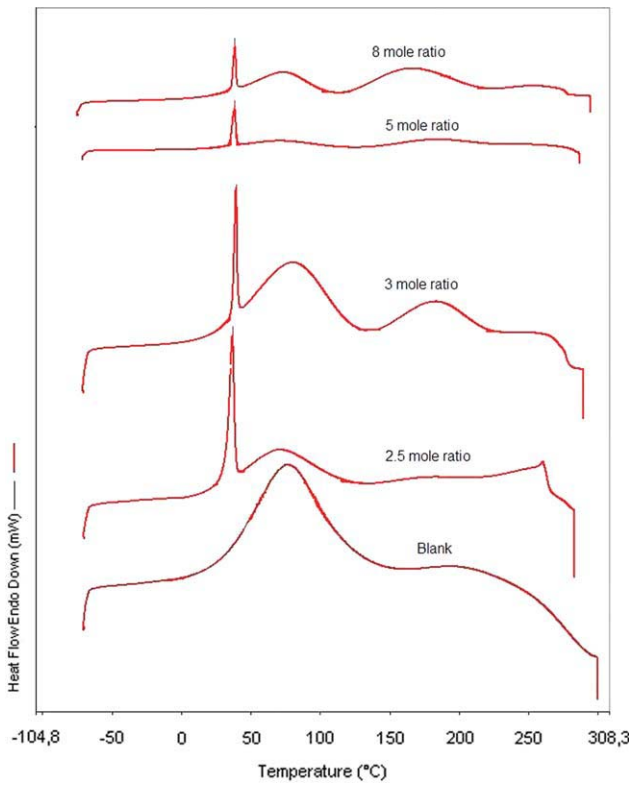

Figure 6 Thermographs of melamine-formaldehyde microcapsules. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

endothermic peaks may be that boiling phenomena of organic solvent. The decomposition or melting peaks of terbinafine was not observed from thermographs. Thermal behavior of terbinafine was completely screened by melamine-formaldehyde shell. This fact can be caused by microencapsulation of terbinafine.

Contact angles and their hysteresis are listed in Table I. The greatest contact angle was measured for 2.5 mole ratio. Contact angle data of melamine-formaldehyde microcapsules at 3 : 1, 5 : 1 and 8 : 1 mole ratios were 73.22°, 66.68°, and 64.25°, respectively, and changed into more hydrophilic polymer nature relatively. This fact can be due to exceed formaldehyde may lead increasing of OH groups in the polymer. Coullerez et al.,[24] who observed 68° contact angle with deionized water, reported that melamine-formaldehyde cured resin shows nonpolar surface behavior due to the low polarity of the s-triazine ring, which can oriented at the top of the surface.

TABLE I
Contact Angle Values and Hysteresis (Δθ)

Mole ratio of MF	Contact angle (°)	Δθ (θ*a*-θ*r*)[a]
2.5	101.74	1.96
3	73.22	4.09
5	66.68	6.93
8	64.25	15.78

[a] Advancing (θ*a*) and receding (θ*r*) contact angles measured in degrees.

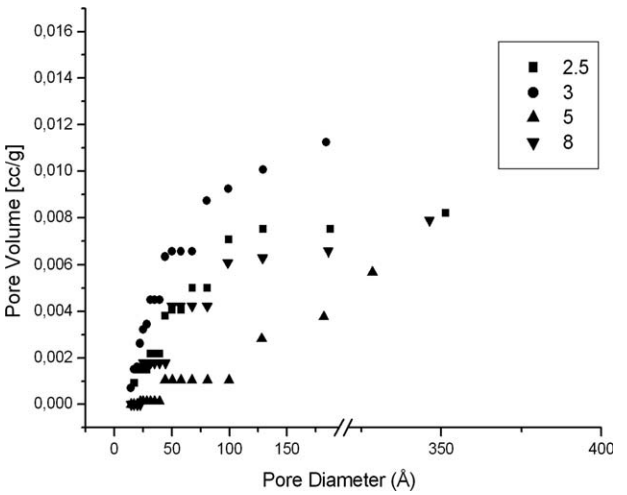

Figure 7 Pore diameter distribution of melamine-formaldehyde microcapsules.

Another important characteristic of a solid–liquid interface is the contact angle hysteresis (Δθ), which is the difference between the contact angle at the front of the droplet (advancing contact angle, θ*a*) and the contact angle at the back of the droplet (receding contact angle, θ*r*) for a droplet moving along the solid surface. As can be seen from the hysteresis values (Table I), one can realize that hysteresis decreases with increasing melamine-formaldehyde mole ratio.

BET surface areas of melamine-formaldehyde microcapsules at 5 : 2, 3 : 1, 5 : 1, and 8 : 1 mole ratios were 3.806, 9.171, 0.676, 1.414 m^2/g, respectively. Pore diameter distribution is presented in Figure 7. As can be seen in Figure 7, mass distributions for all mole ratios were observed between 19

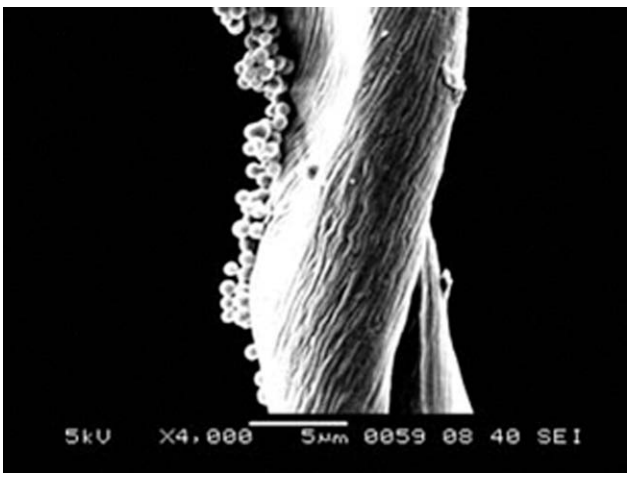

Figure 8 Attached melamine-formaldehyde microcapsules onto cotton fibers.

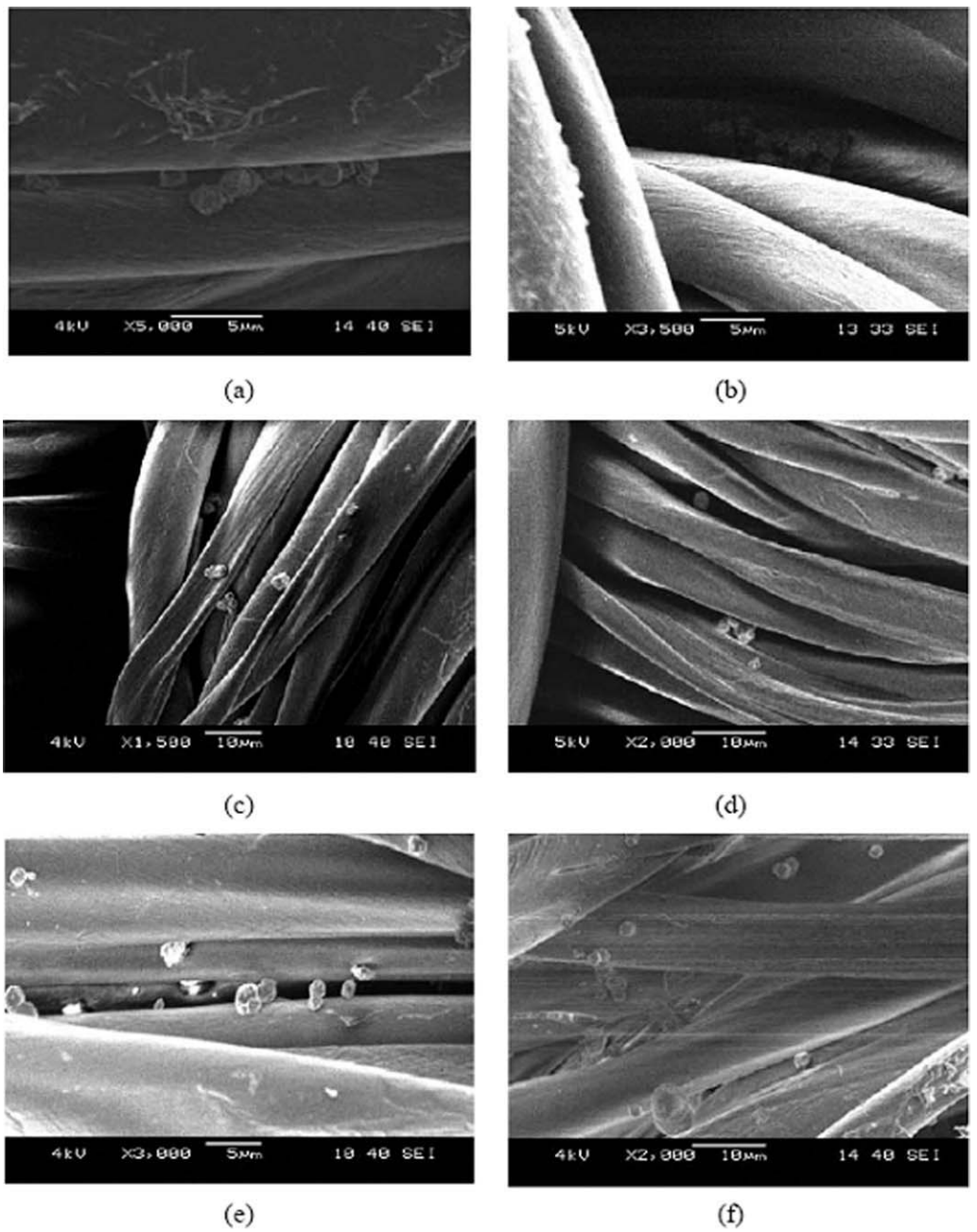

Figure 9 SEM photographs of cotton fabrics after various washing cycles: (a) 1 washing cycle (b) 5 washing cycles (c) 10 washing cycles (d) 15 washing cycles (e) 20 washing cycles (f) 25 washing cycles.

and 50 Å due to mesoporous structure of microcapsules. However distributions of pore diameters at macroporous region were also observed.

Preparation of antifungal functional fabric

The cotton fabric was impregnated by dispersion, which consist of microcapsule and crosslinking agent. Crosslinking agent modified dihydroxy ethylene urea reacts with cellulose backbone via OH groups of both cellulose and dihydroxy ethylene urea in acid catalysis. During the condensation reaction between cellulose and dihydroxy ethylene urea, a polycondensation reaction can be occurred between two of dihydroxy ethylene urea. Thus a network is placed between cellulose macromolecules, which consist of condensation product of dihydroxy ethylene urea. Dihydroxy ethylene urea also reacts with methylolmelamine, which is condensation product of melamine and formaldehyde. Two possible ways of linking between wall polymer and crosslinking agent can be occurred: either between hydroxyl and methylol groups producing ether bridge, or between hydroxyl group and amino

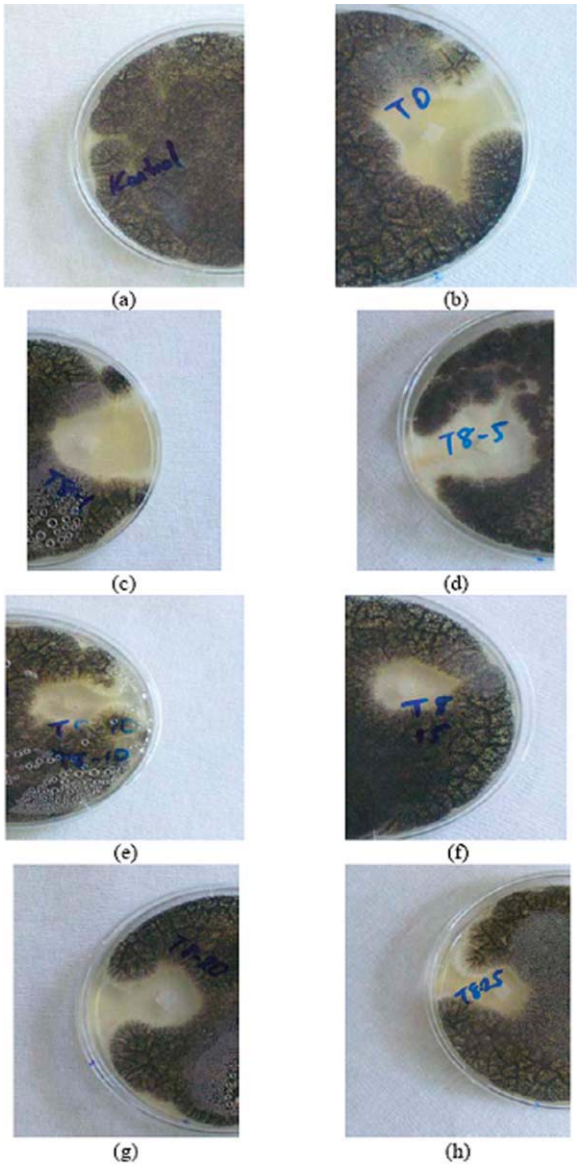

Figure 10 Antifungal test results using *A. niger*: (a) control (b) 1 washing cycle (c) 5 washing cycles (d) 10 washing cycles (e) 15 washing cycles (f) 20 washing cycles (g) 25 washing cycles. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

group. Besides role of linking bridge between microcapsule and cellulose, dihydroxy ethylene urea can act as coating agent to attach the capsules onto fiber. Figure 8 shows the attached microcapsules onto fibers. As can be seen attached microcapsules were also coated by crosslinking agent.

Unique morphological properties of cotton fiber may give advantage to coating process. Because of fiber surface wrinkles and reversal axis, the coated microcapsules could be attached to fiber surface at many points. Contact points of microcapsules to fiber surface may yield more strength to washing fastness.

Textiles should require long-term fastness properties, such as washing fastness, light fastness, crocking fastness and so forth, at the point view of end

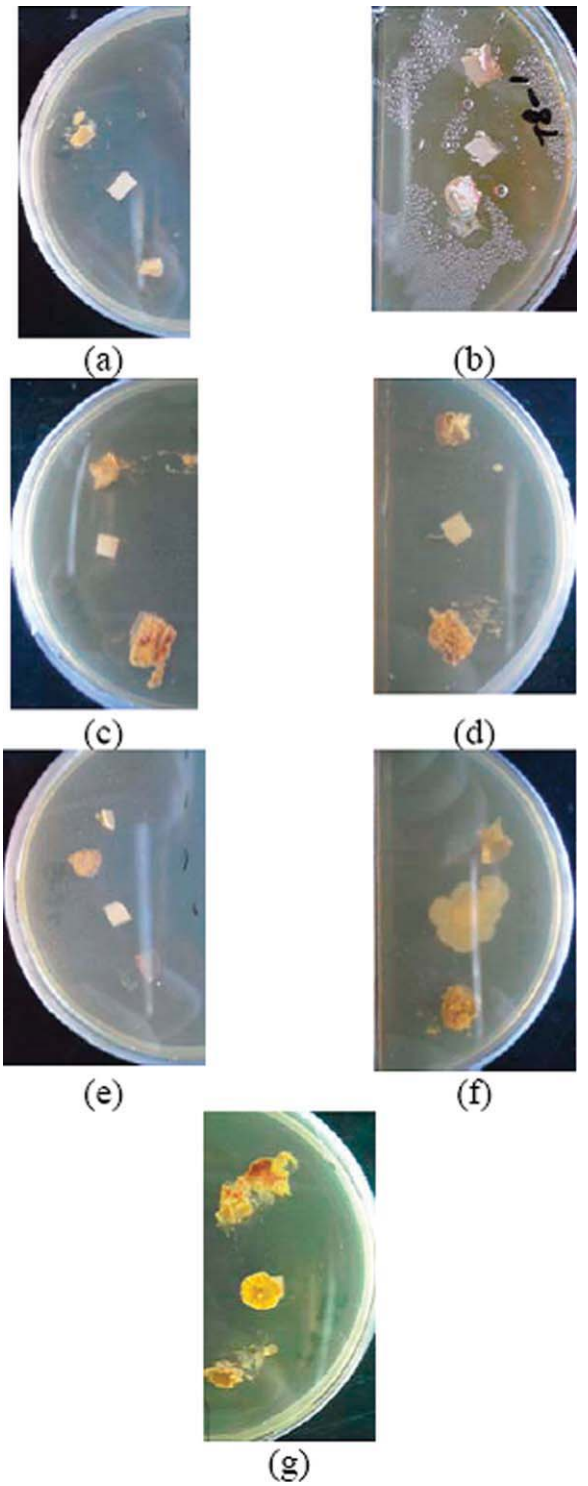

Figure 11 Antifungal test results using Trichophyton rubrum: (a) unwashed (b) 1 washing cycle (c) 5 washing cycles (d) 10 washing cycles (e) 15 washing cycles (f) 20 washing cycles (g) 25 washing cycles. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

users. Figure 9 shows SEM photographs after various washing cycles. Microcapsules were onto cotton fibers even after 25 washing cycles.

Antifungal assessment

Figure 10 shows antifungal test results, which were achieved by using *A. niger* culture. Inhibition zone was gradually decreasing with increasing washing cycle, however antifungal properties of applied fabrics were remained up to 25 washing cycles. Antifungal properties remained *T. rubrum* (Fig. 11), at 10 and 15 washing cycles. Nevertheless *T. rubrum* growth was observed at 20 and 25 washing cycles.

CONCLUSION

In this work, terbinafine, allylamine based antifungal agent, was microencapsulated by *in situ* polymerization using melamine and formaldehyde monomers. Four different mole ratios of melamine and formaldehyde were applied.

Microcapsules had spherical shape and contact angle of polymers were decreasing with increasing of mole ratio. Thermal behavior and XRD peaks of terbinafine were completely screened by melamine-formaldehyde shell at 8 : 1 mole ratio. The characteristic FTIR bands of melamine-formaldehyde polymer and N—CH_3 stretching of terbinafine at 2773 cm^{-1} were observed at all mole ratios.

Microcapsules were successfully applied cotton fabric, using crosslinking agent based on dihydroxyethyleneurea, by padding method. Microcapsules existed after 25 washing cycles. Antifungal properties of applied fabrics were still remained up to 25 washing cycles for *A. niger* and 15 washing cycles for *T. rubrum.*

As a final statement, this work shows antifungal or antimycotic fabrics can be built by microencapsulation. Further studies will be focused on controlled released of microencapsulated antifungal agents.

This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK) under Grant No. MAG-104M265.

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